



Parental socioeconomic status and risk of cerebral palsy in the child

Forthun, Ingeborg; Strandberg-Larsen, Katrine; Wilcox, Allen J.; Moster, Dag; Petersen, Tanja Gram; Vik, Torstein; Lie, Rolv Terje; Uldall, Peter; Tollanes, Mette Christophersen

Published in:

International Journal of Epidemiology

DOI:

[10.1093/ije/dyy139](https://doi.org/10.1093/ije/dyy139)

Publication date:

2018

Document version

Publisher's PDF, also known as Version of record

Document license:

[CC BY](https://creativecommons.org/licenses/by/4.0/)

Citation for published version (APA):

Forthun, I., Strandberg-Larsen, K., Wilcox, A. J., Moster, D., Petersen, T. G., Vik, T., ... Tollanes, M. C. (2018). Parental socioeconomic status and risk of cerebral palsy in the child: evidence from two Nordic population-based cohorts. *International Journal of Epidemiology*, 47(4), 1298-1306. <https://doi.org/10.1093/ije/dyy139>



Miscellaneous

Parental socioeconomic status and risk of cerebral palsy in the child: evidence from two Nordic population-based cohorts

Ingeborg Forthun,^{1,2*} Katrine Strandberg-Larsen,³ Allen J Wilcox,⁴ Dag Moster,^{1,2} Tanja Gram Petersen,³ Torstein Vik,⁵ Rolv Terje Lie,¹ Peter Uldall⁶ and Mette Christophersen Tollånes^{7,8}

¹Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway, ²Department of Pediatrics, Haukeland University Hospital, Bergen, Norway, ³Section of Epidemiology, Department of Public Health, University of Copenhagen, Copenhagen, Denmark, ⁴Epidemiology Branch, National Institute of Environmental Health Sciences, Durham, NC, USA, ⁵Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway, ⁶Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark, ⁷Department of Health Promotion, Norwegian Institute of Public Health, Oslo, Norway and ⁸Norwegian Quality Improvement of Laboratory Examinations (Noklus), Haralds plass Deaconess Hospital, Bergen, Norway

*Corresponding author. Department of Global Public Health and Primary Care, University of Bergen, P.O. Box 7804, N-5020 Bergen, Norway. E-mail: Ingeborg.Forthun@uib.no

Editorial decision 31 May 2018; Accepted 13 June 2018

Abstract

Background: We investigated whether the risk of cerebral palsy (CP) in the child varies by parents' socioeconomic status, in Denmark and Norway.

Methods: We included almost 1.3 million children born in Denmark during 1981–2007 and 2.4 million children born in Norway during 1967–2007, registered in the Medical Birth registries. Data on births were linked to Statistics Denmark and Norway to retrieve information on parents' education and relationship status and, in Denmark, also income. CP diagnoses were obtained from linkage with national registries. We used multivariate log-binomial regression models to estimate relative risk (RR) of CP according to parental socioeconomic status.

Results: There was a strong trend of decreasing risk of CP with additional education of both the mother and the father. These trends were nearly identical for the two parents, with a one-third reduction in risk for those with the highest education compared with parents with the lowest education. When both parents had high education, risk of CP was further reduced (RR 0.58, 0.53–0.63). Women with partners had a reduction in risk (RR 0.79, 0.74–0.85) compared with single mothers overall. Risk patterns were stable over time, across countries and within spastic bilateral and unilateral CP. Household income was not associated with risk of CP.

Conclusions: Risk of CP in two Scandinavian countries was lower among educated parents and mothers with a partner, but unrelated to income. Factors underlying this stable association with education are unknown, but could include differences in potentially modifiable lifestyle factors and health behaviours.

Key words: Cerebral palsy, socioeconomic status, registries, cohort, Denmark, Norway

Key Messages

- We did parallel studies in Denmark and Norway, investigating the associations between different measures of parental socioeconomic status and risk of having a child with CP.
- We found a strong reduction in risk of CP among parents with higher education and mothers with partners, but no association with income.
- These gradients were stable over the study period.
- There is a wide range of possible underlying causal mechanisms for these associations, at least some of which are potentially preventable.

Introduction

Cerebral palsy (CP) is the most common physical disability in children; about 2 per 1000 live-born are later diagnosed with CP.¹ CP is characterized by disturbances of motor function, with a range of associated neurological problems. There are four major subtypes according to clinical presentation. Underlying causes are unknown in most cases, but antenatal factors are considered to be important.^{2,3}

Social inequality in risk has been reported for outcomes strongly associated with CP, including preterm birth, low birthweight and intrauterine growth restriction.^{4,5} Findings on parental socioeconomic status (SES) and risk of CP in the child, however, have been inconsistent. Most studies have reported an increasing risk of CP with decreasing SES,^{6–8} but not all.⁹ CP subtypes may have different aetiologies,¹⁰ but few of the previous studies have investigated SES in relation to subtypes.

