

Reproductive outcomes following induced abortion: a national register based cohort study in Scotland

Journal:	BMJ Open
Manuscript ID:	bmjopen-2012-000911
Article Type:	Research
Date Submitted by the Author:	20-Jan-2012
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Primary Subject Heading :	Reproductive medicine, obstetrics and gynaecology
Secondary Subject Heading:	Epidemiology
Keywords:	Fetal medicine < OBSTETRICS, Maternal medicine < OBSTETRICS, PERINATOLOGY, REPRODUCTIVE MEDICINE
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Reproductive outcomes following induced abortion: a national register based cohort study in Scotland Siladitya Bhattacharya¹, Alison Lowit¹ Sohinee Bhattacharya^{1*}, Amalraj Raja¹, Amanda J Lee¹, Tahir Mahmood², Allan Templeton¹ ¹Division of Applied Health Sciences, University of Aberdeen ²Forth Park Hospital, Kirkcaldy *Corresponding author

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All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf and declare: The Chief Scientist Office Scotland funded the study; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

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Funding for this research was obtained from a research grant from the Chief Scientist's Office in Scotland (CZG_2_403) but the funding body played no role in the design, analysis or interpretation of the results.

Ethical Approval: Approval was obtained from the Privacy Advisory Committee of the Information and Services Division of the National Health Service in Scotland

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1 2 3	Abstract
4 5	
6	Objective: To investigate reproductive outcomes in women following induced
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9	abortion (IA).
10	Design: Retrospective cohort study
11 12	Setting: Hospital admissions between 1981 and 2007 in Scotland.
13	Participants: Data were extracted on all women who had an IA, a miscarriage or
14	a live birth from the Scottish Morbidity Records. A total of 120,033, 457,477 and
15 16	47,355 women with a documented second pregnancy following an IA, livebirth
17	and miscarriage respectively were identified.
18	Outcomes: Obstetric and perinatal outcomes, especially preterm delivery in a
19	
20 21	second ongoing pregnancy following an IA were compared with those in
22	primigravidae, as well as those who had a miscarriage or live birth in their first
23	pregnancy. Outcomes after surgical and medical termination as well as after one
24 25	or more consecutive IAs were compared.
26	Results: IA in a first pregnancy increased the risk of spontaneous preterm birth
27	compared to that in primigravidae [Adjusted relative risk (Adj. RR) 1.37, 95%
28 29	Confidence Interval (CI) 1.32, 1.42] or women with an initial live birth [Adj. RR
30	
31	1.66, 95% CI 1.58-1.74], but not in comparison with women with a previous
32	miscarriage [Adj. RR 0.85, 95% CI 0.79-0.91].
33 34	Surgical abortion increased the risk of spontaneous preterm birth compared to
35	medical abortion [Adj. RR 1.25, 95% CI 1.07-1.45)]. The adjusted relative risks
36	(95% CI) for spontaneous preterm delivery following two, three and four
37 38	consecutive IAs were 0.94 (0.81-1.10), 1.06 (0.76-1.47) and 0.92 (0.53-1.61)
39	respectively.
40	Conclusion: The risk of preterm birth after induced abortion is lower than that
41	
42 43	after miscarriage but higher than that in a first pregnancy or after a previous live
44	birth. This risk is not increased further in women who undergo two or more
45	consecutive induced abortions. Surgical abortion appears to be associated with an
46 47	increased risk of spontaneous preterm birth in comparison with medical
48	termination of pregnancy.
49	
50 51	Background
51 52	Background
53	Many women start their reproductive careers with an abortion in their first
54	programmy In 2011, 12,926 phortians were performed in Contland (account 2rd
55 56	pregnancy. In 2011, 12,826 abortions were performed in Scotland (accessed 3^{rd}
50 57	November 2011) with the highest rates in women aged 16-19 years 1 . What is
58	

 not yet entirely clear is the effect these abortions may have on subsequent childbearing. Following the legalisation of abortion in 1967, initial research on the effects of an induced abortion on subsequent pregnancies showed no evidence of an increased risk of miscarriage, preterm delivery or low birth weight ^{2,3}. Much of the work in the subject has been hampered by methodological limitations. Randomised controlled studies are not feasible in this context and researchers have looked to observational studies. Many of the published studies have been limited by small sample sizes, self-reported outcomes and the inability to adjust for many potential confounders. A recent review ⁴ reported that six out of twelve relevant studies found an association between induced abortion and preterm birth, as well placenta praevia. More recently a number of large studies found no increased risk of placenta praevia, but reported an association with preterm ⁵⁻⁷ and very preterm delivery ⁸⁻¹⁰. The clinical implications of this are profound as preterm delivery, with its associated problems, remains one of the most significant challenges in obstetrics.

Over a quarter of induced abortions in Scotland in 2005 were repeat procedures¹. While the reproductive sequelae of repeat abortions are unclear, the available literature suggests that the risk of preterm delivery is increased by multiple abortions ^{5,6,8,11}.

Changes in the technique of induced abortion have to be taken into account when assessing their impact on future reproduction. In 1992, 83.6% of terminations were carried out surgically, falling to 60.6% in 1998 and 40.7% in 2006, with the remainder being carried out medically ¹. A number of studies ¹²⁻¹⁴ have compared these methods in terms of safety, efficacy and short term complications, but data on subsequent reproductive outcomes is scant. A recent study ¹⁵ found no difference in reproductive outcomes (ectopic, miscarriage and preterm delivery) following medically and surgically induced abortions, but was unable to adjust for known confounders such as smoking.

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In view of the high current rates of induced abortion, it is essential that women, and those involved in their care, are aware of the reproductive consequences of induced abortion.

The Scottish Morbidity Record (SMR) system in Scotland covers a national population and has captured data on medical and surgical abortions for many years. Over 99.3% of abortions in Scotland are carried out in NHS premises and are recorded in the SMR system. As these data are based on clinical records, any potential bias created by underreporting will be removed. The availability of this large national dataset provides an ideal opportunity to link records on abortion (SMR01) with maternity records (SMR02) in order to explore the risk of preterm delivery and other maternal and perinatal outcomes in women following one or more episodes of induced abortion. The data would also allow a meaningful comparison of outcomes following alternative forms of induced abortion (i.e. medical versus surgical).

The primary aim of this study was to investigate reproductive outcomes in women following induced abortion. In particular we wished to answer the following research questions: 1) Is an induced abortion *in a first pregnancy* associated with spontaneous preterm birth or other adverse obstetric or perinatal outcomes in the second pregnancy? 2) Is an induced abortion performed *after an initial singleton livebirth* associated with spontaneous preterm birth or adverse obstetric or perinatal outcomes in the next pregnancy? 3) Do any of these associations differ by method of induced abortion (i.e. surgical versus medical)? 4) Is the risk of adverse obstetric or perinatal outcomes associated with increasing number of terminations?

Methods

A retrospective cohort study design was used on routinely collected anonymised data extracted from the ISD database. Approval was obtained from the Privacy

Advisory Committee of the Information and Statistics Division (ISD) of the National Health Service, Scotland.

To answer research question 1, data were extracted from the ISD databases (SMR01 and 02) on women aged 15-55 years who had an induced abortion (IA), a miscarriage, or a livebirth in their first pregnancy between 1981 and 2007 which was followed by a second pregnancy event. Reproductive outcomes in the subsequent pregnancy of women who had an IA in their first pregnancy (exposed cohort) were compared with those in two unexposed comparison groups: women in their second pregnancy after a miscarriage in their first pregnancy (Group 1) and women in their second pregnancy after a livebirth in their first pregnancy (Group 2). In addition to these two unexposed cohorts, obstetric and perinatal outcomes in a pregnancy following IA in a first pregnancy (exposed cohort) were also compared with first pregnancy outcomes in women in Group 2 i.e. a primigravid cohort.

To explore outcomes following early pregnancy loss after an initial livebirth (research question 2), data were extracted on all women (15-55 years of age) who had an induced abortion, a miscarriage, or a livebirth, in their second pregnancy (following a livebirth in their first pregnancy) between 1981 and 2007 from the ISD databases (SMR01 and 02) and followed up to identify a third pregnancy event. Reproductive, obstetric and perinatal outcomes in women who had an IA after a singleton term first pregnancy (exposed group) were compared with those in two unexposed groups: (1) women in their third pregnancy following a singleton term delivery in the first pregnancy following two singleton term deliveries.

Women treated by different methods of induced abortion (surgical or medical) in a first pregnancy were compared in terms of reproductive, obstetric and perinatal outcomes (research question 3). Finally, to answer research question 4,

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reproductive and perinatal outcomes were compared between groups of women who had 1, 2, 3 and 4 previous consecutive induced abortions.

Data extraction

The following variables were identified by matching SMR01 and SMR02 datasets between the years 1981 and 2007.

Demographic data: Age at pregnancy events, smoking, and social class (assessed using Carstairs category of deprivation). Induced abortion data: estimated gestation and method of termination (medical or surgical or both). Reproductive outcomes: miscarriage, abortion, livebirth, ectopic and stillbirth. Obstetric and perinatal outcomes: pre-eclampsia, placenta praevia, placental abruption, preterm delivery, very preterm delivery, low birth weight and the mode of delivery. Spontaneous delivery rates were calculated after excluding women who had induced labour and elective (planned) caesarean section.

Socioeconomic status was assessed using the Carstairs categories of social deprivation ¹⁶ which was divided into quintiles for analysis.

Power calculation

Given the number of sub-groups in the analysis coupled with multiple outcomes, a global sample size calculation was not feasible. Preliminary enquiries with ISD suggested that we could identify at least 260,000 terminations (1981-2007), of which 30% (n=69,000) were estimated to have had a subsequent livebirth and 25.5% (n=66,223) were induced abortions in a first pregnancy.

Using a 1:1 ratio of women with induced abortions in a first pregnancy (exposed cohort 1) and unexposed women, we anticipated having over 90% power, at the two-sided 5% significance level, to detect a difference of 0.5% or more in the chances of a preterm birth (an odds ratio of 1.09) assuming that the prevalence of livebirths in the unexposed group was 6%.

Statistical analysis

In the absence of an ideal comparison group for women with a prior abortion, we used 3 unexposed cohorts which could increase the chance of false positive

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associations (type I error). To minimise this, we used a stringent p-value of ≤ 0.01 to denote statistical significance throughout the statistical analyses. Statistically significant relative risks are shown in bold in the relevant tables. Stata version 11 was used throughout the analysis.

Descriptive statistics were used to summarise reproductive outcomes, maternal & perinatal outcomes and potential predictor variables (age, smoking, Carstairs quintiles) between the various exposure groups for each research question in turn. Appropriate univariate analyses [chi square test for comparing categorical variables across exposure groups, t-test (two group comparison) and ANOVA (multiple group comparison) to compare mean differences in age at pregnancy event] across exposure groups were performed.

A generalised linear model was used with Poisson family and robust variance estimator to ascertain the relationship between exposure (first pregnancy induced abortion) and various reproductive outcomes (still birth, miscarriage, ectopic and induced abortion), maternal and perinatal outcomes (pre-eclampsia, placentaprevia, abruption placenta) after adjusting for potential confounders (maternal age, year of delivery, smoking, Carstairs category at relevant pregnancy & interpregnancy interval between exposed and relevant pregnancy). For the outcome of induction of labour, pre-eclampsia, placenta previa and placental abruption were also entered into the model. Similarly, the model pertaining to the outcome low birth weight was also adjusted for gestational age.

As smoking data were not routinely collected before 1992, and rarely collected for women having an induced abortion or miscarriage, smoking status was missing for a high percentage of women. This sometimes led to non-convergence of the statistical models. Therefore, a sensitivity analysis was carried out by re-running all of the multivariate models following exclusion of the smoking variable to determine if the overall effect sizes remained of similar magnitude. This was found to be so.

Results

Demographic characteristics of primigravida, as well as women who had an abortion, livebirth or a miscarriage in their first pregnancy are shown in Table 1. Women with a previous induced abortion were younger and more socially deprived in comparison with women with a livebirth or miscarriage in their first pregnancy. The interpregnancy interval was longest for the abortion group and shortest in women with an initial miscarriage.

Reproductive outcomes following IA, miscarriage and livebirth are shown in Table 2. IA in the first pregnancy increased the risk of having an induced abortion, miscarriage or ectopic pregnancy in the second pregnancy as compared with an initial livebirth. Compared to those who had an initial miscarriage, women who had an IA in their first pregnancy were less likely to have a subsequent still birth, miscarriage or ectopic pregnancy but more likely to have a second induced abortion.

Perinatal outcomes in the next ongoing pregnancy following IA are compared with those in primigravidae and women with an initial a livebirth or miscarriage in Table 2. Compared with women having a previous livebirth, an IA put women at higher risk of pre-eclampsia, abruptio placenta, induction of labour, spontaneous preterm and very preterm delivery (<34 weeks) and delivery of a low birth weight baby (<2500 g).

In comparison with women with a previous miscarriage, a history of IA decreased women's chances of developing pre-eclampsia and spontaneous preterm and very preterm delivery. Risks of pre-eclampsia, placental abruption, delivery of a low birth weight baby and spontaneous preterm and very preterm birth were significantly higher following IA than in primigravid women. The risk of preeclampsia in women with a previous IA was higher that in primigravid women but lower than in women with a previous miscarriage (Table 2).

The demographic characteristics of women who had a livebirth in a first pregnancy and then went on to have induced abortion, livebirth or a miscarriage

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in their second pregnancy are shown in Table 3. Women with an induced abortion in their second pregnancy were younger, belonged to a more deprived social group and were more likely to be smokers than women who had a livebirth or miscarriage in their second pregnancy.

Table 4 shows that reproductive outcomes following an induced abortion, livebirth or miscarriage in the second pregnancy in a cohort of women who had a livebirth in their first pregnancy. The risk of miscarriage in a third pregnancy was reduced in women who had either an IA or a livebirth in a second pregnancy, but the risks of another induced abortion were higher than in women with a previous miscarriage.

Compared to women with two previous livebirths, women with a livebirth followed by an IA were more likely to have pre-eclampsia, placenta praevia, induced labour and spontaneous preterm or very preterm birth (Table 4). They were also more likely to deliver low birthweight babies (<2500g). Women with an IA in a second pregnancy were not at any higher risk of perinatal complications in comparison with women with a previous miscarriage with the exception of an increased risk of having a low birthweight baby.

In records where the method of IA was clearly recorded, 52,560 women were noted to have had surgical and 16,702, medical abortions. As Table 5 shows, reproductive outcomes were comparable in the two groups except for a lower risk of a second induced abortion following surgical termination of pregnancy. The adjusted relative risk of miscarriage, ectopic pregnancy, placenta praevia and spontaneous preterm delivery (<37 weeks) were higher after surgical termination of pregnancy.

Table 6 summarises the perinatal outcomes in subsequent pregnancies following one or more consecutive IAs. The adjusted relative risks of having a low birth weight baby, an induction of labour, preterm birth or very preterm birth were not significantly increased by two, three or four consecutive IAs versus one IA.

Discussion

Principal findings

Our results indicate that women who undergo induced abortion in the first pregnancy have an increased risk of spontaneous preterm labour in comparison with primigravid women or those with a previous livebirth. This risk is lower than that faced by women with a previous miscarriage.

A livebirth prior to an IA does not appear to reduce perinatal risks in women who remain at higher risk of spontaneous preterm birth than primigravidae. Surgical termination appears to be associated with a higher chance of spontaneous preterm (but not very preterm) birth than medical IA. There does not appear to be a statistically significant dose dependent effect of IA on future adverse perinatal outcomes. Women with three or four consecutive induced abortions were not at significantly higher risk of spontaneous preterm birth in comparison with women who have had one termination of pregnancy.

Strengths

To our knowledge this is the largest population based study of reproductive outcomes following an induced abortion. In addressing this question we have been able to compare outcomes after medical and surgical abortion and explore the dose dependent effect of abortion on future preterm delivery. An added strength is use of national data and the ability to discriminate between spontaneous and overall preterm birth as an outcome.

Our analysis is based on data collected over a number of years. In acknowledgement of changes in clinical practice during this time, we have adjusted for year of pregnancy. The choice of an appropriate comparison group to women with a history of induced abortion is problematic. Women who become pregnant after having an induced abortion in a first pregnancy are gravida 2 and para 0. It is impossible to control for both gravidity and parity unless the unexposed cohort have had a prior pregnancy which did not lead to a delivery. Other comparison groups can be either women in their first ongoing pregnancies (gravidity 1 parity 0), or in their second ongoing pregnancies after a previous

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delivery (gravidity 2 parity 1). We feel that our strategy comparing the exposed cohort to all three of the above groups adds validity to our results.

Limitations

The main limitations of this study stem from unrecorded and missing data in relation to certain potential confounding factors within the dataset. For example, smoking data were only available for 50% of women; data on body mass index were unavailable, while data on gestational age at termination were missing in the majority of cases. The actual method of termination (medical versus surgical) was unrecorded in around 25% of all cases while a large number of women appeared to have both medical as well as surgical treatment. Parity number was less reliable in the early years of data collection. This may reflect problems with coding and could potentially affect the quality of our results. In addition the analysis of such a large population based dataset has the capacity to produce statistically significant differences which may or may not be clinically relevant, although this has been minimised by our use of a 1% significance level throughout.

Comparison with previous studies

The association between induced abortion and preterm birth found in this study is consistent with previously published work ¹⁷. Two recent meta-analyses suggest that women who have had an IA are at higher risk of preterm birth in subsequent pregnancies ^{18,19}. Our study shows that after adjustment, women with a previous abortion have an increased chance of a subsequent spontaneous preterm birth and very pre-term birth compared with primigravidae or those who have had a previous livebirth, but at lower risk compared to women who have had a previous miscarriage. Women who had a livebirth before an induced abortion are also more likely to have a spontaneous preterm birth compared to women with two previous livebirths.

Our results did not suggest an increased risk of miscarriage after an induced abortion which is in keeping with ⁴ review of literature. In contrast, Sun and

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colleagues ²⁰ demonstrated an association between surgical abortion and miscarriage in a subsequent pregnancy. Literature on the association between IA and miscarriage or ectopic pregnancy is sparse and conflicting. Thus our findings of increase in ectopic rates after IA compared to women with a previous livebirth merit further study. The higher odds of having a second induced abortion following induced abortion in a first pregnancy as shown in our study have been reported elsewhere ²¹⁻²³.

Available data are suggestive of an association between IA and placenta previa ^{24,} ²⁵, but no association with abruptio placenta ^{26,27}. We found that women in their second pregnancy after an initial induced abortion in the first were at higher odds of placental abruption but women in their third pregnancy after an induced abortion in their second pregnancy had higher odds of placenta previa but not abruptio placenta. Published evidence supports a decreased risk of pre-eclampsia after an IA ^{28,29}. Our results suggest that the risk of pre-eclampsia following IA is higher than that faced by primigravid and parous women but lower than after a previous miscarriage.

Since the introduction of medical abortion there has been much speculation about the rival merits of medical and surgical techniques in terms of future reproductive outcomes. Analysis of Danish data has failed to demonstrate a difference in key outcomes such as preterm birth between medical and surgical abortion ¹⁵ in a study which was unable to identify spontaneous versus induced preterm birth. Our results based on the analysis of a larger cohort and with the ability to identify spontaneous preterm births show a clear association with surgical abortion. As we were unable to adjust for gestational age, we cannot rule out the possibility that surgical abortions may have been performed at a more advanced stage of pregnancy requiring a greater degree of cervical dilatation – thus leading to future preterm labour.

A dose dependent relationship between the number of IAs and future preterm birth has been shown in a number of previous studies ¹⁷. The results of our analysis do not support this. Given our inability to adjust for a number of potential confounders, this needs to be investigated further.

Meaning of the results

 These results confirm previously noted association between abortion and the risk of preterm birth, but highlight the importance of interpreting the data in context. Thus the increased risk of spontaneous preterm birth is marked in comparison with two of our unexposed cohorts, but reduced in comparison with that in women with a previous early pregnancy loss. This emphasises the continuum between miscarriage and spontaneous preterm birth and underlines the fact that the risk of the latter after IA is lower than after what is widely regarded as a common complication of early pregnancy. These data should be useful in a clinical context whilst counselling women contemplating pregnancy or attending an early pregnancy clinic.

Conclusions

The risk of spontaneous preterm birth following an induced abortion is higher in comparison with women in their first pregnancy or after a previous livebirth, but lower than in women with a previous miscarriage. A successful pregnancy leading to a livebirth prior to an induced abortion does not appear to ameliorate this risk while more than one abortion does not appear to increase it. Medical abortion appears to be associated with a lower risk of spontaneous preterm birth in comparison with surgical termination of pregnancy. The results of this study should help provide women as well as health professionals with accurate information to inform clinical decision making and service delivery models for termination of pregnancy.

Contribution to authorship

AT conceived the idea for the study. SB was the Principal Investigator. He designed the study along with SohB, AT, ALee and TM, led the funding

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application, managed the project, interpreted the results and wrote the first draft
of the paper. ALo cleaned the data and performed some of the initial analyses.
SohB co-wrote the funding application, facilitated data manipulation, interpreted
the results and helped to draft the paper. EAR performed the statistical analysis
and interpreted the results with input from ALee. All authors commented on, and
contributed to the final draft of the paper.

Acknowledgements

We thank staff at ISD Scotland for extraction of data from the Scottish Morbidity Records Database and Margery Heath for secretarial assistance.

Funding

The Chief Scientist Office Scotland funded the study. The views expressed are those of the authors and not the funding body.

