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Efficacy of Misoprostol Alone for First-Trimester Medical Abortion: A Systematic Review

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Abstract

Objective: To summarize available data on the effectiveness and safety of single-agent misoprostol for medical abortion in the first trimester.

Data Sources: We searched Medline, CABI, Cochrane, EMBASE, LILACS, and the Web of Science, and ClinicalTrials.gov for English language studies that evaluated misoprostol alone for abortion of viable pregnancy in the first trimester.

Methods of Study Selection: Our search yielded 1562 citations, of which 38 included data from 53 trial groups that met our inclusion and exclusion criteria.

Tabulation, Integration, and Results: We abstracted data about each trial group, including study characteristics, treatment regimen, clinical protocol, number of women treated and followed, and numbers with outcomes of interest. We used meta-analytic methods and logistic regression to examine factors associated with surgical intervention after treatment. Among all 12,829 evaluable women, 2536 (meta-analytic estimate 22.0%, 95% CI 18.8%, 25.5%) had surgical uterine evacuation. Multiple factors were significantly associated with this proportion, including misoprostol amount per dose and route of administration, loss to follow-up rate, publication date, geographic region, number of misoprostol doses, duration of dosing, and time between dosing and evaluation. Of 6359 evaluable women, 384 (meta-analytic estimate 6.8%, 95% CI 5.3%, 8.5%) had ongoing pregnancy. At most 26 of 12,184 evaluable women (meta-analytic estimate 0.7%, 95% CI 0.4%, 1.0%) were transfused or hospitalized for abortion-related reasons. In trials that provided satisfaction data, most of women were satisfied or very satisfied with the treatment (meta-analytic estimate 78%, 95% CI 71%, 85%).

Conclusions: Misoprostol alone is effective and safe and is a reasonable option for women seeking abortion in the first trimester. Research is indicated to further refine the regimen and to establish efficacy in the late first trimester.

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PRECIS

Treatment regimens that contain only misoprostol can be effective and safe for first-trimester medical abortion.

INTRODUCTION

For early medical abortion, the primary regimens recommended by current clinical guidelines include two drugs: mifepristone and misoprostol. Because mifepristone potentiates the abortifacient action of misoprostol, the combination is highly effective, resulting in complete abortion in more than 95% of women through 63 days of gestation^{1,2} and 93% between 64 and 70 days.^{2,3} However, mifepristone is costly and is unavailable in many settings. In the United States, although the drug is approved for marketing, the Food and Drug Administration has imposed restrictions on its distribution that substantially limit both patients' and providers' access to it.⁴ For women who cannot obtain mifepristone, use of misoprostol alone, which is inexpensive and is widely used for various obstetric and gastrointestinal indications, can serve as an important alternative option. A systematic review published in 2007 found that the efficacy of misoprostol single-agent regimens at gestational ages ≤ 63 days ranged from 84% to 96%,⁵ but since then, additional studies have been published. We performed this systematic review to summarize available data on the effectiveness and safety of medical abortion with misoprostol alone in the first trimester of pregnancy. The primary outcome of our analysis was surgical evacuation of the uterus to complete the abortion; secondary outcomes were viable ongoing pregnancy after taking the prescribed misoprostol regimen, transfusions and hospitalizations.

SOURCES

We registered our systematic review protocol on PROSPERO (CRD42018083589) before beginning data collection and followed MOOSE guidelines⁶ in reporting the results. With the assistance of a librarian, we searched six databases (Medline, CABI, Cochrane, EMBASE, LILACS, and the Web of Science,) on November 17, 2017, and ClinicalTrials.gov on June 20 2018, for English language studies that evaluated misoprostol alone for medical abortion of a known or presumed viable pregnancy in the first trimester. We did not exclude studies based on study design, date, or any other criteria. Our search strategy for Medline is indicated in Box 1.

Search strategies for other databases were substantively similar. In addition, we reviewed the reference lists of relevant articles, and we contacted experts in the field for information about any published or unpublished trials not discovered in our search.