A socioeconomic gradient in CP risk could change over time, with changes in educational attainment, parental age, income, social policy and health behaviours, and improvements in antenatal, obstetric and neonatal care. This has previously not been investigated in Denmark and Norway where redistributive tax systems, social policies and free access to education aim to reduce socioeconomic differences.¹¹ Denmark and Norway are similar in terms of language, culture, history and health care systems,¹² and both countries offer pregnant women antenatal care free of charge. The aim of this study was to investigate various measures of familial SES and their associations with risk of

CP in children, to describe any changes over time and to explore possible differences by CP subtype.

Methods

Study population

We had two large population-based cohorts available. In Denmark, we used data on all live-born children registered in the Danish Medical Birth Registry (MBR)¹³ during 1981–2007, who survived first year of life. CP status was obtained through record linkage with the Danish Cerebral Palsy Registry (CPR).¹⁴ The registry covered only the eastern part of Denmark before 1995, thus only children born to mothers resident in the eastern part of Denmark were included for the birth years 1981–94. The CPR has CP subtype information and does not include children with post-neonatal causes of CP.

In Norway, we used data from the Norwegian Medical Birth Registry (MBRN)¹⁵ on all children born during 1967–2007 who survived the first year of life. CP diagnoses were collected by linkage to the Norwegian National Insurance Scheme (NAV)¹⁶ and the Norwegian Patient Registry (NPR).¹⁷ A person with CP was defined as someone having received a benefit or disability pension on the basis of ICD-9 codes 342–344 or ICD-10 codes G80–G83 registered in the NAV, or having been registered in the NPR with ICD-10 code G80 on at least two occasions. CP diagnoses from the NAV were available during 1967–2013 and have previously been validated, revealing some under-

reporting of mild cases.¹⁸ Data from the NPR included all diagnoses from in- and outpatient hospital visits during 2008–15. We could not distinguish between postneonally acquired and congenital CP cases in Norway, nor did we have reliable information on CP subtypes.

Measures of socioeconomic status

We use education as the primary measure of parents' SES, since education is the measure that most strongly predicts maternal and child health.¹⁹ Information on highest attained maternal and paternal educational levels were retrieved from record linkage with Statistics Denmark²⁰ and Statistic Norway at end of follow-up (1 October 2010 in Denmark and 1 October 2013 in Norway). In the Danish cohort, we also had information on highest attained or ongoing maternal and paternal education in the year of delivery. The educational systems are similar in Denmark and Norway, and the standards for classification of education have the same overall structure. Maternal and paternal education were categorized as 'primary and lower secondary', 'upper secondary and short non-tertiary', 'bachelor's degree' and 'master's and doctorate degree'.

As additional measures of parental SES, we used relationship status and household income. Information on relationship status came from Statistics Denmark and the Norwegian Medical Birth Registry, and was categorized as 'single mother' or 'with partner'. Information on household income was available only in Denmark, and was calculated as the sum of the mother's and father's disposable income as of January 1st in the year before birth of the child, divided by the square root of household size.²¹ To account for inflation, household income was categorized in quintiles relative to all mothers giving birth in a given year.

Covariates and statistical analyses

We estimated crude and adjusted relative risks (RR) using log-binomial models overall and for each time period (1967–80, 1981–90, 1991–2000, 2001–07). Adjustments were based on discussion of a directed acyclic graph (Supplementary Figure 1, available as Supplementary data at *IJE* online).²² When using parental educational attainment or relationship status as the exposure, we considered year of delivery, included as a continuous variable, and parental age [<20 , 20–24, 25–29 (reference), 30–34, 35–39, 40–44 and ≥ 45 (≥ 40 for mothers)] as possible confounders. We combined the results for Denmark and Norway using meta-analyses with random-effect models (no evidence of heterogeneity between pairs of RRs). When using household income as the exposure, we considered parental educational attainment in year of delivery and age as possible

confounders. We investigated whether the effect of relationship status varied by maternal education, and whether the effect of maternal education varied by household income, by stratification and by including an interaction term in the models.

The total burden of educational inequalities in risk of CP in the population may have changed over time as more parents take higher education. We explored this by calculating the relative index of inequality (RII) across time periods and cohorts.²³ Unlike the RR, the RII accounts for changes in the educational distribution over time. The RII was calculated by ranking the four educational groups for maternal and paternal education from the lowest to the highest within the same birth year, and allocating a score (ranging from 0–1) that equals the midpoint of the category's range in the cumulative distribution. For instance, if 24% of the mothers had only primary or lower secondary education in 1990, they would be allocated a score of 0.12, and if the next group of mothers constituted 42%, they would be allocated a score of 0.45 (0.24 + 0.42/2) etc. Using this score as a continuous exposure variable in the model for a given time period, its estimated coefficient expresses the RII during that period. The RII can be interpreted as the relative risk of having a child with CP, comparing hypothetical parents at the top with parents at the bottom of the educational hierarchy.²⁴ A small RII indicates a large difference in risk of CP between those at the bottom and top of the educational hierarchy. Trends in RII over time were assessed by including an interaction term with score by time period.

To test the robustness of our results, we repeated all analyses after excluding mothers with foreign country of origin and immigrant status. A socioeconomic gradient in CP may be explained at least in part by the association of SES with preterm birth. Analyses adjusting for preterm birth as a mediating variable are subject to bias.²⁵ With that caveat, we carried out sensitivity analyses including only term-born children (gestational week 37 + 0 to 42 + 6). For these analyses, we removed likely errors in gestational age by excluding children with an absolute birthweight-by-gestational-age z-score exceeding 5 standard deviations.²⁶ Finally, we conducted separate analyses of CP cases from each of the two data sources used to identify CP cases in the Norwegian cohort. All analyses were performed using Stata, version 14, and robust standard errors were applied to account for possible sibship dependency.

