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Methods for managing miscarriage

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[Intervention Review]

Methods for managing miscarriage: a network meta-analysis

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A B S T R A C T

Background

Miscarriage, defined as the spontaneous loss of a pregnancy before 24 weeks' gestation, is common with approximately 25% of women experiencing a miscarriage in their lifetime. An estimated 15% of pregnancies end in miscarriage. Miscarriage can lead to serious morbidity, including haemorrhage, infection, and even death, particularly in settings without adequate healthcare provision. Early miscarriages occur during the first 14 weeks of pregnancy, and can be managed expectantly, medically or surgically. However, there is uncertainty about the relative effectiveness and risks of each option.

Objectives

To estimate the relative effectiveness and safety profiles for the different management methods for early miscarriage, and to provide rankings of the available methods according to their effectiveness, safety, and side-effect profile using a network meta-analysis.

Search methods

We searched the Cochrane Pregnancy and Childbirth's Trials Register (9 February 2021), ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) (12 February 2021), and reference lists of retrieved studies.

Selection criteria

We included all randomised controlled trials assessing the effectiveness or safety of methods for miscarriage management. Early miscarriage was defined as less than or equal to 14 weeks of gestation, and included missed and incomplete miscarriage. Management of late miscarriages after 14 weeks of gestation (often referred to as intrauterine fetal deaths) was not eligible for inclusion in the review. Cluster- and quasi-randomised trials were eligible for inclusion. Randomised trials published only as abstracts were eligible if sufficient information could be retrieved. We excluded non-randomised trials.

Data collection and analysis

At least three review authors independently assessed the trials for inclusion and risk of bias, extracted data and checked them for accuracy. We estimated the relative effects and rankings for the primary outcomes of complete miscarriage and composite outcome of death or serious complications. The certainty of evidence was assessed using GRADE. Relative effects for the primary outcomes are reported

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subgrouped by the type of miscarriage (incomplete and missed miscarriage). We also performed pairwise meta-analyses and network meta-analysis to determine the relative effects and rankings of all available methods.

Main results

Our network meta-analysis included 78 randomised trials involving 17,795 women from 37 countries. Most trials (71/78) were conducted in hospital settings and included women with missed or incomplete miscarriage. Across 158 trial arms, the following methods were used: 51 trial arms (33%) used misoprostol; 50 (32%) used suction aspiration; 26 (16%) used expectant management or placebo; 17 (11%) used dilatation and curettage; 11 (6%) used mifepristone plus misoprostol; and three (2%) used suction aspiration plus cervical preparation. Of these 78 studies, 71 (90%) contributed data in a usable form for meta-analysis.

Complete miscarriage

Based on the relative effects from the network meta-analysis of 59 trials (12,591 women), we found that five methods may be more effective than expectant management or placebo for achieving a complete miscarriage:

· suction aspiration after cervical preparation (risk ratio (RR) 2.12, 95% confidence interval (CI) 1.41 to 3.20, low-certainty evidence),

· dilatation and curettage (RR 1.49, 95% CI 1.26 to 1.75, low-certainty evidence),

· suction aspiration (RR 1.44, 95% CI 1.29 to 1.62, low-certainty evidence),

· mifepristone plus misoprostol (RR 1.42, 95% CI 1.22 to 1.66, moderate-certainty evidence),

· misoprostol (RR 1.30, 95% CI 1.16 to 1.46, low-certainty evidence).

The highest ranked surgical method was suction aspiration after cervical preparation. The highest ranked non-surgical treatment was mifepristone plus misoprostol. All surgical methods were ranked higher than medical methods, which in turn ranked above expectant management or placebo.

Composite outcome of death and serious complications

Based on the relative effects from the network meta-analysis of 35 trials (8161 women), we found that four methods with available data were compatible with a wide range of treatment effects compared with expectant management or placebo:

· dilatation and curettage (RR 0.43, 95% CI 0.17 to 1.06, low-certainty evidence),

· suction aspiration (RR 0.55, 95% CI 0.23 to 1.32, low-certainty evidence),

· misoprostol (RR 0.50, 95% CI 0.22 to 1.15, low-certainty evidence),

· mifepristone plus misoprostol (RR 0.76, 95% CI 0.31 to 1.84, low-certainty evidence).

Importantly, no deaths were reported in these studies, thus this composite outcome was entirely composed of serious complications, including blood transfusions, uterine perforations, hysterectomies, and intensive care unit admissions. Expectant management and placebo ranked the lowest when compared with alternative treatment interventions.

Subgroup analyses by type of miscarriage (missed or incomplete) agreed with the overall analysis in that surgical methods were the most effective treatment, followed by medical methods and then expectant management or placebo, but there are possible subgroup differences in the effectiveness of the available methods.

Authors' conclusions

Based on relative effects from the network meta-analysis, all surgical and medical methods for managing a miscarriage may be more effective than expectant management or placebo. Surgical methods were ranked highest for managing a miscarriage, followed by medical methods, which in turn ranked above expectant management or placebo. Expectant management or placebo had the highest chance of serious complications, including the need for unplanned or emergency surgery. A subgroup analysis showed that surgical and medical methods may be more beneficial in women with missed miscarriage compared to women with incomplete miscarriage. Since type of miscarriage (missed and incomplete) appears to be a source of inconsistency and heterogeneity within these data, we acknowledge that the main network meta-analysis may be unreliable. However, we plan to explore this further in future updates and consider the primary analysis as separate networks for missed and incomplete miscarriage.

P L A I N   L A N G U A G E   S U M M A R Y

Which management option is best when women experience an early miscarriage?

What is the issue?

Miscarriage is the most common cause of pregnancy loss and one of the most common complications in early pregnancy. An estimated 15% of pregnancies will end in miscarriage, with 25% of women experiencing a miscarriage in their lifetime. Miscarriage can lead to serious complications, including haemorrhage and infection, and even death, particularly in low-income countries. Miscarriage is generally defined as the spontaneous loss of a pregnancy before 24 weeks' gestation. Most miscarriages happen in the first 14 weeks, and are known as early miscarriages.

Why is this important?

Miscarriage can be managed expectantly (waiting for the pregnancy tissue to pass naturally), medically (tablets given to make the womb expel the pregnancy tissue) or surgically (removal of the pregnancy tissue during surgery). However, there is uncertainty about the effectiveness, safety, and side effects of the available methods for managing a miscarriage. The aim of this Cochrane Review is to find out which method is the most effective and safest with the least side effects. We collected and analysed all the relevant studies to answer this question.

What evidence did we find?

We searched for evidence in February 2021 and identified 78 studies involving 17,795 women. Most women were managed in hospitals. Women were diagnosed with missed (also called silent miscarriage where no pregnancy tissue has been expelled and there is no bleeding or pain) or incomplete miscarriage (already started to bleed or have pain and perhaps expelled some pregnancy tissue). We found evidence for six different methods of managing a miscarriage; three surgical methods (suction aspiration plus cervical preparation, dilatation and curettage, or suction aspiration), two medical methods (mifepristone plus misoprostol or misoprostol alone), and expectant management or placebo.

The analysis suggested that all three surgical methods and both medical methods may be more effective than expectant management or placebo for completing the process of miscarriage. Suction aspiration plus cervical preparation was the best method of miscarriage management followed by dilatation and curettage, and suction aspiration alone. The two medical methods of mifepristone combined with misoprostol, and misoprostol alone were ranked fourth and fifth best methods, respectively.

From the available data, we cannot learn much for the outcome of death or serious complications. No deaths were reported in the studies that contributed towards this outcome. Amongst the serious complications, the majority were women who required blood transfusions, some had womb perforations related to surgery or required further life-saving procedures. We could not know which method is best for this outcome due to limited data. However, expectant management or placebo was associated with more serious complications compared with the alternative treatment options.

We also looked separately at women suffering from an incomplete miscarriage compared to those suffering from a missed miscarriage. For both groups of women, all three surgical methods and both medical methods were found to be more effective than expectant management or placebo for providing a definitive treatment for a miscarriage. These analyses for incomplete and missed miscarriages agreed with the overall analysis in that surgical methods were better for providing a definitive treatment for a miscarriage than medical methods, which in turn were better than expectant management or placebo. However, the benefits for women with missed miscarriages undergoing any management method other than expectant management or placebo were far greater compared to women with incomplete miscarriages. This is probably because expectant management or placebo is more effective in women in whom the process of miscarriage has already started compared with women in whom the process is yet to start.

What does this mean?

All methods were generally more effective for managing a miscarriage compared with expectant management or placebo, but surgical methods were more effective than medical methods. Expectant management or placebo has the lowest chance of successfully treating a miscarriage and has the highest chance of serious complications and the need for unplanned or emergency surgery. In this review we found that the benefits for women with missed miscarriages undergoing any management method other than expectant management or placebo were far greater compared to women with incomplete miscarriages.

SUMMARY OF FINDINGS

Summary of findings 1.   Complete miscarriage

Medical and surgical management compared with expectant management or placebo for treating missed early miscarriage

Patient or population: women with missed miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: complete miscarriage

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention
Suction aspiration plus cervical preparation	2.12 (1.41 to 3.20)	⊕⊕⊖⊖ LOW[a]	Not reported by included studies	-	2.12 (1.41 to 3.20)	⊕⊕⊖⊖ LOW[b]	640 per 1000	1000 per 1000	360 more per 1,000 (from 182 more to 577 more)
Suction aspiration	1.44 (1.29 to 1.62)	⊕⊕⊖⊖ LOW[c]	1.27 (1.08 to 1.48)	⊕⊕⊕⊖ MODERATE[d]	1.72 (1.44 to 2.06)	⊕⊕⊕⊖ MODERATE[f]	640 per 1000	922 per 1000	282 more per 1,000 (from 186 more to 397 more)
Dilation and curettage	1.49 (1.26 to 1.75)	⊕⊕⊖⊖ LOW[c]	1.25 (1.12 to 1.39)	⊕⊕⊕⊖ MODERATE[e]	1.55 (1.29 to 1.86)	⊕⊕⊖⊖ LOW[b]	640 per 1000	954 per 1000	314 more per 1,000 (from 166 more to 480 more)
Mifepristone plus misoprostol	1.42 (1.22 to 1.66)	⊕⊕⊕⊖ MODERATE[g]	1.59 (1.01 to 2.51)	⊕⊕⊕⊖ MODERATE[d]	1.40 (1.16 to 1.70)	⊕⊕⊕⊖ MODERATE[f]	640 per 1000	909 per 1000	269 more per 1,000 (from 141 more to 422 more)
Misoprostol	1.30 (1.16 to 1.46)	⊕⊕⊕⊖	1.85 (1.35 to 2.55)	⊕⊕⊕⊖	1.14 (0.99 to 1.31)	⊕⊕⊕⊖	640 per 1000	832 per 1000	192 more per 1,000 (from 102 more to 294 more)

LOW[c]	MODERAT-E[d]	MODER-ATE[f]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect..

[a] Network evidence downgraded -2 due to low certainty indirect evidence (no intransitivity, incoherence, or imprecision)
[b] Indirect evidence downgraded -2 due to limitations in study design
[c] Network evidence downgraded -2 due to moderate certainty direct evidence and incoherence between direct and indirect estimates (no intransitivity, or imprecision)
[d] Direct evidence downgraded -1 due to severe unexplained statistical heterogeneity
[e] Direct evidence downgraded -1 due to serious imprecision
[f] Indirect evidence downgraded -1 due to severe unexplained statistical heterogeneity
[g] Network evidence downgraded -1 due to moderate certainty indirect evidence (no intransitivity, incoherence, or imprecision)

Summary of findings 2.   Complete miscarriage (missed miscarriage subgroup)

Medical and surgical management compared with expectant management or placebo for treating missed early miscarriage

Patient or population: women with missed miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: complete miscarriage

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention

Suction aspiration plus cervical preparation	Not estimable	-	Not reported by included studies	-	Not estimable	-	Not estimable	Not estimable	Not estimable
Suction aspiration	2.43 (1.69 to 3.49)	⊕⊕⊕⊖ MODERATE[b]	1.88 (1.68 to 2.12)	⊕⊕⊕⊕ HIGH	3.35 (1.94 to 5.81)	⊕⊖⊖⊖ VERY LOW[a]	455 per 1000	942 per 1000	487 more per 1000 (from 402 more to 580 more)
Dilation and curettage	2.07 (1.19 to 3.59)	⊕⊕⊕⊕ HIGH	Not reported by included studies	-	Not estimable	-	455 per 1000	1000 per 1000	545 more per 1000 (from 313 more to 847 more)
Mifepristone plus misoprostol	1.82 (1.28 to 2.58)	⊕⊕⊕⊖ MODERATE[b]	1.25 (1.09 to 1.45)	⊕⊕⊕⊕ HIGH	2.40 (1.58 to 3.65)	⊕⊕⊕⊖ MODERATE[c]	455 per 1000	828 per 1000	373 more per 1000 (from 127 more to 719 more)
Misoprostol	1.67 (1.18 to 2.37)	⊕⊕⊖⊖ LOW[e]	3.18 (1.48 to 6.85)	⊕⊕⊕⊖ MODERATE[d]	1.16 (0.81 to 1.67)	⊕⊕⊕⊖ MODERATE[c]	455 per 1000	760 per 1000	305 more per 1000 (from 82 more to 623 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Indirect evidence downgraded -3 due to multiple crucial limitations in study design, severe unexplained statistical heterogeneity and imprecision
[b] Network evidence downgraded -1 due to high certainty direct evidence and incoherence between direct and indirect estimates (no intransitivity, or imprecision)
[c] Indirect evidence downgraded -1 due to severe unexplained statistical heterogeneity
[d] Direct evidence downgraded -1 due to severe unexplained statistical heterogeneity
[e] Network evidence downgraded -2 due to moderate certainty indirect evidence and incoherence between direct and indirect estimates (no intransitivity, or imprecision)

Summary of findings 3.   Complete miscarriage (incomplete miscarriage subgroup)

Medical and surgical management compared with expectant management or placebo for treating incomplete early miscarriage

Patient or population: women with incomplete miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: complete miscarriage

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Quality of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention
Suction aspiration plus cervical preparation	Not estimable	-	Not reported by included studies	-	Not estimable	-	Not estimable	Not estimable	Not estimable
Suction aspiration	1.19 (1.09 to 1.31)	⊕⊕⊕⊖ MODERATE[c]	1.20 (0.85 to 1.69)	⊕⊖⊖⊖ VERY LOW[a]	1.28 (1.11 to 1.48)	⊕⊕⊖⊖ LOW[b]	767 per 1000	913 per 1000	146 more per 1000 (from 69 more to 238 more)
Dilation and curettage	1.19 (1.08 to 1.31)	⊕⊕⊕⊖ MODERATE[f]	1.25 (1.12 to 1.39)	⊕⊕⊕⊖ MODERATE[d]	1.15 (1.02 to 1.30)	⊕⊖⊖⊖ VERY LOW[e]	767 per 1000	913 per 1000	146 more per 1000 (from 61 more to 238 more)
Mifepristone plus misoprostol	1.08 (0.87 to 1.34)	⊕⊖⊖⊖ VERY LOW[h]	1.08 (0.90 to 1.30)	⊕⊖⊖⊖ VERY LOW[g]	Not estimable	-	767 per 1000	828 per 1000	61 more per 1000 (from 100 fewer to 261 more)
Misoprostol	1.14 (1.03 to 1.25)	⊕⊕⊕⊖ MODERATE[j]	1.04 (0.70 to 1.54)	⊕⊕⊖⊖ LOW[i]	1.12 (1.02 to 1.24)	⊕⊖⊖⊖ VERY LOW[e]	767 per 1000	874 per 1000	107 more per 1000 (from 23 more to 192 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Direct evidence downgraded -3 due to multiple crucial limitations in study design, severe unexplained statistical heterogeneity and imprecision
[b] Indirect evidence downgraded -2 due to serious imprecision
[c] Network evidence downgraded -1 due to low certainty indirect evidence upgraded by 1 as it was downgraded for imprecision
[d] Direct evidence downgraded -1 due to serious imprecision
[e] Indirect evidence downgraded -3 due to multiple crucial limitations in study design, severe unexplained statistical heterogeneity and imprecision
[f] Network evidence downgraded -1 due to moderate certainty direct evidence (no intransitivity, incoherence, or imprecision)
[g] Direct evidence downgraded -3 due to multiple crucial limitations in study design and imprecision
[h] Network evidence downgraded -3 due to very low certainty direct evidence (no intransitivity, incoherence, or imprecision)
[i] Direct evidence downgraded -2 due to serious imprecision
[j] Network evidence downgraded -1 due to low certainty direct evidence upgraded by 1 as network evidence is precise

Summary of findings 4.   Composite outcome of death or serious complication

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with missed or incomplete miscarriage at ≤14 weeks gestation

