BMJ Open

Educational disparities in perinatal health in Denmark in the first decade of the 21st century: A register study of 649,905 children

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023531
Article Type:	Research
Date Submitted by the Author:	13-Apr-2018
Complete List of Authors:	Bilsteen, Josephine; Department of Public Health, University of Copenhagen Andresen, Josefine; Departmetn of Public Health, University of Copenhagen Mortensen, Laust; Department of Public Health, University of Copenhagen Hansen, Anne; Department of Public Health, University of Copehagen Andersen, Anne-Marie; Department of Public Health, University of Copenhagen
Keywords:	Health inequalities, Congenital anomalies, Preterm birth, Small-for-gestational age, Stillbirth, Infant mortality

Educational disparities in perinatal health in Denmark in the first decade of the 21st century: A register study of 649,905 children

Josephine Funck Bilsteen[1*], jfbi@sund.ku.dk

Josefine Bernhard Andresen[1], vln522@alumni.ku.dk

Laust Hvas Mortensen[1] lamo@sund.ku.dk

Anne Vinkel Hansen[1] avih@sund.ku.dk

Anne-Marie Nybo Andersen[1] amny@sund.ku.dk

[1] Section of Social Medicine, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

* Corresponding author.

Section of Social Medicine, Department of Public Health, University of Copenhagen,

Øster Farimagsgade 5, 1014 Copenhagen K, Denmark.

Email: josephinefbilsteen@gmail.com, telephone: +45 41 66 13 81

Word count: 3,749

ABSTRACT

Objective: To investigate socioeconomic differences in six perinatal health outcomes in Denmark in the first decade of the 21st century.

Design: A population-based cohort study.

Setting: Danish national registries.

Participants: A total 646,829 live born children and 3,076 stillborn children (≥22+0 weeks of gestation) born in Denmark from 2000 through 2009. We excluded children with implausible relations between birth weight and gestational age (n=644), children without information on maternal country of origin (n=138), and implausible values of maternal year of birth (n=36).

Main outcome measures: We investigated the following perinatal health outcomes: Stillbirth, neonatal and post-neonatal mortality, small-for-gestational age, preterm birth grated into moderate preterm, very preterm, and extremely preterm, and congenital anomalies registered in the first year of life.

Results: Maternal educational level was inversely associated with all adverse perinatal outcomes. For all examined outcomes the risk association displayed a clear gradient across the educational levels. The associations remained after adjustment for maternal age, maternal country of origin and calendar year. Compared to mothers with vocational education mothers with more than 15 years of education had an adjusted odds ratio for stillbirth of 0.64 [95% CI 0.56-0.73]. The corresponding adjusted odds ratios for neonatal mortality, post-neonatal mortality, congenital anomalies, moderate preterm birth, and small-for-gestational age were, respectively, 0.79 [95% CI 0.67-0.93], 0.56 [95% CI 0.41-0.77], 0.87 [95% CI 0.83-0.92], 0.79 [95% CI 0.76-0.82] and 0.81 [95% CI 0.79-0.84].

Conclusion: Substantial educational inequalities in perinatal health were still present in the Denmark in first decade of the 21st century.

Keywords: Health inequalities; Stillbirth, Infant mortality; Congenital anomalies; Preterm birth; Small-for-gestational age.

ARTICLE SUMMARY

Strengths and limitations of this study

- Danish national registries with high degree of completeness and quality were used in this study.
- The large study population enabled investigation of rare perinatal outcomes.
- The grading of maternal education into five categories enabled detailed investigation of the educational gradients.
- Congenital anomalies are not registered for stillbirths and spontaneous abortions during the study period and as a consequence we could only estimate risk among live born children.

INTRODUCTION

The Nordic countries are generally regarded as egalitarian and have a low prevalence of adverse perinatal outcomes. However in the 1980s and 1990s strong socioeconomic gradients in adverse perinatal outcomes were observed in Denmark, Finland, Norway and Sweden. Several studies documented socioeconomic inequalities in respectively stillbirth, preterm birth, birth weight, infant mortality in all of the Nordic countries[1–4] but studies have been inconclusive with regards to congenital anomalies.[5–8]

During the first decade of the 21st century economic inequality rose in Denmark and elsewhere[9–11], but it is unclear what impact this has had on inequalities in perinatal health. Perinatal health measures, such as infant mortality, are used internationally as indicators of population health status. In addition, perinatal outcomes such as preterm birth and foetal growth are predictive at the individual level for health later in life. Several studies have found that low birth weight is related to the risk of chronic diseases in adulthood, such as type 2 diabetes and cardiovascular disease.[12,13] The health condition of the mother affects perinatal outcomes, thereby transferring socioeconomic inequality in health from one generation to the next.[13]

Socioeconomic position refers to the economic and social indicators that influence what positions individuals or groups hold within the structure of a society.[14] In this study educational level has been chosen as a measure of socioeconomic position because education is a favourable indicator of socioeconomic position in early adult life. Furthermore education is associated to future occupational status and income.[15]

The aim of this study was to describe the associations between maternal educational level and risk of adverse perinatal outcomes in Denmark during the first decade of the 21st century. The adverse perinatal outcomes of interest in this study were stillbirth, preterm birth, small-for-gestational age (SGA), congenital anomalies, neonatal mortality and post-neonatal mortality.

METHODS

We did a longitudinal register linkage study of all live births and stillbirths in Denmark from 2000 through 2009, as recorded in the Danish Medical Birth Register. Information on maternal educational level from the Population's Education register[16] was linked to information on perinatal health outcomes from the Danish Medical Birth Register[17], the Danish National Patient Register[18], and the Danish Register of Causes of Death [19]. The Danish system of unique person identifiers (CPR-number) was used to link individuals across the different registers in an anonymised data set in Statistics Denmark, which could be assessed via a VPN connection from Department of Public Health, University of Copenhagen.

Study populations

The study population consisted of all live born and stillborn children born in Denmark during the study period. Children were excluded from the study population as illustrated in Figure 1. Maternal year of birth was considered implausible after year 1999 and implausible relations between gestational age and birth weight were defined according to the method described by Alexander et al.[20] After the exclusions Analysis Population 1 consisted of a total of 649,905 live and stillborn children. Analysis population 2 consisted of 646,829 live born when stillborn children were excluded from Analysis Population 1. In the analysis of SGA children missing information on birth weight (n=4388) were not included.

Patient and Public Involvement

Patient and public were not involved as data was obtained from Danish national registers.

Study variables

The main exposure variable of interest was maternal educational level, defined as the highest educational level attained or expected (based on ongoing education) of the mother at the year of birth categorized into five categories: Primary education (≤*9 years*), secondary education (high school *10-12 years*), vocational education *(10-12 years)*, short- and medium-cycle higher education *(12-15 years)*, long-cycle higher education *(>15 years)*, and missing. Since the education register is based on reports from Danish

educational institutions, the category of missing is comprised of individuals who are not registered at any education in Denmark.

Information on birth weight and the outcomes preterm birth and stillbirth were obtained from the Medical Birth Register. SGA was defined as birth weight falling below the 10th percentile of birth weight according to sex-specific intrauterine growth curves presented by Marsàl et al.[21] Preterm birth was divided into extremely preterm birth defined as birth ≥22+0 – 27+6 weeks, very preterm birth defined as birth ≥28+0 – 31+6, and moderately preterm birth defined as birth ≥32+0 – 36+6. The variable stillbirth was defined as foetal death at or after 22 completed gestational weeks. In Denmark, the threshold between spontaneous abortions and stillbirths was changed in 2004 from 28 completed weeks of gestation to 22 completed weeks of gestation. All pregnancies from 2000 to 2003 for which a spontaneous abortion was registered after 22 completed weeks of gestation were recoded into stillbirths. Information on infant mortality was obtained from The Central Person Register and The Danish Register of Causes of Death. Neonatal mortality was defined as death of a live born child before or at day 27 after birth and post-neonatal mortality was defined as death of a live born child at or after day 28 through day 365 after birth. Information on congenital anomalies was obtained from the Danish National Patient Register. The variable congenital anomalies registered in first year of life were defined according to EuroCAT's definitions excluding minor anomalies according to EuroCAT criteria.[22]

Other potential confounders in the analysis were the maternal year of birth *(<1965, 1965-69, 1970-74, 1975-79, ≥1980* maternal age at the time of delivery *(<25 years, 25-29 years, 30-34 years, 35-39 years, ≥40 years),* Offspring's year of birth *(2000-01, 2002-03, 2004-05, 2006-07, 2008-09)*, and country of origin of the mother categorized as Denmark, "Other western country" *(Andorra, Australia, Canada, Iceland, Liechtenstein, Monaco, New Zealand, Norway, San Marino, Switzerland, United States of America, Vatican City State and all EU member countries except Denmark)* or "Non-western country" *(all remaining countries).*

Statistics

Initially, we calculated the prevalence for the six perinatal outcomes by maternal educational level. To investigate the associations between maternal educational level and the perinatal outcomes we used multiple logistic regression analyses and the analysis populations were restricted to children with information on maternal educational level. The a priori chosen model for adjustment included the covariates maternal age, maternal country of origin, and maternal year of birth as these were considered potential confounders. The variable year of birth of the offspring was not included in the model since the variables maternal age at time of delivery and maternal year of birth in combination practically describe the variable. Unadjusted and adjusted odds ratios (OR) were presented with a 95% confidence interval. Additionally, we fitted two models to test robustness of the findings: one adjusted for maternal age only and the second including maternal age, parity and country of origin, and year of birth as covariates. However, since the findings from the two models fitted to test robustness were similar to findings from the other adjusted model their findings are not shown. All statistical analyses were conducted in SAS 9.4.

