



Academic achievement in children with orofacial clefts: A nationwide study in Sweden

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Summary Objective: To investigate if academic achievement among children with non-syndromic orofacial clefts (OFC) differs compared to nonaffected children and whether this association is modified by sex and psychiatric comorbidity.

Methods: A register-based cohort of children born with cleft lip (CL), cleft lip and palate (CLP), and cleft palate only (CPO) in Sweden between 1973 and 2004 ($n = 6286$) was compared to a matched community cohort ($n = 61,352$). Outcomes were academic achievements in mathematics and Swedish in school years 3, 5, 6, 9, and upper secondary school; all subjects' grades in school year 9; and university degree. Binomial-, ordinal logistic-, linear-, and binary logistic regression were used.

Results: For the majority of outcomes, no statistically significant group differences were observed, and generally children with CL were less affected than those with CLP and CPO. Children with CPO demonstrated lower achievement in the third school year (Swedish; aOR 0.54, 95% CI 0.40-0.72, mathematics; aOR 0.54, 95% CI 0.42-0.70), in Swedish in the ninth school year (aOR 0.89, 95% CI 0.80-0.99), and in mathematics in upper secondary school (aOR 0.87, 95% CI 0.76-1.00). Individuals with CPO had reduced odds of graduating from university (aOR 0.81, 95% CI 0.67-0.98). Children with CLP demonstrated lower achievement in mathematics in the third school year (aOR 0.72, 95% CI 0.54-0.95) and in both Swedish and mathematics in the ninth school year (Swedish; aOR 0.89, 95% CI 0.80-0.99, mathematics; aOR 0.87,

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95% CI 0.78-0.97). The majority of outcomes were less favorable in females but not for those with psychiatric comorbidity.

Conclusions: Our findings emphasize the need to screen children with clefts for learning difficulties to provide additional support in school. Girls with OFC appeared to be particularly vulnerable in this regard.

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Orofacial clefts (OFC) are among the most common congenital malformations affecting 2 in 1000 live births in Sweden.¹ OFC includes cleft lip (CL), cleft lip and palate (CLP) and cleft palate only (CPO) and can be part of a genetic syndrome or nonsyndromic. Increasing evidence indicates that children with OFC exhibit more neurodevelopmental conditions and poorer academic achievements than their unaffected peers.²⁻⁷ The etiology of these deficits is not fully elucidated with some studies suggesting that differences in brain development may be of greater importance in this regard than the secondary impact of surgical procedures, early impairment of speech and language, or social stigmatization.⁷ Several studies supporting the neurodevelopmental hypothesis have also shown more structural brain differences among children with OFC.⁸⁻¹³

As there is growing evidence on increased risks for neurodevelopmental conditions among individuals with OFC and because such conditions have previously been associated with poorer academic attainment there is a need to address this possible covariate.¹⁴⁻¹⁹ Academic achievement is an important predictor for health, employment, income, and well-being later in life.^{20,21} Academic achievement among individuals with OFC has been explored in different populations and at different educational levels, but several previous studies have been small and underpowered.⁷ Previous studies have generally found academic achievement to be lower in children with OFCs involving the palate, but have also suggested that this may not primarily be mediated by genetic factors.^{2,4-6,12,22-27} However, studies that considered socio-demographic factors or used siblings as controls have generally found less substantial effects.^{5,24,28,29} In addition, the operationalization of academic achievement has varied substantially, with some studies using registry data on grades or similar outcomes and some utilizing direct testing of academic skills.⁷ Findings regarding a possibly moderating effect of sex have been mixed and psychiatric or neurodevelopmental comorbidities such as ASD, ADHD, or language disorder have not been considered, with some notable exceptions.^{5,24-26}

The aim of this study was to assess academic performance throughout the educational system in a large registry cohort of children born in Sweden with nonsyndromic CL, CLP, and CPO while taking comorbid psychiatric conditions and sex differences into consideration.³⁰⁻³²

Methods

Data sources

Data were obtained from the National Board of Health and Welfare in Sweden and Statistics Sweden. All registers use

the ten-digit National Registration Number (NRN). To secure anonymity, these identifying numbers were replaced with arbitrary numbers in the data received by us, enabling data linkage across registries. The following registers were used: the Swedish Medical Birth Register, National Patient Register, Swedish Cause of Death Register, Register of Total Population, Multi-Generation Register, Migration Register, Census of the population and housing, longitudinal integration database for health insurance and labor market studies, and Swedish School-Grade Register. These databases are described in detail in [Supplementary materials 1](#).

The Uppsala ethics committee approved the study (Reg. No. 2012/363).

Participants

We identified 1825 children with CL, 2220 with CLP, and 2241 with CPO born in Sweden between January 1, 1973 and December 31, 2004, who received the diagnosis of OFC at birth or prior to 5 years of age and were recorded in the SGR.

