



The role of maternal age and pregnancy history in risk of miscarriage

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The role of maternal age and pregnancy history in risk of miscarriage

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What is already known on this topic

- Miscarriage is a common pregnancy outcome with clear recurrence risk.
- An increased risk of miscarriage is observed among both younger and older mothers, although the influence of induced abortions on estimation of the age-associated risk of miscarriage remains unclear.
- Some studies indicate an increased risk of other adverse pregnancy outcomes among women who have a history of miscarriage. Few studies have examined whether the risk of miscarriage is increased after pregnancies with complications.

What this study adds

- A large national registry-based cohort in Norway indicated that the increased risk of miscarriage among both younger and older mothers remained after taking induced abortions into account.
- The risk of miscarriage was increased if the previous pregnancy ended in a preterm delivery, delivery by caesarean section, or had experienced gestational diabetes.
- Women who themselves were born small-for-gestational-age also had an increased risk of miscarriage.

Abstract

Objectives: To estimate the burden of miscarriage in the Norwegian population and to evaluate associations with maternal age and pregnancy history.

Design: Prospective cohort study.

Setting: All registered pregnancies in Norway.

Participants: All Norwegian women who were pregnant between 2009 and 2013, as identified through the Medical Birth Registry of Norway, the Norwegian Patient Registry and the abortion registry.

Main outcome measures: Risk of miscarriage according to the woman's age and pregnancy history using logistic regression.

Results: There were 421,201 pregnancies during the study period. Miscarriage risk was lowest among women age 25-29 years (10%), and rose rapidly after age thirty, reaching 53% among women 45 years and older. There was a strong recurrence risk of miscarriage, with age-adjusted odds ratios (aORs) of 1.5 (95% CI: 1.5 to 1.6) after one miscarriage, 2.2 (95% CI: 2.0 to 2.4) after two, and 4.0 (95% CI: 3.3 to 4.8) after three consecutive miscarriages. Risk was modestly increased if the previous birth ended in a preterm delivery (1.22; 95% CI: 1.12 to 1.29), stillbirth (1.30; 1.11 to 1.54), caesarean section (1.16 95% CI: 1.12 to 1.21), or if woman had gestational diabetes in the previous pregnancy (1.19; 95% CI: 1.05 to 1.36). Risk of miscarriage was slightly higher among women who themselves had been small-for-gestational age (1.08; 95% CI: 1.04 to 1.13).

Conclusions: The risk of miscarriage varies greatly by maternal age, shows a strong pattern of recurrence, and is increased after other adverse pregnancy outcomes.

Introduction

Miscarriage is a common outcome of pregnancy, with most studies reporting 12-15% loss among recognized pregnancies by 20 weeks of gestation.¹⁻⁴ Quantifying the full burden of miscarriage is challenging because rates of pregnancy loss are high around the time that pregnancies are clinically recognized. As a result, the total rate of recognized loss is sensitive to how early women recognize their pregnancies. There is also heterogeneity across countries and studies in distinguishing between miscarriage and stillbirth. Furthermore, the observed miscarriage rate is affected by the competing risk of induced abortion. A general lack of data on induced abortions has made it difficult to determine how seriously this competing risk distorts estimation of miscarriage rates. Based on national registries or population-based cohort studies in Sweden, Finland and Denmark, the reported risk of miscarriage was between 12.9-13.5%.⁵⁻⁷ A previous Norwegian study included all women treated at one of the main hospitals in Oslo between 2000 and 2002, and estimated a miscarriage rate of 12% taking into account induced abortions.⁸

Pregnant women in Norway have access to free health care, and most women with recognised pregnancies who experience loss, or impending loss, contact health-care services. All induced abortions are recorded in an abortion register. Thus, nearly all recognised pregnancies are registered in at least one of the national health registers. The high awareness and education among women regarding early signs of pregnancy, combined with freely available health care and mandatory registration systems, make Norway a favourable setting for studying risk of miscarriage.

Although the cause of most miscarriages is unknown, they presumably result from a complex interplay between parental age, genetic, hormonal, immunological and environmental factors.^{9 10} Genetic factors, including parental chromosomal rearrangements and abnormal embryonic genotypes or karyotypes, may underlie more than half of recurrent miscarriages.¹⁰ Maternal age is the strongest known risk factor, with risk that is slightly elevated among the youngest mothers and then rises sharply among older mothers.^{7 11} There may be shared underlying risk factors for miscarriage and other adverse pregnancy outcomes. Several studies have looked at the association

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3 between history of miscarriages and future risk of other pregnancy complications,¹²⁻¹⁷ but less is
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5 known about how complications might predict future miscarriage risk.¹⁸⁻²⁰
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7 The aim of the current study was to estimate the rate of miscarriage among Norwegian
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9 women and to evaluate the association with age and pregnancy history.
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Methods

The study population consisted of all registered pregnancies in Norway between 2009 and 2013, excluding ectopic pregnancies. Information on pregnancies came from three national health registries: the Medical Birth Registry of Norway (MBRN; established in 1967), the Norwegian Patient Registry (NPR; established in 2008) and the abortion registry (established in 1979). The MBRN includes information on all deliveries and fetal losses after 12 gestational weeks, while the NPR provides information on all women in contact with specialist health care services during pregnancy, therefore providing the opportunity to identify losses before 12 weeks, not captured in the MBRN. The abortion registry is a mandatory and non-identifiable registry containing information from all health-care providers who perform induced abortions. We used this registry to obtain information about the frequency of induced abortions according to age and gestational week. We linked information on live births and fetal deaths identified through the MBRN and NPR using unique personal identification numbers.