Results

There were 2809 children diagnosed with CP among 1 275 819 Danish children (2.2 per 1000), and 6187 CP cases among 2 350 548 Norwegian children (2.6 per 1000). The

distribution of parents' education was similar in the two countries. Education levels were slightly higher in Denmark due to a longer period of recorded data for Norway. During the time period for which data were available for both countries (1981–2007), educational levels were slightly higher in Norway. More Danish than Norwegian mothers were single or immigrants (Table 1).

A gradient in risk of CP was observed for both maternal and paternal education. Compared with offspring of mothers with primary or lower secondary education, CP risk was 17% lower among children of mothers with upper secondary or short non-tertiary education [adjusted relative risk (aRR) 0.83, 95% confidence interval (CI), 0.79 to 0.88], 25% lower among children of mothers with

Table 1. Characteristics of study cohorts, Denmark (1981–2007) and Norway (1967–2007)

	Denmark		Norway	
	Number (%)	Number with CP (per 1000)	Number (%)	Number with CP (per 1000)
Maternal education at end of follow-up				
Primary and lower secondary	241 440 (19)	663 (2.7)	553 934 (24)	1687 (3.0)
Upper secondary and short non-tertiary	587 700 (46)	1286 (2.2)	1 013 274 (43)	2621 (2.6)
Bachelor's degree	311 336 (24)	625 (2.0)	632 070 (27)	1550 (2.5)
Master's or doctorate degree	113 218 (9)	182 (1.6)	121 784 (5)	275 (2.3)
Missing data	22 125 (2)	53 (2.4)	29 486 (1)	54 (1.8)
Paternal education at end of follow-up				
Primary and lower secondary	247 549 (19)	637 (2.6)	507 190 (22)	1549 (3.1)
Upper secondary and short non-tertiary	660 650 (52)	1486 (2.2)	1 146 828 (49)	3018 (2.6)
Bachelor's degree	163 374 (13)	308 (1.9)	425 903 (18)	994 (2.3)
Master's or doctorate degree	143 315 (11)	233 (1.6)	218 705 (9)	468 (2.1)
Missing data	60 931 (5)	145 (2.4)	51 922 (2)	158 (3.0)
Relationship status				
Partner	1 086 367 (85)	2288 (2.1)	2 116 234 (90)	5456 (2.6)
Single mother	176 973 (14)	488 (2.8)	222 382 (9)	705 (3.2)
Missing data	12 479 (1)	33 (2.6)	11 932 (1)	26 (2.2)
Household income				
0 to 20th percentile	248 022 (19)	598 (2.4)	NA	NA
>20th to 40th percentile	248 009 (19)	563 (2.3)	NA	NA
>40th to 60th percentile	248 008 (19)	487 (2.0)	NA	NA
>60th to 80th percentile	248 005 (19)	536 (2.2)	NA	NA
>80th percentile	247 996 (19)	534 (2.2)	NA	NA
Missing data	35 779 (3)	91 (2.5)	NA	NA
Maternal age				
<20	27 659 (2)	72 (2.6)	137 010 (6)	375 (2.7)
20 to 24	207 057 (16)	502 (2.4)	621 590 (26)	1528 (2.5)
25 to 29	470 207 (37)	940 (2.0)	808 142 (34)	2076 (2.6)
30 to 34	399 236 (31)	888 (2.2)	541 912 (23)	1434 (2.6)
35 to 39	148 517 (12)	351 (2.4)	204 050 (9)	655 (3.2)
≥40	23 143 (2)	56 (2.4)	37 812 (2)	119 (3.1)
Paternal age				
<20	7092 (1)	23 (3.2)	30 504 (1)	94 (3.1)
20 to 24	103 509 (8)	272 (2.6)	366 878 (16)	919 (2.5)
25 to 29	358 069 (28)	773 (2.2)	743 708 (32)	1884 (2.5)
30 to 34	437 362 (34)	875 (2.0)	663 066 (28)	1736 (2.6)
35 to 39	238 280 (19)	551 (2.3)	344 913 (15)	954 (2.8)
40 to 44	81 899 (6)	194 (2.4)	127 603 (5)	371 (2.9)
≥45	33 731 (3)	78 (2.3)	55 718 (2)	143 (2.6)
Missing data	15 877 (1)	43 (2.7)	18 158 (1)	86 (4.7)
Non-immigrant mother (Danish/Norwegian)	1 133 103 (89)	2505 (2.2)	2 163 630 (92)	5738 (2.7)
Immigrant mother	141 601 (11)	302 (2.1)	186 115 (8)	449 (2.4)

Missing data less than 0.001 are not shown.
NA, not available.

bachelor's degree (aRR 0.75, 95% CI, 0.71 to 0.80), and 36% lower among those of mothers with master's or doctorate degree (aRR 0.64, 95% CI, 0.56 to 0.71) (Figure 1). Similar associations were observed for paternal education, and in both cohorts (Supplementary Table 1, available as Supplementary data at *IJE* online). The educational levels of mothers and fathers tended to be correlated. When combining them, we found similar educational gradients and independent effects of maternal and paternal education on CP risk (Table 2).

