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Socioeconomic position and the risk of miscarriage: a study within the Danish National Birth Cohort

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Abstract

Objectives: To investigate the relationship between different indicators of socioeconomic position and the risk of miscarriage.

Design: Cohort study.

Setting: 1996-2002, Denmark.

Participants: All first time participants, a total of 89,829 pregnant women, enrolled in the Danish National Birth Cohort were included in the present study. Overall, 4,062 pregnancies ended in miscarriage. Information on education, income and labour market attachment in the year before pregnancy was drawn from national registers.

Main outcome measure: Miscarriage, i.e. fetal death within the first 22 weeks of pregnancy, was the outcome of interest. We estimated Hazard Ratios (HR) of miscarriage using Cox regression analysis with gestational age as the underlying time scale.

Results: Women with <10 years of education had an elevated risk of miscarriage when compared to women with >12 years of education (HR 1.19 (95%CI 1.05 to 1.34)). The HR estimates for the four lowest income quintiles were all increased (HRs between 1.09 and 1.15) as compared to the upper quintile, but did not differ considerably from each other. In general, no statistically significant association was found between labour market attachment and the risk of miscarriage, however, the group of women on disability pension had an increased HR of miscarriage when compared to women who were employed (HR 1.32 (95%CI 0.82 to 2.13)).

Conclusion: Educational level and income were inversely associated with the risk of miscarriage. As these factors most likely are non-causally related to miscarriage, the findings indicate that factors related to social position, probably of the environmental and behavioural type, may affect miscarriage risk. The study highlights the need for studies addressing such exposures in order to prevent miscarriages.

Introduction

Social inequality is demonstrated in most reproductive outcomes, such as preterm birth, intrauterine growth retardation and stillbirth [1;1-4]. This inequality indicates a preventive potential, since the minimum level of these outcomes, in theory, should be attainable for all groups in society. Miscarriage, i.e. fetal death before 22 gestational weeks, is the most frequent adverse pregnancy outcome and affects many women and their relatives. Approximately one out of six clinically recognized pregnancies result in miscarriage[5;6] and identification of even a small potential for prevention may have significant impact for public health.

Given the commonness of miscarriage, surprisingly few studies have investigated the relationship with socioeconomic position, and no consensus about any association has been established. It has been shown that women with low socioeconomic position have an increased risk of miscarriage when measured by educational attainment [7-10] while other studies have not supported this finding [11-13]. When social position has been measured by labour market attachment the associations seem even more unclear [7;12-14]. Two studies that used income as a proxy measure of socioeconomic position did not find an association with the risk of miscarriage [10;13]. The risk of miscarriage according to potential risk factors that is known to display a social gradient, such as alcohol drinking during pregnancy and smoking, have been examined individually [12;15-18 19], but with no consistent results. By examining how different measures of socioeconomic position are associated with the risk of miscarriage, we might be able to come closer to identification of causal risk factors for miscarriage. The aim of this study is to describe how educational level, income, and labour market attachment, respectively, are related to the risk of miscarriage in a large cohort study.

Methods

We used data from the Danish National Birth Cohort (DNBC) which comprises of 100,418 pregnancies recruited in the years 1996-2002. The pregnant women were invited to participate in the cohort at the first antenatal visit at the general practitioner. The women were included in the study if they had posted the informed consent form before gestational week 24, intended to carry the pregnancy to term and were able to complete a telephone interview in Danish. The DNBC is described in details elsewhere[20].

For this study, we excluded women with no information on the date of the consent agreement (n=34), women who entered the cohort after 22 weeks of pregnancy (n=1661), women with no information of the date of the pregnancy outcome (n=81) and women with ectopic pregnancies (n=66) or mola hydatidosa (n=48). Furthermore, in cases where women participated in the cohort more than once (n=8,699), we only included the women's first pregnancy in the analyses to meet the criteria of independent observations in the statistical model. Consequently, 89,829 pregnancies were eligible for analyses in this study.

We used educational level, maternal income and labour market attachment as indicators of the pregnant women's socioeconomic position. This information was retrieved from national registers where the information of highest educational attainment, yearly income and predominant attachment to the labour market are registered on an individual level every year. We used the last information registered before the date of last menstruation period (LMP) of the actual pregnancy. The ISCED (International Standard Class of Education) codes from Statistics Denmark were converted into four educational groups, reflecting the highest completed academic educational attainment or – for women in education – the level completion of the actual education would lead to

(see table 1). Labour market attachment was categorized as: employed, students, unemployed, disability-retired and unknown. To be categorized as unemployed, one had to be unemployed for more than 50% of the time in the year preceding conception. If the period of unemployment was less than half the year, one was categorized as employed. Income was grouped using quintiles based on the taxable income of the women the calendar year before year of LMP.

The outcome measure of interest was miscarriage, defined as death and expulsion of an intrauterine pregnancy before 22 weeks of pregnancy [21]. The gestational age was calculated using the self reported first day in the women's last menstruation period, which was stated on the informed consent form. Information about the occurrence of miscarriage came primarily from the Danish National Patient Registry, where all women who had been diagnosed or treated in a hospital setting were registered. A small minority of the women had no pregnancy outcome in the Danish National Patient Registry, and for these we used information from the participant herself.

To study whether the possible association between socioeconomic position and the risk of miscarriage differed according to gestational age, miscarriage was divided into first and second trimester of pregnancy, including miscarriages at 84 days of gestation in the first trimester miscarriages.

Statistical analyses

The hazard ratios (HR) of miscarriage according to three different measures of socioeconomic position were estimated using Cox regression analysis. Gestational age in days was used as the underlying time variable. We used a model with delayed entry, so that women entered the cohort on the gestational day of inclusion in the study. The follow-up ended at the gestational age at date of miscarriage, emigration, maternal death or the day the woman completed the first 22 weeks of

gestation (154 days), whichever came first. We conducted three sets of analyses estimating the relations between maternal educational level, maternal labour market attachment, maternal income level, respectively and miscarriage. Individual level HR were calculated for each category in comparison to a reference category, defined as the category hypothesized to have the lowest risk of miscarriage. The risk association between the three measures of socioeconomic position and miscarriage was adjusted for maternal age at the time of conception (<25, 25-29, 30-34, 35-39, >/=40 years). We conducted trend tests for the association between the socioeconomic variables and the rate of miscarriage. All statistical analyses were performed with the SAS software package version 9.2.

Results

The mean gestational age of recruitment to the study was 78 days, 10% was recruited before 49 days and 10% was recruited after 112 days of gestation. A total of 4,062 pregnancies resulted in a miscarriage. Of these, 2,146 were early miscarriages and 1,916 were late miscarriages.

Table 1 shows the distribution of the three socioeconomic indicators according to maternal age and demonstrates the expected strong association between age and socioeconomic position.
When examining the effect of age on the risk of miscarriage, we found different effects in the first and the second trimester, i.e. the proportional hazards assumption was not fulfilled for age. In the final regression analyses, we therefore stratified the effect of age according to trimester.

