



ORIGINAL ARTICLE

Spontaneous abortion: A prospective cohort study of younger women from the general population in Denmark. Validation, occurrence and risk determinants

L. $BUSS^1$, J. $TOLSTRUP^{2,3}$, C. $MUNK^1$, T. $BERGHOLT^4$, B. $OTTESEN^5$, M. $GRØNBÆK^{2,3}$ & S. K. $KJAER^1$

¹Department of Virus, Hormones and Cancer, Institute of Cancer Epidemiology, Danish Cancer Society, ²Danish Epidemiology Science Centre at the Institute of Preventive Medicine, Kommunehospitalet, ³Centre for Alcohol Research, National Institute of Public Health, ⁴Department of Obstetrics and Gynaecology, Hvidovre University Hospital, and ⁵Department of Obstetrics and Gynaecology, Rigshospitalet, Copenhagen, Denmark

Abstract

Objective. To assess the occurrence of spontaneous abortion, comparing two different data sources. To estimate the rate of spontaneous abortion over a 2-year period, and examine potential predictors of the risk for incident spontaneous abortion. Methods. We used interview data from a population-based prospective cohort study comprising 11,088 women and data from a linkage of the cohort with the Hospital Discharge Register to compare spontaneous abortions as reported in the interview with those identified in the register. Based on interview data, we estimated the rate of spontaneous abortion during the two-year follow-up. Finally, risk determinants for incident spontaneous abortion were analyzed by means of logistic regression. Results. A total of 654 spontaneous abortions before enrolment in the study were reported by the women compared to 531 abortions found in the register. More than 80% of the spontaneous abortions identified from both sources were recorded in the same year. During follow-up a total of 20.9% of pregnancies intended to be carried to term ended as a spontaneous abortion. In the risk factor analysis, we found that previous spontaneous abortion, being single, never having used oral contraceptives, and use of intrauterine device were associated with increased risk of subsequent spontaneous abortion. In addition, it was indicated that a short interpregnancy interval following a spontaneous abortion may confer an increased risk of abortion in the subsequent pregnancy. Conclusion. We found a high rate of spontaneous abortion in the present study and an acceptable agreement between information obtained by interview and register information. More than 25% of the spontaneous abortions were only reported by the women, and this could not be explained by erroneously reported induced abortions, and may be early, nonhospitalized abortions. We confirm that number of previous spontaneous abortions is a strong determinant, and our data may also indicate a role of previous contraceptive habits. A role of the length of interpregnancy interval in the risk of spontaneous abortion cannot be ruled out.

Key words: Prospective, spontaneous abortion, occurrence, risk factors, Danish women

Introduction

Several studies of the incidence of spontaneous abortions have been based on either self-reported data from selected populations or on data from administrative registers. Very few population-based studies have been published (1).

The number of spontaneous abortions will tend to be underestimated when using data from the registers as these only contain information on hospitalized abortions. However, it is a strength of the register-based studies that selection bias because of non-response and information bias can be ruled out. In contrast, differential misclassification may still exist if specific groups of women are more likely than others to be admitted to hospital for spontaneous abortion.

Correspondence: Susanne Krüger Kjær, Department of Virus, Hormones and Cancer, Institute of Cancer Epidemiology, Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen, Denmark. E-mail: susanne@cancer.dk

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By using questionnaires or interviews it is theoretically possible to obtain information on all previous spontaneous abortions. (i.e. both hospitalized and nonhospitalized). However, the questionnaire data may be weakened by selection bias due to nonresponse. Furthermore, as most questionnaire studies have a retrospective design, they may be less reliable due to recall bias.

It is the aim of the present study to asses the occurrence of spontaneous abortions and to compare the results with two different data sources: self-reported data obtained through a personal interview, and data obtained from a computer linkage with the Danish Hospital Discharge Register. We also estimated the rate of spontaneous abortions over a 2-year period, and finally we examined different factors, primarily reproductive and sexual factors, which could potentially be predictors of the risk for subsequent spontaneous abortion.

