Prior uterine evacuation of pregnancy as independent risk factor for preterm birth: a systematic review and metaanalysis

Gabriele Saccone, MD; Lisa Perriera, MD; Vincenzo Berghella, MD

BACKGROUND: Preterm birth (PTB) is the number one cause of perinatal mortality. Prior surgery on the cervix is associated with an increased risk of PTB. History of uterine evacuation, by either induced termination of pregnancy (I-TOP) or spontaneous abortion (SAB), which involve mechanical and/or osmotic dilatation of the cervix, has been associated with an increased risk of PTB in some studies but not in others.

OBJECTIVE: The objective of the study was to evaluate the risk of PTB among women with a history of uterine evacuation for I-TOP or SAB.

DATA SOURCES: Electronic databases (MEDLINE, Scopus, ClinicalTrials.gov, EMBASE, and Sciencedirect) were searched from their inception until January 2015 with no limit for language.

STUDY ELIGIBILITY CRITERIA: We included all studies of women with prior uterine evacuation for either I-TOP or SAB, compared with a control group without a history of uterine evacuation, which reported data about the subsequent pregnancy.

STUDY APPRAISAL AND SYNTHESIS METHODS: The primary outcome was the incidence of PTB < 37 weeks. Secondary outcomes were incidence of low birthweight (LBW) and small for gestational age (SGA). We planned to assess the primary and the secondary outcomes in the overall population as well as in studies on I-TOP and SAB separately. The pooled results were reported as odds ratio (OR) with 95% confidence interval (CI).

RESULTS: We included 36 studies in this metaanalysis (1,047,683 women). Thirty-one studies reported data about prior uterine evacuation for I-TOP, whereas 5 studies reported data for SAB. In the overall population, women with a history of uterine evacuation for either I-TOP or SAB had a significantly higher risk of PTB (5.7% vs 5.0%; OR, 1.44, 95% CI, 1.09—1.90), LBW (7.3% vs 5.9%; OR, 1.41, 95% CI, 1.22—1.62), and SGA (10.2% vs 9.0%; OR, 1.19, 95% CI, 1.01—1.42) compared with controls. Of the 31 studies on I-TOP, 28 included 913,297 women with a history of surgical I-TOP, whereas 3 included 10,253 women with a prior medical I-TOP. Women with a prior surgical I-TOP had a significantly higher risk of PTB (5.4% vs 4.4%; OR, 1.52, 95% CI, 1.08—2.16), LBW (7.3% vs 5.9%; OR, 1.41, 95% CI, 1.22—1.62), and SGA (10.2% vs 9.0%; OR, 1.19, 95% CI, 1.01—1.42) compared with controls. Women with a prior medical I-TOP had a similar risk of PTB compared with those who did not have a history of I-TOP (28.2% vs 29.5%; OR, 1.50, 95% CI, 1.00—2.25). Five studies, including 124,133 women, reported data about a subsequent pregnancy in women with a prior SAB. In all of the included studies, the SAB was surgically managed. Women with a prior surgical SAB had a higher risk of PTB compared with those who did not have a history of SAB (9.4% vs 8.6%; OR, 1.19, 95% CI, 1.03—1.37).

CONCLUSION: Prior surgical uterine evacuation for either I-TOP or SAB is an independent risk factor for PTB. These data warrant caution in the use of surgical uterine evacuation and should encourage safer surgical techniques as well as medical methods.

Key words: abortion, delivery, miscarriage, preterm termination of pregnancy

Preterm birth (PTB) is the number one cause of perinatal mortality in many countries, including the United States.[1,2] Defining risk factors for prediction of PTB is an important goal for several reasons. First, identifying women at risk allows initiation of risk-specific treatment.[3,4] Second, it may define a population useful for studying particular interventions. Finally, it may provide important insights into the mechanisms leading to PTB.

Prior surgery on the cervix, such as cone biopsy and loop electrosurgical excision procedure, is associated with an increased risk of spontaneous PTB.[5-7] A history of uterine evacuation, by either induced termination of pregnancy (I-TOP) or treatment of spontaneous abortion (SAB) by suction dilation and curettage or by dilation and evacuation (D&E), which may involve mechanical and/or osmotic dilatation of the cervix, has been associated with an increased risk of PTB in some studies but not in others.[8-10]

Some studies have also postulated that the method of uterine evacuation may influence the association (or not) with PTB.[9,10] Moreover, with recent increases in the use of medications (misoprostol and mifepristone), it would be important to assess outcomes in subsequent pregnancies after medical termination of pregnancy as the element of cervical trauma is minimized with these techniques.[11]

The aim of this metaanalysis was to evaluate the risk of PTB among women with a history of uterine evacuation for either I-TOP or SAB.

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Materials and Methods

Search strategy

Electronic databases (ie, MEDLINE, Scopus, ClinicalTrials.gov, EMBASE, Sciencedirect) were searched from their inception until January 2015 with no limit for language. Search terms used were the following key words: low birthweight, premature birth, preterm birth, small for gestational age, miscarriage, pregnancy, premature, newborn, uterine evacuation, abortion, induced abortion, spontaneous abortion, termination of pregnancy, curettage, first trimester, second trimester, mifepristone, misoprostol, laminaria, subsequent, and dilatation and evacuation; dilation and curettage; spontaneous preterm birth.

In addition, the reference lists of all identified articles were examined to identify studies not captured by electronic searches. The electronic search and the eligibility of the studies were independently assessed by the authors (G.S. and V.B.). Differences were resolved by discussion.

Study selection

We included all studies of women with prior uterine evacuation for either I-TOP or SAB, compared with a control group without prior uterine evacuation, which reported data about the subsequent pregnancy. We excluded studies without a control group (eg, case series) as well as studies about stillbirth.

I-TOP was defined as an intervention to voluntarily terminate a pregnancy (ie, induced abortion) by either surgical or medical means so it does not result in a live birth. SAB was defined as spontaneous intrauterine pregnancy loss prior to 20 weeks. Surgical uterine evacuation (for either I-TOP or SAB) was defined as a procedure using surgical instruments, either D&E or vacuum aspiration (VA), to remove the fetus and placenta from the uterus.

D&E was defined as a procedure that includes mechanical cervical dilatation (usually by using uterine dilators of increasing diameter to stretch the cervix) followed by the removal of uterine contents using a combination of suction and instruments (eg, sharp curette, ring clamp, or forceps). VA was defined as evacuation of the uterine contents using an electric vacuum aspirator or manual vacuum aspirator. Medical uterine evacuation (for either I-TOP or SAB) was defined as a nonsurgical uterine evacuation in which pharmaceutical drugs are used to empty the uterus.

TABLE 1
Potential overall, sensitivity, and subgroup analyses planned

Intervention group	Control group
Overall analysis	
Prior uterine evacuation (I-TOP and SAB)	No prior uterine evacuation
Planned sensitivity analyses in women with prior uterine evacuation for I-TOP	
Prior I-TOP	No prior I-TOP
Prior surgical (either D&E or VA) I-TOP	No prior I-TOP
Prior surgical I-TOP by D&E	No prior I-TOP
Prior surgical I-TOP by VA	No prior I-TOP
Prior surgical I-TOP by D&E	Prior surgical I-TOP by VA[a]
Prior medical I-TOP	No prior I-TOP
Planned sensitivity analyses in women with prior uterine evacuation for SAB	
Prior SAB	No prior SAB
Prior surgical (either D&E or VA) SAB	No prior SAB
Prior surgical SAB by VA	No prior SAB
Prior surgical SAB by D&E	No prior SAB
Prior surgical SAB by D&E	Prior surgical SAB by VA[a]
Prior medical SAB	No prior SAB
Planned sensitivity analyses comparing I-TOP with SAB	
Prior uterine evacuation for I-TOP	Prior uterine evacuation for SAB[a]
Planned subgroup analyses in study on I-TOP and in study on SAB, separately	
Only 1 prior uterine evacuation	No prior uterine evacuation
More than 1 prior uterine evacuation	No prior uterine evacuation
More than 1 prior uterine evacuation	Only 1 prior uterine evacuation[a]
Prior uterine evacuation in singletons	No prior uterine evacuation in singletons
Prior uterine evacuation in multiple gestations	No prior uterine evacuation in multiple gestations
Prior uterine evacuation in cohort studies	No prior uterine evacuation in cohort studies
Prior uterine evacuation in case-control studies	No prior uterine evacuation in case-control studies
According to gestational age at uterine evacuation	—

D&E, dilation and evacuation; *I-TOP*, induced termination of pregnancy; *SAB*, spontaneous abortion; *VA*, vacuum aspiration.

[a] Because none of the included studies evaluated this outcome, we used an indirect comparison metaanalysis to assess this outcome.

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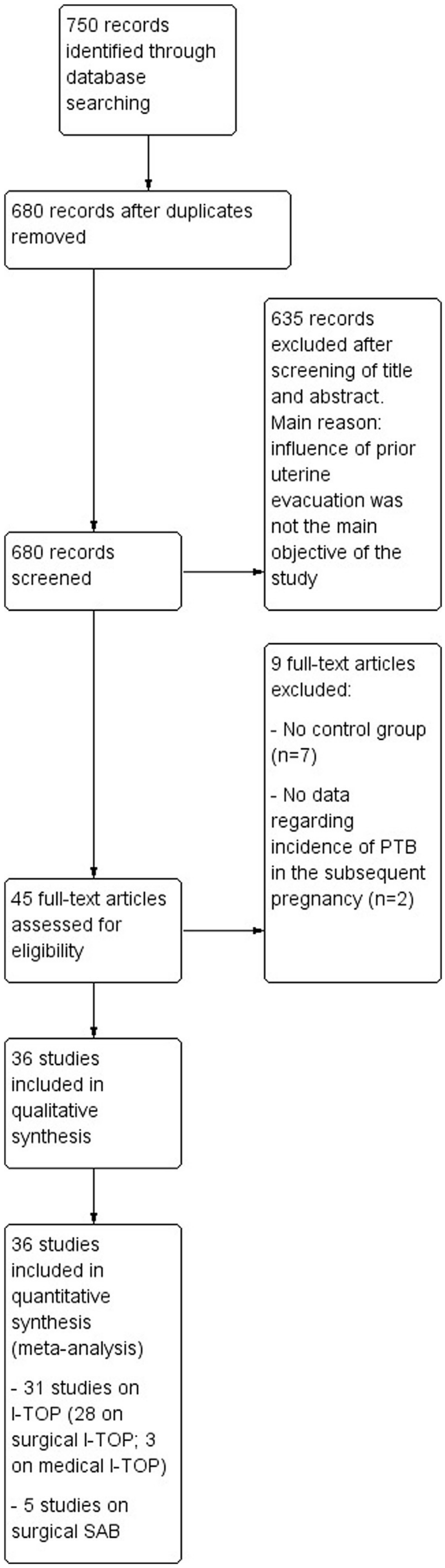
FIGURE 1

Flow diagram of studies identified in the systematic review



I-TOP, induced termination of pregnancy; *PTB*, preterm birth; *SAB*, spontaneous abortion.

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Therefore, we had the potential for several sensitivity analyses according to the type of abortion (Table 1).

Primary and secondary outcomes were planned a priori. The primary outcome was the incidence of PTB (ie, preterm delivery < 37 weeks). Secondary outcomes were neonatal outcomes including incidence of low birthweight (birthweight < 2500 g) and of small for gestational age (birthweight < 10th percentile for gestational age).

We planned to assess the primary and the secondary outcomes in the overall population as well as in studies on I-TOP and SAB, separately. We also planned several subgroup analyses according to the number of prior uterine evacuation; the number of fetuses in the index pregnancy; the gestational age at abortion; or the type of the study (either cohort or case-control study) (Table 1). We assessed these subgroup analyses for only the primary outcome (ie, incidence of PTB) in both surgical and medical I-TOP and SAB, separately and not in the overall combined data (Table 1).

Data extraction and risk of bias assessment

Data abstraction was completed by 2 independent investigators (G.S. and V.B.). Each investigator independently abstracted data from each study separately. Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Differences were resolved by consensus. Information of confounders adjusted and adjusted risk estimates were collected when available. When possible, all authors were contacted for missing data.