We found an inverse association between educational level and the risk of miscarriage (Table 2). Women with compulsory school as the highest educational level had an age adjusted HR of 1.19 (95%CI 1.05 to 1.34) for miscarriage when compared to women with a bachelor level or more (Table 2). Women in the four lowest income quintiles had an increased risk of miscarriage when compared with the group with the highest income level, though only two of the estimates reached statistical significance. Unemployed women and students had the same risk of miscarriage as the employed women. However, the group of women on disability pension had an increased risk of miscarriage compared to women who were employed (HR 1.32(95%CI 0.82 to 2.13)).
For educational level and income level we found significant trends (p-values = 0.01 and 0.04, respectively) while, for labour market attachment, there was no clear trend (p-value = 0.50).

Discussion

This study, based on data from all 89,829 women in the DNBC, displayed a social pattern in the risk of miscarriage. Educational level and income were both inversely associated with the risk of miscarriage.

Apart from maternal age, no etiologic risk factors for miscarriage are well established and few studies have examined the association between socioeconomic position and risk of miscarriage. A few previous studies have reported an association between socioeconomic position and miscarriage[7-10] when socioeconomic position was measured by educational level and labour market attachment, and others found no such association [11-14]. There are several possible explanations for this. Some studies are small with a diminished possibility of detecting a smaller association. Furthermore, two of these studies adjust for earlier miscarriage in their analyses[11;12]. Previous miscarriage is associated with a 60% higher risk of miscarriage[22], suggesting that women vary in their baseline risk for this negative pregnancy outcome. Adjusting for earlier miscarriage may therefore distort the possible association between socioeconomic position and (baseline) risk of miscarriage as we find it less likely that previous miscarriage is a determinant of social position. Another possible explanation may be that only one of the studies uses prospectively collected data.

Why do women with lower socioeconomic position have an increased risk of miscarriage? According to the association we have found between educational level and the risk of miscarriage, it is possible that an overall healthier lifestyle among well educated women may explain part of the effect. This is not a fulfilling explanation though, since some of the typical lifestyle factors seem to be socially patterned in opposite directions in the DNBC. Smoking for instance is socially patterned, with women of low socioeconomic position smoking more than women of higher

socioeconomic position, but smoking is not found to be associated with the risk of miscarriage [12;18]. Alcohol intake during pregnancy is also socially patterned and this exposure is strongly associated with the risk of miscarriage [19]. In the DNBC though, it is the women with high socioeconomic position who have reported to have alcohol intake during their pregnancies [23]. Therefore, typical lifestyle factors cannot solely explain the difference in miscarriage risk we find according to socioeconomic position.

It is known that the ability to make use of the health system depends upon educational level[24;25]. However, it is not clear how this may affect the risk of miscarriage since no preventive measures for this negative pregnancy outcome is known. The association we found between income level and the risk of miscarriage is difficult to interpret. The risk is increased at more or less the same scale for all the income groups compared to the group with the highest income level. A possible explanation could be that the Danish population is relatively homogeneous according to income as compared to other populations[26], and therefore an association would be clearer in countries with a greater distinction in living circumstances between rich and poor[27]. What we wished to examine, looking at the women's employment status before they got pregnant, was whether being outside the labour market had any influence on ones risk of miscarriage. This seems not to be the case. One reasonable explanation might be that in Denmark there is a high social security for people outside the labour market. Another speculation could be that being outside the labour market pose a social risk, while being at the labour market pose several occupational risks and that these risks outweigh each other. The apparently elevated risk of miscarriage for women on disability pension is not surprising, given these women are of remarkable worse health than the rest of the study population.

The present study is based upon a large population and a considerable number of miscarriages, which offers a good foundation to examine the association between different indicators of socioeconomic position and miscarriage. Cohort studies are potentially subject to selection bias due to loss to follow-up. This is a minor issue in this study, since 99,9% of the pregnancy outcomes has been identified. The information we have on the exposure measures are based upon register data which covers almost the whole population, and is therefore not dependent upon the outcome of the pregnancy. To study miscarriage is difficult, since a great part of miscarriages happen very early in the pregnancy period – many even before the women themselves know that they are pregnant[28]. This implies that many women do not have a chance to be recruited for pregnancy cohorts before the miscarriage. The potential bias arising from that fact is taken care of by applying survival analyses with left truncation and gestational age as time variable, but this is why the proportion of pregnancies ending in miscarriage in the DNBC is less than reported in the background population and this is also the explanation why we are restricted from being able to conclude anything about the association between socioeconomic position and the very early miscarriages.

The women participating in the DNBC seems to be somewhat healthier, than the rest of the population[29], though the difference is very moderate and the estimated effect upon the risk estimates obtained in internal comparisons are small. This means that it should be possible to transfer findings based upon the DNBC to the background population. It cannot be excluded though that there is some bias related to selection and, if so, our results are most likely underestimated.

In this study, we were interested in the overall effect of socioeconomic position on the risk of miscarriage. We did not adjust our analyses for typical lifestyle factors, e.g. smoking, alcohol consumption, and body mass index, since we believe them to play a role as mediating factors

between socioeconomic position and the risk of miscarriage. Conditioning on an intermediate will only be of interest if one wishes to examine something different from the overall effect, i.e. the direct effects of the exposure on the outcome [30]. In contrast, maternal age is a strong independent risk factor for miscarriage[31] and also be causally related to social position, and consequently we believe the age-adjusted analyses provide the most accurate estimates.

Conclusion

In this large cohort study we found an inverse association between measures of socioeconomic position and the risk of miscarriage. These findings indicate that at least some of the miscarriages are preventable and highlights the need for further studies addressing which behavioural and environmental exposures, concentrated in groups with lower socioeconomic position, that are causal risk factors for miscarriage.

What is already known on this topic
Social inequality is found in most reproductive outcomes, such as preterm birth, small for gestational age and stillbirth. Around one out of six clinically recognized pregnancies result in a miscarriage. The relationship between socioeconomic position and the risk of miscarriage is not well established.
What this paper adds
Women of lower socioeconomic position seem to have an elevated risk of miscarriage. This indicates that a proportion of miscarriages may be preventable.

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CONTRIBUTORS

A-MNA initiated the study. Study design and analytical strategy were developed by all authors. FNN, LE, SaR made the data management and statistical analyses, supervised by PKA. FNN wrote the first version of the paper and all authors took part in the revision. All authors have seen and approved the final version of the paper.

COMPETING INTERESTS

All authors declare that the answer to the questions on your competing interest form (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

EXCLUSIVE LICENCE

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DATA SHARING STATEMENT

There is no additional data available.

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Table 1: Socioeconomic characteristics of 89,829 women in the Danish National Birth Cohort according to age at conception. Denmark, 1996-2002.