Settings: Hospital

Intervention: multiple interventions (suction aspiration, misoprostol, dilation plus curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management

Outcome: composite outcome of death or serious complication

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention

Suction aspiration plus cervical preparation	Not reported by included studies	-	Not reported by included studies	-	Not reported by included studies	-	Not estimable	Not estimable	Not estimable
Suction aspiration	0.55 (0.23 to 1.32)	⊕⊕⊝⊝ LOW^c	0.43 (0.12 to 1.53)	⊕⊕⊝⊝ LOW^a	0.97 (0.21 to 4.40)	⊕⊕⊝⊝ LOW^b	19 per 1000	10 per 1000	9 fewer per 1000 (from 15 fewer to 6 more)
Dilation and curettage	0.43 (0.17 to 1.06)	⊕⊕⊝⊝ LOW^d	Not reported by included studies	-	0.43 (0.17 to 1.06)	⊕⊕⊝⊝ LOW^b	19 per 1000	8 per 1000	11 fewer per 1000 (from 16 fewer to 1 more)
Mifepristone plus misoprostol	0.76 (0.31 to 1.84)	⊕⊕⊝⊝ LOW^c	0.46 (0.13 to 1.63)	⊕⊕⊝⊝ LOW^a	1.38 (0.37 to 5.17)	⊕⊕⊝⊝ LOW^b	19 per 1000	14 per 1000	5 fewer per 1000 (from 13 fewer to 16 more)
Misoprostol	0.50 (0.22 to 1.15)	⊕⊕⊝⊝ LOW^d	0.96 (0.06 to 15.08)	⊕⊕⊝⊝ LOW^a	0.35 (0.13 to 0.97)	⊕⊕⊝⊝ LOW^b	19 per 1000	10 per 1000	9 fewer per 1000 (from 15 fewer to 3 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

^{a} Direct evidence downgraded -2 due to very serious imprecision

^{b} Indirect evidence downgraded -2 due to very serious imprecision

^{c} Network evidence downgraded -2 due to low certainty direct evidence (no intransitivity or incoherence)

^{d} Network evidence downgraded -2 due to low certainty indirect evidence (no intransitivity or incoherence)

Summary of findings 5.   Need for unplanned/emergency surgical procedure

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with a miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: need for unplanned/emergency surgical procedure

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention
Suction aspiration plus cervical preparation	Not estimable	-	Not reported by included studies	-	Not estimable	-	Not estimable	Not estimable	Not estimable
Suction aspiration	0.37 (0.22 to 0.65)	⊕⊕⊕⊖ MODERATE[b]	0.51 (0.30 to 0.87)	⊕⊕⊕⊕ HIGH	0.13 (0.05 to 0.35)	⊕⊕⊖⊖ LOW[a]	120 per 1000	44 per 1000	76 fewer per 1000 (from 42 fewer to 94 fewer)
Dilation and curettage	0.80 (0.09 to 7.02)	⊕⊖⊖⊖ VERY LOW[c]	Not reported by included studies	-	Not estimable	-	120 per 1000	96 per 1000	24 fewer per 1000 (from 109 fewer to 722 more)
Mifepristone plus misoprostol	0.64 (0.33 to 1.23)	⊕⊕⊖⊖ LOW[e]	0.32 (0.11 to 0.90)	⊕⊕⊕⊖ MODERATE[d]	0.91 (0.43 to 1.93)	⊕⊕⊖⊖ LOW[a]	120 per 1000	77 per 1000	43 less per 1000 (from 80 fewer to 28 more)
Misoprostol	1.04 (0.56 to 1.95)	⊕⊕⊖⊖ LOW[g]	0.67 (0.23 to 1.95)	⊕⊕⊖⊖ LOW[f]	1.28 (0.61 to 2.66)	⊕⊕⊖⊖ LOW[a]	120 per 1000	125 per 1000	5 more per 1000 (from 53 fewer to 114 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Indirect evidence downgraded -2 due to serious imprecision

[b] Network evidence downgraded -1 due to high certainty direct evidence downgraded due to incoherence

[c] Network evidence downgraded -1 due to low certainty indirect loop further downgraded due to imprecision

[d] Direct evidence downgraded -1 due to imprecision

[e] Network evidence downgraded -1 due to moderate certainty direct evidence downgraded due to incoherence

[f] Direct evidence downgraded -2 due to serious imprecision

[g] Network evidence downgraded due to low certainty indirect evidence with imprecision but not further downgraded as indirect evidence previously downgraded for imprecision

Summary of findings 6.   Pain scores (visual analogue scale)

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with a miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: pain scores (visual analogue scale)

Intervention	Anticipated absolute effects[*] (95% CI)		№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard care	**Risk with intervention**			
Suction aspiration plus cervical preparation	The mean pain score was 0	Not reported by included studies	-	-	
Suction aspiration	The mean pain score was 0	Not reported by included studies	-	-	
Dilation and curettage	The mean pain score was 0	Not reported by included studies	-	-	
Mifepristone plus misoprostol	The pain score in the mifepristone plus misoprostol group was on average 0.14 higher (from 0.21 lower to 0.5 higher) than in the		122 (1 RCT)	⊕⊕⊝⊝ LOW [a],[b]	small effect

	expectant management or placebo group			
Misoprostol	The pain score in the misoprostol group was on average 0.33 higher (from 0.08 lower to 0.57 higher) than in the expectant management or placebo group	262 (3 RCTs)	⊕⊕⊖⊖ LOW [a,b]	small effect

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] -1 as patient reported outcome
[b] -1 due to imprecision

Summary of findings 7.   Pelvic inflammatory disease, sepsis or endometritis

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with a miscarriage at ≤14 weeks gestation

Settings: Hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: pelvic inflammatory disease, sepsis or endometritis

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention

Methods for managing miscarriage: a network meta-analysis (Review)

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Suction aspiration plus cervical preparation	Not estimable	-	Not reported by included studies	-	Not estimable	-	Not estimable	Not estimable	Not estimable
Suction aspiration	1.42 (0.88 to 2.28)	⊕⊕⊕⊖ MODERATE^c	1.35 (0.76 to 2.41)	⊕⊕⊕⊖ MODERATE^a	1.55 (0.66 to 3.68)	⊕⊕⊖⊖ LOW^b	36 per 1000	51 per 1000	15 more per 1000 (from 4 fewer to 46 more)
Dilation and curettage	1.85 (1.05 to 3.25)	⊕⊕⊖⊖ VERY LOW^f	3.30 (0.82 to 13.28)	⊕⊕⊖⊖ LOW^d	1.65 (0.89 to 3.06)	⊕⊕⊖⊖ VERY LOW^e	36 per 1000	67 per 1000	31 more 1000 (from 2 more to 81 more)
Mifepristone plus misoprostol	0.90 (0.48 to 1.68)	⊕⊕⊖⊖ LOW^g	0.73 (0.30 to 1.80)	⊕⊕⊖⊖ LOW^d	1.11 (0.47 to 2.64)	⊕⊕⊖⊖ LOW^b	36 per 1000	32 per 1000	4 fewer per 1000 (from 19 fewer to 25 more)
Misoprostol	1.08 (0.62 to 1.88)	⊕⊕⊕⊖ MODERATE^c	1.84 (0.35 to 9.68)	⊕⊕⊖⊖ LOW^d	1.10 (0.56 to 2.16)	⊕⊕⊕⊖ MODERATE^h	36 per 1000	39 per 1000	3 more per 1000 (from 14 fewer to 32 more)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Direct evidence downgraded -1 due to imprecision
[b] Indirect evidence downgraded -2 due to serious imprecision
[c] Network evidence downgraded -1 due to moderate certainty direct evidence not further downgraded due to imprecision as direct evidence previously downgraded for imprecision
[d] Direct evidence downgraded -2 due to serious imprecision
[e] Indirect evidence downgraded -3 due to serious design limitations and imprecision in direct evidence
[f] Network evidence downgraded -3 due to very low certainty indirect evidence, further downgraded -1 for incoherence but upgraded +1 as network is precise
[g] Network evidence downgraded -2 due to low certainty direct evidence, not further downgraded due to imprecision as direct evidence previously downgraded for imprecision

[h] Indirect evidence downgraded -1 due to imprecision in direct evidence

Summary of findings 8. Days of bleeding

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with a miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: days of bleeding

Intervention	Network evidence		Direct evidence		Indirect evidence		Illustrative comparative risks* (95% CI) for NMA estimate		
	Mean difference (95% CI)	Certainty of the evidence (GRADE)	Mean difference (95% CI)	Certainty of the evidence (GRADE)	Mean difference (95% CI)	Certainty of the evidence (GRADE)	Risk with standard care	Risk with intervention	Risk difference with intervention
Suction aspiration plus cervical preparation	Not estimable	-	Not reported by included studies	-	Not estimable	-	Not estimable	Not estimable	Not estimable
Suction aspiration	-2.00 (-3.01 to -0.99)	⊕⊝⊝⊝ VERY LOW[c]	-2.75 (-4.08 to -1.42)	⊕⊕⊝⊝ LOW[a]	-0.73 (-2.12 to 0.66)	⊕⊝⊝⊝ VERY LOW[b]	10 days	8 days	2 days less (from 0.99 days less to 3.01 days less)
Dilation and curettage	-1.96 (-3.48 to -0.45)	⊕⊕⊝⊝ LOW[f]	-1.26 (-2.27 to -0.25)	⊕⊕⊝⊝ LOW[d]	-2.47 (-4.47 to -0.46)	⊕⊝⊝⊝ VERY LOW[e]	10 days	8.04 days	1.96 days less (from 0.45 days less to 3.48 days less)
Mifepristone plus misoprostol	-0.14 (-1.71 to 1.43)	⊕⊝⊝⊝ VERY LOW[h]	0.70 (-0.43 to 1.83)	⊕⊝⊝⊝ VERY LOW[g]	-0.77 (-2.83 to 1.30)	⊕⊝⊝⊝ VERY LOW[b]	10 days	9.86 days	0.14 days less (from 1.71 days less to 1.43 days more)
Misoprostol	-0.47	⊕⊝⊝⊝	0.32 (-2.19 to 2.84)	⊕⊝⊝⊝ VERY LOW[i]	-0.96 (-2.27 to 0.35)	⊕⊕⊝⊝ LOW[i]	10 days	9.53 days	0.47 days less (from 1.53 days less to 0.60 days more)

(-1.53 to 0.60)	VERY LOW[k]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Direct evidence downgraded -2 due to patient reported outcome and significant heterogeneity
[b] Indirect evidence downgraded -4 due to patient reported outcome, significant heterogeneity and serious imprecision
[c] Network evidence downgraded -4 due to low certainty direct evidence, further downgraded due to incoherence and not upgraded as direct grade not downgraded for imprecision
[d] Direct evidence downgraded -2 due to patient reported outcome and imprecision
[e] Indirect evidence downgraded -4 due to very low certainty direct evidence which was due to patient reported outcome, moderate design limitations and serious imprecision
[f] Network evidence downgraded -2 due to low certainty direct evidence, further downgraded -1 for incoherence but upgraded +1 as network is precise and direct evidence was previously downgraded for imprecision
[g] Direct evidence downgraded -3 due to patient reported outcome and serious imprecision
[h] Network evidence downgraded -5 due to very low certainty direct evidence, further downgraded due to incoherence but not even further downgraded due to imprecision as direct evidence previously downgraded for imprecision
[i] Direct evidence downgraded -4 due to patient reported outcome, significant heterogeneity and serious imprecision
[j] Indirect evidence downgraded -2 due to patient reported outcome and significant heterogeneity
[k] Network evidence downgraded -3 due to low certainty indirect evidence downgraded -1 due to imprecision

Summary of findings 9. Women's views/satisfaction

Medical and surgical management compared with expectant management or placebo for treating early miscarriage

Patient or population: women with a miscarriage at ≤14 weeks gestation

Settings: hospital or other healthcare facility

Intervention: multiple interventions (suction aspiration, misoprostol, dilation and curettage, mifepristone plus misoprostol, suction aspiration plus cervical preparation)

Comparison (reference): expectant management or placebo

Outcome: women's views/ satisfaction

Intervention	Narrative synthesis	№ of participants (studies)	Certainty of the evidence	Comments

			(GRADE)
Suction aspiration plus cervical preparation	Not reported by included studies	(0 RCTs)	-
Suction aspiration	2 trials described 92 out of 96 women (98.5%) as being satisfied with suction aspiration compared to 97 out of 99 women (98.0%) for expectant management or placebo. 1 trial used a 10 point numerical scale and found suction aspiration had a satisfaction score of 7.57 from 175 women and expectant management or placebo also had a 7.57 score from 177 women.	547 (3 RCTs)	⊕⊕⊕⊖ MODERATE[a]
Dilatation and curettage	Not reported by included studies	(0 RCTs)	-
Mifepristone plus misoprostol	1 trial used a visual analogue scale and found Mifepristone plus misoprostol had a score of 28.6 (SD 24.8) from 60 women compared to 25.2 (SD 25.6) from 62 women for expectant management or placebo	122 (1 RCT)	⊕⊖⊖⊖ VERY LOW [a,b,c]
Misoprostol	1 trial used a visual analogue scale and found misoprostol had a score of 8.9 (+/- 1.3) compared to 8.7 (+/- 1.5) for expectant management or placebo with 52 women in each arm. 1 trial described 14 out of 16 (87.5%) women as being satisfied with misoprostol compared to 12 out of 16 (75%) women as being satisfied with expectant management or placebo	136 (2 RCTs)	⊕⊕⊖⊖ LOW[a,c]

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] -1 no meta-analysis possible, narrative synthesis was conducted, estimates are not precise
[b] -1 due to design limitations
[c] -1 due to imprecision

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BACKGROUND

Description of the condition

Miscarriage is the most common cause of pregnancy loss. An estimated 15% of pregnancies will end in miscarriage, with 25% of women experiencing a miscarriage in their lifetime (Alberman 1992). This can have emotional and physical impact on both women and their partners extending well beyond the pregnancy (Conway 2000; Geller 2001; Neugebauer 1997).

Miscarriage is generally defined as the spontaneous pregnancy loss before 24 weeks' gestation (Shiers 2003). Most miscarriages happen in the first 14 weeks, and are known as early miscarriages (Alberman 1992). The clinical signs of miscarriage are vaginal bleeding, usually with abdominal pain. Miscarriage can lead to serious morbidity, including haemorrhage and infection, and even death, particularly in low- and middle-income countries (MBRRACE-UK 2016, WHO 2018). A missed miscarriage, also known as a delayed or silent miscarriage, is diagnosed when a non-viable pregnancy is identified on ultrasound scan. Often, women who have missed miscarriage are asymptomatic or have small amounts of vaginal bleeding or pain before the diagnosis is made, but all pregnancy tissue is retained in the uterus. In contrast, incomplete miscarriage is diagnosed when pregnancy tissue has been partly expelled from the uterus (NICE 2019).

Description of the intervention

Miscarriage can be managed expectantly, medically, or surgically. Surgical methods have traditionally been used to manage early miscarriage. Dilatation and curettage uses sharp metal curettage that is often performed in an operating room under regional or general anaesthesia. Sharp curettage is often performed after dilatation of the cervix. Even though, it is a relatively simple procedure, it does carry a small chance of serious complications, such as anaesthetic complications, infection, uterine perforation and Asherman's syndrome. Suction aspiration (electrical or manual vacuum aspiration) has replaced sharp curettage in high-income countries and has a well-documented safety profile and is the recommended surgical method according to the World Health Organization (WHO) safe abortion guidelines (WHO 2009, WHO 2012a). Even so, it is less commonly used in low- and middle-income countries due to lack of equipment and experience. Surgical methods can be combined with an agent to prepare (or ripen) the cervix to avoid the risks of injury from cervical dilation. Commonly used agents include mechanical and pharmacological dilators. The mechanical dilators may use osmotic cervical rods, Foley catheters or laminaria to dilate the cervix. The pharmacological dilators cause cervical ripening by softening and dilation of the cervix. The most common pharmacological dilator is misoprostol, a synthetic prostaglandin E1 analogue that induces cervical ripening and uterine contraction. It is water-soluble and heat-stable (Davies 2001). Oral and sublingual routes have the advantage of rapid onset of action, while the vaginal and rectal routes result in prolonged activity and greater bioavailability (Schaff 2005). Misoprostol is, however, associated with side effects such as diarrhoea, abdominal pain, nausea and vomiting, shivering and pyrexia (Tunçalp 2012).