Reviewers (G.S. and V.B.) independently assessed the risk of bias of the included studies via the Methodological Index for Non-Randomized Studies.[12] Seven domains related to risk of bias were assessed in each study: (1) aim (ie, clearly stated aim), (2) rate (ie, inclusion of consecutive patients and response rate), (3) data (ie, prospective collection of data), (4) bias (ie, unbiased assessment of study endpoints), (5) time (ie, follow-up time appropriate), (6) loss (ie, loss to follow-up), and (7) size (ie, calculation of the study size).[4] Review authors' judgments were categorized as low risk, high risk, or unclear risk of bias. Discrepancies were resolved by discussion.

Data analysis

The data analysis was completed independently by two authors (G.S. and V.B.) using Review Manager 5.3 (Copenhagen, Denmark: The Nordic Cochrane Centre, Cochrane Collaboration, 2014).[13] Discrepancies were resolved by discussion.

Heterogeneity across studies was assessed using the Higgins I^2 test.[13] In case of statistically significant heterogeneity ($I^2 > 0\%$), the random-effects model of DerSimonian and Laird was used; otherwise, in case of no inconsistency in risk estimates (ie, $I^2 = 0\%$), a fixed-effect model was managed. The pooled results were reported as odds ratio (OR) with 95% confidence interval (CI).

For the outcomes not directly assessed by any of the included studies, an indirect comparison metaanalysis was performed (Table 1).[13] In the indirect comparison metaanalyses, data were combined in a 2-stage approach in which outcomes were analyzed in their original study and then summary statistics combined using standard summary data metaanalysis techniques to give an overall measure of effect (summary relative risk with 95% CI).[13]

For studies that reported both unadjusted and adjusted risk for confounders statistically proven, we performed metaanalyses using a generic inverse variance method to obtain the adjusted risk estimate (aOR) of the primary outcome (ie, incidence of PTB).[13,14] We assessed the aOR only for the primary outcome (ie, incidence of PTB) in studies on both surgical and medical I-TOP and SAB, separately.[14]

Before data extraction, the review was registered with the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42015026482). Therefore, all the analyses and the outcomes were planned a priori before the data extraction.

The metaanalysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-Analyses statement.[15]

Results

Study selection and study characteristics

We included 36 studies in this metaanalysis (1,047,683 women).[16-51] The flow of study identification is shown in Figure 1. Risk of publication bias was assessed by visual inspection of funnel plot; the symmetric plot suggested no publication bias (Figure 2). Publication bias, assessed using Begg's and Egger's tests, showed no significant bias ($P = .87$ and $P = .71$, respectively).

Thirty-one studies reported data about prior uterine evacuation for I-TOP, whereas 5 studies reported data regarding prior uterine evacuation for SAB (Tables 2, 3, and 4).[34,40,42,43,51]

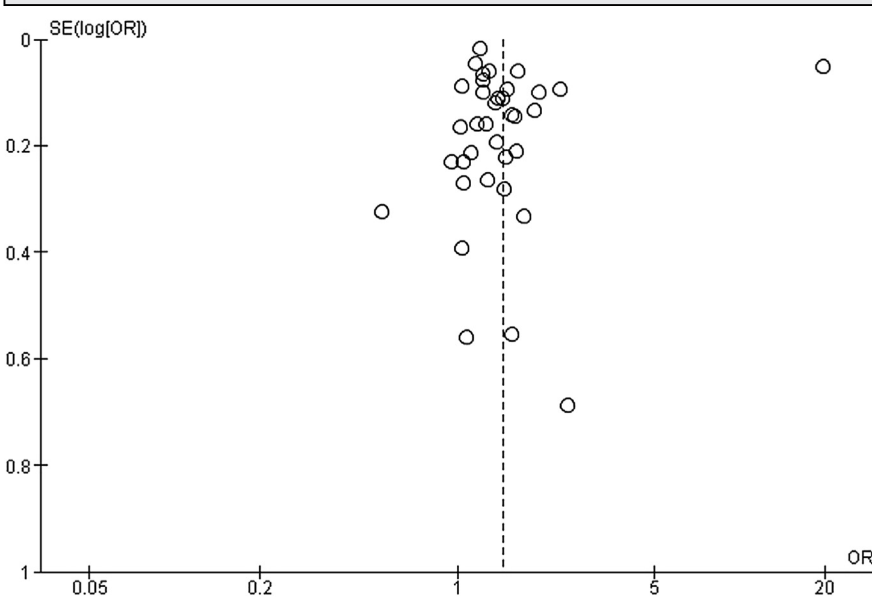
The quality of the studies included in our metaanalysis was assessed by the Methodological Index for Non-Randomized Studies' tool for assessing the risk of bias (Figure 3).[12] Nine of the included studies were retrospective cohorts,[17-19,21,25,26,33,37,44] whereas 9 were prospective cohorts;[22-24,27,29,46,48-50] 11 were case-control studies[16,20,28,31,34,36,38-41,43]; 7 were large, high-quality population-based studies.[30,32,35,42,45,47,51] The majority had a low risk of bias in the aim and the time.

Synthesis of results

Uterine evacuation for induced termination of pregnancy or spontaneous abortion: combined data. In the overall population, women with a history of uterine evacuation for either I-TOP or SAB had a significantly higher risk of PTB (5.7% vs 5.0%; OR, 1.44, 95% CI, 1.09−1.90; Figure 4A; 34 studies, 1,031,320 women), low birthweight (7.3% vs 5.9%; OR, 1.41, 95% CI, 1.22−1.62; Figure 4B; 11 studies, 675,197 women), and small for gestational age (10.2% vs 9.0%; OR, 1.19, 95% CI, 1.01−1.42; Figure 4C; 3 studies, 43,411 women) compared with controls (ie, women without a history of uterine evacuation).

Induced termination of pregnancy. Of the 31 studies reporting data regarding I-TOP, 28 included 913,297 women with a history of surgical I-TOP,[16-33,35-39,41,44-47] whereas 3 included 10,253 women with a prior medical I-TOP (Tables 2 and 3).[48-50] Women with a history of

FIGURE 2
Funnel plot for assessing publication bias



OR, odds ratio.

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TABLE 2
Characteristics of the included studies on surgically induced termination of pregnancy

Study	Study location	Type of study	Number of included women	Method of abortion	GA at abortion	Confounders adjusted	Primary outcome
Pantelakis et al, 1973[16]	Greece	Case-control	4779	Surgical	N/A	None	PTB
Papaevangelou et al, 1973[17]	Greece	Retrospective cohort	3467	Surgical	N/A	None	PTB
Daling and Emmanuel, 1975[18]	Taiwan	Retrospective cohort	1516	Surgical	N/A	None	PTB
Daling and Emmanuel, 1977[19]	United States	Retrospective cohort	553	D&E	N/A	None	PTB
Van der Slikke and Treffers, 1978[20]	The Netherlands	Case-control	3432	Surgical	N/A	None	GA at delivery
World Health Organization, 1979[21]	Europe	Retrospective cohort	3352	Surgical	N/A	None	GA at delivery
Obel, 1979[22]	Denmark	Prospective cohort	497	Surgical	N/A	None	Placental complications
Mandelin and Karjalainen, 1979[23]	Finland	Prospective cohort	696	Surgical	N/A	None	Birthweight
Meirik et al, 1982[24]	Sweden	Prospective cohort	1442	Vacuum	< 13 wks	Marital status, smoking	Birthweight
Linn et al, 1983[25]	United States	Retrospective cohort	9823	Surgical	N/A	Age, ethnicity, smoking, economic status, parity	Birthweight
Meirik et al, 1983[26]	Sweden	Retrospective cohort	1292	Vacuum	< 13 wks	Marital status, smoking	PTB
Meirik et al, 1984[27]	Sweden	Prospective cohort	269	Prostaglandins followed by D&E	< 13 wks	Parity	PTB
Park et al, 1984[28]	Korea	Case-control	681	Surgical	None	N/A	PTB
Frank et al, 1985[29]	United Kingdom	Prospective cohort	1545	Surgical	< 22 wks	Age, marital status, gestational age at entry	LBW
Pickering and Forbes, 1985[30]	United Kingdom	Population-based cohort study	7000	Surgical	N/A	Maternal age, height, sex of infant, marital status, social class	PTB
Lekea-Karanika et al, 1990[31]	Greece	Case-control	4391	Surgical	N/A	Race, smoking	PTB
Martius et al, 1998[32]	Germany	Population-based case-control study	106,124	Surgical	N/A	Gravidity, uterine surgery, type of work, urinary tract infection	PTB
Zhou et al, 1999[33]	Denmark	Retrospective cohort	64,125	Surgical	<14 wks	Maternal age	PTB
Henriet and Kaminski, 2001[35]	French	Population-based cohort study	12,336	Surgical	< 22 wks	Maternal age, parity, education, smoking	SGA

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(continued)

TABLE 2
Characteristics of the included studies on surgically induced termination of pregnancy *(continued)*

Study	Study location	Type of study	Number of included women	Method of abortion	GA at abortion	Confounders adjusted	Primary outcome
Fox-Helias and Blondel, 2000[36]	French	Case-control	17,411	D&E	N/A	None	PTB
Che et al, 2001[37]	China	Retrospective cohort	2707	Vacuum	N/A	Parental age, occupation, education, maternal BMI	PTB
El-Bastawissi et al, 2003[38]	United States	Case-control	654	Surgical	N/A	Maternal age, race, smoking, parity	PTB
Ancel et al, 2004[39]	Europe	Case-control	7721	Surgical	N/A	Maternal age, marital status, social class, smoking, parity	PTB
Moreau et al, 2005[41]	French	Case-control	2561	Surgical	N/A	None	PTB
Raatikainen et al, 2006[44]	Finland	Retrospective cohort	26,967	Vacuum	< 14 wks	Maternal age, weight, marital status, education, smoking, alcohol consumption, parity, uterine surgery	N/A
Bhattacharya et al, 2012[45]	Scotland	Population-based cohort study	577,510	Vacuum	N/A	Maternal age, weight, smoking	PTB
McCarthy et al, 2013[46]	Multicenter	Prospective cohort	4812	D&E	N/A	Maternal age, weight, smoking	PTB
Woolner et al, 2014[47]	Scotland	Population-based cohort study	45,631	D&E	N/A	Smoking, social class	PTB

D&E, dilatation and evacuation; *GA*, gestational age; *LBW*, low birth weight; *N/A*, data not reported in the original study; *PTB*, preterm birth; *SGA*, small for gestational age; *Surgical abortion*, both dilatation and evacuation and vacuum.

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uterine evacuation for I-TOP had a significantly higher risk of PTB (5.5% vs 4.4%; OR, 1.52, 95% CI, 1.09–2.13; Figure 5A, 29 studies, 907,187 women), low birthweight (7.3% vs 5.9%; OR, 1.41, 95% CI, 1.22–1.62; Figure 5B; 11 studies, 675,197 women), and small for gestational age (10.2% vs 9.0%; OR, 1.19, 95% CI, 1.01–1.42; Figure 5C; 3 studies, 43,411 women) compared with controls (ie, women without history of uterine evacuation for I-TOP).

Surgically induced termination of pregnancy

Table 2 shows the characteristics of the included studies on surgical I-TOP.[16-33,35-39,41,44-47] A total of 913,297 women from 28 studies with at least 1 prior surgical I-TOP were included. Seventeen studies reported information on confounders and adjusted risk estimates.[24-33,35,37-39,45-47] Ten studies included only singleton gestations.[17-21,23,32,35,44,46] The vast majority (27 of the 28) stratified data for number of prior I-TOP, whereas 1 did not report informative data about it.[36]

Most of the studies had incidence of PTB as the primary outcome. Regarding the method of abortion, 5 studies defined the procedure as only VA,[24,26,37,44,45] 5 studies defined the procedure as only D&E,[19,27,36,46,47] whereas the others used both methods. One study reported the use of prostaglandins followed by D&E.[27]

Women with a prior surgical I-TOP had a significantly higher risk of PTB (5.4% vs 4.4%; OR, 1.52, 95% CI, 1.08–2.16; Figures 6A; 27 studies, 906,297 women), low birthweight (7.3% vs 5.9%; OR, 1.41, 95% CI, 1.22–1.62; Figure 6B; 11 studies, 675,197 women), and small for gestational age (10.2% vs 9.0%; OR, 1.19, 95% CI, 1.01–1.42; Figure 6C; 3 studies, 43,411 women) compared with controls (ie, women without a history of uterine evacuation for I-TOP).