			Age				
			<25	25-29	30-34	35-39	40+
	n	%	%	%	%	%	%
Educational level							
BA or more (>12 years)	12,378	13.8	4.94	13.5	16.9	16.3	16.5
Higher edu. (less than BA degree)	26,627	29.6	13.8	31.8	31.9	34.1	36.7
Upper sec. edu. & vocational training	39,221	43.7	52.4	44.1	41.8	37.7	20.1
Compulsory school (<10 years)	10,753	11.9	27.9	9.7	8.4	10.9	13.9
Unknown	850	0.9	0.9	0.9	1.0	1.0	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Income quintile							
>80%	17,728	19.7	2.2	13.5	29.3	35.5	38.6
60-80%	17,725	19.7	8.9	19.8	23.4	22.4	19.5
40-60%	17,723	19.7	16.5	21.2	19.9	17.8	18.7
20-40%	17,724	19.7	28.3	22.5	15.2	12.8	10.8
<20%	17,772	19.7	42.9	21.9	10.8	9.9	9.7
Unknown	1,207	1.3	1.3	1.2	1.4	1.7	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Labour market attachment							
Employed	74,738	83.2	68.7	82.5	88.6	88.0	85.0
Student	6,584	7.3	16.0	9.2	3.2	2.1	1.1
Unemployed (> 50% of the year)	2,766	3.1	2.2	3,0	3.3	3.8	5.0
Disability pension	238	0.3	0.1	0.2	0.3	0.7	1.7
Unknown	5,503	6.1	13.4	5.2	4.6	5.5	7.1
n	89,829	100	12,449	37,114	29,864	9,420	982

Table 2: The risk of miscarriage according to educational level, income and labour market attachment, respectively. Risks are expressed in hazard ratios (HR). The Danish National Birth Cohort.

		Crude		Age adjusted	
Educational level (n=88,958)	No events	HR	95%CI	HR	95%CI
BA or more (>12 years)	589	1			
Higher edu. (less than BA degree)	1239	1,01	(0.92-1.11)	1,02	(0.93-1.13)
Upper sec. edu. & vocational training	1668	0,97	(0.88-1.06)	1,01	(0.92-1.11)
Compulsory school (<10 years)	527	1,14	(1.01-1.28)	1,19	(1.05-1.34)
Income quintile (n = 88,602)					
>80 %	785	1		1	
60 - 80 %	787	1,01	(0.91-1.11)	1,1	(0.99-1.21)
40 - 60%	796	1,03	(0.93-1.13)	1,15	(1.04-1.27)
20 - 40%	740	0,93	(0.84-1.03)	1,09	(0.99-1.22)
<20%	773	0,95	(0.86-1.05)	1,15	(1.03-1.27)
Employment status (n= 84,306)					
Employed	3398	1		1	
Student	295	0,91	(0.81-1.03)	1,03	(0.91-1.16)
Unemployed (>50% of the year)	128	1,04	(0.87-1.25)	1,01	(0.84-1.20)
Disability pension	17	1,61	(1.00-2.60)	1,32	(0.82-2.13)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*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
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
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
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
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
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
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

*Give information separately for exposed and unexposed groups.

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 http://www.strobe-statement.org.

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Socioeconomic position and the risk of miscarriage: a study within the Danish National Birth Cohort

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Abstract

Objectives: To investigate the relationship between different indicators of socioeconomic position and the risk of miscarriage.

Design: Cohort study.

Setting: 1996-2002, Denmark.

Participants: All first time participants, a total of 89,829 pregnant women, enrolled in the Danish National Birth Cohort were included in the present study. Overall, 4,062 pregnancies ended in miscarriage. Information on education, income and labour market attachment in the year before pregnancy was drawn from national registers.

Main outcome measure: Miscarriage, i.e. fetal death within the first 22 weeks of pregnancy, was the outcome of interest. We estimated Hazard Ratios (HR) of miscarriage using Cox regression analysis with gestational age as the underlying time scale.

Results: Women with <10 years of education had an elevated risk of miscarriage when compared to women with >12 years of education (HR 1.19 (95%CI 1.05 to 1.34)). The HR estimates for the four lowest income quintiles were all increased (HRs between 1.09 and 1.15) as compared to the upper quintile, but did not differ considerably from each other. In general, no statistically significant association was found between labour market attachment and the risk of miscarriage, however, the group of women on disability pension had an increased HR of miscarriage when compared to women who were employed (HR 1.32 (95%CI 0.82 to 2.13)).

Conclusion: Educational level and income were inversely associated with the risk of miscarriage. As these factors most likely are non-causally related to miscarriage, the findings indicate that factors related to social position, probably of the environmental and behavioural type, may affect miscarriage risk. The study highlights the need for studies addressing such exposures in order to prevent miscarriages.

Introduction

Social inequality is demonstrated in most reproductive outcomes, such as preterm birth, intrauterine growth retardation and stillbirth [1-4]. This inequality indicates a preventive potential, since the minimum level of these outcomes, in theory, should be attainable for all groups in society. Miscarriage, i.e. fetal death before 22 gestational weeks, is the most frequent adverse pregnancy outcome and affects many women and their relatives. Approximately one out of six clinically recognized pregnancies result in miscarriage[5;6] and identification of even a small potential for prevention may have significant impact for public health.

Given the commonness of miscarriage, surprisingly few studies have investigated the relationship with socioeconomic position, and no consensus about any association has been established. It has been shown that women with low socioeconomic position have an increased risk of miscarriage when measured by educational attainment [7-10] while other studies have not supported this finding [11-13]. When social position has been measured by labour market attachment the associations seem even more unclear [7;12-14]. Two studies that used income as a proxy measure of socioeconomic position did not find an association with the risk of miscarriage [10;13]. The risk of miscarriage according to potential risk factors that are known to display a social gradient, such as alcohol drinking during pregnancy and smoking, have been examined individually [12;15-19], but with no consistent results. By examining how different measures of socioeconomic position are associated with the risk of miscarriage, we might be able to come closer to identification of more proximal causal risk factors for miscarriage.

The aim of this study is to describe how educational level, income, and labour market attachment, respectively, are related to the risk of miscarriage in a large cohort study.

Methods

We used data from the Danish National Birth Cohort (DNBC) which comprises of 100,418 pregnancies recruited in the years 1996-2002. The pregnant women were invited to participate in the cohort at the first antenatal visit at the general practitioner. The women were included in the study if they had posted the informed consent form before gestational week 24, intended to carry the pregnancy to term and were able to complete a telephone interview in Danish. The DNBC is described in details elsewhere[20].

For this study, we excluded women with no information on the date of the consent agreement (n=34), women who entered the cohort after 22 weeks of pregnancy (n=1661), women with no information of the date of the pregnancy outcome (n=81) and women with ectopic pregnancies (n=66) or mola hydatidosa (n=48). Furthermore, in cases where women participated in the cohort more than once (n=8,699), we only included the women's first pregnancy in the analyses to meet the criteria of independent observations in the statistical model. Consequently, 89,829 pregnancies were eligible for analyses in this study.