Material and methods

Study population

First examination (enrolment). From May 1991 to January 1993 we established a population-based cohort of Danish women with the overall aim of assessing the role of human papillomavirus infections for development of cervical neoplasia. Details about the enrolment procedure have been described previously (2). Briefly, a random sample of 17,949 women (20-29 years of age) was drawn from the general female population living in Copenhagen by means of the computerized Central Population Register. A total of 1,643 women had moved out of the study area before contact. During a 1.5-year period, 11,088 women (68%) were included in the study. The study was approved by the Scientific Ethical Committee of Copenhagen and Frederiksberg Municipality, Denmark.

Second examination (follow-up). About 2 years after the enrolment, the entire cohort was invited for a second examination, and from October 1993 to January 1995, 8,656 women (\sim 80%) were included in the second phase of the study.

Interviews

Besides having a gynecological examination and blood samples taken, all participants were interviewed by female interviewers (nurses) especially trained for this task. Both at enrolment and at follow-up, the interview included questions about demographic variables, contraceptive use, sexual habits, cervical screening history, smoking habits, and previous sexually transmitted diseases. Information about reproductive history including number of pregnancies, year of each pregnancy, outcome of each pregnancy (live birth, still birth, ectopic pregnancy, induced abortion, and spontaneous abortion) was also collected.

Register linkage

Since 1968, all Danish inhabitants have been assigned a unique personal identification number, comprising information on sex and date of birth. These identification numbers are registered in the computerized Central Population Register, and allow correct linkage of information between different sources or registers. The study cohort of 11,088 women was linked to the population-based Danish Hospital Discharge Register, which contains data on virtually all (~99%) the somatic hospitalizations in Denmark since 1977 (3,4). For each discharge, this computerized register contains information (related to the personal identification number of the patient) on the dates of admission/discharge, up to 20 diagnoses, and every surgical procedure performed during the respective admission.

By means of the linkage, we obtained information on all hospitalized spontaneous abortions since January 1977 (when the women in the cohort were between 6 and 13 years of age). The diagnoses are recorded and classified according to the International Classification of Diseases, 8th and 10th revision, and the coding numbers included to define spontaneous abortion in this study include the following ICD-8 codes: 634.61, 643, 644, 645.1, and 645.7, and ICD-10 codes: O01.1, O02.0, O02.1, O02.9, and O03. The birth diagnoses include the following ICD-8 codes: 650–666, and ICD-10 codes: O60, O63–O70, and O80–O84.

Data analysis

Comparison of interview data with Hospital Discharge Register data. In the present study, we compared the information on previous spontaneous abortions as provided by the participants at the enrolment interview with the information covering the same period registered in the Hospital Discharge Register. In the Hospital Discharge Registry the exact date of the spontaneous abortion was provided whereas only the year was available from the interview. If a spontaneous abortion was recorded from both sources (interview and Hospital Discharge Registry), it was considered to occur in the same year, if the year provided by the woman in the interview was the same as registered in the Hospital Discharge

Register +/- one month (i.e. December in the previous year to January in the next year).

Occurrence of spontaneous abortions. Based on interview data from the first examination and the second examination, we estimated the rate of spontaneous abortions during the follow-up period as a proportion of all pregnancies intended to be carried to term i.e. number of spontaneous abortions divided by the sum of number of live births, still births, spontaneous abortions and ectopic pregnancies. Women who were pregnant at enrolment were excluded from this analysis. Among women who were pregnant at the second examination, we only included those who were ≥28 weeks pregnant. In the same way, the rate of spontaneous abortions was estimated based on data from the Hospital Discharge Register.

Risk determinants for spontaneous abortion. We also examined risk determinants for incident spontaneous abortions in the follow-up period between the two examinations (mean time 2.1 years (range: 1.6-3.4 years)) in women who were not currently pregnant at enrolment in the study. Cases were defined as women who at the second interview reported a spontaneous abortion between the two examinations and/or had been registered in the Hospital Discharge Register with a diagnosis of spontaneous abortion during this time period. The group of non-cases included women who at the second interview reported to have given birth between the two interviews or were pregnant ≥28 weeks of gestation and/or were registered with a birth diagnosis in the Hospital Discharge Register in the same time period or during the following 12 weeks after the time of the second interview (corresponding to being ≥28 weeks pregnant at the time of the second interview). If a woman experienced both a spontaneous abortion and a live birth, the first occurring event defined her case/noncase status.