RESULTS

The distributions of maternal educational level by maternal age, maternal country of origin and calendar year of birth are presented in Table 1. In Denmark, maternal completed and on-going educational level increased during the study period as shown in Table 1. The proportion of mothers born outside Denmark was higher among mothers with missing educational level.

Table 1 Maternal age, year of birth, and country of origin, and offspring's year of birth by educational level, all children born in Denmark 2000-2009

	All children	Primary education	Vocational education	Secondary education	Short and medium-cycle higher education	Long-cycle higher education	Missing
	n=649,905	n=106,129	n=222,744	n=46,026	n=185,417	n=94,168	n=15,421
	%	%	%	%	%	%	%
Maternal age							
<25	12.3	32.6	12.2	17.8	3.8	2.3	20.0
25-29	33.5	30.9	37.4	31.2	25.4	26.2	34.6
30-34	36.3	23.0	34.5	32.6	42.1	46.9	28.0
35-39	15.3	11.0	13.8	15.8	16.4	21.1	14.0
≥40	2.6	2.4	2.1	2.6	2.7	3.5	3.4
Maternal year of birth							
<1965	4.2	4.1	3.8	4.6	4.3	4.8	4.5
1965-69	16.5	12.3	16.4	17.6	17.0	20.7	12.6

1970-74	33.5	24.0	33.0	32.4	37.6	39.6	24.2
1975-79	30.6	28.8	32.0	27.9	31.8	28.3	31.1
≥1980	15.2	30.8	14.8	17.6	9.8	6.7	27.7
Maternal country of origin							
Denmark	86.2	74.7	91.0	77.6	93.2	92.0	10.7
Western countries	3.1	1.3	1.9	3.8	2.6	4.3	26.3
Non-western countries	10.7	24.0	7.2	18.6	4.3	3.7	63.0
Year of birth (offspring)							
2000-2001	20.5	24.2	22.3	23.7	17.9	16.0	20.2
2002-2003	19.9	21.1	20.9	22.1	18.8	18.0	14.9
2004-2005	20.0	19.6	20.1	20.1	20.6	20.0	12.6
2006-2007	20.0	18.0	19.1	18.2	21.5	22.2	21.0
2008-2009	19.7	17.1	17.7	15.9	21.2	23.8	31.3

The prevalence of stillbirth, neonatal mortality, post-neonatal mortality, congenital anomalies, SGA, and three degrees of preterm birth, respectively, by maternal educational level are shown in Table 2. Women with the shortest education had a higher prevalence of all of the adverse perinatal outcomes compared to women with higher educational level. The group of women with unknown educational level had the highest prevalence of stillbirth and SGA compared to the women with known educational level.

Table 2 Prevalence of adverse perinatal outcome by educational level, Denmark, 2000-2009

	Stillbirth	**Neonatal mortality**	**Post-neonatal mortality**	**Congenital anomalies**	**SGA**	**Moderate preterm birth 32+0-36+6**	**Very preterm birth 28+0-31+6**	**Extreme preterm birth <28+0**
	n=3,076	n=1,688	n=648	n=19,449	n=59,979	n=36,610	n=4,670	n=1,843
	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000
Primary education	6.7	3.6	1.9	34.9	125.9	64.5	8.3	4.1
Vocational education	4.8	2.7	1.0	30.7	95.1	60.0	7.8	3.0
Secondary education	4.0	2.5	1.0	28.2	94.2	52.7	7.0	2.4
Short and medium-	4.3	2.2	0.7	28.7	77.9	53.7	6.6	2.3
Long-cycle higher	3.1	2.1	0.5	27.1	77.9	48.8	6.3	2.4
Missing	7.1	3.0	1.2	28.9	126.5	51.2	5.9	3.1

Table 3 shows the relative risks, expressed as adjusted and unadjusted OR, of respectively stillbirth, neonatal mortality, post-neonatal mortality, congenital anomalies, SGA, and moderately preterm birth, very preterm birth, and extremely preterm birth, with mothers with vocational education as the comparison group. Compared to mothers with vocational education mothers with primary education had a statistically significant increased OR for stillbirth, neonatal mortality, post-neonatal mortality, congenital

anomalies, moderate preterm birth, very preterm birth, extreme preterm birth and SGA. Women with short and medium-cycle higher education and women with long-cycle higher education had a statistically significant lower risk of all the six perinatal outcomes compared to women with vocational education. These results indicated consistently inverse educational gradients in the risk of adverse perinatal outcomes. The gradients were consistent after adjusting for maternal age, maternal country of origin and calendar year. The estimates were almost identical in analyses with adjustment for maternal age only and with adjustment for maternal age, maternal country of origin, calendar year and parity (results not shown).

Table 3 Adverse perinatal outcome by maternal educational level, all births Denmark, 2000-2009

	OR	CI: 95 %	aOR	95 %
Stillbirth				
Primary education	1.39	1.26-1.53	1.34	1.21-1.49
Vocational education	1.00		1.00	
Secondary education	0.84	0.71-0.98	0.80	0.69-0.94
Short and medium-cycle higher education	0.89	0.81-0.97	0.89	0.81-0.97
Long-cycle higher education	0.64	0.57-0.73	0.63	0.56-0.72
Neonatal mortality				
Primary education	1.33	1.17-1.51	1.29	1.12-1.48
Vocational education	1.00		1.00	
Secondary education	0.92	0.76-1.13	0.90	0.73-1.10
Short and medium-cycle higher education	0.79	0.70-0.90	0.80	0.71-0.92
Long-cycle higher education	0.79	0.67-0.93	0.79	0.67-0.93
Post-neonatal mortality[a]				
Primary education	1.94	1.59-2.36	1.81	1.47-2.22
Vocational education	1.00		1.00	
Secondary education	1.02	0.74-1.41	0.98	0.71-1.36
Short and medium-cycle higher education	0.74	0.59-0.92	0.76	0.61-0.95
Long-cycle higher education	0.55	0.41-0.75	0.57	0.44-0.78
Congenital anomalies				
Primary education	1.14	1.10-1.19	1.13	1.08-1.18
Vocational education	1.00		1.00	
Secondary education	0.92	0.86-0.97	0.91	0.86-0.97
Short and medium-cycle higher education	0.93	0.90-0.97	0.93	0.89-0.96
Long-cycle higher education	0.88	0.84-0.92	0.87	0.83-0.91
Moderate preterm birth 32+0-36+6[b]				
Primary education	1.08	1.05-1.11	1.12	1.08-1.15
Vocational education	1.00		1.00	
Secondary education	0.87	0.83-0.91	0.89	0.85-0.93
Short and medium-cycle higher education	0.89	0.86-0.91	0.88	0.85-0.90
Long-cycle higher education	0.80	0.78-0.83	0.79	0.76-0.82
Very preterm birth 28+0-31+6[b]				
Primary education	1.06	0.98-1.15	1.10	1.01-1.20
Vocational education	1.00		1.00	
Secondary education	0.89	0.79-1.01	0.91	0.80-1.03
Short and medium-cycle higher education	0.83	0.77-0.90	0.82	0.76-0.88
Long-cycle higher education	0.80	0.73-0.88	0.78	0.71-0.86
Extreme preterm birth <28+0[b]				
Primary education	1.36	1.20-1.54	1.35	1.19-1.54
Vocational education	1.00		1.00	
Secondary education	0.79	0.64-0.96	0.78	0.63-0.96

Short and medium-cycle higher education	0.77	0.68-0.87	0.76	0.67-0.86
Long-cycle higher education	0.78	0.67-0.91	0.76	0.65-0.88
SGA				
Primary education	1.37	1.34-1.40	1.28	1.25-1.32
Vocational education	1.00		1.00	
Secondary education	0.99	0.95-1.02	0.95	0.92-0.99
Short and medium-cycle higher education	0.80	0.79-0.82	0.82	0.80-0.84
Long-cycle higher education	0.80	0.78-0.83	0.82	0.80-0.84

OR: Crude odds ratio, aOR: Odds ratio adjusted for maternal age, maternal country of origin and calendar year.
[a]*Compared to children who were alive 365 days after birth.*
[b]*Compared to children born from 37+0 - 41+6*

DISCUSSION

In a population register study of perinatal outcomes in Denmark we found consistent inverse educational gradients for all perinatal outcomes in the study period, with higher rates of adverse outcomes in children of women with lower educational levels. Adjustments for maternal age, country of origin, parity and calendar year did not chance the gradients.

