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Birth outcomes after induced abortion: a nationwide register-based study of first births in Finland

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STUDY QUESTION: Is the perinatal health of first-born children affected by the mother's previous induced abortion(s) (IAs)?

SUMMARY ANSWER: Prior IAs, particularly repeat IAs, are correlated with an increased risk of some health problems at first birth; even in a country with good health care quality.

WHAT IS KNOWN ALREADY: A positive association between IA and risk of preterm birth or a dose–response effect has been found in some previous studies. Limited information and conflicting results on other infant outcomes are available.

STUDY DESIGN, SIZE AND DURATION: Nationwide register-based study including 300 858 first-time mothers during 1996–2008 in Finland.

PARTICIPANTS/MATERIALS, SETTING AND METHODS: All the first-time mothers with a singleton birth (obtained from the Medical Birth Register) in the period 1996-2008 (n = 300858) were linked to the Abortion Register for the period 1983-2008.

MAIN RESULTS AND THE ROLE OF CHANCE: Of the first-time mothers, 10.3% (n = 31083) had one, 1.5% had two and 0.3% had three or more IAs. Most IAs were surgical (88%) performed before 12 weeks (91%) and carried out for social reasons (97%). After adjustment, perinatal deaths and very preterm birth (<28 gestational week) suggested worse outcomes after IA. Increased odds for very preterm birth were seen in all the subgroups and exhibited a dose–response relationship: 1.19 [95% confidence interval (CI) 0.98-1.44] after one IA, 1.69 (1.14-2.51) after two and 2.78 (1.48-5.24) after three IAs. Increased odds for preterm birth (<37 weeks) and low birthweight (<2500 g and <1500 g) were seen only among mothers with three or more IAs: 1.35 (1.07-1.71), 1.43 (1.12-1.84) and 2.25 (1.43-3.52), respectively.

LIMITATIONS, REASONS FOR CAUTION: Observational studies like ours, however large and well-controlled, will not prove causality.

WIDER IMPLICATIONS OF THE FINDINGS: In terms of public health and practical implications, health education should contain information of the potential health hazards of repeat IAs, including very preterm birth and low birthweight in subsequent pregnancies. Health care professionals should be informed about the potential risks of repeat IAs on infant outcomes in subsequent pregnancy.

STUDY FUNDING/COMPETING INTEREST(S): National Institute for Health and Welfare and the Academy of Finland. No competing interests.

Key words: induced abortion / termination of pregnancy / birth outcomes / prematurity / low birthweight / register study

Introduction

Induced abortion (IA) is one of the most common gynecological procedures performed on women but the impact of IAs on women's subsequent childbearing has not yet been properly studied (van Oppenraaij et al., 2009; Lowit et al., 2010).

Many previous studies (Henriet and Kaminski, 2001; Ancel et al., 2004; Ngyen et al., 2004; Moreau et al., 2005; Freak-Poli et al., 2009; Voigt et al., 2009) and reviews (van Oppenraaij et al., 2009; Shah and Zao, 2009; Swingle et al., 2009; Lowit et al., 2010) have found a positive association between IA and risk of preterm birth or a dose-response effect (i.e. the risk of preterm birth increased with

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increasing number of IAs). Some smaller studies did not find the association (Reime et al., 2008) or it disappeared after adjustment for confounding factors (Raatikainen et al., 2006). The limited data on the association between low birthweight and pre-birth IA have produced conflicting results (Zhou et al., 2000; Henriet and Kaminski, 2001; Raatikainen et al., 2006; Parazzini et al., 2007; Reime et al., 2008).

Most of the recent original studies have been based on small sample-sizes (Henriet and Kaminski, 2001; Ancel et al., 2004; Ngyen et al., 2004; Raatikainen et al., 2006; Parazzini et al., 2007; Reime et al., 2008) and on women's self-reports on exposure (Henriet and Kaminski, 2001; Ancel et al., 2004; Ngyen et al., 2004; Moreau et al., 2005; Raatikainen et al., 2006; Parazzini et al., 2007; Reime et al., 2008; Freak-Poli et al., 2009; Voigt et al., 2009), while the most important confounding factors have not always been controlled for (Zhou et al., 2000; Henriet and Kaminski, 2001; Ancel et al., 2004; Moreau et al., 2005; Raatikainen et al., 2006; Parazzini et al., 2007; Reime et al., 2008; Freak-Poli et al., 2009; Voigt et al., 2009). Furthermore, the type of procedures used, the gestational age at the time of abortion and the number of previous IAs vary substantially (Atrash and Hogue, 1990). Thus, there is a clear need for further studies, particularly from countries with high-quality IA services and reliable information on IAs. Compared with other European countries, Finland has a low rate of IA: 8.9 per 1000 women aged 15-49 (Gissler et al., 2011). According to Finnish legislation enacted in 1970 with updates in 1978 and 1985, a woman needs permission with a legal indication (social, medical or ethical reasons) for IA, although the legislation is interpreted liberally up to 12 weeks. An IA can be legally performed up to 20 weeks, and in cases of a confirmed medical condition of the fetus, up to 24 weeks. Illegal IAs and IAs done outside of Finland are believed to be exceptional.