STUDY SELECTION

Two authors (MH and EGR) separately reviewed the title, abstract, and full text if necessary of each paper identified by the search to select all language reports of studies that included women with viable pregnancies who were treated in the first trimester (91 days or less) with

misoprostol alone to cause abortion. The same two authors then reviewed each selected study together and systematically abstracted relevant data about these women into a custom database. We excluded women who received abortifacient drugs other than misoprostol, women who were treated in the second trimester, women who had missed abortions or non-viable pregnancies before treatment, and women who did not take any misoprostol after study enrollment. Some studies evaluated more than one misoprostol regimen; in our abstraction process, we recorded data about women who received each regimen in each study as a separate trial group.

The primary data abstracted included the number of women treated with the misoprostol regimen in each group, details of the misoprostol regimen (specifically, the number of misoprostol doses provided, the amount of misoprostol in each dose and route of administration, and the intervals between doses), abortion outcomes (specifically, whether surgical evacuation of the uterus was performed and whether the patient had a viable ongoing pregnancy at the time of surgery), the numbers of reported hospitalizations and transfusions, and information about patient satisfaction. We also recorded data about specified factors that we postulated could cause heterogeneity or bias in assessment of efficacy and safety, including information about the trial design, conduct, and publication, the maximum gestational age and other inclusion criteria, location of misoprostol administration (facility or home), follow-up rates, and timing and method of outcome assessment. We contacted some authors to obtain additional data or to clarify details about the studies. We used our judgment to interpret certain details in some reports and to correct apparent errors and inconsistencies.

We combined data across groups to estimate the proportion of patients who had surgical evacuation of the uterus to complete the abortion and viable ongoing pregnancy using meta-analytic methods, conducted in R, version 3.5.0, with the “metafor” package, version 2.0.^{7,8} We applied the Freeman-Tukey double arcsine transformation, and we report p-values from the chi-square test of heterogeneity and associated I^2 statistic. We calculated estimates and 95% confidence intervals using the DerSimonian-Laird random-effects model.

To explore possible explanations for heterogeneity among trial groups in the proportions who had surgery, we examined associations between this outcome and selected characteristics of the trial groups. Many of these characteristics were highly correlated across trial groups, with numerous zero cells in cross-classifications. Therefore, we opted to present only unadjusted results. We used generalized estimating equations with a logistic link and an independence working correlation matrix to control for nesting of trial groups within paper. The response for the models was the ratio of the number of surgeries to the number of evaluable patients for each trial group (conducted in SAS, version 9.4, SAS Institute, Cary, NC, USA); thus model results were weighted by trial group sample size. We included all trial groups in our examination of misoprostol amount per dose and route of administration. We restricted our examination of other factors to groups treated with an initial dose of 800 mcg misoprostol administered vaginally, the most common combination, because most characteristics did not vary across groups treated with other dose-route combinations. We categorized each characteristic considering both clinical interest and the distribution of the data, and we estimated odds ratios and 95% confidence intervals. We

tested for linear trends using linear contrasts of model parameters. We made no adjustment for multiple comparisons. In reviewing the results, we focused on associations that were both substantial (odds ratio >1.5 or <0.67) and significant ($p < 0.05$).

To further evaluate the association between number of misoprostol doses and efficacy, we estimated the proportion of women reported to have had complete abortion after taking only the doses required for all women in that trial group before any doses that were contingent on abortion status. This analysis included only those trial groups that reported these data. We estimated unadjusted odds ratios with confidence intervals and tested for linear trend as described above for amount of misoprostol in the initial dose.

We assessed safety by computing the proportion of women across all trial groups who were reported to have been hospitalized or receive transfusions after treatment. We did not abstract data on non-serious side effects because ascertainment and reporting was not standardized across studies.

RESULTS

Our search yielded 1562 unique citations, of which 37 reported at least one group of women who were treated with misoprostol alone for abortion of viable pregnancy at ≤ 91 days of gestation^{9–45} and one additional group in which the maximum gestational age was 98 days⁴⁶ (Figure 1). We included the last of these because most of the women in the study were ≤ 91 days; the mean gestational age was 64 days. We also identified one additional study (ClinicalTrials.gov Identifier: NCT02299401) that has to date been published only as an abstract, but the authors declined to provide final data for this review because of concern about jeopardizing the planned primary publication.