Medical methods of management of miscarriage include various agents. They usually involve a synthetic prostaglandin and the most commonly used prostaglandin is misoprostol. Other synthetic prostaglandins are available, such as gemeprost or dinoprost, but these agents are less frequently used in this setting. Mifepristone is a progesterone antagonist that interferes with the production or functioning of progesterone and can initiate shedding of pregnancy tissue. Mifepristone has been used alone for terminating unwanted pregnancies, but more frequently is used in combination with misoprostol to manage early miscarriage. It is considered to be more useful in women with missed miscarriages where a non-viable pregnancy is identified on ultrasound scan, and pregnancy tissue is retained in the uterus. In women with incomplete miscarriage, the anti-progesterone effect of mifepristone is considered less useful and treatment is aimed to stimulate uterine contractility often with misoprostol alone. Expectant management involves no surgical or medical intervention, with the expectation that the miscarriage will happen naturally.

Why it is important to do this review

Several Cochrane Reviews have compared an individual method for managing miscarriage with another method or with expectant management (Lemmers 2019; Kim 2017; Nanda 2012; Tuncalp 2010). However, a standard pairwise meta-analysis can only compare two methods that have been directly compared in head-to-head trials (direct evidence). In the absence of a single high-quality randomised controlled trial that compares all methods for managing miscarriage, uncertainty remains about which is the most effective. For the management of miscarriage with multiple competing treatment methods, not all of which have been directly compared, a network meta-analysis may be better able to allow for all possible comparisons to be made so we can determine which method is most effective (Caldwell 2005; Caldwell 2010). A network meta-analysis simultaneously pools all the available direct and indirect evidence on relative treatment effects, within a single coherent analysis. Indirect evidence is obtained by inferring the relative effectiveness of two competing methods through a common comparator. Thus, a network meta-analysis produces estimates of the relative effects of each method compared with every other in a network, even though some pairs may not have been directly compared, and has the potential to reduce the uncertainty in treatment effect estimates (Caldwell 2005). It also allows for the calculation of the probability that each method is the best for any given outcome and can be used to identify gaps in the evidence base (Caldwell 2005).

OBJECTIVES

To estimate the relative effectiveness and safety profiles for the different management methods for early miscarriage, and to provide rankings of the available methods according to their effectiveness, safety, and side-effect profile using a network meta-analysis.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled comparisons that assessed the effectiveness or safety of methods for miscarriage management. Cluster-randomised trials and quasi-randomised trials were eligible for inclusion. Randomised trials published only as abstracts were eligible if sufficient information could be retrieved. We excluded non-randomised trials.

Types of participants

We included all studies that included women who were being treated for early miscarriage (pregnancy loss at less than or equal to 14 weeks of gestation), diagnosed by ultrasound or clinically alone. We included women with both missed and incomplete miscarriage. Late miscarriages after 14 weeks of gestation (often referred to as intrauterine fetal deaths) was not eligible for inclusion in the review. We considered for inclusion studies conducted in all settings regardless of the age of women.

Types of interventions

All interventions were eligible for inclusion, and the following were included in the review: suction aspiration, suction aspiration plus cervical preparation, dilatation and curettage, mifepristone plus misoprostol, misoprostol, and expectant management or placebo.

We included regimens irrespective of their dose as long as they were in the therapeutic range that are recommended in international guidelines. Multi-arm trials that compared different dosages, regimens or routes of one drug, but also compared those versus another drug or method, were included. For the multi-arm trials, we merged the intervention arms of different dosages, regimens or routes of the same drug together for the global analysis of all outcomes and did not treat them as separate independent comparisons. We did not include trials that compared exclusively different dosages, regimens or routes of administration of the same drug. The review was restricted to studies that evaluated drugs or interventions administered by healthcare professionals.

We classified the comparisons within a study as follows:

- suction aspiration plus cervical preparation = any surgical management that involves suction aspiration with cervical preparation agents;
- suction aspiration = any surgical management that involves suction aspiration without any cervical preparation agents;
- dilatation and curettage = any surgical treatment involving sharp metal curette;
- mifepristone plus misoprostol = any medical management with the combined use of mifepristone plus misoprostol at any dose, route or regimen;
- misoprostol = any medical management with the use of misoprostol alone at any dose, route or regimen;
- expectant management = any management that does not involve any surgical or medical treatment.

Types of outcome measures

We estimated the relative effects and rankings of the competing methods of miscarriage management for the following outcomes.

Primary outcomes

- Complete miscarriage: this is defined as evidence of complete evacuation of uterine contents based on clinical findings or ultrasound examination after a specific time period as defined in the primary studies. Outcomes were pooled regardless of the timeframe for assessment.
- Composite outcome of death or serious complications (e.g. uterine perforation, need for further life-saving procedures including hysterectomy, blood transfusion or intensive care unit admission).

Secondary outcomes

- Need for unplanned/emergency surgical procedure.
- Pain scores (visual analogue scale).
- Pelvic inflammatory disease, sepsis or endometritis.
- Mean volumes of blood loss (mL).
- Change in haemoglobin measurements before and after the miscarriage.
- Days of bleeding.
- Cervical tear.
- Women's views or satisfaction.
- Mean duration of hospital stay (days).
- Re-admission to hospital.
- Nausea.
- Vomiting.
- Diarrhoea.
- Pyrexia.
- Anxiety score.
- Depression score.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Electronic searches

We searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (9 February 2021).

The Register is a database containing over 27,000 reports of controlled trials in the field of pregnancy and childbirth. It represents over 30 years of searching. For full current search methods used to populate Pregnancy and Childbirth's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link.

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. hand searches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set that

has been fully accounted for in the relevant review sections (Included studies, Excluded studies, Studies awaiting classification or Ongoing studies).

In addition, we searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports (Feb 12 2021) using the terms listed in Appendix 1.

Searching other resources

We retrieved additional relevant references cited in papers identified through the above search strategy. We screened citations and abstracts and searched for the full texts of studies identified as abstracts. If required, we sought information from primary authors to investigate whether these studies meet eligibility criteria, and to obtain outcome and study data. If this was not possible, we only included abstracts if we could extract sufficient information to satisfy our eligibility criteria and the study authors reported the outcomes of interest. Trials that compared at least two of the drugs or interventions were eligible and we searched for all possible comparisons formed by the drugs or interventions of interest. We did not apply any language or date restrictions.

Data collection and analysis

Selection of studies

At least two review authors (JG, HJ, VD) retrieved and independently assessed for inclusion all the potential studies we identified as a result of the search strategy. Any disagreements were resolved through discussion or, when required, with consultation with a third review author (IDG). We created a PRISMA study flow diagram to map out the number of records identified, included and excluded (Figure 1).

Figure 1. Study flow diagram.
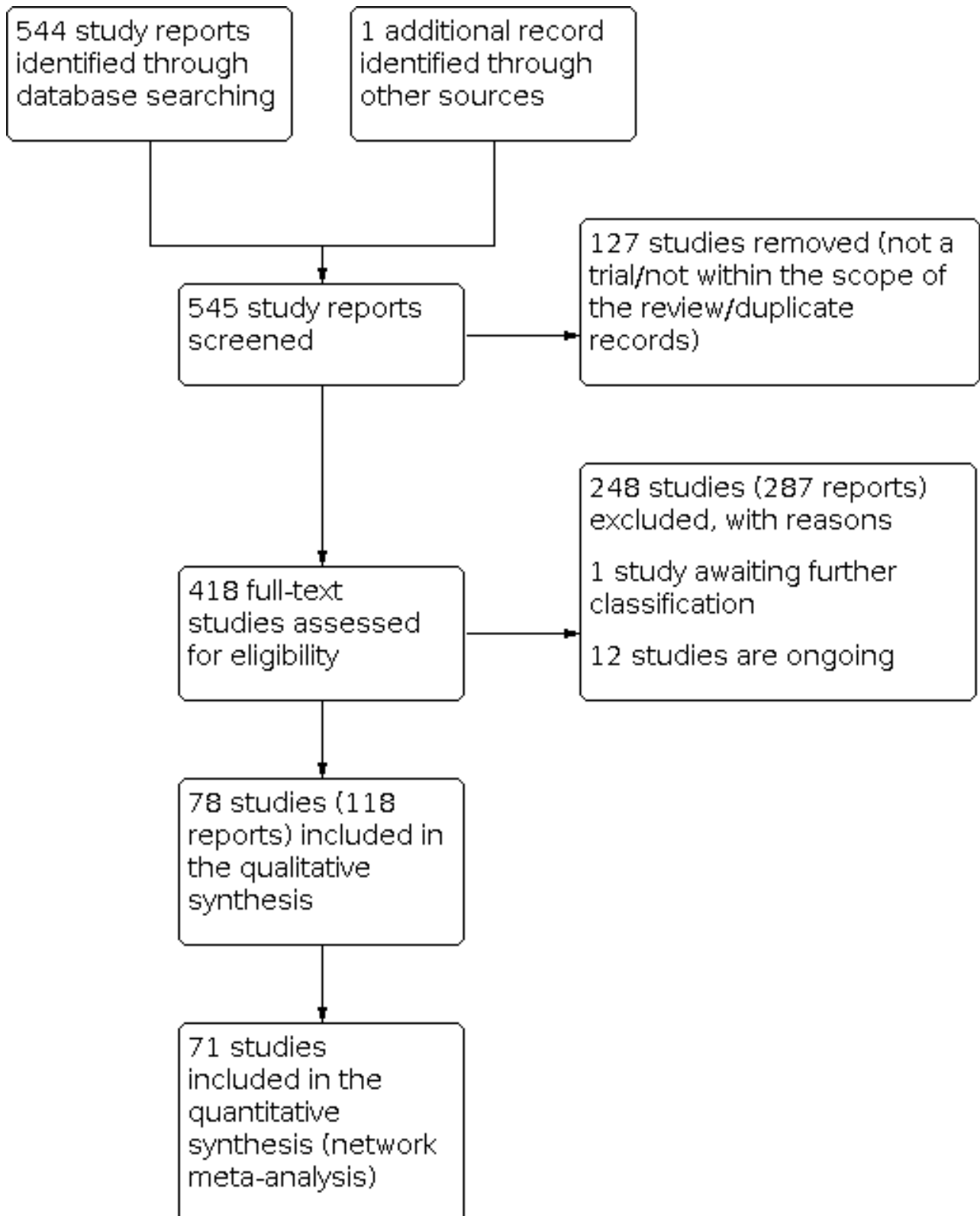
Data extraction and management

We designed an electronic form to extract data. For eligible studies, at least three review authors (JG, AP, HJ, AD, LB, VD) independently extracted the data using the form. We resolved discrepancies through discussion or, when required, with consultation with a seventh review author (IDG). We entered data into Review Manager

5 (RevMan 5.4) software and it was checked for accuracy (RevMan 2014). When information regarding any of the above was unclear, we attempted to contact the authors of the original reports to provide further details. We extracted the following data.

Methods extracted

1. Study design
2. Sequence generation
3. Allocation sequence concealment
4. Blinding
5. Attrition
6. Study protocol and inconsistencies compared with the published report
7. Financial support and conflicts of interest
8. Other concerns about bias

Data extracted

From each included study we extracted the number of participants, along with the inclusion and exclusion criteria. We also extracted the interventions being compared including the healthcare setting, and their respective primary and secondary outcomes relevant to this review. We extracted all relevant arm level data (e.g. number of events and number of participants for binary outcomes and means and standard deviations per study arm for continuous outcomes). Participants in the network could in principle have been randomised to any of the methods being compared. For example, a woman with an early miscarriage could be equally likely to be randomised to dilatation and curettage, misoprostol, suction aspiration, suction aspiration plus cervical preparation, mifepristone plus misoprostol or expectant management or placebo. All of these six interventions were of direct interest.

Data on potential effect modifiers

From each included study we extracted the following study, intervention and population characteristics that may act as effect modifiers:

- gestational age (less than or equal to nine weeks versus greater than nine weeks of gestation);
- type of miscarriage (incomplete versus missed miscarriage);
- healthcare setting (inpatient versus outpatient);
- dosage, regimen, and route of drug administration (sublingual, rectal, oral).

Other data

From each included study we extracted the following additional information:

- country or countries in which the study was performed;
- date of publication;
- type of publication (full-text publication, abstract publication, unpublished data);
- trial registration reference.

Assessment of risk of bias in included studies

At least two review authors (JG, HJ, AD, LB, VD) independently assessed the risk of bias for each included study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of*

Interventions (Higgins 2011). Any disagreement was resolved by discussion or by involving another review author (AP, IDG).

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the methods as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding would have been unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as at:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We state whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or has been supplied by the trial authors, we have re-included missing data in the analyses which we undertook.

We assessed methods as at:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups or not exceeding 10% for the primary outcomes of the review);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation or exceeding 10% for the primary outcomes of the review);
- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias.

We assessed the methods as:

- low risk of bias (where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and so cannot be used; the study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we have about other possible sources of bias.

We assessed whether each study was free of other problems that could put it at risk of bias:

- low risk of other bias;
- high risk of other bias;
- unclear whether there is risk of other bias.

(7) Overall risk of bias

We made explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses (see the 'Sensitivity analysis' section). For our primary outcomes, we combined quality items and judged trials as "A" if they were at low risk of bias and if they include an adequate random sequence generation, allocation concealment, blinding, no selective reporting and with little loss to follow-up (less than 10%) and free of other bias. Trials were judged at "B" if they were at moderate risk of bias and if they demonstrated serious limitations in key criteria excluding randomisation and allocation concealment, for example unclear concealment of allocation. Alternatively, trials were considered to be "C" or at high risk of bias if they had serious limitations in the randomisation sequence (quasi-randomised) or lack of allocation concealment, or small blocked randomisation (<10) or other very serious, crucial methodological limitations such as lack of blinding for a subjective outcome. We explored the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis for information about how the risk of bias was incorporated in the sensitivity analysis.

Measures of treatment effect

Relative treatment effects

For dichotomous data, we present results as a summary risk ratio (RR) with 95% confidence interval (CIs). For continuous data, we used the mean difference (MD) if outcomes are measured in the same way between trials. We used the standardised mean difference (SMD) to combine trials that measured the same outcome, but used different methods. If the target parameter is the effect of change in a continuous measure, such as the change in haemoglobin between baseline and post-miscarriage, where possible, we accounted for the within-patient correlation between baseline and post-miscarriage estimates (Dias 2013). For the network meta-analysis (NMA,) zero events were handled by deleting the relevant cells. These are summarised in forest plots displaying the results from pairwise, indirect and network (combining direct and indirect) analyses for the comparisons between the different methods of miscarriage management.

Relative treatment ranking

We also estimated the ranking probabilities for all methods of miscarriage management of being at each possible rank for each intervention (conditional on the model and specified vague priors). Then we obtained a treatment hierarchy using the surface under the cumulative ranking curve (SUCRA). SUCRA can also be expressed as a percentage of effectiveness or side effects of a treatment that would be ranked first without uncertainty; the larger the SUCRA the higher its rank among all available methods (Salanti 2011). The probabilities to rank the treatments are estimated under a Bayesian model with flat priors, assuming that the posterior distribution of the parameter estimates is approximated by a normal distribution with mean and variance equal to the frequentist estimates and variance–covariance matrix. Rankings are constructed drawing 1000 samples from their approximate posterior density. For each draw, the linear predictor is evaluated for each study, and the largest linear predictor is noted (White 2011).

Unit of analysis issues

Cluster-randomised trials

We planned to include cluster-randomised trials in the analyses along with individually-randomised trials. We planned to adjust their sample sizes using the methods described in the Handbook (Higgins 2011), using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial, or from a study of a similar population. If we had used ICCs from other sources, we planned to report this and to conduct sensitivity analyses to investigate the effect of variation in the ICC. Had we identified both cluster-randomised trials and individually-randomised trials, we planned to synthesise the relevant information. In cluster-randomised trials, particular biases to consider include:

• recruitment bias;
• baseline imbalance;
• loss of clusters;
• incorrect analysis; and
• comparability with individually-randomised trials.

We would have considered it reasonable to combine the results from both cluster-randomised trials and individually-randomised trials if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit was considered to be unlikely. We planned to also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit. We planned to include cluster-randomised trials in the analyses along with individually-randomised trials, but none were found.

Cross-over trials

Cross-over trials are not eligible for inclusion in this review.

Multi-arm trials

We included multi-arm trials and accounted for the correlation between the effect sizes in the network meta-analysis. We treated multi-arm studies as multiple independent comparisons in pairwise meta-analyses.

Dealing with missing data

For included studies, we noted levels of attrition. We explored the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis. We imputed missing standard deviations and errors using standard techniques where possible (Higgins 2011). For all outcomes, we performed analyses, as far as possible, on a modified intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses, and we analysed all participants in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

Assessment of clinical and methodological heterogeneity

To evaluate the presence of clinical heterogeneity, we examined trial and study population characteristics across all eligible trials that compared each pair of interventions. We assessed the presence of clinical heterogeneity within each pairwise comparison by comparing these characteristics.