Pregnancy outcomes and identification of unique pregnancies

We identified live births and fetal deaths after 12 gestational weeks from the MBRN. A fetal death at 20 gestational weeks or later and/or with a birthweight of 500 grams or more was considered a stillbirth, while fetal deaths before 20 gestational weeks with a birthweight less than 500 grams were considered a miscarriage. Hospital discharges in the NPR are coded according to International Classification of Diseases (ICD) version 10. We included the following ICD-10 codes to capture early miscarriages: hydatidiform mole (O01); blighted ovum and nonhydatidiform mole (O02.0); missed abortion (O02.1); other specified abnormal products of conception (O02.8); abnormal product of conception, unspecified (O02.9); spontaneous abortion (O03); and threatened abortion (O02.0). Pregnancies in the NPR are not registered with unique pregnancy IDs, and follow-up visits during the same pregnancy could produce multiple registrations. We therefore took steps to ensure that records reflected unique pregnancies. First, we required a minimum of 6 weeks (42

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3 days) between two successive records of miscarriage to consider them distinct pregnancies. Second,
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5 we required that a record of a miscarriage in the NPR should be at least 6 weeks after a registered
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7 delivery to the same women in the MBRN. Third, we excluded registered miscarriages that occurred
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9 within the gestational period of a registered pregnancy to the same woman in the MBRN. In the case
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11 of multiple fetuses, the outcome was regarded as a livebirth if all deliveries resulted in live births, as
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13 a miscarriage if there was at least one miscarriage but no stillbirth, and as a stillbirth if at least one of
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15 the deliveries resulted in a stillbirth but none in a miscarriage. A multiple birth could thus result in
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17 both a miscarriage and a stillbirth, but only if there was a discrepancy in the birthweight between the
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19 fetuses.
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25 *Pregnancy history*

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27 For the analysis of previous pregnancy outcomes, women were categorized as having no
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29 previous pregnancy, live birth, stillbirth or miscarriage. Neonatal death in a previous live birth was
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31 defined as death within the first 28 days after delivery. We also obtained information on
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33 complications in the previous live-birth pregnancy, including preterm delivery (<37 gestational
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35 weeks), post-term delivery (≥42 gestational weeks), small-for-gestational-age, large-for-gestational-
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37 age, pre-eclampsia, gestational diabetes, and delivery by caesarean section. Small-for-gestational-age
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39 was defined as birthweight below the 10th percentile, and large-for-gestational-age as birthweight
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41 above the 90th percentile, using sex-and-gestational-week-specific birthweight distributions. Delivery
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43 by caesarean section was further subdivided into emergency (“acute”), planned (“elective”) or
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45 unspecified.
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50 For mothers born in Norway (75% of our population), we also obtained information from the
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52 MBRN on conditions of the woman’s own birth. These included whether the mother was delivered
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54 preterm, small-for-gestational-age, large-for-gestational-age, or in a pregnancy with pre-eclampsia.
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Statistical analysis

Rate of miscarriages can be calculated as number of miscarriages among all ongoing pregnancies in each gestational week. An induced abortion that occurs at a gestational age when most miscarriages would have already occurred should be in the denominator at least as a partial count, so if those are omitted the apparent rate of miscarriage will be inflated. In the absence of data on the gestational week of induced abortion (which is rarely available), there is no precise way to take the induced abortions into account. One practical approach that has been suggested is to include half of the induced abortions in the denominator.²¹

The Norwegian data provide gestational-week distributions for all induced abortions according to maternal age, which allow us to directly estimate the number of pregnancies that would have resulted in a miscarriage if the pregnancy had not been terminated. Because the Norwegian data do not include gestational-age information for miscarriages, we applied rates of gestational-week-specific risk of miscarriage derived from a population with miscarriage rates similar to those in Norway.²² We subsequently estimated the risk of miscarriage by adding the estimated number of induced abortions that would have ended in a miscarriage to the numerator, and including all pregnancies ending in induced abortions in the denominator (See the online supplement for details).

The great majority of induced abortions in Norway occurred soon after recognition of pregnancy, so that our correction for induced abortions made only a very small difference in the estimated overall risk of miscarriages. This was also true when we calculated the age-associated risk of miscarriage, for which there were large differences in the occurrence of induced abortions by age. With this reassurance that the early induced abortions in Norway produce little distortion in miscarriage risk, we excluded induced abortions from the remaining analyses.