The 38 papers included 42 studies conducted in at least 16 countries over at least the past 24 years (Appendix 1, available online at <http://links.lww.com/xxx>). Of these studies, 21 were non-comparative case series studies, 7 were randomized trials or cohort studies comparing different misoprostol-only regimens, and 14 were randomized trials or cohort studies comparing misoprostol-only regimens to other abortion treatments (aspiration, methotrexate, or misoprostol combined with mifepristone, methotrexate, tamoxifen, letrozole, or laminaria).

The 42 studies included 53 trial groups of women treated with misoprostol alone (Table 1). The total number of treated subjects in all groups combined was 13,573. The two largest groups, both retrospective case series in anonymous Latin American countries where abortion was legally restricted, constituted 44% of this total.^{9,10} Over all groups, 744 women (5%) were lost before abortion outcome was ascertained. The proportion lost was 0–7% in 51 groups; the proportions in the other two groups, which were the two largest, were 10% and 13%. Our analysis included 12,829 evaluable women across all trial groups.

The admission criteria for all studies were broad: in general, any woman requesting medical abortion who had no medical contraindication to the abortifacient drug treatment and whose gestational age was less than a specified maximum (42–98 days) was eligible. In 48 groups, which included 95% of evaluable women, gestational age was routinely determined by

ultrasound. One study included only women aged ≤ 17 years,⁴³ one included only women with ≥ 2 prior cesarean deliveries,²⁶ and one included only women with gestational ages of 64–84 days.¹⁸

The 53 groups used a multitude of misoprostol regimens. In all groups, women were required to take a specified minimum number (1 to 5) of doses of misoprostol vaginally, buccally, orally, sublingually, or by a combination of routes (Table 1). In all but 4 groups,^{13,14,21} the initial dose was 800 mcg or was administered vaginally; the combination 800 mcg vaginally was used in 31 groups that collectively included 10,010 (78%) of the evaluable women. Misoprostol was moistened before vaginal insertion in 41% of evaluable women who took the drug by that route. In 39 of the 48 groups in which more than one dose was allowed, subsequent doses used the same amount per dose and route of misoprostol as the first dose. Multiple doses were administered 3–48 hours apart, such that the longest duration of the required treatment was 96 hours. In 35 groups (38% of evaluable women), if complete abortion had not occurred after the required doses, women were instructed to take additional contingent doses up to a specified maximum, after which a decision regarding surgical intervention was made. The maximum total number of allowed doses (required + contingent) in any group was 6, and the maximum duration of dosing if all allowed doses were taken was 14 days. Across all groups, most women were instructed to take no more than 3 doses within a maximum of 48 hours. Nine studies,^{18–24,43,45} 7 of which were conducted by the same group of investigators, provided extra misoprostol to some or all women who were determined not to need surgery in order to evacuate “remains” from the uterus or for an unspecified reason, and one study provided a dose of misoprostol to all women who were scheduled for surgery.³⁰ We did not count those extra doses in this analysis because they were given after the outcome had been determined and thus did not contribute to the outcome. In at least 24 groups (83% of evaluable women), women were allowed to take some or all of the misoprostol doses at home.

In 46 groups (79% of evaluable women), all women were assessed with ultrasound before the decision of whether to perform surgery, whereas in 6 groups, ultrasound was used only if clinically indicated, and in one group, abortions were provided by community health workers who apparently rarely used ultrasound.⁴² The earliest point at which surgical intervention was considered varied from 24 hours to 14 days after the first misoprostol dose. No paper provided explicit criteria for the decision to resort to surgical uterine evacuation, hospitalization or transfusion.

Among all 12,829 evaluable subjects (Table 1), 2,536 (20%) underwent surgical uterine evacuation (meta-analytic estimate 22.0%, 95% CI 18.8%, 25.5%). Across trial groups, the proportion with this outcome ranged from 0 to 77% (Figure 2, Panel A). More than 90% of the evaluable subjects were in trial groups in which the failure proportion was 24% or less.