A comparison group from the population was created by randomly including 10 individuals without OFC for each participant with OFC ($n = 61,352$), matching for month and year of birth, sex, and county of birth.

Comorbid diagnoses of congenital malformations, deformations, and chromosomal abnormalities (ICD-8 and 9 codes 740-759 and ICD-10 codes Q00-Q99, except for the facial cleft codes (749 in ICD-8 and 9 and Q35-Q37 in ICD-10) were identified as syndromic indicators in both cases and in the comparison group.

Exposure

The exposure was a diagnosis of CL, CLP, or CPO as indicated in the NPR by their international classification of diseases ICD-8, ICD-9, or ICD-10 diagnoses. The ICD-codes for CL were 749.10-749.13 (ICD-8), 749B (ICD-9), and Q36 (ICD-10); for CLP, the codes were 749.20-749.24 (ICD-8), 749C (ICD-9), and Q37 (ICD-10); and for CPO, the codes were 749.00 (ICD-8), 749A (ICD-9), and Q35 (ICD-10).

Outcome measures

We utilized results from national standardized tests (NSTs), average percentile grade for all subjects in the ninth school year, grades in the ninth school year, in upper secondary school for both mathematics and Swedish, as well as having a university degree as the outcome measures. We estimated the proportion of passed tests among NSTs in mathematics

Table 1 Translation matrix of grades between the grading systems.

Calculated grade value	1973-1994	1994-2011	2012-2013
1	1	Not passed	F
2	2 and 3	Pass	E and D
3	4	Pass with distinction	C and B
4	5	Pass with excellence	A

and Swedish, based on up to seven different tests in mathematics and up to eight different tests in Swedish for each individual in the cohorts and then investigated odds ratios for the passed tests. In upper secondary school, we utilized grades in the first mathematics and Swedish courses that are common to all Swedish upper secondary schools. The various procedures for NSTs and the systems for reporting grades in Sweden were changed multiple times across the study period and outcomes were translated for comparability using the translation matrix depicted in [Table 1](#). For a more in-depth description of these different procedures used across the study period, see [Supplementary materials 2](#).

We identified all individuals born before 1990 with a university degree.

The process for reporting achievements in year 6 NSTs changed between 2012 and 2013, and the 2013 tests were only reported as a final grade of the given test instead of the number of passed subtests. Because of these changes, we decided to exclude the results from the sixth school year's 2013 standardized tests.

For all analyses of achievements in Swedish throughout the educational system, we excluded children who followed the curriculum with Swedish as their second language. All subjects were observed from their date of birth until outcome, emigration, death, or end of the study on December 31, 2012, whichever occurred first.

Covariates

We used the same covariates for the multivariable analyses as in previous research on the psychiatric morbidity in OFC.¹⁴ We controlled for several confounders such as gestational complications and somatic indicators, year and season of birth, sex, congenital malformations or known genetic syndromes, parental psychiatric morbidity, and sociodemographic factors among parents.

Information on psychiatric diagnoses was extracted from the NPR with ICD-codes 290-315 (ICD-8), 290-319 (ICD-9), and F00-F99 (ICD-10) and on suicide attempts extracted from the NPR using the codes E950-E959 (ICD-8 and 9) and X60-X84 (ICD-10). Information on deaths by suicide was retrieved from the Swedish Cause of Death Register using the codes E950-E959 (ICD-8 and 9) and X60-X84 (ICD-10).

Perinatal variables were collected from the MBR. Gestational age at birth was dichotomized into term birth (≥ 37 gestational weeks) or preterm birth (< 37 gestational weeks). Small for gestational age (SGA) was defined as less

than -2 standard deviations (SD). Birth weight was defined as low if < 2500 g. Low Apgar score was defined as < 7 at 5 min after birth. A binary variable was created for gestational complications (preterm, SGA, low Apgar, and low birth weight) and was used in the models.

Sociodemographic variables and parental mental health were accessed through linkage via the MGR to the biological parents. Age of the parent or the mean of the ages of both parents at the time of birth was identified depending on the availability of data.

Data on maternal country of birth from the MBR were aggregated across regions: Sweden, other Nordic countries, and other countries. Information on the educational level of parents was retrieved from the LISA database. Parental education was entered into the model as a categorical variable using five categories according to the Swedish Education Terminology: 0-9 years, 10-11 years, 12-14 years, and > 14 years (university). The highest level of education obtained by either of the parents was used in the analysis.

Parental psychiatric morbidity was defined as having at least one psychiatric diagnosis using the same diagnostic codes as in the OFC and comparison groups using an ordinal variable which would take the value of 0 if none of the parents had psychiatric morbidity, 1 if only one parent had psychiatric morbidity, and 2 if both parents had psychiatric morbidity. The variable was treated as time varying in analyses.