For women (both cases and non-cases) who did not participate in the second phase of the study, the follow-up period was defined as the mean time between the two examinations among women who participated on both occasions, and they were followed up by register linkage only.

Finally, we assessed the association between interpregnancy interval and risk of spontaneous abortion. We had no information on gestational length, so we estimated the time of conception by subtracting 9 weeks from the date of spontaneous abortion, and 40 weeks from the date of childbirth. As the exact date of termination of the respective pregnancy was not obtained at the interview, only women registered in the Hospital Discharge Register could be included in the interpregnancy analyses.

The association between a potential risk determinant and spontaneous abortion was analyzed using multivariate logistic regression with simultaneous adjustment for possible confounders. A variable was retained in the statistical model if it was significantly associated with the outcome or if it affected the estimates of the other variables. The measure of association was the odds ratio (OR) with 95% confidence interval (CI). We have previously reported on the association between spontaneous abortion and alcohol and caffeine consumption in the same population, but are restricted to those women replying to a dietary questionnaire (5). As adjustment for neither alcohol nor caffeine intake changed the findings in the present paper, only results from the larger, nonrestricted data analysis are presented in this paper.

Results

Comparison of interview data with Hospital Discharge Register data

In all, 575 women reported 654 spontaneous abortions occurring before enrolment in the study (Table I). According to the Hospital Discharge Register, 479 women had experienced 531 spontaneous abortions in that period. Most of the spontaneous abortions (n=459) were identified from both sources. However, 195 abortions were only reported by the women, and fewer (n=72)were only registered in the Hospital Discharge Register.

In the group of 459 abortions identified by the women as well as in the Hospital Discharge Register, 373 abortions (81%) were recorded in the same calendar year. In 67 abortions (15%),

Table I. Previous spontaneous abortions as reported in a personal interview and/or registered in the Danish Hospital Discharge Register among 11,088 women aged 20-29 years

| D1 | Hospital Discharge Register | | | | | |
|-----------------------|-----------------------------|-----------|-----------|--|--|--|
| Personal interview | Ever spontaneous abortion | | | | | |
| | Yes | No | Total | | | |
| Yes | 459 (408)* | 195 (167) | 654 (575) | | | |
| No | 72 (71) | | | | | |
| Total | 531 (479) | | | | | |

^{*}Number of women in parentheses.

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there was a one-year difference, and in 19 abortions (4%), a two-year difference was observed (data not shown).

Among the 195 spontaneous abortions only reported by the women, 4 had a record of extrauterine pregnancy in the same time period in the Hospital Discharge Register, 10 had a record of legally induced abortion, and 181 had no gynecologic or obstetric record in the Hospital Discharge Register (data not shown).

In Table II, the 72 spontaneous abortions that were only found in the Hospital Discharge Register, are shown. A total of 55 abortions were classified as *abortus alius definitus* (ICD-8: 643.80) or just *spontaneous abortion* (ICD-8: 643.90). In this group, 23 were reported by the women as induced abortion; two as extrauterine pregnancy; and in 30 cases, no reproductive outcome was reported. Among the six abortions coded in the registry as *missed abortion*, five were reported by the women as induced abortion and one as a stillbirth. Finally, there were 11 cases with an unspecific abortion diagnosis, *abortion ut provocatus et spontaneous non indicatus* (ICD-8: 644.9). These were all reported in the interview as induced abortions.

Occurrence of spontaneous abortions

In the period between the first and the second examination, 2,433 pregnancies occurred in the cohort as reported by the women. Of these, 312 pregnancies were present at the second examination but had lasted for less than 28 weeks and were thus excluded, leaving 2,121 pregnancies for study. A total of 499 pregnancies ended as an induced abortion and consequently there were 1,622