We calculated the odds ratio (OR) of miscarriage according to pregnancy history by logistic regression, using cluster variance estimation to account for women with multiple pregnancies during the study period. To evaluate recurrence risk of miscarriage, we examined the risk among those who had one, two and three previous consecutive miscarriages, as compared to the risk of miscarriage

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3 among women having their first pregnancy. The multivariable model was adjusted for age and age
4 squared, to capture the non-linear relationship between age and risk of miscarriage.⁷ We conducted
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6 a sensitivity analysis of the risk according to the outcome of the previous pregnancy adjusting for
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8 inter-pregnancy interval, where we assigned all miscarriages to have a gestational age of 8 weeks.
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10 We also conducted a sensitivity analysis of the risk according to complications in the previous
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12 pregnancy where we adjusted for maternal smoking during the previous pregnancy, for the
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14 approximately 80% of pregnancies with this information available. All analyses were conducted using
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17 Stata version 14 (Statacorp, Texas).
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23 *Patient and public involvement*

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25 No patients were involved in setting the research question or the outcome measures, nor were they
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27 involved in developing plans for recruitment, design, or implementation of the study. No patients
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29 were asked to advise on interpretation or writing up of results. There are no plans to disseminate the
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31 results of the research to study participants or the relevant patient community.
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Results

There were 421,201 pregnancies registered in Norway between 2009 and 2013 (Figure 1). Among these, 299,178 resulted in live birth, 1,317 resulted in stillbirth, 76,903 resulted in induced abortion, and 43,803 resulted in miscarriage (Table 1). After correcting for induced abortions, the overall risk of miscarriage was 12.8%.

Age-specific risk of miscarriage

Risk of miscarriage varied substantially across age groups (Table 1). The age-associated risk of miscarriage showed a J-shaped pattern (Figure 2). The lowest risk was observed among women 25-29 years of age (9.8%), with the absolute lowest risk at age 27 (9.5%), and the highest risk at age 45 years and older (53.6%). We also observed a modest risk increase among the youngest mothers (<20 years) (Figure 2). Adjustment for induced abortions made very little difference in the age-specific risks, except for a modest risk decrease in the oldest and youngest categories (Table 1).

Pregnancy history and miscarriage risk

Risk of miscarriage was increased among women whose prior pregnancy ended in a stillbirth (adjusted OR 1.30; 95% CI: 1.11 to 1.53) or miscarriage (adjusted OR 1.65; 1.59 to 1.71), compared to women with no previous pregnancy (Table 2). Risk was also higher for women with a history of neonatal death, although the numbers were small and the estimate imprecise (Table 2). Associations were similar in our sensitivity analysis adjusting for inter-pregnancy-interval (eTable 1). There was a strong recurrence risk of miscarriage, which remained after adjustment for mother's age. After one miscarriage, the adjusted OR of another was 1.54 (95% CI: 1.48 to 1.60). This increased to 2.21 after two consecutive miscarriages (95% CI: 2.03 to 2.41) and 3.97 after three consecutive miscarriages (95% CI: 3.29 to 4.78) (Table 3).

Pregnancy complications and miscarriage risk

Other adverse outcomes in previous pregnancies also predicted higher risk of miscarriage. Miscarriage risk was higher if the previous live birth was preterm (adjusted OR 1.22; 1.12 to 1.29), if the previous pregnancy included a diagnosis of gestational diabetes (adjusted OR 1.19; 95% CI: 1.05 to 1.36), or if the pregnancy was delivered by caesarean section (adjusted OR 1.16; 95% CI: 1.12 to 1.21) (Table 4). Women whose previous delivery had been post-term had a slightly reduced risk of miscarriage (adjusted OR 0.84; 95% CI: 0.79 to 0.90). There was weak evidence for an increased risk after delivery of infants small-for-gestational-age, large-for-gestational-age, or with a congenital malformation (Table 4). Pre-eclampsia in the previous pregnancy was not associated with increased miscarriage risk. The associations between complications in the previous pregnancy and miscarriage remained similar when adjusting for inter-pregnancy interval and smoking in the previous pregnancy (eTables 1 and 2).

Using information from the women's own birth record, we identified a modest increased miscarriage risk if the woman herself had been born small-for-gestational-age (adjusted RR 1.08; 95% CI: 1.04 to 1.13) (Table 5). In contrast, there was no evidence of increased risk for women exposed to pre-eclampsia in utero, or for women born large-for-gestational-age, preterm, or post-term (Table 5).

Discussion

Miscarriage is a common outcome of pregnancy, but the rate is challenging to estimate because it is subject to inconsistent registration and documentation. Few countries have population registries, but miscarriage data in Norway has been consistently collected since 2008. In this first exploration of the Norwegian register data, we are able to confirm some observations with new precision, and present associations not previously reported.