We found strong evidence of heterogeneity across trial groups in the proportion of subjects who ultimately had surgery ($p < 0.001$, $I^2 = 94.2\%$). In unadjusted analyses, this proportion was significantly associated with characteristics of the initial misoprostol dose (Table 2). Among groups treated vaginally, the odds of surgery decreased with the amount of misoprostol in the initial dose (linear trend $p < 0.001$); groups treated with 800 mcg had

about one quarter the risk of surgery as groups treated with 200 mcg. Among groups treated with 800 mcg in the initial dose, oral administration was associated with nearly a 3-fold higher risk of surgery than vaginal administration, whereas risks were similar in groups who took the drug sublingually, buccally, and vaginally.

In the 31 groups treated initially with 800 mcg vaginally, the proportion of women who had surgery was significantly associated with numerous group characteristics (Table 3). Some of these were details of the clinical protocol: the risk of surgery declined with increases in both the allowed number of misoprostol doses and the duration of dosing (linear trend $p = 0.01$ for both associations). Surgery was less common in groups in which the misoprostol was moistened before vaginal insertion and in groups in which the decision to perform surgery was delayed until 4–7 days after treatment. Surgery was also associated with other characteristics of the studies; for example, the two groups with loss rates $>10\%$ had higher surgery rates than groups with no loss, later studies had higher rates than earlier ones, and studies conducted in Asia and Latin America had higher rates than those conducted in North America. Many of the group characteristics were correlated with each other: for example, groups that were given more doses also had longer duration of dosing and were more likely to use moistened tablets if the route of administration was vaginal, and both of the two studies with $>10\%$ loss took place in Latin America and did not report using moistened tablets.

Data on abortion status after only the required misoprostol doses was available from 42 trial groups (Table 4). In these groups, each woman was evaluated to determine abortion completeness after she took all of the required doses but before any additional doses. Complete abortion was significantly more common after 3 doses than after only one, but no significant linear trend was apparent by number of doses from 1 to 5 ($p=0.73$).

In 36 groups, researchers noted the number of surgical interventions performed for ongoing pregnancy. Of the 6359 evaluable women in these groups (50% of the total), 384 (6%) had ongoing pregnancies (meta-analytic estimate 6.8%, 95% CI 5.3%, 8.5%, heterogeneity: $p < 0.001$, $I^2 = 81.7\%$). The proportion across groups ranged from 0 to 33%; more than 90% of the women were in groups in which no more than 11% of subjects had ongoing pregnancy (Figure 2, Panel B). The 384 ongoing pregnancies constituted 39% of the 989 medical abortion failures in these groups.

Across the 38 papers, 14 women were hospitalized for abortion-related reasons and 12 received transfusions. Excluding the studies in which women were or may have been hospitalized routinely throughout the abortion process,^{13,14,18,26,27,33,46} the sum of these numbers (26) constitutes at most 0.2% of the total 12,184 evaluable women (meta-analytic estimate 0.7%, 95% CI 0.4%, 1.0%). No deaths or ectopic pregnancies were reported.

Women in 20 groups provided information about satisfaction about the treatment regimen (Appendix 1, <http://links.lww.com/xxx>). In these groups, 2549 of 2961 women (86%; meta-analytic estimate 78%, 95% CI 71%, 85%) said that they were satisfied or very satisfied, and 2396 of 2832 (85%; meta-analytic estimate 76%, 95% CI 76%, 82%) said that they would use the method if needed in the future.

DISCUSSION

Data from 42 studies that included nearly 13,000 evaluable women indicate that misoprostol used alone can be effective and safe for inducing abortion in the first trimester. Across all studies, about 78% of women had complete abortions without recourse to surgery, and viable pregnancy was terminated in more than 93%. The reported incidence of serious complications requiring hospitalization or transfusion was at most 0.2%. Most women were satisfied with the treatment.