The purpose of this study was to examine birth outcomes of first-born children by mother's IA history in Finland, which has good IA and birth services and relatively few IAs. Our hypothesis was that having one IA does not affect birth outcomes, but having several may result in poorer birth outcomes. The study was based on nationwide obligatory health registers and took into account mothers' background characteristics, previous miscarriages and ectopic pregnancies.

Materials and Methods

All first-time mothers with a singleton birth were identified in the nation-wide Finnish Medical Birth Register (MBR) for the period 1996–2008 and linked to the data in the Abortion Register (AR) for the period 1983–2008. The MBR was started in 1987 and includes all births occurring in Finland (THL, 2012a). The register contains information on mothers' background, care during pregnancy and delivery and infants' health up to the age of 7 days. The AR has been operating since 1950, and computerized data have been available since 1983 (Gissler et al., 1996, 2004). The AR is based on obligatory notification from physicians (THL, 2012b). The AR includes information on reasons for IA, date, method and gestational weeks of IA, as well as information on woman's sociodemographic and obstetric background. According to data quality studies, the coverage and accuracy of both registers are very good and the contents correspond well to the information found in medical records (Gissler et al., 1995, 1996).

Mother's first birth was identified from the MBR, and her IAs prior to that date were checked from the AR (notifications) and the MBR (mothers' own information). Mothers were classified according to the

information in the AR by the number of IAs before the first birth: no IA, one IA, two IAs and three or more IAs. Mothers who, according to the MBR, had an IA history but in whom no IAs were found in the AR were classified as 'IA history unknown'. If there was a discrepancy in the number of IAs between the MBR and AR, the AR information was used (n = 5950).

Birth outcomes by the mother's number of IAs were calculated. The following were used as outcome indicators: very low birthweight (<1500 g), low birthweight (<2500 g), very preterm birth (<28 weeks), preterm birth (<37 weeks), low one-minute Apgar scores (0–6) and perinatal death (from 22 weeks). Differences in mothers' background characteristics were studied by cross tabulations and chi-square tests. In the MBR, the socioeconomic position of the mother is defined by using her own occupation at the time of delivery, which is collected routinely from maternity hospitals and classified automatically in the MBR into eight categories according to the national classification by Statistics Finland. In this study, classification into four categories was used: upper white-collar workers, lower white-collar workers, blue-collar workers and others (entrepreneurs, students, pensioners, unemployed women and women with an unclassified position).

Logistic regression (odds ratios and 95% confidence intervals) was used to adjust for background variables considered confounders. Confounders were selected on the basis of previous literature on maternal risk factors on birth outcomes and their availability and quality in the used health registers (Gissler et al., 1995, 1996). The original confounder list included maternal age, marital status, socioeconomic position, urbanity, smoking during pregnancy, previous ectopic pregnancies and miscarriages, as well as method, indication and timing of IA. Of those, only statistically significant variables (P < 0.1) were included in the model. All the variables related to IAs (method, indication and timing) were excluded, since their inclusion did not improve the model. First, adjustment was made for social background (maternal age, marital status, socioeconomic position, urbanity and smoking during pregnancy). Second, data were adjusted for previous ectopic pregnancies and miscarriages. Mothers with an unknown history of IAs were excluded from the logistic regression analyses. Statistical analyses were performed by SAS,

Ethical approval for the study was obtained from the Ethics committee of the National Institute for Health and Welfare (THL), while THL also gave permission to use the registers in this study.

Results

In total, $300\,858$ first-time mothers with singleton births in the period 1996–2008 were identified from the MBR. According to the AR, 31 083 (10.3%) had had one, 4417 (1.5%) two and 942 (0.3%) three or more IAs before the first birth; 226 mothers (0.08%) had an unknown history of IA. Of IAs, 88% were surgical, 91% were made before 12 weeks and 97% were made for social reasons.