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TABLE 1: Demographic characteristics at first pregnancy of women who had induced abortion, livebirth or miscarriagein their first pregnancy

			Outcome in fi	rst pregna	ncy	
	0.	Induced abortion N=120,033	Live birth N=457,477	p-value	Miscarriage N=47,355	p-value
Mean Age (SD)		24.68 (7.56)	24.89 (5.11)	<0.001	26.26 (6.13)	<0.001
	1	17265 (17.1)	79705 (18.0)	<0.001	8403 (18.8)	<0.001
	2	18538 (18.3)	81661 (18.4)		8206 (18.4)	
Carstairs Category 1,2	3	19530 (19.3)	84559 (19.1)		8794 (19.7)	
	4	21135 (20.9)	92504 (20.9)		9426 (21.1)	
	5	24615 (24.4)	105313 (23.7)		9788 (21.9)	
	Never	1014 (42.3)	112744 (48.4)	<0.001	4892 (39.8)	<0.001
	Current	676 (28.2)	72182 (31.0)		2044 (16.6)	
	Former	85 (3.5)	22140 (9.5)		533 (4.3)	
Smoking status ²	Not known	622 (26.0)	26088 (11.2)		4818 (39.2)	
	Total	2397	233154		12287	
	Missing	117636 (98.0)	224323 (49.0)		35068 (74.1)	
Interpregnancy interval in Weeks	Median (IQR)	165 (78, 321)	139 (95, 213)	<0.001	65 (47, 104)	<0.001

Values are n (%) unless otherwise specified

¹ Carstairs categories 1 = least deprived, 5 = most deprived

² Percentage based on available information for each group

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TABLE 2: Reproductive and perinatal outcomes following induced abortion, miscarriage or live birth in first pregnancy

Outcome of 2 nd pregnancy	Outcom	Outcome in First pregnancy			Crude	and Adjusted (Adj.) Relativ (99% CI) ¹	ve Risk
	Induced abortion N=120033	Live birth N=457477	Miscarriage N=47355		Induced abortion vs Live birth	Induced abortion vs Miscarriage	
Live birth	67336 (56.1)	355674 (77.7)	36479 (77.0)		Crude 0.72 (0.71, 0.73) Adj. 0.74 (0.73, 0.74)	Crude 0.72 (0.72, 0.73) Adj. 0.69 (0.69, 0.70)	
Still birth	409 (0.34)	1406 (0.31)	247 (0.52)		Crude 1.11 (0.96, 1.28) Adj. 1.06 (0.91, 1.24)	Crude 0.65 (0.53, 0.80) Adj. 0.58(0.46, 0.74)	
Miscarriage	7965 (6.6)	30669 (6.7)	6197 (13.1)		Crude 0.99 (0.96, 1.02) Adj. 1.05(1.01, 1.08)	Crude 0.51 (0.49, 0.53) Adj. 0.56(0.54, 0.59)	
Ectopic	1115 (0.9)	2939 (0.6)	499 (1.1)		Crude 1.45 (1.32, 1.58) Adj. 1.36(1.23, 1.50)	Crude 0.88 (0.77, 1.01) Adj. 0.83(0.71, 0.97)	
Induced abortion	43208 (36.0)	66789 (14.6)	3933 (8.3)		Crude 2.47 (2.43, 2.50) Adj. 2.30(2.27, 2.33)	Crude 4.33 (4.16, 4.51) Adj. 4.64(4.44, 4.85)	
Outcomes in ongoing pregnancies	N=67745	N=357080	N=36726	Primigravida N=457477			Induced abortion vs Primigravida
Pre-eclampsia	1583 (2.3)	2982 (0.8)	922 (2.5)	8649 (1.9)	Crude 2.80 (2.58, 3.03) Adj. 2.42 (2.21, 2.65)	Crude 0.93 (0.84, 1.03) Adj. 0.83 (0.73, 0.94)	Crude 1.24 (1.15, 1.32) Adj. 1.26 (1.17, 1.35)
Placentaprevia	385 (0.6)	1919 (0.5)	289 (0.8)	2042 (0.5)	Crude 1.06 (0.92, 1.22) Adj. 1.09 (0.93, 1.28)	Crude 0.72 (0.59, 0.88) Adj. 0.79 (0.62, 1.01)	Crude 1.27 (1.10, 1.47) Adj. 1.05 (0.91, 1.22)
Abruptio placenta	339 (0.5)	1197 (0.3)	173 (0.5)	1770 (0.4)	Crude 1.49 (1.27, 1.75) Adj. 1.49 (1.25, 1.77)	Crude 1.06 (0.84, 1.35) Adj. 1.00 (0.76, 1.32)	Crude 1.30 (1.11, 1.51) Adj. 1.28 (1.10, 1.50)
Induction of labour ²	18044 (26.6)	69482 (19.5)	10347 (28.2)	120080 (26.3)	Crude 1.37 (1.34, 1.39) Adj. 1.33 (1.30, 1.35)	Crude 0.95 (0.92, 0.97) Adj. 0.98 (0.95, 1.01)	Crude 1.01 (1.00, 1.03) Adj. 1.00 (0.99, 1.02)
Low birth weight $< 2500g^3$	5385 (8.0)	16309 (4.6)	3101 (8.5)	28735 (6.3)	Crude 1.74 (1.67, 1.81) Adj. 1.24 (1.17, 1.31)	Crude 0.94 (0.89, 1.00) Adj. 0.96 (0.90, 1.03)	Crude 1.27 (1.22, 1.31) Adj. 1.08 (1.04, 1.13)
Outcomes in spontaneous births	N= 45656	N=255220	N=23751	N=318217			
Spontaneous preterm birth <37 weeks	4224 (9.3)	13453 (5.3)	2376 (10.0)	21891 (6.9)	Crude 1.76 (1.68, 1.83) Adj. 1.66 (1.58, 1.74)	Crude 0.92 (0.86, 0.97) Adj. 0.85 (0.79, 0.91)	Crude 1.35 (1.29, 1.40) Adj. 1.37 (1.32, 1.42)
Spontaneous very preterm birth <34 weeks	1512 (3.3)	3994 (1.6)	865 (3.6)	7154 (2.3)	Crude 2.12 (1.96, 2.29) Adj. 2.00 (1.83, 2.18)	Crude 0.90 (0.82, 1.01) Adj. 0.86 (0.76, 0.98)	Crude 1.47 (1.37, 1.58) Adj. 1.52 (1.41, 1.63)

Values are n (%) unless otherwise specified

¹ Adjusted for maternal age, year of delivery, Carstairs at first pregnancy & interpregnancy interval.

² Further adjusted for pre-eclampsia, placenta previa & abruptio placenta.

³ Low birth weight also adjusted for gestational age.

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		Outcome in second pregnancy following an initial livebirth				
	\mathbf{k}	Induced abortion N=30527	Live birth N=125855	p-value	Miscarriage N=22404	p-value
Mean Age (SD)		N=30327 26.04 (5.85)	N=125855 26.15 (4.68)	<0.001	N=22404 28.41 (5.42)	0.001
	1	3523 (12.8)	20264 (16.5)		4498 (20.9)	
	2	4304 (15.6)	21985 (17.9)		4079 (18.9)	
Carstairs Category ^{1,2}	3	5186 (18.8)	23425 (19.0)	<0.001	4312 (20.0)	<0.001
	4	6243 (22.6)	25979 (21.1)		4447 (20.6)	
	5	8370 (30.3)	31395 (25.5)		4235 (19.6)	
	Never	393 (39.7)	32464 (48.5)		3165 (46.1)	
	Current	313 (31.6)	20658 (30.9)		1169 (17.0)	
Smoking status ²	Former	43 (4.3)	5359 (8.0)	<0.001	282 (4.1)	0.001
	Not known	241 (24.3)	8482 (12.7)		2243 (32.7)	
	Total	990	66963		6859	
	Missing	29537 96.8)	58892 (46.8)		15545 (69.4)	
Interpregnancy interval	Median(IQR)	108 (61, 209)	152 (96, 256)	<0.001	60 (48, 87)	<0.001

TABLE 3: Demographic characteristics of women who had induced abortion, livebirth or miscarriage after an initial livebirth

Percentage based on available information for each group

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TABLE 4: Reproductive and perinatal outcomes in women who had induced abortion, livebirth or miscarriage following a livebirth in the first pregnancy

Outcome of 3 rd pregnancy	Outco	ome of second pre	egnancy	-	d (Adj.) Relative Risk % CI) ¹
	Induced abortion N=30527	Live birth N=125855	Miscarriage N=22404	Induced abortion vs Live birth	Induced abortion vs Miscarriage
Live birth	18562 (60.8)	85014 (67.5)	17745 (79.2)	Crude 0.90 (0.89, 0.91) Adj. 0.88 (0.87, 0.89)	Crude 0.77 (0.76, 0.78) Adj. 0.77 (0.76, 0.78)
Still birth	84 (0.3)	426 (0.3)	69 (0.3)	Crude 0.81 (0.60, 1.11) Adj. 0.76 (0.55, 1.06)	Crude 0.89 (0.59, 1.36) Adj. 0.86 (0.54, 1.37)
Miscarriage	2005 (6.6)	8778 (7.0)	2869 (12.8)	Crude 0.94 (0.89, 1.00) Adj. 0.93 (0.88, 1.00)	Crude 0.51 (0.48, 0.55) Adj. 0.67 (0.62, 0.72)
Ectopic	339 (1.1)	1064 (0.9)	181 (0.8)	Crude 1.31 (1.12, 1.54) Adj. 1.31 (1.11, 1.56)	Crude 1.38 (1.09, 1.74) Adj. 1.16 (0.90, 1.50)
Induced abortion	9537 (31.2)	30573 (24.3)	1540 (6.9)	Crude 1.29 (1.25, 1.32) Adj. 1.33 (1.30, 1.37)	Crude 4.55 (4.25, 4.86) Adj. 4.37 (4.06, 4.70)
Outcomes in ongoing pregnancies	Induced Abortion N=18646	Live birth N=85440	Miscarriage N=17814		d (Adj.) Relative Risk % CI) ²
Pre-eclampsia	144 (0.8)	567 (0.7)	165 (0.9)	Crude 1.16 (0.92, 1.48) Adj. 1.40 (1.10, 1.79)	Crude 0.83 (0.62, 1.12) Adj. 0.91 (0.66, 1.27)
Placenta previa	183 (1.0)	473 (0.6)	133 (0.8)	Crude 1.77 (1.42, 2.22) Adj. 1.78 (1.40, 2.25)	Crude 1.32 (0.98, 1.76) Adj. 1.34 (0.97, 1.84)
Abruptio placenta	91 (0.5)	325 (0.4)	66 (0.4)	Crude 1.28 (0.95, 1.74) Adj. 1.28 (0.93, 1.77)	Crude 1.32 (0.87, 2.00) Adj. 1.32 (0.83, 2.10)
Induction of labour ³	4298 (23.1)	18239 (21.4)	3968 (22.3)	Crude 1.08 (1.04, 1.12) Adj. 1.11 (1.07, 1.16)	Crude 1.03 (0.98, 1.09) Adj. 1.01 (0.96, 1.07)
Low birth weight $<2500^4$	1086 (5.8)	3905 (4.6)	784 (4.4)	Crude 1.28 (1.17, 1.39) Adj. 1.36 (1.21, 1.51)	Crude 1.32 (1.17, 1.49) Adj. 1.04 (0.90, 1.21)
Outcomes in spontaneous births	Induced abortion N=12868	Live birth N=59220	Miscarriage N=12056	<u></u>	
Spontaneous preterm birth <37 weeks	859 (6.7)	3035 (5.1)	644 (5.3)	Crude 1.30 (1.18, 1.43) Adj. 1.27 (1.14, 1.40)	Crude 1.25 (1.10, 1.42) Adj. 1.14 (0.99, 1.32)
Spontaneous very preterm birth <34 weeks	282 (2.2)	929 (1.6)	189 (1.6)	Crude 1.40 (1.17, 1.66) Adj. 1.36 (1.13, 1.64)	Crude 1.40 (1.10, 1.78) Adj. 1.33 (1.01, 1.74)

Values are n (%) unless otherwise specified

¹ Adjusted for age, year of delivery, carstairs at second pregnancy & interpregnancy interval

² Adjusted for maternal age, year of pregnancy, Carstairs category at second pregnancy & interpregnancy interval

³ Further adjusted for pre-eclampsia, placenta previa & abruptio placenta

⁴ Low birth weight also adjusted for gestational age

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TABLE 5: Reproductive outcomes following medical and surgical abortion

Reproductive outcomes in next (2 nd) pregnancy	Surgical termination in first pregnancy N=52560	Medical termination in first pregnancy N=16702	Surgical vs Medical induced abortion Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹
Live birth	28285 (53.8)	9785 (58.6)	Crude 0.92 (0.90, 0.94) Adj. 1.44 (1.41, 1.48)
Still birth	151 (0.3)	57 (0.3)	Crude 0.84 (0.56, 1.26) Adj. 0.98 (0.57, 1.69)
Miscarriage	3723 (7.1)	1200 (7.2)	Crude0.99 (0.91, 1.07)Adj. 1.45 (1.30, 1.62)
Ectopic	599 (1.1)	120 (0.7)	Crude1.59 (1.23, 2.05)Adj. 1.78 (1.29, 2.45)
Induced Abortion	19802 (37.7)	5540 (33.2)	Crude1.14 (1.10, 1.17)Adj. 0.44 (0.42, 0.46)
Outcome in ongoing pregnancy	N=28, 436	N=9842	
Pre-Eclampsia	688 (2.4)	316 (3.2)	Crude0.75 (0.63, 0.90)Adj.1.12 (0.90, 1.39)
Placenta praevia	248 (0.9)	23 (0.2)	Crude3.73 (2.13, 6.54)Adj. 2.23 (1.17, 4.26)
Abruptio placentae	160 (0.6)	40 (0.4)	Crude 1.38 (0.88, 2.18) Adj. 1.09 (0.63, 1.88)
Birth weight ² <2500 g	2407 (8.5)	697 (7.1)	Crude 1.19 (1.07, 1.33) Adj. 1.12 (0.97, 1.28)
Spontaneous births	N=18126 ³	N=6474 ³	
Preterm <37 wks	1768 (9.8)	533 (8.2)	Crude1.18 (1.05, 1.34)Adj. 1.25 (1.07, 1.45)
Very Preterm <34 wks	633 (3.5)	217 (3.4)	Crude 1.04 (0.86, 1.27) Adj. 1.09 (0.84, 1.40)

Values are n (%) unless otherwise specified

¹ All relative risks have been adjusted for maternal age, year of event, Carstairs category at the previous & interpregnancy interval

² Low birth weight also adjusted for gestational age

³ Only spontaneous delivery considered among live & still birth

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TABLE 6: Comparisons of perinatal outcomes following one or more induced abortions

	No of co	onsecutive previ	ous induced al	portions	Crude		abortion	tive Risks for perir s compared to 1 al onfidence Interval)	oortion	comes after 2, 3
	1 N=25348	2 N=3622	3 N=565	4 N=225		2 vs 1 ⁴		3 vs 1 ⁴		4 vs 1 ⁴
Low birth weight	2188 (8.6)	325 (9.0)	54 (9.6)	20 (8.9)	Crude	1.04 (0.90, 1.20)	Crude	1.11 (0.79, 1.55)	Crude	1.03 (0.59, 1.79)
<2500g ^{2, 3}	2100 (0.0)	323 (9.0)	54 (9.6)	20 (8.9)	Adj.	0.92 (0.77, 1.11)	Adj.	0.99 (0.73, 1.34)	Adj.	0.54 (0.25, 1.16)
Induction of labour	6919 (27.3)	1005 (27.8)	170 (30.1)	72 (32.0)	Crude	1.02 (0.94, 1.09)	Crude	1.10 (0.93, 1.30)	Crude	1.17 (0.91, 1.51)
	0919 (27.3)	1005 (27.8)	170 (30.1)	72 (32.0)	Adj.	1.02 (0.95, 1.10)	Adj.	1.11 (0.94, 1.31)	Adj.	1.20 (0.93, 1.55)
	N=16275	N=2285	N=347	N=136						
Spontaneous					Crude	1.03 (0.88, 1.22)	Crude	1.04 (0.69, 1.55)	Crude	1.43 (0.84, 2.44)
preterm birth <37 weeks	1676 (10.3)	243 (10.6)	37 (10.7)	20 (14.7)	Adj.	0.94 (0.81, 1.10)	Adj.	1.06 (0.76, 1.47)	Adj.	0.92 (0.53, 1.61)
Spontaneous					Crude	1.01 (0.76, 1.35)	Crude	1.30 (0.70, 2.41)	Crude	1.76 (0.76, 4.05)
preterm birth <34weeks	613 (3.8)	87 (3.8)	17 (4.9)	9 (6.6)	Adj.	0.96 (0.71, 1.28)	Adj.	1.14 (0.60, 2.14)	Adj.	1.61 (0.69, 3.72)

Values are n (%) unless otherwise specified

¹ All relative risks have been adjusted for maternal age, year of event, Carstairs category & interpregnancy interval.

² Low birth weight also adjusted for gestational age

³ Percentage calculated based on number available in the group

Comparison group is women with 1 IA

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		Supplemental file: STROB	E Statement					
	Chec	Checklist of items that should be included in reports of cohort stud						
	ltem No	Recommendation	Location within manuscript					
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 	Title & Abstract: Line 51 Abstract: Lines 52 - 97					
		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	Introduction: Lines 112 - 159					
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction: Lines 161- 170					
Methods								
Study design	4	Present key elements of study design early in the paper	Methodology: Line 173					
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods Lines 178-181					
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 	Methods: Lines 178 - 207 Not applicable					
		exposed and unexposed						
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods: Lines 213 - 221					
Data sources/ measuremen t	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	Methods: Lines 210 - 211.					
Bias	9	Describe any efforts to address potential sources of bias	The only possible source of bias could be misclassification of variables as routinely collected data are used. We think that the large dataset should					

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			compensate for that.
Study size	10	Explain how the study size was	All available data were
		arrived at	included.
			Power calculation: line
			225 -235.
Quantitative	11	Explain how quantitative variables	Statistical analysis:
variables		were handled in the analyses. If	Lines 238-267
		applicable, describe which groupings	
		were chosen and why	
Statistical	12	(a) Describe all statistical methods,	Statistical analysis:
methods		including those used to control for	Lines 238-267
		confounding	
		(b) Describe any methods used to	Methods: Lines 203 -
		examine subgroups and interactions	207
		(c) Explain how missing data were	Methodology: Lines
		addressed	152 - 159
		(d) If applicable, explain how loss to	Not applicable.
		follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	Methodology Lines
			261-267
Results			
Participants	13*	(a) Report numbers of individuals at	Results: Lines 176 -
		each stage of study—eg numbers	177
		potentially eligible, examined for	
		eligibility, confirmed eligible, included	
		in the study, completing follow-up,	
		and analysed	
		(b) Give reasons for non-participation	Not applicable
		at each stage	
		(c) Consider use of a flow diagram	The whole population
			was selected
Descriptive	14*	(a) Give characteristics of study	Tables 1 and 3
data		participants (eg demographic, clinical,	
		social) and information on exposures	
		and potential confounders	
		(b) Indicate number of participants	Tables 1 and 3
		with missing data for each variable of	
		interest	
		(c) Summarise follow-up time (eg,	Table 1 and 3
		average and total amount)	
Outcome	15*	Report numbers of outcome events or	Tables 2,4,5
data		summary measures over time	
Main results	16	(a) Give unadjusted estimates and, if	Table 2, 4, 5
	_	applicable, confounder-adjusted	, ,
		estimates and their precision (eg,	
		95% confidence interval). Make clear	
		which confounders were adjusted for	
		-	
		and why they were included	

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		continuous variables were	
		categorized	
Other	17	Report other analyses done—eg	Results: Lines 266-7
analyses		analyses of subgroups and	
		interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference	Discussion: Lines 341-
		to study objectives	353
Limitations	19	Discuss limitations of the study, taking	Discussion: Lines 377-
		into account sources of potential bias	389
		or imprecision. Discuss both direction	
		and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation	Discussion: Lines 439-
		of results considering objectives,	449
		limitations, multiplicity of analyses,	
		results from similar studies, and other	
		relevant evidence	
Generalis-	21	Discuss the generalisability (external	Discussion: Lines 363-
ability		validity) of the study results	373

Other information	ation		
Funding	22	Give the source of funding and the role of the funders	Lines 479-480
		for the present study and, if applicable, for the	
		original study on which the present article is based	



Reproductive outcomes following induced abortion: a national register based cohort study in Scotland

Journal:	BMJ Open	
Manuscript ID:	bmjopen-2012-000911.R1	
Article Type:	Research	
Date Submitted by the Author:	24-May-2012	
Complete List of Authors:	Bhattacharya, Siladitya; University of Aberdeen, Institute of Applied Health Sciences Lowit, Alison; University of Aberdeen, Institute of Applied Health Sciences Bhattacharya, Sohinee; University of Aberdeen, Public Health Raja, Edwin Amalraj; University of Aberdeen, Medical Statistics, Dept. of Public Health Lee, Amanda; University of Aberdeen, Medical Statistics, Dept. of Public Health Mahmood, Tahir; Forth Park Hospital, Obstetrics and Gynaecology Templeton, Allan; University of Aberdeen, Institute of Applied Health Sciences	
<pre>Primary Subject Heading: Reproductive medicine, obstetrics and gynaecology</pre>		
Secondary Subject Heading: Epidemiology		
Keywords:	Fetal medicine < OBSTETRICS, Maternal medicine < OBSTETRICS, PERINATOLOGY, REPRODUCTIVE MEDICINE	
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2	1	Reproductive outcomes following induced abortion: a national register
3 4	1	Reproductive outcomes following induced abortion: a national register
5	2	based cohort study in Scotland
6 7	3	Siladitya Bhattacharya ¹ , Alison Lowit ¹ Sohinee Bhattacharya ^{1*} , Edwin A Raja ¹ ,
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28 29	18	
30	19	All authors have completed the Unified Competing Interest form at
31 32	20	http://www.icmje.org/coi_disclosure.pdf and declare: The Chief Scientist Office Scotland
33	21	funded the study; no financial relationships with any organisations that might have an
34	22	interest in the submitted work in the previous three years; no other relationships or
35 36	23	activities that could appear to have influenced the submitted work
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Abstract

39 Background

The impact of induced abortions on subsequent childbearing is of major importance to women. Some published studies have shown a link between induced abortion and subsequent preterm birth but existing studies have been largely unable to disentangle spontaneous and induced preterm delivery. The primary aim of this study was to investigate reproductive outcomes in women following induced abortion.