Important strengths of our study include the population-based design, the prospective collection of the data, and the availability of information from the woman's own birth record. Limitations include likely under ascertainment of early miscarriages. The patient registry captures only miscarriages that led to a consultation with specialist health-care services. Women who had contact only with their general practitioner are therefore not in the patient registry. However, in Norway, most women who recognizes a miscarriage are likely to receive care from a specialist. There are potential confounding factors for which we did not have information, including maternal ethnicity, education and body-mass index. Notably, our findings for risk of miscarriage according to complications in the previous pregnancy did not change after adjustment for smoking in the previous pregnancy. It is possible that father's age might contribute to the increased miscarriage risk associated with maternal age.¹¹ Unfortunately, the father's identity was not recorded in the patient registry which made us unable to adjust for paternal age.

Overall risk of miscarriage in Norway was 12.8%. This risk is remarkably similar to reports from other Nordic countries.⁵⁻⁷ It is also similar to the risk reported from smaller studies in Norway, United States and Canada.^{2-4,8} This consistency with other studies, especially with prospective studies with full ascertainment of early miscarriages, provides some reassurance that the Norwegian registries capture the majority of recognized miscarriages.

As expected,^{7,11} miscarriage risk was strongly related to maternal age. The risk was moderately increased (15.8%) for women under the age of twenty, reaching a nadir (9.5%) at age 27, and then rising nearly linearly after the age of 30 to reach 54% at ages 45 and older (Figure 2). The

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3 increased risk among young women is a curious finding. In a Danish study, the apparent increase
4 among younger women did not persist after a crude adjustment for induced abortions.⁷ When we
5 made a similar crude adjustment (adding half of induced abortions to the denominator), the increase
6 among the youngest women was likewise mostly removed, but when we made the more precise
7 adjustment, the higher risk among the youngest women persisted. This may indicate unrecognized
8 social causes of miscarriage, or an effect of reproductive immaturity. The fact that our careful
9 adjustment for induced abortions made little difference to any of the age estimates may be
10 explained by the fact that induced abortion in Norway occur very early (84% within the first 9 weeks).

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21 Women vary in their risk of miscarriage at a given age, for reasons that are not well
22 understood. If a miscarriage marks a woman as being at relatively higher risk, then this risk is
23 expressed in subsequent pregnancies. Controlling for maternal age, the odds ratio for miscarriage
24 increased from 1.54 after one miscarriage to 2.21 after two and 3.97 after three. Recurrence risk has
25 been previously reported, although not with this precision or to this extent.²³

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32 We found evidence that certain other pregnancy outcomes cluster with miscarriage risk,
33 suggesting that these outcomes may share underlying causes. Specifically, miscarriage risk was
34 moderately increased among women who had experienced a stillbirth, preterm delivery or
35 gestational diabetes in their previous pregnancy. No previous studies have considered those
36 pregnancy outcomes as risk factors for miscarriage. Our results for preterm delivery are supported by
37 the temporally reverse association, meaning an increase in preterm birth following miscarriage.^{14 16 24-}
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27 Possible shared pathways include cervical insufficiency and infections,^{14 16 24-27} although these are
speculative. There are few clues in the literature suggesting that glucose metabolism abnormalities
may increase miscarriage risk.²⁸⁻³¹

Unexpectedly, there was a small increased risk of miscarriage among women who were
small-for-gestational-age at their own birth. There is no obvious mechanisms for this finding, and it
remains to be confirmed in future studies. However, there could be shared risk-related exposures
between mothers and daughters, e.g. smoking, that could potentially explain this association.

