

# Preterm birth is associated with lower academic attainment at age 12 years

**Citation for published version (APA):**

van Beek, P. E., Leemhuis, A. G., Abu-Hanna, A., Pajkrt, E., Aarnoudse-Moens, C. S. H., van Baar, A. L., Andriessen, P., & Ravelli, A. C. J. (2022). Preterm birth is associated with lower academic attainment at age 12 years: a matched cohort study by linkage of population-based datasets. *Journal of Pediatrics*, 251, 60-66.e3. <https://doi.org/10.1016/j.jpeds.2022.07.049>

**Document license:**

TAVERNE

**DOI:**

[10.1016/j.jpeds.2022.07.049](https://doi.org/10.1016/j.jpeds.2022.07.049)

**Document status and date:**

Published: 01/12/2022

**Document Version:**

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

[www.tue.nl/taverne](http://www.tue.nl/taverne)

**Take down policy**

If you believe that this document breaches copyright please contact us at:

[openaccess@tue.nl](mailto:openaccess@tue.nl)

providing details and we will investigate your claim.



# Preterm Birth is Associated with Lower Academic Attainment at Age 12 Years: A Matched Cohort Study by Linkage of Population-Based Datasets

Pauline E. van Beek, MD, PhD<sup>1</sup>, Aleid G. Leemhuis, MD, PhD<sup>2,\*</sup>, Ameen Abu-Hanna, PhD<sup>3</sup>, Eva Pajkrt, MD, PhD<sup>4</sup>, Cornelieke S. H. Aarnoudse-Moens, PhD<sup>5</sup>, Anneloes L. van Baar, PhD<sup>6</sup>, Peter Andriessen, MD, PhD<sup>1,7</sup>, and Anita C. J. Ravelli, PhD<sup>3,4</sup>

**Objective** To compare academic attainment at age 12 years in preterm children born below 30 weeks of gestation with matched term-born peers, using standardized, nationwide and well-validated school tests.

**Study design** This population-based, national cohort study was performed by linking perinatal data from the nationwide Netherlands Perinatal Registry with educational outcome data from Statistics Netherlands and included 4677 surviving preterm children born at 25<sup>0/7</sup>-29<sup>6/7</sup> weeks of gestational age and 366 561 controls born at 40 weeks of gestational age in 2000-2007. First, special education participation rate was calculated. Subsequently, all preterm children with academic attainment test data derived at age 12 years were matched to term-born children using year and month of birth, sex, parity, socioeconomic status, and maternal age. Total, language, and mathematics test scores and secondary school level advice were compared between these 2 groups.

**Results** Children below 30 weeks of gestation had a higher special education participation rate (10.2% vs 2.7%,  $P < .001$ ) than term-born peers. Preterm children had lower total ( $-0.37$  SD; 95% CI  $-0.42$  to  $-0.31$ ), language ( $-0.21$  SD; 95% CI  $-0.27$  to  $-0.15$ ), and mathematics ( $-0.45$  SD; 95% CI  $-0.51$  to  $-0.38$ ) z scores, and more often a prevocational secondary school level advice (62% vs 46%,  $P < .001$ ).

**Conclusions** A substantial proportion of children born before 30 weeks of gestation need special education at the end of elementary schooling. These children have significant deficits on all measures of academic attainment at age 12 years, especially mathematics, compared with matched term-born peers. (*J Pediatr* 2022;251:60-6).

Despite ongoing improvements in the management of extremely preterm infants, there is a recognized increased risk of subsequent disability.<sup>1</sup> A large body of research indicates that children born very preterm are at increased risk of adverse long-term outcome.<sup>2</sup> Findings are generally consistent and indicate that a large proportion of preterm-born children and their families face major challenges, including significant developmental delay, cognitive impairments, and behavioral and emotional problems.<sup>3-6</sup>

Academic attainment provides an important measure of long-term outcome of very preterm children because it has substantial, causal effects on health and opportunities in life.<sup>7,8</sup> However, most information on academic attainment is retrieved from tests performed in follow-up clinics where matched term-born controls are not always available. In the Netherlands, several registries contain individual information on special education participation, results of a standardized nationwide academic attainment test administered at the end of elementary school at grade 6, and data on personalized advices regarding the level of secondary school.

Therefore, the aim of this study was to assess academic attainment (including special education) at the end of elementary school, in preterm children born below 30 weeks of gestation in comparison with that of matched term-born peers. The second aim was to evaluate the academic attainment measures within the group of preterm children to detect potential gestational age-related gradients.

From the <sup>1</sup>Department of Neonatology, Máxima Medical Center, Veldhoven, the Netherlands; <sup>2</sup>Department of Neonatology, Emma Children's Hospital, Amsterdam University Medical Centers, Amsterdam, the Netherlands; <sup>3</sup>Department of Medical Informatics, Amsterdam Public Health Research Institute, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; <sup>4</sup>Department of Obstetrics and Gynecology, Amsterdam Reproduction and Development Research Institute, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; <sup>5</sup>Department of Neonatology and Pediatrics, Emma Children's Hospital, Amsterdam Reproduction and Development, Amsterdam UMC Location AMC, Amsterdam, the Netherlands; <sup>6</sup>Child and Adolescent Studies, Utrecht University, Utrecht, the Netherlands; and <sup>7</sup>Department of Applied Physics, School of Medical Physics and Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands

\*Former publication name was van Wassenaer-Leemhuis.

This project has been funded by an unrestricted grant from *Stichting Tiny and Anny van Doorne Fonds*. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the article. Access to the micro-data analysis environment of Statistics Netherlands data for this study (project 8617) was given by Statistics Netherlands. In addition, the privacy commission of Perined (approval number 19.43) approved the study in 2019. The authors declare no conflicts of interest.

CITO    Centraal Instituut voor Toets Ontwikkeling  
SES    Socioeconomic status

0022-3476/\$ - see front matter. © 2022 Elsevier Inc. All rights reserved.  
<https://doi.org/10.1016/j.jpeds.2022.07.049>

## Methods

This national, population-based cohort study included all preterm surviving children, born between 25<sup>0/7</sup> and 29<sup>6/7</sup> completed weeks of gestation between January 1, 2000 and December 31, 2007. For comparison, all term survivors born at 40 completed weeks of (40<sup>0/7</sup>-40<sup>6/7</sup>) gestation in the same study period were included. Infants with congenital malformations were excluded from the study. Patients were not involved in any stage of this research process.