Statistical analysis

The data were analyzed using the statistical software Stata v.15.³³ We analyzed academic achievement at five different time points throughout the educational system, in the three different subgroups of CL, CLP, and CPO and separate stratified analyses comparing those with and without a registered psychiatric diagnostic code until the event of the observed academic outcome.

Binomial regression with logit link function and cluster robust standard errors was used to investigate odds ratios for the number of succeeded NST subtests in mathematics and Swedish, considering the number of subtests that were performed. We used ordinal logistic regression with cluster robust standard errors to investigate odds ratios for grades in mathematics and Swedish. Conditional logistic regression with cluster robust standard errors was used to investigate the odds ratio of the binary outcome of university degree.

For the continuous covariate concerning parental age, restricted cubic spline with three knots was used to avoid forcing the relationship to the outcomes to be linear. Depending on the variation in the variable concerning year of birth, this variable was either excluded, included as a categorical variable, or included using restricted cubic spline with three knots.

In order to examine a possible moderating effect of sex, we estimated separate models where an interaction term of sex and the exposure CL, CLP, CPO with or without psychiatric comorbidity was included.

Results

Descriptive data regarding the cohorts are shown in [Tables 2-5](#). A total of 1825 children with CL, 2220 children with

Table 2 Descriptive characteristics of individuals with orofacial clefts and the matched comparison cohorts.

	Cleft lip (CL)		Cleft lip and palate (CLP)		Cleft palate only (CPO)	
	Affected individuals, n (%)	Comparison cohort, n (%)	Affected individuals, n (%)	Comparison cohort, n (%)	Affected individuals, n (%)	Comparison cohort, n (%)
Total sample	1825	17,806	2220	21,689	2241	21,857
Male	1161 (63.6%)	11,313 (63.5%)	1497 (67.4%)	14,619 (67.4%)	1053 (47.0%)	10,278 (47.0%)
Female	664 (36.4%)	6493 (36.5%)	723 (32.6%)	7070 (32.6%)	1188 (53.0%)	11,579 (53.0%)
Year of Birth						
1965-1974	130 (7.1%)	1300 (7.3%)	206 (9.3%)	2060 (9.5%)	151 (6.7%)	1510 (6.9%)
1975-1984	510 (27.9%)	5096 (28.6%)	606 (27.3%)	6057 (27.9%)	532 (23.7%)	5319 (24.3%)
1985-1994	659 (36.1%)	6436 (36.1%)	865 (39.0%)	8457 (39.0%)	905 (40.4%)	8853 (40.5%)
Gestational Complications						
Yes	209 (12.9%)	1618 (10.2%)	299 (15.8%)	1845 (9.7%)	324 (16.0%)	1908 (9.7%)
No	1415 (87.1%)	14,295 (89.8%)	1599 (84.2%)	17,087 (90.3%)	1695 (84.0%)	17,775 (90.3%)
Congenital malformations, deformations, and chromosomal abnormalities						
Yes	275 (15.1%)	1244 (7.0%)	485 (21.8%)	1504 (6.9%)	691 (30.8%)	1511 (6.9%)
No	1550 (84.9%)	16,562 (93.0%)	1735 (78.2%)	20,185 (93.1%)	1550 (69.2%)	20,346 (93.1%)
Mean age of parents	29.9	30.0	29.8	29.8	30.5	30.1
Maternal Region of Birth						
Sweden	1538 (89%)	14,668 (86.4%)	1832 (90.7%)	17,610 (87.1%)	1834 (86.8%)	18,072 (86.8%)
Other Nordic country	74 (4.3%)	779 (4.6%)	83 (4.1%)	861 (4.3%)	111 (5.3%)	912 (4.4%)
Outside Nordic countries	116 (6.7%)	1530 (9.0%)	104 (5.2%)	1744 (8.6%)	169 (8.0%)	1847 (8.9%)
Parental education						
0-9 years	108 (6%)	1105 (6.3%)	133 (6.1%)	1357 (6.3%)	137 (6.2%)	1209 (5.6%)
10-11 years	541 (30.1%)	4965 (28.2%)	661 (30.5%)	6115 (28.5%)	683 (30.9%)	5887 (27.3%)
12-14 years	632 (35.1%)	6393 (36.3%)	791 (36.5%)	7669 (35.8%)	802 (36.2%)	7854 (36.4%)
> 14	519 (28.8%)	5131 (29.2%)	582 (26.9%)	6306 (29.4%)	591 (26.7%)	6653 (30.8%)

CLP, 2241 children with CPO, and a total of 61,352 matched children without cleft participated in the analyses. On a majority of the outcomes, no group differences were observed between OFC cases and controls. Significant differences are presented below.