Our analysis identified some treatment characteristics that were associated with higher effectiveness. The chance of surgical uterine evacuation decreased significantly as the amount of misoprostol in the initial dose increased and was lower in trial groups that administered this dose vaginally, sublingually, or buccally rather than orally. Among groups in which the dose was 800 mcg vaginally, surgical intervention was substantially less common if women were permitted to take at least four doses, if these doses were taken over an interval of more than 48 hours, and if the tablets were moistened before insertion. Among all 53 groups, 20 were treated with at least three doses, the first of which consisted of at least 800 mcg misoprostol administered vaginally (moistened), sublingually, or buccally; of the 5338 evaluable women in these groups, 87% aborted without surgery.

The data reviewed here have many strengths: the studies were conducted in numerous diverse settings, the study populations were typical abortion clients unselected except with respect to gestational age, and follow-up rates were high. The variety of regimens and clinical protocols used in the 42 included studies enabled us to examine multiple factors that may contribute to the likelihood of surgical intervention following treatment with misoprostol alone. Our analysis of all of these studies provides insights not available from only the 7 individual studies published to date that directly compared different misoprostol-only regimens or protocols.

However, our analysis also had significant limitations. Two studies contributed 44% of the patients, and thus these studies dominated the analysis. We evaluated trial group characteristics, not data from individual women. Furthermore, we could examine only those characteristics that were reported consistently across studies, and because of the high degree of correlation between these characteristics across trial groups, we restricted our analysis primarily to groups treated with one particular misoprostol amount-route combination. We looked at each characteristic separately rather than simultaneously in an adjusted multivariable analysis, and as a result, the associations that we identified are certainly affected by confounding and should not be interpreted as proof of causality. For example, moistening of vaginally administered tablets was associated with higher numbers of allowed doses, and both were associated with lower surgery rates; our analysis did not establish the extent to which either factor may have been independently responsible for improved regimen effectiveness. Nevertheless, this finding is consistent with other data. In particular, wetting the tablets has been shown to improve vaginal absorption of misoprostol⁴⁷ and enhance cervical dilation before surgical abortion,⁴⁸ and two randomized trials have suggested that it decreases risk of surgical intervention in first trimester medical abortion.^{36,49} Our finding that surgery was less common in trial groups without loss to follow-up may be explained by

the fact that indications for surgery (abortion failure, bleeding) prompt patients to seek care. It suggests that the true risk among all treated patients may be lower than our estimate.

Despite these limitations, currently available data suggest that misoprostol as a single agent is a reasonable option for women seeking abortion in the first trimester. This treatment is clearly less effective than standard regimens that also contain mifepristone,^{1,2} and thus enhanced vigilance should be recommended to detect potential failures. Nevertheless, misoprostol alone may be preferred by some women because it may be easier to obtain, less costly, or have other advantages. Further research is indicated to refine the regimen, addressing issues such as the optimal misoprostol amount per dose and dosing intervals if the drug is administered sublingually or buccally, which may be more convenient for women than vaginal insertion, and the efficacy of these regimens in the late first trimester.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Box 1. Search strategy for Medline

(Early trimester OR less than ten weeks OR early pregnancy OR first trimester OR less than thirteen weeks) AND (Medical abortion OR medical termination OR oral medication abortion OR oral medication termination OR non-surgical abortion OR non-surgical termination OR elective abortion OR termination of pregnancy OR induced abortion OR induced termination of pregnancy) AND (misoprostol OR cytotec) AND (single agent OR single-agent OR alone OR only).

Figure 1.
Study selection flow diagram.

Figure 2. Group size by percent of women with surgical uterine evacuation (**A**) and ongoing pregnancy (**B**). Meta-analytic estimate of population proportion indicated by the *solid line* with 95% CI indicated by band. The trial groups to the left of the dashed lines contained 90% of patients.

Table 1.