Table II. Types of discrepancies in the 72 spontaneous abortions only registered in the Hospital Discharge Register as spontaneous abortions

| Diagnosis in the Hospital Discharge Register | Diagnosis as reported by the women in the interview |
|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| Spontaneous abortion (ICD-8 codes: 643.80; 643.90) (<i>n</i> = 55) | Induced abortion $(n = 23)$ Extrauterine pregnancy $(n = 2)$ No reproductive event reported $(n = 30)$ |
| Missed abortion (ICD-8 code: 634.10) | Induced abortion $(n=5)$ Stillbirth $(n=1)$ |
| Abortion, spontaneous or induced (ICD-8-code: 644.9) (n = 11) | Induced abortion $(n=11)$ |

pregnancies that were intended to be carried to term. All in all, 339 (20.9%) of the pregnancies ended as spontaneous abortions, 36 (2.2%) were extrauterine pregnancies, and 1,247 pregnancies (76.9%) resulted in childbirths. When the spontaneous abortions were assessed in the same way on the basis of the Hospital Discharge Register data, the spontaneous abortion rate was 16.3%.

Risk determinants for incident spontaneous abortion

A total of 343 women reported and/or were registered with a spontaneous abortion in the follow-up period and were thus defined as cases. Likewise, 1,578 experienced a live birth and constituted the non-cases. In Table III the odds ratios for incident spontaneous abortion associated with a variety of factors are shown. Age was related to the risk of spontaneous abortion, the OR being 1.5 (95% CI: 1.1-2.2) for 20-23-year-old women compared to older women (27-29 years of age). Similarly, marital status was a significant risk factor whereas schooling was not related to the risk of subsequent spontaneous abortion. Ever having experienced an induced abortion was not strongly related to the risk of subsequent spontaneous abortion. In contrast, history of two or more previous spontaneous abortions was strongly associated with an increased risk (OR = 2.3; 95% CI: 1.1-4.5), also when adjustment was made for total number of previous pregnancies and/or previous induced abortions (data not shown). Number of pregnancies in itself was also a significant risk factor in the univariate analysis, but after adjustment for other risk factors, including number of previous spontaneous abortions, no association remained.

While having ever used oral contraceptives seemed to decrease the risk of incident spontaneous abortion (OR = 0.8; 95% CI: 0.6-1.0), previous use of intrauterine devices (IUD) significantly increased the risk (OR = 1.3; 95% CI: 1.0-1.8), however none of the trends for duration reached statistical significance. In contrast, neither previous pelvic inflammatory disease, self-reported chlamydia infection nor lifetime number of sexual partners were related to the risk of spontaneous abortion. The overall risk factor pattern did not change when the analysis was restricted to include either only the women with self-reported spontaneous abortion or only women with a spontaneous abortion registered in the Hospital Discharge Register (data not shown).

The effect of different interpregnancy intervals on the outcome of the subsequent pregnancy was assessed in women who had previously been