The risk of PTB was still significantly higher after adjusting for confounders statistically proven, including marital status, smoking, age, ethnicity, economic status, parity, maternal height, race, social class, gestational age at entry,

TABLE 3
Characteristics of the included studies on medically induced termination of pregnancy

Study	Study location	Type of study	Number of included women	Method of abortion	GA at abortion	Confounders adjusted	Primary outcome
Zhu et al, 2009[48]	China	Prospective cohort	9363	200 mg mifepristone	< 14 wks	None	Placental complications
Mirmilstein et al, 2009[49]	Australia	Prospective cohort	154	400 μg misoprostol	14-24 wks	None	PTB
Winer et al, 2009[50]	France	Prospective cohort	736	200 mg mifepristone followed by 400 μg misoprostol	< 22 wks	None	PTB

GA, gestational age; *PTB*, preterm birth.

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gravidity, parity, parental age, education, body mass index, uterine surgery, type of work, alcohol consumption, urinary tract infection, and sex of the infant (aOR, 1.25, 95% CI, 1.13−1.38; Figure 7; 16 studies, 874,080 women).

Subgroup analysis: method of abortion. Comparing the women with a prior surgical I-TOP with those who did not, both VA (3.6% vs 3.1%; OR, 1.20, 95% CI, 1.16−1.24; Figure 8; 5 studies, 609,912 women) and D&E (5.5% vs 4.3%; OR, 1.39, 95% CI, 1.08−1.80; Figure 9; 5 studies, 68,679 women) were associated with an increased risk of PTB. Moreover, by using an indirect comparison metaanalysis, we found that women who received D&E had a significantly higher risk of PTB compared with those who received VA (5.5% vs 3.6%; OR, 1.54, 95% CI, 1.38−1.73).

Subgroup analysis: number of prior I-TOP. Women with only 1 prior surgical I-TOP had a significantly higher risk of PTB compared with those who did not have any prior I-TOP (5.1% vs 4.4%; OR, 1.53, 95% CI, 1.02−2.31; Figure 10A; 23 studies, 875,356 women). Women with more than 1 prior surgical I-TOP had a significantly higher risk of PTB compared with those without any prior I-TOP (23.4% vs 8.6%; OR, 1.98, 95% CI, 1.46−2.68; Figure 10B; 9 studies, 165,085 women). Moreover, by using an indirect comparison metaanalysis, we found that women with more than 1 prior surgical I-TOP had a significantly higher risk of PTB compared with those who had only 1 prior surgical I-TOP (23.4% vs 5.1%; OR, 5.65, 95% CI, 5.10−6.25).

Subgroup analysis: number of fetuses. In a subgroup analysis of studies in which only singleton gestations in the index pregnancy were enrolled, women with a history of surgical I-TOP had a significantly higher risk of PTB compared with controls (9.6% vs 6.6%; OR, 1.45, 95% CI, 1.27−1.65; Figure 11; 10 studies, 152,668 women). No separate data about multiple gestations were reported in any studies.

TABLE 4
Characteristics of the included studies on spontaneous abortion

Study	Study location	Type of study	Number of included women	Method of abortion	GA at abortion	Confounders adjusted	Primary outcome
Doyle 2000[34]	Taiwan	Case-control	12,273	Surgical	N/A	None	PTB
Nguyen et al, 2004[40]	Vietnam	Case-control	1709	Surgical	N/A	None	PTB
Smith et al, 2006[42]	Scotland	Population-based case-control	84,391	Surgical	N/A	None	PTB
Selo-Ojeme and Tewari, 2006[43]	United Kingdom	Case-control	206	Surgical	N/A	None	PTB
Freak-Poli et al, 2009[51]	Australia	Population-based case-control study	25,554	Surgical	< 20 wks	None	N/A

D&E, dilatation and evacuation; *GA*, gestational age; *LBW*, low birth weight; *N/A*, data not reported in the original study; *PTB*, preterm birth; *SGA*, small for gestational age; *Surgical abortion*, either dilatation and evacuation or vacuum.

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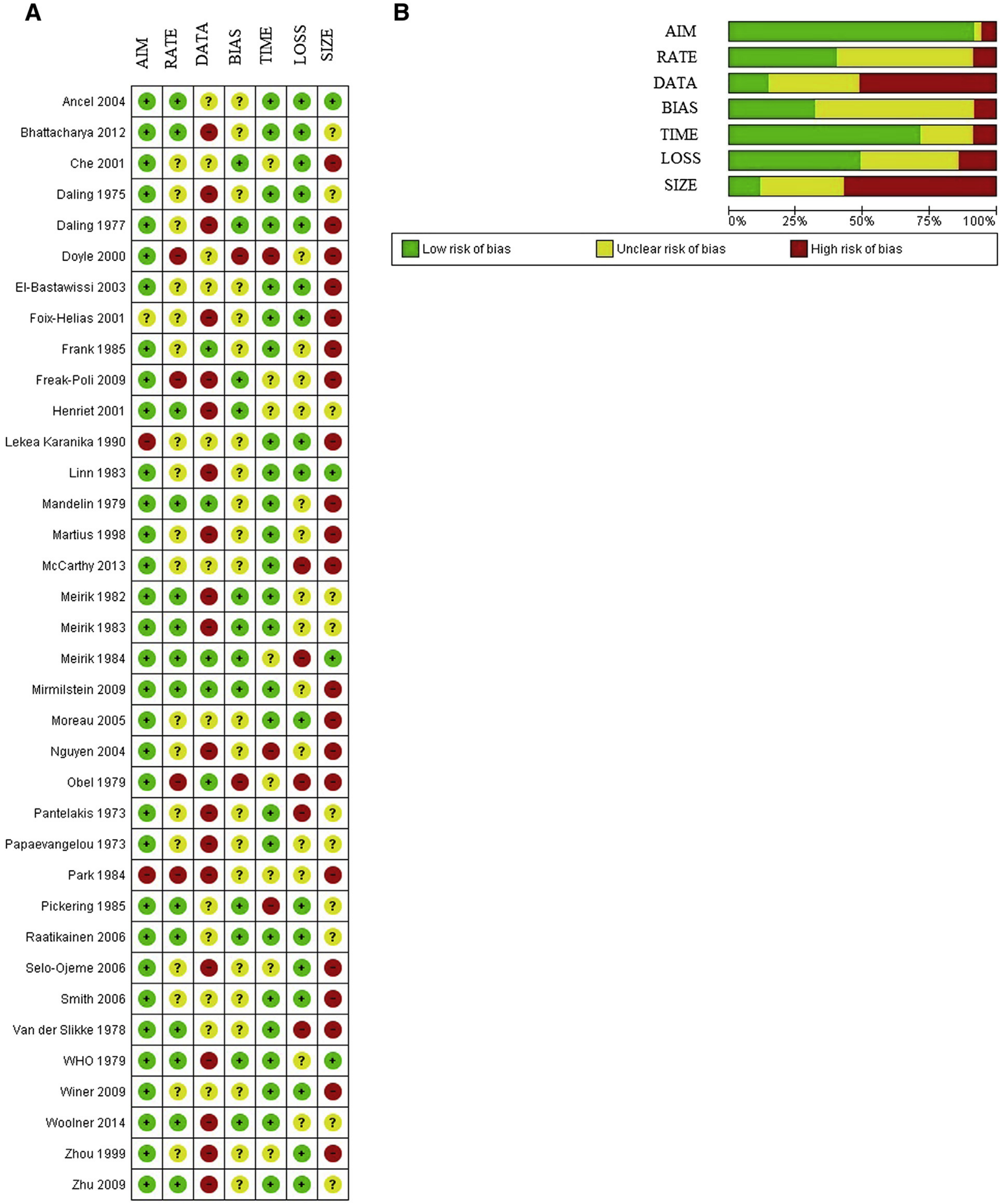
FIGURE 3
Assessment of risk of bias



A, Summary of the risk of bias for each study. *Plus sign* indicates a low risk of bias; *minus sign* indicates a high risk of bias; *question mark* indicates an unclear risk of bias. **B,** Risk of bias graph about each risk of the bias item presented as percentages across all included studies.

Aim, clearly stated aim; *Bias*, unbiased assessment of study endpoints; *Data*, prospective collection of data; *Loss*, loss to follow-up; *Rate*, inclusion of consecutive patients and response rate; *Size*, calculation of the study size; *Time*, follow-up time appropriate.

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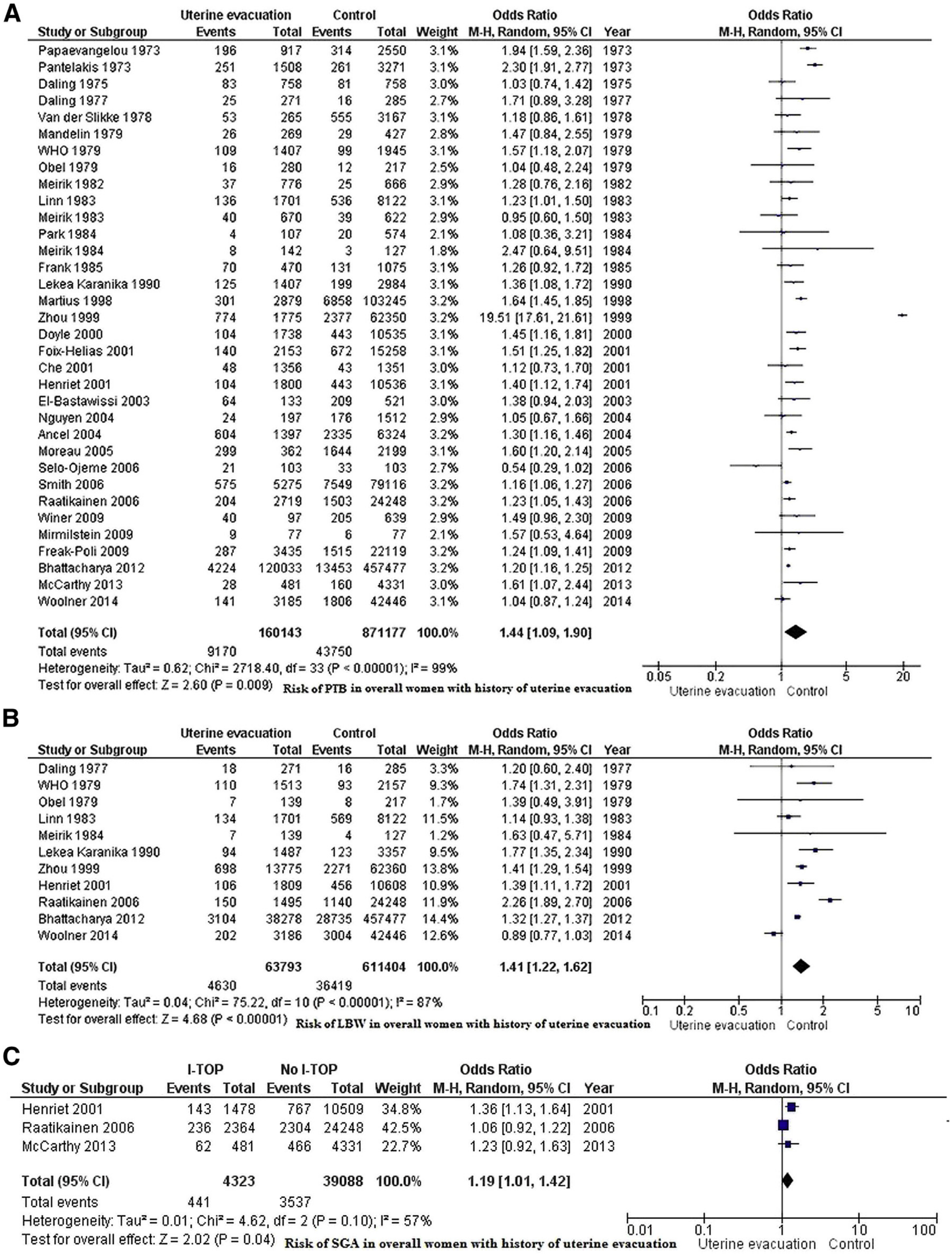
FIGURE 4