School year 3—age 10

Mathematics

Children with CLP and CPO demonstrated poorer performance in NSTs in mathematics than children without clefts (CLP: aOR 0.72, 95% CI 0.54-0.95 and CPO: aOR 0.54, 95% CI 0.42-0.70). Children with CLP without comorbid psychiatric conditions also showed lower odds of passed tests compared to non-cleft children (aOR 0.71, 95% CI 0.53-0.96) but children with CLP and psychiatric comorbidity did not show any poorer results compared to non-cleft children with psychiatric conditions (aOR 0.70, 95% CI 0.30-1.62). Children with CPO without psychiatric comorbidity presented lower odds than non-cleft peers without psychiatric comorbidity to succeed at NSTs in mathematics (aOR 0.56, 95% CI 0.43-0.74) and children with CPO and comorbid psychiatric conditions presented even lower odds of passing compared to non-exposed children with psychiatric conditions (OR 0.33, 95% CI 0.15-0.74) (Tables 5-7) (Tables S1-S3). No significant differences were observed for the CL group.

Swedish

Children with CPO had a lower probability of passing the Swedish NSTs than their peers without clefts (aOR 0.54, 95% CI 0.40-0.72). Children with CPO with no comorbid psychiatric conditions had lower odds of passing the NSTs than their peers without clefts and no psychiatric comorbidity (aOR 0.62, 95% CI 0.45-0.86). Children with CPO and comorbid psychiatric conditions also had lower odds of passing the Swedish NSTs than non-cleft children with comorbid psychiatric conditions (aOR 0.33, 95% CI 0.14-0.76) (Tables 5-7) (Tables S1-S3). As for outcomes in mathematics, no significant differences were observed for the CL group.

School year 5 or 6—age 12-13

Mathematics and Swedish

The years 5 and 6 NSTs did not reveal any significantly poorer results among CL, CLP, or CPO than unaffected peers in the comparison groups (Tables 6-8).

School year 9—age 16

Mathematics

Students with CLP and CPO had significantly reduced odds of receiving a high grade in mathematics (CLP: aOR 0.87, 95% CI 0.78-0.97 and CPO: aOR 0.81, 95% CI 0.73-0.91). Again,

Table 3 Descriptive academic outcomes CL.

Academic outcomes	CL total		CL without psychiatric comorbidity		CL with psychiatric comorbidity	
	Exposed		Exposed		Exposed	
	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed
Mathematics						
National tests Year 3	247 (87.3)	2322 (90.4)	221 (88.7)	1936 (91.0)	26 (75.3)	96 (82.6)
National tests Year 5 or 6	176 (88.8)	1641 (90.1)	162 (88.8)	1393 (90.6)	14 (89.3)	66 (81.5)
Final grade Year 9	n, (% with high achievement ^a)	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Upper secondary School grade Year 12	484 (35.5)	4933 (38.3)	474 (36.5)	4582 (38.8)	10 (15.2)	76 (23.2)
Swedish						
National tests Year 3	n, % passed	n, % passed	n, % passed tests	n, % passed	n, % passed	n, % passed
National tests Year 5 or 6	237 (91.5)	2111 (93.8)	212 (91.8)	1761 (94.1)	25 (88.9)	94 (87.1)
Final grade Year 9	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Upper secondary School grade Year 12	170 (90.9)	1512 (91.4)	156 (91.2)	1279 (91.9)	14 (87.7)	70 (85.4)
All school subjects						
Average percentile grade Year 9	n, mean	n, mean	n, mean	n, mean	n, mean	n, mean
Having University degree	1364, 47.4	12,879, 50.0	1298, 48.3	11,821, 50.6	66, 29.5	327, 32.9
Higher education						
Having University degree	n, %	n, %	n, %	n, %	n, %	n, %
	168 (17.7)	2023 (21.3)	160 (20.1)	1571 (22.1)	8 (5.2)	49 (10.5)

^a High achievement is defined as achieving a grade 3 or 4 in a grade scale 1-4.

Table 4 Descriptive academic outcomes CLP.