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3 We also observed a small increase in miscarriage risk after caesarean section. A meta-
4 analysis of caesarean section and subsequent risk of miscarriage reported inconsistent effects, with
5 RR/OR estimates ranging from 0.76 to 1.32.¹⁹ This meta-analysis did not pool the results from
6 individual studies due to the heterogeneity among studies, including varying definitions of
7 miscarriage/early fetal demise. It is possible that the underlying problem leading to delivery by
8 caesarean section also increases risk of miscarriage in the subsequent pregnancy.¹⁹ We did not have
9 sufficient detailed information to explore the role of factors necessitating delivery by caesarean
10 section.
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21 In sum, population-based data from Norway enable precise estimates of miscarriage risk
22 related to mother's age, with the lowest risk at age 27. Risk of miscarriage increases as much as four-
23 fold after three consecutive previous miscarriages. Exploratory associations suggest that miscarriage
24 risk is linked to previous pregnancy complications (stillbirth, preterm delivery) and gestational
25 diabetes. More focused studies of these associations may lead to new insights regarding underlying
26 causes of miscarriage.
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3 Contributors: MCM, AJW and SEH conceived and designed the study. SEH obtained access to data.
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5 MCM conducted the data analysis and drafted the initial version of the manuscript. CRW and NHM
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7 provided important insight during the data analysis. All authors contributed in the interpretation of
8
9 the data and critically revised the manuscript. MCM has full access to the data to all of the data in the
10
11 study and can take responsibility for the integrity of the data and the accuracy of the data analysis.
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13 The corresponding author attests that all listed authors meet authorship criteria and that no others
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15 meeting the criteria have been omitted.
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59 Data sharing: No additional data available.
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5 Transparency: The lead author (MCM) affirms that the manuscript is an honest, accurate, and
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7 transparent account of the study being reported; that no important aspects of the study have been
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9 omitted; and that any discrepancies from the study as planned have been explained.
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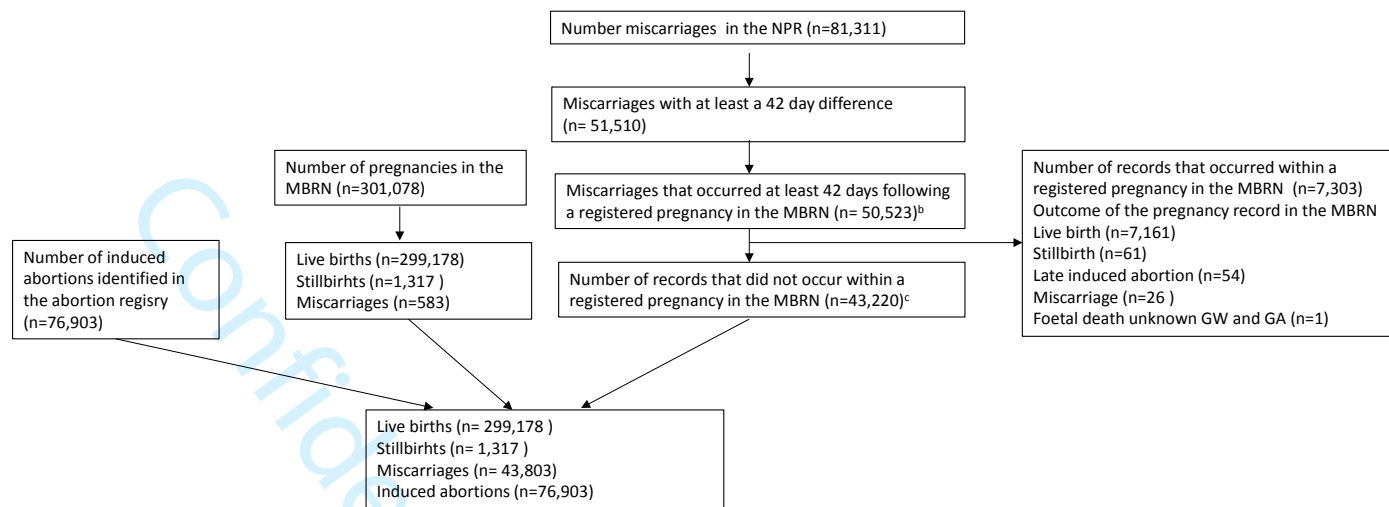
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Figure 1 Pregnancies identified in the Norwegian health registries between January 2009 and December 2013