4647 Methods

Data were extracted on all women (aged 15-55 years) who had an induced abortion, a miscarriage, a livebirth, or an ongoing pregnancy and live delivery in their first pregnancy recorded between 1981 and 2007 in the Scottish Morbidity Records databases. Obstetric and perinatal outcomes in a second ongoing pregnancy following an induced abortion were compared with those in primigravidae, as well as those who had had a miscarriage or livebirth in their first pregnancy. Spontaneous preterm birth rates were also compared in women following surgical and medical termination as well as after one or more consecutive induced abortions.

5758 Findings

A total of 120,033, 457,477 and 47,355 women with a documented second pregnancy following an initial induced abortion (IA), livebirth and miscarriage respectively between 1981 and 2007 were identified. Data from first pregnancies from the 457,477 women who had an initial livebirth constituted a third unexposed cohort of primigravidae. Women who underwent an initial induced abortion were younger and more socially deprived than those who had a livebirth or a miscarriage (p < 0.001). The livebirth group contained the highest proportion of current smokers, followed by the abortion group.

Women with an induced abortion in a first pregnancy had a higher risk of spontaneous preterm live birth in the next pregnancy than women in their first pregnancies [Adjusted relative risk (Adj. RR) 1.37, 99% Confidence Interval (CI) 1.32, 1.43] or women who had a livebirth in their first pregnancy [Adj. RR 1.66, 99% CI 1.58-1.74], but a lower risk in comparison with women with a previous miscarriage [Adj. RR 0.85, 99% CI 0.79-0.92]

Following an initial induced abortion, women were more likely to be diagnosed with placental abruption than either primigravidae [Adj. RR 1.28, 99% CI 1.10-

 1.50] or women with a previous livebirth [Adj. RR 1.49, 99% CI 1.25-1.77]. The
risk of pre-eclampia was higher in women with previous induced abortion in
comparison with primigravidae [Adj. RR 1.26, 99% CI 1.17-1.35] or women with
a previous livebirth [Adj. RR 2.42, 99% CI 2.21- 2.65].

In comparison with women who had an initial miscarriage, women with an IA in their first pregnancy were less likely to have a subsequent miscarriage [Adj. RR 0.56, 99% CI 0.54-0.590] or ectopic pregnancy [Adj. RR 0.83, 95% CI 0.71-0.97] but more likely to have a second induced abortion [Adj. RR 4.64, 99% CI 4.44-4.85]. They were less prone to develop pre-eclampsia [Adj. RR 0.83, 99% CI 0.73-0.94] in their next ongoing pregnancy.

Surgical abortion was associated with a higher chance of spontaneous preterm birth in the next ongoing pregnancy than medical abortion [Adj. RR 1.25, 99% CI 1.07-1.45)]. Compared with primigravid women, the risk of spontaneous preterm delivery was higher after surgical (Adj. RR 1.45 (1.37, 1.55) but not medical abortion (1.11 (0.99, 1.24). The adjusted relative risks (99% CI) for spontaneous preterm birth in the next ongoing pregnancy following two, three and four consecutive IAs in comparison with a single IA were 1.02 (0.86-1.21), 1.01 (0.66-1.55) and 1.38 (0.71-2.70) respectively.

97 Interpretation

Induced abortion in a first pregnancy is associated with a higher risk of spontaneous pretermbirth in a subsequent pregnancy than that in primigravidae or women with a previous livebirth, but is lower than that observed in women with an initial miscarriage. This is the first study to show that surgical, but not medical abortion appears to be associated with an increased risk of spontaneous preterm birth.

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106 Background

Many women start their reproductive careers with an abortion in their first pregnancy. In 2009, 13,005 abortions were performed in Scotland with the highest rates in women aged 16-19 years ¹. What is not yet entirely clear is the effect these abortions may have on subsequent childbearing. It has been believed that infection, cervical trauma and endometrial curettage associated with induced abortion could lead to future infertility, ectopic, preterm delivery and placenta praevia, but the data from existing observational studies are mixed $^{2-18}$ Following the legalisation of abortion in 1967, initial research on the effects of an induced abortion on subsequent pregnancies showed no evidence of an increased risk of miscarriage, preterm delivery or low birth weight^{19, 20}. Much of the work in the subject has been hampered by methodological limitations; randomised controlled studies are not feasible in this context and researchers have looked to observational studies. Many of the published studies have been limited by small sample sizes, self-reported outcomes and inability to adjust for many potential confounders. A recent review ²¹ reported that half of the twelve relevant studies found an association between induced abortion and preterm birth as well placenta praevia. More recently a number of large studies found no increased risk of placenta praevia, but supported an association with preterm ^{18, 22, 23} and verv preterm delivery ^{24, 25} The clinical implications of this are profound as reducing the incidence of preterm delivery, with its considerable associated problems, remains one of the most significant challenges in obstetrics.

Over a quarter of induced abortions in Scotland in 2005 were repeat procedures ¹ [ISD, personal communication]. While the reproductive sequalae of repeat abortions are unclear, the available literature suggests that the risk of preterm delivery is increased by multiple abortions ^{18, 22, 24, 26}.

Changes in the technique of abortion have to be taken into account when assessing their impact on future reproduction. In 1992, 83.6% of terminations were carried out surgically, falling to 60.6% in 1998 and 40.7% in 2006, with the reminder being carried out medically ¹accessed 23 March 2010. A number of studies ²⁷⁻²⁹ have compared these methods in terms of safety, efficacy and short term complications but data on subsequent reproductive outcomes is scant. A recent study ³⁰ found no difference in reproductive outcomes (ectopic, miscarriage and preterm delivery) following medically and surgically induced abortions, but was unable to adjust for known confounders such as smoking.

 In view of the high current rates of induced abortion, it is important for women and those involved in their care to be aware of any potential associations with future reproductive outcomes.

The Scottish Morbidity Record (SMR) system in Scotland covers a national population and has captured data on medical and surgical abortion for many years. Over 99.3% of abortions in Scotland are carried out in NHS premises and are recorded in the SMR system. As these data are based on clinical records, any potential bias created by underreporting will be removed. The availability of this large national dataset provides an ideal opportunity to link records on abortion (SMR01) with maternity records (SMR02) in order to explore the risk of preterm delivery and other maternal and perinatal outcomes in women following one of more episodes of induced abortion. The data would also allow a meaningful comparison of outcomes following alternative forms of induced abortion (i.e. medical versus surgical).

The primary aim of this study was to investigate reproductive outcomes in women following induced abortion. In particular we wished to answer the following research questions: 1) Is an induced abortion in a first pregnancy associated with spontaneous preterm birth or other adverse obstetric or perinatal outcomes in the second pregnancy? 2) Is an induced abortion performed after a singleton term first pregnancy associated with spontaneous preterm birth or adverse obstetric or perinatal outcomes in the next pregnancy? 3) Do any of these associations differ by method of induced abortion (i.e. surgical versus medical)? 4) Is the risk of adverse obstetric or perinatal outcomes associated with increasing number of terminations?

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170 Methods

A retrospective cohort study design was used on routinely collected data
extracted from the Information and Statistics Division (ISD) database. Approval
was obtained from the Privacy Advisory Committee of the National Health
Service, Scotland.

Data were extracted from the ISD databases (SMR01 and 02) on women aged 15-55 years who had an induced abortion, a miscarriage, a live birth, or an ongoing pregnancy and live delivery in their first pregnancy between 1981 and 2007 followed by a second pregnancy event. Reproductive outcomes in the subsequent pregnancy of women who had an IA in their first pregnancy (exposed

cohort) were compared with those in two unexposed groups: 1) women in their second pregnancy after a miscarriage in their first pregnancy and 2) women in their second pregnancy after a live birth in their first pregnancy. In addition to these two unexposed cohorts, obstetric and perinatal outcomes in the subsequent pregnancy of women who had an IA in their first pregnancy (exposed group), were also compared with those women in their first pregnancy.

To explore outcomes following early pregnancy loss after an initial livebirth, data were extracted on all women (15-55 years of age) who had an induced abortion, a miscarriage, or a live birth, in their second pregnancy (following a live birth in their first pregnancy) between 1981 and 2007 from the ISD databases (SMR01 and 02) and followed up to identify a third pregnancy event. Reproductive, obstetric and perinatal outcomes in women who had an IA after a singleton term first pregnancy (exposed group), were compared with those in two unexposed groups: 1) women in their third pregnancy following a singleton term delivery in the first pregnancy and a miscarriage in the second pregnancy and 2) women in their third pregnancy following two singleton term deliveries

Women treated by different methods of induced abortion (surgical or medical) in a first pregnancy were compared in terms of reproductive, obstetric and perinatal outcomes. Finally, to answer research question 4, reproductive and perinatal outcomes were compared between women who had 1, 2, 3 and 4 previous consecutive induced abortions and women with no previous abortions. Each group of women was independent of the others – for example women who had 3 abortions were excluded from the group with 2 abortions. For each analysis, except research question 4, the women were matched on parity as the risk of adverse obstetric outcomes is dependent on parity with primiparous women suffering the highest risk.

210 Data extracted

The following variables were identified by matching SMR01 and SMR02 datasetsbetween the years 1981 and 2007.

Demographic details: Age at pregnancy events, smoking status, and social class (assessed using Carstairs category of deprivation) in the exposed group were compared with each of the 3 unexposed cohorts

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Induced abortion details: estimated gestation and method of termination (medical or surgical or both) were recorded for the exposed group. Reproductive outcomes: miscarriage, abortion, livebirth, ectopic, stillbirth in the exposed group were compared with the unexposed cohorts. Obstetric and perinatal outcomes: The incidence of pre-eclampsia, placenta praevia, placental abruption, preterm delivery, very preterm delivery, low birth weight and the mode of delivery in the exposed cohort were compared with each of the 3 unexposed cohorts. Spontaneous delivery rates (including live and stillbirth) were calculated after excluding women who had induced labour and elective (planned) caesarean section.

Socioeconomic status was assessed using the Carstairs index ³¹ which was
 divided into quintiles for analysis.

Power Calculation

Given the number of sub-groups in the analysis coupled with multiple outcomes, a global sample size calculation was not feasible. Preliminary enquiries with ISD suggested that we could identify at least 260,000 terminations (1981-2007), of which 30% (n=69,000) were estimated to have had a subsequent live birth and 25.5% (n=66,223) were induced abortions in a first pregnancy.

Using a 1:1 ratio of women with induced abortions in a first pregnancy (exposed cohort) and unexposed women, we anticipated having over 90% power, at the two-sided 5% significance level, to detect a difference of 0.5% or more in the chances of a preterm birth (ie, an odds ratio of 1.09) assuming that the prevalence of live births in the unexposed group was 6%.

245 Statistical Analysis

In the absence of an ideal comparison group for women with a prior abortion, we used 3 unexposed cohorts which could increase the chance of false positive associations (type I error). To help minimise this, we used a stringent p-value of ≤ 0.01 to denote statistical significance throughout the statistical analyses.

A generalised linear model was used with Poisson family and robust variance estimator to ascertain the relationship between exposure (first pregnancy induced abortion) and various reproductive outcomes (still birth, miscarriage, ectopic and induced abortion), maternal and perinatal outcomes (pre-eclampsia, placentaprevia, abruption placenta) after adjusting for potential confounders (maternal

age, year of delivery, smoking & carstairs at relevant pregnancy). For the outcome of induction of labour, pre-eclampsia, placenta previa and placental abruption were also entered into the model. Similarly, the outcome low birth weight was also adjusted for gestational age. Stata version 11 was used for the analysis and a stringent p-value of ≤ 0.01 was used to denote statistical significance throughout.

As smoking data were not routinely collected in the maternity database (SMR02) before 1992, and rarely recorded for women having an induced abortion or miscarriage. Thus self-reported smoking status, collected at antenatal booking visit, though available for some women was non-randomly missing for a high percentage of women. This sometimes led to non-convergence of the statistical models. Therefore, a sensitivity analysis was carried out by re-running all of the multivariate models excluding the smoking variable to determine if the overall effect sizes remained of similar magnitude. This was found to be so.

271 Results

Demographic characteristics of women who had an abortion in their first pregnancy were compared with those who had either a live birth or a miscarriage in their first pregnancy and with primigravida women (Table 1). Women with a previous induced abortion were significantly older, more socially deprived and more likely to be smokers than primigravida women or those who had a live birth or a miscarriage in a previous pregnancy.

 Table 2 presents reproductive outcomes in a subsequent pregnancy following IA, livebirth and miscarriage in the first pregnancy. As Table 2 shows, an IA in the first pregnancy increased the risks of having a still birth or an induced abortion in the second pregnancy as compared with an initial livebirth. Compared to those who had an initial miscarriage, women who had an IA in their first pregnancy were less likely to have a subsequent miscarriage or ectopic pregnancy, but more likely to have another induced abortion.

Perinatal outcomes in the next ongoing pregnancy following IA are also compared with those in primigravida and women who have had a livebirth or miscarriage in Table 2. Compared with women having a previous livebirth, an IA put women at higher risk of pre-eclampsia, abruptio placenta, induction of labour, spontaneous preterm and very preterm delivery (<32weeks) extremely preterm (< 28 weeks) and delivery of a low birth weight baby (<2500 g) but not placenta praevia.

In comparison with women with a previous miscarriage, a history of IA decreased women's chances of developing pre-eclampsia and spontaneous preterm and very preterm delivery. Risks of pre-eclampsia, placental abruption (but not placenta praevia), delivery of a low birth weight baby and spontaneous preterm, very preterm and extremely preterm birth were significantly higher following IA than in primigravid women. The risk of pre-eclampsia in women with a previous IA was higher than in primigravid women but lower than in women with a previous miscarriage (Table 2).

The demographic characteristics of women who had a livebirth in a first pregnancy and then went on to have induced abortion, live birth or a miscarriage in their second pregnancy are shown in Table 3. Women with an induced abortion in their second pregnancy were younger, belonged to a more deprived social group and were more likely to be smokers than women who had a live birth in their second pregnancy. Compared to women who had a miscarriage in their second pregnancy, women with a previous induced abortion were older, belonged to more deprived social classes and were more likely to smoke.

As Table 4 shows, IA in the second pregnancy increased the risks of having ectopic or an induced abortion in the third pregnancy as compared with an initial livebirth. The risk of miscarriage in a third pregnancy was reduced in women who had either an IA in a second pregnancy, but the risks of another induced abortion were higher than in women with a previous miscarriage.

Compared to women with two previous livebirths, women with a livebirth followed by an IA were more likely to have pre-eclampsia, placenta praevia, induced labour, low birthweight and spontaneous preterm, very preterm and extremely preterm birth (Table 4). Women with an IA in a second pregnancy were not at any significantly higher risk of perinatal complications in comparison with women with a previous miscarriage.

In records where the method of IA was clearly recorded, 52,560 women were noted to have had surgical and 16,702, medical abortions. As Table 5 shows, reproductive outcomes were comparable in the two groups except for a lower risk of a second induced abortion following surgical termination of pregnancy. The adjusted relative risk of miscarriage, ectopic pregnancy, placenta praevia and spontaneous preterm delivery (<37 weeks) were significantly higher after surgical termination. In comparison with primigravid women i.e. no previous abortion,

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women with a medical abortion had an increased risk of placental abruption, but not spontaneous preterm, very preterm or extremely preterm delivery. In contrast, women with a surgical abortion had higher risks of all three types of spontaneous preterm delivery. They also had an increased risk of preeclampsia, placenta praevia, abruption and low birthweight babies. More women had repeat abortion following surgical termination of pregnancy, and fewer went on to have a livebirth in comparison with primigravid women and those who had medical terminations.

Table 6 summarises the risk of spontaneous preterm delivery in subsequent pregnancies following one or more consecutive IAs in comparison to those with no previous abortions (primigravid women). The adjusted relative risks of spontaneous preterm birth, (< 37 weeks) was incrementally increased in women undergoing 1, 2, 3 and 4 induced abortions. The adjusted relative risk of spontaneous very preterm delivery (< 32 weeks) was increased after 1 and 4 induced abortions. While the adjusted relative risk of spontaneous extremely preterm delivery (<28weeks) was increased by 2 and 4 previous induced abortions. Additional induced abortions did not increase the adjusted relative risks of any type of spontaneous preterm birth after termination of pregnancy.

353 Discussion

Principal findings

Our results suggest that an induced abortion in the first pregnancy predisposes women to higher maternal and perinatal risks in comparison to women with a previous live birth. Compared to an initial miscarriage, an induced abortion in a first pregnancy led to a higher subsequent risk of miscarriage or ectopic pregnancy, induced abortion and pre-eclampsia. Women with a previous induced abortion face increased risks of antepartum haemorrhage and spontaneous preterm birth than women in their first pregnancy.

A livebirth prior to an IA does not appear to ameliorate perinatal risks in women who are at higher risk of spontaneous preterm birth than primigravida. Surgical termination appears to be associated with a higher chance of spontaneous preterm birth than medical IA. There does not appear to be a dose dependent effect of IA on future adverse perinatal outcomes. Women with three or four consecutive induced abortions were not at significantly higher risk of spontaneous

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preterm birth in comparison with women who have had one termination ofpregnancy.

375 Strengths

To our knowledge this is the largest population based study of reproductive outcomes following an induced abortion. Registry based previous studies reporting preterm birth rates as an outcome have been unable to discriminate between spontaneous and induced preterm delivery; this is one of the first papers to be able to calculate and report spontaneous preterm birth rates after induced abortion.

We have acknowledged changes in clinical practice over the years during which data were collected and have adjusted for year of pregnancy in the regression models. The choice of an appropriate comparison group to women with a history of induced abortion is problematic. Women who are pregnant again after having undergone an induced abortion in a previous (first) pregnancy are gravida 2 and parity 0. It is impossible to control for both gravidity and parity unless the unexposed cohort have had a prior pregnancy which did not lead to a delivery. Other comparison groups can be either women in their first ongoing pregnancies (gravidity 1 parity 0), or in their second ongoing pregnancies after a previous delivery (gravidity 2 parity 1). We feel that our strategy comparing the exposed cohort to all three of the above groups adds validity to our results.

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395 Limitations

The main limitations of this study stem from unrecorded and missing data in relation to certain potential confounding factors within the dataset. For example, smoking data were only available for 50% of women; data on body mass index were unavailable while data on gestational age at termination was missing in the majority of cases. The actual method of termination (medical versus surgical) was unrecorded in around 25% of all cases, while a large number of women appeared to have both medical as well as surgical treatment. Parity number was less reliable in the early years of data collection. This may reflect problems with coding and could potentially affect the quality of our results. In addition, the analysis of such a large population based dataset has the capacity to produce statistically significant differences which may or may not be clinically relevant,

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407 although this has been minimised by our use of a stringent 1% significance level408 throughout.

Defining an ideal reference group is a challenge in studies exploring outcomes after induced abortion. While we have partially addressed this issue by using more than one unexposed cohort, our data do not allow us to adjust for potential differences in pregnancy intentions between groups, which can impact on antenatal care and perinatal outcomes.

Unrecorded data relating to key potential confounders cannot exclude the possibility that some associations are not explained by abortion itself but by special circumstances of women seeking abortion which also increases their risk of complications in pregnancy. We ran a separate analysis to identify previous pregnancy complications in women who either had an induced abortion, miscarriage or livebirth in a second pregnancy. As supplementary Table A shows, induced abortion in the second pregnancy was not significantly associated with increased relative risk (99% confidence interval) of preeclampsia, placenta praevia, placental abruption and low birthweight respectively compared to either livebirth [0.99 (0.85, 1.16); 1.29 (0.99, 1.67) 1.32 (0.96, 1.82) 1.08 (0.98, 1.18)] or miscarriage [0.79 (0.65, 0.96) 1.17 (0.81, 1.69) 1.08 (0.70, 1.68) 1.14 (1.00, 1.30)].

Comparison with previous studies

The association between induced abortion and preterm birth found in this study is consistent with previously published work ³². Two recent meta-analyses suggest that women who have had an IA are at higher risk of preterm birth in subsequent pregnancies ^{33, 34}. Our study shows that after adjustment women with a previous abortion have an increased chance of a subsequent preterm birth and very pre-term birth compared with primigravidae or those who have had a previous live birth, but at no significantly greater risk compared to women who have had a previous miscarriage. Women who had a live birth before an induced abortion are more likely to have a preterm birth compared to women with two previous live births.

Our results did not suggest a signficant increased risk of miscarriage after an induced abortion which is in keeping with a review of literature ²¹. In contrast, Sun (2003)³⁵ demonstrated an association between surgical abortion and miscarriage in a subsequent pregnancy. Literature on the association between IA and miscarriage or ectopic pregnancy is sparse and conflicting. The increased risk of having a second termination following

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induced abortion in a first pregnancy highlighted in our study has been
reported elsewhere ³⁶⁻³⁸. While women who had an abortion were more likely to
have a subsequent abortion, but they may also be more likely to have an
unintended pregnancy. This should be seen a potential risk factor which should be
explored in future studies.