### Data Collection

Gestational age was based on the last menstrual period, ultrasound measurement before 20 weeks of gestation, or a combination of both. If estimation by ultrasound measurement differed by >6 days from the last menstrual period, then the ultrasound measurement was considered the dominant one. Variables used from the Perinatal Registry included gestational age, birth weight, sex, parity (0, 1, or  $\geq 2$ ), maternal age, socioeconomic status (SES), and ethnicity (White/non-White). SES was area-based and assessed using scores defined by the Netherlands Institute for Social and Cultural Research based on the 4-digit postal code at birth.

The national perinatal data from the Netherlands Perinatal Registry were linked using deterministic linkage with the national population datasets obtained from Statistics Netherlands (97% linkage was achieved). The Netherlands Perinatal Registry ([www.perined.nl](http://www.perined.nl)) contains population-based information regarding pregnancy, delivery, neonatal (re)admissions, and pregnancy outcomes, as registered by midwives, obstetricians, and pediatricians/neonatologists. Statistics Netherlands plays the role of a third trusted party for data linkage in the Netherlands and performed the linkage between the perinatal registry and data from Statistics Netherlands. After linkage, the cases were pseudonymized by Statistics Netherlands. In accordance with national regulations confidentiality was maintained by following the guidelines of disclosure of identities of individual persons, enterprises, institutions, or households by Statistics Netherlands ([www.microdata.nl](http://www.microdata.nl)). Access to the micro-data analysis environment of Statistics Netherlands data for this study (project 8617) was given by Statistics Netherlands. In addition, the privacy commission of Perined (approval number 19.43) approved the study in 2019. Analysis output was checked on whether it satisfies the privacy regulations of Statistics Netherlands before it was released for use in this study.

### Outcome Measurements

From Statistics Netherlands, education data on the 5 outcome measures of academic attainment were collected: special education participation, the total, language, and mathematics scores of the standardized nationwide academic attainment test at age 12 years and based on the total score the personalized advice for the level of secondary school.

First, the need for special education was determined for all surviving children at 25-29 and 40 weeks of gestation. All children with learning, behavioral, sensory, or physical

disabilities that require special education are annually registered in a national compulsory registry. Special education was defined as an educational setting in a separate school, designed to accommodate educational, behavioral, and/or medical needs of children who could not be adequately addressed in a regular school environment.

Second, all children who had registered outcome measures from the standardized nationwide academic attainment test (*Centraal Instituut voor Toets Ontwikkeling* [CITO] test) at age 11-12 years were selected from all surviving preterm children born at 25-29 weeks of gestation, and matched with term-born peers of whom the same data were retrieved (the matching procedure is described in the Matching section). Children who attended special education were not routinely excluded from the CITO-test system. Approximately two-thirds of the elementary schools use this standardized nationwide test that was available for linkage and analyses.<sup>9,10</sup> Other education test outcomes that may be used in elementary school settings were not available for analysis. The academic attainment test is administered in schools on 3 consecutive days in the final year of elementary school when the child is 11 or 12 years of age, and consists of 240 multiple-choice items assessing different intellectual skills. The outcome measures of the test include a total, language, and mathematics score, presented as z scores. The total score is usually presented as a standardized score between 501 and 550 (mean 535 = z score 0, SD 10, eg, score of 527 corresponds with z score of -0.8). This standardized score is used to support the advice concerning the type of secondary school. Secondary education in the Netherlands is uniquely divided into 4 types from the first year onward and ranges from prevocational to preuniversity type. A score below 537 indicates an advice for prevocational secondary school type.

### Matching

In the linked dataset with birth and academic attainment test results available, each preterm child was matched to a term-born child born at 40 completed weeks of gestation, using exact matching. Matching variables included year of birth (2000-2007), month of birth (1-12), sex (male/female), parity (categorized as 0, 1,  $\geq 2$ ), SES in quintiles (categorized as very low, low, middle, high, very high), and maternal age (categorized as <25, 25-27, 28-34, and  $\geq 35$  years).

### Statistical Analyses

Before matching, the need for special education was compared between all very preterm children and all children born at 40 weeks of gestation using a  $\chi^2$  test. After matching, baseline characteristics of very preterm children with and without individual academic attainment test results available (ie, matched and nonmatched children) were compared using Student t tests for continuous variables and  $\chi^2$  tests for categorical variables.

For the first aim, all 5 outcome measures of academic attainment were compared between very preterm children and their matched term peers using a Student t test or  $\chi^2$  test. Linear and logistic regression analyses with and without adjustment (for sex, parity, maternal age, SES, and ethnicity)

were performed to calculate an aOR or mean difference in academic attainment outcome measurements between very preterm children and children born at 40 weeks of gestation.

For the second aim, to test whether there was an association between gestational age and academic attainment within the very preterm children, an ANOVA test or  $\chi^2$  test was performed comparing the 5 different groups of completed weeks of gestation (25 up to 29 weeks) for all 5 outcome measures. An adjusted linear or logistic regression including gestational age (completed weeks) was performed within the group of very preterm children to calculate adjusted mean differences or ORs within the very preterm children, using 29-week children as a reference.

Two sensitivity analyses for the 3 continuous test score outcome measurements were done. Linear regression analysis was repeated by excluding children who had individual test-score results but attended special education. Second, sensitivity analysis was performed of the matched cohort excluding the 2007 births because late entry to elementary school or to repeat a year could have reduced the number of children with education scores in the last available year 2019.

A *P* value of <.05 was considered statistically significant. Calculations were performed within the microdata environment of Statistics Netherlands, using SPSS v 25 (IBM SPSS Statistics 25).