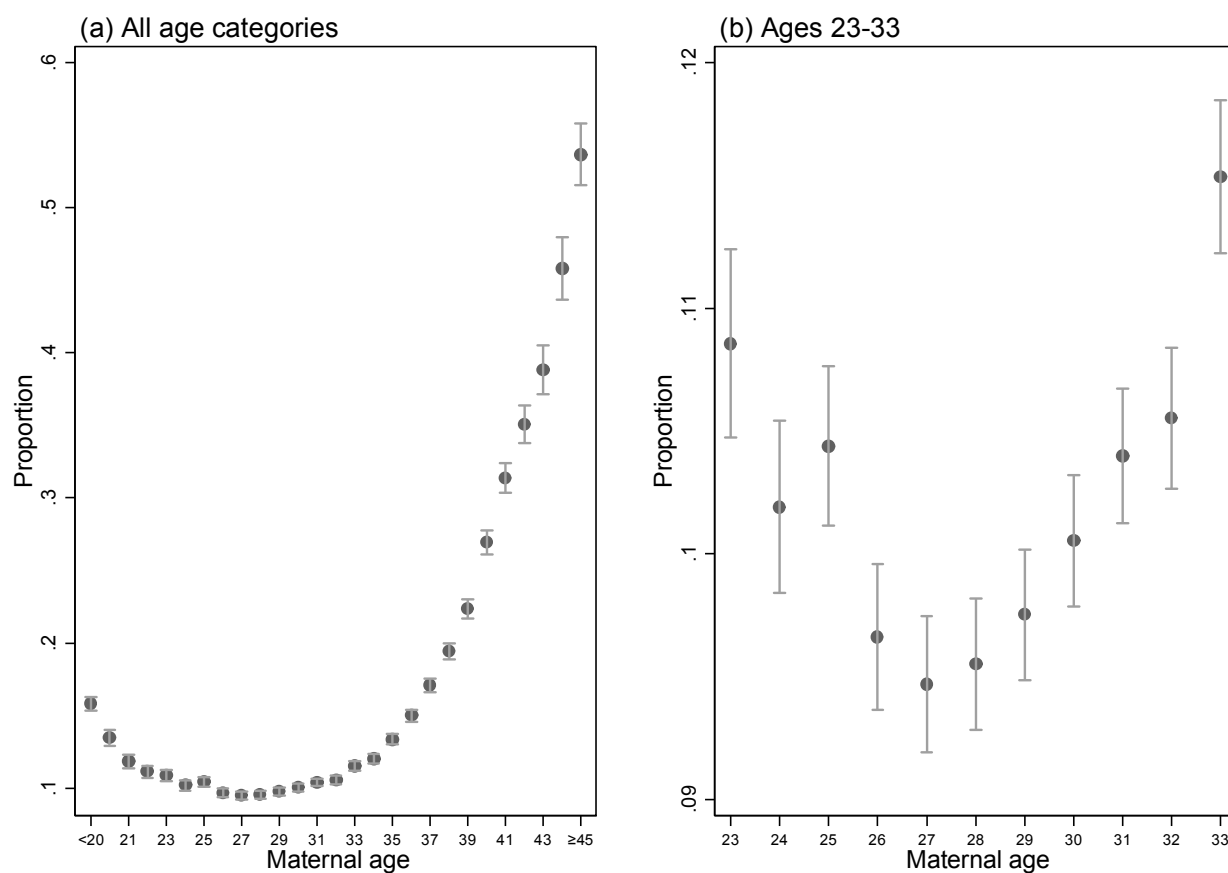


^a Includes ICD10 codes O01 (Hydatidiform mole), O02.0 (Blighted ovum and nonhydatidiform mole), O02.1 (Missed abortion), O02.8 (Other specified abnormal products of conception), O02.9 (Abnormal product of conception, unspecified), O03 (Spontaneous abortion), and O20.0 (Threatened abortion).

^b This data cleaning ensures that the miscarriage/abortion registered in the NPR was not also captured in the MBRN

^c This cleaning ensures that a miscarriage/abortion registered in the NPR did not occur within a registered pregnancy in the MBRN (birth date minus gestational age in days set as cut off)

Figure 2 Illustration of the risk of miscarriage according to maternal age



Includes the estimated number of induced abortions that would have resulted in a miscarriage in the numerator of the risk calculations and all induced abortions in the denominator.

Review Only

Table 1 Frequency of pregnancy outcomes in Norway between 2009 and 2013 by maternal age (n=421,201)

Age group	Total number of pregnancies	Live births % (N)	Stillbirths % (N)	Induced abortions % (N)	Proportion miscarriages excluding induced abortions from the denominator % (N)	Proportion miscarriages including induced abortions that would have resulted in a miscarriage in the numerator and all induced abortions in the denominator % (N)
Younger than 20	17,066	33.9 (5,792)	0.2 (28)	59.1 (10,083)	16.7 (1,163)	15.8 (2,698)
20-24	70,829	61.2 (43,373)	0.2 (172)	30.8 (21,811)	11.2 (5,473)	11.3 (7,987)
25-29	122,137	77.0 (94,022)	0.3 (352)	14.4 (17,591)	9.7 (10,172)	9.8 (11,910)
30-34	123,266	79.2 (97,631)	0.3 (402)	10.8 (13,312)	10.8 (11,921)	10.8 (13,362)
35-39	68,502	70.9 (48,590)	0.4 (300)	14.3 (9,793)	16.7 (9,819)	16.7 (11,414)
40-44	18,076	51.7 (9,340)	0.3 (59)	22.2 (4,004)	33.2 (4,673)	32.2 (5,820)
45 or older	1,315	32.7 (430)	0.3 (4)	23.5 (309)	56.9 (572)	53.6 (705)
Missing	10	0	0	0	100 (10)	0
Total	421,201	71.0 (299,178)	0.3 (1,317)	18.3 (76,903)	12.7 (43,803)	1.28 (53,906)

Table 2 Risk of miscarriage in Norway between 2009 and 2013 according to the outcome of **the previous pregnancy** (live birth, stillbirth, miscarriage or a neonatal death) (n= 315,963*)

Previous pregnancy	Total number of pregnancies excluding induced abortions	Number of miscarriages % (N) ^a	Adjusted for age OR (95% CI)
No previous registered pregnancy	127,150	11.6 (14,791)	Ref
Live birth	157,763	12.2 (19,170)	0.91 (0.89 to 0.94)
Stillbirth	1,175	17.5 (205)	1.30 (1.11 to 1.53)
Miscarriage	29,434	21.1 (6,214)	1.65 (1.59 to 1.71)
Neonatal death	441	17.0 (75)	1.28 (0.97 to 1.64)

*105,238 pregnancies excluded from the analysis because of unknown pregnancy history or because their previous or current pregnancy was an induced abortion.