Mothers with partners had a lower risk of having a child with CP compared with single mothers (Figure 1).

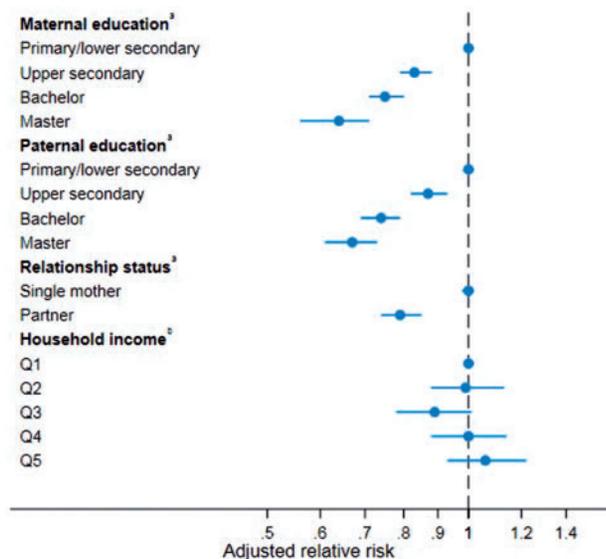


Figure 1. Adjusted relative risks of CP for Denmark and Norway (combined with meta-analysis) by maternal and paternal education at end of follow-up (2010 in Denmark and 2013 in Norway), marital status in year of delivery and household income in the year before delivery. ^aAdjusted for year of delivery and maternal age (in analysis on maternal education and relationship status) and paternal age (in analysis on paternal education). ^bOnly in Denmark, adjusted for maternal and paternal education and maternal and paternal age in year of delivery.

This finding did not vary with maternal educational level (*P*-values tests for interaction 0.32 in Denmark and 0.53 in Norway). Income data were available only for the Danish cohort. Household income was unrelated to the risk of CP after adjusting for parents' age and education in the year of delivery (Figure 1). CP risk did not vary significantly by household income within any of the educational groups (*P*-value for interaction 0.31).

The proportion of parents with higher education increased during the study period, particularly among mothers. In Denmark, the proportion of mothers with higher education rose from 30% in 1981–90 to 38% in 2001–07. The corresponding figures were 32% and 50% in Norway. Even so, the RII for risk of CP remained stable over time. However, a reduction in the RII was found for paternal education in Norway, as a result of converging absolute risk

Table 3. Time trends in the relative index of inequality^a (RII) (95% confidence interval) for maternal and paternal education at end of follow-up (2010 in Denmark and 2013 in Norway) in Denmark and Norway

	Denmark	Norway
Maternal education		
1967 to 1980	NA	0.65 (0.55, 0.77)
1981 to 1990	0.62 (0.47, 0.82)	0.66 (0.54, 0.80)
1991 to 2000	0.61 (0.49, 0.76)	0.70 (0.58, 0.83)
2001 to 2007	0.63 (0.48, 0.82)	0.63 (0.50, 0.79)
<i>P</i> for trend	0.67	0.92
Paternal education		
1967 to 1980	NA	0.56 (0.47, 0.67)
1981 to 1990	0.63 (0.48, 0.84)	0.60 (0.49, 0.73)
1991 to 2000	0.67 (0.54, 0.83)	0.70 (0.59, 0.85)
2001 to 2007	0.63 (0.48, 0.83)	0.71 (0.57, 0.89)
<i>P</i> for trend	0.83	0.03

^aAdjusted for maternal age (in analysis on maternal education) and paternal age (in analysis on paternal education).

NA, not available.

Table 2. Number in total (%) and relative risk (95% confidence interval) of CP for Denmark and Norway (combined with meta-analysis) by combinations of parental education^a at end of follow-up (2010 in Denmark and 2013 in Norway)

Maternal education	Paternal education					
	Low		Intermediate		High	
	Number (%)	Adjusted ^b RR (95% CI)	Number (%)	Adjusted ^b RR (95% CI)	Number (%)	Adjusted ^b RR (95% CI)
Low	308 647 (9)	1.00 (reference)	389 684 (11)	0.82 (0.76, 0.90)	61 813 (2)	0.69 (0.58, 0.82)
Intermediate	335 209 (10)	0.77 (0.70, 0.85)	962 730 (28)	0.75 (0.69, 0.81)	265 750 (8)	0.67 (0.60, 0.74)
High	97 443 (3)	0.82 (0.71, 0.94)	442 203 (13)	0.70 (0.64, 0.77)	616 847 (18)	0.58 (0.53, 0.63)

^aThe group 'low' includes primary and lower secondary education, 'intermediate' includes upper secondary and short non-tertiary education and 'high' includes bachelor's, master's and doctorate degree.

^bAdjusted for year of delivery and maternal and paternal age.