Primary and secondary outcomes in women with uterine evacuation for induced termination of pregnancy or spontaneous abortion



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Study or Subgroup	Uterine evacuation Events	Uterine evacuation Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Papaevangelou 1973	196	917	314	2550	3.1%	1.94 [1.59, 2.36]	1973
Pantelakis 1973	251	1508	261	3271	3.1%	2.30 [1.91, 2.77]	1973
Daling 1975	83	758	81	758	3.0%	1.03 [0.74, 1.42]	1975
Daling 1977	25	271	16	285	2.7%	1.71 [0.89, 3.28]	1977
Van der Slikke 1978	53	265	555	3167	3.1%	1.18 [0.86, 1.61]	1978
Mandelin 1979	26	269	29	427	2.8%	1.47 [0.84, 2.55]	1979
WHO 1979	109	1407	99	1945	3.1%	1.57 [1.18, 2.07]	1979
Obel 1979	16	280	12	217	2.5%	1.04 [0.48, 2.24]	1979
Meirik 1982	37	776	25	666	2.9%	1.28 [0.76, 2.16]	1982
Linn 1983	136	1701	536	8122	3.1%	1.23 [1.01, 1.50]	1983
Meirik 1983	40	670	39	622	2.9%	0.95 [0.60, 1.50]	1983
Park 1984	4	107	20	574	2.1%	1.08 [0.36, 3.21]	1984
Meirik 1984	8	142	3	127	1.8%	2.47 [0.64, 9.51]	1984
Frank 1985	70	470	131	1075	3.1%	1.26 [0.92, 1.72]	1985
Lekea Karanika 1990	125	1407	199	2984	3.1%	1.36 [1.08, 1.72]	1990
Martius 1998	301	2879	6858	103245	3.2%	1.64 [1.45, 1.85]	1998
Zhou 1999	774	1775	2377	62350	3.2%	19.51 [17.61, 21.61]	1999
Doyle 2000	104	1738	443	10535	3.1%	1.45 [1.16, 1.81]	2000
Foix-Helias 2001	140	2153	672	15258	3.1%	1.51 [1.25, 1.82]	2001
Che 2001	48	1356	43	1351	3.0%	1.12 [0.73, 1.70]	2001
Henriet 2001	104	1800	443	10536	3.1%	1.40 [1.12, 1.74]	2001
El-Bastawissi 2003	64	133	209	521	3.0%	1.38 [0.94, 2.03]	2003
Nguyen 2004	24	197	176	1512	2.9%	1.05 [0.67, 1.66]	2004
Ancel 2004	604	1397	2335	6324	3.2%	1.30 [1.16, 1.46]	2004
Moreau 2005	299	362	1644	2199	3.1%	1.60 [1.20, 2.14]	2005
Selo-Ojeme 2006	21	103	33	103	2.7%	0.54 [0.29, 1.02]	2006
Smith 2006	575	5275	7549	79116	3.2%	1.16 [1.06, 1.27]	2006
Raatikainen 2006	204	2719	1503	24248	3.2%	1.23 [1.05, 1.43]	2006
Winer 2009	40	97	205	639	2.9%	1.49 [0.96, 2.30]	2009
Mirmilstein 2009	9	77	6	77	2.1%	1.57 [0.53, 4.64]	2009
Freak-Poli 2009	287	3435	1515	22119	3.2%	1.24 [1.09, 1.41]	2009
Bhattacharya 2012	4224	120033	13453	457477	3.2%	1.20 [1.16, 1.25]	2012
McCarthy 2013	28	481	160	4331	3.0%	1.61 [1.07, 2.44]	2013
Woolner 2014	141	3185	1806	42446	3.1%	1.04 [0.87, 1.24]	2014
Total (95% CI)		**160143**		**871177**	**100.0%**	**1.44 [1.09, 1.90]**	
Total events	9170		43750				

Heterogeneity: Tau² = 0.62; Chi² = 2718.40, df = 33 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.60 (P = 0.009) **Risk of PTB in overall women with history of uterine evacuation**

B

Study or Subgroup	Uterine evacuation Events	Uterine evacuation Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Daling 1977	18	271	16	285	3.3%	1.20 [0.60, 2.40]	1977
WHO 1979	110	1513	93	2157	9.3%	1.74 [1.31, 2.31]	1979
Obel 1979	7	139	8	217	1.7%	1.39 [0.49, 3.91]	1979
Linn 1983	134	1701	569	8122	11.5%	1.14 [0.93, 1.38]	1983
Meirik 1984	7	139	4	127	1.2%	1.63 [0.47, 5.71]	1984
Lekea Karanika 1990	94	1487	123	3357	9.5%	1.77 [1.35, 2.34]	1990
Zhou 1999	698	13775	2271	62360	13.8%	1.41 [1.29, 1.54]	1999
Henriet 2001	106	1809	456	10608	10.9%	1.39 [1.11, 1.72]	2001
Raatikainen 2006	150	1495	1140	24248	11.9%	2.26 [1.89, 2.70]	2006
Bhattacharya 2012	3104	38278	28735	457477	14.4%	1.32 [1.27, 1.37]	2012
Woolner 2014	202	3186	3004	42446	12.6%	0.89 [0.77, 1.03]	2014
Total (95% CI)		**63793**		**611404**	**100.0%**	**1.41 [1.22, 1.62]**	
Total events	4630		36419				

Heterogeneity: Tau² = 0.04; Chi² = 75.22, df = 10 (P < 0.00001); I² = 87%
Test for overall effect: Z = 4.68 (P < 0.00001) **Risk of LBW in overall women with history of uterine evacuation**

C

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Henriet 2001	143	1478	767	10509	34.8%	1.36 [1.13, 1.64]	2001
Raatikainen 2006	236	2364	2304	24248	42.5%	1.06 [0.92, 1.22]	2006
McCarthy 2013	62	481	466	4331	22.7%	1.23 [0.92, 1.63]	2013
Total (95% CI)		**4323**		**39088**	**100.0%**	**1.19 [1.01, 1.42]**	
Total events	441		3537				

Heterogeneity: Tau² = 0.01; Chi² = 4.62, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 2.02 (P = 0.04) **Risk of SGA in overall women with history of uterine evacuation**

Forest plot for primary outcome (ie, risk of preterm birth) and for secondary outcomes (ie, low birthweight, small for gestational age) in overall women with a history of uterine evacuation for either induced termination of pregnancy or spontaneous abortion. **A,** Risk for PTB. **B,** Risk for LBW. **C,** Risk for SGA.

CI, confidence interval; *LBW*, low birthweight; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth; *SGA*, small for gestational age.

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FIGURE 5

Primary and secondary outcomes in induced termination of pregnancy

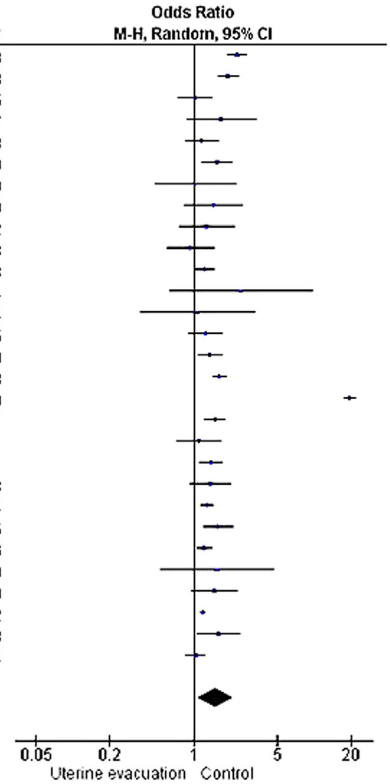
A

Study or Subgroup	Uterine evacuation Events	Uterine evacuation Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Pantelakis 1973	251	1508	261	3271	3.7%	2.30 [1.91, 2.77]	1973
Papaevangelou 1973	196	917	314	2550	3.6%	1.94 [1.59, 2.36]	1973
Daling 1975	83	758	81	758	3.6%	1.03 [0.74, 1.42]	1975
Daling 1977	25	271	16	285	3.2%	1.71 [0.89, 3.28]	1977
Van der Slikke 1978	53	265	555	3167	3.6%	1.18 [0.86, 1.61]	1978
WHO 1979	109	1407	99	1945	3.6%	1.57 [1.18, 2.07]	1979
Obel 1979	16	280	12	217	3.1%	1.04 [0.48, 2.24]	1979
Mandelin 1979	26	269	29	427	3.4%	1.47 [0.84, 2.55]	1979
Meirik 1982	37	776	25	666	3.4%	1.28 [0.76, 2.16]	1982
Meirik 1983	40	670	39	622	3.5%	0.95 [0.60, 1.50]	1983
Linn 1983	136	1701	536	8122	3.6%	1.23 [1.01, 1.50]	1983
Meirik 1984	8	142	3	127	2.3%	2.47 [0.64, 9.51]	1984
Park 1984	4	107	20	574	2.7%	1.08 [0.36, 3.21]	1984
Frank 1985	70	470	131	1075	3.6%	1.26 [0.92, 1.72]	1985
Lekea Karanika 1990	125	1407	199	2984	3.6%	1.36 [1.08, 1.72]	1990
Martius 1998	301	2879	6858	103245	3.7%	1.64 [1.45, 1.85]	1998
Zhou 1999	774	1775	2377	62350	3.7%	19.51 [17.61, 21.61]	1999
Foix-Helias 2001	140	2153	672	15258	3.7%	1.51 [1.25, 1.82]	2001
Che 2001	48	1356	43	1351	3.5%	1.12 [0.73, 1.70]	2001
Henriet 2001	104	1800	443	10536	3.6%	1.40 [1.12, 1.74]	2001
El-Bastawissi 2003	64	133	209	521	3.5%	1.38 [0.94, 2.03]	2003
Ancel 2004	604	1397	2335	6324	3.7%	1.30 [1.16, 1.46]	2004
Moreau 2005	299	362	1644	2199	3.6%	1.60 [1.20, 2.14]	2005
Raatikainen 2006	204	2719	1503	24248	3.7%	1.23 [1.05, 1.43]	2006
Mirmilstein 2009	9	77	6	77	2.7%	1.57 [0.53, 4.64]	2009
Winer 2009	40	97	205	639	3.5%	1.49 [0.96, 2.30]	2009
Bhattacharya 2012	4224	120033	13453	457477	3.7%	1.20 [1.16, 1.25]	2012
McCarthy 2013	28	481	160	4331	3.5%	1.61 [1.07, 2.44]	2013
Woolner 2014	141	3185	1806	42446	3.7%	1.04 [0.87, 1.24]	2014
Total (95% CI)		**149395**		**757792**	**100.0%**	**1.52 [1.09, 2.13]**	
Total events	8159		34034				

Heterogeneity: Tau² = 0.79; Chi² = 2665.25, df = 28 (P < 0.00001); I² = 99%

Test for overall effect: Z = 2.46 (P = 0.01)