Figure 1: Flow-chart of the population included in this study

We used educational level, maternal income and labour market attachment as indicators of the pregnant women's socioeconomic position. This information was retrieved from national registers where the information of highest educational attainment, yearly income and predominant attachment to the labour market are registered on an individual level every year. We used the last information registered before the date of last menstruation period (LMP) of the actual pregnancy. The ISCED (International Standard Class of Education) codes from Statistics Denmark were converted into four educational groups, reflecting the highest completed academic educational attainment or – for women in education – the level completion of the actual education would lead to (see table 1). Labour market attachment was categorized as: employed, students, unemployed, disability-retired and unknown. To be categorized as unemployed, one had to be unemployed for more than 50% of the time in the year preceding conception. If the period of unemployment was less than half the year, one was categorized as employed. Income was grouped using quintiles based on the taxable income of the women the calendar year before year of LMP.

The outcome measure of interest was miscarriage, defined as death and expulsion of an intrauterine pregnancy before 22 weeks of pregnancy [21]. The gestational age was calculated using the self reported first day in the woman's last menstrual period, which was stated on the informed consent form. Information about the occurrence of miscarriage came primarily from the Danish National Patient Registry, where all women who had been diagnosed or treated in a hospital setting were registered. A small minority of the women had no pregnancy outcome in the Danish National Patient Registry, and for these we used information from the participant herself.

To study whether the possible association between socioeconomic position and the risk of miscarriage differed according to gestational age, miscarriage was divided into first and second

trimester of pregnancy, including miscarriages at 84 days of gestation in the first trimester miscarriages.

Statistical analyses

The hazard ratios (HR) of miscarriage according to three different measures of socioeconomic position were estimated using Cox regression analysis. Gestational age in days was used as the underlying time variable. We used a model with delayed entry, so that women entered the cohort on the gestational day of inclusion in the study. The follow-up ended at the gestational age at date of miscarriage, emigration, maternal death or the day the woman completed the first 22 weeks of gestation (154 days), whichever came first. We conducted three sets of analyses estimating the relations between maternal educational level, maternal labour market attachment, maternal income level, respectively and miscarriage. Individual level HR were calculated for each category in comparison to a reference category, defined as the category hypothesized to have the lowest risk of miscarriage. The risk association between the three measures of socioeconomic position and miscarriage was adjusted for maternal age at the time of conception (<25, 25-29, 30-34, 35-39, >/=40 years). Furthermore, we conducted a multivariate analysis where we included all three indicators of socioeconomic position and maternal age. We conducted trend tests for the association between the socioeconomic variables and the rate of miscarriage using Wald's test for trend. All statistical analyses were performed with the SAS software package version 9.2.

The DNBC data collection was approved by the Danish Scientific Ethics Committee and this particular study was, according to Danish legislation, approved by the Danish Data Protection Agency.

Results

The mean gestational age of recruitment to the study was 78 days, 10% were recruited before 49 days and 10% were recruited after 112 days of gestation. A total of 4,062 pregnancies resulted in a miscarriage. Of these, 2,146 were first trimester miscarriages and 1,916 were second trimester miscarriages.

Table 1: Socioeconomic characteristics of 89,829 women in the Danish National Birth Cohort according to age. Denmark, 1996-2002.

			Age				
			<25	25-29	30-34	35-39	40+
	n	%	%	%	%	%	%
Educational level							
BA or more (>12 years)	12,378	13.8	4.94	13.5	16.9	16.3	16.5
Higher edu. (less than BA degree)	26,627	29.6	13.8	31.8	31.9	34.1	36.7
Upper sec. edu. & vocational training	39,221	43.7	52.4	44.1	41.8	37.7	20.1
Compulsory school (<10 years)	10,753	11.9	27.9	9.7	8.4	10.9	13.9
Unknown	850	0.9	0.9	0.9	1.0	1.0	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Income quintile							
>80%	17,728	19.7	2.2	13.5	29.3	35.5	38.6
60-80%	17,725	19.7	8.9	19.8	23.4	22.4	19.5
40-60%	17,723	19.7	16.5	21.2	19.9	17.8	18.7
20-40%	17,724	19.7	28.3	22.5	15.2	12.8	10.8
<20%	17,772	19.7	42.9	21.9	10.8	9.9	9.7
Unknown	1,207	1.3	1.3	1.2	1.4	1.7	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Labour market attachment							
Employed	74,738	83.2	68.7	82.5	88.6	88.0	85.0
Student	6,584	7.3	16.0	9.2	3.2	2.1	1.1
Unemployed (> 50% of the year)	2,766	3.1	2.2	3,0	3.3	3.8	5.0
Disability pension	238	0.3	0.1	0.2	0.3	0.7	1.7
Unknown	5,503	6.1	13.4	5.2	4.6	5.5	7.1
n	89,829	100	12,449	37,114	29,864	9,420	982

Table 1 shows the distribution of the three socioeconomic indicators according to maternal age and demonstrates the expected strong association between age and socioeconomic position.

When examining the effect of age on the risk of miscarriage, we found different effects in the first and the second trimester, i.e. the proportional hazards assumption was not fulfilled for age. In the final regression analyses, we therefore stratified the effect of age according to trimester.

Table 2: The risk of miscarriage according to educational level, income level and labour market attachment, respectively, in the Danish National Birth Cohort. Risks are expressed in HR.

		Crude		Age adjusted	
Educational level (n=88,958)	No events	HR	95%CI	HR	95%CI
BA or more (>12 years)	589	1			
Higher edu. (less than BA degree)	1239	1,01	(0.92-1.11)	1,02	(0.93-1.13)
Upper sec. edu. & vocational training	1668	0,97	(0.88-1.06)	1,01	(0.92-1.11)
Compulsory school (<10 years)	527	1,14	(1.01-1.28)	1,19	(1.05-1.34)
Income quintile (n = 88,602)					
>80 %	785	1		1	
60 - 80 %	787	1,01	(0.91-1.11)	1,1	(0.99-1.21)
40 - 60%	796	1,03	(0.93-1.13)	1,15	(1.04-1.27)
20 - 40%	740	0,93	(0.84-1.03)	1,09	(0.99-1.22)
<20%	773	0,95	(0.86-1.05)	1,15	(1.03-1.27)
Employment status (n= 84,306)					
Employed	3398	1		1	
Student	295	0,91	(0.81-1.03)	1,03	(0.91-1.16)
Unemployed (>50% of the year)	128	1,04	(0.87-1.25)	1,01	(0.84-1.20)
Disability pension	17	1,61	(1.00-2.60)	1,32	(0.82-2.13)

The association between measures of socioeconomic position and miscarriage did not differ with trimester of pregnancy, why the overall associations between educational level, income and labour market attachment, respectively and miscarriage are presented. We found an inverse association between educational level and the risk of miscarriage (Table 2). Women with compulsory school as the highest educational level had an age adjusted HR of 1.19 (95%CI 1.05 to 1.34) for miscarriage when compared to women with a bachelor level or more (Table 2). Women in the four lowest income quintiles had an increased risk of miscarriage when compared with the group with the highest income level, though only two of the estimates reached statistical significance. Unemployed women and students had the same risk of miscarriage as the employed women. However, the group of women on disability pension had an increased risk of miscarriage compared to women who were employed (HR 1.32(95%CI 0.82 to 2.13)).