Compared with mothers with no previous IAs, mothers with previous IAs were more often smokers, single, from urban areas and from a lower socioeconomic position, and had had miscarriages and ectopic pregnancies before their first birth (Table I).

In the unadjusted analysis, all poor birth outcomes increased by the number of IAs (Table II). Poor outcomes were rare among the mothers with an unknown history of IAs, with numbers being too low to judge their risk.

After adjustment for social background, very preterm birth (<28 gestational week) suggested worse outcomes (Table III). By the number of IAs, the risk of very preterm birth was seen in all the

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Table I Background variables of the Finnish first-time mothers at the time of birth during 1996–2008 by the number of previous induced abortions^a.

Background variable ^b	Number of previous induced abortions											
	0 (n = 264 190)		l (n = 31 083)		2 (n = 4417)		3+ (n = 942)		Unknown history ^c (n = 226)		Total (n = 300 858)	
	n	%	n	%	n	%	n	%	n	%	n	%
Age group												
< 20 years	15 759	6.0	2411	7.8	249	5.6	26	2.8	10	4.4	18 455	6.
20-24	66 434	25.1	8668	27.9	1128	25.5	194	20.6	48	21.2	76 472	25.
25-29	98 392	37.2	9613	30.9	1320	29.9	295	31.3	77	34.1	109 697	36.
30-34	60 284	22.8	6805	21.9	1069	24.2	249	26.4	59	26.1	68 466	22.
35-39	19601	7.4	2949	9.5	534	12.1	133	14.1	25	11.1	23 242	7.7
40+	3719	1.4	637	2.0	117	2.6	45	4.8	7	3.1	4525	1
Unknown	1	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.0
Area												
Urban	1 84 926	70.0	22 59 1	72.7	3365	76.2	720	76.4	109	48.2	211711	70.
Semi-urban	39 389	14.9	4251	13.7	517	11.7	104	11.0	70	31.0	44 33 I	14.
Rural	39 405	14.9	4209	13.5	519	11.8	116	12.3	36	15.9	44 285	14.
Abroad	470	0.2	32	0.1	16	0.4	2	0.2	11	4.9	531	0.
Marital status												
Married	1 29 295	48.9	9785	31.5	1188	26.9	272	28.9	86	38.1	I 40 626	46.
Cohabiting	93 223	35.3	13813	44.4	1972	44.6	365	38.7	112	49.6	1 09 485	36.
Single	32 654	12.4	6202	20.0	1092	24.7	262	27.8	22	9.7	40 232	13.
Unknown	9018	3.4	1283	4.1	165	3.7	43	4.6	6	2.7	10515	3.
Socioeconomic position												
Upper white-collar	42 55 1	16.1	3211	10.3	362	8.2	73	7.7	21	9.3	46218	18.
Lower white-collar	79 354	30.0	9101	29.3	1223	27.7	245	26.0	47	20.8	89 970	35.
Blue-collar	30 749	11.6	5169	16.6	840	19.0	178	18.9	20	8.8	36 956	14.
Other ^d	111536	42.2	13 602	43.8	1992	45.1	446	47.3	138	61.1	127714	31.
Smoker ^e	39 200	14.8	9285	29.9	1821	41.2	433	46.0	48	21.2	50 787	16.
History of miscarriage	26 476	10.0	3671	11.8	613	13.9	129	13.7	21	9.3	30 910	10.
History of ectopic pregnancy	2533	1.0	418	1.3	87	2.0	21	2.2	I	0.4	3060	1.0

 $^{^{\}mathrm{a}}$ Induced abortions in the AR during 1983–2008.

subgroups (even though not always statistically significant), as was a dose–response effect (Table III). Risk of very low birthweight ($<1500\,\mathrm{g}$) was similar, but was statistically significant only among women with three or more IAs. Risks of preterm birth (<37 weeks) and low birthweight ($<2500\,\mathrm{g}$) were seen only among mothers with three or more IAs. Low Apgar scores were not related to IAs. Results on perinatal deaths suggested a small increase after IA, but most comparisons were statistically non-significant (Table III). The largest increase was after three IAs.

Because the overall risk of perinatal death was lower than risks in each subgroup, we also did a sub-analysis excluding the women who had a discrepancy in the number of abortions recorded in the AR and the MBR (Table III). The results remained similar.