Risk of PTB in women with history of I-TOP



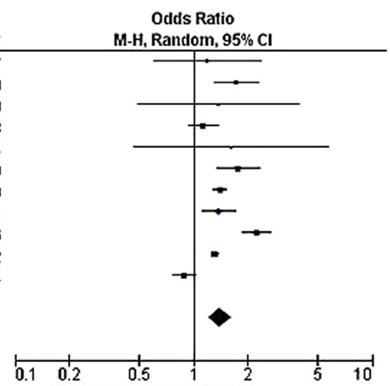
B

Study or Subgroup	Uterine evacuation Events	Uterine evacuation Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Daling 1977	18	271	16	285	3.3%	1.20 [0.60, 2.40]	1977
WHO 1979	110	1513	93	2157	9.3%	1.74 [1.31, 2.31]	1979
Obel 1979	7	139	8	217	1.7%	1.39 [0.49, 3.91]	1979
Linn 1983	134	1701	569	8122	11.5%	1.14 [0.93, 1.38]	1983
Meirik 1984	7	139	4	127	1.2%	1.63 [0.47, 5.71]	1984
Lekea Karanika 1990	94	1487	123	3357	9.5%	1.77 [1.35, 2.34]	1990
Zhou 1999	698	13775	2271	62360	13.8%	1.41 [1.29, 1.54]	1999
Henriet 2001	106	1809	456	10608	10.9%	1.39 [1.11, 1.72]	2001
Raatikainen 2006	150	1495	1140	24248	11.9%	2.26 [1.89, 2.70]	2006
Bhattacharya 2012	3104	38278	28735	457477	14.4%	1.32 [1.27, 1.37]	2012
Woolner 2014	202	3186	3004	42446	12.6%	0.89 [0.77, 1.03]	2014
Total (95% CI)		**63793**		**611404**	**100.0%**	**1.41 [1.22, 1.62]**	
Total events	4630		36419				

Heterogeneity: Tau² = 0.04; Chi² = 75.22, df = 10 (P < 0.00001); I² = 87%

Test for overall effect: Z = 4.68 (P < 0.00001)

Risk of LBW in women with history of I-TOP



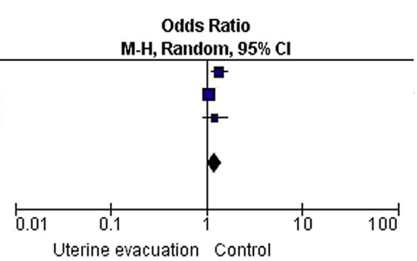
C

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Henriet 2001	143	1478	767	10509	34.8%	1.36 [1.13, 1.64]	2001
Raatikainen 2006	236	2364	2304	24248	42.5%	1.06 [0.92, 1.22]	2006
McCarthy 2013	62	481	466	4331	22.7%	1.23 [0.92, 1.63]	2013
Total (95% CI)		**4323**		**39088**	**100.0%**	**1.19 [1.01, 1.42]**	
Total events	441		3537				

Heterogeneity: Tau² = 0.01; Chi² = 4.62, df = 2 (P = 0.10); I² = 57%

Test for overall effect: Z = 2.02 (P = 0.04)

Risk of SGA in women with history of I-TOP



Forest plot for primary outcome (ie, risk of preterm birth) and for secondary outcomes (ie, low birthweight, small for gestational age) in women with a history of uterine evacuation for induced termination of pregnancy. **A,** Risk for PTB. **B,** Risk for LBW. **C,** Risk for SGA.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *LBW*, low birthweight; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth; *SGA*, small for gestational age.

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FIGURE 6

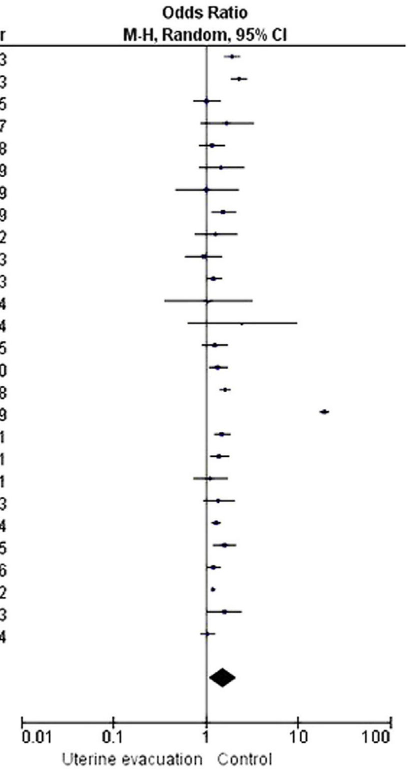
Primary and secondary outcomes in uterine evacuation for surgically induced termination of pregnancy

A

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Papaevangelou 1973	196	917	314	2550	3.9%	1.94 [1.59, 2.36]	1973
Pantelakis 1973	251	1508	261	3271	3.9%	2.30 [1.91, 2.77]	1973
Daling 1975	83	758	81	758	3.8%	1.03 [0.74, 1.42]	1975
Daling 1977	25	271	16	285	3.5%	1.71 [0.89, 3.28]	1977
Van der Slikke 1978	53	265	555	3167	3.8%	1.18 [0.86, 1.61]	1978
Mandelin 1979	26	269	29	427	3.6%	1.47 [0.84, 2.55]	1979
Obel 1979	16	280	12	217	3.3%	1.04 [0.48, 2.24]	1979
WHO 1979	109	1407	99	1945	3.8%	1.57 [1.18, 2.07]	1979
Meirik 1982	37	776	25	666	3.6%	1.28 [0.76, 2.16]	1982
Meirik 1983	40	670	39	622	3.7%	0.95 [0.60, 1.50]	1983
Linn 1983	136	1701	536	8122	3.9%	1.23 [1.01, 1.50]	1983
Park 1984	4	107	20	574	2.8%	1.08 [0.36, 3.21]	1984
Meirik 1984	8	142	3	127	2.5%	2.47 [0.64, 9.51]	1984
Frank 1985	70	470	131	1075	3.8%	1.26 [0.92, 1.72]	1985
Lekea Karanika 1990	125	1407	199	2984	3.9%	1.36 [1.08, 1.72]	1990
Martius 1998	301	2879	6858	103245	3.9%	1.64 [1.45, 1.85]	1998
Zhou 1999	774	1775	2377	62350	3.9%	19.51 [17.61, 21.61]	1999
Foix-Helias 2001	140	2153	672	15258	3.9%	1.51 [1.25, 1.82]	2001
Henriet 2001	104	1800	443	10536	3.9%	1.40 [1.12, 1.74]	2001
Che 2001	48	1356	43	1351	3.7%	1.12 [0.73, 1.70]	2001
El-Bastawissi 2003	64	133	209	521	3.8%	1.38 [0.94, 2.03]	2003
Ancel 2004	604	1397	2335	6324	3.9%	1.30 [1.16, 1.46]	2004
Moreau 2005	299	362	1644	2199	3.8%	1.60 [1.20, 2.14]	2005
Raatikainen 2006	204	2719	1503	24248	3.9%	1.23 [1.05, 1.43]	2006
Bhattacharya 2012	4224	120033	13453	457477	3.9%	1.20 [1.16, 1.25]	2012
McCarthy 2013	28	481	160	4331	3.7%	1.61 [1.07, 2.44]	2013
Woolner 2014	141	3185	1806	42446	3.9%	1.04 [0.87, 1.24]	2014
Total (95% CI)		**149221**		**757076**	**100.0%**	**1.52 [1.08, 2.16]**	
Total events	8110		33823				

Heterogeneity: Tau² = 0.80; Chi² = 2665.34, df = 26 (P < 0.00001); I² = 99%

Test for overall effect: Z = 2.37 (P = 0.02)



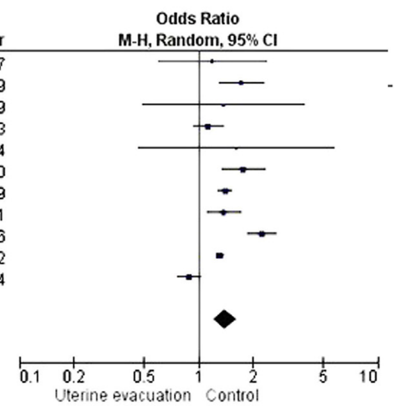
Risk of PTB in women with history of surgical I-TOP

B

Study or Subgroup	Uterine evacuation Events	Uterine evacuation Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Daling 1977	18	271	16	285	3.3%	1.20 [0.60, 2.40]	1977
WHO 1979	110	1513	93	2157	9.3%	1.74 [1.31, 2.31]	1979
Obel 1979	7	139	8	217	1.7%	1.39 [0.49, 3.91]	1979
Linn 1983	134	1701	569	8122	11.5%	1.14 [0.93, 1.38]	1983
Meirik 1984	7	139	4	127	1.2%	1.63 [0.47, 5.71]	1984
Lekea Karanika 1990	94	1487	123	3357	9.5%	1.77 [1.35, 2.34]	1990
Zhou 1999	698	13775	2271	62360	13.8%	1.41 [1.29, 1.54]	1999
Henriet 2001	106	1809	456	10608	10.9%	1.39 [1.11, 1.72]	2001
Raatikainen 2006	150	1495	1140	24248	11.9%	2.26 [1.89, 2.70]	2006
Bhattacharya 2012	3104	38278	28735	457477	14.4%	1.32 [1.27, 1.37]	2012
Woolner 2014	202	3186	3004	42446	12.6%	0.89 [0.77, 1.03]	2014
Total (95% CI)		**63793**		**611404**	**100.0%**	**1.41 [1.22, 1.62]**	
Total events	4630		36419				

Heterogeneity: Tau² = 0.04; Chi² = 75.22, df = 10 (P < 0.00001); I² = 87%

Test for overall effect: Z = 4.68 (P < 0.00001)



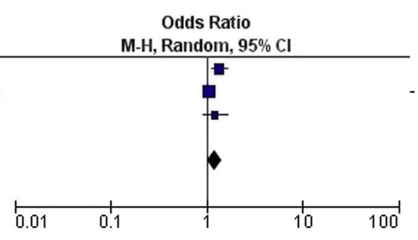
Risk of LBW in women with history of surgical I-TOP

C

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Henriet 2001	143	1478	767	10509	34.8%	1.36 [1.13, 1.64]	2001
Raatikainen 2006	236	2364	2304	24248	42.5%	1.06 [0.92, 1.22]	2006
McCarthy 2013	62	481	466	4331	22.7%	1.23 [0.92, 1.63]	2013
Total (95% CI)		**4323**		**39088**	**100.0%**	**1.19 [1.01, 1.42]**	
Total events	441		3537				

Heterogeneity: Tau² = 0.01; Chi² = 4.62, df = 2 (P = 0.10); I² = 57%

Test for overall effect: Z = 2.02 (P = 0.04)



Risk of SGA in women with history of surgical I-TOP

Forest plot for primary outcome (ie, risk of preterm birth) and for secondary outcomes (ie, low birthweight, small for gestational age) in women with a history of uterine evacuation for surgically induced termination of pregnancy. **A,** Risk for PTB. **B,** Risk for LBW. **C,** Risk for SGA.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *LBW*, low birthweight; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth; *SGA*, small for gestational age.