Table 4. Prevalence of subtypes of CP (per 1000) and relative risk (95% confidence interval) by maternal and paternal education^a at end of follow-up (2010) in Denmark only (1981–2007)

	Maternal education		Paternal education	
	With subtype of CP (per 1000)	Adjusted ^b RR (95% CI)	With subtype of CP (per 1000)	Adjusted ^b RR (95% CI)
Unilateral spastic CP				
Low	196 (0.8)	1.00 (reference)	191 (0.8)	1.00 (reference)
Intermediate	447 (0.8)	0.90 (0.76, 1.07)	514 (0.8)	0.99 (0.83, 1.17)
High	283 (0.7)	0.77 (0.64, 0.94)	190 (0.6)	0.78 (0.63, 0.96)
Bilateral spastic CP				
Low	388 (1.6)	1.00 (reference)	359 (1.5)	1.00 (reference)
Intermediate	657 (1.1)	0.75 (0.66, 0.86)	758 (1.1)	0.85 (0.75, 0.97)
High	395 (0.9)	0.63 (0.54, 0.73)	273 (0.9)	0.67 (0.57, 0.79)
Dyskinetic CP				
Low	55 (0.2)	1.00 (reference)	56 (0.2)	1.00 (reference)
Intermediate	127 (0.2)	0.99 (0.72, 1.37)	153 (0.2)	1.09 (0.80, 1.50)
High	85 (0.2)	0.89 (0.62, 1.27)	51 (0.2)	0.78 (0.53, 1.16)
Ataxic CP				
Low	21 (0.1)	1.00 (reference)	29 (0.1)	1.00 (reference)
Intermediate	40 (0.1)	0.82 (0.48, 1.41)	41 (0.1)	0.55 (0.33, 0.90)
High	34 (0.1)	0.96 (0.54, 1.70)	22 (0.1)	0.61 (0.34, 1.10)

^aThe group 'low' includes primary and lower secondary education, 'intermediate' includes 'upper secondary and short non-tertiary education' and 'high' includes both bachelor's, master's and doctorate degree.

^bAdjusted for year of delivery and maternal age (in analysis on maternal education) and paternal age (in analysis on paternal education).

of CP for the educational groups over time. Due to the lack of validated data on CP diagnoses in the Norwegian cohort, this result should be interpreted with caution (Table 3).

Information on CP subtypes was available only in the Danish cohort. There were 939 children diagnosed with unilateral spastic CP, 1469 diagnosed with bilateral spastic CP, 276 with dyskinetic CP, 97 with ataxic CP and 28 without a classified CP subtype. Higher parental education was associated with reduced risks of having children with both the unilateral and bilateral spastic CP subtypes (Table 4). For the dyskinetic and ataxic subtypes, numbers were not large enough to assess trends by SES.

Using parental education in the year of delivery rather than at end of follow-up had practically no influence on the results (Supplementary Table 2, available as Supplementary data at *IJE* online, Danish data only). Parental education in the year of delivery and at end of follow-up was highly correlated (Pearson's correlation = 0.9). Similarly, results did not change in any important way when including only children born at term, or when excluding immigrant mothers (Supplementary Table 3, available as Supplementary data at *IJE* online). Educational gradients in CP were similar for both maternal and paternal education when restricting analysis to cases from the Norwegian National Insurance Scheme or to cases from the National Patient Registry (Supplementary Table 4, available as Supplementary data at *IJE* online).

Discussion

Higher levels of parental educational attainment were associated with reduced risk of CP. We found independent effects of maternal and paternal education, and the educational gradient remained stable over recent decades. A lower risk of CP in the child was also observed for mothers with partners compared with single mothers, independent of education. In contrast, we found no gradient in risk of CP by household income.

There has been a large increase in the proportion of parents with higher education, especially among mothers. If the parents remaining in the lowest educational group become more marginalized, this could lead to an increase in educational inequalities in risk of CP over time. However, little or no changes in the RII over time suggest that the educational differences in risk are persistent, but perhaps not related to the burden of belonging to a lower educated group than others. The association between parental SES and CP may operate through mediating lifestyle factors, such as poor diet, obesity, type 2 diabetes, cigarette smoking and psychosocial factors. All of these have been associated with SES,^{19,27} and obesity and smoking increased the risk of CP in large prospective studies conducted in Denmark, Norway and Sweden,^{28–31} whereas the role of dietary factors, type-2 diabetes and psychosocial factors in CP have been less explored. Other potential

mediating factors include genitourinary infections and use of paracetamol during pregnancy; both differed by socioeconomic status and were associated with risk of CP in three large prospective Danish studies.^{28,32,33} Utilization of antenatal care may also differ between mothers of low and high SES, even though high-quality antenatal care is available for all pregnant women in Denmark and Norway free of charge. On the other hand, part of the educational gradient could be due to common underlying causes of parental education and CP, for example a subclinical neurodevelopmental disorder in the parent that affect his or her educational attainment and increases the risk of having a child with CP.^{34,35}