Further adjustment for history of miscarriage and ectopic pregnancy had only a marginal effect on adverse birth outcomes after IAs (Table III).

Discussion

In our study, after adjusting for mothers' background characteristics, mothers who had had one pre-birth IA had only marginally increased risks of some outcomes. After two previous IAs, the risk of very preterm birth was increased statistically significantly. With the exception of low Apgar scores, the studied adverse birth outcomes were more common among mothers having had three or more IAs. Taking into account previous miscarriages and ectopic pregnancies did not notably change the results.

 $^{^{}b}P$ -value for chi-square test < 0.001 for every background variable when comparing the groups by the number of induced abortions.

^cHistory of induced abortion in the Medical Birth Register but no induced abortions in the AR.

^dOther = entrepreneurs, students, pensioners, unemployed women and women with an unclassified position.

^eSmoking during pregnancy.

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Table II Birth outcomes of first-time Finnish mothers during 1996-2008 by the number of previous induced abortions^a.

Outcome	Number of previous induced abortions												
	0 (n = 264 190)		l (n = 31 083)		2 (n = 4417)		3+ (n = 942)		Unknown history ^b (n = 226)		Total (n = 300 858)		
	n	/1000°	n	/1000°	n	/1000°	n	/1000°	n	/1000°	n	/1000°	
Very preterm <28 gestational week	837	3	120	4	26	6	10	11	0	0	993	3	
Preterm <37 gestational week	14 705	56	1737	60	269	63	77	84	8	35	16796	56	
Very low birthweight $<$ 1500 g	2087	8	266	9	46	11	20	22	0	0	2419	8	
Low birthweight <2500 g	11 097	42	1353	47	224	52	70	76	8	35	12752	42	
Apgar scores I min 0-6	17 595	67	1997	69	317	74	73	80	17	75	19 999	66	
Perinatal death	1272	5	187	6	29	7	9	10	1	4	1498	5	

^aInduced abortions in the AR during 1983-2008.

Owing to the large number of IAs carried out every year, even a very small increase in risk of poor birth outcomes could have significant public health implications. The majority of previous studies of birth outcomes after pre-birth IA have had methodological problems. Prior to our study, only one large-scale study with reliable data on the exposure (IA) in a country with good IA and birth services and relatively few IAs (Denmark) had been published (Zhou et al., 2000). Our study was the first that can at least partly control for the most important confounding factors, such as smoking and socioeconomic position. Furthermore, we were able to study more outcomes than just the low-birthweight variable investigated in the Danish study (Zhou et al., 2000).

Our large national register-based study covered all the first-time mothers having a singleton birth in the period 1996-2008 and all the IAs carried out in Finland in the period 1983-2008. Data on birth outcomes received from the MBR are considered reliable (Gissler et al., 1995). We did not have information on IA before 1982 or on IAs performed in other countries. Earlier studies assessing the completeness of the Finnish AR found that 99% of IAs were reported to the register and at least 95% of the information matched with medical records (Gissler et al., 1996; Heikinheimo et al., 2008). We found 226 first-time mothers—0.08% of all the studied first-time mothers—in the MBR whose IA history was unknown. As the IA information in the MBR is originally based on mothers' information, some of these may be miscarriages; others may have been mistakes or IAs done while the woman was outside Finland or prior to 1983. Poor outcomes were rare among these mothers. Women who had a discrepancy in the number of IAs between the registers were classified according to the AR and analyses were made that both included and excluded them, which had only marginal effects on the results.

As in previous studies (Raatikainen et al., 2006; Heikinheimo et al., 2008; Niinimäki et al., 2009), we found that the demographic and reproductive profiles of first-time mothers who had had a pre-birth IA differed from those of the first-time mothers who had had no pre-birth IAs. Most risk factors such as smoking, lower socioeconomic position and previous miscarriages and ectopic pregnancies were more common among primiparous women who had experienced IA. In the logistic regression analyses, we were able to adjust for these

confounding factors. However, poor birth outcomes may still be due to mothers' characteristics that could not be controlled for. The risk of repeat IAs is highly associated with low socioeconomic position, which is also a risk factor for prematurity and perinatal mortality. Most IAs in our study were made during the first trimester (91%).