Characteristics of studies

	Trial groups N=53		Evaluable women N=12829	
	n	%	n	%
Number of treated women per group				
3–100	27	51%	1247	10%
101–500	19	36%	3472	27%
501–720	5	9%	2766	22%
2805–3225	2	4%	5344	42%
Lost to follow-up				
None	39	74%	4484	35%
10%	12	23%	3001	23%
>10%	2	4%	5344	42%
Publication date				
1994–1999	14	26%	1609	13%
2000–2004	14	26%	5093	40%
2005–2009	18	34%	5237	41%
2010-present	7	13%	890	7%
Study design				
randomized trial	23	43%	3315	26%
non-randomized prospective	24	45%	3527	27%
non-randomized retrospective	6	11%	5987	47%
Region				
Latin or South America	11	21%	7664	60%
North America	11	21%	1023	8%
Asia	17	32%	980	8%
other or multiple	14	26%	3162	25%
Planned maximum gestational age				
42–56 days	19	36%	4173	33%
57–63 days	17	32%	4563	36%
64–70 days	7	13%	3247	25%
71 days	10	19%	846	7%
First misoprostol dose and route				
200 mcg vaginal	2	4%	111	1%
400 mcg vaginal	4	8%	160	1%
600 mcg vaginal	1	2%	89	1%
800 mcg vaginal	31	58%	10010	78%
800 mcg buccal	3	6%	584	5%
800 mcg sublingual	2	4%	1021	8%
800 mcg oral	4	8%	119	1%
1000 mcg vaginal	1	2%	300	2%
400 mcg vaginal + 400 mcg sublingual	1	2%	149	1%

	Trial groups N=53		Evaluable women N=12829	
	n	%	n	%
400 mcg vaginal + 400 mcg oral	1	2%	5	0%
800 mcg vaginal + 400 mcg buccal	1	2%	98	1%
800 mcg vaginal + 400 mcg sublingual	1	2%	76	1%
800 mcg oral + 400 mcg sublingual	1	2%	107	1%
Misoprostol moistened before vaginal administration*				
no or not stated	20	47%	6543	59%
Yes	23	53%	4455	41%
Number of required doses				
1	34	64%	3598	28%
2	7	13%	3374	26%
3	9	17%	5651	44%
4	2	4%	186	1%
5	1	2%	20	0%
Duration of required dosing				
0 (only 1 required dose)	34	64%	3598	28%
1–24h	16	30%	6251	49%
25–48h	1	2%	2900	23%
73h–7d	2	4%	80	1%
Total number of allowed doses				
1	5	9%	330	3%
2	11	21%	3069	24%
3	25	47%	8059	63%
4	5	9%	458	4%
5	1	2%	20	0%
6	6	11%	893	7%
Maximum duration of dosing if all allowed contingent doses were taken				
0 (only 1 dose allowed)	5	9%	330	3%
1–24h	19	36%	4995	39%
25–48h	13	25%	5682	44%
49–72h	4	8%	269	2%
73h–7d	9	17%	1155	9%
>7d	3	6%	398	3%
Protocol permitted patient to take misoprostol at home				
all	9	17%	5188	40%
some	15	28%	5483	43%
none	29	55%	2158	17%
Evaluated by ultrasound prior to decision to perform surgery				
all patients	46	87%	10199	79%
some or no patients	7	13%	2630	21%
Earliest timing of decision re. surgery				

	Trial groups N=53		Evaluable women N=12829	
	n	%	n	%
24h	2	4%	128	1%
25–48h	7	13%	438	3%
49–72h	12	23%	4685	37%
73h–7d	16	30%	1864	15%
>7d	16	30%	5714	45%

^aDenominator for percents include only trial groups and evaluable women who took the first dose by the vaginal route.

Table 2.Surgical uterine evacuation by misoprostol dose and route^a

	Evaluable women	Women who had surgical uterine evacuation		Adjusted OR ^b	
		N	%	OR	95% CI
First dose administered vaginally					
200 mcg	111	83	75%	1	
400 mcg	160	99	62%	0.55	(0.52, 0.57)
600 mcg	89	32	36%	0.19	(0.14, 0.26)
800 mcg	10010	1895	19%	0.08	(0.05, 0.12)
1000 mcg	300	21	7%	0.03	(0.02, 0.04)
First dose 800 mcg					
vaginal route	10010	1895	19%	1	
buccal route	584	104	18%	0.93	(0.49, 1.76)
sublingual route	1021	191	19%	0.99	(0.76, 1.27)
oral route	119	62	52%	4.66	(3.61, 6.01)
combinations of routes	154	20	13%	0.64	(0.46, 0.89)

^aTable includes 53 trial groups.^bConfidence intervals are adjusted for clustering by paper.