## Results

The total very preterm study population (gestational age 25-29 weeks) consisted of 5777 live born infants without congenital anomalies, of whom 81% (*n* = 4677) survived to

discharge. Within the study period, 366 777 live born infants were born at 40 weeks of gestational age, of whom 99.5% (*n* = 366 561) survived to discharge (Figure; available at [www.jpeds.com](http://www.jpeds.com)). Special education information was available for all the included very preterm and term children. Information on the standardized nationwide academic attainment test (ie, CITO test) was available for 2233 very preterm children. Children without education test results available (*n* = 2444) were more frequently male (57% vs 51%), from low SES (47% vs 41%), lower maternal age (29.5 years vs 30.4 years), and had lower birth weight (1090 g vs 1123 g) (Table I; available at [www.jpeds.com](http://www.jpeds.com)). Furthermore, 2231 (99.9%) of the 2233 very preterm children with test results available could be exactly matched to 2231 children born at 40 weeks of gestational age with test results available. The control group born at 40 weeks of gestation was comparable with the very preterm infants for all factors used for matching (Table II).

### Very Preterm Children with Term Born Children

Among all 4677 surviving very preterm children, 10.2% (*n* = 476) attended special education, compared with 2.7% (*n* = 10 065) of the children born at 40 weeks of gestation (mean difference 7.4% [95% CI 6.6%-8.4%]) (Table III).

Among the matched 2231 very preterm children, mean total z score was -0.26, which was lower compared with 0.11 in the matched term control group (mean difference -0.37 [95% CI -0.42 to -0.31]). Mean language z score was -0.12 among the very preterm children compared with 0.08 among term children (mean difference -0.21 [95% CI -0.27 to -0.15]), and mean mathematics z score was -0.35

**Table II.** Description of the matched cohort with data available, consisting of 2231 very preterm children born at 25-29 weeks total and 2231 children born at 40 weeks of gestation (left part), and for all very preterm children separately for each completed gestational age week

	Very preterm birth		Control group		Very preterm birth					Total <i>n</i> = 4462
	25-29 wk	40 wk	<i>P</i> value	25 wk	26 wk	27 wk	28 wk	29 wk	<i>P</i> value	
	<i>n</i> = 2231	<i>n</i> = 2231		<i>n</i> = 95	<i>n</i> = 254	<i>n</i> = 451	<i>n</i> = 604	<i>n</i> = 827		
Birthweight (g)	1123 (337)	3560 (442)	<.001*	880 (424)	913 (276)	1034 (375)	1152 (329)	1243 (261)	<.001*	2341 (1280)
Matching variables										
Male sex	1139 (51.1)	1139 (51.1)	1.00	40 (42.1)	113 (44.5)	240 (53.2)	324 (53.6)	422 (51.0)	.04*	2278 (51.1)
Parity			1.00						.01*	
0	1505 (67.5)	1505 (67.5)		48 (50.5)	174 (68.5)	310 (68.7)	404 (66.9)	569 (68.8)		3010 (67.5)
1	476 (21.3)	476 (21.3)		33 (34.7)	46 (18.1)	90 (20.0)	125 (20.7)	182 (22.0)		952 (21.3)
2+	250 (11.2)	250 (11.2)		14 (14.7)	34 (13.4)	51 (11.3)	75 (12.4)	76 (9.2)		500 (11.2)
Maternal age (y)	30.4 (4.9)	30.2 (4.8)	.30	30.0 (5.3)	30.4 (5.0)	30.3 (5.0)	30.5 (4.9)	30.4 (4.8)	.93	30.3 (4.9)
Maternal age			1.00						.46	
<25	270 (12.1)	270 (12.1)		13 (13.7)	35 (13.8)	58 (12.9)	63 (10.4)	101 (12.2)		540 (12.1)
25-27	320 (14.3)	320 (14.3)		19 (20.0)	33 (13.0)	67 (14.9)	95 (15.7)	106 (12.8)		640 (14.3)
28-34	1201 (53.8)	1201 (53.8)		43 (45.3)	133 (52.4)	238 (52.8)	318 (52.6)	469 (56.7)		2402 (53.8)
≥35	440 (19.7)	440 (19.7)		20 (21.1)	53 (20.9)	88 (19.5)	128 (21.2)	151 (18.3)		880 (19.7)
SES			1.00						.06	
Very low	471 (21.1)	471 (21.1)		28 (29.5)	45 (17.7)	82 (18.2)	126 (20.9)	190 (23.0)		942 (21.1)
Low	439 (19.7)	439 (19.7)		22 (23.2)	54 (21.3)	103 (22.8)	116 (19.2)	144 (17.4)		878 (19.7)
Middle	454 (20.3)	454 (20.3)		17 (17.9)	49 (19.3)	89 (19.7)	136 (22.5)	163 (19.7)		908 (20.3)
High	474 (21.2)	474 (21.2)		16 (16.8)	63 (24.8)	94 (20.8)	136 (22.5)	165 (20.0)		948 (21.2)
Very high	393 (17.6)	393 (17.6)		12 (12.6)	43 (16.9)	83 (18.4)	90 (14.9)	165 (20.0)		786 (17.6)

Results are presented as *n* (%) or mean (SD).  
\*Significant at a .05 level.

**Table III.** Academic attainment outcome measures for very preterm (gestational age of 25-29 weeks) and term (gestational age of 40 weeks) children

All surviving children (n = 371 238)					
	Very preterm birth (25-29 wk)	Control group (40 wk)	Total	Mean difference (95% CI)/OR (95% CI)	P value
	n = 4677	n = 366 561	n = 371 238		
Special education rate	10.2%	2.7%	2.8%	7.4% (6.6%-8.4%)	<.001*
OR				4.0 (3.6-4.4)	
All matched children (n = 4462)					
	Very preterm birth (25-29 wk)	Control group (40 wk)	Total	Mean difference (95% CI)/OR (95% CI)	P value
	n = 2231	n = 2231	n = 4462		
Total z score (SD)	-0.26 (1.02)	0.11 (0.96)	-0.07 (1.02)	-0.37 (-0.42 to -0.31)	<.001*
Language z score (SD)	-0.12 (1.10)	0.08 (0.98)	-0.02 (1.00)	-0.21 (-0.27 to -0.15)	<.001*
Mathematics z score (SD)	-0.35 (1.06)	0.10 (0.95)	-0.12 (1.03)	-0.45 (-0.51 to -0.38)	<.001*
% prevocational secondary school type advice <sup>†</sup>	61.5%	46.4%	53.9%	15.1% (12.2%-18.0%)	<.001*
OR				1.8 (1.6-2.1)	

The upper one-half of the table shows the number of children who were in special education, calculated for all survivors consisting of 4677 very preterm and 366 561 term children. The lower one-half of the table shows academic achievement test results for the matched cohort, consisting of 2231 very preterm (gestational age of 25-29 weeks) and 2231 term (gestational age of 40 weeks) children.