Assessment of transitivity across treatment comparisons

We assessed the assumption of transitivity by comparing the distribution of potential effect modifiers across the different pairwise comparisons. In this context we expect that the transitivity assumption will hold assuming the following: 1) the common treatment used to compare different miscarriage management drugs indirectly is similar when it appears in different trials (e.g. misoprostol is administered in a similar way in misoprostol versus suction aspiration trials and in misoprostol versus mifepristone plus misoprostol trials); 2) all pairwise comparisons do not differ with respect to the distribution of effect modifiers (e.g. the design and study characteristics of suction aspiration versus misoprostol trials are similar to misoprostol versus mifepristone plus misoprostol trials).

Assessment of statistical heterogeneity and inconsistency

Assumptions when estimating the heterogeneity

In standard pairwise meta-analyses we estimated different heterogeneity variances for each pairwise comparison. In the network meta-analysis, we assumed a common estimate for the heterogeneity variance across the different comparisons.

Measures and tests for heterogeneity

We assessed statistically the presence of heterogeneity within each pairwise comparison using the I^2 statistic and its 95% CI that measures the percentage of variability that cannot be attributed to random error (Higgins 2002). We based the assessment of statistical heterogeneity in the entire network on the magnitude of the heterogeneity variance parameter (τ^2) estimated from the network meta-analysis models. For dichotomous outcomes we compared the magnitude of the heterogeneity variance with the empirical distribution as derived by Turner (Turner 2012). We also estimated a total I^2 statistic value for heterogeneity in the network as described elsewhere (Higgins 2002). The certainty of the evidence was downgraded for inconsistency where $I^2 \geq 60\%$ in line with the World Health Organization standard operating procedures for grading evidence for guidelines (Vogel 2019).

Assessment of statistical inconsistency

The statistical agreement between the various sources of evidence in a network of interventions (consistency) was evaluated by global and local approaches to complement the evaluation of transitivity.

Local approaches for evaluating inconsistency

To evaluate the presence of inconsistency locally we used the loop-specific approach. This method evaluates the consistency assumption in each closed loop of the network separately as the difference between direct and indirect estimates for a specific comparison in the loop (inconsistency factor) (Veroniki 2013). Then, the magnitude of the inconsistency factors and their 95% CIs can be used to infer about the presence of inconsistency in each loop. We assumed a common heterogeneity estimate within each loop.

Global approaches for evaluating inconsistency

To check the assumption of consistency in the entire network we used the "design-by-treatment" model as described by Higgins

and colleagues (Higgins 2012). This method accounts for different sources of inconsistency that can occur when studies with different designs (two-arm trials versus three-arm trials) give different results as well as disagreement between direct and indirect evidence. Using this approach we inferred about the presence of inconsistency from any source in the entire network based on a Chi² test. We performed the design-by-treatment model in STATA using the mvmeta command (StataCorp. 2019).

Inconsistency and heterogeneity are interwoven; to distinguish between these two sources of variability we employed the I² statistic for inconsistency that measures the percentage of variability that cannot be attributed to random error or heterogeneity (within comparison variability).

Assessment of reporting biases

We aimed to minimise the potential impact of these biases by ensuring a comprehensive search for eligible studies and by being alert to duplication of data. If there were 10 or more studies in any of the direct comparisons, we investigated reporting biases (such as publication bias) using funnel plots to explore the possibility of small-study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies) as part of the assessment of the certainty of the direct evidence.

Data synthesis

Methods for direct treatment comparisons

We performed standard pairwise meta-analyses using a random-effects model in Review manager software (Revman 5.4) for every treatment comparison (DerSimonian 1986). The random-effects method (DerSimonian 1986) was used for this analysis to mitigate for the high level of heterogeneity observed. This method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. The standard errors of the study-specific estimates are therefore adjusted to incorporate a measure of the extent of heterogeneity. This results to wider confidence intervals in the presence of heterogeneity, and corresponding claims of statistical significance are more conservative.

Methods for indirect and mixed comparisons

We initially generated and assessed the network diagrams to determine if a network meta-analysis was feasible. Then we performed the network meta-analysis within a frequentist framework using multivariate meta-analysis estimated by restricted maximum likelihood. All analyses were done using Stata statistical software, release 15 (StataCorp, College Station, TX). We used the network suite of Stata commands designed for this purpose (White 2012; White 2015).

Subgroup analysis and investigation of heterogeneity

For the primary outcomes we had planned to carry out the following pre-specified subgroup analyses by using the following effect modifiers.

- gestational age (greater than nine weeks versus less than or equal to nine weeks of gestation);
- type of miscarriage (incomplete versus missed miscarriage);
- type of vacuum aspiration device used (electrical versus manual vacuum aspiration);

- type of healthcare setting (inpatient versus outpatient);
- dosage, regimen, and route of drug administration (sublingual, rectal, oral).

We assessed subgroup differences by evaluating the relative effects and assessment of model fit for the primary outcome of complete miscarriage.

Sensitivity analysis

For the primary outcomes we had planned to perform sensitivity analysis for the following:

- overall risk of bias of the studies (restricted to studies at low risk of overall bias);
- randomisation unit (cluster versus individual);
- use of placebo versus expectant management.
- exclusion of quasi-randomised trials

We assessed differences by evaluating the relative effects and assessment of model fit.

Summary of findings and assessment of the certainty of the evidence

The summary of findings tables present evidence comparing all methods with a reference comparator, expectant management or placebo. Each table describes key features of the evidence relating to a single outcome. There is a table for each important outcome in accordance with the GRADE approach. These outcomes are 1) complete miscarriage, 2) composite outcome of death or serious complication, 3) need for unplanned/emergency surgical procedure, 4) pain scores (visual analogue scale), 5) pelvic inflammatory disease, sepsis or endometritis, 6) days of bleeding, and 7) women's views or satisfaction. We also present tables for two subgroups analyses of the complete miscarriage outcome: 1) missed miscarriage and 2) incomplete miscarriage. We assessed the certainty of the evidence using the GRADE approach as outlined in the GRADE handbook in order to assess the certainty of the body of evidence relating for each outcome for all comparisons. In order to create summary of findings tables, we used GRADEpro GDT, to import data from RevMan 5.4 (RevMan 2014).

We used the GRADE working group's approach (Brignardello-Petersen 2018; Puhan 2014) for rating the certainty of the network meta-analysis effect estimates for all the comparisons and all outcomes. We appraised the certainty of the direct, indirect, and network evidence sequentially (in this order). First, we assessed the certainty of the direct evidence (where available) for a given outcome, and rated the evidence using the standard GRADE approach based on consideration of: study design limitations (risk of bias); inconsistency; imprecision; indirectness and publication bias (Higgins 2011). Study design limitations were assessed using an A, B or C scale with "A" studies being at low risk of bias and "C" studies being at high risk of bias as described before. For objective outcomes, importance was given to method of randomisation, allocation concealment and attrition bias, whereas for subjective outcomes blinding of the assessor was also taken into consideration. On all the network diagrams, of the outcomes where network meta-analysis was possible, we display the certainty of the direct evidence using a colour-coded key as outlined in the figure caption. Then we rated the certainty of the indirect evidence for the same given outcomes, and this was determined based on the lower

of the certainty ratings of the two direct arms forming the dominant 'first-order' loop in the network diagram for this outcome. Our final step was to determine the certainty of network evidence based on: (i) the higher certainty rating of the direct and indirect evidence, (ii) whether the relevant network exhibited 'transitivity', i.e. whether all the comparisons contributing data to the estimate were directly consistent with the PICO question, (iii) consideration of coherence between direct and indirect effect estimates, and (iv) precision of the network effect estimate. At each of these stages, two review authors (JG, AP) independently appraised the certainty ratings for the direct, indirect and network evidence. Disagreements between authors were resolved through discussion and consultation with a third review author (IDG) where necessary.

The certainty of network evidence for each outcome was rated as 'high', 'moderate', 'low' or 'very low' in accordance with the GRADE approach.

- High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate certainty: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;
- Low certainty: our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect;
- Very low certainty: we have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

For ease of comparison when interpreting the relative effects of all methods for managing a miscarriage compared to expectant management or placebo, the summary of findings tables include the effect estimate and certainty judgements for each of the direct evidence, indirect evidence and the network meta-analysis, describing all the findings for a single outcome in each table. The anticipated absolute effects are also included, based on the network effect estimate for each treatment intervention in comparison with expectant management or placebo. The assumed risks in the expectant management or placebo group are based on weighted means of baseline risks from the studies with expectant management or placebo arms in the network meta-analysis. The corresponding risks in the suction aspiration plus cervical preparation, suction aspiration, dilatation plus curettage, mifepristone plus misoprostol, misoprostol groups (and their 95% CIs) are based on the assumed risk in the expectant management or placebo group and the relative effect of the individual treatment intervention, when compared with the expectant management or placebo group (and its 95% CI) as derived from the network meta-analysis.

RESULTS

Description of studies

Results of the search

The results of the search are summarised in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Figure 1). The search of Cochrane Pregnancy and Childbirth's (CPC) Trials Register on 9 February 2021 retrieved in total 544 available records. One further record from additional author searches and manual searching of reference lists was

obtained. We excluded 127 records as duplicates or based on their title and abstract. We examined the full text of 418 records and included in the network meta-analysis 78 randomised trials (reported in 118 publications). We contacted the authors from 38 references for additional data or clarifications. We were able to obtain additional data or clarifications from trial authors for nine randomised trials (Characteristics of included studies). We excluded 248 studies (reported in 287 publications) (Characteristics of excluded studies), one trial (reported in one publication) could not be classified (Characteristics of studies awaiting classification) and 12 studies were still ongoing (Characteristics of ongoing studies).

Included studies

This review included 78 randomised trials, published between 1979 and 2021, involving 17,795 women. All studies were individually randomised; there were no cluster-randomised studies. A number of multi-arm trials were identified: three four-arm trials and five three-arm trials. For the three four-arm trials as there was randomisation based on setting of care as well as intervention, the arms which had the same intervention were combined for the purposes of the network meta-analysis. For two of the three-arm trials, one arm was excluded from the analysis due to reasons detailed in the table of Characteristics of included studies. Most studies were reported in English (86%, 67/78); Four translations were obtained (three Portuguese and one Norwegian). One study was funded by Assistance Publique Hôpitaux de Paris, France (Torre 2012); one study was funded by Committee on Research and Conference Grants, University of Hong Kong (Ngai 2001); two studies were funded by the David and Lucille Packard Foundation (Dabash 2010, Taylor 2011); one study was funded by the Health Services Research Fund of Hong Kong (Chung 1999); one study was funded by the Healthcare Insurers Innovation Foundation, Canada (Hamel 2021); one study was funded by National Institute for Health Research HTA programme, UK (Chu 2020); four studies were funded by National Institutes of Health, USA (Zhang 2005; Davis 2007; Harwood 2008; Schreiber 2018); one study was funded by the Riverside Methodist Hospital Medical Research Foundation, USA (Lister 2005); one study was funded by a South and West NHS Executive research and development grant, UK (Trinder 2006); one study was funded by the Swedish Medical Research Council (Nielsen 1995). All the other 64 studies did not state their source of funding. One study declared consultancy fees from Danco laboratories as a conflict of interest (Schreiber 2018); one study declared the donation of £20,000 from Exelgyn, the manufacturers of mifepristone, which was an intervention used in the trial as a conflict of interest (Trinder 2006); one study declared that two authors had served as consultants to Pfizer as a conflict of interest (Zhang 2005). Ten studies stated that there were no conflicts of interest to declare from any of the authors, and 65 studies did not state whether the authors had any conflicts of interest.

The studies were conducted across 37 countries (including high-, middle- and low-income countries); there were no multi-country trials. The median size of the trials was 180 participants (interquartile range (IQR) 206 (94 to 300)). Most studies were single-centre studies (82%, 64/78); 14 studies were multi-centre studies (18%, 14/78). Most trials (91%, 71/78) were performed in a hospital setting, four were performed in a community setting (5%), two (3%) in a mixed setting, and one (1%) of unspecified setting. Six of the studies only recruited women with an early first trimester miscarriage (less than or equal to nine weeks of gestation) with

the majority (61/78) only specifying a gestational age of less than or equal to 14 weeks of gestation; a specific cut-off in terms of gestational age was not specified in 11 out of 78 studies. Thirty-six out of 78 studies were based purely on women with an incomplete miscarriage, 17 studies on women with a missed miscarriage, 19 had a mixed population of women with either a missed or incomplete miscarriage and in six studies the type of miscarriage was not specified.

Of the 78 included studies, 71 (90%) contributed data to the analysis, seven studies did not present the data in a usable form for meta-analysis or narrative synthesis. Across the 71 trials (158 trial arms) that contributed data for analysis, the following agents were used either as intervention or comparison:

- 51 trial arms (33%) used misoprostol;
- 50 trial arms (32%) used suction aspiration;
- 26 trial arms (16%) used expectant management or placebo;
- 17 trial arms (11%) used dilatation and curettage;
- 11 trial arms (6%) used mifepristone plus misoprostol;
- 3 trial arms (2%) used suction aspiration plus cervical preparation.

Of the 51 trial arms that used misoprostol, the concentrations of the first dose administered were as follows: 19 of 51 (37%) used 800 micrograms, 17 of 51 (33%) used 400 micrograms, 13 of 51 (23%) used 600 micrograms, 1 of 51 (2%) used 200 micrograms, and 1 of 51 (2%) did not specify the dose of misoprostol. The routes of administration used for misoprostol was as follows: 26 of 51 (51%) gave misoprostol vaginally, 19 of 51 (37%) orally, 2 of 51 (4%) vaginally or orally, 2 of 51 (4%) sublingually, and 2 of 51 (4%) did not specify the route of administration.

Of the 11 trial arms that assessed the effectiveness of mifepristone, six of 11 (55%) used a 200 milligram dose of mifepristone, four of 11 (36%) used a 600 milligram dose and one of 11 (9%) used a dose of 400 milligrams. Mifepristone was always taken orally and given in combination with misoprostol, which was taken 24 to 72 hours later. The concentrations of misoprostol administered following mifepristone were as follows: 7 of 11 (64%) used 800 micrograms and 4 of 11 (36%) used 400 micrograms of misoprostol. The routes of administration for misoprostol following mifepristone were as follows: 5 of 11 (46%) gave misoprostol vaginally, 3 of 11 (27%) orally, and 3 of 11 (27%) vaginally or orally.

Of the 59 trials that contributed to the primary outcome, 14 (24%) made the assessment for complete miscarriage on days 1 to 5, 14 (24%) on day 7, 18 (31%) on days 10 to 14 and 9 (15%) over 15 days later. 4 studies (6%) did not specify the timeframe used to assess complete miscarriage.

Excluded studies

We excluded 248 trials (for details see Characteristics of excluded studies). The most common reasons for exclusion were because trials included participants who were over 14 weeks of gestation at the time of recruitment or were based on participants undergoing a termination of pregnancy. Some trials were not randomised, or exclusively investigated doses or routes of administration of the same method of management of miscarriage.