Available literature suggests there is an association between IA and placenta previa ^{39, 40}, but no association with abruptio placenta ^{41, 42}. This study found that women in their second pregnancy after an initial induced abortion in the first were at higher odds of both placenta previa and abruptio placenta, women in their third pregnancy after an induced abortion in their second pregnancy had higher odds of placenta previa, but not abruptio placenta. Published evidence supports a decreased risk of pre-eclampsia after an IA ^{43, 44}. Our results suggest a risk of developing preeclampsia which is on par with primigravid women, but lower than women with a previous miscarriage. The reasons for these associations are unclear and hence any explanations can only be speculative. Problems with placental position and function could occur due to disruption of the endometrium by vigorous curettage. The quality of placental function in a previous pregnancy could influence susceptibility to future preeclampsia.

Since the introduction of medical abortion there has been much speculation about the rival merits of medical and surgical techniques, especially in terms of future reproductive outcomes. Analysis of Danish data has failed to demonstrate a difference in key outcomes such as preterm birth between medical and surgical abortion, but this study was unable to identify spontaneous versus induced preterm birth ³⁰. With our ability to identify spontaneous PTBs, we have shown a clear association with surgical abortion. However, since we were unable to adjust for gestational age, we cannot rule out the possibility that surgical abortions may have been performed at a more advanced stage of pregnancy requiring a greater degree of cervical dilatation - thus leading to future preterm labour. Our results are supported by a recent publication showing that the risk of preterm birth after one or more medical abortions is higher than after surgical abortion and comparable to that in primigravid women ¹¹.

A dose dependent relationship between the number of IAs and future PTB has
 been shown in a number of previous studies ³². The results of our analysis do not

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482 support this. Given our inability to adjust for a number of potential confounders,
483 this needs to be investigated further.

Our data suggest that medical and surgical terminations may impact differently on future reproductive outcomes - with a higher risk of spontaneous preterm birth after surgery. We were unable to disentangle the separate effects of repeated medical and surgical abortion due to a relative paucity of numbers. A recent publication ¹¹ found an increased risk of premature delivery following multiple surgical, but not first trimester, medical induced abortions. While this could reflect the effect of repeated surgical trauma to the cervix, this needs further exploration in future studies with long term periods of follow up.

A key challenge in studying health sequalae after induced abortion is to deal with
potential differences in pregnancy intentions between comparison groups. While
women who had an abortion were more likely to have a subsequent abortion,
they may also be more likely to have an unintended pregnancy, which needs to
be acknowledged as a potential risk factor in future studies.

500 Conclusions

Induced abortion in a first pregnancy is associated with a higher risk of spontaneous preterm birth in a subsequent pregnancy in comparison with primigravid women, but not women with a previous miscarriage. A successful pregnancy leading to a livebirth prior to an induced abortion does not appear to ameliorate this risk while more than one abortion does not significantly increase it. Surgical abortion appears to be associated with an increased risk of spontaneous very preterm birth in comparison with medical termination of pregnancy. The results of this study should help provide women as well as health professionals with accurate information to inform clinical decision making and tailor antenatal care to address women's risk profiles.

AT conceived the idea for the study. SB was the Principal Investigator. He designed the study along with SohB, AT, ALee and TM, led the funding application, managed the project, interpreted the results and wrote the first draft of the paper. ALo cleaned the data and performed some of the initial analyses. SohB co-wrote the funding application, facilitated data manipulation, interpreted the results and helped to draft the paper. EAR performed the statistical analysis and interpreted the results with input from ALee. All authors commented on, and contributed to the final draft of the paper.

520	
521	Acknowledgements
522	We thank staff at ISD Scotland for extraction of data from the Scottish Morbidi
523	Records Database and Margery Heath for secretarial assistance.
524	
525	Funding
526	The Chief Scientist Office Scotland funded the study. The views expressed a
527	those of the authors and not the funding body.
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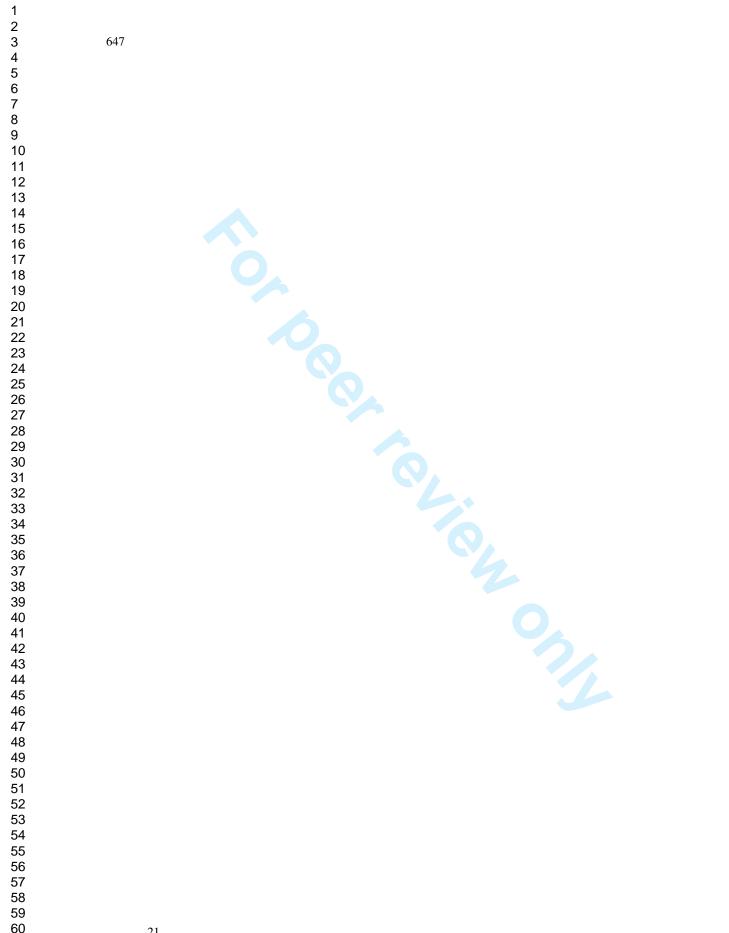


TABLE 1: Demographic characteristics at first pregnancy of women who had induced abortion, livebirth or miscarriage in their first pregnancy

		Outcome in first pregnancy					
	9	Induced abortion N=120,033	Live birth N=457,477	p-value	Miscarriage N=47,355	p-value	
Mean Age (SD)		24.68 (7.56)	24.89 (5.11)	<0.001	26.26 (6.13)	<0.001	
	1	17265 (17.1)	79705 (18.0)	<0.001	8403 (18.8)	< 0.001	
	2	18538 (18.3)	81661 (18.4)		8206 (18.4)		
Carstairs Category ^{1,2}	3	19530 (19.3)	84559 (19.1)		8794 (19.7)		
	4	21135 (20.9)	92504 (20.9)		9426 (21.1)		
	5	24615 (24.4)	105313 (23.7)		9788 (21.9)		
	Never	1014 (42.3)	112744 (48.4)	<0.001	4892 (39.8)	<0.001	
	Current	676 (28.2)	72182 (31.0)	1/	2044 (16.6)		
	Former	85 (3.5)	22140 (9.5)		533 (4.3)		
Smoking status ²	Not known	622 (26.0)	26088 (11.2)		4818 (39.2)		
	Total	2397	233154		12287		
	Missing	117636 (98.0)	224323 (49.0)		35068 (74.1)		
Interpregnancy interval in Weeks	Median (IQR)	165 (78, 321)	139 (95, 213)	<0.001	65 (47, 104)	<0.001	

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12	655 TABLE 2:	R
13 14	Outcome of 2 nd	
15	pregnancy	
16 17		
18	Live birth	
19 20	Live birth	
21	Still birth	
22 23	Miscarriage	
24 25	Ectopic	
26	Induced abortion	
27 28	Outcomes in ongoin pregnancies	ıg
29 30	Pre-eclampsia	
31 32	Placentaprevia	
33 34	Abruptio placenta	
35 36	Induction of labour ²	
37 38	Low birth weight <25	00g
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Values are n (%) unless otherwise specified

Carstairs categories 1 = least deprived, 5 = most deprived

² Percentage based on available information for each group

555 **TABLE 2:** Reproductive and perinatal outcomes following induced abortion, miscarriage or live birth in first pregnancy

4 5	Outcome of 2 nd pregnancy	Outcome in First pregnancy							Crude	and Adjusted (Adj.) Relativ (99% CI) 1	ve Risk
6 7		Induced abortion N=120033	Live birth N=457477	Miscarriage N=47355		Induced abortion vs Live birth	Induced abortion vs Miscarriage				
8 9	Live birth	67336 (56.1)	355674 (77.7)	36479 (77.0)		Crude 0.72 (0.71, 0.73) Adj. 0.74 (0.73, 0.74)	Crude 0.72 (0.72, 0.73) Adj. 0.69 (0.69, 0.70)				
0 1	Still birth	409 (0.34)	1406 (0.31)	247 (0.52)		Crude 1.11 (0.96, 1.28) Adj. 1.06 (0.91, 1.24)	Crude 0.65 (0.53, 0.80) Adj. 0.58(0.46, 0.74)				
2 3	Miscarriage	7965 (6.6)	30669 (6.7)	6197 (13.1)		Crude 0.99 (0.96, 1.02) Adj. 1.05(1.01, 1.08)	Crude 0.51 (0.49, 0.53) Adj. 0.56(0.54, 0.59)				
4 5	Ectopic	1115 (0.9)	2939 (0.6)	499 (1.1)		Crude 1.45 (1.32, 1.58) Adj. 1.36(1.23, 1.50)	Crude 0.88 (0.77, 1.01) Adj. 0.83(0.71, 0.97)				
6	Induced abortion	43208 (36.0)	66789 (14.6)	3933 (8.3)		Crude 2.47 (2.43, 2.50) Adj. 2.30(2.27, 2.33)	Crude 4.33 (4.16, 4.51) Adj. 4.64(4.44, 4.85)				
8	Outcomes in ongoing pregnancies	N=67745	N=357080	N=36726	Primigravida N=457477			Induced abortion vs Primigravida			
9 0	Pre-eclampsia	1583 (2.3)	2982 (0.8)	922 (2.5)	8649 (1.9)	Crude 2.80 (2.58, 3.03) Adj. 2.42 (2.21, 2.65)	Crude 0.93 (0.84, 1.03) Adj. 0.83 (0.73, 0.94)	Crude 1.24 (1.15, 1.32) Adj. 1.26 (1.17, 1.35)			
1 2	Placentaprevia	385 (0.6)	1919 (0.5)	289 (0.8)	2042 (0.5)	Crude 1.06 (0.92, 1.22) Adj. 1.09 (0.93, 1.28)	Crude 0.72 (0.59, 0.88) Adj. 0.79 (0.62, 1.01)	Crude 1.27 (1.10, 1.47) Adj. 1.05 (0.91, 1.22)			
3 4	Abruptio placenta	339 (0.5)	1197 (0.3)	173 (0.5)	1770 (0.4)	Crude 1.49 (1.27, 1.75) Adj. 1.49 (1.25, 1.77)	Crude 1.06 (0.84, 1.35) Adj. 1.00 (0.76, 1.32)	Crude 1.30 (1.11, 1.51) Adj. 1.28 (1.10, 1.50)			
5 6	Induction of labour ²	18044 (26.6)	69482 (19.5)	10347 (28.2)	120080 (26.3)	Crude 1.37 (1.34, 1.39) Adj. 1.33 (1.30, 1.35)	Crude 0.95 (0.92, 0.97) Adj. 0.98 (0.95, 1.01)	Crude 1.01 (1.00, 1.03) Adj. 1.00 (0.99, 1.02)			
7 8	Low birth weight $< 2500g^3$	5385 (8.0)	16309 (4.6)	3101 (8.5)	28735 (6.3)	Crude 1.74 (1.67, 1.81) Adj. 1.24 (1.17, 1.31)	Crude 0.94 (0.89, 1.00) Adj. 0.96 (0.90, 1.03)	Crude 1.27 (1.22, 1.31) Adj. 1.08 (1.04, 1.13)			

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5								
6 7	Outcomes in spontaneous births	N= 45656	N=255220	N=23751	N=318217			
8 9	Spontaneous preterm birth <37 weeks	4224 (9.3)	13453 (5.3)	2376 (10.0)	21891 (6.9)	Crude 1.76 (1.68, 1.83) Adj. 1.66 (1.58, 1.74)	Crude 0.92 (0.86, 0.99) Adj. 0.85 (0.79, 0.92)	Crude 1.35 (1.29, 1.40) Adj. 1.37 (1.32, 1.43)
10 11	Spontaneous very preterm birth <32 weeks	878 (1.9)	2157 (0.9)	513 (2.2)	4051 (1.3)	Crude 2.28 (2.05, 2.52) Adj. 2.20 (1.96, 2.47)	Crude 0.89 (0.77, 1.03) Adj. 0.83 (0.70, 0.99)	Crude 1.51 (1.37, 1.66) Adj. 1.57 (1.43, 1.72)
12 13	Spontaneous very preterm birth <28 weeks	271 (0.6)	651 (0.3)	186 (0.8)	1349 (0.4)	Crude 2.33 (1.93, 2.80) Adj. 2.24 (1.82, 2.76)	Crude 0.76 (0.59, 0.97) Adj. 0.80 (0.60, 1.06)	Crude 1.40 (1.18, 1.66) Adj. 1.49 (1.26, 1.77)
14	Values are n (%) unless oth	erwise specified						
15 16	657 Adjusted for mater	nal age, year of delive	ry, Carstairs at fir	rst pregnancy & ir	nterpregnancy inte	erval.		
17	658 Further adjusted fo	or pre-eclampsia, place	nta previa & abru	iptio placenta.				
18	659 Low birth weight al	so adjusted for gestati	onal age.					
19	660							
20	661							

663 **TABLE 3: Demographic characteristics of women who had induced abortion, livebirth or miscarriage after an initial livebirth**

Induced abortion

N=30527

26.04 (5.85)

3523 (12.8)

4304 (15.6)

5186 (18.8)

6243 (22.6)

8370 (30.3)

Live birth

N=125855

26.15 (4.68)

20264 (16.5)

21985 (17.9)

23425 (19.0)

25979 (21.1)

31395 (25.5)

Outcome in second pregnancy following an initial livebirth

p-value

< 0.001

< 0.001

Miscarriage

N=22404

28.41 (5.42)

4498 (20.9)

4079 (18.9)

4312 (20.0)

4447 (20.6)

4235 (19.6)

p-value

0.001

< 0.001

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Mean Age (SD)

Carstairs Category^{1,2}

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	Never	393 (39.7)	32464 (48.5)		3165 (46.1)	
	Current	313 (31.6)	20658 (30.9)		1169 (17.0)	
Smoking status ²	Former	43 (4.3)	5359 (8.0)	<0.001	282 (4.1)	0.001
	Not known	241 (24.3)	8482 (12.7)		2243 (32.7)	
	Total	990	66963		6859	
	Missing	29537 (96.8)	58892 (46.8)		15545 (69.4)	
Interpregnancy interval	Median(IQR)	108 (61, 209)	152 (96, 256)	<0.001	60 (48, 87)	<0.001

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TABLE 4: Reproductive and perinatal outcomes in women who had induced abortion, livebirth or miscarriage following a

672 livebirth in the first pregnancy

Outcome of 3 rd pregnancy	Outcome of second pregnancy				Crude and Adjusted (Adj.) Relative Risk (99% CI) 1			
	Induced abortion N=30527	Live birth N=125855	Miscarriage N=22404	I	nduced abortion vs Live birth]	nduced abortion vs Miscarriage	
Live birth	18562 (60.8)	85014 (67.5)	17745 (79.2)	Crude Adj.	0.90 (0.89, 0.91) 0.88 (0.87, 0.89)	Crude Adj.	0.77 (0.76, 0.78) 0.77 (0.76, 0.78)	
Still birth	84 (0.3)	426 (0.3)	69 (0.3)	Crude Adj.	0.81 (0.60, 1.11) 0.76 (0.55, 1.06)	Crude Adj.	0.89 (0.59, 1.36) 0.86 (0.54, 1.37)	
Miscarriage	2005 (6.6)	8778 (7.0)	2869 (12.8)	Crude Adj.	0.94 (0.89, 1.00) 0.93 (0.88, 1.00)	Crude Adj.	0.51 (0.48, 0.55) 0.67 (0.62, 0.72)	
Ectopic	339 (1.1)	1064 (0.9)	181 (0.8)	Crude Adj.	1.31 (1.12, 1.54) 1.31 (1.11, 1.56)	Crude Adj.	1.38 (1.09, 1.74) 1.16 (0.90, 1.50)	
Induced abortion	9537 (31.2)	30573 (24.3)	1540 (6.9)	Crude Adj.	1.29 (1.25, 1.32) 1.33 (1.30, 1.37)	Crude Adj.	4.55 (4.25, 4.86) 4.37 (4.06, 4.70)	
Outcomes in ongoing pregnancies	Induced Abortion N=18646	Live birth N=85440	Miscarriage N=17814	Crude and Adjusted (Adj.) Relative Risk (99% CI) ²			lelative Risk	
Pre-eclampsia	144 (0.8)	567 (0.7)	165 (0.9)	Crude Adj.	1.16 (0.92, 1.48) 1.40 (1.10, 1.79)	Crude Adj.	0.83 (0.62, 1.12) 0.91 (0.66, 1.27)	
Placenta previa	183 (1.0)	473 (0.6)	133 (0.8)	Crude Adj.	1.77 (1.42, 2.22) 1.78 (1.40, 2.25)	Crude Adj.	1.32 (0.98, 1.76) 1.34 (0.97, 1.84)	
Abruptio placenta	91 (0.5)	325 (0.4)	66 (0.4)	Crude Adj.	1.28 (0.95, 1.74) 1.28 (0.93, 1.77)	Crude Adj.	1.32 (0.87, 2.00) 1.32 (0.83, 2.10)	
Induction of labour ³	4298 (23.1)	18239 (21.4)	3968 (22.3)	Crude Adj.	1.08 (1.04, 1.12) 1.11 (1.07, 1.16)	Crude Adj.	1.03 (0.98, 1.09) 1.01 (0.96, 1.07)	
Low birth weight $<2500^4$	1086 (5.8)	3905 (4.6)	784 (4.4)	Crude Adj.	1.28 (1.17, 1.39) 1.36 (1.21, 1.51)	Crude Adj.	1.32 (1.17, 1.49) 1.04 (0.90, 1.21)	
Outcomes in spontaneous births	Induced abortion N=12868	Live birth N=59220	Miscarriage N=12056					
Spontaneous preterm birth <37 weeks	859 (6.7)	3035 (5.1)	644 (5.3)	Crude Adj.	1.30 (1.18, 1.43) 1.27 (1.14, 1.40)	Crude Adj.	1.25 (1.10, 1.42) 1.14 (0.99, 1.32)	
Spontaneous very preterm birth <32 weeks	162 (1.3)	495 (0.8)	104 (0.9)	Crude Adj.	1.51 (1.19, 1.90) 1.44 (1.12, 1.84)	Crude Adj.	1.46 (1.06, 2.01) 1.35 (0.93, 1.96)	

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74	birth <	neous very preterm 28 weeks	55 (0.4)	152 (0.3)	38 (0.3)	Crude Adj.	1.67 (1.11, 2.49) 1.59 (1.02, 2.46)	Crude Adj.	1.36 (0.79, 2.33) 1.19 (0.62, 2.30)
		are n (%) unless oth							
75	1	Adjusted for age, ye	ear of delivery, cars	stairs at second pregn	ancy & interpregnanc	y interval			
76	2		nal age, year of pre	gnancy, Carstairs cate	egory at second pregr	ancy & interpre	gnancy interval		
77	3		r pre-eclampsia, pla	acenta previa & abrup	tio placenta				
78	4	Low birth weight als	so adjusted for gest	ational age					
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TABLE 5: Reproductive outcomes following medical and surgical abortion

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Reproductive outcomes in next (2 nd) pregnancy	Primigravida N=457477	Medical termination in first pregnancy N=16702	Surgical termination in first pregnancy N=52560	RR	Medical vs Primigravida Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹	Surgical vs Primigravida Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹	Surgical vs Medical induced abortion Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹
Live birth	355674 (77.7)	9785 (58.6)	28285 (53.8)	Crude Adj.	0.75 (0.74, 0.77) 0.71 (0.70, 0.73)	0.69 (0.69, 0.70) 0.76 (0.75, 0.77)	0.92 (0.90, 0.94) 1.44 (1.41, 1.48)
Still birth	1406 (0.3)	57 (0.3)	151 (0.3)	Crude Adj.	1.11 (0.79, 1.57) 1.15 (0.80, 1.64)	0.93 (0.75, 1.17) 0.95 (0.73, 1.23)	0.84 (0.56, 1.26) 0.98 (0.57, 1.69)
Miscarriage	30669 (6.7)	1200 (7.2)	3723 (7.1)	Crude Adj.	1.07 (1.00, 1.15) 0.98 (0.91, 1.06)	1.06 (1.01, 1.10) 1.03 (0.98, 1.08)	0.99 (0.91, 1.07) 1.45 (1.30, 1.62)
Ectopic	2939 (0.6)	120 (0.7)	599 (1.1)	Crude Adj.	1.12 (0.88, 1.42) 0.99 (0.78, 1.28)	1.77 (1.58, 1.99) 1.80 (1.58, 2.06)	1.59 (1.23, 2.05) 1.78 (1.29, 2.45)
Induced Abortion	66789 (14.6)	5540 (33.2)	19802 (37.7)	Crude Adj.	2.27 (2.21, 2.34) 3.01 (2.91, 3.12)	2.58 (2.54, 2.63) 2.00 (1.96, 2.04)	1.14 (1.10, 1.17) 0.44 (0.42, 0.46)
Outcome in ongoing pregnancy ⁴	N=457477	N=9842	N=28436		C	6	
Pre-Eclampsia	8649 (1.9)	316 (3.2)	688 (2.4)	Crude Adj.	1.70 (1.47, 1.96) 1.01 (0.86, 1.17)	1.28 (1.16, 1.42) 1.14 (1.03, 1.27)	0.75 (0.63, 0.90) 1.12 (0.90, 1.39)
Placenta praevia	2042 (0.5)	23 (0.2)	248 (0.9)	Crude Adj.	0.52 (0.31, 0.90) 0.81 (0.47, 1.40)	1.95 (1.64, 2.32) 1.63 (1.36, 1.95)	3.73 (2.13, 6.54) 2.23 (1.17, 4.26)
Abruptio placentae	1770 (0.4)	40 (0.4)	160 (0.6)	Crude Adj.	1.05 (0.70, 1.58) 1.65 (1.08, 2.52)	1.45 (1.18, 1.80) 1.54 (1.24, 1.91)	1.38 (0.88, 2.18) 1.09 (0.63, 1.88)
Birth weight ²	28735 (6.3)	697 (7.1)	2407 (8.5)	Crude	1.13 (1.03, 1.24)	1.35 (1.28, 1.42)	1.19 (1.07, 1.33)