We did not find a gradient in CP risk by household income (data only available in Denmark). This finding may appear somewhat surprising, but is in line with previous research on the educational gradient in preterm birth in Denmark.³⁶ Household income can vary a lot from year to year and may be less reliable than education as an indicator of parents' SES at time of birth, as most parents will only have recently entered the labour market. Since we used information on parental education at end of follow-up, the fact that some parents will still be in school at time of birth is accounted for. Both Norway and Denmark have succeeded in reducing income inequality through a redistributive tax system and various social policies, and they rank as two of the countries with lowest income inequality among the OECD countries.³⁷ This may make income a poorer marker than education or marital status, both less responsive to social policy. Also, a higher income does not necessarily lead to healthier consumption or behaviours.³⁸

Parental education was associated with risks for the spastic CP subtypes, and in particular spastic bilateral CP. This may be related to the educational gradient in preterm birth,⁵ as spastic bilateral CP is the dominant subtype in children born preterm.³⁹ However, the educational gradient for risk of CP overall persisted when restricting analyses to term births. CP may result from immaturity at birth, but preterm birth and fetal growth restriction may also be the result of underlying pathological processes that also cause CP.^{2,3} Preterm birth and low birthweight are therefore potential colliders on a causal pathway from parental SES to CP, and adjusting for them can bias estimates and distort interpretation.^{25,40} Our analysis restricted to term-born children, should therefore be interpreted with care.

Our results correspond well with some recent research. A prospective study conducted in the USA found a parental educational gradient for spastic CP, in line with our results.⁶ A prospective registry-based study from Sweden found increased odds of CP in children of mothers with low compared with high socioeconomic status, using a combined measure based on education and occupation

of the head of the household.⁷ A population-based registry study conducted in five regions in the UK, using an aggregated area-based measure of socioeconomic status (Carstairs index), found a strong socioeconomic gradient for post-neonatally acquired CP, but results for perinatally acquired CP were less clear.⁸ One US study found no difference in prevalence of CP by maternal education, poverty level or insurance status in the period 1997–2003.⁹ In that study, the prevalence of CP was 3.9 per 1000 children aged 3 to 17 years, which is relatively high. CP case status was defined by parents stating that a doctor or health professional had at some point told them their child had CP, independent of current status. This is likely to have led to false-positive cases. If the probability of seeking health care was affected by parents' SES, this may have influenced the results.

The major strength of our study was the high-quality population-based registry data on almost 1.3 million Danish and 2.4 million Norwegian children. The availability of birth cohorts spanning four decades in Norway and three decades in Denmark enabled investigation of time trends. In addition, we had information on several indicators of SES and, in the Danish cohort, also CP subtypes. This enabled us to explore whether the socioeconomic gradient differed among CP subtypes, something few studies have been able to do.

An important limitation in the Norwegian data was the lack of validated CP diagnoses. If being registered with a CP diagnosis in the Norwegian National Insurance Scheme (NAV) depends on parental SES, this could result in differential misclassification. A previous validation study of CP data from NAV for the birth years 1983–87 found some under-reporting of mild cases.¹⁸ There may be a selection bias on SES in receiving benefits from NAV, but the direction of such possible bias is not known. In the Norwegian Patient Registry (NPR), CP prevalence may be overestimated due to inaccurate diagnoses and diagnoses based on suspected but unconfirmed cases.⁴¹ An association between high parental SES and use of specialist health services has been reported in Norway.⁴² However, a recent study validating the CP cases in the NPR against the more recent Norwegian Cerebral Palsy Registry⁴³ for birth years 1996–2007 found that 86% of CP diagnoses in the patient registry were correct.⁴¹ It was further reported that the prevalence of CP was 2.5 per 1000 when combining validated data from both sources, which corresponds well with the overall prevalence found in the Norwegian cohort in our study. To reduce the problem with false-positives from the NPR, we included only those with a CP diagnosis on at least two separate occasions. We found an educational gradient in CP whether using cases only from NAV or only from the NPR. In addition, the educational

gradient was almost identical to the gradient found in Denmark, where CP cases had been validated. In the Norwegian cohort, unlike the Danish cohort, the post-neonatally acquired CP cases could not be excluded. However, only about 6% of CP cases in Norway have a post-neonatal cause⁴³ and we therefore believe that including them has not influenced our results.

In both cohorts, we excluded all stillborn and infant deaths in the analyses. Children born with CP probably have a higher risk of dying in the first year of life. Since a socioeconomic gradient in infant mortality has been reported in both Denmark and Norway,^{44,45} exclusion of early deaths could bias our estimates towards the null value.

Our information from Norway included only information on parental education at end of follow-up, not at time of delivery. We have to assume that parent's final educational attainment is a reasonable proxy for the underlying, lifelong exposures that contribute to the causal pathways of CP. Within this framework, inherent abilities, family background and childhood SES are regarded as more important than education in itself, as these will directly affect a person's potential for higher education. However, taking higher education may also form a set of enduring cognitive and emotional skills and provide a higher educated social network, which foster health-promoting behaviour.³⁸ Also, having a child with CP may limit parental educational attainment and income, leading to the possibility of reverse causality. A study in Denmark found that having a child with CP initially reduced maternal educational attainment, but this difference had mostly disappeared by the time the child was 15 years old.⁴⁶ However, we found almost identical results when using educational level in the year of delivery and at the end of follow-up (available in the Danish data). This suggests that using education at end of follow-up in Norway probably does not introduce considerable bias in the estimates. If the associations had been stronger for final attained education, it would suggest that CP is more related to the parents' background and their intellectual potential, rather than direct consequences of the process and content of education at the time of pregnancy. However, the strong correlation between education at pregnancy and final attained education make such distinctions difficult.