Risk of bias in included studies

We present summaries of the risk of bias of the included studies for each of the domains we assessed across all studies (Figure 2) and for each included study (Figure 3).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

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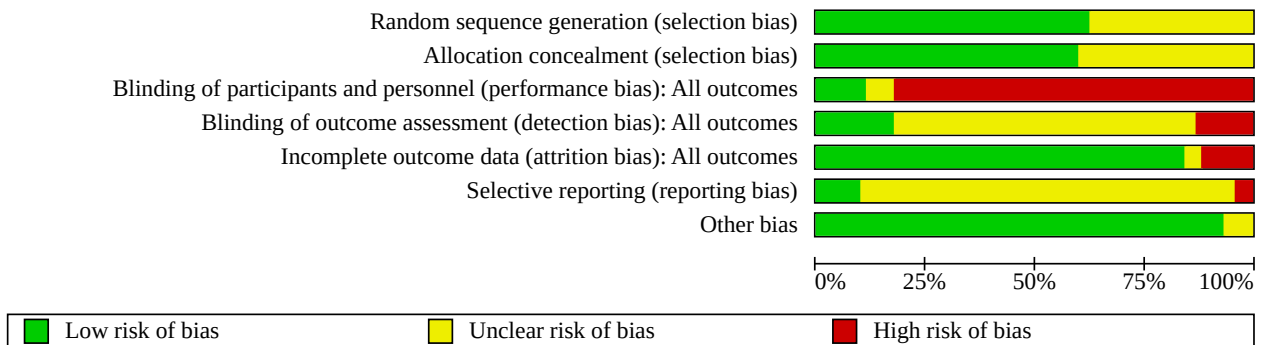
Figure 3.   Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 3.   (Continued)

Study							
de Holanda 2003	?	?	−	?	+	?	?
de Jonge 1995	+	+	−	?	+	?	+
Demetroulis 2001	+	+	−	?	+	?	+
Fernlund 2018	+	+	−	−	+	+	+
Fonseca 1997	?	?	?	?	+	?	+
Ganguly 2010	+	+	−	+	+	?	+
Gazvani 2000	?	?	−	?	+	?	+
Graziosi 2004	+	+	−	+	?	?	?
Hamel 2021	+	+	+	+	+	+	+
Harwood 2008	+	+	−	?	+	?	+
Ibiyemi 2018	+	+	−	−	−	?	+
Igogo 2015	?	?	−	?	+	?	+
Kaluaarachchi 2015	?	?	−	?	+	?	+
Karlsen 2001	?	+	−	?	+	?	+
Kashif 2020	?	?	−	?	+	?	+
Kittiwatanakul 2012	+	+	−	?	+	?	+
Kong 2013	+	+	−	?	+	?	+
Kovavisarach 2002	?	?	?	?	+	?	+
Kyaw 2015	+	?	−	?	+	?	+
Lee 2001	+	+	−	?	−	−	+
Lister 2005	+	+	+	?	+	?	+
Machtinger 2002	?	?	−	?	?	?	+
Machtinger 2004	?	?	−	?	+	?	?
Montesinos 2011	+	+	−	?	−	−	?
Moodliar 2005	+	+	−	?	+	?	+
Muffley 2002	+	+	−	?	+	?	?
Nadarajah 2014	+	+	−	−	+	?	+
Nasreen 2009	?	?	−	?	−	?	+
Ngai 2001	+	+	−	?	+	?	+
Nielsen 1995	+	+	−	?	+	?	+
Nielsen 1999	?	?	−	−	+	?	+
Niinimaki 2006	+	+	−	?	+	?	+
Nwafor 2020	+	+	−	−	+	?	+
Patua 2013	+	?	−	+	+	?	+
Pereira 2006	?	?	−	−	+	?	+
Phusaanantakul 2010	+	+	+	+	+	−	+
Sahin 2001	?	?	−	?	+	?	+
Salam 2016	?	?	?	?	+	?	+
Schreiber 2018	+	+	−	+	+	+	+
Schwarzler 2003	?	?	−	?	+	?	+
Shaheen 2017	?	?	−	−	+	?	+
Shaikh 2008	?	?	−	?	+	?	+
Shelley 2005	+	+	−	?	+	?	+
Shuaib 2013	?	?	−	?	+	?	+
Shwekerela 2007	+	+	−	?	+	?	+
Sinha 2018	+	+	+	+	+	+	+
Stockheim 2006	+	+	−	?	+	?	+

Figure 3. (Continued)

Allocation

Adequate sequence generation was found to have been used in 49 of 78 trials (63%) and these trials were judged to be at low risk of bias. In 29 of 78 trials (37%) the description of sequence generation was not clearly stated and hence they were at unclear risk of bias. In 47 of 78 trials (60%) there was a clear description of adequate allocation concealment. However, in 31 of 78 trials (40%) the description of allocation concealment was inadequate and so these trials were at unclear risk of bias. Many of the trials with inadequate information about sequence generation or allocation concealment were abstracts or other forms of short communications, which had limited word counts. Most of the trials which had inadequate description of random sequence generation also gave inadequate information regarding allocation concealment.

Blinding

Only 9 of 78 trials (12%) had blinding of participants and personnel and hence were judged to be at low risk of bias. Four of 78 trials (5%) had unclear information regarding blinding of patients and personnel and were therefore judged to be at unclear risk of bias with the remaining 65 of 78 trials (83%) unblinded to either patients or personnel or both and therefore at high risk of bias. In the majority of these unblinded trials, the nature of the intervention and comparator, for example with misoprostol versus suction curettage, meant blinding was not practically possible rather than being a result of poor trial design. Blinding of the outcome assessor of the primary outcome of complete miscarriage was inadequately described in 56 of 78 trials (72%) meaning these were judged to be at unclear risk of bias. In 9 of 78 trials (12%) the outcome assessor was unblinded meaning these were at high risk of bias. Only in 12 of 78 trials (15%) was it clearly stated that the outcome assessor was blinded meaning these trials were at low risk of bias.

Incomplete outcome data

There were 66 of 78 trials (85%) that had minimal missing outcome data (less than 10%) and balanced in numbers across intervention groups with similar reasons for missing data across groups, and were therefore at low risk of attrition bias. Nine of 78 trials (12%) were judged to be at high risk of attrition bias due to losing over 10% of their participant population to follow up. Three of 78 trials (3%) were judged to be at unclear risk of attrition bias as not enough

information was provided to assess whether or not the handling of incomplete data was appropriate.

Selective reporting

Only eight of 78 trials (10%) pre-specified all outcomes in publicly available study protocols and were judged to be at low risk of reporting bias. Three of 78 trials (4%) did not report all pre-specified outcomes as reported in their published protocols or methodology within the main report and were judged to be at high risk of bias for selective reporting. For most trials (67 of 78 trials; 86%), we were unable to identify a published protocol and the risk of reporting bias was judged to be unclear.

Other potential sources of bias

In 73 of 78 trials (94%) there were no other potential sources of bias detected and so these were judged to be at low risk of bias. Five of 78 trials (6%) were judged to be at unclear risk of bias; one because it was not explained why one arm of the trial was greater than 50% larger than the other arm despite random allocation and no indication of randomisation other than in a 1:1 ratio, one because a vaginal lubricant was co-administered with the vaginal misoprostol for some participants which the authors acknowledge may have affected the rate of absorption of the medication, one because the method of outcome assessment varied between sites where the trial was conducted, and one because the research group accepted a donation of £20,000 from Exelgyn, the manufacturers of mifepristone. The majority of comparisons contained less than 10 studies, therefore investigation of publication bias was not valid. The comparison of suction aspiration vs misoprostol for the outcomes of nausea, vomiting and diarrhoea were downgraded for publication bias.

Overall risk of bias

For the comparison of suction aspiration versus misoprostol, 7 of 23 (30%) trials were judged to be at high overall risk of bias, and 16 of 23 (70%) trials at low overall risk of bias. For the comparison of suction aspiration versus dilatation & curettage, 2 of 5 (40%) trials were judged to be at high overall risk of bias, and 3 of 5 (60%) at low overall risk of bias. For the comparison of misoprostol versus mifepristone plus misoprostol, 2 of 7 (29%) trials were judged to be at high overall risk of bias, and 5 of 7 (71%) at low overall risk of bias. For the comparison of misoprostol versus dilatation & curettage,

2 of 4 (50%) trials were judged to be at high overall risk of bias, and 2 of 4 (50%) at low overall risk of bias. For the comparison of misoprostol versus suction aspiration plus cervical preparation, the single trial was judged to be at high overall risk of bias. For the comparison of misoprostol versus expectant or placebo, 1 of 10 (10%) trials were judged to be at high overall risk of bias, and 9 of 10 (90%) at low overall risk of bias. For the comparison of mifepristone plus misoprostol versus expectant or placebo, 1 of 3 (33%) trials were judged to be at high overall risk of bias, and 2 of 3 (67%) at low overall risk of bias. For the comparison of suction aspiration versus mifepristone plus misoprostol, suction aspiration versus expectant or placebo, and dilatation & curettage versus expectant or placebo, all trials were judged to be at low overall risk of bias.

Effects of interventions

See: **Summary of findings 1** Complete miscarriage; **Summary of findings 2** Complete miscarriage (missed miscarriage subgroup); **Summary of findings 3** Complete miscarriage (incomplete miscarriage subgroup); **Summary of findings 4** Composite outcome of death or serious complication; **Summary of findings 5** Need for unplanned/emergency surgical procedure; **Summary of findings 6** Pain scores (visual analogue scale); **Summary of findings 7** Pelvic inflammatory disease, sepsis or endometritis; **Summary of findings 8** Days of bleeding; **Summary of findings 9** Women's views/satisfaction

See: Summary of findings 1 for the main comparison "complete miscarriage" and Summary of findings 4 for the second primary outcome "composite outcome of death or serious complication". Summary of findings 5, Summary of findings 6, Summary of findings 7, Summary of findings 8 and Summary of findings 9, present the effects of interventions from other important secondary outcomes such as "need for unplanned/ emergency surgical procedure", "pain scores (visual analogue scale)", "pelvic inflammatory disease, sepsis or endometritis", "days of bleeding", "women's views or satisfaction" respectively. Summary of findings 2 and Summary of findings 3 present the effects of the subgroup analyses of women with a missed miscarriage and women with an incomplete miscarriage respectively for the primary outcome of "complete miscarriage".

Please note that all of the analyses presented in the Data and analyses section relate to the 'direct evidence' and were used as per our methods to grade the evidence. The results from Data and analyses were also used to check the direction of effect in the subgroups, and subgroup analyses are presented for the outcome of complete miscarriage where a high level of global statistical inconsistency and heterogeneity was observed.

The following section presents the results as reported in all of the figures (Figure 4 to Figure 5). The figures present the results from the network diagrams, the forest plots with the pairwise, indirect and network (combining direct and indirect) effect estimates and the cumulative rankograms for all the outcomes with available data. The figures present the results for different methods for managing miscarriage in comparison to expectant management or placebo and different methods for managing miscarriage.

Figure 4. Network diagram for outcome of complete miscarriage. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Figure 5. Cumulative rankogram comparing each of the methods of management of a miscarriage for incomplete miscarriage subgroup analysis for the outcome of complete miscarriage. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.

Primary outcomes

Complete miscarriage

The network diagram for the outcome of complete miscarriage is presented in Figure 4. Misoprostol was the most frequently investigated method of miscarriage management (45 of 63 trial arms [71%]) for this outcome (Figure 4).

Relative effects from the network meta-analysis of 59 trials, suggested that suction aspiration plus cervical preparation (risk ratio (RR) 2.12, 95% confidence interval (CI) 1.41 to 3.20, *low-certainty evidence*), dilatation and curettage (RR 1.49, 95% CI 1.26 to 1.75, *low-certainty evidence*), suction aspiration (RR 1.44, 95% CI 1.29 to 1.62, *low-certainty evidence*), mifepristone plus misoprostol (RR 1.42, 95% CI 1.22 to 1.66, *moderate-certainty evidence*) and misoprostol (RR 1.30, 95% (CI) 1.16 to 1.46, *low-certainty evidence*) may be more effective in achieving complete miscarriage compared with expectant management or placebo (Figure 6; Summary of findings 1).

Figure 6. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of complete miscarriage.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	1.27 (1.08, 1.48)
Indirect	1.72 (1.44, 2.06)
Network	1.44 (1.29, 1.62)
Suction aspiration plus cervical preparation vs Expectant or placebo	
Network	2.12 (1.41, 3.20)
Misoprostol vs Expectant or placebo	
Direct	1.85 (1.35, 2.55)
Indirect	1.14 (0.99, 1.31)
Network	1.30 (1.16, 1.46)
Mifepristone plus misoprostol vs Expectant or placebo	
Direct	1.59 (1.01, 2.51)
Indirect	1.40 (1.16, 1.70)
Network	1.42 (1.22, 1.66)
Dilatation & curettage vs Expectant or placebo	
Direct	1.25 (1.12, 1.39)
Indirect	1.55 (1.29, 1.86)
Network	1.49 (1.26, 1.75)
Suction aspiration vs Suction aspiration plus cervical preparation	
Network	0.68 (0.46, 1.01)
Suction aspiration vs Misoprostol	
Direct	1.07 (1.05, 1.10)
Indirect	1.05 (0.89, 1.24)
Network	1.11 (1.04, 1.19)
Suction aspiration vs Mifepristone plus misoprostol	
Direct	1.29 (0.96, 1.73)
Indirect	0.94 (0.81, 1.08)
Network	1.01 (0.89, 1.16)
Suction aspiration vs Dilatation & curettage	
Direct	1.02 (0.99, 1.06)
Indirect	0.89 (0.72, 1.09)
Network	0.97 (0.85, 1.10)
Misoprostol vs Suction aspiration plus cervical preparation	
Direct	0.61 (0.52, 0.72)
Network	0.61 (0.41, 0.91)
Misoprostol vs Mifepristone plus misoprostol	
Direct	0.87 (0.79, 0.97)
Indirect	0.99 (0.80, 1.22)
Network	0.91 (0.81, 1.03)
Misoprostol vs Dilatation & curettage	
Direct	0.73 (0.57, 0.93)
Indirect	0.96 (0.81, 1.13)
Network	0.87 (0.77, 1.00)
Mifepristone plus misoprostol vs Suction	

Figure 6.   (Continued)

Based on these results, about 640 per 1000 women having expectant management or placebo would have a complete miscarriage compared with 1000 having suction aspiration plus cervical preparation, 954 for dilatation and curettage, 922 for suction aspiration, 909 for mifepristone plus misoprostol and 832 per 1000 women for misoprostol (Summary of findings 1).

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for completing a miscarriage are shown in Figure 7. Treatment hierarchies are presented with the surface under the cumulative ranking curve (SUCRA); the larger the SUCRA the higher its rank among all available methods of managing a miscarriage. Ranking indicates the cumulative probability of being the best method of managing a miscarriage, the second best, the third best, etc. A SUCRA of 100% means the method of miscarriage management is the best and a SUCRA of 0% means the method of miscarriage management is the worst. The highest ranked method for managing a miscarriage was suction aspiration plus cervical preparation (SUCRA 98.2%), followed by dilatation and curettage (SUCRA 68.2%), and suction aspiration (SUCRA 58.4%). Mifepristone plus misoprostol ranked fourth (53.2%), followed by misoprostol (SUCRA 22.1%), and expectant management or placebo (SUCRA 0%) coming last.

Figure 7. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of complete miscarriage. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
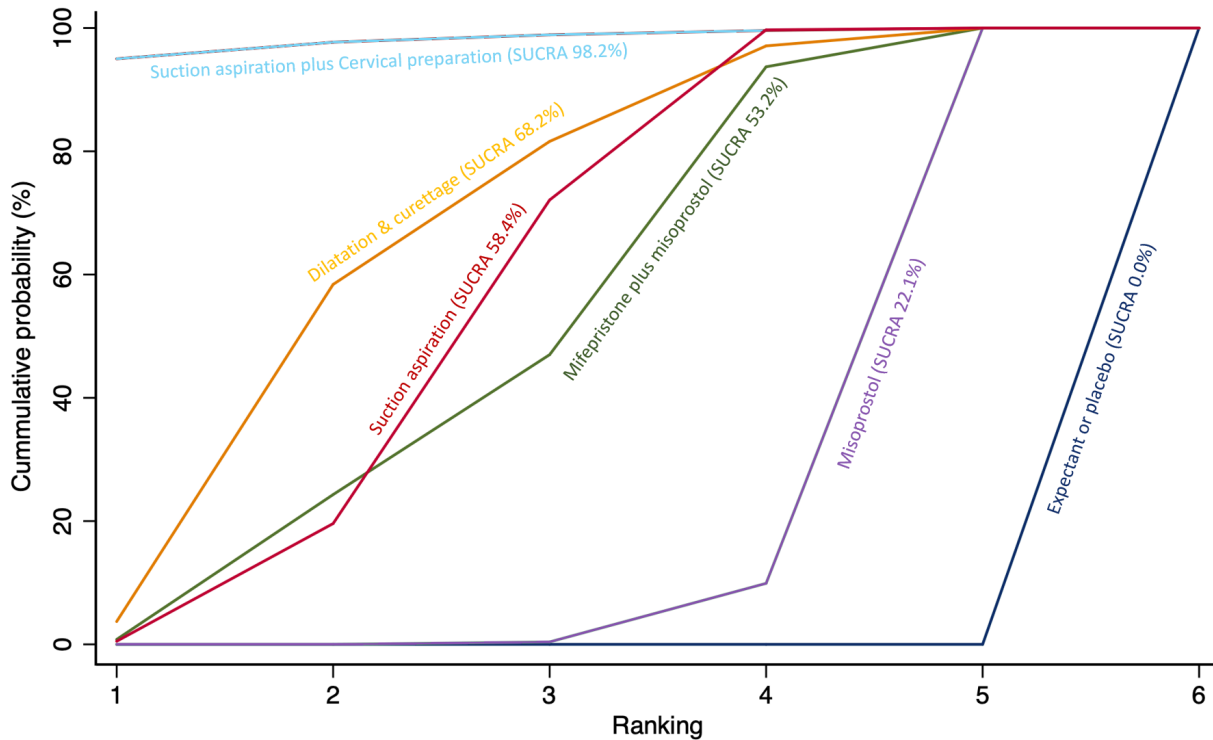
Composite outcome of death or serious complication