Table 3 Recurrence risk of miscarriages in Norway between 2009 and 2013 after one, two and three consecutive miscarriages (n=156,584*)

Previous miscarriages	Total number of pregnancies excluding induced abortions	Total number of miscarriages % (N)	Adjusted for age OR (95% CI)
No previous registered pregnancy	127,150	11.6 (14,791)	Ref
The previous pregnancy ended in a miscarriage	25,575	19.8 (5,051)	1.54 (1.48 to 1.60)
The two previous pregnancies ended in a miscarriage	3,208	27.7 (890)	2.21 (2.03 to 2.41)
The three previous pregnancies ended in a miscarriage	651	41.9 (273)	3.97 (3.29 to 4.78)

*264,617 pregnancies excluded from the analysis because of unknown pregnancy history or because the woman's previous or current pregnancy was an induced abortion or because the previous pregnancy was a live birth or a stillbirth.

Table 4 Risk of miscarriage in Norway between 2009 and 2013 according to complications in **the previous live birth pregnancy** (n= 158,204*)

Exposure	Exposure group	Total number of pregnancies excluding induced abortions	Number of miscarriages % (N)	Adjusted for age OR (95% CI)
Gestational age	Preterm	8,639	14.7 (1,261)	1.22 (1.12 to 1.29)
	Term	136,286	12.2 (16,436)	Ref
	Post term	11,602	11.1 (1,272)	0.84 (0.79 to 0.90)
Fetal growth	Small	13,014	12.6 (1,642)	1.06 (1.01 to 1.12)
	Normal	130,366	12.0 (15,595)	Ref
	Large	13,109	13.2 (1,727)	1.05 (0.99 to 1.10)
Congenital malformation	No	150,791	12.1 (18,288)	Ref
	Yes	7,413	12.9 (957)	1.07 (0.99 to 1.14)
Preeclampsia	No	152,266	12.2 (18,505)	Ref
	Yes	5,938	12.5 (740)	1.04 (0.96 to 1.13)
Gestational diabetes	No	156,405	12.1 (18,962)	Ref
	Yes	1,799	15.7(283)	1.19 (1.05 to 1.36)
Caesarean section	No	135,858	11.8 (16,029)	Ref
	Yes	22,346	14.4 (3,216)	1.16 (1.12 to 1.21)
	Acute	6,284	16.7 (1,047)	1.29 (1.20 to 1.39)
	Elective	15,918	13.5 (2,149)	1.11 (1.06 to 1.17)
	Unspecified	144	13.9 (20)	1.04 (0.63 to 1.70)

*127,150 pregnancies excluded because the woman had no prior registered pregnancy; 1,175 pregnancies excluded because the prior pregnancy was a stillbirth, 29,434 pregnancies excluded because the prior pregnancy was a miscarriage; and 105,238 pregnancies excluded because the outcome of the prior pregnancy was unknown or an induced abortion.

Table 5 Risk of miscarriages in Norway between 2009 and 2013 according to the **women's own** pregnancy outcome (n=258,954*)

Exposure	Category	Total number of pregnancies excluding induced abortions	Number of miscarriages % (N) ^a	Adjusted for age OR (95% CI)
Gestational age	Preterm	10,599	13.2 (1,396)	1.05 (0.99 to 1.12)
	Term	194,910	12.6 (24,462)	Ref
	Post term	38,044	13.0 (4,955)	1.04 (1.00 to 1.08)
Fetal growth	Small	26,397	13.6 (3,598)	1.08 (1.04 to 1.13)
	Normal	195,358	12.6 (24,571)	Ref
	Large	21,548	12.2 (2,618)	0.97 (0.93 to 1.02)
Pre-eclampsia	No	252,346	12.7 (31,951)	Ref
	Yes	6,608	12.9 (852)	1.06 (0.98 to 1.15)

*76,903 pregnancies excluded because they resulted in an induced abortion; 1,412 pregnancies excluded because the woman was born before the medical birth registry was set up (in 1967); and 83,932 pregnancies excluded because the woman was born outside of Norway.

Online supplement methods

We estimated the number of induced abortions that would have resulted in a miscarriage if the pregnancy had not been terminated, using published data on the gestational-week-specific risk of miscarriage.¹⁹ We used this published data to estimate the cumulative probability of fetal death up to and including gestational week 20 for pregnancies terminated at different gestational weeks. The frequency of induced abortions according to maternal age gestational week at the time of the procedure was available from the abortion registry.

The expected number of miscarriage per induced abortion that happens at week k will be computable as 1 minus the probability that a k -week pregnancy survives to week 20:

$$\text{Let } R_k = \exp\left\{\sum_{j=k}^{20} \ln(1 - p_j)\right\}$$

This denotes the probability of survival to week 20, given alive at the start of week k (when the induced abortion occurred), so that 1 minus that is the probability of miscarriage given survival up to week k .