| Baseline variables | n | % spontaneous abortion | OR# | OR## | (95% CI) |
|-------------------------------|-------|------------------------|----------|----------|-----------|
| Age | | | | | |
| 20-23 | 374 | 20.3 | 1.3 | 1.5 | (1.1-2.2) |
| 24-26 | 717 | 18.4 | 1.2 | 1.3 | (1.0-1.7) |
| 27-29 | 830 | 16.3 | 1.0 | 1.0 | |
| Schooling | | | | | |
| <10 | 678 | 18.4 | 1.0 | 1.0 | (0.7-1.2) |
| >11 | 1,240 | 17.5 | 1.0 | 1.0 | |
| Marital status | | | | | |
| Married/cohabiting | 1,514 | 16.3 | 1.0 | 1.0 | |
| Single | 405 | 24.0 | 1.6* | 1.6 | (1.2-2.1) |
| No. of pregnancies | | | | | |
| Not previously pregnant | 943 | 15.4 | 1.0 | 1.0 | |
| 1 | 585 | 20.3 | 1.5* | 1.0 | (0.6-1.4) |
| 2 | 247 | 18.2 | 1.3 | 0.8 | (0.6-1.2) |
| >3 | 143 | 23.8 | 1.9* | 0.9 | (0.6-1.6) |
| Previous spontaneous abortion | | | | | |
| Not previously pregnant | 943 | 15.4 | 0.7 | 0.7 | (0.6-1.0) |
| 0 | 803 | 19.3 | 1.0 | 1.0 | |
| 1 | 138 | 21.7 | 1.3 | 1.2 | (0.8-1.8) |
| >2 | 37 | 35.4 | 2.6* | 2.3 | (1.1-4.5) |
| Previous induced abortion | | | | | |
| Not previously pregnant | 943 | 15.4 | 0.8 | 0.8 | (0.6-1.1) |
| 0 | 409 | 18.6 | 1.0 | 1.0 | |
| >1 | 569 | 21.4 | 1.2 | 1.2 | (0.8-1.6) |
| Use of oral contraceptives | | | | | |
| Never | 228 | 21.1 | 1.0 | 1.0 | |
| Ever | 1,692 | 17.4 | 0.8 | 0.8 | (0.6-1.0) |
| Duration of OC use: trend: | | | p = 0.06 | p = 0.21 | |
| Use of IUD | | | | | |
| Never | 1,352 | 16.6 | 1.0 | 1.0 | |
| Ever | 568 | 21.0 | 1.5* | 1.3 | (1.0-1.8) |
| Duration of IUD use: Trend: | | | p = 0.38 | p = 0.23 | |
| No. of sex partners | | | | | |
| 1-4 | 577 | 17.7 | 1.0 | 1.0 | |
| 5-9 | 573 | 17.3 | 1.0 | 0.9 | (0.7-1.3) |
| 10-19 | 473 | 17.3 | 1.0 | 0.9 | (0.6-1.3) |
| >20 | 295 | 20.3 | 1.3 | 1.0 | (0.7-1.5) |
| PID | | | | | |
| Never | | 17.3 | 1.0 | 1.0 | |
| Ever | | 19.3 | 1.2 | 1.0 | (0.8-1.3) |
| History of chlamydia | | | | | |
| Never | | 17.4 | 1.0 | 1.0 | |
| Ever | | 20.3 | 1.2 | 1.1 | (0.8-1.5) |

[#]Adjusted for age.

pregnant (Table IV). In women who had given birth at the last pregnancy, especially a longer interval (\geq 37 months) was associated with a pattern of increased risk of spontaneous abortion (OR =1.8; 95% CI: 0.7–4.5 versus 19–24 months), however without reaching statistical significance. If the pre-

vious pregnancy was a spontaneous abortion, we observed that a shorter pregnancy interval tended to increase the risk of the subsequent pregnancy ending as a spontaneous abortion (OR = 2.1; 95% CI: 0.5-7.5 for ≤ 6 month-interval versus ≥ 25 months).

^{##}Adjusted for age, marital status, number of previous spontaneous abortions and having ever used IUD.

^{*95%} CI excludes 1.0.

Missing values are excluded from the analysis.

IUD, intrauterine device; PID, pelvic inflammatory disease.

Table IV. Odds ratios for spontaneous abortion associated with different potential risk determinants

| | n | % spontaneous abortion | OR# | OR## | (95% CI) | OR& | (95% CI) |
|---------------------------|---------------|------------------------|-----|------|-----------|-----|-----------|
| Interval since last birth | 1 | | | | | | |
| <12 months | | 12.9 | 1.4 | 1.4 | (0.4-4.9) | 1.3 | (0.4-4.8) |
| 13-18 months | 69 | 13.0 | 1.4 | 1.3 | (0.5-3.9) | 1.3 | (0.5-3.8) |
| 19-24 months | 70 | 10.0 | 1.0 | 1.0 | | 1.0 | |
| 25-36 months | 137 | 13.1 | 1.4 | 1.4 | (0.6-3.6) | 1.4 | (0.6-3.5) |
| >37 months | 131 | 15.3 | 1.7 | 1.7 | (0.7-4.3) | 1.8 | (0.7-4.5) |
| Interval since last spon | taneous abort | ion | | | | | |
| <6 months | 21 | 28.6 | 2.5 | 2.5 | (0.7-9.6) | 2.1 | (0.5-7.5) |
| 7-12 months | 17 | 23.5 | 1.9 | 1.9 | (0.4-8.3) | 1.6 | (0.4-7.2) |
| 13-24 months | 22 | 22.9 | 1.9 | 1.9 | (0.5-7.7) | 1.6 | (0.5-7.6) |
| >25 months | 36 | 13.9 | 1.0 | 1.0 | | 1.0 | |

#Adjusted for age.

##Adjusted for age and number of previous spontaneous abortions.