Academic outcomes	CLP total		CLP without psychiatric comorbidity		CLP with psychiatric comorbidity	
	Exposed	Unexposed	Exposed	Unexposed	Exposed	Unexposed
Mathematics	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed
National tests Year 3	244 (88.5)	2286 (91.5)	216 (89.1)	1907 (91.9)	28 (83.7)	105 (86.9)
National tests Year 5 or 6	185 (89.3)	1695 (90.9)	169 (89.2)	1449 (91.1)	16 (90.3)	74 (83.7)
	n, (%)with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Final grade Year 9	570 (34.8)	5980 (38.6)	545 (35.7)	5471 (39.3)	25 (22.3)	103 (22.7)
Upper secondary School grade Year 12	393 (44.7)	3308 (47.6)	373 (45.5)	2992 (48.3)	20 (32.8)	98 (29.8)
Swedish	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed
National tests Year 3	236 (91.0)	2099 (93.4)	209 (91.4)	1756 (93.8)	27 (87.9)	103 (86.2)
National tests Year 5 or 6	180 (90.4)	1569 (91.2)	164 (90.8)	1333 (91.7)	16 (86.7)	73 (80.2)
	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Final grade Year 9	647 (40.1)	6511 (43.5)	619 (41.1)	5940 (44.0)	28 (25.7)	120 (27.2)
Upper secondary School grade Year 12	425 (48.2)	3513 (50.8)	398 (48.5)	3134 (50.8)	27 (43.5)	136 (41.2)
All school subjects	n, mean	n, mean	n, mean	n, mean	n, mean	n, mean
Average percentile grade Year 9	1638, 46.3	15,488, 49.8	1525, 47.4	13,929, 50.6	113, 31.1	454, 30.0
Higher education	n, %	n, %	n, %	n, %	n, %	n, %
Having a University degree	228 (18.6)	2588 (21.1)	212 (21.2)	1953 (21.8)	16 (7.1)	57 (9.1)

^a High achievement is defined as achieving a grade 3 or 4 in a grade scale 1-4.

Table 5 Descriptive academic outcomes CPO.

Academic outcomes	CPO total		CPO without psychiatric comorbidity		CPO with psychiatric comorbidity	
	Exposed	Unexposed	Exposed	Unexposed	Exposed	Unexposed
Mathematics	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed
National tests Year 3	281 (84.4)	2675 (91.8)	247 (85.6)	2210 (92.1)	34 (75.4)	138 (86.7)
National tests Year 5 or 6	228 (88.0)	2097 (90.8)	207 (89.2)	1802 (91.3)	21 (76.2)	88 (80.2)
	n,(%)with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Final grade Year 9	521 (33.4)	5781 (39.3)	498 (34.3)	5192 (39.5)	23 (20.5)	136 (30.6)
Upper secondary School grade Year 12	363 (42.0)	3305 (48.0)	336 (42.5)	2896 (48.5)	27 (36.5)	128 (37.6)
Swedish	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed	n, % passed
National tests Year 3	270 (90.2)	2450 (94.8)	236 (91.6)	2015 (95.1)	34 (79.5)	141 (89.7)
National tests Year 5 or 6	226 (90.2)	1978 (92.9)	202 (91.7)	1679 (93.9)	24 (77.3)	91 (79.9)
	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a	n, % with high achievement ^a
Final grade Year 9	723 (47.2)	7151 (50.6)	684 (48.1)	6443 (51.0)	39 (8.9)	167 (38.3)
Upper secondary School grade Year 12	450 (51.8)	3983 (57.6)	418 (52.7)	3439 (57.5)	32 (42.7)	166 (48.8)
All school subjects	n, mean	n, mean	n, mean	n, mean	n, mean	n, mean
Average percentile grade Year 9	1562, 47.9	14,696, 52.7	1450, 48.9	13,141, 53.2	112, 34.3	444, 38.1
Higher education	n, %	n, %	n, %	n, %	n, %	n, %
Having a University degree	202 (17.8)	2683 (23.6)	187 (20.9)	2004 (25.1)	15 (6.2)	56 (9.9)

^a High achievement is defined as achieving a grade 3 or 4 in a grade scale 1-4.

Table 6 Academic achievements among children with CL.

Academic outcomes	CL total		CL without psychiatric comorbidity		CL with psychiatric comorbidity	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Mathematics						
^a National tests Year 3	0.78	0.59-1.03	0.79	0.58-1.06	0.59	0.25-1.35
^a National tests Year 5 or 6	0.89	0.61-1.29	0.85	0.58-1.27	3.59	0.65-19.92
^b Final grade Year 9	0.91	0.81-1.02	0.93	0.82-1.05	0.60	0.36-1.01
^b Upper secondary School grade Year 12	1.00	0.86-1.16	1.00	0.86-1.16	0.93	0.43-2.03
Swedish	aOR	95% CI	aOR	95% CI	aOR	95% CI
^a National tests Year 3	0.75	0.55-1.04	0.74	0.52-1.06	0.94	0.44-2.00
^a National tests Year 5 or 6	1.01	0.70-1.47	0.98	0.66-1.46	1.84	0.68-4.97
^b Final grade Year 9	0.94	0.83-1.06	0.96	0.85-1.09	0.67	0.37-1.21
^b Upper secondary school grade Year 12	1.02	0.88-1.19	1.06	0.91-1.23	0.62	0.33-1.18
All school subjects Year 9	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
^c Average percentile grade	-1.65	-3.19 to -0.11	-1.39	-2.97 to -0.18	11.01	-14.93-36.94
Higher education	aOR	95% CI	aOR	95% CI	aOR	95% CI
^d Having a University degree	0.86	0.70-1.07	0.89	0.71-1.12	missing	missing

Models were adjusted for perinatal complications, congenital malformations and chromosomal abnormalities, sex, year of birth, parental age, maternal country of birth, parental psychiatric disorders, and educational level.