An educational gradient in SGA was found in this study. This result is consistent with previous Nordic studies, which have reported socioeconomic inequalities in SGA.[5,23–28] Socioeconomic differences have been found in preterm birth as an overall outcome[5,23,24,29] and in preterm birth categorised according to gestational age.[3,26,28,30,31] This study found an educational gradient in moderate, very and extremely preterm birth. Consistently with previous studies[32–34] an educational gradient was found in stillbirth in this study. This study observed educational gradients in neonatal and post-neonatal mortality. Socioeconomic inequalities have been found in earlier Nordic studies in neonatal mortality[28,32,35–38] and also in post-neonatal mortality.[32,35,36,38]

We used population-covering register individual-based data with minimal sources of selection and information bias. The data from the Danish Medical Birth Register used in this study are of high quality.[17] The size of the study population enabled investigation of relatively rare perinatal outcomes like post-neonatal mortality. The data used from Statistics Denmark were all variables collected for administrative purposes, which according to the documentation from Statistics Denmark were so-called high quality variables.[39] Some limitations of the study should be discussed. In Denmark the registers

only obtain information on congenital anomalies for live births. The prevalence of congenital anomalies is presumably higher among stillbirths, spontaneous and induced abortions than among live births.[40] A socioeconomic gradient in stillbirth was observed in this study and consequently the socioeconomic gradient in congenital anomalies could be underestimated. In order to understand the true association between socioeconomic position and congenital anomalies it is essential to include information on congenital anomalies for live births, stillbirths, induced abortions and spontaneous abortions.

In contrast to several previous studies we did not adjust for lifestyle factors such as smoking, alcohol intake, BMI, and physical activity. In this study we were interested in estimating the overall effect of maternal educational level on adverse perinatal outcome and as a consequence we did not adjust for lifestyle factors as these were believed to mediate the association.

Previous Nordic studies that investigated the association between socioeconomic position and congenital anomalies reported inconsistent results.[5–8] In this study a statistically significant educational gradient in congenital anomalies was observed. The discrepancy between the association of this study and the associations of previous studies might be related to different socioeconomic measures used in the studies, variation in number of participants, differences in types of congenital anomalies included and different study populations in regard to inclusion of stillbirths.

The general level of education in Denmark increased during the study period. The proportion of women who attained primary school and no further education declined slightly during the study period. However, educational inequality in adverse perinatal outcomes was still observed. A contributing explanation of the inequality is likely to be found in a possible selection of women with the lowest educational level.[37] The group of women with primary education becomes more highly selected and thereby more socially vulnerable[41] and this may contribute to the higher risk of adverse perinatal outcomes. The educational distribution of mothers who give birth changes over time and also differs in the relatively similar Nordic

Welfare states this should make generalizations to other cohorts difficult. Nevertheless, socioeconomic differences in perinatal outcomes has been observed in different countries and in different time periods[4].

A possible part of the explanation of the observed educational differences is an overall healthier lifestyle among women with higher socioeconomic position. Certain lifestyle risk factors are more common among lower socioeconomic groups than among higher socioeconomic groups. For instance the prevalence of smokers is highest among women with lower educational level in Denmark[42] and smoking is associated with a higher risk of several adverse perinatal outcomes.[40] To investigate the mediating factors between socioeconomic position and adverse perinatal outcomes was beyond the scope of this article. However in order to reduce socioeconomic inequality in perinatal health future studies should focus on the mediating mechanisms in the association of socioeconomic position and adverse perinatal outcome

CONCLUSION

Socioeconomic inequality in perinatal health was observed in Denmark in the first decade of the 21st century. Maternal educational gradients were evident in the rare but serious outcomes such as congenital anomalies and foetal and infant mortality. The socioeconomically patterned risk of preterm birth and growth restriction is worrying because it may be the first tracks on the way to socioeconomic inequalities in health later in life. Interventions to diminish socioeconomic inequality in the earliest phases of life are still needed.

Figure 1: Flowchart of the study populations

LIST OF ABBREVIATIONS

SGA: Small-for-gestational age OR: Odds ratios

DECLARATIONS

Ethics approval and consent to participate: According to Danish legislation no ethical permission is required for register-based research, however, the study was approved by the local data protection authorities.

Consent for publication: Not applicable.

Availability of data and material: The data that support the findings of this study are available from Statistics Denmark but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Statistics Denmark.

Competing interests: The authors declare that they have no competing interests

Funding: This project was partly supported by the NordForsk grant no. 75970 for the project Contingent Life Courses.

Author contributions: AMNA, JA and JB designed the study. JA and JB analysed the data with assistance from AMNA, AVH and LM. JA and JB interpreted the data and prepared the first draft of the manuscript, which was revised by AMNA, AVH and LM. All authors read and approved the final manuscript.

Acknowledgments: We would like to thank Professor David Taylor Robinson for his comments and suggestions.

REFERENCES

1 Rom AL, Mortensen LH, Cnattingius S, *et al.* A comparative study of educational inequality in the risk of stillbirth in Denmark, Finland, Norway and Sweden 1981–2000. *J Epidemiol Community Health* 2012;**66**:240–6. doi:10.1136/jech.2009.101188

2 Arntzen A, Nybo Andersen AM. Social determinants for infant mortality in the Nordic countries, 1980-2001. *Scand J Public Health* 2004;**32**:381–9. doi:10.1080/14034940410029450

3 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. doi:10.1111/j.1365-3016.2008.00977.x

4 Mortensen LH, Helweg-Larsen K, Nybo Andersen A-M. Socioeconomic differences in perinatal health and disease. *Scand J Public Health* 2011;**39**:110–4. doi:10.1177/1403494811405096

5 Räisänen S, Sankilampi U, Gissler M, *et al.* Smoking cessation in the first trimester reduces most obstetric risks, but not the risks of major congenital anomalies and admission to neonatal care: a population-based cohort study of 1 164 953 singleton pregnancies in Finland. *J Epidemiol Community Health* 2014;**68**:159–64. doi:10.1136/jech-2013-202991

6 Olesen C, Thrane N, Rønholt A-M, *et al.* Association between social position and congenital anomalies: A population-based study among 19,874 Danish women. *Scand J Soc Med* 2009;**37**:246–51. doi:10.1177/1403494808100938

7 Morales-Suarez Varela MM, Nohr EA, Llopis-Gonzalez A, *et al.* Socio-occupational status and congenital anomalies. *Eur J Public Health* 2009;**19**:161–7. doi:10.1093/eurpub/ckp003

8 Morales-Suárez-Varela M, Kaerlev L, Jin Liang Zhu, *et al.* Unemployment and pregnancy outcomes: A study within the Danish National Birth Cohort. *Scand J Soc Med* 2011;**39**:449–56. doi:10.1177/1403494811407672

9 Piketty T, Goldhammer A. *Capital in the twenty-first century*. Cambridge Massachusetts: : The Belknap Press of Harvard University Press 2014.

10 OECD. An overview of growing income inequalities in OECD countries: Main Findings. *Divid We Stand Why Inequal Keeps Rising* 2011;:25:21-45.

11 Statistics Denmark. *Indkomster 2011.* Denmark: : Statistics Denmark 2013.

12 Fall CHD. Fetal Programming and the Risk of Noncommunicable Disease. *Indian J Pediatr* 2013;**80**:13–20. doi:10.1007/s12098-012-0834-5

13 Gluckman PD, Hanson MA, Cooper C, *et al.* Effect of In Utero and Early-Life Conditions on Adult Health and Disease. *N Engl J Med* 2008;**359**:61–73. doi:10.1056/NEJMra0708473

14 Lynch J, Kaplan G. Socioeconomic position. In: Berkman LF, Kawachi I, eds. *Social Epidemiology*. Oxford University Press 2000.