&Adjusted for age, number of previous spontaneous abortions, and marital status.

Discussion

Using information from personal interviews, we found that 20.9% of all pregnancies (intended to be carried to term) occurring during a follow-up period of around 2 years ended as spontaneous abortions. The corresponding spontaneous abortion rate was 16.3% when register-based data were used. This is in line with some previous studies (6,7), but is a little higher than in a recent Danish register-based study (13.5%) (8).

The occurrence of spontaneous abortion is difficult to study for a variety of reasons. Most spontaneous abortions occur early in pregnancy and a certain proportion do not lead to medical contact and hospitalization. Therefore, when using registerbased information, the occurrence of spontaneous abortions will tend to be underestimated. In the present study, we found that out of 654 self-reported abortions occurring before entrance in the study, 195 (29.8%) were not registered in the Hospital Discharge Register. Even though the majority of these may be spontaneous abortions not admitted to a hospital, some may have been hospitalized spontaneous abortions which were, wrongly, not registered in the Hospital Discharge Register. The discrepancy could also arise if women reported an induced abortion as a spontaneous abortion. This, however, is not likely to play an important role in the present study as the majority of the 195 self-reported spontaneous abortions had no gynecologic or obstetric record in the Hospital Discharge Register, and only 10 had an induced abortion diagnosis in the relevant time period. Finally, some of the discrepancy could be explained if heavy menstrual bleeding was misinterpreted as spontaneous abortion. Our results are in line with those of a recent prospective community study of 626 pregnant women followed for outcome of pregnancy. Among the women who had a spontaneous abortion, more than 25% were not admitted to hospital (1).

The Danish Hospital Discharge Register has previously been evaluated by the Danish National Board of Health and others (9-12). Within the gynecologic/obstetric area, a recent study on the validity of nonmalignant gynecologic diagnoses/operations reported on a serious problem in the validity of the diagnoses, but a good validity of the coding of the operations (12). An older study reported on a satisfying quality of data concerning abortions (13). In the present study, where the comparison was made between register data and data from a personal interview, we found an acceptable agreement between the two sources – both concerning number of spontaneous abortions (disregarding the issue of potential nonhospitalized early abortions) and concerning the time of the abortion. Among the spontaneous abortions in the Hospital Discharge Register, around 14% were not reported as a spontaneous abortion or were not reported at all by the women (72/531). The majority of these 72 cases were reported by the women as induced abortions, which may be surprising. This may be explained for example if the woman is admitted with a nonviable pregnancy and is having curettage, then she may interpret the procedure as induced rather than spontaneous. Alternatively, the coding for these women could be wrong in the Hospital Discharge Register.

In analytical studies of spontaneous abortion, some methodological problems also exist. When using questionnaires or interviews, it is theoretically possible to obtain information on all previous spontaneous abortions known by the woman (i.e. both hospitalized and nonhospitalized). However, the questionnaire data may be weakened by selection

bias due to nonresponse. In contrast, it is an advantage of the register-based studies that selection bias because of nonresponse and information bias can virtually be ruled out. However, differential misclassification may still exist if specific groups of women are more likely than others to be admitted to hospital for spontaneous abortion. Most of the studies conducted so far using questionnaire/interview information have had a retrospective design, and may thus be less reliable due to recall bias. It is a strength of our study that information on potential risk factors was collected prospectively, and thus independently of the outcome of the subsequent pregnancy.

In the present study we find that the most significant risk factor for incident spontaneous abortion is a history of two or more spontaneous abortions. This association could not be explained by adjusting for total number of pregnancies, previous induced abortions, age, or other confounding factors. This is in line with several previous studies (14-16).

Many studies have shown a higher risk of spontaneous abortion with increasing maternal age, possibly due to an increasing frequency of chromosomal aberrations and higher prevalence of chronic diseases with increasing age (17–19). In a recent Danish study, the risk of spontaneous abortion followed a J-shaped curve with the most substantial increase in risk after the age of 35 years, however, when adjustment was made for induced abortion, the increased risk in the very young women disappeared (8). The results from our study, including women 20–29 years of age, are in line with this, except that the increased risk among the younger women did not disappear after adjustment for the effect of induced abortion. Thus, in spite of a narrow age range in our study, we found that the risk was age dependent with the highest risk occurring among the youngest women in our study population.