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<2500 g				Adj.	1.05 (0.94, 1.17)	1.16 (1.08, 1.23)	1.12 (0.97, 1.28)
Spontaneous births ⁴	N=318217 ³	N=6474 ³	N=18126 ³				
Preterm <37 wks	21891 (6.9)	533 (8.2)	1768 (9.8)	Crude Adj.	1.20 (1.07, 1.33) 1.11 (0.99, 1.24)	1.42 (1.34, 1.51) 1.45 (1.37, 1.55)	1.18 (1.05, 1.34) 1.25 (1.07, 1.45)
Very Preterm <32 wks	4051 (1.3)	123 (1.9)	363 (2.0)	Crude Adj.	1.49 (1.18, 1.89) 1.25 (0.98, 1.60)	1.57 (1.37, 1.81) 1.62 (1.41, 1.87)	1.05 (0.81, 1.38) 1.13 (0.81, 1.58)
Very Preterm <28 wks	1349 (0.4)	35 (0.5)	120 (0.7)	Crude Adj.	1.27 (0.82, 2.00) 0.91 (0.58, 1.44)	1.56 (1.22, 2.00) 1.62 (1.27, 2.07)	1.23 (0.75, 2.01) 1.38 (0.73, 2.61)
³ Only sr	ontaneous delivery co	onsidered among li	ive & still birth				
Only Sp	oontaneous delivery co ative risks comparing	5	medical/surgical ha	ave been	adjusted for maternal a	ge, year of event, Carsta	airs category at the on
4 All rela	,	5	medical/surgical ha	ave been	adjusted for maternal a	ge, year of event, Carsta	airs category at the on

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TABLE 6: Risk of spontaneous preterm delivery following increasing number of induced abortions

1 previous abortion vs 0 2 previous abortions vs 0 3 previous abortions vs 0 4 previous abortions vs 0	Crude RR (99% C.I.) 1.50 (1.41, 1.59) 1.55 (1.32, 1.81) 1.55 (1.04, 2.31)	Adj.RR (99% C.l.)* 1.47 (1.38, 1.57) 1.51 (1.29, 1.77)	Crude RR (99% Cl) 1.70 (1.47, 1.96) 1.48 (1.00, 2.19)	Adj RR(99% Cl) 1.59 (1.37, 1.84) 1.34 (0.91, 2.00)	Crude RR(99% Cl) 1.44 (1.09, 1.87)	Adj RR (99% C 1.24 (0.94, 1.64
2 previous abortions vs 0 3 previous abortions vs 0	1.55 (1.32, 1.81)	1.51 (1.29, 1.77)				1.24 (0.94, 1.64
3 previous abortions vs 0			1.48 (1.00, 2.19)	1.34 (0.91, 2.00)		
	1.55 (1.04, 2.31)			(- ,)	2.27 (1.31, 3.94)	1.89 (1.08, 3.31
4 previous abortions vs 0		1.52 (1.01, 2.27)	1.81 (0.74, 4.46)	1.64 (0.67, 4.06)	1.36 (0.22, 8.37)	1.12 (0.18, 6.96
	2.13 (1.26, 3.64)	2.10 (1.23, 3.59)	4.62 (1.91, 11.19)	4.27(1.76,10.37)	6.94 (1.95, 24.72)	5.96(1.65,21.37
2 previous abortions vs 1	1.03 (0.87, 1.22)	1.02 (0.86, 1.21)	0.87 (0.57, 1.31)	0.84 (0.56, 1.28)	1.58 (0.86, 2.89)	1.52 (0.83, 2.78
3 previous abortions vs 2	1.00 (0.65, 1.54)	1.01 (0.66, 1.55)	1.23 (0.46, 3.27)	1.22 (0.46, 3.26)	0.60 (0.09, 3.99)	0.60 (0.09, 3.97
4 previous abortions vs 3	1.38 (0.71, 2.68)	1.38 (0.71, 2.70)	2.55 (0.72, 9.01)	2.60 (0.74, 9.18)	5.10 (0.56, 46.78)	5.29 (0.58, 48.3
30						
	3 previous abortions vs 2 4 previous abortions vs 3 PTD preterm del	3 previous abortions vs 2 1.00 (0.65, 1.54) 4 previous abortions vs 3 1.38 (0.71, 2.68) PTD preterm delivery 30	3 previous abortions vs 2 1.00 (0.65, 1.54) 1.01 (0.66, 1.55) 4 previous abortions vs 3 1.38 (0.71, 2.68) 1.38 (0.71, 2.70) PTD preterm delivery 30	3 previous abortions vs 2 1.00 (0.65, 1.54) 1.01 (0.66, 1.55) 1.23 (0.46, 3.27) 4 previous abortions vs 3 1.38 (0.71, 2.68) 1.38 (0.71, 2.70) 2.55 (0.72, 9.01) PTD preterm delivery	3 previous abortions vs 2 1.00 (0.65, 1.54) 1.01 (0.66, 1.55) 1.23 (0.46, 3.27) 1.22 (0.46, 3.26) 4 previous abortions vs 3 1.38 (0.71, 2.68) 1.38 (0.71, 2.70) 2.55 (0.72, 9.01) 2.60 (0.74, 9.18) PTD preterm delivery	3 previous abortions vs 2 1.00 (0.65, 1.54) 1.01 (0.66, 1.55) 1.23 (0.46, 3.27) 1.22 (0.46, 3.26) 0.60 (0.09, 3.99) 4 previous abortions vs 3 1.38 (0.71, 2.68) 1.38 (0.71, 2.70) 2.55 (0.72, 9.01) 2.60 (0.74, 9.18) 5.10 (0.56, 46.78) PTD preterm delivery

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Supplementary Table A

Comparison of reproductive and perinatal outcomes in the 1st pregnancy (live birth & full term) in women who had induced abortion, livebirth or miscarriage in the 2nd pregnancy

Outcome of 1st pregnancy	Outco	ome of second pre	gnancy		Relative Risk 9% CI) ¹
Live birth	Induced abortion N=30527	Live birth N=125855	Miscarriage N=22404	Induced abortion vs Live birth	Induced abortion vs Miscarriage
Pre-eclampsia	349 (1.1)	1447 (1.2)	325 (1.5)	0.99 (0.85, 1.16)	0.79 (0.65, 0.96)
Placenta previa	128 (0.4)	409 (0.3)	80 (0.4)	1.29 (0.99, 1.67)	1.17 (0.81, 1.69)
Abruptio placenta	84 (0.3)	262 (0.2)	57 (0.3)	1.32 (0.96, 1.82)	1.08 (0.70, 1.68)
Induction of labour ³	8064 (26.4)	33225 (26.4)	6103 (27.2)	1.00 (0.97, 1.03)	0.97 (0.93, 1.01)
Low birth weight $<2500^4$	972 (3.2)	3727 (3.0)	626 (2.8)	1.08 (0.98, 1.18)	1.14 (1.00, 1.30)

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		study in Scotlar	
		Supplemental file: STROB	
	Cheo	klist of items that should be included	in reports of cohort stud
	ltem No	Recommendation	Location within manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Title & Abstract: Line 51
		(<i>b</i>) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract: Lines 52 - 97
Introduction			
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction: Lines 112 - 159
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction: Lines 161- 170
Methods			
Study design	4	Present key elements of study design early in the paper	Methodology: Line 173
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods Lines 178-181
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 	Methods: Lines 178 - 207 Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods: Lines 213 - 221
Data sources/ measuremen t	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	Methods: Lines 210 - 211.
Bias	9	Describe any efforts to address potential sources of bias	The only possible source of bias could be misclassification of variables as routinely collected data are used. We think that the large dataset should

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			compensate for that.
Study size	10	Explain how the study size was arrived at	All available data were included.
			Power calculation: lines
Quantitative	11	Explain how quantitative variables	225 -235. Statistical analysis:
variables	11	were handled in the analyses. If	Lines 238-267
Vallables		applicable, describe which groupings	
		were chosen and why	
Statistical	12	(<i>a</i>) Describe all statistical methods,	Statistical analysis:
methods	12	including those used to control for	Lines 238-267
		confounding	
		(b) Describe any methods used to	Methods: Lines 203 -
		examine subgroups and interactions	207
		(c) Explain how missing data were	Methodology: Lines
		addressed	152 - 159
		(d) If applicable, explain how loss to	Not applicable.
		follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	Methodology Lines
		_	261-267
Results			
Participants	13*	(a) Report numbers of individuals at	Results: Lines 176 -
•		each stage of study—eg numbers	177
		potentially eligible, examined for	
		eligibility, confirmed eligible, included	
		in the study, completing follow-up,	
		and analysed	
		(b) Give reasons for non-participation	Not applicable
		at each stage	
		(c) Consider use of a flow diagram	The whole population was selected
Descriptive	14*	(a) Give characteristics of study	Tables 1 and 3
data		participants (eg demographic, clinical,	
		social) and information on exposures	
		and potential confounders	
		(b) Indicate number of participants	Tables 1 and 3
		with missing data for each variable of	
		interest	
		(c) Summarise follow-up time (eg,	Table 1 and 3
		average and total amount)	
Outcome	15*	Report numbers of outcome events or	Tables 2,4,5
data		summary measures over time	
Main results	16	(a) Give unadjusted estimates and, if	Table 2, 4, 5
		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	Methods, Tables 2, 4, 5

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		continuous variables were categorized	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results: Lines 266-7
Discussion		•	
Key results	18	Summarise key results with reference to study objectives	Discussion: Lines 341- 353
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	Discussion: Lines 377- 389
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion: Lines 439- 449
Generalis- ability	21	Discuss the generalisability (external validity) of the study results	Discussion: Lines 363- 373

Other information	on		
Funding	22	Give the source of funding and the role of the funders	Lines 479-480
		for the present study and, if applicable, for the	
		original study on which the present article is based	



Reproductive outcomes following induced abortion: a national register based cohort study in Scotland

Journal:	BMJ Open
Manuscript ID:	bmjopen-2012-000911.R2
Article Type:	Research
Date Submitted by the Author:	27-Jun-2012
Complete List of Authors:	Bhattacharya, Siladitya; University of Aberdeen, Institute of Applied Health Sciences Lowit, Alison; University of Aberdeen, Institute of Applied Health Sciences Bhattacharya, Sohinee; University of Aberdeen, Public Health Raja, Edwin Amalraj; University of Aberdeen, Medical Statistics, Dept. of Public Health Lee, Amanda; University of Aberdeen, Medical Statistics, Dept. of Public Health Mahmood, Tahir; Forth Park Hospital, Obstetrics and Gynaecology Templeton, Allan; University of Aberdeen, Institute of Applied Health Sciences
Primary Subject Heading :	Reproductive medicine, obstetrics and gynaecology
Secondary Subject Heading:	Epidemiology
Keywords:	Fetal medicine < OBSTETRICS, Maternal medicine < OBSTETRICS, PERINATOLOGY, REPRODUCTIVE MEDICINE
	SCHOLARONE [™] Manuscripts

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2	1	Perroductive outcomes following induced shortions a national register
3 4	1	Reproductive outcomes following induced abortion: a national register
5 6	2	based cohort study in Scotland
7	3	Siladitya Bhattacharya ¹ , Alison Lowit ¹ Sohinee Bhattacharya ^{1*} , Edwin A Raja ¹ ,
8 9	4	Amanda J Lee ¹ , Tahir Mahmood ² , Allan Templeton ¹
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30	19	All authors have completed the Unified Competing Interest form at
31 32	20	http://www.icmje.org/coi_disclosure.pdf and declare: The Chief Scientist Office Scotland
33	21	funded the study; no financial relationships with any organisations that might have an
34 35	22	interest in the submitted work in the previous three years; no other relationships or
36	23	activities that could appear to have influenced the submitted work
37	24	
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 Objective: To investigate reproductive outcomes in women following induce abortion (IA). Design: Retrospective cohort study Setting: Hospital admissions between 1981 and 2007 in Scotland. Participants: Data were extracted on all women who had an IA, a miscarria a live birth from the Scottish Morbidity Records. A total of 120,033, 457,477 47,355 women with a documented second pregnancy following an IA, livebir and miscarriage respectively were identified. Outcomes: Obstetric and perinatal outcomes, especially preterm delivery in second ongoing pregnancy following an IA were compared with those in primigravidae, as well as those who had a miscarriage or live birth in their fi pregnancy. Outcomes after surgical and medical termination as well as after or more consecutive IAs were compared. Results: IA in a first pregnancy increased the risk of spontaneous preterm I compared to that in primigravidae [Adjusted relative risk (Adj. RR) 1.37, 95 Confidence Interval (CI) 1.32, 1.42] or women with an initial live birth [Adj. 1.66, 95% CI 1.58-1.74], but not in comparison with women with a previous miscarriage [Adj. RR 0.85, 95% CI 0.79-0.91]. Surgical abortion increased the risk of spontaneous preterm birth compared medical abortion [Adj. RR 1.25, 95% CI 1.07-1.45]]. The adjusted relative r (95% CI) for spontaneous preterm delivery following two, three and four consecutive IAs were 0.94 (0.81-1.10), 1.06 (0.76-1.47) and 0.92 (0.53-1.6 respectively. Conclusion: The risk of preterm birth after induced abortion is lower than t after miscarriage but higher than that in a first pregnancy or after a previou birth. This risk is not increased further in women who undergo two or more consecutive induced abortions. Surgical abortion appears to be associated were and source appears to be associated were and source and the respective induced abortion.
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ncreased risk of spontaneous preterm birth in comparison with medical ermination of pregnancy.

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75 Background

Many women start their reproductive careers with an abortion in their first pregnancy. In 2009, 13,005 abortions were performed in Scotland with the highest rates in women aged 16-19 years ¹. What is not yet entirely clear is the effect these abortions may have on subsequent childbearing. It has been believed that infection, cervical trauma and endometrial curettage associated with induced abortion could lead to future infertility, ectopic, preterm delivery and placenta praevia, but the data from existing observational studies are mixed ^{2 -18} Following the legalisation of abortion in 1967, initial research on the effects of an induced abortion on subsequent pregnancies showed no evidence of an increased risk of miscarriage, preterm delivery or low birth weight^{19, 20}. Much of the work in the subject has been hampered by methodological limitations; randomised controlled studies are not feasible in this context and researchers have looked to observational studies. Many of the published studies have been limited by small sample sizes, self-reported outcomes and inability to adjust for many potential confounders. A recent review ²¹ reported that half of the twelve relevant studies found an association between induced abortion and preterm birth as well as placenta praevia. More recently a number of large studies found no increased risk of placenta praevia, but supported an association with preterm ^{18, 22, 23} and very preterm delivery ^{24, 25} The clinical implications of this are profound as reducing the incidence of preterm delivery, with its considerable associated problems, remains one of the most significant challenges in obstetrics.

Over a quarter of induced abortions in Scotland in 2005 were repeat procedures ¹
[ISD, personal communication]. While the reproductive sequalae of repeat
abortions are unclear, the available literature suggests that the risk of preterm
delivery is increased by multiple abortions ^{18, 22, 24, 26}.

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Changes in the technique of abortion have to be taken into account when assessing their impact on future reproduction. In 1992, 83.6% of terminations were carried out surgically, falling to 60.6% in 1998 and 40.7% in 2006, with the remainder being carried out medically ¹. A number of studies ²⁷⁻²⁹ have compared these methods in terms of safety, efficacy and short term complications but data on subsequent reproductive outcomes is scant. A recent study ³⁰ found no difference in reproductive outcomes (ectopic, miscarriage and preterm delivery) following medically and surgically induced abortions, but was unable to adjust for known confounders such as smoking.

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In view of the high current rates of induced abortion, it is important for women and those involved in their care to be aware of any potential associations with future reproductive outcomes.

The Scottish Morbidity Record (SMR) system in Scotland covers a national population and has captured data on medical and surgical abortion for many years. Over 99.3% of abortions in Scotland are carried out in NHS premises and are recorded in the SMR system. As these data are based on clinical records, any potential bias created by underreporting will be removed. The availability of this large national dataset provides an ideal opportunity to link records on abortion (SMR01) with maternity records (SMR02) in order to explore the risk of preterm delivery and other maternal and perinatal outcomes in women following one or more episodes of induced abortion. The data would also allow a meaningful comparison of outcomes following alternative forms of induced abortion (i.e. medical versus surgical).

The primary aim of this study was to investigate reproductive outcomes in women following induced abortion. In particular we wished to answer the following research questions: 1) Is an induced abortion in a first pregnancy associated with spontaneous preterm birth or other adverse obstetric or perinatal outcomes in the second pregnancy? 2) Is an induced abortion performed after a singleton term first pregnancy associated with spontaneous preterm birth or adverse obstetric or perinatal outcomes in the next pregnancy? 3) Do any of these associations differ by method of induced abortion (i.e. surgical versus medical)? 4) Is the risk of adverse obstetric or perinatal outcomes associated with increasing number of terminations?

139 Methods

A retrospective cohort study design was used on routinely collected data
extracted from the Information and Statistics Division (ISD) database. Approval
was obtained from the Privacy Advisory Committee of the National Health
Service, Scotland.

Data were extracted from the ISD databases (SMR01 and 02) on women aged 145 15-55 years who had an induced abortion, a miscarriage, a live birth, or an 147 ongoing pregnancy and live delivery in their first pregnancy between 1981 and 148 2007 followed by a second pregnancy event. Reproductive outcomes in the 149 subsequent pregnancy of women who had an IA in their first pregnancy (exposed

150 cohort) were compared with those in two unexposed groups: 1) women in their 151 second pregnancy after a miscarriage in their first pregnancy and 2) women in 152 their second pregnancy after a live birth in their first pregnancy. In addition to 153 these two unexposed cohorts, obstetric and perinatal outcomes in the subsequent 154 pregnancy of women who had an IA in their first pregnancy (exposed group), 155 were also compared with those women in their first pregnancy.

To explore outcomes following early pregnancy loss after an initial livebirth, data were extracted on all women (15-55 years of age) who had an induced abortion, a miscarriage, or a live birth, in their second pregnancy (following a live birth in their first pregnancy) between 1981 and 2007 from the ISD databases (SMR01 and 02) and followed up to identify a third pregnancy event. Reproductive, obstetric and perinatal outcomes in women who had an IA after a singleton term first pregnancy (exposed group), were compared with those in two unexposed groups: 1) women in their third pregnancy following a singleton term delivery in the first pregnancy and a miscarriage in the second pregnancy and 2) women in their third pregnancy following two singleton term deliveries

Women treated by different methods of induced abortion (surgical or medical) in a first pregnancy were compared in terms of reproductive, obstetric and perinatal outcomes. Finally, to answer research question 4, reproductive and perinatal outcomes were compared between women who had 1, 2, 3 and 4 previous consecutive induced abortions and women with no previous abortions. Each group of women was independent of the others - for example women who had 3 abortions were excluded from the group with 2 abortions. For each analysis, except research question 4, the women were matched on parity as the risk of adverse obstetric outcomes is dependent on parity with primiparous women suffering the highest risk.

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179 Data extracted

The following variables were identified by matching SMR01 and SMR02 datasetsbetween the years 1981 and 2007.

Demographic details: Age at pregnancy events, smoking status, and social class (assessed using Carstairs category of deprivation) in the exposed group were compared with each of the 3 unexposed cohorts

Induced abortion details: estimated gestation and method of termination (medical or surgical or both) were recorded for the exposed group. Reproductive outcomes: miscarriage, abortion, livebirth, ectopic, stillbirth in the exposed group were compared with the unexposed cohorts. Obstetric and perinatal outcomes: The incidence of pre-eclampsia, placenta praevia, placental abruption, preterm delivery, very preterm delivery, low birth weight and the mode of delivery in the exposed cohort were compared with each of the 3 unexposed cohorts. Spontaneous delivery rates (including live and stillbirth) were calculated after excluding women who had induced labour and elective (planned) caesarean section.

Socioeconomic status was assessed using the Carstairs index ³¹ which was
 divided into quintiles for analysis.

Power Calculation

Given the number of sub-groups in the analysis coupled with multiple outcomes, a global sample size calculation was not feasible. Preliminary enquiries with ISD suggested that we could identify at least 260,000 terminations (1981-2007), of which 30% (n=69,000) were estimated to have had a subsequent live birth and 25.5% (n=66,223) were induced abortions in a first pregnancy.