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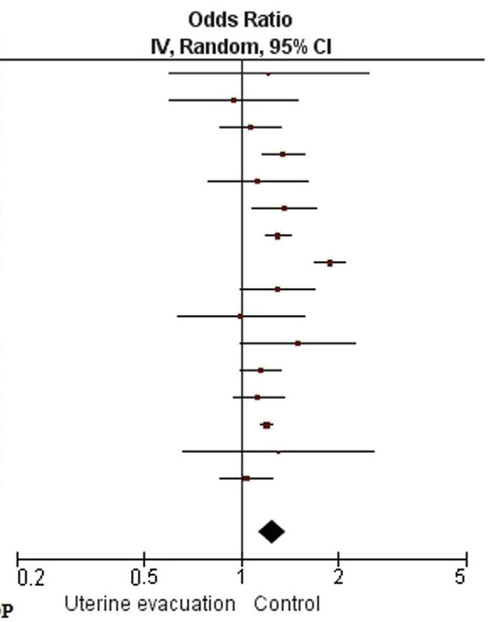
FIGURE 7

Adjusted estimates for primary outcome in surgically induced termination of pregnancy

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Year
Meirik 1982	0.198851	0.364233	1.6%	1.22 [0.60, 2.49]	1982
Meirik 1983	-0.05129	0.233748	3.2%	0.95 [0.60, 1.50]	1983
Linn 1983	0.067659	0.113136	6.9%	1.07 [0.86, 1.34]	1983
Pickering 1985	0.300105	0.077208	8.5%	1.35 [1.16, 1.57]	1985
Frank 1985	0.122218	0.183201	4.4%	1.13 [0.79, 1.62]	1985
Lekea Karanika 1990	0.307485	0.118715	6.7%	1.36 [1.08, 1.72]	1990
Martius 1998	0.262364	0.046159	9.8%	1.30 [1.19, 1.42]	1998
Zhou 1999	0.636577	0.055117	9.5%	1.89 [1.70, 2.11]	1999
Henriet 2001	0.262364	0.135364	6.0%	1.30 [1.00, 1.69]	2001
Che 2001	0	0.233748	3.2%	1.00 [0.63, 1.58]	2001
El-Bastawissi 2003	0.405465	0.212477	3.7%	1.50 [0.99, 2.27]	2003
Ancel 2004	0.139762	0.075314	8.6%	1.15 [0.99, 1.33]	2004
Raatikainen 2006	0.122218	0.092342	7.9%	1.13 [0.94, 1.35]	2006
Bhattacharya 2012	0.182321	0.022959	10.5%	1.20 [1.15, 1.26]	2012
McCarthy 2013	0.264898	0.349489	1.7%	1.30 [0.66, 2.59]	2013
Woolner 2014	0.039221	0.094387	7.8%	1.04 [0.86, 1.25]	2014
Total (95% CI)			**100.0%**	**1.25 [1.13, 1.38]**	

Heterogeneity: Tau² = 0.02; Chi² = 72.92, df = 15 (P < 0.00001)
Test for overall effect: Z = 4.43 (P < 0.00001)



Adjusted estimates forest plot for risk of PTB in women with history of I-TOP

Adjusted estimates forest plot for primary outcome (ie, risk of preterm birth) in women with a history of surgically induced termination of pregnancy.

CI, confidence interval; *IV*, independent variable.

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Subgroup analysis: type of study. Of 28 included studies (Table 2),[16-33,35-39,41,44-47] 9 were case-control,[16,20,28,31,32,36,38,39,41] whereas 19 were cohort studies.[17-19,21-27,29,30,33,35,37,44-47] Comparing I-TOP group with controls, women with a prior surgical I-TOP had a significant higher risk of PTB in the subgroup analysis of only case-control studies (15.7% vs 8.2%; OR, 1.52, 95% CI, 1.31−1.75; 9 studies, 145,193 women), whereas the risk was similar in the subgroup analysis of only cohort studies (4.7% vs 3.7%; OR, 1.55, 95% CI, 0.90−2.68; 18 studies, 761,104 women).

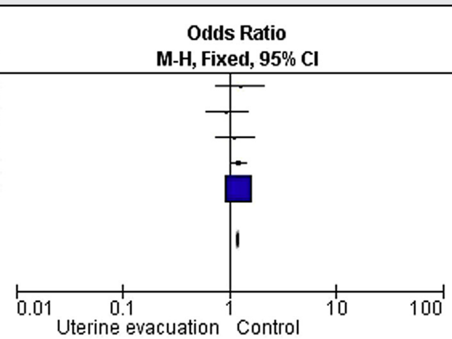
Subgroup analysis: gestational age at abortion. Only 7 studies reported data regarding gestational age at abortion.[24,26,27,29,33,35,44] In subgroup analysis of studies that included only women with a prior first-trimester (< 14 weeks) surgical I-TOP,[24,26,27,33,44] there was no statistically significant difference in the

FIGURE 8

Primary outcome in surgically induced termination of pregnancy with vacuum aspiration

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Meirik 1982	37	776	25	660	0.4%	1.27 [0.76, 2.14]	1982
Meirik 1983	40	670	39	622	0.6%	0.95 [0.60, 1.50]	1983
Che 2001	48	1356	43	1351	0.7%	1.12 [0.73, 1.70]	2001
Raatikainen 2006	204	2719	1503	24248	5.0%	1.23 [1.05, 1.43]	2006
Bhattacharya 2012	4224	120033	13453	457477	93.4%	1.20 [1.16, 1.25]	2012
Total (95% CI)		**125554**		**484358**	**100.0%**	**1.20 [1.16, 1.24]**	
Total events	4553		15063				

Heterogeneity: Tau² = 0.00; Chi² = 1.28, df = 4 (P = 0.87); I² = 0%
Test for overall effect: Z = 10.67 (P < 0.00001)



Risk of PTB in women with history of I-TOP with VA

Forest plot for primary outcome (ie, risk of preterm birth) in women with a history of surgically induced termination of pregnancy with vacuum aspiration.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth; *VA*, vacuum aspiration.

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FIGURE 9

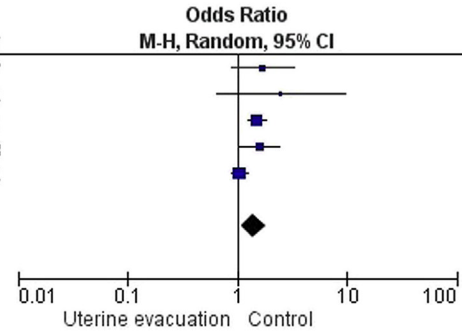
Primary in surgically induced termination of pregnancy with dilatation and evacuation

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Daling 1977	25	271	16	285	11.2%	1.71 [0.89, 3.28]	1977
Meirik 1984	8	142	3	127	3.3%	2.47 [0.64, 9.51]	1984
Foix-Helias 2001	140	2153	672	15258	32.6%	1.51 [1.25, 1.82]	2001
McCarthy 2013	28	481	160	4331	19.6%	1.61 [1.07, 2.44]	2013
Woolner 2014	141	3185	1806	42446	33.3%	1.04 [0.87, 1.24]	2014
Total (95% CI)		**6232**		**62447**	**100.0%**	**1.39 [1.08, 1.80]**	
Total events	342		2657				

Heterogeneity: Tau² = 0.04; Chi² = 11.10, df = 4 (P = 0.03); I² = 64%

Test for overall effect: Z = 2.52 (P = 0.01)

Risk of PTB in women with history of I-TOP with D&E



Forest plot for primary outcome (ie, risk of preterm birth) in women with a history of surgically induced termination of pregnancy with dilatation and evacuation.

CI, confidence interval; *D&C*, dilatation and evacuation; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth.

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risk of PTB comparing I-TOP group with controls (17.5% vs 4.5%; OR, 2.36, 95% CI, 0.39–14.11; Figure 12; 5 studies 94,096 women).

Medically induced termination of pregnancy

Only 3 studies, including 10,253 women, reported data about subsequent pregnancy in women with a prior medical I-TOP (Table 3).[48-50]

One study enrolled women with a prior first-trimester mifepristone I-TOP,[48] 1 study enrolled women with a prior midtrimester misoprostol I-TOP,[49] whereas the other study enrolled women with prior misoprostol and mifepristone I-TOP in either the first or midtrimester.[50] All 3 of the studies were a prospective cohort and enrolled only women with just 1 prior medical I-TOP.

One study reported only data about placental complications as outcomes,[48] and so only 2 studies with 890 women were included in the pooled results for the primary outcome.

Women with a prior medical I-TOP had a similar risk of PTB compared with those who did not have a prior medical I-TOP (28.2% vs 29.5%; OR, 1.50, 95% CI, 1.00–2.25; Figure 13; 2 studies, 890 women). No data were available regarding secondary outcomes. Because of the limited data, assessing subgroup and sensitivity analyses were not feasible. None of the included studies adjusted the incidence of PTB for confounders statistically proven, so assessed the aOR by using generic inverse variance method was not feasible.

Spontaneous termination of pregnancy. Five studies, including 124,133 women, reported data about subsequent pregnancy in women with a prior SAB.[42,43,51] In all of the included studies, the SAB was surgically managed. Two of them were large population-based studies,[42,51] whereas the others were case-control studies (Table 4). Women with prior surgical management of SAB had a higher risk of PTB compared with those who did not have a history of SAB (9.4% vs 8.6%; OR, 1.19, 95% CI, 1.03–1.37; Figure 14; 5 studies, 124,133 women). Because of the limited data, assessing subgroup and sensitivity analyses were not feasible. None of the included studies adjusted the incidence of PTB for confounders statistically proven, so assessing the aOR by using generic inverse variance method was not feasible.

Spontaneous abortion vs induced termination of pregnancy

By using an indirect comparison meta-analysis, we found that women who had a history of uterine evacuation for SAB had a significantly higher risk of PTB compared with those who had a history of uterine evacuation for I-TOP (9.4% vs 5.5%; OR, 1.80, 95% CI, 1.68–1.92).

Comment

Main findings

This metaanalysis evaluated the effect of prior uterine evacuation on future PTB risk. We found that prior surgical uterine evacuation, for either I-TOP or SAB, was an independent risk factor for PTB. A summary of our findings is reported in Table 5. Women with at least 1 prior surgical I-TOP had a significantly higher risk of PTB, low birthweight, and small for gestational age compared with those who did not have any prior surgical I-TOP. Women with more than 1 prior surgical I-TOP had a significantly higher risk of PTB compared with those who had only 1 prior surgical I-TOP.

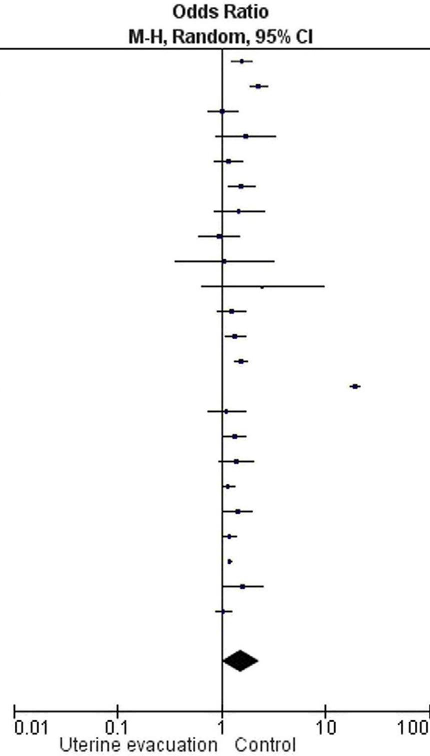
Subgroup analyses revealed a higher risk of PTB for both VA and D&E. The risk of PTB was significantly higher in the D&E group compared with the VA group. Data about medical I-TOP and about SAB were limited. However, we did not find an increased risk of PTB in women with a history of medical I-TOP. The clinical significance of a higher rate of PTB associated with uterine evacuation for SAB vs uterine evacuation for I-TOP is of unclear clinical significance and requires further study (Table 5).