The network diagram for the composite outcome of death or serious complications is presented in Figure 8. Misoprostol was the most frequently investigated method of miscarriage management (24 of 37 trial arms [65%]) for this outcome (Figure 8). This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 8. Network diagram for outcome of composite outcome of death or serious complication. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
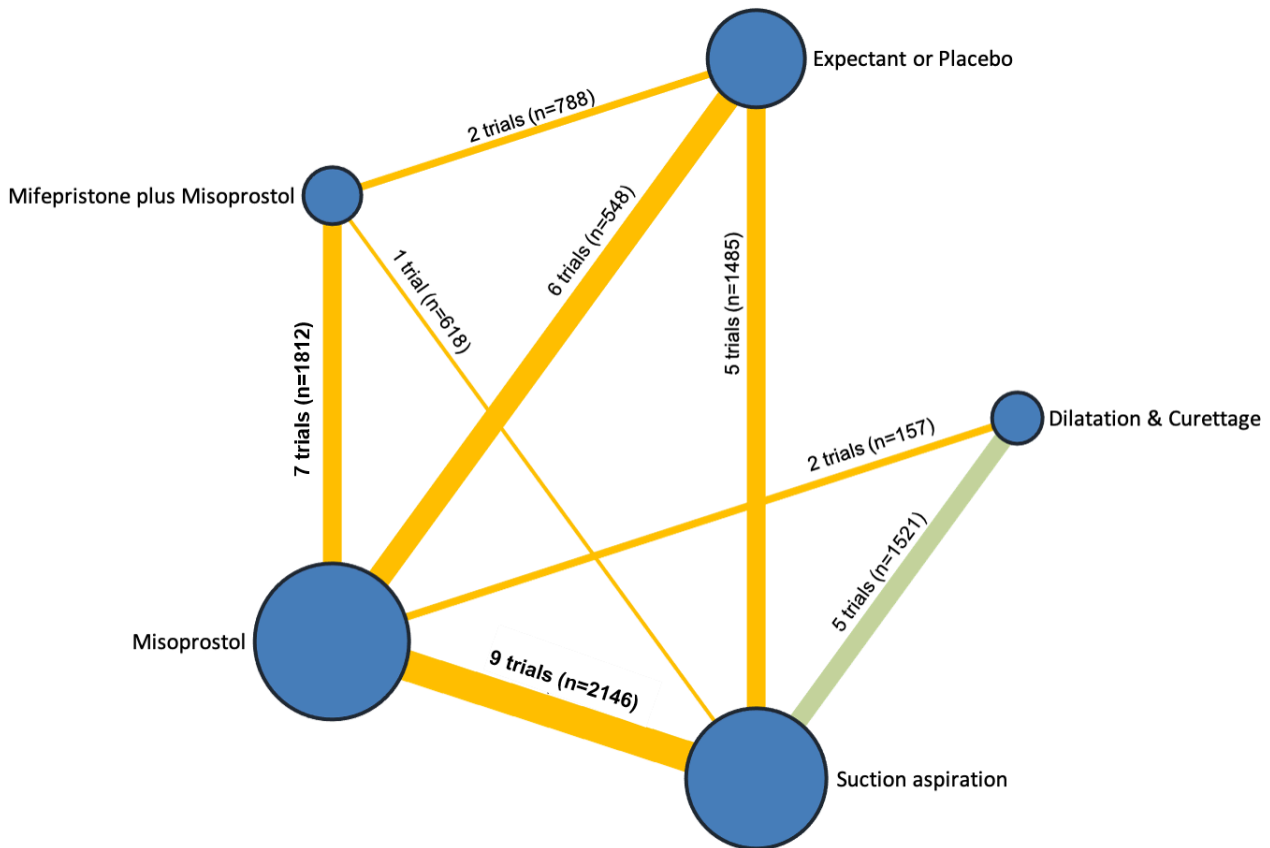
Relative effects from the network meta-analysis of 35 trials suggest that dilatation and curettage (RR 0.43, 95% CI 0.17 to 1.06, *low-certainty evidence*), suction aspiration (RR 0.55, 95% CI 0.23 to 1.32, *low-certainty evidence*), misoprostol (RR 0.50, 95% CI 0.22 to 1.15, *low-certainty evidence*) and mifepristone plus misoprostol (RR 0.76, 95% CI 0.31 to 1.84, *low-certainty evidence*) were compatible with a wide range of treatment effects for death and serious complications compared with expectant management or placebo (Figure 9 Summary of findings 4).

Figure 9.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of composite outcome of death or serious complication.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	0.43 (0.12, 1.53)
Indirect	0.97 (0.21, 4.40)
Network	0.55 (0.23, 1.32)
Misoprostol vs Expectant or placebo	
Direct	0.96 (0.06, 15.08)
Indirect	0.35 (0.13, 0.97)
Network	0.50 (0.22, 1.15)
Mifepristone plus misoprostol vs Expectant or placebo	
Direct	0.46 (0.13, 1.63)
Indirect	1.38 (0.37, 5.17)
Network	0.76 (0.31, 1.84)
Dilatation & curettage vs Expectant or placebo	
Network	0.43 (0.17, 1.06)
Suction aspiration vs Misoprostol	
Direct	1.53 (0.45, 5.16)
Indirect	0.95 (0.42, 2.16)
Network	1.11 (0.58, 2.11)
Suction aspiration vs Mifepristone plus misoprostol	
Direct	0.14 (0.01, 2.74)
Indirect	0.74 (0.27, 2.06)
Network	0.73 (0.30, 1.80)
Suction aspiration vs Dilatation & curettage	
Direct	1.27 (0.80, 2.02)
Indirect	1.52 (0.45, 5.11)
Network	1.29 (0.85, 1.98)
Misoprostol vs Mifepristone plus misoprostol	
Direct	0.50 (0.20, 1.25)
Indirect	1.09 (0.24, 5.03)
Network	0.66 (0.32, 1.36)
Misoprostol vs Dilatation & curettage	
Direct	1.26 (0.54, 2.97)
Indirect	1.05 (0.40, 2.78)
Network	1.16 (0.61, 2.21)
Dilatation & curettage vs Mifepristone plus	

Figure 9. (Continued)

Dilatation & curettage vs Mifepristone plus misoprostol

Network — 0.57 (0.23, 1.41)

.1   1   10

Favours intervention   Favours comparator

It should be noted that death was rare (no deaths across all trials were reported). The reported complications comprised mainly of blood transfusions, but also uterine perforation, need for further life-saving procedures such as hysterectomy (not including surgical completion of miscarriage as a second line intervention as this is reported in the secondary outcome of need for unplanned/emergency surgical procedure), or intensive care unit admission.

Based on these results, about 19 per 1000 women given expectant management or placebo for their miscarriage would experience death or a serious complication compared with 8 per 1000 having dilation and curettage, 10 for suction aspiration, 10 for misoprostol

and 14 per 1000 for mifepristone plus misoprostol (Summary of findings 4).

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the composite outcome of death or serious complication are shown in Figure 10. The highest ranked method for managing a miscarriage for the composite outcome of death or serious complication was dilatation and curettage (SUCRA 84.4%), followed by misoprostol (SUCRA 70.1%), suction aspiration (SUCRA 52.9%), with mifepristone plus misoprostol (SUCRA 31.2%) ranked fourth and expectant management or placebo (SUCRA 10.9%) last.

Figure 10. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of composite outcome of death or serious complication. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
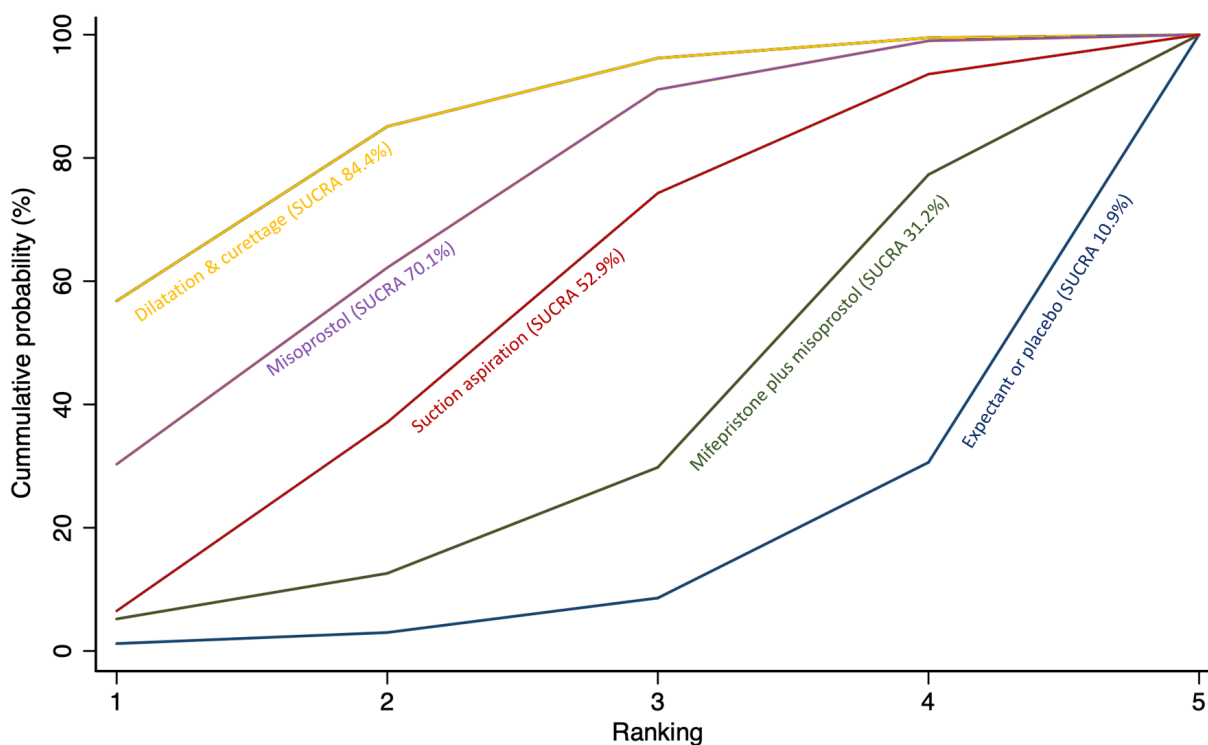
Secondary Outcomes

Need for unplanned/emergency surgical procedure

The network diagram for the outcome of need for unplanned/ emergency surgical procedure is presented in Figure 11. 30 trial

arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 11.   Network diagram for outcome of need for unplanned/ emergency surgical procedure. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
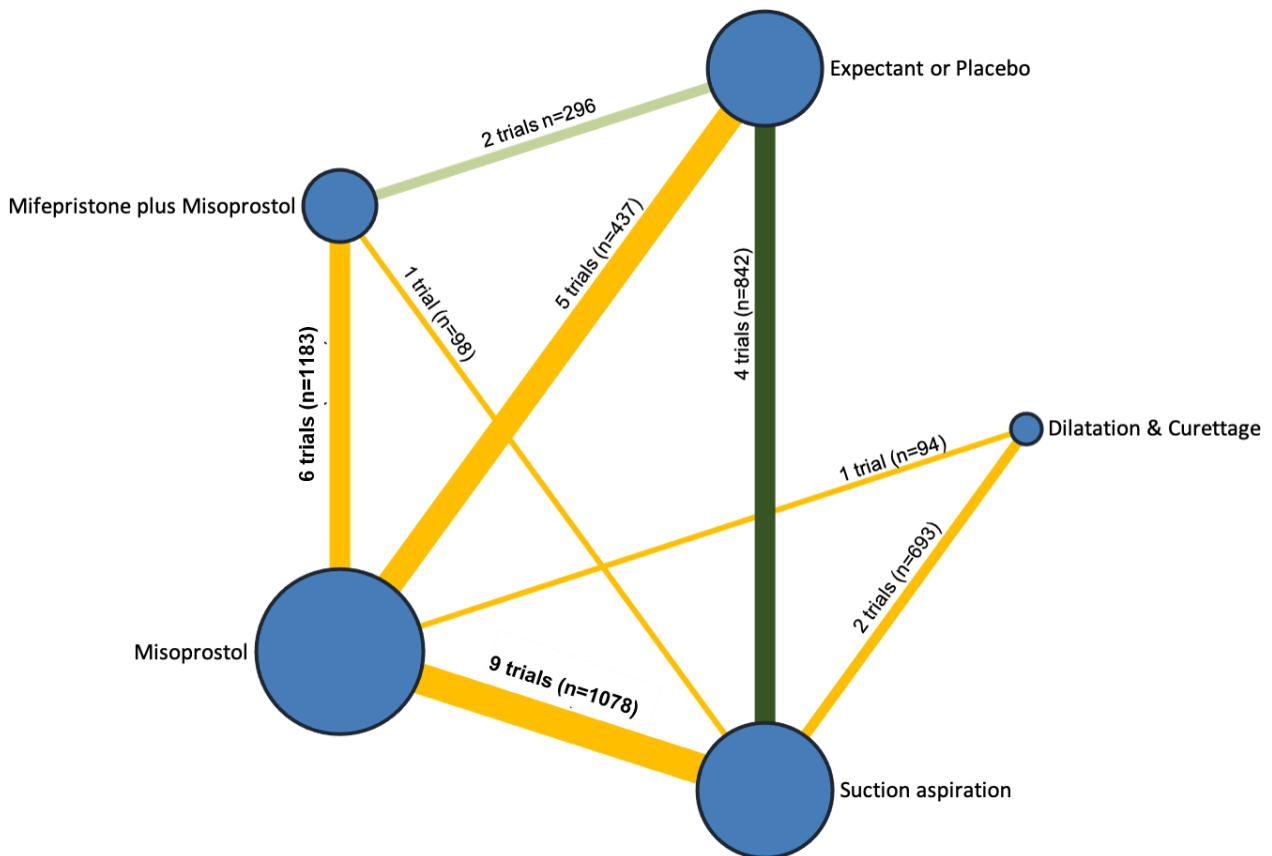
Relative effects from the network meta-analysis of 28 trials, suggest that suction aspiration (RR 0.37, 95% CI 0.22 to 0.65, *moderate-certainty evidence*) probably reduces the need for unplanned/ emergency surgical procedures when compared with expectant management or placebo. For mifepristone plus misoprostol (RR 0.64, 95% CI 0.33 to 1.23, *low-certainty evidence*) we cannot rule out

an important benefit for this outcome. For dilatation and curettage (RR 0.80, 95% CI 0.09 to 7.02, *very low-certainty evidence*) and misoprostol (RR 1.04, 95% CI 0.56 to 1.95, lo*w-certainty evidence*), results are compatible with a wide range of treatment effects (Figure 12, Summary of findings 5).

Figure 12. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of need for unplanned/ emergency surgical procedure.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	0.51 (0.30, 0.87)
Indirect	0.13 (0.05, 0.35)
Network	0.37 (0.22, 0.65)
Misoprostol vs Expectant or placebo	
Direct	0.67 (0.23, 1.95)
Indirect	1.28 (0.61, 2.66)
Network	1.04 (0.56, 1.95)
Mifepristone plus misoprostol vs Expectant or placebo	
Direct	0.32 (0.11, 0.90)
Indirect	0.91 (0.43, 1.93)
Network	0.64 (0.33, 1.23)
Dilatation & curettage vs Expectant or placebo	
Network	0.80 (0.09, 7.02)
Suction aspiration vs Misoprostol	
Direct	0.20 (0.10, 0.38)
Indirect	0.85 (0.35, 2.07)
Network	0.36 (0.20, 0.64)
Suction aspiration vs Mifepristone plus misoprostol	
Direct	1.00 (0.06, 15.54)
Indirect	0.57 (0.29, 1.10)
Network	0.59 (0.31, 1.11)
Suction aspiration vs Dilatation & curettage	
Direct	0.33 (0.01, 8.07)
Indirect	0.36 (0.01, 18.96)
Network	0.46 (0.06, 3.85)
Misoprostol vs Mifepristone plus misoprostol	
Direct	1.55 (1.22, 1.96)
Indirect	4.28 (1.28, 14.30)
Network	1.64 (1.12, 2.39)
Misoprostol vs Dilatation & curettage	
Indirect	1.45 (0.11, 18.81)
Network	1.30 (0.15, 11.11)
Dilatation & curettage vs Mifepristone plus	

Figure 12.   (Continued)

Dilatation & curettage vs Mifepristone plus misoprostol
Network   1.26 (0.14, 11.05)

Favours intervention   Favours comparator

Based on these results, about 120 per 1000 women given expectant management or placebo for their miscarriage would experience unplanned or emergency surgical procedures compared with 44 per 1000 women for suction aspiration, 77 for mifepristone plus misoprostol, 96 for dilatation and curettage and 125 per 1000 women having for misoprostol (Summary of findings 5).

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the need for unplanned/ emergency surgical procedure are shown in Figure 13. The highest ranked method for managing a miscarriage was suction aspiration (SUCRA 92.6%), followed by mifepristone plus misoprostol (SUCRA 64.8%), with dilatation and curettage (SUCRA 43.1%) ranked third, expectant management or placebo (SUCRA 26.6%) fourth and misoprostol (SUCRA 3.0%) last.