Using a 1:1 ratio of women with induced abortions in a first pregnancy (exposed cohort) and unexposed women, we anticipated having over 90% power, at the two-sided 5% significance level, to detect a difference of 0.5% or more in the chances of a preterm birth (ie, an odds ratio of 1.09) assuming that the prevalence of live births in the unexposed group was 6%.

214 Statistical Analysis

In the absence of an ideal comparison group for women with a prior abortion, we used 3 unexposed cohorts which could increase the chance of false positive associations (type I error). To help minimise this, we used a stringent p-value of ≤ 0.01 to denote statistical significance throughout the statistical analyses.

A generalised linear model was used with Poisson family and robust variance estimator to ascertain the relationship between exposure (first pregnancy induced abortion) and various reproductive outcomes (still birth, miscarriage, ectopic and induced abortion), maternal and perinatal outcomes (pre-eclampsia, placentaprevia, abruption placenta) after adjusting for potential confounders (maternal

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age, year of delivery, smoking & carstairs at relevant pregnancy). For the outcome of induction of labour, pre-eclampsia, placenta previa and placental abruption were also entered into the model. Similarly, the outcome low birth weight was also adjusted for gestational age. Stata version 11 was used for the analysis and a stringent p-value of ≤ 0.01 was used to denote statistical significance throughout.

As smoking data were not routinely collected in the maternity database (SMR02) before 1992, and rarely recorded for women having an induced abortion or miscarriage. Thus self-reported smoking status, collected at antenatal booking visit, though available for some women was non-randomly missing for a high percentage of women. This sometimes led to non-convergence of the statistical models. Therefore, a sensitivity analysis was carried out by re-running all of the multivariate models excluding the smoking variable to determine if the overall effect sizes remained of similar magnitude. This was found to be so.

240 Results

Demographic characteristics of women who had an abortion in their first pregnancy were compared with those who had either a live birth or a miscarriage in their first pregnancy and with primigravida women (Table 1). Women with a previous induced abortion were significantly older, more socially deprived and more likely to be smokers than primigravida women or those who had a live birth or a miscarriage in a previous pregnancy.

Table 2 presents reproductive outcomes in a subsequent pregnancy following IA, livebirth and miscarriage in the first pregnancy. As Table 2 shows, women with an IA in the first pregnancy were more at risk of having a still birth or an induced abortion in the second pregnancy as compared with an initial livebirth. Compared to those who had an initial miscarriage, women who had an IA in their first pregnancy were less likely to have a subsequent miscarriage or ectopic pregnancy, but more likely to have another induced abortion.

Perinatal outcomes in the next ongoing pregnancy following IA are also compared with those in primigravida and women who have had a livebirth or miscarriage in Table 2. Compared with women having a previous livebirth, women who had an induced abortion were at higher risk of pre-eclampsia, abruptio placenta, induction of labour, spontaneous preterm and very preterm delivery (<32weeks) extremely preterm (< 28 weeks) and delivery of a low birth weight baby (<2500 g) but not placenta praevia.

In comparison with women with a previous miscarriage, a history of IA was associated with a lower risk of developing pre-eclampsia and spontaneous preterm and very preterm delivery. Risks of pre-eclampsia, placental abruption (but not placenta praevia), delivery of a low birth weight baby and spontaneous preterm, very preterm and extremely preterm birth were significantly higher following IA than in primigravid women. The risk of pre-eclampsia in women with a previous IA was higher than in primigravid women but lower than in women with a previous miscarriage (Table 2).

The demographic characteristics of women who had a livebirth in a first pregnancy and then went on to have induced abortion, live birth or a miscarriage in their second pregnancy are shown in Table 3. Women with an induced abortion in their second pregnancy were younger, belonged to a more deprived social group and were more likely to be smokers than women who had a live birth in their second pregnancy. Compared to women who had a miscarriage in their second pregnancy, women with a previous induced abortion were older, belonged to more deprived social classes and were more likely to smoke.

As Table 4 shows, IA in the second pregnancy was associated with a higher risk of an ectopic or an induced abortion in the third pregnancy as compared with an initial livebirth. The risk of miscarriage in a third pregnancy was lower in women who had an IA in a second pregnancy, but the risks of another induced abortion were higher than in women with a previous miscarriage.

Compared to women with two previous livebirths, women with a livebirth followed by an IA were more likely to have pre-eclampsia, placenta praevia, induced labour, low birthweight and spontaneous preterm, very preterm and extremely preterm birth (Table 4). Women with an IA in a second pregnancy were not at any significantly higher risk of perinatal complications in comparison with women with a previous miscarriage.

In records where the method of IA was clearly recorded, 52,560 women were noted to have had surgical and 16,702, medical abortions. As Table 5 shows, reproductive outcomes were comparable in the two groups except for a lower risk of a second induced abortion following surgical termination of pregnancy. The adjusted relative risk of miscarriage, ectopic pregnancy, placenta praevia and spontaneous preterm delivery (<37 weeks) were significantly higher after surgical

termination. In comparison with primigravid women i.e. no previous abortion, women with a medical abortion had an increased risk of placental abruption, but not spontaneous preterm, very preterm or extremely preterm delivery. In contrast, women with a surgical abortion had higher risks of all three types of spontaneous preterm delivery. They also had an increased risk of preeclampsia, placenta praevia, abruption and low birthweight babies. More women had repeat abortion following surgical termination of pregnancy, and fewer went on to have a livebirth in comparison with primigravid women and those who had medical terminations.

Table 6 summarises the risk of spontaneous preterm delivery in subsequent pregnancies following one or more consecutive IAs in comparison to those with no previous abortions (primigravid women). The adjusted relative risks of spontaneous preterm birth, (< 37 weeks) was incrementally higher in women undergoing 1, 2, 3 and 4 induced abortions. The adjusted relative risk of spontaneous very preterm delivery (< 32 weeks) was higher after 1 and 4 induced abortions, while the adjusted relative risk of spontaneous extremely preterm delivery (<28weeks) was higher following 2 and 4 previous induced abortions. Additional induced abortions were not associated with increased adjusted relative risks of any type of spontaneous preterm birth.

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323 Discussion

Principal findings

Our results suggest that women who had an induced abortion in the first pregnancy were more at risk of maternal and perinatal risks in comparison to women with a previous live birth. Compared to an initial miscarriage, an induced abortion in a first pregnancy was associated with a higher subsequent risk of miscarriage or ectopic pregnancy, induced abortion and pre-eclampsia. Women with a previous induced abortion face increased risks of antepartum haemorrhage and spontaneous preterm birth than women in their first pregnancy.

A livebirth prior to an IA does not appear to be associated with reduced perinatal complications in women who are at higher risk of spontaneous preterm birth than primigravida. Surgical termination appears to be associated with a higher chance of spontaneous preterm birth than medical IA. There does not appear to be a dose dependent effect of IA on future adverse perinatal outcomes.

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Women with three or four consecutive induced abortions were not at significantly
higher risk of spontaneous preterm birth in comparison with women who have
had one termination of pregnancy.

345 Strengths

To our knowledge this is the largest population based study of reproductive outcomes following an induced abortion. Registry based previous studies reporting preterm birth rates as an outcome have been unable to discriminate between spontaneous and induced preterm delivery; this is one of the first papers to be able to calculate and report spontaneous preterm birth rates after induced abortion.

We have acknowledged changes in clinical practice over the years during which data were collected and have adjusted for year of pregnancy in the regression models. The choice of an appropriate comparison group to women with a history of induced abortion is problematic. Women who are pregnant again after having undergone an induced abortion in a previous (first) pregnancy are gravida 2 and parity 0. It is impossible to control for both gravidity and parity unless the unexposed cohort have had a prior pregnancy which did not lead to a delivery. Other comparison groups can be either women in their first ongoing pregnancies (gravidity 1 parity 0), or in their second ongoing pregnancies after a previous delivery (gravidity 2 parity 1). We feel that our strategy comparing the exposed cohort to all three of the above groups adds validity to our results.

365 Limitations

The main limitations of this study stem from unrecorded and missing data in relation to certain potential confounding factors within the dataset. For example, smoking data were only available for 50% of women; data on body mass index were unavailable while data on gestational age at termination was missing in the majority of cases. The actual method of termination (medical versus surgical) was unrecorded in around 25% of all cases, while a large number of women appeared to have both medical as well as surgical treatment. Parity number was less reliable in the early years of data collection. This may reflect problems with coding and could potentially affect the quality of our results. In addition, the analysis of such a large population based dataset has the capacity to produce statistically significant differences which may or may not be clinically relevant,

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 although this has been minimised by our use of a stringent 1% significance levelthroughout.

Defining an ideal reference group is a challenge in studies exploring outcomes after induced abortion. While we have partially addressed this issue by using more than one unexposed cohort, our data do not allow us to adjust for potential differences in pregnancy intentions between groups, which can impact on antenatal care and perinatal outcomes.

Unrecorded data relating to key potential confounders cannot exclude the possibility that some associations are not explained by abortion itself but by special circumstances of women seeking abortion which also increases their risk of complications in pregnancy. We ran a separate analysis to identify previous pregnancy complications in women who either had an induced abortion, miscarriage or livebirth in a second pregnancy. As supplementary Table A shows, induced abortion in the second pregnancy was not significantly associated with increased relative risk (99% confidence interval) of preeclampsia, placenta praevia, placental abruption and low birthweight respectively compared to either livebirth [0.99 (0.85, 1.16); 1.29 (0.99, 1.67) 1.32 (0.96, 1.82) 1.08 (0.98, 1.18)] or miscarriage [0.79 (0.65, 0.96) 1.17 (0.81, 1.69) 1.08 (0.70, 1.68) 1.14 (1.00, 1.30)].

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398 Comparison with previous studies

The association between induced abortion and preterm birth found in this study is consistent with previously published work ³². Two recent meta-analyses suggest that women who have had an IA are at higher risk of preterm birth in subsequent pregnancies ^{33, 34}. Our study shows that after adjustment women with a previous abortion have an increased chance of a subsequent preterm birth and very pre-term birth compared with primigravidae or those who have had a previous live birth, but at no significantly greater risk compared to women who have had a previous miscarriage. Women who had a live birth before an induced abortion are more likely to have a preterm birth compared to women with two previous live births.

409 Our results did not suggest a signficant increased risk of miscarriage after an 410 induced abortion which is in keeping with a review of literature ²¹. In 411 contrast, Sun (2003)³⁵ demonstrated an association between surgical 412 abortion and miscarriage in a subsequent pregnancy. Literature on the 413 association between IA and miscarriage or ectopic pregnancy is sparse and 414 conflicting. The increased risk of having a second termination following

415 induced abortion in a first pregnancy highlighted in our study has been 416 reported elsewhere ³⁶⁻³⁸. While women who had an abortion were more likely to 417 have a subsequent abortion, but they may also be more likely to have an 418 unintended pregnancy. This should be seen a potential risk factor which should be 419 explored in future studies.

Available literature suggests there is an association between IA and placenta previa ^{39, 40}, but no association with abruptio placenta ^{41, 42}. This study found that women in their second pregnancy after an initial induced abortion in the first were at higher odds of both placenta previa and abruptio placenta, women in their third pregnancy after an induced abortion in their second pregnancy had higher odds of placenta previa, but not abruptio placenta. Published evidence supports a decreased risk of pre-eclampsia after an IA ^{43, 44}. Our results suggest a risk of developing preeclampsia which is on par with primigravid women, but lower than women with a previous miscarriage. The reasons for these associations are unclear and hence any explanations can only be speculative. Problems with placental position and function could occur due to disruption of the endometrium by vigorous curettage. The quality of placental function in a previous pregnancy could influence susceptibility to future preeclampsia.

Since the introduction of medical abortion there has been much speculation about the rival merits of medical and surgical techniques, especially in terms of future reproductive outcomes. Analysis of Danish data has failed to demonstrate a difference in key outcomes such as preterm birth between medical and surgical abortion, but this study was unable to identify spontaneous versus induced preterm birth ³⁰. With our ability to identify spontaneous PTBs, we have shown a clear association with surgical abortion. However, since we were unable to adjust for gestational age, we cannot rule out the possibility that surgical abortions may have been performed at a more advanced stage of pregnancy requiring a greater degree of cervical dilatation - thus leading to future preterm labour. Our results are supported by a recent publication showing that the risk of preterm birth after one or more surgical abortions is higher than after medical abortion and comparable to that in primigravid women ¹¹.

A dose dependent relationship between the number of IAs and future PTB has
 been shown in a number of previous studies ³². The results of our analysis do not

 452 support this. Given our inability to adjust for a number of potential confounders,453 this needs to be investigated further.

Our data suggest that medical and surgical terminations may impact differently on future reproductive outcomes - with a higher risk of spontaneous preterm birth after surgery. We were unable to disentangle the separate effects of repeated medical and surgical abortion due to a relative paucity of numbers.

A recent publication ¹¹ found an increased risk of premature delivery following multiple surgical, but not first trimester, medical induced abortions. While this could reflect the effect of repeated surgical trauma to the cervix, this needs further exploration in future studies with long term periods of follow up.

A key challenge in studying health sequalae after induced abortion is to deal with potential differences in pregnancy intentions between comparison groups. While women who had an abortion were more likely to have a subsequent abortion, they may also be more likely to have an unintended pregnancy, which needs to be acknowledged as a potential risk factor in future studies. BMJ Open: first published as 10.1136/bmjopen-2012-000911 on 6 August 2012. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

470 <u>Conclusions</u>

Induced abortion in a first pregnancy is associated with a higher risk of spontaneous preterm birth in a subsequent pregnancy in comparison with primigravid women, but not women with a previous miscarriage. A successful pregnancy leading to a livebirth prior to an induced abortion does not appear to ameliorate this risk while more than one abortion does not significantly increase it. Surgical abortion appears to be associated with an increased risk of spontaneous very preterm birth in comparison with medical termination of pregnancy. The results of this study should help provide women as well as health professionals with accurate information to inform clinical decision making and tailor antenatal care to address women's risk profiles.

AT conceived the idea for the study. SB was the Principal Investigator. He designed the study along with SohB, AT, ALee and TM, led the funding application, managed the project, interpreted the results and wrote the first draft of the paper. ALo cleaned the data and performed some of the initial analyses. SohB co-wrote the funding application, facilitated data manipulation, interpreted the results and helped to draft the paper. EAR performed the statistical analysis and interpreted the results with input from ALee. All authors commented on, and contributed to the final draft of the paper.

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491 Acknowledgements

We thank staff at ISD Scotland for extraction of data from the Scottish MorbidityRecords Database and Margery Heath for secretarial assistance.

495 Funding

The Chief Scientist Office Scotland funded the study. The views expressed arethose of the authors and not the funding body.

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494

499 Contributorship

AT conceived the idea for the study. SB was the Principal Investigator. He 500 501 designed the study along with SohB, AT, ALee and TM, led the funding 502 application, managed the project, interpreted the results and wrote the first draft 503 of the paper. ALo cleaned the data and performed some of the initial analyses. 504 SohB co-wrote the funding application, facilitated data manipulation, interpreted 505 the results and helped to draft the paper. EAR performed the statistical analysis 506 and interpreted the results with input from ALee. All authors commented on, and 507 contributed to the final draft of the paper.



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TABLE 1: Demographic characteristics at first pregnancy of women who had induced abortion, livebirth or miscarriage in their first pregnancy

		Outcome in first pregnancy				
		Induced abortion	Live birth	p-value	Miscarriage	p-value
		N=120,033	N=457,477		N=47,355	
Mean Age (SD)		24.68 (7.56)	24.89 (5.11)	<0.001	26.26 (6.13)	<0.001
	1	17265 (17.1)	79705 (18.0)	<0.001	8403 (18.8)	< 0.001
	2	18538 (18.3)	81661 (18.4)		8206 (18.4)	
Carstairs Category ^{1,2}	3	19530 (19.3)	84559 (19.1)		8794 (19.7)	
	4	21135 (20.9)	92504 (20.9)		9426 (21.1)	
	5	24615 (24.4)	105313 (23.7)		9788 (21.9)	
	Never	1014 (42.3)	112744 (48.4)	<0.001	4892 (39.8)	<0.001
	Current	676 (28.2)	72182 (31.0)		2044 (16.6)	
	Former	85 (3.5)	22140 (9.5)		533 (4.3)	
Smoking status ²	Not known	622 (26.0)	26088 (11.2)		4818 (39.2)	
	Total	2397	233154		12287	
	Missing	117636 (98.0)	224323 (49.0)		35068 (74.1)	
Interpregnancy interval in Weeks	Median (IQR)	165 (78, 321)	139 (95, 213)	<0.001	65 (47, 104)	<0.001

Values are n (%) unless otherwise specified

¹ Carstairs categories 1 = least deprived, 5 = most deprived

² Percentage based on available information for each group

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Outcome of 2 nd pregnancy	Outcome in First pregnancy				Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹			
	Induced abortion N=120033	Live birth N=457477	Miscarriage N=47355		Induced abortion vs Live birth	Induced abortion vs Miscarriage		
Live birth	67336 (56.1)	355674 (77.7)	36479 (77.0)		Crude 0.72 (0.71, 0.73) Adj. 0.74 (0.73, 0.74)	Crude 0.72 (0.72, 0.73) Adj. 0.69 (0.69, 0.70)		
Still birth	409 (0.34)	1406 (0.31)	247 (0.52)		Crude 1.11 (0.96, 1.28) Adj. 1.06 (0.91, 1.24)	Crude 0.65 (0.53, 0.80) Adj. 0.58(0.46, 0.74)		
Miscarriage	7965 (6.6)	30669 (6.7)	6197 (13.1)		Crude 0.99 (0.96, 1.02) Adj. 1.05(1.01, 1.08)	Crude 0.51 (0.49, 0.53) Adj. 0.56(0.54, 0.59)		
Ectopic	1115 (0.9)	2939 (0.6)	499 (1.1)		Crude 1.45 (1.32, 1.58) Adj. 1.36(1.23, 1.50)	Crude 0.88 (0.77, 1.01) Adj. 0.83(0.71, 0.97)		
Induced abortion	43208 (36.0)	66789 (14.6)	3933 (8.3)		Crude 2.47 (2.43, 2.50) Adj. 2.30(2.27, 2.33)	Crude 4.33 (4.16, 4.51) Adj. 4.64(4.44, 4.85)		
Outcomes in ongoing pregnancies	N=67745	N=357080	N=36726	Primigravida N=457477			Induced abortion vs Primigravida	
Pre-eclampsia	1583 (2.3)	2982 (0.8)	922 (2.5)	8649 (1.9)	Crude 2.80 (2.58, 3.03) Adj. 2.42 (2.21, 2.65)	Crude 0.93 (0.84, 1.03) Adj. 0.83 (0.73, 0.94)	Crude 1.24 (1.15, 1.32 Adj. 1.26 (1.17, 1.3	
Placentaprevia	385 (0.6)	1919 (0.5)	289 (0.8)	2042 (0.5)	Crude 1.06 (0.92, 1.22) Adj. 1.09 (0.93, 1.28)	Crude 0.72 (0.59, 0.88) Adj. 0.79 (0.62, 1.01)	Crude 1.27 (1.10, 1.47 Adj. 1.05 (0.91, 1.22	
Abruptio placenta	339 (0.5)	1197 (0.3)	173 (0.5)	1770 (0.4)	Crude 1.49 (1.27, 1.75) Adj. 1.49 (1.25, 1.77)	Crude 1.06 (0.84, 1.35) Adj. 1.00 (0.76, 1.32)	Crude 1.30 (1.11, 1.51 Adj. 1.28 (1.10, 1.5	
Induction of labour ²	18044 (26.6)	69482 (19.5)	10347 (28.2)	120080 (26.3)	Crude 1.37 (1.34, 1.39) Adj. 1.33 (1.30, 1.35)	Crude 0.95 (0.92, 0.97) Adj. 0.98 (0.95, 1.01)	Crude 1.01 (1.00, 1.03 Adj. 1.00 (0.99, 1.02	
Low birth weight $< 2500g^3$	5385 (8.0)	16309 (4.6)	3101 (8.5)	28735 (6.3)	Crude 1.74 (1.67, 1.81) Adj. 1.24 (1.17, 1.31)	Crude 0.94 (0.89, 1.00) Adj. 0.96 (0.90, 1.03)	Crude 1.27 (1.22, 1.31 Adj. 1.08 (1.04, 1.1	
Outcomes in spontaneous births	N= 45656	N=255220	N=23751	N=318217				
Spontaneous preterm birth <37 weeks	4224 (9.3)	13453 (5.3)	2376 (10.0)	21891 (6.9)	Crude 1.76 (1.68, 1.83) Adj. 1.66 (1.58, 1.74)	Crude 0.92 (0.86, 0.97) Adj. 0.85 (0.79, 0.91)	Crude 1.35 (1.29, 1.40 Adj. 1.37 (1.32, 1.4	
Spontaneous very preterm birth <34 weeks	1512 (3.3)	3994 (1.6)	865 (3.6)	7154 (2.3)	Crude 2.12 (1.96, 2.29) Adj. 2.00 (1.83, 2.18)	Crude 0.90 (0.82, 1.01) Adj. 0.86 (0.76, 0.98)	Crude 1.47 (1.37, 1.58 Adj. 1.52 (1.41, 1.6	

TABLE 2: Reproductive and perinatal outcomes following induced abortion, miscarriage or live birth in first pregnancy

Values are n (%) unless otherwise specified

Adjusted for maternal age, year of delivery, Carstairs at first pregnancy & interpregnancy interval.

Further adjusted for pre-eclampsia, placenta previa & abruptio placenta.

Low birth weight also adjusted for gestational age.