For educational level and income level we found significant trends (p-values = 0.01 and 0.04, respectively) while, for labour market attachment, there was no clear trend (p-value = 0.50).

Table 3: The association between miscarriage and educational level, income level and labour market attachment, respectively, in the Danish National Birth Cohort. Risks are expressed in HR and are adjusted for maternal age and mutually adjusted for the different indicators of socioeconomic position (n=83.470)

Educational level	HR	95%CI
BA or more (>12 years)	1	
Higher edu. (less than BA degree)	1.03	(0.91-1.11)
Upper sec. edu. & vocational training	1.01	(0.89-1.09)
Compulsory school (<10 years)	1.13	(0.98-1.29)
Income quintile		
>80 %	1	
60 - 80 %	1,09	(0.99-1.21)
40 - 60%	1,13	(1.02-1.26)
20 - 40%	1.11	(1.00-1.23)
<20%	1.13	(1.01-1.27)
Employment status		
Employed	1	
Student	1.02	(0.89-1.16)
Unemployed (>50% of the year)	0.95	(0.79-1.14)
Disability pension	0.99	(0.57-1.72)

A multivariate model where all three measures of socioeconomic position and maternal age were included revealed essentially the same results for income and educational level, while the elevated risk for women on disability pension disappeared (table 3).

Discussion

This study, based on data from all 89,829 women in the DNBC, displayed a social pattern in the risk of miscarriage. Educational level and income were both inversely associated with the risk of miscarriage.

Apart from maternal age, no life style risk factors for miscarriage are well established and few studies have examined the association between socioeconomic position and risk of miscarriage. A few previous studies have reported an association between socioeconomic position and miscarriage[7-10] when socioeconomic position was measured by educational level and labour market attachment, and others found no such association [11-14]. There are several possible explanations for this. Some studies are small with a diminished possibility of detecting a smaller association. Furthermore, two of these studies adjust for earlier miscarriage in their analyses[11;12]. Previous miscarriage is associated with a 60% higher risk of miscarriage[22], suggesting that women vary in their baseline risk for this negative pregnancy outcome. Adjusting for earlier miscarriage may therefore distort the possible association between socioeconomic position and (baseline) risk of miscarriage, as we find it less likely that previous miscarriage is a determinant of social position. Another possible explanation may be that only one of the studies uses prospectively collected data. Why do women with lower socioeconomic position have an increased risk of miscarriage? According to the association we have found between educational level and the risk of miscarriage, it

is possible that an overall healthier lifestyle among well educated women may explain part of the effect. This is not a fulfilling explanation though, since some of the typical lifestyle factors seem to be socially patterned in opposite directions in the DNBC. Smoking for instance is socially patterned, with women of low socioeconomic position smoking more than women of higher socioeconomic position, but studies on the effect of smoking on miscarriage risk are not consistent, and there are several studies reporting no effect of smoking on miscarriage risk [12;18;23]. Alcohol intake during pregnancy is also socially patterned and this exposure is strongly associated with the risk of miscarriage [19]. In the DNBC though, women with high socioeconomic position more frequently reported to have an alcohol intake during their pregnancies [24]. Therefore, typical lifestyle factors cannot solely explain the difference in miscarriage risk we find according to socioeconomic position.

It is known that the ability to make use of the health system depends upon educational level[25;26]. However, it is not clear how this may affect the risk of miscarriage since no preventive or curative measures for this negative pregnancy outcome is known. The association we found between income level and the risk of miscarriage is difficult to interpret. The risk is increased at more or less the same scale for all the income groups compared to the group with the highest income level. A possible explanation could be that the Danish population is relatively homogeneous according to income as compared to other populations[27], and therefore an association would be clearer in countries with a greater distinction in living circumstances between rich and poor[28]. What we wished to examine, looking at the women's employment status before they got pregnant, was whether being outside the labour market had any influence on ones risk of miscarriage. This seems not to be the case. One reasonable explanation might be that in Denmark there is a high social security for people outside the labour market. Another speculation could be that being outside the

labour market pose a social risk, while being at the labour market pose several occupational risks and that these risks outweigh each other. The apparently elevated risk of miscarriage for women on disability pension is not surprising, given these women are of remarkable worse health than the rest of the study population. However, the association seems to disappear when we adjust for income and educational level. A possible explanation for this may be that that these women all have a low income and that mutually adjustment in this case probably is over adjustment.

The present study is based upon a large population and a considerable number of miscarriages, which offers a good foundation to examine the association between different indicators of socioeconomic position and miscarriage. Cohort studies are potentially subject to selection bias due to loss to follow-up. This is a minor issue in this study, since 99.9% of the pregnancy outcomes have been identified. The information we have on the exposure measures are based upon register data which covers almost the whole population, and is therefore not dependent upon the outcome of the pregnancy. To study miscarriage is difficult, since a great part of miscarriages happen very early in the pregnancy period – many even before the women themselves know that they are pregnant[29]. This implies that many women do not have a chance to be recruited for pregnancy cohorts before the miscarriage. The potential bias arising from that fact is taken care of by applying survival analyses with left truncation and gestational age as time variable, but this is why the proportion of pregnancies ending in miscarriage in the DNBC is less than reported in the background population and this is also the explanation why we are restricted from being able to conclude anything about the association between socioeconomic position and the very early miscarriages before gestational week 6.

The women participating in the DNBC seem to be somewhat healthier than the rest of the population[30], though the difference is very moderate and the estimated effect upon the risk estimates

obtained in internal comparisons are small. This means that it should be possible to transfer findings based upon the DNBC to the background population. It cannot be excluded though that there is some bias related to selection and, if so, our results are most likely underestimated.

In this study, we were interested in the overall effect of socioeconomic position on the risk of miscarriage. We did not adjust our analyses for typical lifestyle factors, e.g. smoking, alcohol consumption, and body mass index, since we believe them to play a role as mediating factors between socioeconomic position and the risk of miscarriage. Conditioning on an intermediate will only be of interest if one wishes to examine something different from the overall effect, i.e. the direct effects of the exposure on the outcome [31]. In contrast, maternal age is a strong independent risk factor for miscarriage[32] and is also causally related to social position, and consequently we believe that the age-adjusted analyses provide the most accurate estimates.

Conclusion

In this large cohort study we found an inverse association between measures of socioeconomic position and the risk of miscarriage. These findings indicate that at least some of the miscarriages are preventable and highlights the need for further studies addressing which behavioural and environmental exposures, concentrated in groups with lower socioeconomic position, that are causal risk factors for miscarriage.

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CONTRIBUTORS

A-MNA initiated the study. Study design and analytical strategy were developed by all authors. FNN, LE, SaR made the data management and statistical analyses, supervised by PKA. FNN wrote the first version of the paper and all authors took part in the revision. All authors have seen and approved the final version of the paper.

COMPETING INTERESTS

All authors declare that the answer to the questions on your competing interest form (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

EXCLUSIVE LICENCE

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DATA SHARING STATEMENT

There is no additional data available.