In contrast to some earlier studies (Ancel et al., 2004; Moreau et al., 2005; Freak-Poli et al., 2009; Voigt et al., 2009), we did not find any significant increased risk of preterm birth after one IA (Henriet and Kaminski, 2001; Ancel et al., 2004; Freak-Poli et al., 2009; Shah and Zao, 2009; Voigt et al., 2009). Neither did we find a dose—response effect between the number of pre-birth IAs and preterm birth. An increased risk of preterm birth was found only after three or more pre-birth IAs. In keeping with some earlier findings, we found a dose—response effect between the number of pre-birth IAs and very preterm birth (Moreau et al., 2005; Freak-Poli et al., 2009; Shah and Zao, 2009; Voigt et al., 2009).

Our study's finding of a stronger association of pre-birth IA with very preterm birth than with preterm birth is in line with the findings of some earlier studies (Lumley, 1998; Ancel et al., 2004; Moreau et al., 2005). It has been suggested that both infections before and after IA and surgical procedures may be the underlying mechanisms for the increased risk of very preterm births in subsequent pregnancies (Henriet and Kaminski, 2001; Ancel et al., 2004). Women with a history of IA have had an increased risk of intra-amniotic infection, intra-partum infection and infections of their infants. A relationship has been found between previous IA and preterm birth after placenta previa and other maternal hemorrhage (Ancel et al., 2004), and it has been suggested that the surgical IA, by damaging the endometrium, may increase faulty placentation, causing preterm delivery in subsequent pregnancy. Furthermore, surgical IA may cause mechanical trauma to the cervix, increasing the risk of cervical insufficiency (Ancel et al., 2004). In repeat IAs, women are repeatedly exposed to these potentially harmful effects.

Eighty-eight percent of the IAs in this study were done surgically. The women with three or more IAs had twice as many (2.2 versus I.0%) ectopic pregnancies as there were in women with no IAs. This may reflect a previous history of pelvic inflammatory disease and Chlamydia infections, which are also risk factors for preterm

^bHistory of induced abortion in the Medical Birth Register but no induced abortions in the AR.

^cNumber per 1000 births.

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Table III Crude and adjusted ORs and 95% Cls for birth outcomes of Finnish first-time mothers during 1996–2008 comparing those having had one or more previous induced abortions with those with a history of no induced abortions, by the number of abortions.

Birth outcome	Crude and adjusted odds ratios and 95% CI											
	0 versus	s I	0 versus	s 2	0 versus	3+	0 versus I +					
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI				
Very preterm <28 gestat	ional week							• • • • • • • • • • • • • • • • • • • •				
Crude Model	1.22	1.01-1.48	1.86	1.26-2.76	3.38	1.80-6.32	1.34	1.13-1.60				
Adjusted Model I ^a	1.20	0.99-1.45	1.71	1.15-2.54	2.81	1.49-5.29	1.28	1.07-1.53				
Adjusted Model II ^b	1.19	0.98-1.44	1.69	1.14-2.51	2.78	1.48-5.24	1.27	1.06-1.52				
Preterm <37 gestational	week											
Crude Model	1.00	0.95-1.06	1.10	0.97-1.25	1.51	1.20-1.91	1.03	0.98-1.08				
Adjusted Model I ^a	0.98	0.93-1.03	1.02	0.90-1.15	1.36	1.07-1.72	0.99	0.95-1.04				
Adjusted Model II ^b	0.98	0.93-1.03	1.01	0.89-1.15	1.35	1.07-1.71	0.99	0.94-1.04				
Very low birthweight < I	500 g											
Crude Model	1.08	0.95-1.23	1.32	0.99-1.77	2.72	1.75-4.25	1.15	1.02-1.29				
Adjusted Model I ^a	1.04	0.91-1.18	1.14	0.84-1.54	2.26	1.44-3.53	1.06	0.94-1.20				
Adjusted Model II ^b	1.03	0.91-1.18	1.13	0.84-1.54	2.25	1.43-3.52	1.06	0.94-1.19				
Low birthweight <2500 g	5											
Crude Model	1.04	0.98-1.10	1.22	1.06-1.40	1.83	1.43-2.34	1.08	1.02-1.14				
Adjusted Model I ^a	0.96	0.90-1.01	1.02	0.89-1.18	1.44	1.12-1.84	0.98	0.93-1.03				
Adjusted Model II ^b	0.96	0.90-1.01	1.02	0.89-1.18	1.43	1.12-1.84	0.98	0.93-1.03				
Apgar scores I min 0-6												
Crude Model	0.96	0.92-1.01	1.08	0.97 - 1.22	1.18	0.93 - 1.50	0.98	0.94-1.03				
Adjusted Model I ^a	0.95	0.90 - 1.00	1.05	0.93-1.18	1.11	0.87-1.41	0.97	0.93-1.02				
Adjusted Model II ^b	0.95	0.90 - 1.00	1.05	0.93-1.18	1.10	0.86-1.41	0.97	0.93-1.02				
Perinatal death												
Crude Model	1.25	1.07-1.46	1.37	0.94-1.98	1.99	1.03-3.85	1.28	1.11-1.48				
Adjusted Model I ^a	1.19	1.02-1.39	1.16	0.79-1.71	1.70	0.88-3.30	1.15	0.99-1.34				
Adjusted Model I ^c	1.15	0.98-1.36	1.16	0.79-1.71	1.70	0.87-3.29	1.17	1.01-1.36				
Adjusted Model II ^b	1.19	1.02-1.39	1.16	0.79 - 1.70	1.70	0.87-3.29	1.15	0.99-1.34				