FIGURE 10
Primary outcome of prior terminations of pregnancy in surgically induced termination of pregnancy

A

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Papaevangelou 1973	133	731	314	2550	4.5%	1.58 [1.27, 1.98]	1973
Pantelakis 1973	251	1508	261	3271	4.5%	2.30 [1.91, 2.77]	1973
Daling 1975	83	758	81	758	4.4%	1.03 [0.74, 1.42]	1975
Daling 1977	25	271	16	285	4.1%	1.71 [0.89, 3.28]	1977
Van der Slikke 1978	53	265	555	3167	4.5%	1.18 [0.86, 1.61]	1978
WHO 1979	109	1407	99	1945	4.5%	1.57 [1.18, 2.07]	1979
Mandelin 1979	26	269	29	427	4.2%	1.47 [0.84, 2.55]	1979
Meirik 1983	40	670	39	622	4.3%	0.95 [0.60, 1.50]	1983
Park 1984	4	107	20	574	3.5%	1.08 [0.36, 3.21]	1984
Meirik 1984	8	142	3	127	3.1%	2.47 [0.64, 9.51]	1984
Frank 1985	70	470	131	1075	4.5%	1.26 [0.92, 1.72]	1985
Lekea Karanika 1990	125	1407	199	2984	4.5%	1.36 [1.08, 1.72]	1990
Martius 1998	251	2532	6858	103245	4.6%	1.55 [1.35, 1.77]	1998
Zhou 1999	774	1775	2377	62350	4.6%	19.51 [17.61, 21.61]	1999
Che 2001	48	1356	43	1351	4.4%	1.12 [0.73, 1.70]	2001
Henriet 2001	83	1487	443	10536	4.5%	1.35 [1.06, 1.71]	2001
El-Bastawissi 2003	64	133	209	521	4.4%	1.38 [0.94, 2.03]	2003
Ancel 2004	389	964	2335	6324	4.6%	1.16 [1.01, 1.33]	2004
Moreau 2005	238	294	1644	2199	4.5%	1.43 [1.06, 1.95]	2005
Raatikainen 2006	173	2364	1503	24248	4.5%	1.19 [1.01, 1.41]	2006
Bhattacharya 2012	4224	120033	13453	457477	4.6%	1.20 [1.16, 1.25]	2012
McCarthy 2013	24	415	160	4331	4.3%	1.60 [1.03, 2.49]	2013
Woolner 2014	141	3185	1806	42446	4.5%	1.04 [0.87, 1.24]	2014
Total (95% CI)		**142543**		**732813**	**100.0%**	**1.53 [1.02, 2.31]**	
Total events	7336		32578				

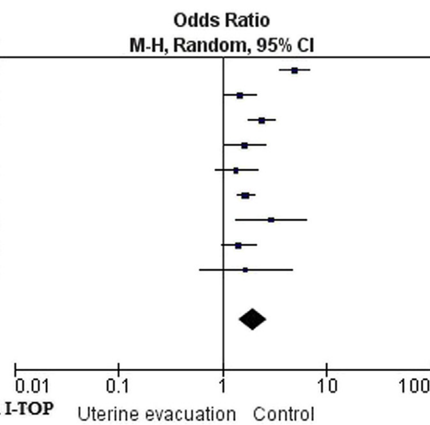
Heterogeneity: Tau² = 0.97; Chi² = 2664.60, df = 22 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.03 (P = 0.04) **Risk of PTB in women with only one prior surgical I-TOP**



B

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Papaevangelou 1973	63	186	314	3350	12.8%	4.95 [3.58, 6.86]	1973
Linn 1983	34	359	536	8122	12.3%	1.48 [1.03, 2.13]	1983
Martius 1998	50	347	6858	103245	13.1%	2.37 [1.75, 3.20]	1998
Henriet 2001	21	313	443	10536	11.3%	1.64 [1.04, 2.58]	2001
El-Bastawissi 2003	39	82	209	521	11.1%	1.35 [0.85, 2.16]	2003
Ancel 2004	215	433	2355	6324	14.1%	1.66 [1.37, 2.02]	2004
Moreau 2005	61	68	1644	2199	7.5%	2.94 [1.34, 6.47]	2005
Raatikainen 2006	31	355	1503	24248	12.2%	1.45 [1.00, 2.10]	2006
McCarthy 2013	4	66	160	4331	5.6%	1.68 [0.60, 4.68]	2013
Total (95% CI)		**2209**		**162876**	**100.0%**	**1.98 [1.46, 2.68]**	
Total events	518		14022				

Heterogeneity: Tau² = 0.16; Chi² = 44.70, df = 8 (P < 0.00001); I² = 82%
Test for overall effect: Z = 4.38 (P < 0.0001) **Risk of PTB in women with more than one prior surgical I-TOP**



Forest plot for primary outcome (ie, risk of preterm birth) according to number of prior termination of pregnancy in women with history of surgically induced termination of pregnancy. **A,** Women with only 1 prior surgical I-TOP. **B,** Women with more than 1 prior surgical I-TOP.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth.

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Comparison with existing literature

One other metaanalysis has evaluated the risk of PTB in women with prior surgical I-TOP.[10] Shah and Zao[10] showed that a previous surgical I-TOP was associated with an increased risk of PTB. However, it did not include all currently available studies, outcomes considered were different, subgroup and sensitivity analyses were not performed, the number of included women was lower, and medical I-TOP and SAB were not analyzed.[10]

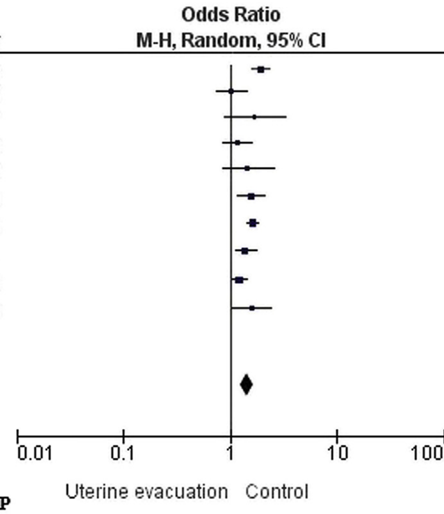
Strengths and limitations

Our study has several strengths. To our knowledge, no prior metaanalysis on this issue is as large, up to date, or comprehensive. The number of the included women is large. Most of the included studies had incidence of PTB as the

FIGURE 11
Primary outcome in singleton gestations with surgically induced termination of pregnancy

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Papaevangelou 1973	196	917	314	2550	13.4%	1.94 [1.59, 2.36]	1973
Daling 1975	83	758	81	758	8.8%	1.03 [0.74, 1.42]	1975
Daling 1977	25	271	16	285	3.3%	1.71 [0.89, 3.28]	1977
Van der Slikke 1978	53	265	555	3167	9.1%	1.18 [0.86, 1.61]	1978
Mandelin 1979	26	269	29	427	4.3%	1.47 [0.84, 2.55]	1979
WHO 1979	109	1407	99	1945	10.2%	1.57 [1.18, 2.07]	1979
Martius 1998	301	2879	6858	103245	16.5%	1.64 [1.45, 1.85]	1998
Henriet 2001	104	1800	443	10536	12.5%	1.40 [1.12, 1.74]	2001
Raatikainen 2006	204	2719	1503	24248	15.3%	1.23 [1.05, 1.43]	2006
McCarthy 2013	28	481	160	4331	6.6%	1.61 [1.07, 2.44]	2013
Total (95% CI)		**11766**		**151492**	**100.0%**	**1.45 [1.27, 1.65]**	
Total events	1129		10058				

Heterogeneity: Tau² = 0.02; Chi² = 23.40, df = 9 (P = 0.005); I² = 62%
Test for overall effect: Z = 5.57 (P < 0.00001)



Risk of PTB in singleton gestations with history of surgical I-TOP

Forest plot for primary outcome (ie, risk of preterm birth) in singleton gestations with a history of surgically induced termination of pregnancy.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth.

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primary outcome. We planned several subgroup and sensitivity analyses to reduce the heterogeneity between the studies and to have higher-quality data.

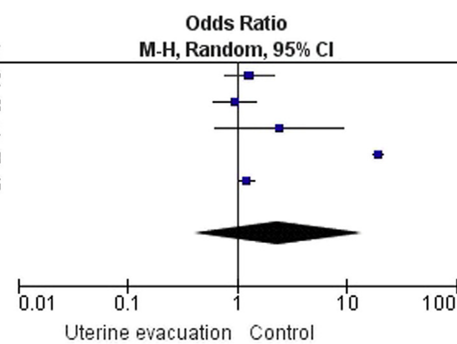
Limitations of our study are inherent to the limitations of the included studies. Most of the studies did not report a mechanism of surgical abortion and did not control appropriately for confounders. Only 6 studies included parity, an important determinant of preterm delivery, as a potential confounder.[25,27,32,35,38,44] Women who have induced abortions typically have a lower socioeconomic status, are more likely to smoke, and generally have other risk factors for PTB.[1-4]

In all of the included studies, cervical dilatation was performed mechanically using uterine dilators; none of them used balloon catheter or laminaria. No studies reported the size or type of dilators used for surgical I-TOP to analyze the effect of cervical trauma related to the size of dilators. Most of the included studies did not report gestational age of prior surgical TOP to analyze whether late surgical TOP has different effect than early surgical TOP. Some studies compared women with prior surgical TOP to nulliparous women whereas others to multiparous women.

FIGURE 12
Primary outcome in first-trimester surgically induced termination of pregnancy

Study or Subgroup	I-TOP Events	I-TOP Total	No I-TOP Events	No I-TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Meirik 1982	37	776	25	666	20.2%	1.28 [0.76, 2.16]	1982
Meirik 1983	40	670	39	622	20.3%	0.95 [0.60, 1.50]	1983
Meirik 1984	8	143	3	127	18.4%	2.45 [0.64, 9.44]	1984
Zhou 1999	774	1775	2377	62350	20.5%	19.51 [17.61, 21.61]	1999
Raatikainen 2006	204	2719	1503	24248	20.5%	1.23 [1.05, 1.43]	2006
Total (95% CI)		**6083**		**88013**	**100.0%**	**2.36 [0.39, 14.11]**	
Total events	1063		3947				

Heterogeneity: Tau² = 4.05; Chi² = 1145.63, df = 4 (P < 0.00001); I² = 100%
Test for overall effect: Z = 0.94 (P = 0.35)



Risk of PTB in women with history of first trimester surgical I-TOP

Forest plot for primary outcome (ie, risk of preterm birth) in women with a history of first-trimester (< 14 weeks) surgically induced termination of pregnancy.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth.

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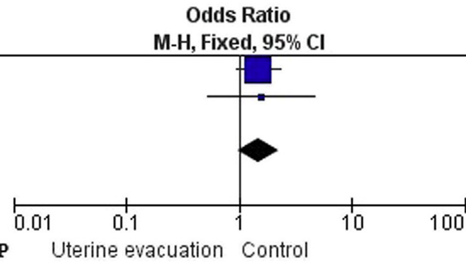
FIGURE 13
Primary outcome in medically induced termination of pregnancy

Study or Subgroup	I-TOP Events	I-TOP Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Winer 2009	40	97	205	639	85.7%	1.49 [0.96, 2.30]	2009
Mirmilstein 2009	9	77	6	77	14.3%	1.57 [0.53, 4.64]	2009
Total (95% CI)		**174**		**716**	**100.0%**	**1.50 [1.00, 2.25]**	
Total events	49		211				

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.95 (P = 0.05)



Risk of PTB in women with history of medical I-TOP

Forest plot for primary outcome (ie, risk of preterm birth) in women with a history of medically induced termination of pregnancy.

CI, confidence interval; *I-TOP*, induced termination of pregnancy; *M-H*, Mantel-Haenszel test; *PTB*, preterm birth.

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Half of more than 1 million women included in this metaanalysis were drawn from a single national register-based cohort study.[45] In this study, Bhattacharya et al[45] reported that data regarding smoking were frequently missing and that the interpregnancy interval was much shorter in the I-TOP group compared with the controls. Moreover, the specific methods of abortion were not well described.[45] Bhattacharya et al also found no increased risk of PTB after the first I-TOP.

There were no randomized controlled trials included in the metaanalysis and no studies comparing prior medical with prior surgical uterine evacuation. Data about medical I-TOP and about SAB were limited. Search strategies for retrieving studies in electronic databases are limited, and this could have influenced our findings. Study on surgical I-TOP did not report data regarding previous cervical preparation with cervical ripening, which could lead to less cervical injury; only 1 study reported the use of prostaglandins before D&E.[27]

None of the included studies reported data about the type of VA, whether electric vacuum aspirator or manual vacuum aspirator. Because women face a stigma when reporting on an induced abortion, women in the case or control group could have omitted I-TOP from their medical history, which would lead to underreporting of abortion in the control group and underreporting of the number of abortions in the case group. This recall bias has the potential to have a dramatic impact on the risk of PTB associated with uterine evacuation procedures, particularly if abortion were underreported in the control group.

Data regarding PTB referred to both spontaneous and indicated as the etiology of PTB. Most outcomes had a very high statistically heterogeneity, and this was a major shortcoming of the metaanalysis. Notably, the PTB rate in the control group ranged widely from approximately 4% to approximately 29%. Whereas most of the comparisons are statistically significant (Table 5), their clinical significance may be valued by some clinicians and patients as less compelling; for example, the difference in the incidence of PTB in women with a prior uterine evacuation is just 0.7% higher in absolute numbers (5.7%) than in women without prior uterine evacuation (5.0%).