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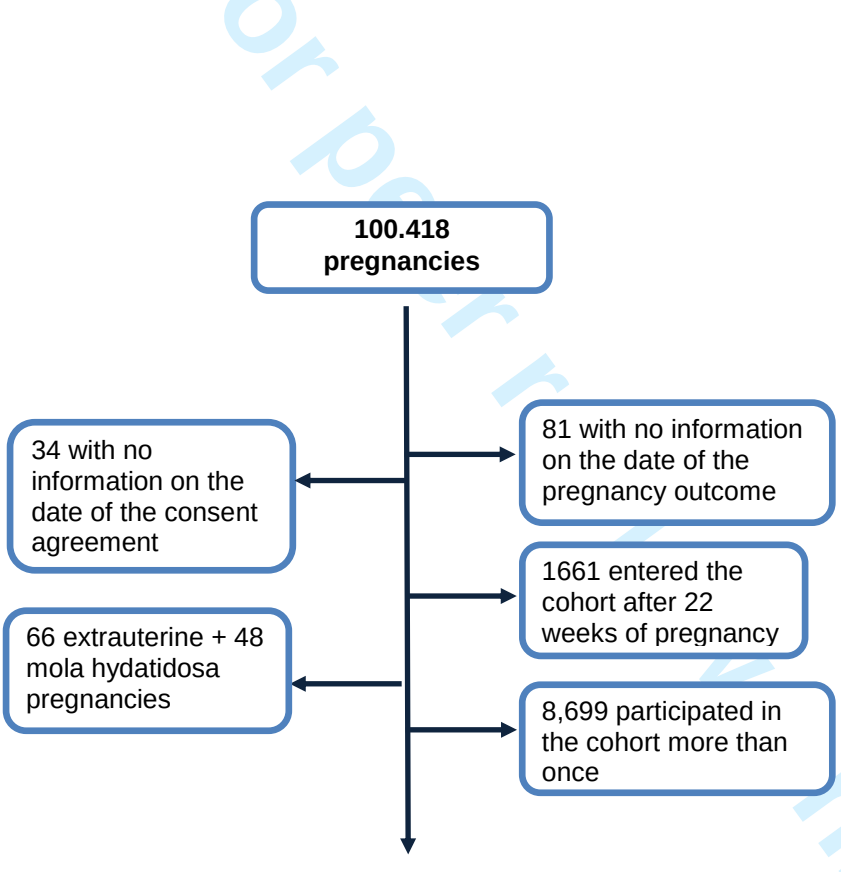

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Main outcome measure: Miscarriage, i.e. fetal death within the first 22 weeks of pregnancy, was the outcome of interest. We estimated Hazard Ratios (HR) of miscarriage using Cox regression analysis with gestational age as the underlying time scale.

Results: Women with <10 years of education had an elevated risk of miscarriage when compared to women with >12 years of education (HR 1.19 (95%CI 1.05 to 1.34)). The HR estimates for the four lowest income quintiles were all increased (HRs between 1.09 and 1.15) as compared to the upper quintile, but did not differ considerably from each other. In general, no statistically significant association was found between labour market attachment and the risk of miscarriage, however, the group of women on disability pension had an increased HR of miscarriage when compared to women who were employed (HR 1.32 (95%CI 0.82 to 2.13)).

Conclusion: Educational level and income were inversely associated with the risk of miscarriage. As these factors most likely are non-causally related to miscarriage, the findings indicate that factors related to social position, probably of the environmental and behavioural type, may affect miscarriage risk. The study highlights the need for studies addressing such exposures in order to prevent miscarriages.

Introduction

Social inequality is demonstrated in most reproductive outcomes, such as preterm birth, intrauterine growth retardation and stillbirth [1;1-4]. This inequality indicates a preventive potential, since the minimum level of these outcomes, in theory, should be attainable for all groups in society. Miscarriage, i.e. fetal death before 22 gestational weeks, is the most frequent adverse pregnancy outcome and affects many women and their relatives. Approximately one out of six clinically recognized pregnancies result in miscarriage[5;6] and identification of even a small potential for prevention may have significant impact for public health.

Given the commonness of miscarriage, surprisingly few studies have investigated the relationship with socioeconomic position, and no consensus about any association has been established. It has been shown that women with low socioeconomic position have an increased risk of miscarriage when measured by educational attainment [7-10] while other studies have not supported this finding [11-13]. When social position has been measured by labour market attachment the associations seem even more unclear [7;12-14]. Two studies that used income as a proxy measure of socioeconomic position did not find an association with the risk of miscarriage [10;13]. The risk of miscarriage according to potential risk factors that are known to display a social gradient, such as alcohol drinking during pregnancy and smoking, have been examined individually [12;15-18 19], but with no consistent results. By examining how different measures of socioeconomic position are associated with the risk of miscarriage, we might be able to come closer to identification of more proximal causal risk factors for miscarriage.

The aim of this study is to describe how educational level, income, and labour market attachment, respectively, are related to the risk of miscarriage in a large cohort study.

Methods

We used data from the Danish National Birth Cohort (DNBC) which comprises of 100,418 pregnancies recruited in the years 1996-2002. The pregnant women were invited to participate in the cohort at the first antenatal visit at the general practitioner. The women were included in the study if they had posted the informed consent form before gestational week 24, intended to carry the pregnancy to term and were able to complete a telephone interview in Danish. The DNBC is described in details elsewhere[20].

For this study, we excluded women with no information on the date of the consent agreement (n=34), women who entered the cohort after 22 weeks of pregnancy (n=1661), women with no information of the date of the pregnancy outcome (n=81) and women with ectopic pregnancies (n=66) or mola hydatidosa (n=48). Furthermore, in cases where women participated in the cohort more than once (n=8,699), we only included the women's first pregnancy in the analyses to meet the criteria of independent observations in the statistical model. Consequently, 89,829 pregnancies were eligible for analyses in this study.

Figure 1: Flow-chart of the population included in this study

We used educational level, maternal income and labour market attachment as indicators of the pregnant women's socioeconomic position. This information was retrieved from national registers where the information of highest educational attainment, yearly income and predominant attachment to the labour market are registered on an individual level every year. We used the last information registered before the date of last menstruation period (LMP) of the actual pregnancy. The ISCED (International Standard Class of Education) codes from Statistics Denmark were converted into four educational groups, reflecting the highest completed academic educational attainment or – for women in education – the level completion of the actual education would lead to (see table 1). Labour market attachment was categorized as: employed, students, unemployed, disability-retired and unknown. To be categorized as unemployed, one had to be unemployed for more than 50% of the time in the year preceding conception. If the period of unemployment was less than half the year, one was categorized as employed. Income was grouped using quintiles based on the taxable income of the women the calendar year before year of LMP.