15 Galobardes B, Shaw M, Lawlor DA, *et al.* Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;**60**:7–12. doi:10.1136/jech.2004.023531

16 Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health* 2011;**39**:91–4. doi:10.1177/1403494810394715

17 Bliddal M, Broe A, Pottegård A, *et al.* The Danish Medical Birth Register. *Eur J Epidemiol* 2018;**33**:27–36. doi:10.1007/s10654-018-0356-1

18 Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health* 2011;**39**:30–3. doi:10.1177/1403494811401482

19 Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health* 2011;**39**:26–9. doi:10.1177/1403494811399958

20 Alexander G, Himes J, Kaufman R, *et al.* A united states national reference for fetal growth. *Obstet Gynecol* 1996;**87**:163–8. doi:10.1016/0029-7844(95)00386-X

21 Marsál K, Persson P-H, Larsen T, *et al.* Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr* 1996;**85**:843–8. doi:10.1111/j.1651-2227.1996.tb14164.x

22 Eurocat. EUROCAT Guide 1.4 and Reference Documents (2013). http://www.eurocat-network.eu/content/Full%20Guide%201%204.pdf

23 Gissler M, Rahkonen O, Arntzen A, *et al.* Trends in socioeconomic differences in Finnish perinatal health 1991–2006. *J Epidemiol Community Health* 2009;**63**:420–5. doi:10.1136/jech.2008.079921

24 Mortensen LH, Lauridsen JT, Diderichsen F, *et al.* Income-related and educational inequality in small-for-gestational age and preterm birth in Denmark and Finland 1987-2003. *Scand J Public Health* 2010;**38**:40–5. doi:10.1177/1403494809353820

25 Räisänen S, Gissler M, Sankilampi U, *et al.* Contribution of socioeconomic status to the risk of small for gestational age infants – a population-based study of 1,390,165 singleton live births in Finland. *Int J Equity Health* 2013;**12**:28. doi:10.1186/1475-9276-12-28

26 Li X, Sundquist J, Sundquist K. Parental occupation and risk of small-for-gestational-age births: a nationwide epidemiological study in Sweden. *Hum Reprod* 2010;**25**:1044–50. doi:10.1093/humrep/deq004

27 Mortensen LH, Diderichsen F, Arntzen A, *et al.* Social inequality in fetal growth: a comparative study of Denmark, Finland, Norway and Sweden in the period 1981-2000. *J Epidemiol Community Health* 2008;**62**:325–31. doi:10.1136/jech.2007.061473

28 Gisselmann MD, Hemström Ö. The contribution of maternal working conditions to socio-economic inequalities in birth outcome. *Soc Sci Med* 2008;**66**:1297–309. doi:10.1016/j.socscimed.2007.11.036

29 Thompson JMD, Irgens LM, Rasmussen S, *et al.* Secular trends in socio-economic status and the implications for preterm birth. *Paediatr Perinat Epidemiol* 2006;**20**:182–7. doi:10.1111/j.1365-3016.2006.00711.x

30 Morgen CS, Bjørk C, Andersen PK, *et al.* Socioeconomic position and the risk of preterm birth--a study within the Danish National Birth Cohort. *Int J Epidemiol* 2008;**37**:1109–20. doi:10.1093/ije/dyn112

31 Räisänen S, Gissler M, Saari J, *et al.* Contribution of risk factors to extremely, very and moderately preterm births - register-based analysis of 1,390,742 singleton births. *PloS One* 2013;**8**:e60660. doi:10.1371/journal.pone.0060660

32 Carlsen F, Grytten J, Eskild A. Maternal education and risk of offspring death; changing patterns from 16 weeks of gestation until one year after birth. *Eur J Public Health* 2014;**24**:157–62. doi:10.1093/eurpub/ckt065

33 Högberg L, Cnattingius S. The influence of maternal smoking habits on the risk of subsequent stillbirth: is there a causal relation? *BJOG Int J Obstet Gynaecol* 2007;**114**:699–704. doi:10.1111/j.1471-0528.2007.01340.x

34 Kesmodel U, Wisborg K, Olsen SF, *et al.* Moderate alcohol intake during pregnancy and the risk of stillbirth and death in the first year of life. *Am J Epidemiol* 2002;**155**:305–12.

35 Arntzen A, Mortensen L, Schnor O, *et al.* Neonatal and postneonatal mortality by maternal education--a population-based study of trends in the Nordic countries, 1981-2000. *Eur J Public Health* 2008;**18**:245–51. doi:10.1093/eurpub/ckm125

36 Arntzen A, Samuelsen SO, Bakketeig LS, *et al.* Socioeconomic status and risk of infant death. A population-based study of trends in Norway, 1967-1998. *Int J Epidemiol* 2004;**33**:279–88. doi:10.1093/ije/dyh054

37 Gisselmann MD. Education, infant mortality, and low birth weight in Sweden 1973-1990: emergence of the low birth weight paradox. *Scand J Public Health* 2005;**33**:65–71. doi:10.1080/14034940410028352

38 Johansson S, Villamor E, Altman M, *et al.* Maternal overweight and obesity in early pregnancy and risk of infant mortality: a population based cohort study in Sweden. *BMJ* 2014;**349**:g6572–g6572. doi:10.1136/bmj.g6572

39 Højkvalitetsvariable. http://www.dst.dk/da/TilSalg/Forskningsservice/Dokumentation/hoejkvalitetsvariable (accessed 20 May 2015).

40 Wilcox AJ. *Fertility and pregnancy: an epidemiologic perspective*. Oxford ; New York: : Oxford University Press 2010.

41 Mortensen LH, Diderichsen F, Davey Smith G, *et al.* Time is on whose side? Time trends in the association between maternal social disadvantage and offspring fetal growth. A study of 1 409 339 births in Denmark, 1981-2004. *J Epidemiol Community Health* 2009;**63**:281–5. doi:10.1136/jech.2008.076364

42 Illemann Christensen A, Statens Institut for Folkesundhed. *Sundhed og sygelighed i Danmark 2010 & udviklingen siden 1987*. Statens Institut for Folkesundhed 2012.

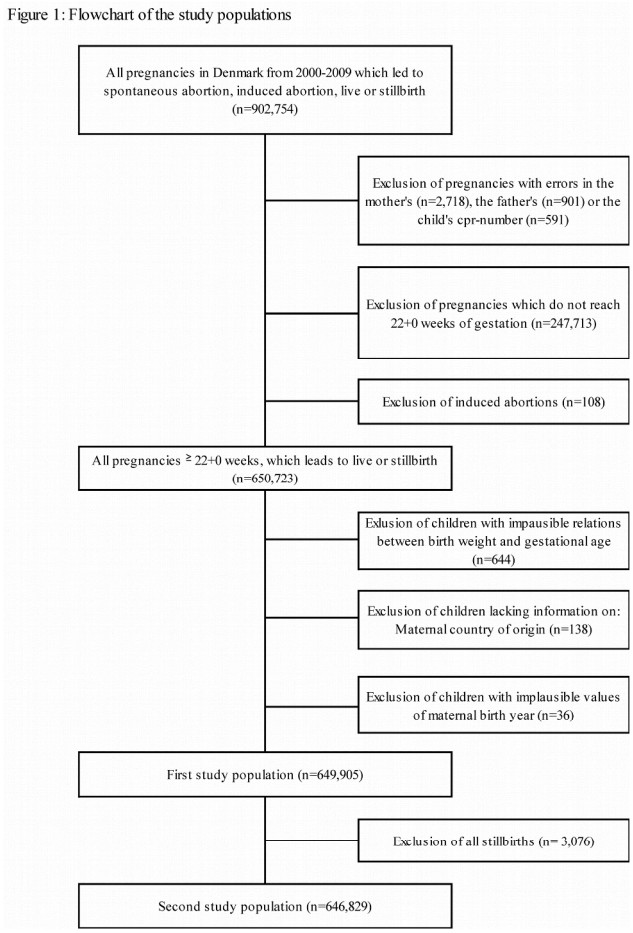

Figure 1 Flow chart

209x297mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	5 + Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	5-7
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-7 + Figure 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, pp 7-8
		(b) Indicate number of participants with missing data for each variable of interest	Figure 1
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2 pp 8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3 pp 9-10
		(*b*) Report category boundaries when continuous variables were categorized	5-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Considered
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Educational disparities in perinatal health in Denmark in the first decade of the 21st century: A register-based cohort study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-023531.R1
Article Type:	Research
Date Submitted by the Author:	13-Jul-2018
Complete List of Authors:	Bilsteen, Josephine; Department of Public Health, University of Copenhagen Andresen, Josefine; Department of Public Helath, University of Copenhagen Mortensen, Laust; Department of Public Health, University of Copenhagen Hansen, Anne; Department of Public Health, University of Copehagen Andersen, Anne-Marie; Department of Public Health, University of Copenhagen
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Paediatrics
Keywords:	Health inequalities, Congenital anomalies, Preterm birth, Small-for-gestational age, Stillbirth, Infant mortality

Educational disparities in perinatal health in Denmark in the first decade of the 21st century: A register-based cohort study

Josephine Funck Bilsteen[1*], jfbi@sund.ku.dk

Josefine Bernhard Andresen[1], vln522@alumni.ku.dk

Laust Hvas Mortensen[1] lamo@sund.ku.dk

Anne Vinkel Hansen[1] avih@sund.ku.dk

Anne-Marie Nybo Andersen[1] amny@sund.ku.dk

[1] Section of Social Medicine, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

* Corresponding author.