 $^{^{}a}$ Adjusted for social factors: age, marital status, socioeconomic position, urbanity, smoking; women with missing information in the AR (n = 226, 0.08%) excluded.

birth (Paavonen, 2012). However, adjusting for previous miscarriages or ectopic pregnancies did not notably change our findings.

Preterm birth has been the most studied outcome, and there are very few data on other birth outcomes (van Oppenraaij et al., 2009). As with the Danish study (Zhou et al., 2000), we could not find a strong association between low birthweight and a previous IA, although in contrast to the Danish study, we did find an increased risk after three or more previous IAs and a dose—response effect in very low birthweight as described in one previous meta-analysis (Shah and Zao, 2009). Contrary to previous studies that found no difference with relatively small sample sizes, we found a small increased risk of perinatal death after one pre-birth IA (van Oppenraaij et al., 2009). We found the highest risk after three or more IAs, but even our sample was not large enough to enable statistical significance.

Our result of a non-existing association between low Apgar scores and pre-birth IA(s) is in line with the findings of previous studies (van Oppenraaij et al., 2009).

Only a few studies have taken into account the method of IA when studying the association between poor birth outcomes and pre-birth IAs, and those taking it into account did not find any differences by the IA method (Atrash and Hogue, 1990; Yimin et al., 2003; Virk et al., 2007). According to a recent Finnish study, medical IA offered a good alternative to surgical methods without increasing the risk of repeat IAs, but with an increased risk of short-term adverse events (Niinimäki et al., 2009). In 2010, the majority (90%) of IAs in Finland were carried out by medical methods (THL, 2012b). During our study period (1983–2008) most IAs were carried out by surgical methods. In the future, when the number of IAs carried out by

 $^{^{\}mathrm{b}}$ Adjusted additionally for miscarriage and ectopic pregnancy; women with missing information in the AR ($n=226,\,0.08\%$) excluded.

Excluding women who had a history of induced abortion in the Medical Birth Register but not in the AR (n = 226) and those with a discrepancy in the number of induced abortions between the Medical Birth Register and the AR (n = 5950).

No induced abortion, $n = 264\,$ 190 (a reference group), I induced abortion $n = 31\,$ 083, 2 induced abortions n = 4417, 3+ induced abortions n = 942, 1 or more induced abortions, $n = 36\,$ 442.

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medical methods is high enough (but surgical IAs still exist), a large-scale study should be done that compares the birth outcomes in the subsequent pregnancy by the method of IA.

In conclusion, our study confirms those previous findings suggesting that prior repeat IAs are correlated with an increased the risk of (very) preterm birth and (very) low birthweight at first birth. From a public health perspective, information on increased risk of very preterm birth after IAs and its dose—response effect is intrinsically important. In terms of practical implications, it must be noted that observational studies like ours, however large and well-controlled, will not prove causality. For example, our finding of an increased risk following several IAs may be due to some confounding that we could not control for. However, as there are also other reasons to avoid IAs and particularly repeat IAs, sexuality education should contain information of the potential health hazards of IAs, including for subsequent pregnancies. Health care professionals should be informed about the potential risks of repeat IAs on birth outcomes in subsequent pregnancy.

Authors' roles

R.K.: participated in the interpretation of data, drafting and design of the article and in the modification of the final version. M.G.: participated in the interpretation and analysis of data, planning the article, revising the draft critically and approving the final version. M.N.: participated in the interpretation of data, revising the draft critically and approving the final version. E.H.: participated in the conception and design of the article, interpretation of data, revising the draft critically and approving the final version.

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Conflict of interest

None declared.

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