Results are presented as mean (SD), unless reported otherwise.

\*Significant at a .05 level.

†Number of children who received prevocational secondary school type advice = standardized score <537.

among preterm children compared with 0.10 among term children (mean difference -0.45 [95% CI -0.51 to -0.38]). Among very preterm children, more children (61.5%) received an advice for prevocational secondary school type compared with 46.4% among the control group (mean difference 15.1% [95% CI 12.2%-18.0%]).

All academic outcome measurements were significantly lower among all separate 25-29 weeks of gestational age groups compared with 40-week gestational age children, both for crude scores as well as after adjustment (Table IV; available at [www.jpeds.com](http://www.jpeds.com)). Children born at 25 weeks had a higher risk for prevocational secondary school type advice compared with those born at 40 weeks (OR 3.1, 95% CI 1.9-5.0).

### Gradient in Academic Attainment within Very Preterm Children

Special education rate decreased from 15.3% among 25-week children to 9.2% among 29-week children (Table V). Total z score increased from -0.67 among 25-week children to -0.17 among 29-week children, language z score increased from -0.44 among 25-week children to -0.04 among 29-week children, and mathematics z score increased from -0.44 among 25-week children to -0.04 among 29-week children. The percentage in advice for prevocational secondary school type decreased from 74.7% among 25-week children to 58.4% among 29-week children. All academic outcome measurements were significantly lower among 25-week children compared with 29 weeks of gestational age children, using both crude as well as adjusted scores.

### Sensitivity Analyses

All academic outcome measures were similar when all children who attended special education were excluded from

the analyses (Table VI; available at [www.jpeds.com](http://www.jpeds.com)). Similar outcome results were found when the children who were born in 2007 were excluded (Table VII; available at [www.jpeds.com](http://www.jpeds.com)).

## Discussion

In this national cohort study covering 8 years of birth, the effect of very preterm birth (25-29 weeks of gestation) on school-based academic attainment at age 12 years, at the end of elementary schooling, was assessed by comparing the results of very preterm children with term-born peers matched for important factors. Academic attainment was assessed using 5 outcome domains, and consistently significant deficits were seen in all 5 measurements. Special schooling rate was about 4 times higher in very preterm children, the results on the national academic attainment test were lower by 0.21-0.45 SD and very preterm children received 1.3 times more often a prevocational secondary school advice, compared with children born at 40 weeks of gestation. Within the group of very preterm children (25-29 weeks of gestation), a gradual improvement in academic attainment scores was seen with every increasing completed week of gestation.

This study reports precise and unique results after successful record linkage between 2 large national registries. Instead of study- or hospital-based results, it provides population- and school-based long-term outcome data for a large sample of very preterm-born children. The linkage of this individual-level registry data from Statistics Netherlands combined with the population-based perinatal registry has provided an invaluable opportunity to determine the impact of prematurity on individual outcomes later in life. Because of the matching, bias because of selection and selective loss-to-follow-up is limited, making the results a valuable

**Table V. Academic attainment outcome measures for 2231 very preterm (gestational age of 25-29 weeks) children, presented for each gestational age week**

All survived children (n = 4677)					
	25 wk	26 wk	27 wk	28 wk	29 wk
	n = 249	n = 582	n = 905	n = 1250	n = 827
% children attending special education	15.3%	12.4%	10.3%	9.4%	9.2%
Crude OR (95%CI)	1.79 (1.22-2.62)	1.40 (1.04-1.88)	1.14 (0.89-1.49)	1.03 (0.80-1.33)	ref
aOR (95% CI)	1.79 (1.21-2.64)	1.44 (0.89-1.50)	1.14 (0.87-1.50)	1.02 (0.80-1.32)	ref
All matched children (n = 2231)					
	25 wk	26 wk	27 wk	28 wk	29 wk
	n = 95	n = 254	n = 451	n = 604	n = 827
Total z score (SD)	-0.67 (1.12)	-0.33 (0.97)	-0.29 (1.08)	-0.25 (1.02)	-0.17 (1.02)
Crude difference (95%CI)	-0.50 (-0.72 to -0.28)*	-0.16 (-0.30 to -0.01)*	-0.11 (-0.23 to 0.01)	-0.08 (-0.18 to 0.03)	ref
Adjusted difference (95% CI)	-0.41 (-0.62 to -0.19)*	-0.13 (-0.27 to 0.02)	-0.10 (-0.21 to 0.02)	-0.06 (-0.11 to 0.06)	ref
Language z score (SD)	-0.44 (1.10)	-0.19 (0.91)	-0.16 (1.08)	-0.13 (0.97)	-0.04 (1.01)
Crude difference (95%CI)	-0.40 (-0.64 to -0.16)*	-0.14 (-0.30 to 0.05)	-0.12 (-0.24 to 0.01)	-0.09 (-0.20 to 0.02)	ref
Adjusted difference (95% CI)	-0.34 (-0.57 to -0.11)*	-0.13 (-0.28 to 0.02)	-0.11 (-0.23 to 0.02)	-0.07 (-0.18 to 0.04)	ref
Mathematics z score (SD)	-0.69 (1.18)	-0.43 (1.00)	-0.38 (1.10)	-0.35 (1.06)	-0.26 (1.04)
Crude difference (95%CI)	-0.43 (-0.67 to -0.18)*	-0.18 (-0.34 to -0.02)*	-0.12 (-0.25 to 0.01)	-0.09 (-0.21 to 0.03)	ref
Adjusted difference (95% CI)	-0.35 (-0.59 to -0.10)*	-0.13 (-0.29 to -0.03)*	-0.11 (-0.24 to 0.02)	-0.08 (-0.20 to 0.04)	ref
% children with standardized score <537 <sup>†</sup>	74.7%	67.3%	62.1%	60.6%	58.4%
Crude OR (95%CI)	2.1 (1.3-3.4)*	1.5 (1.1-2.0)*	1.2 (0.9-1.5)	1.1 (0.9-1.4)	ref
aOR (95% CI)	1.8 (1.1-3.0)*	1.4 (1.1-1.9)*	1.1 (0.9-1.4)	1.1 (0.9-1.3)	ref