Table 3.

Surgical uterine evacuation by trial characteristics in groups treated with 800 mcg misoprostol vaginally

	Trial groups N=31	Evaluable women N=10010	Women who had surgical uterine evacuation N=1895		OR ^a		
			N	%	OR	95% CI	
Number of treated women per group							
3–100	15	823	193	23%	1		
101–500	11	2098	209	10%	0.36	0.21	0.61
501–720	3	1745	242	14%	0.53	0.30	0.93
2805, 3225	2	5344	1251	23%	1.00	0.62	1.60
Lost to follow-up in group							
0	22	2991	390	13%	1		
>0 to 10%	7	1675	254	15%	1.19	0.81	1.75
>10%	2	5344	1251	23%	2.04	1.56	2.66
Publication date							
1994–1999	8	1342	164	12%	1		
2000–2004	12	4704	859	18%	1.60	0.91	2.82
2005–present	11	3964	872	22%	2.03	1.39	2.96
Study design							
randomized	12	1602	311	19%	1		
prospective cohort or case series	15	2603	284	11%	0.51	0.35	0.74
retrospective cohort or case series	4	5805	1300	22%	1.20	0.82	1.74
Region							
North America	6	841	95	11%	1		
Asia	12	668	157	24%	1.97	1.25	3.11
Latin or South America	8	7102	1426	20%	2.41	1.16	5.03
other or multiple	5	1399	217	16%	1.44	0.95	2.20
Planned maximum gestational age							
42–56 days	14	3905	743	19%	1		
57–63 days	11	2742	380	14%	0.68	0.43	1.09
63 days	6	3363	772	23%	1.27	0.85	1.89
Misoprostol moistened before vaginal administration							
no or not stated	11	6093	1419	23%	1		
yes	20	3917	476	12%	0.46	0.35	0.60
Total number of allowed doses							
1	4	305	78	26%	1		
2	8	2862	656	23%	0.87	0.47	1.60
3	16	6221	1106	18%	0.63	0.30	1.31
4+	3	622	55	9%	0.28	0.14	0.57
Maximum duration of dosing if all allowed contingent doses were taken							
0 (only 1 dose allowed)	4	305	78	26%	1		

	Trial groups N=31	Evaluable women N=10010	Women who had surgical uterine evacuation N=1895		OR ^a		
			N	%	OR	95% CI	
1–24h	9	3759	817	22%	0.81	0.42	1.54
25–48h	9	5138	910	18%	0.63	0.29	1.37
>48 h	9	808	90	11%	0.36	0.16	0.82
Protocol permitted patient to take misoprostol at home							
all or some	13	8558	1663	19%	1		
none	18	1452	232	16%	0.79	0.49	1.26
Evaluated by ultrasound prior to decision to perform surgery							
all patients	29	8985	1729	19%	1		
some or no patients	2	1025	166	16%	0.81	0.62	1.06
Earliest timing of decision re. surgery							
72h	10	4403	893	20%	1		
73h-7d	8	1087	133	12%	0.55	0.31	0.96
>7d	13	4520	869	19%	0.94	0.59	1.49

^a Confidence intervals are adjusted for clustering by paper.

Table 4.

Complete abortion after required misoprostol doses, by number of doses required

Number of required misoprostol doses	Groups N=42	Evaluable women N=12072	Complete abortion without surgery N=9074		OR ^a		
	n	n	n	%	OR	95% CI	
1	25	3232	2221	69%			
2	6	3156	2343	74%	1.31	0.98	1.75
3	8	5478	4355	79%	1.77	1.30	2.40
4	2	186	141	76%	1.43	0.49	4.16
5	1	20	14	70%	1.06	0.89	1.27

^a Confidence intervals are adjusted for clustering by paper