Section of Social Medicine, Department of Public Health, University of Copenhagen,

Øster Farimagsgade 5, 1014 Copenhagen K, Denmark.

Email: jfbi@sund.ku.dk, telephone: +4541661381

Word count: 5,575

ABSTRACT

Objective: To investigate socioeconomic differences in six perinatal health outcomes in Denmark in the first decade of the 21st century.

Design: A population-based cohort study.

Setting: Danish national registries.

Participants: A total of 646,829 live born children and 3,076 stillborn children (≥22+0 weeks of gestation) born in Denmark from 2000 through 2009. We excluded children with implausible relations between birth weight and gestational age (n=644), children without information on maternal country of origin (n=138), and implausible values of maternal year of birth (n=36).

Main outcome measures: We investigated the following perinatal health outcomes: Stillbirth, neonatal and post-neonatal mortality, small-for-gestational age, preterm birth grated into moderate preterm, very preterm, and extremely preterm, and congenital anomalies registered in the first year of life.

Results: Maternal educational level was inversely associated with all adverse perinatal outcomes. For all examined outcomes the risk association displayed a clear gradient across the educational levels. The associations remained after adjustment for maternal age, maternal country of origin and calendar year. Compared to mothers with vocational education mothers with more than 15 years of education had an adjusted risk ratio for stillbirth of 0.64 [95% CI 0.56-0.72]. The corresponding adjusted risk ratios for neonatal mortality, post-neonatal mortality, congenital anomalies, moderate preterm birth, and small-for-gestational age were, respectively, 0.79 [95% CI 0.67-0.93], 0.57 [95% CI 0.41-0.78], 0.87 [95% CI 0.83-0.91], 0.80 [95% CI 0.77-0.83] and 0.83 [95% CI 0.81-0.85].

Conclusion: Substantial educational inequalities in perinatal health were still present in the Denmark in first decade of the 21st century.

Keywords: Health inequalities; Stillbirth, Infant mortality; Congenital anomalies; Preterm birth; Small-for-gestational age.

ARTICLE SUMMARY

Strengths and limitations of this study

- Danish national registries with high degree of completeness and quality were used in this study.
- The large study population enabled investigation of rare perinatal outcomes.
- The grading of maternal education into five categories enabled detailed investigation of the educational gradients.
- Congenital anomalies are not registered for stillbirths and spontaneous abortions during the study period and as a consequence we could only estimate risk among live born children.

INTRODUCTION

The Nordic countries are generally regarded as egalitarian and have a low prevalence of adverse perinatal outcomes. However in the 1980s and 1990s strong socioeconomic gradients in adverse perinatal outcomes were observed in Denmark, Finland, Norway and Sweden. Several studies documented socioeconomic inequalities in respectively stillbirth, preterm birth, birth weight, infant mortality in all of the Nordic countries[1–4] but studies have been inconclusive with regards to congenital anomalies.[5–8]

During the first decade of the 21st century economic inequality rose in Denmark and elsewhere[9–11], but it is unclear what impact this has had on inequalities in perinatal health. Perinatal health measures, such as infant mortality, are used internationally as indicators of population health status. In addition, perinatal outcomes such as preterm birth and foetal growth are predictive at the individual level for health later in life. Several studies have found that low birth weight is related to the risk of chronic diseases in adulthood, such as type 2 diabetes and cardiovascular disease.[12,13] The health condition of the mother affects perinatal outcomes, thereby transferring socioeconomic inequality in health from one generation to the next.[13]

Socioeconomic position refers to the economic and social indicators that influence what positions individuals or groups hold within the structure of a society.[14] In this study educational level has been chosen as a measure of socioeconomic position because education is a favourable indicator of socioeconomic position in early adult life. Furthermore education is associated to future occupational status and income.[15]

The aim of this study was to describe the associations between maternal educational level and risk of adverse perinatal outcomes in Denmark during the first decade of the 21st century. The adverse perinatal outcomes of interest in this study were stillbirth, preterm birth, small-for-gestational age (SGA), congenital anomalies, neonatal mortality and post-neonatal mortality.

METHODS

We did a longitudinal register linkage study of all live births and stillbirths in Denmark from 2000 through 2009, as recorded in the Danish Medical Birth Register. Information on maternal educational level from the Population's Education register[16] was linked to information on perinatal health outcomes from the Danish Medical Birth Register[17], the Danish National Patient Register[18], and the Danish Register of Causes of Death [19]. The Danish system of unique person identifiers (CPR-number) was used to link individuals across the different registers in an anonymised data set in Statistics Denmark, which could be assessed via a VPN connection from Department of Public Health, University of Copenhagen. According to Danish legislation no ethical permission is required for register-based research; however, the study was approved by the local data protection authorities.

Study populations

The study population consisted of all live born and stillborn children born in Denmark during the study period. Children were excluded from the study population as illustrated in Figure 1. Children whose mothers were born after 1999 were excluded. Furthermore, we excluded children with implausible relations between gestational age and birth weight defined according to the method described by Alexander et al.[20] After the exclusions Analysis Population 1 consisted of a total of 649,905 live and stillborn children. Analysis population 2 consisted of 646,829 live born when stillborn children were excluded from Analysis Population 1. In the analysis of SGA children missing information on birth weight (n=4388) were not included.

Patient and Public Involvement

As this is a whole population register-based study we did not recruit individuals. Patients and public were not involved in development of the research question, the design, or conduct of this study. We planned to disseminate the results of this study through open access publication.

Study variables

The main exposure variable of interest was maternal educational level, defined as the highest educational level attained or expected (based on ongoing education) of the mother at the year of birth categorized into five categories: Primary education (*≤9 years*), secondary education (high school *10-12 years*), vocational education *(10-12 years)*, short- and medium-cycle higher education *(12-15 years)*, long-cycle higher education *(>15 years)*, and missing. Since the education register is based on reports from Danish educational institutions, the category of missing is comprised of individuals who are not registered at any education in Denmark.

Information on birth weight and the outcomes preterm birth and stillbirth were obtained from the Medical Birth Register. SGA was defined as birth weight falling below the 10th percentile of birth weight according to sex-specific intrauterine growth curves presented by Marsàl et al.[21] Preterm birth was divided into extremely preterm birth defined as birth ≥22+0 – 27+6 weeks, very preterm birth defined as birth ≥28+0 – 31+6, and moderately preterm birth defined as birth ≥32+0 – 36+6. The variable stillbirth was defined as foetal death at or after 22 completed gestational weeks. In Denmark, the threshold between spontaneous abortions and stillbirths was changed in 2004 from 28 completed weeks of gestation to 22 completed weeks of gestation. All pregnancies from 2000 to 2003 for which a spontaneous abortion was registered after 22 completed weeks of gestation were recoded into stillbirths. Information on infant mortality was obtained from The Central Person Register and The Danish Register of Causes of Death. Neonatal mortality was defined as death of a live born child before or at day 27 after birth and post-neonatal mortality was defined as death of a live born child at or after day 28 through day 365 after birth. Information on congenital anomalies was obtained from the Danish National Patient Register. The variable congenital anomalies registered in first year of life were defined according to EuroCAT's definitions excluding minor anomalies according to EuroCAT criteria.[22]

Other potential confounders in the analysis were the maternal year of birth *(<1965, 1965-69, 1970-74, 1975-79, ≥1980* maternal age at the time of delivery *(<25 years, 25-29 years, 30-34 years, 35-39 years, ≥40 years),* Offspring's year of birth *(2000-01, 2002-03, 2004-05, 2006-07, 2008-09)*, and country of origin of the mother categorized as Denmark, "Other western country" *(Andorra, Australia, Canada,*

Iceland, Liechtenstein, Monaco, New Zealand, Norway, San Marino, Switzerland, United States of America, Vatican City State and all EU member countries except Denmark) or "Non-western country" *(all remaining countries).*

Statistics

Initially, we calculated the prevalence for the six perinatal outcomes by maternal educational level. To investigate the associations between maternal educational level and the perinatal outcomes we used multiple logistic regression analyses and the analysis populations were restricted to children with information on maternal educational level. The a priori chosen model for adjustment included the covariates maternal age, maternal country of origin, and maternal year of birth as these were considered potential confounders. The variable year of birth of the offspring was not included in the model since the variables maternal age at time of delivery and maternal year of birth in combination practically describe the variable. Unadjusted and adjusted risk ratios (RR) were presented with a 95% confidence interval. Additionally, we fitted two models to test robustness of the findings: one adjusted for maternal age only and the second including maternal age, parity and country of origin, and year of birth as covariates. However, since the findings from the two models fitted to test robustness were similar to findings from the other adjusted model their findings are not shown. All statistical analyses were conducted in SAS 9.4.