Even though most spontaneous abortions occur in the group of married/cohabiting women, we find an increased risk among single women. Although single women may tend to be younger and may have a different social status, the association remained significant after adjustment for confounders in line with some previous studies (16,19). In contrast, we observed no relationship between spontaneous abortion and schooling, which may be somewhat surprising in the light of the fact that education is considered a proxy measure for social status.

There is controversy in the literature concerning the role of contraceptive habits and risk of subsequent spontaneous abortion. Some studies report on a protective effect of previous oral contraceptive use (20,21), whereas others find no association (16). It has been hypothesized that the effect could be explained if fertile women use oral contraceptives more often and that they may have a better reproductive outcome than less fertile women. In the present study we find a borderline statistically significantly protective effect of ever/never having used oral contraceptives and a nonsignificant indication of a decreasing risk with duration of use. In contrast, it has been suggested that IUD use, history of pelvic inflammatory disease, and previous sexually transmitted diseases such as chlamydia increase the risk of spontaneous abortion (16,22,23). In our study we observe a significantly increased risk with having ever/never used an IUD and a nonsignificantly increasing trend with increasing duration of IUD use, but no association with previous pelvic inflammatory disease, self-reported chlamydia infection or lifetime number of sexual partners. Thus, although our data seem to indicate an increased risk in relation to IUD and a protective effect of OC use, this still needs confirmation from other studies.

Several studies on interpregnancy intervals have focused on perinatal outcomes like still birth, preterm birth, and low birth weight, and have consistently found an increased risk of an adverse outcome related to short intervals (24). Recently, an increased risk was also found for longer interpregnancy intervals after adjustment was made for a variety of sociodemographic, behavioral, and biologic risk factors (25). However, the literature has been less consistent with regard to the role of longer interpregnancy intervals. The results of our present study are in line with those in a recent Danish registerbased study finding that women with about two years since the last pregnancy resulting in a birth have the lowest risk of spontaneous abortion (26). However, our data indicating an increased risk of spontaneous abortion in a pregnancy initiated shortly after a previous spontaneous abortion are at variance with those in the other Danish study. The reason for this discrepancy is unknown, but for one thing the age distributions of the study populations are different from each other as the women in our study were quite young (20-29 years at enrolment). It should also be taken into account that our results, although showing a trend, are based only on a limited number of women. Another limitation of our study is that we were only able to study interpregnancy intervals up to ≥ 25 months. It is a drawback that in none of these two Danish studies was there any information on whether the pregnancy was planned or not. Short interpregnancy intervals are more likely to occur in unplanned pregnancies, and unplanned pregnancies have been suggested to

be more frequent in women exposed to a higher level of economic, social, or psychological stress (24). Thus, it is still unclear how much these factors contribute to the observed risk related to short interpregnancy intervals, i.e. how much of the increased risk can be attributed to a higher occurrence of other risk factors among women with short interpregnancy intervals and how much can be attributed to biological factors related to short interpregnancy itself. Similarly, it is not known whether a long interpregnancy interval in itself is associated with an adverse outcome like spontaneous abortion or other perinatal adverse outcomes or it is merely a marker for an increased risk due to other factors like secondary infertility (24).

In summary, we find a high incidence of spontaneous abortion when measured by means of a personal interview and when assessed through information from the Hospital Discharge Register. We found an acceptable agreement between the two sources with regard to number of spontaneous abortions (disregarding the issue of nonhospitalized abortions) and regarding the timing of the abortion.

The results of our study provide supportive evidence that having two or more previous spontaneous abortions is the strongest predictor for a spontaneous abortion to occur in the subsequent pregnancy. Our data also point to a potential role of previous contraceptive habits. Finally, we find an indication that both a short and a longer interpregnancy interval following childbirth increase the risk of spontaneous abortion. In addition, we cannot rule out that getting pregnant shortly after a spontaneous abortion may increase the risk of another spontaneous abortion. However, it should be emphasized that these findings need to be confirmed in larger studies taking into account previous subfertility as well as additional risk factors assessing social and psychological stress.

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