Results are presented as % or as mean (SD). Differences are presented relative to 29-week children and presented as mean difference or OR with 95% CI. Adjusted differences are adjusted for sex, parity, SES, maternal age, and ethnicity.

\*Significant at a .05 level.

<sup>†</sup>Number of children who received prevocational secondary school type advice.

addition to the existing literature on academic outcomes of very preterm children.

Among all surviving preterm children, 10.2% participated in special education, compared with 2.7% in children born at 40 weeks of gestation, showing an almost 4-fold increase in special education attendance. This proportion, however, is lower than the 19% of the preterm-born children (<32 weeks) from the Dutch POPS cohort born in 1983 that needed special education at 9 years of age in 1992, which may reflect improvements in neonatal and educational care over time.<sup>11</sup> Internationally, this decline in preterm infants attending special education has not clearly been described. Also, it is important to realize that the Dutch government executed legislation in 2014 that required schools to include children in the regular school system as much as possible, which may also have caused some reduction in the attendance of special education since then.

Although 10.2% of the surviving preterm children attended special elementary education, the remaining 90% of all very preterm children in this study completed regular elementary school. Moreover, although academic test results were lower in preterm children attending mainstream education, differences were within range of only one-half a SD. The school-based setting of the current study shows that a significant proportion of all very preterm infants is capable to finish regular elementary school.

Recently, a meta-analysis of McBride was published, summarizing academic outcomes of school-aged children born preterm, compared with children born at term.<sup>12</sup> Children born preterm showed significantly lower scores in reading

comprehension (-0.53 SD) and applied mathematical problems (-0.76 SD). The differences between very preterm and their matched term-born peers were smaller in the current study (language -0.21, mathematics -0.45), which may be explained by the fact that the outcome measure in the current study was mainly measured in children in mainstream education, thus largely without children in special education. This is different from many follow-up studies in which testing is done in all children, without any distinction made between mainstream and special education. Our results confirm the difficulties found for preterm children born at 25 to 29 weeks of gestation in general and especially in the mathematical domain.

Consistent with previous studies, this study has shown that children born below 30 weeks of gestation are less likely to complete regular elementary school education and are more likely to have poorer academic attainment at the end of elementary schooling than both their term-born peers and more mature-born counterparts.<sup>2,13</sup> Therefore it is imperative to upskill educational professionals in relation to understanding the impact of preterm birth and to raise the awareness of prematurity among teachers.<sup>7</sup> One study demonstrated that 5-year-old pupils who received educational support were exactly the children with worse cognitive outcomes on follow-up based tests, which would point at accurate awareness of teachers if there are learning problems.<sup>14</sup> This study shows that within the education system, very preterm children require long-term support for cognitive and behavioral problems to allow for later life success. Given that almost all teachers will be responsible for the management of a (very) preterm

child during their career, these results are of significant public health and educational concern.<sup>15</sup>

The strengths of this study include the large population-based datasets representing a school-based school setting over multiple years, the exactly matched term control group and the 5 different measures of academic attainment including special education rate. As participation in special education is captured in an obligatory register, no participation bias could have occurred for this outcome measure. However, this study has some limitations. Approximately two-thirds of the elementary schools use the standardized nationwide test (ie, CITO test) that was available for linkage and analyses.<sup>9</sup> In addition, availability of CITO data depended on permission of schools for sharing individual data of their pupils and willingness of schools to administrate academic attainment test on an individual level as this is not an obligatory register. Therefore, 62% of term children with the CITO education outcomes available were in line with our expectations. However, among the very preterm children, data on school outcome at age 12 years was unavailable for a higher percentage of very preterm children compared with term-born children (52% vs 38%). It was unclear why preterm children did have data available less often. Second, children with and without test data available were different in a few baseline characteristics. A very low or low SES appeared in 47.4% of the 2444 cases with unavailable test data and appeared in 40.8% of the 2233 cases with available test data. This might have influence the absolute test results found in our study. However, all very preterm children were exactly matched to term children using multiple variables including SES. Therefore, the expected impact on the presented differences is limited.

As children included in this study were born between 2000 and 2007, the long-term results of this study may not necessarily be applicable to the current-born generation of infants born below 30 weeks of gestation. Children born at 24 weeks of gestation could not be included in this study because they did not survive during the years our cohort was born. Lowering the threshold for active management of extremely preterm infants results in improved outcome for infants born at higher gestational ages. Preterm infants born at 24 weeks of gestation after the implementation of the guideline modification in 2010 will reach the age of 11-12 years in the upcoming years, after which their academic attainment results can be evaluated.

The age of 12 years is on the verge of secondary school, in which an increased demand will be seen on planning and other executive functioning skills of the children. Studying registry-based outcomes in very preterm-born young adults in future studies may therefore be of additional value.

This study showed that preterm children born at 25 to 29 weeks of gestation have significant deficits in several measures of academic attainment at age 11-12 years, compared with their term-born peers. However, the large majority of the children were in mainstream education at age 12 years. A gradual improvement was seen with every increasing completed week of gestation from 25 to 29 weeks for all

academic outcome measurements. The use of population-based, school-based registry of academic attainment may be of considerable added value in evaluating long-term outcomes of very preterm children. ■

*We thank the Dutch perinatal registration for the use of the Perined data. We thank Statistics Netherlands for using the national education and special school data and for setting-up and facilitate the microdata environment.*

Submitted for publication Feb 8, 2022; last revision received Jul 4, 2022; accepted Jul 21, 2022.