RESULTS

The distributions of maternal educational level by maternal age, maternal country of origin and calendar year of birth are presented in Table 1. In Denmark, maternal completed and on-going educational level increased during the study period as shown in Table 1. The proportion of mothers born outside Denmark was higher among mothers with missing educational level.

Table 1 Maternal age, year of birth, and country of origin, and offspring's year of birth by educational level, all children born in Denmark 2000-2009

	All children	Primary education	Vocational education	Secondary education	Short and medium-cycle higher education	Long-cycle higher education	Missing
	n=649,905	n=106,129	n=222,744	n=46,026	n=185,417	n=94,168	n=15,421

	%	%	%	%	%	%	%
Maternal age							
<25	12.3	32.6	12.2	17.8	3.8	2.3	20.0
25-29	33.5	30.9	37.4	31.2	25.4	26.2	34.6
30-34	36.3	23.0	34.5	32.6	42.1	46.9	28.0
35-39	15.3	11.0	13.8	15.8	16.4	21.1	14.0
≥40	2.6	2.4	2.1	2.6	2.7	3.5	3.4
Maternal year of birth							
<1965	4.2	4.1	3.8	4.6	4.3	4.8	4.5
1965-69	16.5	12.3	16.4	17.6	17.0	20.7	12.6
1970-74	33.5	24.0	33.0	32.4	37.6	39.6	24.2
1975-79	30.6	28.8	32.0	27.9	31.8	28.3	31.1
≥1980	15.2	30.8	14.8	17.6	9.8	6.7	27.7
Maternal country of origin							
Denmark	86.2	74.7	91.0	77.6	93.2	92.0	10.7
Western countries	3.1	1.3	1.9	3.8	2.6	4.3	26.3
Non-western countries	10.7	24.0	7.2	18.6	4.3	3.7	63.0
Year of birth (offspring)							
2000-2001	20.5	24.2	22.3	23.7	17.9	16.0	20.2
2002-2003	19.9	21.1	20.9	22.1	18.8	18.0	14.9
2004-2005	20.0	19.6	20.1	20.1	20.6	20.0	12.6
2006-2007	20.0	18.0	19.1	18.2	21.5	22.2	21.0
2008-2009	19.7	17.1	17.7	15.9	21.2	23.8	31.3

The prevalence of stillbirth, neonatal mortality, post-neonatal mortality, congenital anomalies, SGA, and three degrees of preterm birth, respectively, by maternal educational level are shown in Table 2. Women with the shortest education had a higher prevalence of all of the adverse perinatal outcomes compared to women with higher educational level. The group of women with unknown educational level had the highest prevalence of stillbirth and SGA compared to the women with known educational level.

Table 2 Prevalence of adverse perinatal outcome by educational level, Denmark, 2000-2009

	Stillbirth	**Neonatal mortality**	**Post-neonatal mortality**	**Congenital anomalies**	**SGA**	**Moderate preterm birth 32+0-36+6**	**Very preterm birth 28+0-31+6**	**Extreme preterm birth <28+0**
	n=3,076	n=1,688	n=648	n=19,449	n=59,979	n=36,610	n=4,670	n=1,843
	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000	Per 1000
Primary education	6.7	3.6	1.9	34.9	125.9	64.5	8.3	4.1
Vocational education	4.8	2.7	1.0	30.7	95.1	60.0	7.8	3.0
Secondary education	4.0	2.5	1.0	28.2	94.2	52.7	7.0	2.4
Short and medium-	4.3	2.2	0.7	28.7	77.9	53.7	6.6	2.3
Long-cycle higher	3.1	2.1	0.5	27.1	77.9	48.8	6.3	2.4
Missing	7.1	3.0	1.2	28.9	126.5	51.2	5.9	3.1

Table 3 shows the relative risks, expressed as adjusted and unadjusted RR, of respectively stillbirth, neonatal mortality, post-neonatal mortality, congenital anomalies, SGA, and moderately preterm birth, very preterm birth, and extremely preterm birth, with mothers with vocational education as the comparison group. Compared to mothers with vocational education mothers with primary education had a statistically significant increased RR for stillbirth, neonatal mortality, post-neonatal mortality, congenital anomalies, moderate preterm birth, very preterm birth, extreme preterm birth and SGA. Women with short and medium-cycle higher education and women with long-cycle higher education had a statistically significant lower risk of all the six perinatal outcomes compared to women with vocational education. These results indicated consistently inverse educational gradients in the risk of adverse perinatal outcomes. The gradients were consistent after adjusting for maternal age, maternal country of origin and calendar year. The estimates were almost identical in analyses with adjustment for maternal age only and with adjustment for maternal age, maternal country of origin, calendar year and parity (results not shown).

Table 3 Adverse perinatal outcome by maternal educational level, all births Denmark, 2000-2009

	RR	95 % CI	aRR	95 % CI
Stillbirth				
Primary education	1.39	1.26-1.53	1.34	1.21-1.48
Vocational education	1.00		1.00	
Secondary education	0.84	0.71-0.98	0.81	0.69-0.94
Short and medium-cycle higher education	0.89	0.81-0.97	0.89	0.81-0.98
Long-cycle higher education	0.65	0.57-0.74	0.64	0.56-0.72
Neonatal mortality				
Primary education	1.33	1.16-1.51	1.29	1.12-1.47
Vocational education	1.00		1.00	
Secondary education	0.92	0.76-1.13	0.90	0.73-1.10
Short and medium-cycle higher education	0.79	0.70-0.90	0.80	0.71-0.92
Long-cycle higher education	0.79	0.67-0.93	0.79	0.67-0.93
Post-neonatal mortality[a]				
Primary education	1.93	1.59-2.35	1.81	1.47-2.22
Vocational education	1.00		1.00	
Secondary education	1.02	0.74-1.41	0.98	0.71-1.36
Short and medium-cycle higher education	0.74	0.59-0.92	0.76	0.61-0.95
Long-cycle higher education	0.55	0.41-0.75	0.57	0.42-0.78
Congenital anomalies				
Primary education	1.14	1.09-1.18	1.13	1.08-1.18
Vocational education	1.00		1.00	
Secondary education	0.92	0.86-0.98	0.91	0.86-0.97
Short and medium-cycle higher education	0.94	0.90-0.97	0.93	0.90-0.97
Long-cycle higher education	0.88	0.84-0.92	0.87	0.83-0.91
Moderate preterm birth 32+0-36+6[b]				
Primary education	1.07	1.04-1.10	1.11	1.08-1.14
Vocational education	1.00		1.00	
Secondary education	0.88	0.84-0.92	0.89	0.86-0.93
Short and medium-cycle higher education	0.89	0.87-0.92	0.89	0.86-0.91

Long-cycle higher education	0.81	0.79-0.84	0.80	0.77-0.83
Very preterm birth 28+0-31+6[b]				
Primary education	1.06	0.98-1.15	1.10	1.01-1.20
Vocational education	1.00		1.00	
Secondary education	0.89	0.79-1.01	0.91	0.81-1.03
Short and medium-cycle higher education	0.83	0.77-0.90	0.82	0.76-0.89
Long-cycle higher education	0.80	0.73-0.88	0.78	0.71-0.86
Extreme preterm birth <28+0[b]				
Primary education	1.36	1.20-1.54	1.35	1.19-1.54
Vocational education	1.00		1.00	
Secondary education	0.79	0.64-0.96	0.78	0.63-0.96
Short and medium-cycle higher education	0.77	0.68-0.87	0.76	0.67-0.86
Long-cycle higher education	0.78	0.67-0.91	0.76	0.65-0.89
SGA				
Primary education	1.32	1.30-1.35	1.25	1.22-1.28
Vocational education	1.00		1.00	
Secondary education	0.99	0.96-1.02	0.96	0.93-0.99
Short and medium-cycle higher education	0.82	0.80-0.84	0.83	0.82-0.85
Long-cycle higher education	0.82	0.80-0.84	0.83	0.81-0.85

RR: Crude risk ratio, aRR: Risk ratio adjusted for maternal age, maternal country of origin and calendar year.
[a]Compared to children who were alive 365 days after birth.
[b]Compared to children born from 37+0 - 41+6

DISCUSSION

In a population register study of perinatal outcomes in Denmark we found consistent inverse educational gradients for all perinatal outcomes in the study period, with higher rates of adverse outcomes in children of women with lower educational levels. Adjustments for maternal age, country of origin, parity and calendar year did not chance the gradients.