^a The outcome measure is the number of passed subtests. Binomial regression derived adjusted odds ratios (aOR) express the odds to pass a subtest among the exposed compared to the unexposed.

^b The outcome measure is the final grade in the ordinal scale: Ordinal logistic regression derived aORs express the odds for higher grade among the exposed compared to the unexposed.

^c The outcome is continuous grade. The linear regression derived coefficient expresses the adjusted mean difference between the exposed and unexposed.

^d The outcome is having obtained a university degree. The conditional logistic regression derived aORs express the odds for a university degree among the exposed compared to the unexposed.

no significant differences were observed for the CL group. Children with CLP and CPO without psychiatric comorbidity also demonstrated lower odds of receiving a high grade in mathematics compared to their peers without clefts and no psychiatric comorbidity (CLP no psych: aOR 0.89, 95% CI 0.80-0.99 and CPO no psych: aOR 0.83, 95% CI 0.74-0.93) (Tables 6-8).

Moderation analyses showed that females with CPO drive the association, with lower odds of receiving a high final grade in mathematics (female aOR 0.72 95% CI 0.62-0.84 and male aOR 0.93, 95% CI 0.79-1.10, sex interaction $p = .023$), both without psychiatric comorbidity (female aOR 0.75, 95% CI 0.64-0.87 and male aOR 0.95, 95% CI 0.80-1.11, interaction $p = .039$) and with psychiatric comorbidity (female aOR 0.52, 95% CI 0.28-0.97 and male aOR 1.11, 95% CI 0.61-2.00) (Tables S1-S3).

Swedish

Children with CLP had reduced odds of receiving a high grade in Swedish (aOR 0.89, 95% CI 0.80-0.99). Females with CL had reduced odds of receiving a high grade in Swedish but no such association was seen among males (female aOR 0.78, 95% CI 0.65-0.95 and male aOR 1.06, 95% CI 0.91-1.23, sex interaction $p = .015$). This association was also present among females with CL without psychiatric comorbidity (female aHR 0.81, 95% CI 0.66-0.98, sex interaction $p = .02$) (Tables 6-8, S1-S3).

Average percentile grade

Individuals with CL, CLP, and CPO had lower average percentile grade for all subjects when finishing compulsory school compared to unaffected peers (CL coefficient -1.65, 95% CI -3.19 to -0.11), CLP coefficient -2.71, 95% CI (-4.07 to -1.36), and CPO coefficient -3.23, 95% CI (-4.72 to -1.74)). This association was also significant among individuals with CLP and CPO without psychiatric comorbidity (CLP coefficient -2.39, 95% CI (-3.80 to -0.98) and CPO coefficient -2.91, 95% CI (-4.37 to -1.45)), but not when psychiatric comorbidity was present. Females with CLP and CPO were more negatively affected than males (CLP female coefficient -5.22, 95% CI (-7.86)-(-2.59), male coefficient -1.56, 95% CI (-3.17)-0.05, sex interaction p -value 0.022), CPO female coefficient -4.59, 95% CI (-6.61)-(-2.58), male coefficient -1.62, 95% CI (-3.71) - 0.46, sex interaction $p = 0.039$) (Tables 6-8, S1-S3).

Upper secondary school

Mathematics

At upper secondary school, individuals with CL demonstrated no association with lower grades in mathematics whereas students with CLP and CPO in total and without concurrent psychiatric conditions had significantly reduced odds of receiving a high grade in mathematics (CLP in total: aOR 0.85, 95% CI 0.75-0.98; CLP without psychiatric comorbidity: aOR 0.85, 95% CI 0.74-0.98; CPO in total: aOR

Table 7 Academic achievements among children with CLP.