The outcome measure of interest was miscarriage, defined as death and expulsion of an intrauterine pregnancy before 22 weeks of pregnancy [21]. The gestational age was calculated using the self reported first day in the woman's last menstrual period, which was stated on the informed consent form. Information about the occurrence of miscarriage came primarily from the Danish National Patient Registry, where all women who had been diagnosed or treated in a hospital setting were registered. A small minority of the women had no pregnancy outcome in the Danish National Patient Registry, and for these we used information from the participant herself.

To study whether the possible association between socioeconomic position and the risk of miscarriage differed according to gestational age, miscarriage was divided into first and second

trimester of pregnancy, including miscarriages at 84 days of gestation in the first trimester miscarriages.

Statistical analyses

The hazard ratios (HR) of miscarriage according to three different measures of socioeconomic position were estimated using Cox regression analysis. Gestational age in days was used as the underlying time variable. We used a model with delayed entry, so that women entered the cohort on the gestational day of inclusion in the study. The follow-up ended at the gestational age at date of miscarriage, emigration, maternal death or the day the woman completed the first 22 weeks of gestation (154 days), whichever came first. We conducted three sets of analyses estimating the relations between maternal educational level, maternal labour market attachment, maternal income level, respectively and miscarriage. Individual level HR were calculated for each category in comparison to a reference category, defined as the category hypothesized to have the lowest risk of miscarriage. The risk association between the three measures of socioeconomic position and miscarriage was adjusted for maternal age at the time of conception (<25, 25-29, 30-34, 35-39, >/=40 years). Furthermore, we conducted a multivariate analysis where we included all three indicators of socioeconomic position and maternal age. We conducted trend tests for the association between the socioeconomic variables and the rate of miscarriage using Wald's test for trend. All statistical analyses were performed with the SAS software package version 9.2.

The DNBC data collection was approved by the Danish Scientific Ethics Committee and this particular study was, according to Danish legislation, approved by the Danish Data Protection Agency.

Results

The mean gestational age of recruitment to the study was 78 days, 10% were recruited before 49 days and 10% were recruited after 112 days of gestation. A total of 4,062 pregnancies resulted in a miscarriage. Of these, 2,146 were first trimester miscarriages and 1,916 were second trimester miscarriages.

Table 1: Socioeconomic characteristics of 89,829 women in the Danish National Birth Cohort according to age. Denmark, 1996-2002.

			Age				
			<25	25-29	30-34	35-39	40+
	n	%	%	%	%	%	%
Educational level							
BA or more (>12 years)	12,378	13.8	4.94	13.5	16.9	16.3	16.5
Higher edu. (less than BA degree)	26,627	29.6	13.8	31.8	31.9	34.1	36.7
Upper sec. edu. & vocational training	39,221	43.7	52.4	44.1	41.8	37.7	20.1
Compulsory school (<10 years)	10,753	11.9	27.9	9.7	8.4	10.9	13.9
Unknown	850	0.9	0.9	0.9	1.0	1.0	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Income quintile							
>80%	17,728	19.7	2.2	13.5	29.3	35.5	38.6
60-80%	17,725	19.7	8.9	19.8	23.4	22.4	19.5
40-60%	17,723	19.7	16.5	21.2	19.9	17.8	18.7
20-40%	17,724	19.7	28.3	22.5	15.2	12.8	10.8
<20%	17,772	19.7	42.9	21.9	10.8	9.9	9.7
Unknown	1,207	1.3	1.3	1.2	1.4	1.7	2.8
n	89,829	100	12,449	37,114	29,864	9,420	982
Labour market attachment							
Employed	74,738	83.2	68.7	82.5	88.6	88.0	85.0
Student	6,584	7.3	16.0	9.2	3.2	2.1	1.1
Unemployed (> 50% of the year)	2,766	3.1	2.2	3,0	3.3	3.8	5.0
Disability pension	238	0.3	0.1	0.2	0.3	0.7	1.7
Unknown	5,503	6.1	13.4	5.2	4.6	5.5	7.1
n	89,829	100	12,449	37,114	29,864	9,420	982

Table 1 shows the distribution of the three socioeconomic indicators according to maternal age and demonstrates the expected strong association between age and socioeconomic position.

When examining the effect of age on the risk of miscarriage, we found different effects in the first and the second trimester, i.e. the proportional hazards assumption was not fulfilled for age. In the final regression analyses, we therefore stratified the effect of age according to trimester.

Table 2: The risk of miscarriage according to educational level, income level and labour market attachment, respectively, in the Danish National Birth Cohort. Risks are expressed in HR.

		Crude		Age adjusted	
Educational level (n=88,958)	No events	HR	95%CI	HR	95%CI
BA or more (>12 years)	589	1			
Higher edu. (less than BA degree)	1239	1,01	(0.92-1.11)	1,02	(0.93-1.13)
Upper sec. edu. & vocational training	1668	0,97	(0.88-1.06)	1,01	(0.92-1.11)
Compulsory school (<10 years)	527	1,14	(1.01-1.28)	1,19	(1.05-1.34)
Income quintile (n = 88,602)					
>80 %	785	1		1	
60 - 80 %	787	1,01	(0.91-1.11)	1,1	(0.99-1.21)
40 - 60%	796	1,03	(0.93-1.13)	1,15	(1.04-1.27)
20 - 40%	740	0,93	(0.84-1.03)	1,09	(0.99-1.22)
<20%	773	0,95	(0.86-1.05)	1,15	(1.03-1.27)
Employment status (n= 84,306)					
Employed	3398	1		1	
Student	295	0,91	(0.81-1.03)	1,03	(0.91-1.16)
Unemployed (>50% of the year)	128	1,04	(0.87-1.25)	1,01	(0.84-1.20)
Disability pension	17	1,61	(1.00-2.60)	1,32	(0.82-2.13)

The association between measures of socioeconomic position and miscarriage did not differ with trimester of pregnancy, why the overall associations between educational level, income and labour market attachment, respectively and miscarriage are presented. We found an inverse association between educational level and the risk of miscarriage (Table 2). Women with compulsory school as the highest educational level had an age adjusted HR of 1.19 (95%CI 1.05 to 1.34) for miscarriage when compared to women with a bachelor level or more (Table 2). Women in the four lowest income quintiles had an increased risk of miscarriage when compared with the group with the highest income level, though only two of the estimates reached statistical significance. Unemployed women and students had the same risk of miscarriage as the employed women. However, the group of women on disability pension had an increased risk of miscarriage compared to women who were employed (HR 1.32(95%CI 0.82 to 2.13)).

For educational level and income level we found significant trends (p-values = 0.01 and 0.04, respectively) while, for labour market attachment, there was no clear trend (p-value = 0.50).