Figure 13.   Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of need for unplanned/ emergency surgical procedure. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
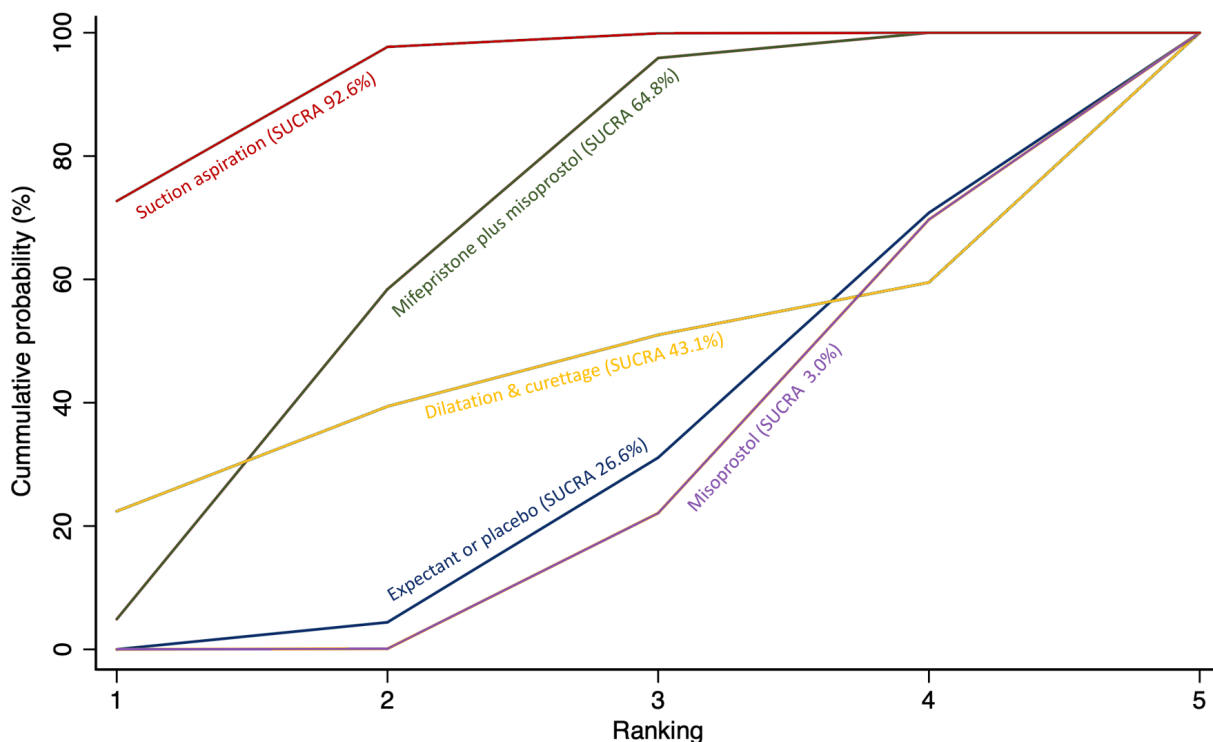
Pain scores (visual analogue scale)

The network diagram for the outcome of pain scores (visual analogue scale) is presented in Figure 14. 13 trials contributed

towards this outcome. This outcome was not reported for any trial involving suction curettage plus cervical preparation.

Figure 14. Network diagram for outcome of pain score (visual analogue scale). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Due to the small number of trials reporting this outcome, network meta-analysis was not possible, and so were unable to produce network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis (Data and analyses).

Pairwise meta-analysis of three trials found misoprostol may cause a slightly higher pain score compared to expectant management or placebo (standardised mean difference (SMD) 0.33, 95% CI 0.08 to 0.57, *low-certainty evidence*) (Analysis 8.4). One further trial compared mifepristone plus misoprostol to expectant management or placebo but we cannot rule out a small difference in pain scores for this comparison (SMD 0.14, 95% CI -0.21 to 0.50, *low-certainty evidence*) (Analysis 10.4).

Pelvic Inflammatory disease, sepsis or endometritis

The network diagram for the outcome of pelvic inflammatory disease, sepsis or endometritis is presented in Figure 15. 41 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

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Figure 15. Network diagram for outcome of pelvic inflammatory disease, sepsis or endometritis. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
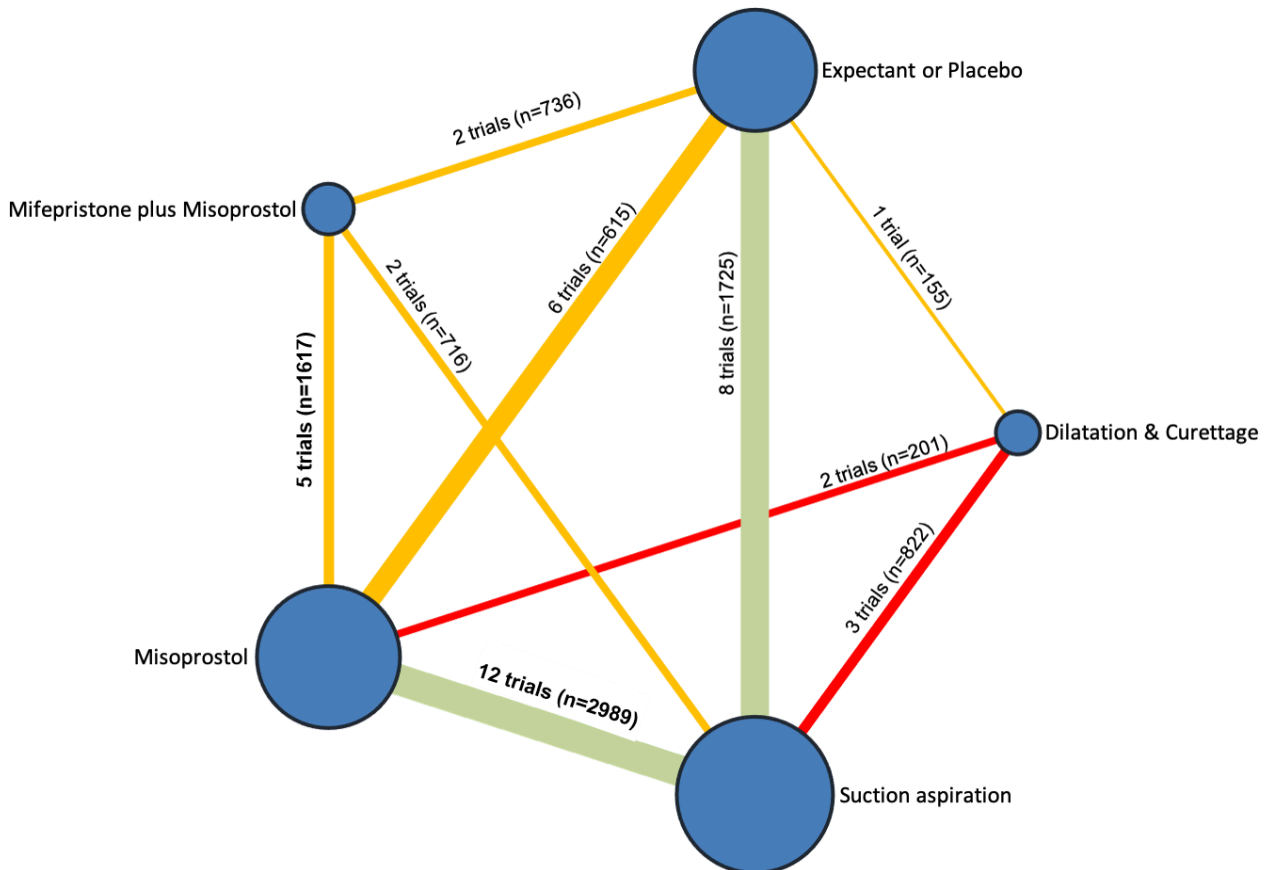
Relative effects from the network meta-analysis of 39 trials, suggest that mifepristone plus misoprostol (RR 0.90, 95% CI 0.48 to 1.68, *low-certainty evidence*), misoprostol (RR 1.08, 95% CI 0.62 to 1.88, *moderate-certainty evidence*) and suction aspiration (RR 1.42, 95% CI 0.88 to 2.28, *moderate-certainty evidence*) were compatible with a wide range of treatment effects for pelvic inflammatory disease, sepsis or endometritis when compared with expectant management or placebo. However, dilatation and curettage (RR 1.85, 95% CI 1.05 to 3.25, *very low-certainty evidence*) may increase the risk of pelvic inflammatory disease, sepsis or endometritis when compared with expectant management or placebo, but the evidence is very uncertain (Figure 16, Summary of findings 7).

Figure 16.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of pelvic inflammatory disease, sepsis or endometritis.
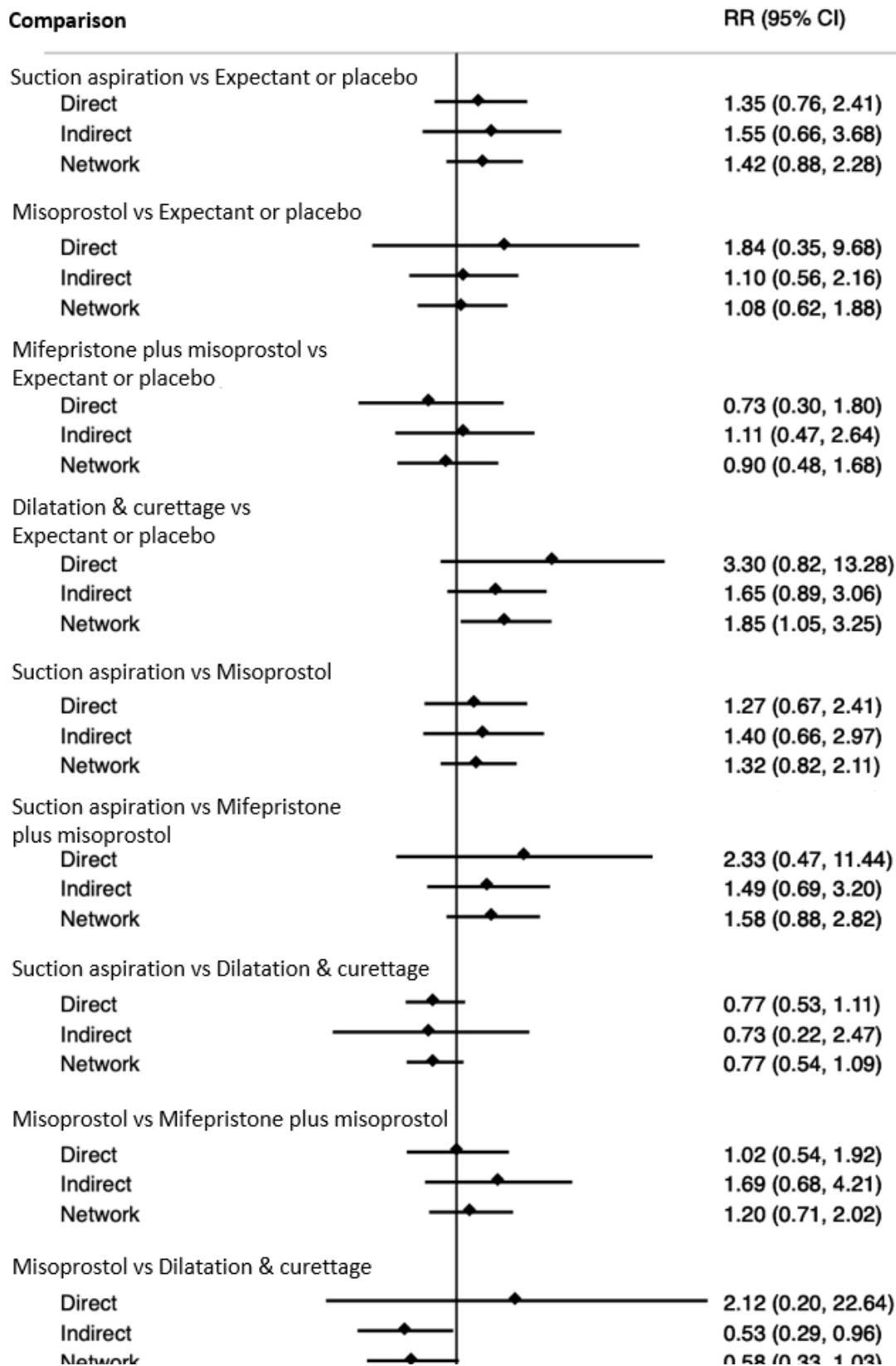
Figure 16. (Continued)
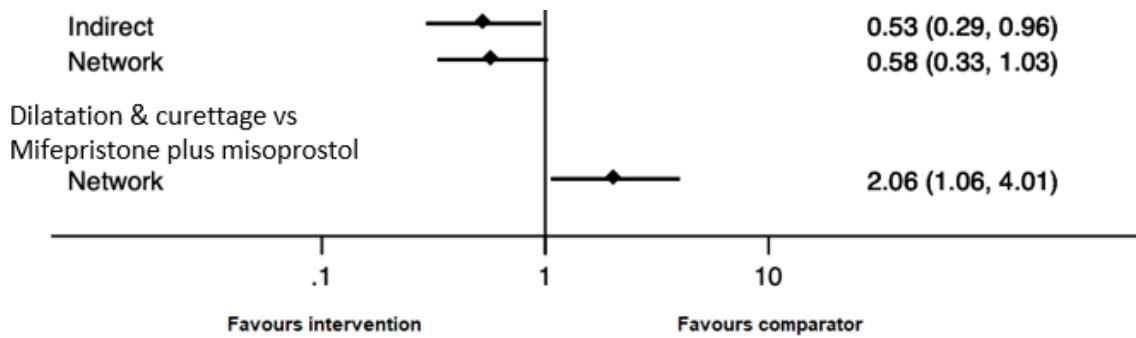
Based on these results, about 36 per 1000 women given expectant management or placebo for their miscarriage would experience pelvic inflammatory disease, sepsis or endometritis compared with 32 per 1000 women for mifepristone plus misoprostol, 39 for misoprostol, 51 for suction aspiration, and 67 per 1000 women having dilatation and curettage (Summary of findings 7).

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for pelvic inflammatory disease, sepsis or endometritis are shown in Figure 17. The highest ranked method for managing a miscarriage for the outcome of pelvic inflammatory disease, sepsis or endometritis was mifepristone plus misoprostol (SUCRA 83.4%), followed by expectant management or placebo (SUCRA 71.4%), misoprostol (SUCRA 62.7%), with suction aspiration (SUCRA 29.3%) ranked fourth and dilatation and curettage (SUCRA 3.2%) last.

Figure 17.   Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of pelvic inflammatory disease, sepsis or endometritis. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
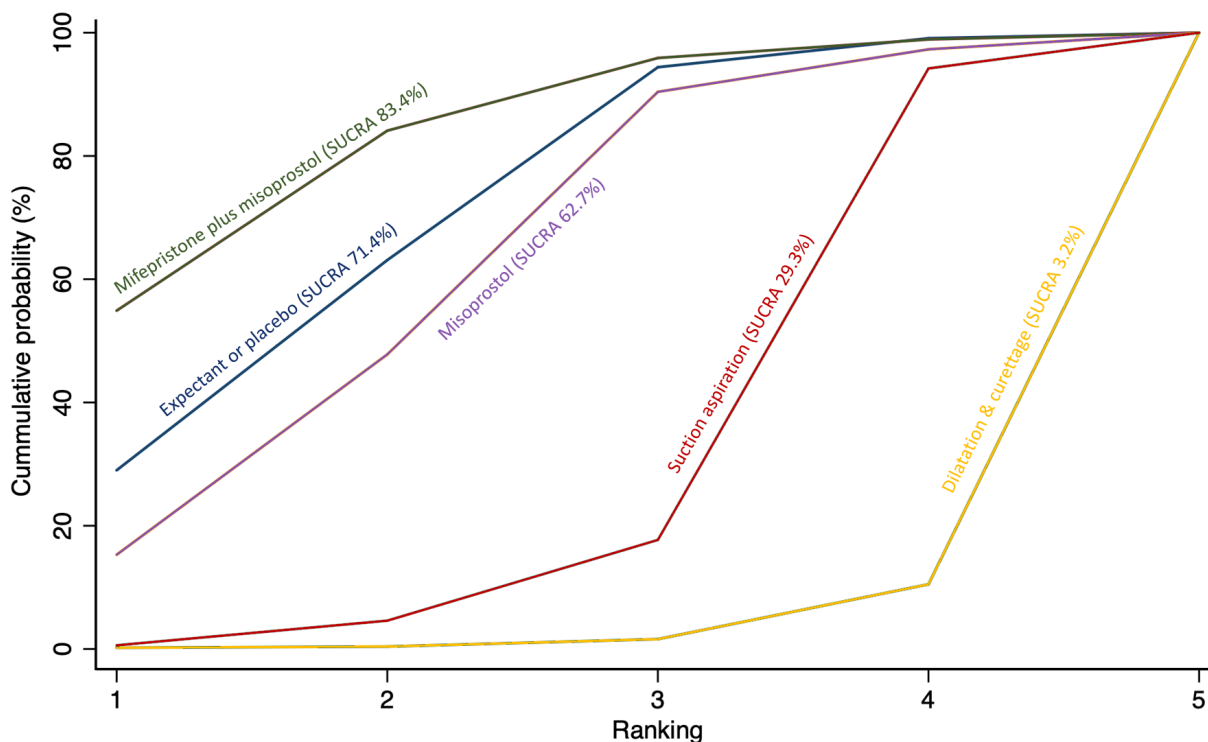
Mean volumes of blood loss (millilitres (mL)

The network diagram for the outcome of mean volumes of blood loss (mL) is presented in Figure 18. Four trials contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation. Due to the small number of trials reporting this outcome, we were unable to produce network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis. One trial found suction aspiration may cause smaller volumes of blood loss compared to expectant management or placebo (mean difference (MD) -23.00, 95% CI -40.41 to -5.59).