Academic outcomes	CLP total		CLP without psychiatric comorbidity		CLP with psychiatric comorbidity	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Mathematics						
^a National tests Year 3	0.72	0.54-0.95	0.71	0.53-0.96	0.70	0.30-1.62
^a National tests Year 5 or 6	0.83	0.56-1.22	0.83	0.55-1.23	1.43	0.25-8.25
^b Final grade Year 9	0.87	0.78-0.97	0.89	0.80-0.99	0.83	0.51-1.33
^b Upper secondary School grade Year 12	0.85	0.75-0.98	0.85	0.74-0.98	1.11	0.63-1.96
Swedish						
^a National tests Year 3	0.75	0.55-1.03	0.75	0.53-1.06	0.94	0.37-2.42
^a National tests Year 5 or 6	0.94	0.66-1.35	0.95	0.66-1.39	1.24	0.33-4.60
^b Final grade Year 9	0.89	0.80-0.99	0.91	0.81-1.02	0.83	0.54-1.26
^b Upper secondary school grade Year 12	0.94	0.81-1.08	0.95	0.82-1.10	0.91	0.50-1.66
All school subjects Year 9	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
^c Average percentile grade	-2.71	-4.07 to -1.36	-2.39	-3.80 to -0.98	-6.88	-19.24-5.49
Higher education						
^d Having a University degree	0.90	0.74-1.08	0.99	0.81-1.21	0.40	0.08-1.99

Models were adjusted for perinatal complications, congenital malformations and chromosomal abnormalities, sex, year of birth, parental age, maternal country of birth, parental psychiatric disorders, and educational level.

^a The outcome measure is the number of passed subtests. Binomial regression derived adjusted odds ratios (aOR) express the odds to pass a subtest among the exposed compared to the unexposed.

^b The outcome measure is the final grade in ordinal scale: Ordinal logistic regression derived aORs express the odds for higher grade among the exposed compared to the unexposed.

^c The outcome is continuous grade. The linear regression derived coefficient expresses the adjusted mean difference between exposed and unexposed.

^d The outcome is having obtained a university degree. The conditional logistic regression derived aORs express the odds for a university degree among the exposed compared to the unexposed.

0.87, 95% CI 0.76-0.999; and CPO without psychiatric comorbidity: aOR 0.86, 95% CI 0.74-0.996) (Tables 6-8).

Females with CLP and CPO were more negatively affected with even lower odds of receiving a high grade in mathematics (CLP female: aOR 0.64, 95% CI 0.50-0.81; CLP male: aOR 0.98, 95% CI 0.83-1.15; sex interaction: p-value.004; CPO female: aOR 0.76, 95% CI 0.64-0.92; and CPO male: aOR 1.04, 95% CI 0.84-1.28; sex interaction p-value.032) (Tables S1-S3).

Swedish

There was no association with lower odds for a high grade in Swedish in Upper Secondary School among individuals with clefts (Tables 6-8, S1-S3).

University degree

Individuals with CPO had reduced odds of graduating from university than their unaffected peers (CPO aOR 0.81, $p = 0.033$) (Tables 6-8, S1-S3).

Discussion

We examined academic achievement among children born with OFC throughout the educational system in Sweden, from primary school until university. We found that children

with CLP and CPO had poorer academic achievement on some but not all outcomes than their non-cleft peers already in primary school, whereas individuals with CPO exhibited associations into university level education. When comparing individuals with psychiatric comorbidity, poorer achievement was only found for children with CPO in the third-year NSTs in mathematics and Swedish. In addition, analyses of sex differences pointed to lower achievement in females, especially in the CPO cohort. On most outcomes, no significant associations between OFC and academic outcome were found, which must be considered a hopeful message for individuals with OFC and their families alongside the possible implications of these associations.

In the subgroup of children with psychiatric comorbidity, we found poorer results only among children with CPO in the third-year NSTs in mathematics and Swedish, compared to children with psychiatric comorbidity without CPO. On the contrary, poorer academic achievements were more evident among children with CLP without psychiatric comorbidity from primary school up to upper secondary school and for CPO also at university level, compared to children without psychiatric comorbidity and without clefts. A possible explanation for this finding may be yet undiagnosed neurodevelopmental conditions among children with OFC but may perhaps more likely be explained by cognitive difficulties mediating the relationship in this group, irrespective of psychiatric comorbidity.

Table 8 Academic achievements among children with CPO.

Academic outcomes	CPO total		CPO without psychiatric comorbidity		CPO with psychiatric comorbidity	
	aOR	95% CI	aOR	95% CI	aOR	95% CI
Mathematics						
^a National tests Year 3	0.54	0.42-0.70	0.56	0.43-0.74	0.33	0.15-0.74
^a National tests Year 5 or 6	0.79	0.57-1.09	0.83	0.59-1.17	0.91	0.31-2.73
^b Final grade Year 9	0.81	0.73-0.91	0.83	0.74-0.93	0.78	0.50-1.21
^b Upper secondary School grade Year 12	0.87	0.76-0.999	0.86	0.74-0.996	1.01	0.59-1.72
Swedish	aOR	95% CI	aOR	95% CI	aOR	95% CI
^a National tests Year 3	0.54	0.40-0.72	0.62	0.45-0.86	0.33	0.14-0.76
^a National tests Year 5 or 6	0.75	0.54-1.04	0.77	0.53-1.11	1.06	0.49-2.30
^b Final grade Year 9	0.93	0.83-1.03	0.94	0.84-1.05	0.93	0.59-1.45
^b Upper secondary School grade Year 12	0.92	0.79-1.07	0.95	0.81-1.12	0.80	0.47-1.35
All school subjects Year 9	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
^c Average percentile grade	-3.23	-4.72 to -1.74	-2.91	-4.37 to -1.45	-7.18	-21.12-6.76
Higher education	aOR	95% CI	aOR	95% CI	aOR	95% CI
^d Having a University degree	0.81	0.67-0.98	0.88	0.71-1.08	missing	missing

Models were adjusted for perinatal complications, congenital malformations and chromosomal abnormalities, sex, year of birth, parental age, maternal country of birth, parental psychiatric disorders, and educational level.