An educational gradient in SGA was found in this study. This result is consistent with previous Nordic studies, which have reported socioeconomic inequalities in SGA.[5,23–28] Socioeconomic differences have been found in preterm birth as an overall outcome[5,23,24,29] and in preterm birth categorised according to gestational age.[3,26,28,30,31] This study found an educational gradient in moderate, very and extremely preterm birth. Consistently with previous studies[32–34] an educational gradient was found in stillbirth in this study. This study observed educational gradients in neonatal and post-neonatal mortality. Socioeconomic inequalities have been found in earlier Nordic studies in neonatal mortality[28,32,35–38] and also in post-neonatal mortality.[32,35,36,38]

Previous Nordic studies that investigated the association between socioeconomic position and congenital anomalies reported inconsistent results.[5–8] In accordance with a previous Danish study[6] this study found a statistically significant educational gradient in congenital anomalies. Both studies used maternal educational level as a measure of socioeconomic position whereas the other studies used occupation[5,8] or a combination of occupation and education[7]. The differences in findings regarding socioeconomic differences in congenital anomalies are likely to be related to the use of different socioeconomic measures.

We used population-covering register individual-based data with minimal sources of selection and information bias. The data from the Danish Medical Birth Register used in this study are of high quality.[17] The size of the study population enabled investigation of relatively rare perinatal outcomes like post-neonatal mortality. Information on education was collected for administrative purposes, and according to the documentation from Statistics Denmark the education variable was a so-called high quality variable.[39] A limitation of this study is that the Danish registers only obtained information on congenital anomalies for live births. The prevalence of congenital anomalies is presumably higher among stillbirths, spontaneous and induced abortions than among live births.[40] Consequently, the socioeconomic gradient in congenital anomalies observed in this study could be underestimated. In order to understand the true association between socioeconomic position and congenital anomalies it is essential to include information on congenital anomalies for live births, stillbirths, induced abortions and spontaneous abortions.

In contrast to several previous studies we did not adjust for lifestyle factors such as smoking, alcohol intake, BMI, and physical activity. In this study we were interested in estimating the overall effect of maternal educational level on adverse perinatal outcome and as a consequence we did not adjust for lifestyle factors as these were believed to mediate the association. It could be debated whether maternal age is a mediator or a confounder in the association. In this study we assumed that maternal age affects maternal education since young women have not had the opportunity to undergo as much education as older women. As a consequence we considered maternal age a confounder. Both singletons and multiples

were included in the analyses as we do not think the associations between maternal education and the adverse perinatal outcomes differ between singletons and multiples when the estimates are adjusted for maternal age and other potential confounders.

The general level of education in Denmark increased during the study period. The proportion of women who attained primary school and no further education declined slightly during the study period. However, educational inequality in adverse perinatal outcomes was still observed. A contributing explanation of the inequality is likely to be found in a possible selection of women with the lowest educational level.[37] The group of women with primary education becomes more highly selected and thereby more socially vulnerable[41] and this may contribute to the higher risk of adverse perinatal outcomes. The educational distribution of mothers who give birth changes over time and also differs in the relatively similar Nordic Welfare states this should make generalizations to other cohorts difficult. Nevertheless, socioeconomic differences in perinatal outcomes has been observed in different countries and in different time periods[4].

Educational inequality in perinatal outcomes persists in the 21st century. A possible part of the explanation of this is an overall healthier lifestyle among women with higher socioeconomic position. Certain lifestyle risk factors are more common among lower socioeconomic groups than among higher socioeconomic groups. For instance the prevalence of smokers is highest among women with lower educational level in Denmark[42] and smoking is associated with a higher risk of several adverse perinatal outcomes.[40] To investigate the mediating factors between socioeconomic position and adverse perinatal outcomes was beyond the scope of this article. However, in order to reduce socioeconomic inequality in perinatal health future studies should focus on the mediating mechanisms in the association of socioeconomic position and adverse perinatal outcome

CONCLUSION

Socioeconomic inequality in perinatal health was observed in Denmark in the first decade of the 21st century. Maternal educational gradients were evident in the rare but serious outcomes such as congenital

anomalies and foetal and infant mortality. The socioeconomically patterned risk of preterm birth and growth restriction is worrying because it may be the first tracks on the way to socioeconomic inequalities in health later in life. Interventions to diminish socioeconomic inequality in the earliest phases of life are still needed.

Figure 1: Flowchart of the study populations

LIST OF ABBREVIATIONS

SGA: Small-for-gestational age RR: Risk ratios

DECLARATIONS

Ethics approval and consent to participate: According to Danish legislation no ethical permission is required for register-based research; however, the study was approved by the local data protection authorities.

Consent for publication: Not applicable.

Availability of data and material: The data that support the findings of this study are available from Statistics Denmark but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Statistics Denmark.

Competing interests: The authors declare that they have no competing interests

Funding: This project was partly supported by the NordForsk grant no. 75970 for the project Contingent Life Courses.

Author contributions: AMNA, JA and JB designed the study. JA and JB analysed the data with assistance from AMNA, AVH and LM. JA and JB interpreted the data and prepared the first draft of the manuscript, which was revised by AMNA, AVH and LM. All authors read and approved the final manuscript.

Acknowledgments: We would like to thank Professor David Taylor Robinson for his comments and suggestions.

REFERENCES

1 Rom AL, Mortensen LH, Cnattingius S, *et al.* A comparative study of educational inequality in the risk of stillbirth in Denmark, Finland, Norway and Sweden 1981–2000. *J Epidemiol Community Health* 2012;**66**:240–6. doi:10.1136/jech.2009.101188

2 Arntzen A, Nybo Andersen AM. Social determinants for infant mortality in the Nordic countries, 1980-2001. *Scand J Public Health* 2004;**32**:381–9. doi:10.1080/14034940410029450

3 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. doi:10.1111/j.1365-3016.2008.00977.x

4 Mortensen LH, Helweg-Larsen K, Nybo Andersen A-M. Socioeconomic differences in perinatal health and disease. *Scand J Public Health* 2011;**39**:110–4. doi:10.1177/1403494811405096

5 Räisänen S, Sankilampi U, Gissler M, *et al.* Smoking cessation in the first trimester reduces most obstetric risks, but not the risks of major congenital anomalies and admission to neonatal care: a population-based cohort study of 1 164 953 singleton pregnancies in Finland. *J Epidemiol Community Health* 2014;**68**:159–64. doi:10.1136/jech-2013-202991

6 Olesen C, Thrane N, Rønholt A-M, *et al.* Association between social position and congenital anomalies: A population-based study among 19,874 Danish women. *Scand J Soc Med* 2009;**37**:246–51. doi:10.1177/1403494808100938

7 Morales-Suarez Varela MM, Nohr EA, Llopis-Gonzalez A, *et al.* Socio-occupational status and congenital anomalies. *Eur J Public Health* 2009;**19**:161–7. doi:10.1093/eurpub/ckp003

8 Morales-Suárez-Varela M, Kaerlev L, Jin Liang Zhu, *et al.* Unemployment and pregnancy outcomes: A study within the Danish National Birth Cohort. *Scand J Soc Med* 2011;**39**:449–56. doi:10.1177/1403494811407672

9 Piketty T, Goldhammer A. *Capital in the twenty-first century*. Cambridge Massachusetts: : The Belknap Press of Harvard University Press 2014.

10 OECD. An overview of growing income inequalities in OECD countries: Main Findings. *Divid We Stand Why Inequal Keeps Rising* 2011;:25:21-45.

11 Statistics Denmark. *Indkomster 2011.* Denmark: : Statistics Denmark 2013.

12 Fall CHD. Fetal Programming and the Risk of Noncommunicable Disease. *Indian J Pediatr* 2013;**80**:13–20. doi:10.1007/s12098-012-0834-5

13 Gluckman PD, Hanson MA, Cooper C, *et al.* Effect of In Utero and Early-Life Conditions on Adult Health and Disease. *N Engl J Med* 2008;**359**:61–73. doi:10.1056/NEJMra0708473

14 Lynch J, Kaplan G. Socioeconomic position. In: Berkman LF, Kawachi I, eds. *Social Epidemiology*. Oxford University Press 2000.