Reprint requests: Pauline E. van Beek, MD, PhD, Department of Pediatrics, Máxima Medical Center, PO Box 7777, 5500 MB Veldhoven, the Netherlands. E-mail: [pauline.van.beek@mmc.nl](mailto:pauline.van.beek@mmc.nl)

## Data Statement

Data sharing statement available at [www.jpeds.com](http://www.jpeds.com).

## References

- McNicholas F, Healy E, White M, Sherdian-Pereira M, O'Connor N, Coakley S, et al. Medical, cognitive and academic outcomes of very low birth weight infants at age 10-14 years in Ireland. *Ir J Med Sci* 2014;183:525-32.
- Johnson S, Marlow N. Early and long-term outcome of infants born extremely preterm. *Arch Dis Child* 2017;102:97-102.
- Twilhaar ES, Wade RM, de Kieviet JF, van Goudoever JB, van Elburg RM, Oosterlaan J. Cognitive outcomes of children born extremely or very preterm since the 1990s and associated risk factors: a meta-analysis and meta-regression. *JAMA Pediatr* 2018;172:361-7.
- Linsell L, Malouf R, Johnson S, Morris J, Kurinczuk JJ, Marlow N. Prognostic factors for behavioral problems and psychiatric disorders in children born very preterm or very low birth weight: a systematic review. *J Dev Behav Pediatr* 2016;37:88-102.
- Allotey J, Zamora J, Cheong-See F, Kalidindi M, Arroyo-Manzano D, Asztalos E, et al. Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children. *BJOG* 2018;125:16-25.
- Sarda SP, Sarri G, Siffel C. Global prevalence of long-term neurodevelopmental impairment following extremely preterm birth: a systematic literature review. *J Int Med Res* 2021;49:3000605211028026.
- O'Nions E, Wolke D, Johnson S, Kennedy E. Preterm birth: educational and mental health outcomes. *Clin Child Psychol Psychiatry* 2021;26:750-9.
- Twilhaar ES, de Kieviet JF, Aarnoudse-Moens CS, van Elburg RM, Oosterlaan J. Academic performance of children born preterm: a meta-analysis and meta-regression. *Arch Dis Child Fetal Neonatal Ed* 2018;103:F322-30.
- Lubbe Mvd. The End of Primary School Test. Cito, The Netherlands 2007.
- van der Straaten TFK, Briaire JJ, Dirks E, Soede W, Rieffe C, Frijns JHM. The school career of children with hearing loss in different primary educational settings-a large longitudinal nationwide study. *J Deaf Stud Deaf Educ* 2021;26:405-16.
- Hille ET, den Ouden AL, Bauer L, van den Oudenrijn C, Brand R, Verloove-Vanhorick SP. School performance at nine years of age in very premature and very low birth weight infants: perinatal risk factors and predictors at five years of age. Collaborative Project on Preterm and Small for Gestational Age (POPS) Infants in The Netherlands. *J Pediatr* 1994;125:426-34.
- McBryde M, Fitzallen GC, Liley HG, Taylor HG, Bora S. Academic outcomes of school-aged children born preterm: a systematic review and meta-analysis. *JAMA Netw Open* 2020;3:e202027.

13. Mathiasen R, Hansen BM, Andersen AM, Forman JL, Greisen G. Gestational age and basic school achievements: a national follow-up study in Denmark. *Pediatrics* 2010;126:1553.
14. van Veen S, Aarnoudse-Moens CSH, Oosterlaan J, van Sonderen L, de Haan TR, van Kaam AH, et al. Very preterm born children at early school age: healthcare therapies and educational provisions. *Early Hum Dev* 2018;117:39-43.
15. Johnson S, Gilmore C, Gallimore I, Jaekel J, Wolke D. The long-term consequences of preterm birth: what do teachers know? *Dev Med Child Neurol* 2015;57:571-7.

## 50 Years Ago in *THE JOURNAL OF PEDIATRICS*

### Sudden Infant Death Syndrome: 50 Years Later

French JW, Beckwith JB, Graham CB, Guntheroth WG. Lack of postmortem radiographic evidence of nasopharyngeal obstruction in the sudden infant death syndrome. *J Pediatr* 1972;81:1145-8.

In this 1972 article, which appeared *The Journal*, French et al evaluated the size of the nasopharyngeal airway on postmortem radiographs obtained as part of 100 consecutive autopsies performed on infants dying suddenly and unexpectedly. Of this group, 22 of the deaths were explained by autopsy and 78 remained unexplained and presumed due to sudden infant death syndrome (SIDS). Radiographic nasopharyngeal mean airway diameter measurements were similar in the 2 groups. The authors concluded that nasopharyngeal airway obstruction was unlikely to be a “significant factor” in SIDS.

Fifty years later, the search for causal factors or markers for sudden unexpected infant deaths continues. Recently, butyrylcholinesterase, an enzyme that is part of the cholinergic autonomic nervous system, was identified as a potential biomarker for infants dying of SIDS.<sup>1</sup> This case-control study demonstrated lower butyrylcholinesterase-specific activity in dried blood spot cards obtained on day 2-3 of life for infants who subsequently died of SIDS compared with surviving controls or infants dying of other causes. Yet to be understood is how this finding relates to a clinical phenomenon that reaches peak incidence at 2-4 months of age—one of the essential epidemiologic features of SIDS.

The results of case-control studies in the 1980s and 1990s identified the prone sleep position as a consistent risk factor for SIDS. Subsequent public health campaigns emphasizing prone infant sleep and safe infant sleep practices (Back to Sleep, Safe to Sleep) successfully reduced rates of SIDS. However, despite steep initial declines in SIDS rates in the 1990's, little additional progress has been made worldwide since 2000.<sup>2</sup>

In a recent Perspective piece, Goldstein et al describe the challenges of conducting basic science research in sudden unexpected infant death/SIDS. They note that “the perception of SIDS has shifted from a medical mystery to a sleep accident.”<sup>3</sup> They add “one impediment to understanding risk and making headway in pathogenesis has been the failure to refine the SIDS phenotype.” They suggest that eventual success in basic science SIDS research will require a return to a focus on the essential features that served to characterize SIDS as it was originally framed in 1969<sup>4</sup> and further defined in the years that followed. These core features should necessarily remain the guideposts for all future basic science research.