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		Outcome in second pregnancy following an initial livebirth				
		Induced abortion N=30527	Live birth N=125855	p-value	Miscarriage N=22404	p-value
Mean Age (SD)		26.04 (5.85)	26.15 (4.68)	<0.001	28.41 (5.42)	0.001
	1	3523 (12.8)	20264 (16.5)		4498 (20.9)	
	2	4304 (15.6)	21985 (17.9)		4079 (18.9)	<0.001
Carstairs Category ^{1,2}	3	5186 (18.8)	23425 (19.0)	<0.001	4312 (20.0)	
	4	6243 (22.6)	25979 (21.1)		4447 (20.6)	
	5	8370 (30.3)	31395 (25.5)		4235 (19.6)	
	Never	393 (39.7)	32464 (48.5)		3165 (46.1)	0.001
	Current	313 (31.6)	20658 (30.9)]	1169 (17.0)	
Smoking status ²	Former	43 (4.3)	5359 (8.0)	<0.001	282 (4.1)	
Smoking Status	Not known	241 (24.3)	8482 (12.7)		2243 (32.7)	
	Total	990	66963		6859	
	Missing	29537 96.8)	58892 (46.8)		15545 (69.4)	
Interpregnancy interval	Median(IQR)	108 (61, 209)	152 (96, 256)	<0.001	60 (48, 87)	<0.001

TABLE 3: Demographic characteristics of women who had induced abortion, livebirth or miscarriage after an initial livebirth

Percentage based on available information for each group

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TABLE 4: Reproductive and perinatal outcomes in women who had induced abortion, livebirth or miscarriage following a livebirth in the first pregnancy

Outcome of 3 rd pregnancy	Outcome of second pregnancy			Crude and Adjusted (Adj.) Relative Risk (99% CI) 1		
	Induced abortion N=30527	Live birth N=125855	Miscarriage N=22404	Induced abortion vs Live birth	Induced abortion vs Miscarriage	
Live birth	18562 (60.8)	85014 (67.5)	17745 (79.2)	Crude 0.90 (0.89, 0.91) Adj. 0.88 (0.87, 0.89)	Crude 0.77 (0.76, 0.78) Adj. 0.77 (0.76, 0.78)	
Still birth	84 (0.3)	426 (0.3)	69 (0.3)	Crude 0.81 (0.60, 1.11) Adj. 0.76 (0.55, 1.06)	Crude 0.89 (0.59, 1.36) Adj. 0.86 (0.54, 1.37)	
Miscarriage	2005 (6.6)	8778 (7.0)	2869 (12.8)	Crude 0.94 (0.89, 1.00) Adj. 0.93 (0.88, 1.00)	Crude 0.51 (0.48, 0.55) Adj. 0.67 (0.62, 0.72)	
Ectopic	339 (1.1)	1064 (0.9)	181 (0.8)	Crude 1.31 (1.12, 1.54) Adj. 1.31 (1.11, 1.56)	Crude 1.38 (1.09, 1.74) Adj. 1.16 (0.90, 1.50)	
Induced abortion	9537 (31.2)	30573 (24.3)	1540 (6.9)	Crude 1.29 (1.25, 1.32) Adj. 1.33 (1.30, 1.37)	Crude 4.55 (4.25, 4.86) Adj. 4.37 (4.06, 4.70)	
Outcomes in ongoing pregnancies	Induced Abortion N=18646	Live birth N=85440	Miscarriage N=17814	Crude and Adjusted (Adj.) Relative Risk (99% CI) ²		
Pre-eclampsia	144 (0.8)	567 (0.7)	165 (0.9)	Crude 1.16 (0.92, 1.48) Adj. 1.40 (1.10, 1.79)	Crude 0.83 (0.62, 1.12) Adj. 0.91 (0.66, 1.27)	
Placenta previa	183 (1.0)	473 (0.6)	133 (0.8)	Crude 1.77 (1.42, 2.22) Adj. 1.78 (1.40, 2.25)	Crude 1.32 (0.98, 1.76) Adj. 1.34 (0.97, 1.84)	
Abruptio placenta	91 (0.5)	325 (0.4)	66 (0.4)	Crude 1.28 (0.95, 1.74) Adj. 1.28 (0.93, 1.77)	Crude 1.32 (0.87, 2.00) Adj. 1.32 (0.83, 2.10)	
Induction of labour ³	4298 (23.1)	18239 (21.4)	3968 (22.3)	Crude 1.08 (1.04, 1.12) Adj. 1.11 (1.07, 1.16)	Crude 1.03 (0.98, 1.09) Adj. 1.01 (0.96, 1.07)	
Low birth weight $<2500^4$	1086 (5.8)	3905 (4.6)	784 (4.4)	Crude 1.28 (1.17, 1.39) Adj. 1.36 (1.21, 1.51)	Crude 1.32 (1.17, 1.49) Adj. 1.04 (0.90, 1.21)	
Outcomes in spontaneous births	Induced abortion N=12868	Live birth N=59220	Miscarriage N=12056	21		
Spontaneous preterm birth <37 weeks	859 (6.7)	3035 (5.1)	644 (5.3)	Crude 1.30 (1.18, 1.43) Adj. 1.27 (1.14, 1.40)	Crude 1.25 (1.10, 1.42) Adj. 1.14 (0.99, 1.32)	
Spontaneous very preterm birth <34 weeks	282 (2.2)	929 (1.6)	189 (1.6)	Crude 1.40 (1.17, 1.66) Adj. 1.36 (1.13, 1.64)	Crude 1.40 (1.10, 1.78) Adj. 1.33 (1.01, 1.74)	

Values are n (%) unless otherwise specified

¹ Adjusted for age, year of delivery, carstairs at second pregnancy & interpregnancy interval

² Adjusted for maternal age, year of pregnancy, Carstairs category at second pregnancy & interpregnancy interval

³ Further adjusted for pre-eclampsia, placenta previa & abruptio placenta

⁴ Low birth weight also adjusted for gestational age

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TABLE 5: Reproductive outcomes following medical and surgical abortion

Reproductive outcomes in next (2 nd) pregnancy	Surgical termination in first pregnancy N=52560	Medical termination in first pregnancy N=16702	Surgical vs Medical induced abortion Crude and Adjusted (Adj.) Relative Risk (99% CI) ¹		
Live birth	28285 (53.8)	9785 (58.6)	Crude 0.92 (0.90, 0.94) Adj. 1.44 (1.41, 1.48)		
Still birth	151 (0.3)	57 (0.3)	Crude 0.84 (0.56, 1.26) Adj. 0.98 (0.57, 1.69)		
Miscarriage	3723 (7.1)	1200 (7.2)	Crude0.99 (0.91, 1.07)Adj. 1.45 (1.30, 1.62)		
Ectopic	599 (1.1)	120 (0.7)	Crude1.59 (1.23, 2.05)Adj. 1.78 (1.29, 2.45)		
Induced Abortion	19802 (37.7)	5540 (33.2)	Crude1.14 (1.10, 1.17)Adj. 0.44 (0.42, 0.46)		
Outcome in ongoing pregnancy	N=28, 436	N=9842			
Pre-Eclampsia	688 (2.4)	316 (3.2)	Crude 0.75 (0.63, 0.90) Adj. 1.12 (0.90, 1.39)		
Placenta praevia	248 (0.9)	23 (0.2)	Crude3.73 (2.13, 6.54)Adj. 2.23 (1.17, 4.26)		
Abruptio placentae	160 (0.6)	40 (0.4)	Crude 1.38 (0.88, 2.18) Adj. 1.09 (0.63, 1.88)		
Birth weight ² <2500 g	2407 (8.5)	697 (7.1)	Crude 1.19 (1.07, 1.33) Adj. 1.12 (0.97, 1.28)		
Spontaneous births	N=18126 ³	N=6474 ³			
Preterm <37 wks	1768 (9.8)	533 (8.2)	Crude1.18 (1.05, 1.34)Adj. 1.25 (1.07, 1.45)		
Very Preterm <34 wks	633 (3.5)	217 (3.4)	Crude 1.04 (0.86, 1.27) Adj. 1.09 (0.84, 1.40)		

Values are n (%) unless otherwise specified

¹ All relative risks have been adjusted for maternal age, year of event, Carstairs category at the previous & interpregnancy interval

² Low birth weight also adjusted for gestational age

³ Only spontaneous delivery considered among live & still birth

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TABLE 6: Comparisons of perinatal outcomes following one or more induced abortions

	No of consecutive previous induced abortions			Crude and Adjusted ¹ (Adj.) Relative Risks for perinatal outcomes after 2, 3 and 4 abortions compared to 1 abortion (99% confidence Interval)						
	1 N=25348	2 N=3622	3 N=565	4 N=225		2 vs 1 ⁴		3 vs 1 ⁴		4 vs 1 ⁴
Low birth weight <2500g ^{2, 3}	2188 (8.6)	325 (9.0)	54 (9.6)	20 (8.9)	Crude Adj.	1.04 (0.90, 1.20) 0.92 (0.77, 1.11)	Crude Adj.	1.11 (0.79, 1.55) 0.99 (0.73, 1.34)	Crude Adj.	1.03 (0.59, 1.79) 0.54 (0.25, 1.16)
Induction of labour	6919 (27.3)	1005 (27.8)	170 (30.1)	72 (32.0)	Crude Adj.	1.02 (0.94, 1.09) 1.02 (0.95, 1.10)	Crude Adj.	1.10 (0.93, 1.30) 1.11 (0.94, 1.31)	Crude Adj.	1.17 (0.91, 1.51) 1.20 (0.93, 1.55)
	N=16275	N=2285	N=347	N=136						
Spontaneous preterm birth <37 weeks	1676 (10.3)	243 (10.6)	37 (10.7)	20 (14.7)	Crude Adj.	1.03 (0.88, 1.22) 0.94 (0.81, 1.10)	Crude Adj.	1.04 (0.69, 1.55) 1.06 (0.76, 1.47)	Crude Adj.	1.43 (0.84, 2.44) 0.92 (0.53, 1.61)
Spontaneous preterm birth <34weeks	613 (3.8)	87 (3.8)	17 (4.9)	9 (6.6)	Crude Adj.	1.01 (0.76, 1.35) 0.96 (0.71, 1.28)	Crude Adj.	1.30 (0.70, 2.41) 1.14 (0.60, 2.14)	Crude Adj.	1.76 (0.76, 4.05) 1.61 (0.69, 3.72)

Values are n (%) unless otherwise specified

¹ All relative risks have been adjusted for maternal age, year of event, Carstairs category & interpregnancy interval.

² Low birth weight also adjusted for gestational age

³ Percentage calculated based on number available in the group

Comparison group is women with 1 IA

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Reproductive outcomes following induced abortion: a national register 1 2 based cohort study in Scotland Siladitya Bhattacharya¹, Alison Lowit¹ Sohinee Bhattacharya^{1*}, Edwin A Raja¹, 3 Amanda J Lee¹, Tahir Mahmood², Allan Templeton¹ 4 5 ¹Division of Applied Health Sciences, University of Aberdeen 6 ²Forth Park Hospital, Kirkcaldy 7 8 *Corresponding author 9 All correspondence to: 10 Sohinee Bhattacharya Lecturer, Obstetric Epidemiology 11 12 University of Aberdeen 13 Dugald Baird Centre for Research on Women's Health 14 Aberdeen Maternity Hospital AB25 2ZL 15 Tel: +44 (0)1224 438441 16 17 e-mail: sohinee.bhattacharya@abdn.ac.uk 18 19 All authors have completed the Unified Competing Interest form at 20 http://www.icmje.org/coi_disclosure.pdf and declare: The Chief Scientist Office Scotland 21 funded the study; no financial relationships with any organisations that might have an 22 interest in the submitted work in the previous three years; no other relationships or 23 activities that could appear to have influenced the submitted work 24 25 The Corresponding Author has the right to grant on behalf of all authors and does grant on 26 behalf of all authors, a worldwide licence to the Publishers and its licensees in perpetuity, 27 in all forms, formats and media (whether known now or created in the future), to (i) 28 publish, reproduce, distribute, display and store the Contribution, (ii) translate the 29 Contribution into other languages, create adaptations, reprints, include within collections 30 and create summaries, extracts and/or, abstracts of the Contribution, (iii) create any other 31 derivative work(s) based on the Contribution, (iv) to exploit all subsidiary rights in the 32 Contribution, (v) the inclusion of electronic links from the Contribution to third party 33 material where-ever it may be located; and, (vi) licence any third party to do any or all of 34 the above. 35 36

 Abstract Background The impact of induced abortions on subsequent childbearing is of major importance to women. Some published studies have shown a link between induced abortion and subsequent preterm birth but existing studies have been largely unable to disentangle spontaneous and induced preterm delivery. The primary aim of this study was to investigate reproductive outcomes in women following induced abortion. Methods Data were extracted on all women (aged 15-55 years) who had an induced abortion, a miscarriage, a livebirth, or an ongoing pregnancy and live delivery in their first pregnancy recorded between 1981 and 2007 in the Scottish Morbidity Records databases. Obstetric and perinatal outcomes in a second ongoing pregnancy following an induced abortion were compared with those in primigravidae, as well as those who had had a miscarriage or livebirth in their first pregnancy. Spontaneous preterm birth rates were also compared in women following surgical and medical termination as well as after one or more consecutive induced abortions. Findings A total of 120,033, 457,477 and 47,355 women with a documented second pregnancy following an initial induced abortion (IA), livebirth and miscarriage respectively between 1981 and 2007 were identified. Data from first pregnancies from the 457,477 women who had an initial livebirth constituted a third unexposed cohort of primigravidae. Women who underwent an initial induced abortion were younger and more socially deprived than those who had a livebirth or a miscarriage (p < 0.001). The livebirth group contained the highest proportion of current smokers, followed by the abortion group.

Women with an induced abortion in a first pregnancy had a higher risk of spontaneous preterm live birth in the next pregnancy than women in their first pregnancies [Adjusted relative risk (Adj. RR) 1.37, 99% Confidence Interval (CI) 1.32, 1.43] or women who had a livebirth in their first pregnancy [Adj. RR 1.66, 99% CI 1.58-1.74], but a lower risk in comparison with women with a previous miscarriage [Adj. RR 0.85, 99% CI 0.79-0.92]

Following an initial induced abortion, women were more likely to be diagnosed with placental abruption than either primigravidae [Adj. RR 1.28, 99% CI 1.10BMJ Open: first published as 10.1136/bmjopen-2012-000911 on 6 August 2012. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

1.50] or women with a previous livebirth [Adj. RR 1.49, 99% CI 1.25-1.77]. The
risk of pre-eclampia was higher in women with previous induced abortion in
comparison with primigravidae [Adj. RR 1.26, 99% CI 1.17-1.35] or women with
a previous livebirth [Adj. RR 2.42, 99% CI 2.21- 2.65].

In comparison with women who had an initial miscarriage, women with an IA in their first pregnancy were less likely to have a subsequent miscarriage [Adj. RR 0.56, 99% CI 0.54-0.590] or ectopic pregnancy [Adj. RR 0.83, 95% CI 0.71-0.97] but more likely to have a second induced abortion [Adj. RR 4.64, 99% CI 4.44-4.85]. They were less prone to develop pre-eclampsia [Adj. RR 0.83, 99% CI 0.73-0.94] in their next ongoing pregnancy.

Surgical abortion was associated with a higher chance of spontaneous preterm birth in the next ongoing pregnancy than medical abortion [Adj. RR 1.25, 99% CI 1.07-1.45)]. Compared with primigravid women, the risk of spontaneous preterm delivery was higher after surgical (Adj. RR 1.45 (1.37, 1.55) but not medical abortion (1.11 (0.99, 1.24). The adjusted relative risks (99% CI) for spontaneous preterm birth in the next ongoing pregnancy following two, three and four consecutive IAs in comparison with a single IA were 1.02 (0.86-1.21), 1.01 (0.66-1.55) and 1.38 (0.71-2.70) respectively.

97 Interpretation

Induced abortion in a first pregnancy is associated with a higher risk of spontaneous pretermbirth in a subsequent pregnancy than that in primigravidae or women with a previous livebirth, but is lower than that observed in women with an initial miscarriage. This is the first study to show that surgical, but not medical abortion appears to be associated with an increased risk of spontaneous preterm birth.

106 Background

Many women start their reproductive careers with an abortion in their first pregnancy. In 2009, 13,005 abortions were performed in Scotland with the highest rates in women aged 16-19 years ¹. What is not yet entirely clear is the effect these abortions may have on subsequent childbearing. It has been believed that infection, cervical trauma and endometrial curettage associated with induced abortion could lead to future infertility, ectopic, preterm delivery and placenta praevia, but the data from existing observational studies are mixed ^{2 -18} Following the legalisation of abortion in 1967, initial research on the effects of an induced abortion on subsequent pregnancies showed no evidence of an increased risk of miscarriage, preterm delivery or low birth weight^{19, 20}. Much of the work in the subject has been hampered by methodological limitations; randomised controlled studies are not feasible in this context and researchers have looked to observational studies. Many of the published studies have been limited by small sample sizes, self-reported outcomes and inability to adjust for many potential confounders. A recent review ²¹ reported that half of the twelve relevant studies found an association between induced abortion and preterm birth as well as placenta praevia. More recently a number of large studies found no increased risk of placenta praevia, but supported an association with preterm ^{18, 22, 23} and very preterm delivery ^{24, 25} The clinical implications of this are profound as reducing the incidence of preterm delivery, with its considerable associated problems, remains one of the most significant challenges in obstetrics.

Over a quarter of induced abortions in Scotland in 2005 were repeat procedures ¹ [ISD, personal communication]. While the reproductive sequalae of repeat abortions are unclear, the available literature suggests that the risk of preterm delivery is increased by multiple abortions ^{18, 22, 24, 26}. BMJ Open: first published as 10.1136/bmjopen-2012-000911 on 6 August 2012. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

Changes in the technique of abortion have to be taken into account when assessing their impact on future reproduction. In 1992, 83.6% of terminations were carried out surgically, falling to 60.6% in 1998 and 40.7% in 2006, with the remainder being carried out medically ¹. A number of studies ²⁷⁻²⁹ have compared these methods in terms of safety, efficacy and short term complications but data on subsequent reproductive outcomes is scant. A recent study ³⁰ found no difference in reproductive outcomes (ectopic, miscarriage and preterm delivery) following medically and surgically induced abortions, but was unable to adjust for known confounders such as smoking.

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In view of the high current rates of induced abortion, it is important for women
 and those involved in their care to be aware of any potential associations with
 future reproductive outcomes.

The Scottish Morbidity Record (SMR) system in Scotland covers a national population and has captured data on medical and surgical abortion for many years. Over 99.3% of abortions in Scotland are carried out in NHS premises and are recorded in the SMR system. As these data are based on clinical records, any potential bias created by underreporting will be removed. The availability of this large national dataset provides an ideal opportunity to link records on abortion (SMR01) with maternity records (SMR02) in order to explore the risk of preterm delivery and other maternal and perinatal outcomes in women following one or more episodes of induced abortion. The data would also allow a meaningful comparison of outcomes following alternative forms of induced abortion (i.e. medical versus surgical).

The primary aim of this study was to investigate reproductive outcomes in women following induced abortion. In particular we wished to answer the following research questions: 1) Is an induced abortion in a first pregnancy associated with spontaneous preterm birth or other adverse obstetric or perinatal outcomes in the second pregnancy? 2) Is an induced abortion performed after a singleton term first pregnancy associated with spontaneous preterm birth or adverse obstetric or perinatal outcomes in the next pregnancy? 3) Do any of these associations differ by method of induced abortion (i.e. surgical versus medical)? 4) Is the risk of adverse obstetric or perinatal outcomes associated with increasing number of terminations?

170 Methods

A retrospective cohort study design was used on routinely collected data extracted from the Information and Statistics Division (ISD) database. Approval was obtained from the Privacy Advisory Committee of the National Health Service, Scotland.

Data were extracted from the ISD databases (SMR01 and 02) on women aged 15-55 years who had an induced abortion, a miscarriage, a live birth, or an ongoing pregnancy and live delivery in their first pregnancy between 1981 and 2007 followed by a second pregnancy event. Reproductive outcomes in the subsequent pregnancy of women who had an IA in their first pregnancy (exposed

cohort) were compared with those in two unexposed groups: 1) women in their second pregnancy after a miscarriage in their first pregnancy and 2) women in their second pregnancy after a live birth in their first pregnancy. In addition to these two unexposed cohorts, obstetric and perinatal outcomes in the subsequent pregnancy of women who had an IA in their first pregnancy (exposed group), were also compared with those women in their first pregnancy.

To explore outcomes following early pregnancy loss after an initial livebirth, data were extracted on all women (15-55 years of age) who had an induced abortion, a miscarriage, or a live birth, in their second pregnancy (following a live birth in their first pregnancy) between 1981 and 2007 from the ISD databases (SMR01 and 02) and followed up to identify a third pregnancy event. Reproductive, obstetric and perinatal outcomes in women who had an IA after a singleton term first pregnancy (exposed group), were compared with those in two unexposed groups: 1) women in their third pregnancy following a singleton term delivery in the first pregnancy and a miscarriage in the second pregnancy and 2) women in their third pregnancy following two singleton term deliveries

Women treated by different methods of induced abortion (surgical or medical) in a first pregnancy were compared in terms of reproductive, obstetric and perinatal outcomes. Finally, to answer research question 4, reproductive and perinatal outcomes were compared between women who had 1, 2, 3 and 4 previous consecutive induced abortions and women with no previous abortions. Each group of women was independent of the others - for example women who had 3 abortions were excluded from the group with 2 abortions. For each analysis, except research question 4, the women were matched on parity as the risk of adverse obstetric outcomes is dependent on parity with primiparous women suffering the highest risk.

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210 Data extracted

The following variables were identified by matching SMR01 and SMR02 datasets between the years 1981 and 2007.