After having randomly assigned a proportion of the induced abortions to have resulted in a miscarriage based on this calculated cumulative probability of miscarriage, we estimated the age specific relative risks (RR) of miscarriage using age 26 as the reference, as this was the median age of women in the publication from which we obtained the gestational week specific risk of miscarriage. We then used these initial estimated age-specific RRs to calculate maternal age and gestational week specific cumulative risk of miscarriage, and used these estimated probabilities to randomly assign a proportion of induced abortions to have resulted in a miscarriage. This process was repeated for a total of 40 iterations until we saw that the age-specific RRs of miscarriage were approaching their limit values. To estimate the confidence intervals of the age-specific risk of miscarriage, we then used the final obtained age-specific RRs to randomly assign the proportion of induced abortions that would have resulted in a miscarriage for a total of 1000 imputed data sets. The absolute proportion of miscarriage was then estimated as the mean across these imputed datasets. The confidence intervals for the proportions were then estimated using Rubin's rules:

$$\sigma^2 = \bar{U} + \left\{1 + \frac{1}{m}\right\} B$$

$$\text{Where } \bar{U} = \frac{1}{m} \{ \hat{p}_j (1 - \hat{p}_j) / n_j \}$$

is the within imputation variance;

$$\text{And } B = \frac{1}{m-1} \left\{ \sum_{j=k}^m (\hat{p}_j - \bar{p}) \right\}^2$$

is the between imputation variance.

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eTable 1 Risk of miscarriage according to whether the previous pregnancy ended in a live birth, stillbirth, miscarriage or a neonatal death (n= 315,963*)

Previous pregnancy	Total number of pregnancies excluding induced abortions	Number of miscarriages % (N) ^a	Adjusted for age OR (95% CI)	Adjusted for age and inter-pregnancy interval
Live birth	157,763	12.2 (19,170)	Ref	Ref
Stillbirth	1,175	17.5 (205)	1.43 (1.22 to 1.67)	1.57 (1.34 to 1.84)
Miscarriage	29,434	21.1 (6,214)	1.80 (1.74 to 1.86)	2.03 (1.93 to 2.13)
Neonatal death	441	17.0 (75)	1.38 (1.07 to 1.79)	1.52 (1.17 to 1.19)

*105,238 pregnancies excluded from the analysis because of unknown pregnancy history or because their previous or current pregnancy was an induced abortion.

eTable 2 Risk of miscarriages by whether **the previous pregnancy** was a live birth with a pregnancy complication (n= 158,204)

Exposure	Exposure group	Total number of pregnancies excluding induced abortions	Number of miscarriages % (N)	Adjusted for age OR (95% CI)	Adjusted for age and inter-pregnancy interval OR (95% CI)	Adjusted for age, inter-pregnancy interval and smoking OR (95% CI)*
Gestational age	Preterm	8,639	14.7 (1,261)	1.22 (1.12 to 1.29)	1.20 (1.13 to 1.28)	1.19 (1.11 to 1.28)
	Term	136,286	12.2 (16,436)	Ref	Ref	Ref
	Post term	11,602	11.1 (1,272)	0.84 (0.79 to 0.90)	0.84 (0.79 to 0.90)	0.84 (0.79 to 0.91)
Fetal growth	Small	13,014	12.6 (1,642)	1.06 (1.01 to 1.12)	1.06 (1.00 to 1.12)	1.04 (0.97 to 1.10)
	Normal	130,366	12.0 (15,595)	Ref	Ref	Ref
	Large	13,109	13.2 (1,727)	1.05 (0.99 to 1.10)	1.03 (0.97 to 1.09)	1.03 (0.97 to 1.10)
Congenital malformation	No	150,791	12.1 (18,288)	Ref	Ref	Ref
	Yes	7,413	12.9 (957)	1.07 (0.99 to 1.14)	1.07 (1.00 to 1.15)	1.07 (0.99 to 1.16)
Preeclampsia	No	152,266	12.2 (18,505)	Ref	Ref	Ref
	Yes	5,938	12.5 (740)	1.04 (0.96 to 1.13)	1.03 (0.95 to 1.11)	1.02 (0.93 to 1.12)
Gestational diabetes	No	156,405	12.1 (18,962)	Ref	Ref	Ref
	Yes	1,799	15.7(283)	1.19 (1.05 to 1.36)	1.25 (1.10 to 1.43)	1.22 (1.06 to 1.41)
Caesarean section	No	135,858	11.8 (16,029)	Ref	Ref	Ref
	Yes	22,346	14.4 (3,216)	1.16 (1.12 to 1.21)	1.18 (1.13 to 1.23)	1.17 (1.12 to 1.23)
	Acute	6,284	16.7 (1,047)	1.29 (1.20 to 1.39)	1.31 (1.22 to 1.41)	1.32 (1.21 to 1.43)
	Elective	15,918	13.5 (2,149)	1.11 (1.06 to 1.17)	1.13 (1.08 to 1.19)	1.12 (1.06 to 1.18)
	Unspecified	144	13.9 (20)	1.04 (0.63 to 1.70)	0.97 (0.59 to 1.60)	1.11 (0.64 to 1.91)

*Restricted to the 80% of pregnancies that had information on smoking in the previous pregnancy. This models adjusts for maternal smoking in the prior pregnancy.