**Patrick L. Carolan, MD**  
Department of Pediatrics  
Children's Minnesota  
Minneapolis, Minnesota

## References

1. Harrington CT, Hafid NA, Waters KA. Butyrylcholinesterase is a potential biomarker for sudden infant death syndrome. *EBioMedicine* 2022;80:104041. <https://doi.org/10.1016/j.ebiom.2022.104041>
2. Park S, Han JH, Hwang J, Yon DK, Lee SW, Kim JH, et al. The global burden of sudden infant death syndrome from 1990 to 2019: a systematic analysis from the Global Burden of Disease Study 2019. *QJM* 2022;hcac093.<https://doi.org/10.1093/qjmed/hcac093>
3. Goldstein RD, Kinney HC, Guttmacher AE. Only halfway there with sudden infant death syndrome. *N Engl J Med* 2022;386:1873-5.
4. Bergman AB, Beckwith JB, Ray CG, eds. *Sudden Infant Death Syndrome: Proceedings of the International Conference on Causes of Sudden Death in Infants 1969*. Seattle (WA): University of Washington Press; 1970.



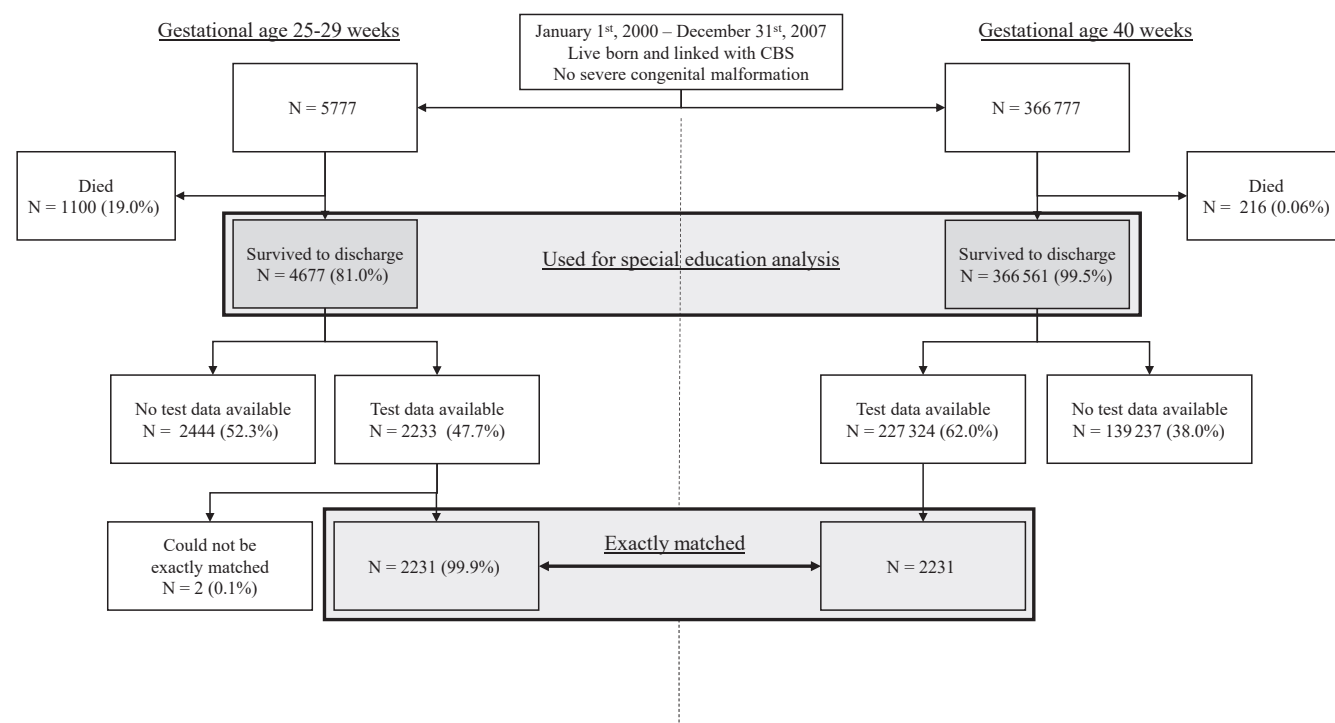


Figure. Flowchart. CBS, Statistics Netherlands (Centraal Bureau voor Statistiek).

Table I. Baseline characteristics among 4677 surviving very preterm children born at 25-29 weeks of gestation, compared between all very preterm children with testing data available (n = 2233) vs very preterm children with testing data unavailable (n = 2444)

	Including children who attended special education		P value
	Testing data available	Testing data unavailable	
	n = 2233	n = 2444	
Male sex	1142 (51.1%)	1391 (56.9%)	<.001*
Parity			.07
0	1500 (67.2%)	1603 (65.6%)	
1	477 (21.4%)	506 (20.7%)	
2+	256 (11.5%)	335 (13.7%)	
Maternal age	30.4 (4.9)	29.5 (5.3)	<.001*
SES			<.001*
Very low	471 (21.1%)	623 (25.5%)	
Low	440 (19.7%)	536 (21.9%)	
Middle	455 (20.4%)	511 (20.9%)	
High	475 (21.3%)	407 (16.7%)	
Very high	392 (17.6%)	367 (15.0%)	
Birth weight	1123 (337)	1090 (324)	<.001*

\*Significant at a .05 level.