Conclusion

Parents with more education had substantially lower risk of having a child with cerebral palsy, as did mothers with a partner. These gradients in risk were persistent over the complete study period in both Denmark and Norway. There is a wide range of possible underlying causal mechanisms, at least some of which are potentially preventable. These mechanisms deserve further exploration.

Supplementary Data

Supplementary data are available at *IJE* online.

Funding

This work was funded by the Western Norway Regional Health Authority [to I.F.] and by the Intramural Program of the NIH, National Institute of Environmental Health Sciences [to A.J.W.].

Acknowledgements

We thank Anne Vinkel Hansen and Abdulfatah Adam (former and current Data Administrator at the Section of Epidemiology, University of Copenhagen, Denmark) for help with data management in the Danish cohort.

Author Contributions

M.C.T. proposed and planned the study. K.S-L. and D.M provided the data and planned the study. I.F. planned the study, analysed the data and wrote the first draft of the manuscript. All authors interpreted the data, critically revised drafts of the manuscript and approved the final manuscript. I.F. is the guarantor, has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest: All the authors declare no conflict of interest.

References

- Sellier E, Platt MJ, Andersen GL, Krageloh-Mann I, De La Cruz J, Cans C. Decreasing prevalence in cerebral palsy: a multi-site European population-based study, 1980 to 2003. *Dev Med Child Neurol* 2016;**58**:85–92.
- Jacobsson B, Hagberg G. Antenatal risk factors for cerebral palsy. *Best Pract Res Clin Obstet Gynaecol* 2004;**18**:425–36.
- Nelson KB, Blair E. Prenatal factors in singletons with cerebral palsy born at or near term. *N Engl J Med* 2015;**373**:946–53.
- Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA. Socioeconomic disparities in adverse birth outcomes: a systematic review. *Am J Prev Med* 2010;**39**:263–72.
- Petersen CB, Mortensen LH, Morgen CS *et al.* Socio-economic inequality in preterm birth: a comparative study of the Nordic countries from 1981 to 2000. *Paediatr Perinat Epidemiol* 2009;**23**:66–75.
- Durkin MS, Maenner MJ, Benedict RE *et al.* The role of socio-economic status and perinatal factors in racial disparities in the risk of cerebral palsy. *Dev Med Child Neurol* 2015;**57**:835–43.
- Hjern A, Thorngren-Jerneck K. Perinatal complications and socio-economic differences in cerebral palsy in Sweden – a national cohort study. *BMC Pediatr* 2008;**8**:49.
- Dolk H, Pattenden S, Bonellie S *et al.* Socio-economic inequalities in cerebral palsy prevalence in the United Kingdom: a register-based study. *Paediatr Perinat Epidemiol* 2010;**24**: 149–55.
- Boyle CA, Boulet S, Schieve LA *et al.* Trends in the prevalence of developmental disabilities in US children, 1997–2008. *Pediatrics* 2011;**127**:1034–42.