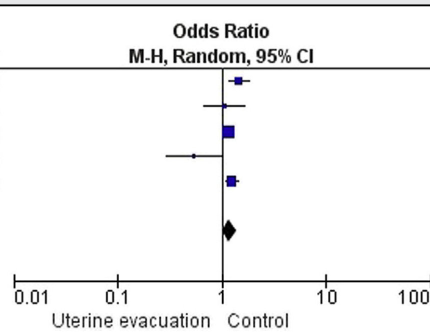
Implications

The are many methods of abortion.[52-61] The procedure used depends largely on the stage of pregnancy and the size of the

FIGURE 14
Primary outcome in spontaneous abortion

Study or Subgroup	Spontaneous TOP Events	Spontaneous TOP Total	No TOP Events	No TOP Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Doyle 2000	104	1738	443	10535	21.0%	1.45 [1.16, 1.81]	2000
Nguyen 2004	24	197	176	1512	8.1%	1.05 [0.67, 1.66]	2004
Smith 2006	575	5275	7549	79116	35.6%	1.16 [1.06, 1.27]	2006
Selo-Ojeme 2006	21	103	33	103	4.6%	0.54 [0.29, 1.02]	2006
Freak-Poli 2009	287	3435	1515	22119	30.7%	1.24 [1.09, 1.41]	2009
Total (95% CI)		**10748**		**113385**	**100.0%**	**1.19 [1.03, 1.37]**	
Total events	1011		9716				

Heterogeneity: Tau² = 0.01; Chi² = 9.95, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 2.35 (P = 0.02)



Risk of PTB in women with history of SAB

Forest plot for primary outcome (ie, risk of preterm birth) in women with a history of spontaneous abortion.

M-H, Mantel-Haenszel test; *CI*, confidence interval; *PTB*, preterm birth; *SAB*, spontaneous abortion.

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TABLE 5

Summary of the pooled results for the risk of preterm birth

Intervention group	Control group	Results, n, %[a]	OR, 95% CI
Overall analysis			—
Women with prior uterine evacuation (both I-TOP and SAB)	Women with no prior uterine evacuation	9170/160,143 (5.7%) vs 43,750/871,177 (5.0%)	OR, 1.44, 95% CI, 1.09–1.90[b]
Planned sensitivity analyses in women with prior uterine evacuation for I-TOP			—
Women with prior I-TOP (either surgical or medical)	Women with no prior I-TOP	8159/149,395 (5.5%) vs 34,034/757,792 (4.4%)	OR, 1.52, 95% CI, 1.09–2.13[b]
Women with prior surgical (either D&E or VA) I-TOP	Women with no prior I-TOP	8110/149,221 (5.4%) vs 33,823/757,076 (4.4%)	OR, 1.52, 95% CI, 1.08–2.16[b]
Women with prior surgical I-TOP by VA	Women with no prior I-TOP	4553/125,554 (3.6%) vs 15,063/484,358 (3.1%)	OR, 1.20, 95% CI, 1.16–1.24[b]
Women with prior surgical I-TOP by D&E	Women with no prior I-TOP	342/6232 (5.5%) vs 2657/ 62,447 (4.3%)	OR, 1.39, 95% CI, 1.08–1.80[b]
Women with prior surgical I-TOP by D&E	Women with prior surgical I-TOP by VA	342/6232 (5.5%) vs 4553/ 125,554 (3.6%)	OR, 1.54, 95% CI, 1.38–1.73[b]
Women with prior medical I-TOP	Women with no prior I-TOP	49/174 (28.2%) vs 211/716 (29.5%)	OR, 1.50, 95% CI, 1.–2.25
Planned subgroup analyses in women with prior uterine evacuation for I-TOP			
Women with only one prior surgical (either D&E or VA) I-TOP	Women with no prior I-TOP	7,336/142,543 (5.1%) vs 32,578/732,813 (4.4%)	OR, 1.53, 95% CI, 1.02–2.31[b]
Women with more than one prior surgical (either D&E or VA) I-TOP	Women with no prior I-TOP	518/2,209 (23.4%) vs 14,022/162,876 (5.1%)	OR, 1.98, 95% CI, 1.46–2.68[b]
Women with more than one prior surgical (either D&E or VA) I-TOP	Women with only one prior surgical (either D&E or VA) I-TOP	518/2209 (23.4%) vs 7336/ 142,543 (5.1%)	OR, 5.65, 95% CI, 5.10 to 6.25
Women with prior surgical (either D&E or VA) I-TOP with singleton gestation in the index pregnancy	Women with no prior surgical (either D&E or VA) I-TOP with singleton gestation in the index pregnancy	1129/11,766 (9.6%) vs 10,058/151,492 (6.6%)	OR, 1.45, 95% CI, 1.27 to 1.65[b]
Women with prior surgical (either D&E or VA) I-TOP with multiple gestation in the index pregnancy	Women with no prior surgical (either D&E or VA) I-TOP with multiple gestation in the index pregnancy	—	Not feasible
Women with prior surgical (either D&E or VA) I-TOP in only cohort studies	Women with no prior surgical (either D&E or VA) I-TOP in only cohort studies	6568/139,372 (4.7%) vs 22,714/621,732 (3.7%)	OR, 1.55, 95% CI, 0.90–2.68
Women with prior surgical (either D&E or VA) I-TOP in only case-control studies	Women with no prior surgical (either D&E or VA) I-TOP in only case-control studies	1542/9849 (15.7%) vs 11,109/135,344 (8.2%)	OR, 1.52, 95% CI, 1.31–1.75[b]
Women with prior surgical (either D&E or VA) I-TOP in the first trimester ($<$ 14 wks)	Women with no prior surgical (either D&E or VA) I-TOP in the first trimester ($<$ 14 wks)	1063/6083 (17.5%) vs 3947/ 88,013 (4.5%)	OR, 2.36, 95% CI, 0.39–14.11
Planned sensitivity analyses in women with prior uterine evacuation for SAB			—
Women with prior surgical (either D&E or VA) SAB	Women with no prior SAB	1,011/10,748 (9.4%) vs 9,716/113,385 (8.6%)	OR, 1.19, 95% CI, 1.03–1.37[b]
Women with prior surgical SAB by VA	Women with no prior SAB	—	Not feasible
Women with prior surgical SAB by D&E	Women with no prior SAB	—	Not feasible
Women with prior surgical SAB by D&E	Women with prior surgical SAB by VA	—	Not feasible
Women with prior medical SAB	Women with no prior SAB	—	Not feasible

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TABLE 5
Summary of the pooled results for the risk of preterm birth *(continued)*

Intervention group	Control group	Results, n, %[a]	OR, 95% CI
Planned subgroup analyses in women with prior uterine evacuation for SAB			
Women with only 1 prior SAB	Women with no prior SAB	—	Not feasible
Women with more than 1 prior SAB	Women with no prior SAB	—	Not feasible
Women with more than 1 prior SAB	Women with only 1 prior SAB	—	Not feasible
Women with prior SAB with singleton gestation in the index pregnancy	Women with no prior SAB with singleton gestation in the index pregnancy	—	Not feasible
Women with prior SAB with multiple gestation in the index pregnancy	Women with no prior SAB with multiple gestation in the index pregnancy	—	Not feasible
Women with prior SAB in only case-control studies	Women with no prior SAB in only case-control studies	—	Not feasible
Women with prior SAB in only cohort studies	Women with no prior SAB in only cohort studies	—	Not feasible
Subgroup analysis according to gestational age at prior uterine evacuation for SAB		—	Not feasible
Planned analysis in women with prior uterine evacuation for SAB vs women with prior uterine evacuation for I-TOP			
Women with prior SAB	Women with prior I-TOP	1011/10,748 (9.4%) vs 8159/149,395 (5.5%)	OR, 1.80, 95% CI, 1.68–1.92[b]

CI, confidence interval; *D&E*, dilation and evacuation; *I-TOP*, induced termination of pregnancy; *OR*, odds ratio; *SAB*, spontaneous abortion; *VA*, vacuum aspiration.

[a] Data are presented as number in the intervention group vs number in the control group (with percentages); [b] Statistically significant.

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fetus.[52] Dilatation of the cervix is required during surgical methods of abortion.[52] In contrast to normal birth, during which the dilation occurs slowly over a period of many hours, during a surgical abortion, the cervix is usually mechanically stretched.[53] This stretching of the cervix may result in permanent physical injury to the cervix.[53] Osmotic dilators are often used to reduce the need for mechanical dilation. Osmotic dilators are inserted into the cervix prior to the procedure, and they absorb water and swell, gradually stretching the cervix open.[54]

VA or suction dilation and curettage may be used to evacuate the uterus up to 16 weeks' gestation. This is the most common way to evacuate the uterus in the developed world.[55,56] In gestations above 8-12 weeks, misoprostol is often used in combination with mechanical dilation to prepare the cervix prior to evacuation.[57] General and/or local anesthesia is given to the pregnant woman and her cervix is quickly dilated.

Surgical evacuation with the added insertion of a spoon-shaped scraper (curette) is not the preferred method to evacuate the uterus because it is associated with more complications.[52] Compared with labor-induction abortion, surgical uterine evacuation offers a more predictable timing of evacuation and greater cost savings.[52] Moreover, this surgical procedure also allows women to avoid the labor-like process of a medical induction. Medical abortion is effective throughout the first and the second trimester; however, in randomized trials it has been shown to have greater complications when compared with surgical uterine evacuation.[58] It is the termination of pregnancy by stimulation of labor-like contractions that cause eventual expulsion of the fetus and placenta from the uterine cavity.[59] The combination of mifepristone and misoprostol is the most effective and fastest regimen.[60] Typically, mifepristone 200 mg is followed by the use of misoprostol 24-48 hours later.[61]

The biological plausibility to explain the higher risk of PTB in women with a history of uterine evacuation is not completely clear. However, 3 main hypotheses can be made. Previous studies have suggested that infectious diseases following surgical uterine evacuation account for the increased risk of PTB.[62,63] The increased risk of PTB could result from the overt or covert infection following surgically uterine evacuation[62] as well as from mechanical trauma to the cervix, leading to increased risk of cervical insufficiency.[5,6,8]

The greater mechanical dilation of the cervix obtained during the D&E compared to VA[58-59] could explain the higher risk of PTB in women with a prior D&E compared with those with a history of VA. Moreover, surgical procedures including curettage during D&E may result in scar tissue that may increase the probability of faulty placental implantation. Indeed, same studies reported an association between prior D&E and subsequent complications such as preeclampsia, pregnancy loss, placenta previa, and placenta accreta.[41,45-47,64,65]

Data about medical I-TOP are very limited.[48-50] However, studies comparing medical I-TOP with surgical I-TOP in the first trimester showed that medical I-TOP was probably safer than a surgical one with respect to the influence on subsequent pregnancy[66,67] and is not associated with placental complications.[48] So, provided there is no contraindication, medical I-TOP may be the preferred choice for evacuating the uterus in the first trimester, especially for those women without a child and for those who want to avoid surgery and anesthesia.[66,68,69] Furthermore, medical abortion is associated with higher acceptability.[68,69]

Conclusions

In summary, this metaanalysis found that prior surgical evacuation of the uterus may be an independent risk factor for PTB. These data warrant caution in the use of standard surgical evacuation for either I-TOP or SAB and should encourage better surgical methods, perhaps with cervical ripening before evacuation as well as medical and minimally invasive methods for mechanical cervical dilation such as osmotic dilators). However, patient preference for the type of abortion experience should drive the decision making.

Women should be given the choice between a surgical and medical procedure and should also be informed of the realistic and accurate risk of the procedures and the risk in the subsequent pregnancy. Because of the limitations of the studies included in our metaanalysis, it is difficult to definitively recommend that surgical abortion should be avoided and that medical methods should be preferentially offered.

To be able to make a definitive statement regarding risk of PTB associated with medical and surgical abortion, more research is needed. In particular, there is a need for randomized controlled trials that investigate whether technical interventions (eg, cervical preparation before uterine evacuation) diminish the risk of PTB associated with surgical uterine evacuation and for randomized trials comparing surgical and medical evacuation of the uterus. ■

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