15 Galobardes B, Shaw M, Lawlor DA, *et al.* Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;**60**:7–12. doi:10.1136/jech.2004.023531

16 Jensen VM, Rasmussen AW. Danish Education Registers. *Scand J Public Health* 2011;**39**:91–4. doi:10.1177/1403494810394715

17 Bliddal M, Broe A, Pottegård A, *et al.* The Danish Medical Birth Register. *Eur J Epidemiol* 2018;**33**:27–36. doi:10.1007/s10654-018-0356-1

18 Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health* 2011;**39**:30–3. doi:10.1177/1403494811401482

19 Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health* 2011;**39**:26–9. doi:10.1177/1403494811399958

20 Alexander G, Himes J, Kaufman R, *et al.* A united states national reference for fetal growth. *Obstet Gynecol* 1996;**87**:163–8. doi:10.1016/0029-7844(95)00386-X

21 Marsál K, Persson P-H, Larsen T, *et al.* Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr* 1996;**85**:843–8. doi:10.1111/j.1651-2227.1996.tb14164.x

22 Eurocat. EUROCAT Guide 1.4 and Reference Documents (2013). http://www.eurocat-network.eu/content/Full%20Guide%201%204.pdf

23 Gissler M, Rahkonen O, Arntzen A, *et al.* Trends in socioeconomic differences in Finnish perinatal health 1991–2006. *J Epidemiol Community Health* 2009;**63**:420–5. doi:10.1136/jech.2008.079921

24 Mortensen LH, Lauridsen JT, Diderichsen F, *et al.* Income-related and educational inequality in small-for-gestational age and preterm birth in Denmark and Finland 1987-2003. *Scand J Public Health* 2010;**38**:40–5. doi:10.1177/1403494809353820

25 Räisänen S, Gissler M, Sankilampi U, *et al.* Contribution of socioeconomic status to the risk of small for gestational age infants – a population-based study of 1,390,165 singleton live births in Finland. *Int J Equity Health* 2013;**12**:28. doi:10.1186/1475-9276-12-28

26 Li X, Sundquist J, Sundquist K. Parental occupation and risk of small-for-gestational-age births: a nationwide epidemiological study in Sweden. *Hum Reprod* 2010;**25**:1044–50. doi:10.1093/humrep/deq004

27 Mortensen LH, Diderichsen F, Arntzen A, *et al.* Social inequality in fetal growth: a comparative study of Denmark, Finland, Norway and Sweden in the period 1981-2000. *J Epidemiol Community Health* 2008;**62**:325–31. doi:10.1136/jech.2007.061473

28 Gisselmann MD, Hemström Ö. The contribution of maternal working conditions to socio-economic inequalities in birth outcome. *Soc Sci Med* 2008;**66**:1297–309. doi:10.1016/j.socscimed.2007.11.036

29 Thompson JMD, Irgens LM, Rasmussen S, *et al.* Secular trends in socio-economic status and the implications for preterm birth. *Paediatr Perinat Epidemiol* 2006;**20**:182–7. doi:10.1111/j.1365-3016.2006.00711.x

30 Morgen CS, Bjørk C, Andersen PK, *et al.* Socioeconomic position and the risk of preterm birth--a study within the Danish National Birth Cohort. *Int J Epidemiol* 2008;**37**:1109–20. doi:10.1093/ije/dyn112

31 Räisänen S, Gissler M, Saari J, *et al.* Contribution of risk factors to extremely, very and moderately preterm births - register-based analysis of 1,390,742 singleton births. *PloS One* 2013;**8**:e60660. doi:10.1371/journal.pone.0060660

32 Carlsen F, Grytten J, Eskild A. Maternal education and risk of offspring death; changing patterns from 16 weeks of gestation until one year after birth. *Eur J Public Health* 2014;**24**:157–62. doi:10.1093/eurpub/ckt065

33 Högberg L, Cnattingius S. The influence of maternal smoking habits on the risk of subsequent stillbirth: is there a causal relation? *BJOG Int J Obstet Gynaecol* 2007;**114**:699–704. doi:10.1111/j.1471-0528.2007.01340.x

34 Kesmodel U, Wisborg K, Olsen SF, *et al.* Moderate alcohol intake during pregnancy and the risk of stillbirth and death in the first year of life. *Am J Epidemiol* 2002;**155**:305–12.

35 Arntzen A, Mortensen L, Schnor O, *et al.* Neonatal and postneonatal mortality by maternal education--a population-based study of trends in the Nordic countries, 1981-2000. *Eur J Public Health* 2008;**18**:245–51. doi:10.1093/eurpub/ckm125

36 Arntzen A, Samuelsen SO, Bakketeig LS, *et al.* Socioeconomic status and risk of infant death. A population-based study of trends in Norway, 1967-1998. *Int J Epidemiol* 2004;**33**:279–88. doi:10.1093/ije/dyh054

37 Gisselmann MD. Education, infant mortality, and low birth weight in Sweden 1973-1990: emergence of the low birth weight paradox. *Scand J Public Health* 2005;**33**:65–71. doi:10.1080/14034940410028352

38 Johansson S, Villamor E, Altman M, *et al.* Maternal overweight and obesity in early pregnancy and risk of infant mortality: a population based cohort study in Sweden. *BMJ* 2014;**349**:g6572–g6572. doi:10.1136/bmj.g6572

39 Højkvalitetsvariable. http://www.dst.dk/da/TilSalg/Forskningsservice/Dokumentation/hoejkvalitetsvariable (accessed 20 May 2015).

40 Wilcox AJ. *Fertility and pregnancy: an epidemiologic perspective*. Oxford ; New York: : Oxford University Press 2010.

41 Mortensen LH, Diderichsen F, Davey Smith G, *et al.* Time is on whose side? Time trends in the association between maternal social disadvantage and offspring fetal growth. A study of 1 409 339 births in Denmark, 1981-2004. *J Epidemiol Community Health* 2009;**63**:281–5. doi:10.1136/jech.2008.076364

42 Illemann Christensen A, Statens Institut for Folkesundhed. *Sundhed og sygelighed i Danmark 2010 & udviklingen siden 1987*. Statens Institut for Folkesundhed 2012.

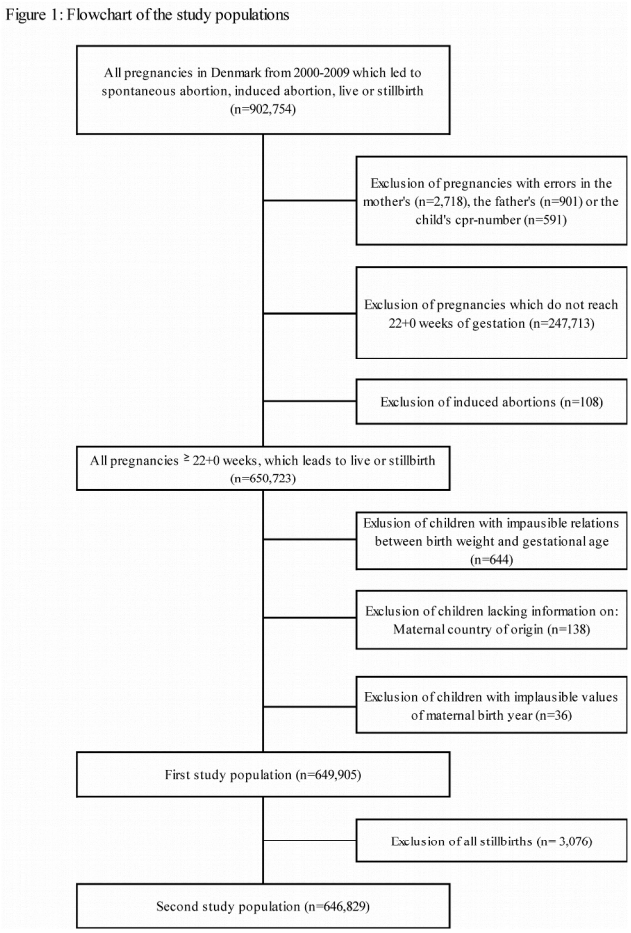

Figure 1: Flowchart of the study populations

209x297mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	5 + Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	5-7
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-7 + Figure 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, pp 7-8
		(b) Indicate number of participants with missing data for each variable of interest	Figure 1
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2 pp 8-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3 pp 9-10
		(*b*) Report category boundaries when continuous variables were categorized	5-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Considered
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.