Demographic details: Age at pregnancy events, smoking status, and social class (assessed using Carstairs category of deprivation) in the exposed group were compared with each of the 3 unexposed cohorts

Induced abortion details: estimated gestation and method of termination (medical or surgical or both) were recorded for the exposed group. Reproductive outcomes: miscarriage, abortion, livebirth, ectopic, stillbirth in the exposed group were compared with the unexposed cohorts. Obstetric and perinatal outcomes: The incidence of pre-eclampsia, placenta praevia, placental abruption, preterm delivery, very preterm delivery, low birth weight and the mode of delivery in the exposed cohort were compared with each of the 3 unexposed cohorts. Spontaneous delivery rates (including live and stillbirth) were calculated after excluding women who had induced labour and elective (planned) caesarean section.

229 Socioeconomic status was assessed using the Carstairs index ³¹ which was 230 divided into quintiles for analysis.

Power Calculation

Given the number of sub-groups in the analysis coupled with multiple outcomes, a global sample size calculation was not feasible. Preliminary enquiries with ISD suggested that we could identify at least 260,000 terminations (1981-2007), of which 30% (n=69,000) were estimated to have had a subsequent live birth and 25.5% (n=66,223) were induced abortions in a first pregnancy.

 Using a 1:1 ratio of women with induced abortions in a first pregnancy (exposed cohort) and unexposed women, we anticipated having over 90% power, at the two-sided 5% significance level, to detect a difference of 0.5% or more in the chances of a preterm birth (ie, an odds ratio of 1.09) assuming that the prevalence of live births in the unexposed group was 6%.

245 Statistical Analysis

In the absence of an ideal comparison group for women with a prior abortion, we used 3 unexposed cohorts which could increase the chance of false positive associations (type I error). To help minimise this, we used a stringent p-value of ≤ 0.01 to denote statistical significance throughout the statistical analyses.

A generalised linear model was used with Poisson family and robust variance estimator to ascertain the relationship between exposure (first pregnancy induced abortion) and various reproductive outcomes (still birth, miscarriage, ectopic and induced abortion), maternal and perinatal outcomes (pre-eclampsia, placentaprevia, abruption placenta) after adjusting for potential confounders (maternal

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age, year of delivery, smoking & carstairs at relevant pregnancy). For the outcome of induction of labour, pre-eclampsia, placenta previa and placental abruption were also entered into the model. Similarly, the outcome low birth weight was also adjusted for gestational age. Stata version 11 was used for the analysis and a stringent p-value of ≤ 0.01 was used to denote statistical significance throughout.

As smoking data were not routinely collected in the maternity database (SMR02) before 1992, and rarely recorded for women having an induced abortion or miscarriage. Thus self-reported smoking status, collected at antenatal booking visit, though available for some women was non-randomly missing for a high percentage of women. This sometimes led to non-convergence of the statistical models. Therefore, a sensitivity analysis was carried out by re-running all of the multivariate models excluding the smoking variable to determine if the overall effect sizes remained of similar magnitude. This was found to be so.

271 Results

272 Demographic characteristics of women who had an abortion in their first 273 pregnancy were compared with those who had either a live birth or a miscarriage 274 in their first pregnancy and with primigravida women (Table 1). Women with a 275 previous induced abortion were significantly older, more socially deprived and 276 more likely to be smokers than primigravida women or those who had a live birth 277 or a miscarriage in a previous pregnancy.

Table 2 presents reproductive outcomes in a subsequent pregnancy following IA, livebirth and miscarriage in the first pregnancy. As Table 2 shows, women with an IA in the first pregnancy were more at risk of having a still birth or an induced abortion in the second pregnancy as compared with an initial livebirth. Compared to those who had an initial miscarriage, women who had an IA in their first pregnancy were less likely to have a subsequent miscarriage or ectopic pregnancy, but more likely to have another induced abortion.

Perinatal outcomes in the next ongoing pregnancy following IA are also compared with those in primigravida and women who have had a livebirth or miscarriage in Table 2. Compared with women having a previous livebirth, women who had an induced abortion were at higher risk of pre-eclampsia, abruptio placenta, induction of labour, spontaneous preterm and very preterm delivery (<32weeks) extremely preterm (< 28 weeks) and delivery of a low birth weight baby (<2500 g) but not placenta praevia.

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In comparison with women with a previous miscarriage, a history of IA was associated with a lower risk of developing pre-eclampsia and spontaneous preterm and very preterm delivery. Risks of pre-eclampsia, placental abruption (but not placenta praevia), delivery of a low birth weight baby and spontaneous preterm, very preterm and extremely preterm birth were significantly higher following IA than in primigravid women. The risk of pre-eclampsia in women with a previous IA was higher than in primigravid women but lower than in women with a previous miscarriage (Table 2).

The demographic characteristics of women who had a livebirth in a first pregnancy and then went on to have induced abortion, live birth or a miscarriage in their second pregnancy are shown in Table 3. Women with an induced abortion in their second pregnancy were younger, belonged to a more deprived social group and were more likely to be smokers than women who had a live birth in their second pregnancy. Compared to women who had a miscarriage in their second pregnancy, women with a previous induced abortion were older, belonged to more deprived social classes and were more likely to smoke.

As Table 4 shows, IA in the second pregnancy was associated with a higher risk of an ectopic or an induced abortion in the third pregnancy as compared with an initial livebirth. The risk of miscarriage in a third pregnancy was lower in women who had an IA in a second pregnancy, but the risks of another induced abortion were higher than in women with a previous miscarriage.

Compared to women with two previous livebirths, women with a livebirth followed by an IA were more likely to have pre-eclampsia, placenta praevia, induced labour, low birthweight and spontaneous preterm, very preterm and extremely preterm birth (Table 4). Women with an IA in a second pregnancy were not at any significantly higher risk of perinatal complications in comparison with women with a previous miscarriage.

In records where the method of IA was clearly recorded, 52,560 women were noted to have had surgical and 16,702, medical abortions. As Table 5 shows, reproductive outcomes were comparable in the two groups except for a lower risk of a second induced abortion following surgical termination of pregnancy. The adjusted relative risk of miscarriage, ectopic pregnancy, placenta praevia and spontaneous preterm delivery (<37 weeks) were significantly higher after surgical

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termination. In comparison with primigravid women i.e. no previous abortion, 332 333 women with a medical abortion had an increased risk of placental abruption, but 334 not spontaneous preterm, very preterm or extremely preterm delivery. In 335 contrast, women with a surgical abortion had higher risks of all three types of 336 spontaneous preterm delivery. They also had an increased risk of preeclampsia, 337 placenta praevia, abruption and low birthweight babies. More women had repeat 338 abortion following surgical termination of pregnancy, and fewer went on to have a 339 livebirth in comparison with primigravid women and those who had medical 340 terminations.

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Table 6 summarises the risk of spontaneous preterm delivery in subsequent 342 343 pregnancies following one or more consecutive IAs in comparison to those with no previous abortions (primigravid women). The adjusted relative risks of 344 spontaneous preterm birth, (< 37 weeks) was incrementally higher in women 345 undergoing 1, 2, 3 and 4 induced abortions. The adjusted relative risk of 346 347 spontaneous very preterm delivery (< 32 weeks) was higher after 1 and 4 348 induced abortions. while the adjusted relative risk of spontaneous extremely 349 preterm delivery (<28weeks) was higher following 2 and 4 previous induced abortions. Additional induced abortions were not associated with increased 350 351 adjusted relative risks of any type of spontaneous preterm birth.

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354 **Discussion**

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356 Principal findings

Our results suggest that women who had an induced abortion in the first pregnancy were more at risk of maternal and perinatal risks in comparison to women with a previous live birth. Compared to an initial miscarriage, an induced abortion in a first pregnancy was associated with a higher subsequent risk of miscarriage or ectopic pregnancy, induced abortion and pre-eclampsia. Women with a previous induced abortion face increased risks of antepartum haemorrhage and spontaneous preterm birth than women in their first pregnancy.

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A livebirth prior to an IA does not appear to be associated with reduced perinatal complications in women who are at higher risk of spontaneous preterm birth than primigravida. Surgical termination appears to be associated with a higher chance of spontaneous preterm birth than medical IA. There does not appear to be a dose dependent effect of IA on future adverse perinatal outcomes.

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Women with three or four consecutive induced abortions were not at significantly higher risk of spontaneous preterm birth in comparison with women who have

372 had one termination of pregnancy.

376 Strengths

To our knowledge this is the largest population based study of reproductive outcomes following an induced abortion. Registry based previous studies reporting preterm birth rates as an outcome have been unable to discriminate between spontaneous and induced preterm delivery; this is one of the first papers to be able to calculate and report spontaneous preterm birth rates after induced abortion.

We have acknowledged changes in clinical practice over the years during which data were collected and have adjusted for year of pregnancy in the regression models. The choice of an appropriate comparison group to women with a history of induced abortion is problematic. Women who are pregnant again after having undergone an induced abortion in a previous (first) pregnancy are gravida 2 and parity 0. It is impossible to control for both gravidity and parity unless the unexposed cohort have had a prior pregnancy which did not lead to a delivery. Other comparison groups can be either women in their first ongoing pregnancies (gravidity 1 parity 0), or in their second ongoing pregnancies after a previous delivery (gravidity 2 parity 1). We feel that our strategy comparing the exposed cohort to all three of the above groups adds validity to our results.

396 Limitations

The main limitations of this study stem from unrecorded and missing data in relation to certain potential confounding factors within the dataset. For example, smoking data were only available for 50% of women; data on body mass index were unavailable while data on gestational age at termination was missing in the majority of cases. The actual method of termination (medical versus surgical) was unrecorded in around 25% of all cases, while a large number of women appeared to have both medical as well as surgical treatment. Parity number was less reliable in the early years of data collection. This may reflect problems with coding and could potentially affect the quality of our results. In addition, the analysis of such a large population based dataset has the capacity to produce statistically significant differences which may or may not be clinically relevant,

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 although this has been minimised by our use of a stringent 1% significance levelthroughout.

Defining an ideal reference group is a challenge in studies exploring outcomes after induced abortion. While we have partially addressed this issue by using more than one unexposed cohort, our data do not allow us to adjust for potential differences in pregnancy intentions between groups, which can impact on antenatal care and perinatal outcomes.

Unrecorded data relating to key potential confounders cannot exclude the possibility that some associations are not explained by abortion itself but by special circumstances of women seeking abortion which also increases their risk of complications in pregnancy. We ran a separate analysis to identify previous pregnancy complications in women who either had an induced abortion, miscarriage or livebirth in a second pregnancy. As supplementary Table A shows, induced abortion in the second pregnancy was not significantly associated with increased relative risk (99% confidence interval) of preeclampsia, placenta praevia, placental abruption and low birthweight respectively compared to either livebirth [0.99 (0.85, 1.16); 1.29 (0.99, 1.67) 1.32 (0.96, 1.82) 1.08 (0.98, 1.18)] or miscarriage [0.79 (0.65, 0.96) 1.17 (0.81, 1.69) 1.08 (0.70, 1.68) 1.14 (1.00, 1.30)].

Comparison with previous studies

The association between induced abortion and preterm birth found in this study is consistent with previously published work ³². Two recent meta-analyses suggest that women who have had an IA are at higher risk of preterm birth in subsequent pregnancies ^{33, 34}. Our study shows that after adjustment women with a previous abortion have an increased chance of a subsequent preterm birth and very pre-term birth compared with primigravidae or those who have had a previous live birth, but at no significantly greater risk compared to women who have had a previous miscarriage. Women who had a live birth before an induced abortion are more likely to have a preterm birth compared to women with two previous live births.

Our results did not suggest a signficant increased risk of miscarriage after an induced abortion which is in keeping with a review of literature ²¹. In contrast, Sun (2003)³⁵ demonstrated an association between surgical abortion and miscarriage in a subsequent pregnancy. Literature on the association between IA and miscarriage or ectopic pregnancy is sparse and conflicting. The increased risk of having a second termination following

induced abortion in a first pregnancy highlighted in our study has been reported elsewhere ³⁶⁻³⁸. While women who had an abortion were more likely to have a subsequent abortion, but they may also be more likely to have an unintended pregnancy. This should be seen a potential risk factor which should be explored in future studies.

Available literature suggests there is an association between IA and placenta previa ^{39, 40}, but no association with abruptio placenta ^{41, 42}. This study found that women in their second pregnancy after an initial induced abortion in the first were at higher odds of both placenta previa and abruptio placenta, women in their third pregnancy after an induced abortion in their second pregnancy had higher odds of placenta previa, but not abruptio placenta. Published evidence supports a decreased risk of pre-eclampsia after an IA ^{43, 44}. Our results suggest a risk of developing preeclampsia which is on par with primigravid women, but lower than women with a previous miscarriage. The reasons for these associations are unclear and hence any explanations can only be speculative. Problems with placental position and function could occur due to disruption of the endometrium by vigorous curettage. The quality of placental function in a previous pregnancy could influence susceptibility to future preeclampsia.

Since the introduction of medical abortion there has been much speculation about the rival merits of medical and surgical techniques, especially in terms of future reproductive outcomes. Analysis of Danish data has failed to demonstrate a difference in key outcomes such as preterm birth between medical and surgical abortion, but this study was unable to identify spontaneous versus induced preterm birth ³⁰. With our ability to identify spontaneous PTBs, we have shown a clear association with surgical abortion. However, since we were unable to adjust for gestational age, we cannot rule out the possibility that surgical abortions may have been performed at a more advanced stage of pregnancy requiring a greater degree of cervical dilatation - thus leading to future preterm labour. Our results are supported by a recent publication showing that the risk of preterm birth after one or more surgical abortions is higher than after medical abortion and comparable to that in primigravid women ¹¹.

A dose dependent relationship between the number of IAs and future PTB has
 been shown in a number of previous studies ³². The results of our analysis do not

 support this. Given our inability to adjust for a number of potential confounders,this needs to be investigated further.

Our data suggest that medical and surgical terminations may impact differently on future reproductive outcomes - with a higher risk of spontaneous preterm birth after surgery. We were unable to disentangle the separate effects of repeated medical and surgical abortion due to a relative paucity of numbers.

490 A recent publication ¹¹ found an increased risk of premature delivery following 491 multiple surgical, but not first trimester, medical induced abortions. While this 492 could reflect the effect of repeated surgical trauma to the cervix, this needs 493 further exploration in future studies with long term periods of follow up.

A key challenge in studying health sequalae after induced abortion is to deal with potential differences in pregnancy intentions between comparison groups. While women who had an abortion were more likely to have a subsequent abortion, they may also be more likely to have an unintended pregnancy, which needs to be acknowledged as a potential risk factor in future studies. BMJ Open: first published as 10.1136/bmjopen-2012-000911 on 6 August 2012. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected by copyright

501 Conclusions

Induced abortion in a first pregnancy is associated with a higher risk of spontaneous preterm birth in a subsequent pregnancy in comparison with primigravid women, but not women with a previous miscarriage. A successful pregnancy leading to a livebirth prior to an induced abortion does not appear to ameliorate this risk while more than one abortion does not significantly increase it. Surgical abortion appears to be associated with an increased risk of spontaneous very preterm birth in comparison with medical termination of pregnancy. The results of this study should help provide women as well as health professionals with accurate information to inform clinical decision making and tailor antenatal care to address women's risk profiles.

AT conceived the idea for the study. SB was the Principal Investigator. He designed the study along with SohB, AT, ALee and TM, led the funding application, managed the project, interpreted the results and wrote the first draft of the paper. ALo cleaned the data and performed some of the initial analyses. SohB co-wrote the funding application, facilitated data manipulation, interpreted the results and helped to draft the paper. EAR performed the statistical analysis and interpreted the results with input from ALee. All authors commented on, and contributed to the final draft of the paper.

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522 Acknowledgements

- 523 We thank staff at ISD Scotland for extraction of data from the Scottish Morbidity
- 524 Records Database and Margery Heath for secretarial assistance.

Funding 526

- 527 The Chief Scientist Office Scotland funded the study. The views expressed are S. Ins and those of the authors and not the funding body. 528
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Supplementary Table A

Comparison of reproductive and perinatal outcomes in the 1st pregnancy (live birth & full term) in women who had induced abortion, livebirth or miscarriage in the 2nd pregnancy

Outcome of 1st pregnancy	Outco	ome of second preg	nancy	Crude Relative Risk (99% CI) ¹		
Live birth	Induced abortion N=30527	Live birth N=125855	Miscarriage N=22404	Induced abortion vs Live birth	Induced abortion vs Miscarriage	
Pre-eclampsia	349 (1.1)	1447 (1.2)	325 (1.5)	0.99 (0.85, 1.16)	0.79 (0.65, 0.96)	
Placenta previa	128 (0.4)	409 (0.3)	80 (0.4)	1.29 (0.99, 1.67)	1.17 (0.81, 1.69)	
Abruptio placenta	84 (0.3)	262 (0.2)	57 (0.3)	1.32 (0.96, 1.82)	1.08 (0.70, 1.68)	
Induction of labour ³	8064 (26.4)	33225 (26.4)	6103 (27.2)	1.00 (0.97, 1.03)	0.97 (0.93, 1.01)	
Low birth weight <2500 ⁴	972 (3.2)	3727 (3.0)	626 (2.8)	1.08 (0.98, 1.18)	1.14 (1.00, 1.30)	

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	Cheo Item No 1	Supplemental file: STROB klist of items that should be included Recommendation (a) Indicate the study's design with a	
abstract	ltem No	Recommendation	Location within
abstract	No		
Title and abstract Introduction	1	(a) Indicate the study's design with a	
			Title & Abstract: Line
Introduction		commonly used term in the title or the abstract	51
Introduction		(b) Provide in the abstract an	Abstract: Lines 52 - 97
Introduction		informative and balanced summary of	
Introduction		what was done and what was found	
Background/	2	Explain the scientific background and	Introduction: Lines 112
rationale		rationale for the investigation being reported	- 159
Objectives	3	State specific objectives, including	Introduction: Lines 161-
		any prespecified hypotheses	170
Methods	1		
Study design	4	Present key elements of study design	Methodology: Line 173
		early in the paper	
Setting	5	Describe the setting, locations, and	Methods Lines
-		relevant dates, including periods of	178-181
		recruitment, exposure, follow-up, and	
		data collection	
Participants	6	(a) Give the eligibility criteria, and the	Methods: Lines 178 -
•		sources and methods of selection of	207
		participants. Describe methods of	
		follow-up	
		(b) For matched studies, give	Not applicable
		matching criteria and number of	
		exposed and unexposed	
Variables	7	Clearly define all outcomes,	Methods: Lines 213 -
		exposures, predictors, potential	221
		confounders, and effect modifiers.	
		Give diagnostic criteria, if applicable	
Data	8*	For each variable of interest, give	Methods: Lines 210 -
sources/		sources of data and details of	211.
measuremen		methods of assessment	
t		(measurement). Describe	
		comparability of assessment methods	
		if there is more than one group	
Bias	9	Describe any efforts to address	The only possible
		potential sources of bias	source of bias could be
			misclassification of
			variables as routinely
			collected data are
			used. We think that the

			compensate for that.
Study size	10	Explain how the study size was	All available data were
		arrived at	included.
			Power calculation: lines
			225 -235.
Quantitative variables	11	Explain how quantitative variables	Statistical analysis:
		were handled in the analyses. If	Lines 238-267
		applicable, describe which groupings	
		were chosen and why	
Statistical	12	(a) Describe all statistical methods,	Statistical analysis:
methods		including those used to control for	Lines 238-267
		confounding	
		(b) Describe any methods used to	Methods: Lines 203 -
		examine subgroups and interactions	207
		(c) Explain how missing data were	Methodology: Lines
		addressed	152 - 159
		(d) If applicable, explain how loss to	Not applicable.
		follow-up was addressed	
		(<u>e</u>) Describe any sensitivity analyses	Methodology Lines
			261-267
Results			
Participants	13*	(a) Report numbers of individuals at	Results: Lines 176 -
		each stage of study—eg numbers	177
		potentially eligible, examined for	
		eligibility, confirmed eligible, included	
		in the study, completing follow-up,	
		and analysed	
		(b) Give reasons for non-participation	Not applicable
		at each stage	
		(c) Consider use of a flow diagram	The whole population
			was selected
Descriptive	14*	(a) Give characteristics of study	Tables 1 and 3
data		participants (eg demographic, clinical,	
		social) and information on exposures	
		and potential confounders	
		(b) Indicate number of participants	Tables 1 and 3
		with missing data for each variable of	
		interest	
		(c) Summarise follow-up time (eg,	Table 1 and 3
		average and total amount)	
Outcome	15*	Report numbers of outcome events or	Tables 2,4,5
data		summary measures over time	
Main results	16	(a) Give unadjusted estimates and, if	Table 2, 4, 5
		applicable, confounder-adjusted	
		estimates and their precision (eg,	
		95% confidence interval). Make clear	
		which confounders were adjusted for	
		and why they were included	

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		[1
		continuous variables were	
		categorized	
Other	17	Report other analyses done—eg	Results: Lines 266-7
analyses		analyses of subgroups and	
		interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference	Discussion: Lines 341-
		to study objectives	353
Limitations	19	Discuss limitations of the study, taking	Discussion: Lines 377-
		into account sources of potential bias	389
		or imprecision. Discuss both direction	
		and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation	Discussion: Lines 439-
		of results considering objectives,	449
		limitations, multiplicity of analyses,	
		results from similar studies, and other	
		relevant evidence	
Generalis-	21	Discuss the generalisability (external	Discussion: Lines 363-
ability		validity) of the study results	373

Other inform	ation				
Funding	22	Give the source of funding and the role of the funders	Lines 479-480		
		for the present study and, if applicable, for the			
		original study on which the present article is based			