Table 3: The association between miscarriage and educational level, income level and labour market attachment, respectively, in the Danish National Birth Cohort. Risks are expressed in HR and are adjusted for maternal age and mutually adjusted for the different indicators of socioeconomic position (n=83.470)

Educational level	HR	95%CI
BA or more (>12 years)	1	
Higher edu. (less than BA degree)	1.03	(0.91-1.11)
Upper sec. edu. & vocational training	1.01	(0.89-1.09)
Compulsory school (<10 years)	1.13	(0.98-1.29)
Income quintile		
>80 %	1	
60 - 80 %	1,09	(0.99-1.21)
40 - 60%	1,13	(1.02-1.26)
20 - 40%	1.11	(1.00-1.23)
<20%	1.13	(1.01-1.27)
Employment status		
Employed	1	
Student	1.02	(0.89-1.16)
Unemployed (>50% of the year)	0.95	(0.79-1.14)
Disability pension	0.99	(0.57-1.72)

A multivariate model where all three measures of socioeconomic position and maternal age were included revealed essentially the same results for income and educational level, while the elevated risk for women on disability pension disappeared (table 3).

Discussion

This study, based on data from all 89,829 women in the DNBC, displayed a social pattern in the risk of miscarriage. Educational level and income were both inversely associated with the risk of miscarriage.

Apart from maternal age, no life style risk factors for miscarriage are well established and few studies have examined the association between socioeconomic position and risk of miscarriage. A few previous studies have reported an association between socioeconomic position and miscarriage[7-10] when socioeconomic position was measured by educational level and labour market attachment, and others found no such association [11-14]. There are several possible explanations for this. Some studies are small with a diminished possibility of detecting a smaller association. Furthermore, two of these studies adjust for earlier miscarriage in their analyses[11;12]. Previous miscarriage is associated with a 60% higher risk of miscarriage[22], suggesting that women vary in their baseline risk for this negative pregnancy outcome. Adjusting for earlier miscarriage may therefore distort the possible association between socioeconomic position and (baseline) risk of miscarriage, as we find it less likely that previous miscarriage is a determinant of social position. Another possible explanation may be that only one of the studies uses prospectively collected data. Why do women with lower socioeconomic position have an increased risk of miscarriage? According to the association we have found between educational level and the risk of miscarriage, it

is possible that an overall healthier lifestyle among well educated women may explain part of the effect. This is not a fulfilling explanation though, since some of the typical lifestyle factors seem to be socially patterned in opposite directions in the DNBC. Smoking for instance is socially patterned, with women of low socioeconomic position smoking more than women of higher socioeconomic position, but studies on the effect of smoking on miscarriage risk are not consistent, and there are several studies reporting no effect of smoking on miscarriage risk [12;18;32]. Alcohol intake during pregnancy is also socially patterned and this exposure is strongly associated with the risk of miscarriage [19]. In the DNBC though, women with high socioeconomic position more frequently reported to have an alcohol intake during their pregnancies [23]. Therefore, typical lifestyle factors cannot solely explain the difference in miscarriage risk we find according to socioeconomic position.

It is known that the ability to make use of the health system depends upon educational level[24;25]. However, it is not clear how this may affect the risk of miscarriage since no preventive or curative measures for this negative pregnancy outcome is known. The association we found between income level and the risk of miscarriage is difficult to interpret. The risk is increased at more or less the same scale for all the income groups compared to the group with the highest income level. A possible explanation could be that the Danish population is relatively homogeneous according to income as compared to other populations[26], and therefore an association would be clearer in countries with a greater distinction in living circumstances between rich and poor[27]. What we wished to examine, looking at the women's employment status before they got pregnant, was whether being outside the labour market had any influence on ones risk of miscarriage. This seems not to be the case. One reasonable explanation might be that in Denmark there is a high social security for people outside the labour market. Another speculation could be that being outside the

labour market pose a social risk, while being at the labour market pose several occupational risks and that these risks outweigh each other. The apparently elevated risk of miscarriage for women on disability pension is not surprising, given these women are of remarkable worse health than the rest of the study population. However, the association seems to disappear when we adjust for income and educational level. A possible explanation for this may be that that these women all have a low income and that mutually adjustment in this case probably is over adjustment.

The present study is based upon a large population and a considerable number of miscarriages, which offers a good foundation to examine the association between different indicators of socioeconomic position and miscarriage. Cohort studies are potentially subject to selection bias due to loss to follow-up. This is a minor issue in this study, since 99.9% of the pregnancy outcomes have been identified. The information we have on the exposure measures are based upon register data which covers almost the whole population, and is therefore not dependent upon the outcome of the pregnancy. To study miscarriage is difficult, since a great part of miscarriages happen very early in the pregnancy period – many even before the women themselves know that they are pregnant[28]. This implies that many women do not have a chance to be recruited for pregnancy cohorts before the miscarriage. The potential bias arising from that fact is taken care of by applying survival analyses with left truncation and gestational age as time variable, but this is why the proportion of pregnancies ending in miscarriage in the DNBC is less than reported in the background population and this is also the explanation why we are restricted from being able to conclude anything about the association between socioeconomic position and the very early miscarriages before gestational week 6.

The women participating in the DNBC seem to be somewhat healthier than the rest of the population[29], though the difference is very moderate and the estimated effect upon the risk estimates

obtained in internal comparisons are small. This means that it should be possible to transfer findings based upon the DNBC to the background population. It cannot be excluded though that there is some bias related to selection and, if so, our results are most likely underestimated.

In this study, we were interested in the overall effect of socioeconomic position on the risk of miscarriage. We did not adjust our analyses for typical lifestyle factors, e.g. smoking, alcohol consumption, and body mass index, since we believe them to play a role as mediating factors between socioeconomic position and the risk of miscarriage. Conditioning on an intermediate will only be of interest if one wishes to examine something different from the overall effect, i.e. the direct effects of the exposure on the outcome [30]. In contrast, maternal age is a strong independent risk factor for miscarriage[31] and is also causally related to social position, and consequently we believe that the age-adjusted analyses provide the most accurate estimates.

Conclusion

In this large cohort study we found an inverse association between measures of socioeconomic position and the risk of miscarriage. These findings indicate that at least some of the miscarriages are preventable and highlights the need for further studies addressing which behavioural and environmental exposures, concentrated in groups with lower socioeconomic position, that are causal risk factors for miscarriage.

What is already known on this topic
Social inequality is found in most reproductive outcomes, such as preterm birth, small for gestational age and stillbirth. Around one out of six clinically recognized pregnancies result in a miscarriage. The relationship between socioeconomic position and the risk of miscarriage is not well established.
What this paper adds
Women of lower socioeconomic position seem to have an elevated risk of miscarriage. This indicates that a proportion of miscarriages may be preventable.

ACKNOWLEDGEMENTS

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CONTRIBUTORS

A-MNA initiated the study. Study design and analytical strategy were developed by all authors. FNN, LE, SaR made the data management and statistical analyses, supervised by PKA. FNN wrote the first version of the paper and all authors took part in the revision. All authors have seen and approved the final version of the paper.

COMPETING INTERESTS

All authors declare that the answer to the questions on your competing interest form (http://bmj.com/cgi/content/full/317/7154/291/DC1) are all No and therefore have nothing to declare.

EXCLUSIVE LICENCE

DATA SHARING STATEMENT

There is no additional data available.

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*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
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
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
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
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
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
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
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
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

*Give information separately for exposed and unexposed groups.

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 http://www.strobe-statement.org.