^a The outcome measure is the number of passed subtests. Binomial regression derived adjusted odds ratios (aOR) express the odds to pass a subtest among the exposed compared to the unexposed.

^b The outcome measure is the final grade in ordinal scale: Ordinal logistic regression derived aORs express the odds for higher grade among the exposed compared to the unexposed.

^c The outcome is continuous grade. The linear regression derived coefficient expresses the adjusted mean difference between exposed and unexposed.

^d The outcome is having obtained a university degree. The conditional logistic regression derived aORs express the odds for a university degree among the exposed compared to the unexposed.

Children with CLP and CPO presented lower academic achievements than CL, in line with our previous study where children with CLP and CPO were more susceptible to having neurodevelopmental conditions than CL.¹⁴ A possible explanation of these findings could be a differential impact on brain development among different subtypes of OFC, supporting the hypothesis of neurodevelopmental differences as an important common mechanism for the association between OFC and lower academic achievements.^{23,29}

In line with some previous findings in OFC, we also detected sex differences with poorer academic outcomes in the later school years among females than males.^{5,24,25} Undiagnosed neurodevelopmental conditions among females with OFC may be a possible explanation, as the diagnostic criteria for neurodevelopmental conditions such as ADHD and ASD have been criticized for poor sensitivity regarding capturing females with ADHD/ASD-related difficulties.³⁴

The achievements in mathematics were generally more negatively affected than the achievements in Swedish. These findings are in contrast to those in several previous studies that either found no difference across subjects²² or lower achievement in language-specific subjects.³⁵ However, previous studies suggest lower achievement in mathematics among individuals with neuropsychiatric conditions.^{36,37}

An alternative explanation to our findings, or at least a set of possible mediating factors, are the various somatic symptoms related to OFC, such as obstructive sleep apnea, hearing impairments, or secondary effects such as missing school days owing to clinic appointments and refraining from speaking up in class owing to cleft-related speech difficulties.^{38,39} However, all children in Sweden undergo visual and hearing assessments as part of the pediatric national care program to detect impairments before starting elementary school. Thus, impaired hearing is unlikely to explain the poorer school performance in this cohort.

Strengths and limitations

A major strength of this study is the use of a nationwide register-based cohort with long follow-up time, enabling us to include a large number of participants adjusting for several possible confounders. We also investigated academic outcomes among children with OFC and children without OFC with and without psychiatric comorbidity at the time of the academic assessment separately. Previous studies on academic achievement and OFC have not adequately addressed these issues.^{40,41} The use of NSTs and grades to measure academic outcomes rather than relying on a single type of outcome measure^{4,24} is also an important strength.

A potential weakness of our study design is the possibility of unidentified syndromic cases that can be associated with intellectual disability or other psychiatric conditions as well as breathing, hearing, and visual impairments. This is expected to have occurred more often in the earlier born individuals of the cohort and we have adjusted for calendar year to eliminate this risk. We have also tried to take into consideration any possible unidentified associated congenital malformations and syndromes by adjusting for all ICD-codes for malformations in the analyses and not the

known syndromes alone. However, our results showing lower achievement in CPO could be partially explained by such genetic factors given the differential pathway of gene transmission recently identified for the different subtypes of OFC.⁴² The long time period studied and nature of our data did not permit us to study time-related trends in outcomes, which is a potential weakness. We also acknowledge that although this potential confounder was partially rectified by using a matrix translation across different outcomes, we cannot rule out that some of the associations observed are an artifact of an impact of cleft on real-world outcomes in society that has changed over time.

Conclusions

This study has shown that children with nonsyndromic CLP and CPO exhibit less favorable academic achievement than nonaffected peers throughout the educational system, especially in mathematics. The findings emphasize the need to screen children with clefts for needs in terms of special education and that children with CL appear to have more favorable academic outcomes than other types of OFC.

Ethical approval

The Uppsala Ethics Committee approved the study (Reg. No. 2012/363).

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Declaration of Competing Interest

None declared.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.bjps.2025.12.037](https://doi.org/10.1016/j.bjps.2025.12.037).

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