10. Stanley FBE, Alberman E. *Cerebral Palsies: Epidemiology and Causal Pathways*. London: MacKeith Press, 2000.
11. Dahl E, Fritzell J, Lahelma E, Martikainen P, Kunst A, Mackenbach JP. Welfare state regimes and health inequalities. In: Siegrist J, Marmot M (eds). *Social Inequalities in Health: New Evidence and Policy Implications*. New York, NY: Oxford University Press, 2006.
12. Lyttkens CH, Christiansen T, Häkkinen U, Kaarboe O, Sutton M, Welander A. The core of the Nordic health care system is not empty. *Nordic J Health Econ* 2016;**4**:7–27.
13. Knudsen LB, Olsen J. The Danish Medical Birth Registry. *Dan Med Bull* 1998;**45**:320–23.
14. Uldall P, Michelsen SI, Topp M, Madsen M. The Danish Cerebral Palsy Registry. A registry on a specific impairment. *Dan Med Bull* 2001;**48**:161–63.
15. Irgens LM. The Medical Birth Registry of Norway. Epidemiological research and surveillance throughout 30 years. *Acta Obstet Gynecol Scand* 2000;**79**:435–39.
16. Norwegian Ministry of Labour and Social Affairs. *The Norwegian Social Insurance Scheme*, 2018. (10 April 2018, date last accessed).
17. Norwegian Directorate of Health. *Norsk pasientregister—et sentralt helseregister* [In English: Norwegian Patient Registry—A Central Health Registry]. 2018.. (18 April 2018, date last accessed).
18. Moster D, Lie RT, Irgens LM, Bjerkedal T, Markestad T. The association of Apgar score with subsequent death and cerebral palsy: a population-based study in term infants. *J Pediatr* 2001;**138**:798–803.
19. Kramer MS, Seguin L, Lydon J, Goulet L. Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Paediatr Perinat Epidemiol* 2000;**14**:194–210.
20. Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health* 2011;**39**:91–94.
21. Organization for Economic Cooperation and Development (OECD). *Project on Income Distribution and Poverty. What are Equivalence Scales?* 2018. (20 October 2017, date last accessed).
22. Hernan MA, Hernandez-Diaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. *Am J Epidemiol* 2002;**155**:176–84.
23. Mackenbach JP, Kunst AE. Measuring the magnitude of socioeconomic inequalities in health: an overview of available measures illustrated with two examples from Europe. *Soc Sci Med* 1997;**44**:757–71.
24. Hayes LJ, Berry G. Sampling variability of the Kunst-Mackenbach relative index of inequality. *J Epidemiol Community Health* 2002;**56**:762–65.
25. Wilcox AJ, Weinberg CR, Basso O. On the pitfalls of adjusting for gestational age at birth. *Am J Epidemiol* 2011;**174**:1062–68.
26. Skjaerven R, Gjessing HK, Bakketeig LS. New standards for birth weight by gestational age using family data. *Am J Obstet Gynecol* 2000;**183**:689–96.
27. Cameron AJ, Spence AC, Laws R, Hesketh KD, Lioret S, Campbell KJ. A review of the relationship between socioeconomic position and the early-life predictors of obesity. *Curr Obes Rep* 2015;**4**:350–62.
28. Streja E, Miller JE, Bech BH *et al.* Congenital cerebral palsy and prenatal exposure to self-reported maternal infections, fever, or smoking. *Am J Obstet Gynecol* 2013;**209**:332.e1–10.
29. Forthun I, Wilcox AJ, Strandberg-Larsen K *et al.* Maternal pre-pregnancy BMI and risk of cerebral palsy in offspring. *Pediatrics* 2016;**138**:e20160874.
30. Villamor E, Tedroff K, Peterson M *et al.* Association between maternal body mass index in early pregnancy and incidence of cerebral palsy. *JAMA* 2017;**317**:925–36.
31. Thorngren-Jerneck K, Herbst A. Perinatal factors associated with cerebral palsy in children born in Sweden. *Obstet Gynecol* 2006;**108**:1499–505.
32. Miller JE, Pedersen LH, Streja E *et al.* Maternal infections during pregnancy and cerebral palsy: a population-based cohort study. *Paediatr Perinat Epidemiol* 2013;**27**:542–52.
33. Petersen TG, Liew Z, Andersen AN *et al.* Use of paracetamol, ibuprofen or aspirin in pregnancy and risk of cerebral palsy in the child. *Int J Epidemiol* 2018;**47**:121–30.
34. Tollanes MC, Wilcox AJ, Lie RT, Moster D. Familial risk of cerebral palsy: population based cohort study. *BMJ* 2014;**349**:g4294.
35. Tollanes MC, Wilcox AJ, Stoltenberg C, Lie RT, Moster D. Neurodevelopmental disorders or early death in siblings of children with cerebral palsy. *Pediatrics* 2016;**138**:e20160269.
36. Morgen CS, Bjork C, Andersen PK, Mortensen LH, Nybo Andersen AM. Socioeconomic position and the risk of preterm birth—a study within the Danish National Birth Cohort. *Int J Epidemiol* 2008;**37**:1109–20.
37. Organization for Economic Cooperation and Development (OECD). *In It Together: Why Less Inequality Benefits All*. Paris: OECD Publishing, 2015.
38. Glymour M, Avendano M, Kawachi I. Socioeconomic status and health. In: Berkman LKI, Glymour M (eds). *Social Epidemiology*. New York, NY: Oxford University Press, 2014.
39. Korzeniewski SJ, Birbeck G, DeLano MC, Potchen MJ, Paneth N. A systematic review of neuroimaging for cerebral palsy. *J Child Neurol* 2008;**23**:216–27.
40. Ananth CV, Schisterman EF. Confounding, causality, and confusion: the role of intermediate variables in interpreting observational studies in obstetrics. *Am J Obstet Gynecol* 2017;**217**:167–75.
41. Hollung SJ, Vik T, Wiik R, Bakken IJ, Andersen GL. Completeness and correctness of cerebral palsy diagnoses in two health registers: implications for estimating prevalence. *Dev Med Child Neurol* 2017;**59**:402–06.
42. Grøholt E-K, Nordhagen R. Ulikhet i helse og helsetjenestebruk hos nordiske barn etter foreldrenes utdannelse. *Nord J Epidemiol* 2009;**12**:47–54.
43. Andersen GL, Irgens LM, Haagaas I, Skranes JS, Meberg AE, Vik T. Cerebral palsy in Norway: prevalence, subtypes and severity. *Eur J Paediatr Neurol* 2008;**12**:4–13.
44. Arntzen A, Samuelsen SO, Bakketeig LS, Stoltenberg C. Socioeconomic status and risk of infant death. A population-based study of trends in Norway, 1967–98. *Int J Epidemiol* 2004;**33**:279–88.
45. Olsen O, Madsen M. Effects of maternal education on infant mortality and stillbirths in Denmark. *Scand J Public Health* 1999;**27**:128–36.
46. Michelsen SI, Flachs EM, Madsen M, Uldall P. Parental social consequences of having a child with cerebral palsy in Denmark. *Dev Med Child Neurol* 2015;**57**:768–75.