**Table IV. Academic attainment outcome measures for very preterm (gestational age of 25-29 weeks) and term (gestational age of 40 weeks) children**

<b>All survived children (n = 4677 preterm + n = 366 561 term)</b>						
	<u>25 wk</u>	<u>26 wk</u>	<u>27 wk</u>	<u>28 wk</u>	<u>29 wk</u>	<u>40 wk</u>
	n = 249	n = 582	n = 905	n = 1250	n = 1691	n = 366 561
%children attending special education	15.3%	12.4%	10.3%	9.4%	9.2%	2.7%
Crude OR (95%CI)	6.4 (4.5-9.0)*	5.0 (4.5-9.0)*	4.1 (3.3-5.0)*	3.7 (3.1-4.7)*	3.6 (3.0-4.2)*	ref
aOR (95% CI)	6.7 (4.7-9.5)*	4.9 (3.8-6.4)*	3.9 (3.1-4.8)*	3.4 (2.8-4.1)*	3.3 (2.8-4.0)*	ref
<b>All matched children (n = 2231 preterm + n = 2231 term)</b>						
	<u>25 wk</u>	<u>26 wk</u>	<u>27 wk</u>	<u>28 wk</u>	<u>29 wk</u>	<u>40 wk</u>
	n = 95	n = 254	n = 451	n = 604	n = 827	n = 2231
Total z score (SD)	-0.67 (1.12)	-0.33 (0.97)	-0.29 (1.08)	-0.25 (1.02)	-0.17 (1.02)	0.11
Crude difference (95%CI)	-0.79 (-0.99 to -0.58)*	-0.44 (-0.57 to -0.31)*	-0.40 (-0.50 to -0.30)*	-0.36 (-0.45 to -0.27)*	-0.29 (-0.37 to -0.21)*	ref
Adjusted difference (95% CI)	-0.70 (-0.90 to -0.50)*	-0.43 (-0.55 to -0.30)*	-0.40 (-0.49 to -0.30)*	-0.35 (-0.44 to -0.27)*	-0.30 (-0.37 to -0.22)*	ref
Language z score (SD)	-0.44 (1.10)	-0.19 (0.91)	-0.16 (1.08)	-0.13 (0.97)	-0.04 (1.01)	0.08
Crude difference (95%CI)	-0.53 (-0.75 to -0.30)*	-0.27 (-0.41 to -0.14)*	-0.24 (-0.35 to -0.14)*	-0.22 (-0.31 to -0.12)*	-0.13 (-0.21 to -0.04)*	Ref
Adjusted difference (95% CI)	-0.46 (-0.68 to -0.24)*	-0.27 (-0.40 to -0.14)*	-0.24 (-0.35 to -0.14)*	-0.21 (-0.30 to -0.12)*	-0.14 (-0.22 to -0.06*)	ref
Mathematics z score (SD)	-0.69 (1.18)	-0.43 (1.00)	-0.38 (1.10)	-0.35 (1.06)	-0.26 (1.04)	0.10
Crude difference (95%CI)	-0.79 (-1.02 to -0.56)*	-0.54 (-0.68 to -0.40)*	-0.48 (-0.59 to -0.37)*	-0.45 (-0.55 to -0.35)*	-0.36 (-0.44 to -0.27)*	Ref
Adjusted difference (95% CI)	-0.72 (-0.94 to -0.49)*	-0.51 (-0.64 to -0.37)*	-0.49 (-0.59 to -0.38)*	-0.45 (-0.55 to -0.36)*	-0.37 (-0.34 to -0.28)*	ref
%children with standardized score <537 <sup>†</sup>	74.7%	67.3%	62.1%	60.6%	58.4%	46.4%
Crude OR (95%CI)	3.4 (2.1-5.5)*	2.4 (1.8-3.1)*	1.9 (1.5-2.3)*	1.7 (1.5-2.1)*	1.6 (1.4-1.9)*	ref
aOR (95% CI)	3.1 (1.9-5.0)*	2.4 (1.8-3.1)*	1.9 (1.6-2.4)*	1.8 (1.5-2.2)*	1.7 (1.4-2.0)*	ref

Results are presented as % or as mean (SD). Differences are presented relative to 40-week children, and presented as mean difference or OR with 95% CI. Adjusted differences are adjusted for sex, parity, SES, maternal age, and ethnicity.

\*Significant at a .05 level.

<sup>†</sup>Number of children who received prevocational secondary school type advice.

**Table VI.** Academic attainment outcome measures for very preterm (gestational age of 25-29 weeks) and term (gestational age of 40 weeks) children, excluding children who attended special education

All matched children – Excluding children who attended special education					
	Very preterm birth (25-29 wk)	Control group (40 wk)	Total	Mean difference (95% CI)/OR (95% CI)	P value
	n = 2174	n = 2214	n = 4388	crude	crude
Total z score	-0.24	0.12	-0.06	-0.35 (-0.29 to -0.41)	<.001*
Language z score	-0.12	0.09	-0.01	-0.20 (-0.14 to -0.26)	<.001*
Mathematics z score	-0.33	0.10	-0.11	-0.44 (-0.37 to -0.50)	<.001*
% prevocational secondary school type advice <sup>†</sup>	61.1%	46.3%	53.6%	14.8% (11.9%-17.8%)	<.001*
OR				1.8 (1.6-2.1)	

Results are presented as mean (SD), unless reported otherwise.

\*Significant at a .05 level.

†Number of children who received prevocational secondary school type advice = standardized score <537.

**Table VII.** Academic attainment outcome measures for very preterm (gestational age of 25-29 weeks) and term (gestational age of 40 weeks) children, excluding children who were born in 2007

All matched children – Excluding children who were born in 2007					
	Very preterm birth (25-29 wk)	Control group (40 wk)	Total	Mean difference (95% CI)/OR (95% CI)	P value
	n = 2113	n = 2113	n = 4226		
Total z score	-0.27	0.10	-0.08	-0.37 (-0.31 to -0.43)	<.001*
Language z score	-0.13	0.08	-0.02	-0.21 (-0.15 to -0.27)	<.001*
Mathematics z score	-0.35	0.10	-0.12	-0.45 (-0.38 to -0.51)	<.001*
% children with standardized score <537 <sup>†</sup>	61.9%	46.7%	54.3%	15.1% (12.2%-18.2%)	<.001*
OR				1.9 (1.7-2.1)	

Results are presented as mean (SD), unless reported otherwise.

\*Significant at a .05 level.

†Number of children who received prevocational secondary school type advice = standardized score <537.