Figure 18. Network diagram for outcome of mean volumes of blood loss (millilitres). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. Multi-arm trials contribute to more than one comparison.

Change in haemoglobin measurements before and after the miscarriage

The network diagram for the outcome of change in haemoglobin measurements before and after the miscarriage is presented in Figure 19. 15 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

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Figure 19. Network diagram for outcome of change in haemoglobin measurements before and after the miscarriage. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 13 trials, suggest that dilatation and curettage (MD 0.50, 95% CI 0.06 to 0.93, *low-certainty evidence*) may cause a change in haemoglobin measurement before and after the miscarriage when compared with expectant management or placebo. Misoprostol (MD 0.25, 95% CI -0.01 to 0.52, *low-certainty evidence*) and mifepristone plus misoprostol (MD 0.23, 95% CI -0.23 to 0.70, *moderate-*certainty evidence*) may make little or no difference to this outcome when compared to expectant management or placebo. Suction aspiration (MD 0.09, 95% CI -0.15 to 0.32, *very low-certainty evidence*) makes little or no difference to this outcome when compared with expectant management or placebo, but the evidence is very uncertain (Figure 20).

Figure 20.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of change in haemoglobin measurements before and after the miscarriage.
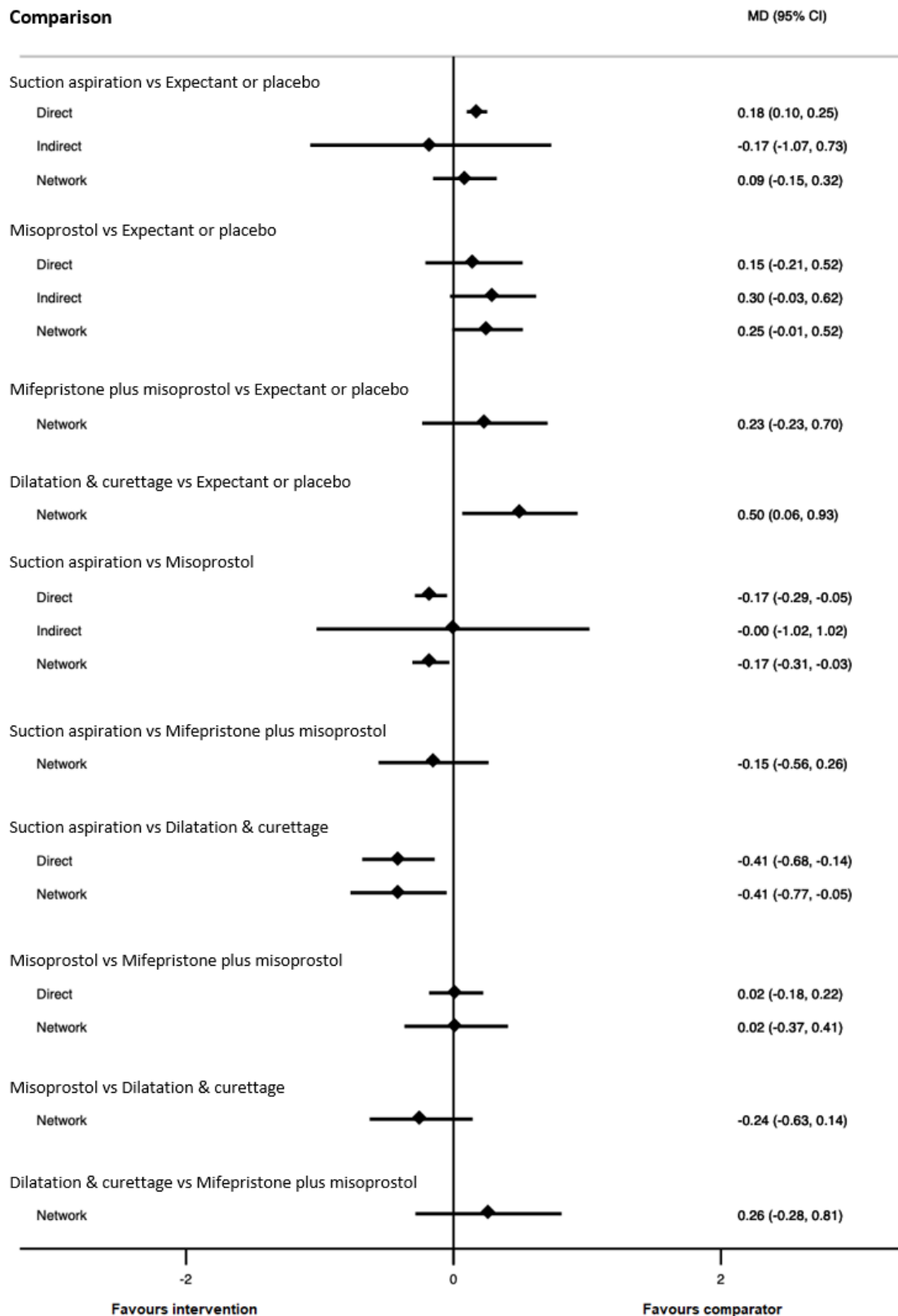
Figure 20. (Continued)

Favours intervention   Favours comparator

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of change in haemoglobin measurements before and after the miscarriage are shown in Figure 21. The highest ranked method for managing a miscarriage for the outcome of change in haemoglobin measurements before and after the miscarriage was expectant management or placebo (SUCRA 88.2%), followed by suction aspiration (SUCRA 74.1%), mifepristone plus misoprostol (SUCRA 46.2%), with misoprostol (SUCRA 34.6%) ranked fourth and dilatation and curettage (SUCRA 6.9%) last.

Figure 21. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of change in haemoglobin measurements before and after the miscarriage. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
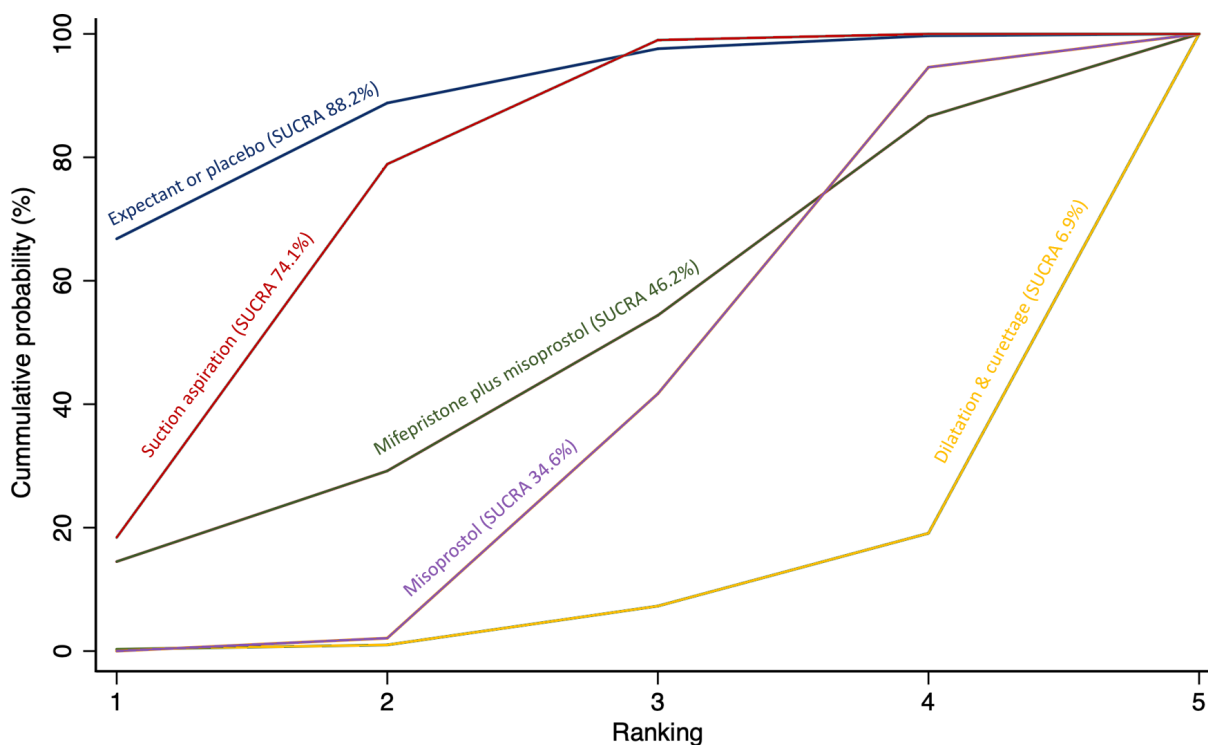
Days of bleeding

The network diagram for the outcome of days of bleeding is presented in Figure 22. 20 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 22.   Network diagram for outcome of days of bleeding. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 18 trials suggest that dilatation and curettage (MD -1.96, 95% CI -3.48 to -0.45, *low-certainty evidence*) may cause less days of bleeding when compared with expectant management or placebo. Suction aspiration (MD -2.00, 95% CI -3.01 to -0.99, *very low-certainty evidence*) may cause less days of bleeding when compared to expectant management or placebo, but the evidence is very uncertain. Misoprostol (MD -0.47, 95% CI -1.53 to 0.60, *very low-certainty evidence*) and mifepristone plus misoprostol (MD -0.14, 95% CI -1.71 to 1.43, *very low-certainty evidence*), were compatible with a wide range of treatment effects for days of bleeding when compared to expectant management or placebo (Figure 23, Summary of findings 8).

Figure 23.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of days of bleeding.

Comparison	MD (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	-2.75 (-4.08, -1.42)
Indirect	-0.73 (-2.12, 0.66)
Network	-2.00 (-3.01, -0.99)
Misoprostol vs Expectant or placebo	
Direct	0.32 (-2.19, 2.84)
Indirect	-0.96 (-2.27, 0.35)
Network	-0.47 (-1.53, 0.60)
Mifepristone plus misoprostol vs Expectant or placebo	
Direct	0.70 (-0.43, 1.83)
Indirect	-0.77 (-2.83, 1.30)
Network	-0.14 (-1.71, 1.43)
Dilatation & curettage vs Expectant or placebo	
Direct	-1.26 (-2.27, -0.25)
Indirect	-2.47 (-4.47, -0.46)
Network	-1.96 (-3.48, -0.45)
Suction aspiration vs Misoprostol	
Direct	-1.13 (-1.83, -0.42)
Indirect	-2.96 (-4.59, -1.33)
Network	-1.54 (-2.35, -0.72)
Suction aspiration vs Mifepristone plus misoprostol	
Network	-1.86 (-3.44, -0.28)
Suction aspiration vs Dilatation & curettage	
Direct	-0.30 (-1.30, 0.70)
Indirect	0.13 (-1.82, 2.08)
Network	-0.04 (-1.50, 1.43)
Misoprostol vs Mifepristone plus misoprostol	
Direct	0.02 (-0.03, 0.07)
Indirect	-1.35 (-4.00, 1.30)
Network	-0.32 (-1.77, 1.12)
Misoprostol vs Dilatation & curettage	
Direct	2.60 (1.27, 3.93)
Indirect	0.89 (-0.93, 2.71)
Network	1.50 (0.01, 2.99)
Dilatation & curettage vs Mifepristone plus misoprostol	

Figure 23. (Continued)

Dilatation & curettage vs Mifepristone plus misoprostol
Network

-1.82 (-3.81, 0.17)

Favours intervention — Favours comparator

Based on these results, women given expectant management or placebo for their miscarriage, would experience 10 days of bleeding compared with 8 days of bleeding for women having suction aspiration, 8.04 days for women having dilatation and curettage, 9.53 days for women having misoprostol and 9.86 days of bleeding for women having mifepristone plus misoprostol (Summary of findings 8).

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of days of bleeding are shown in Figure 24. The highest ranked method for managing a miscarriage for the outcome of days of bleeding was suction aspiration (SUCRA 87.9%), followed by dilatation and curettage (SUCRA 85.1%), misoprostol (SUCRA 37.2%) with mifepristone plus misoprostol (SUCRA 24.7%) ranked fourth and expectant management or placebo (SUCRA 15.1%) last.

Figure 24. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of days of bleeding. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
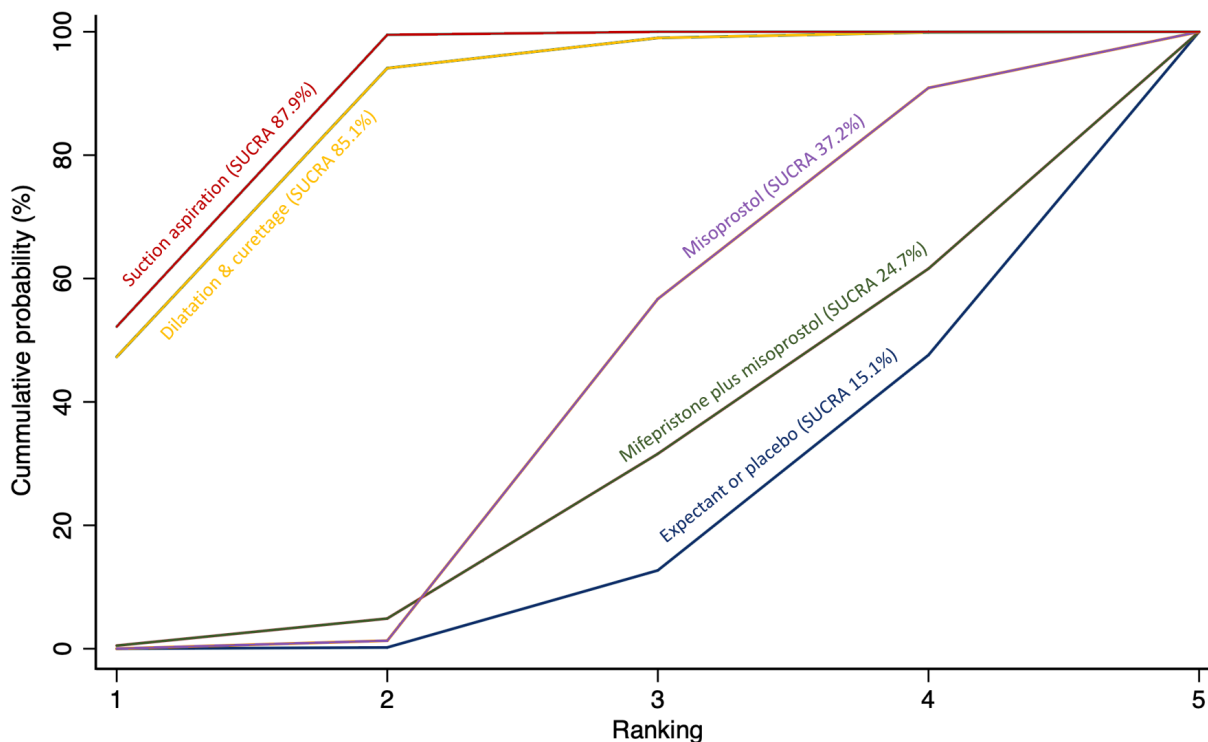
Cervical Tear

Due to the infrequency at which cervical tears occurred across all studies where it was reported, we were unable to produce a network diagram, network relative effects and a rankogram.

Direct evidence is presented only from pairwise meta-analysis. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Only eight trials reported this outcome with five reporting no cervical tears for either intervention it was comparing. The most frequently investigated intervention for this outcome was suction aspiration with seven trials out of eight. Pairwise meta-analysis suggests that we cannot rule out a substantial harm of suction aspiration compared with misoprostol (3 trials, RR 7.18, 95% CI 0.84 to 61) and substantial benefit for suction aspiration compared with dilatation and curettage (2 trials, RR 0.49, 95% CI 0.20 to 1.18) (Analysis 3.8).

Women's views or satisfaction

There was significant heterogeneity in the methods of reporting women's views or satisfaction across all the studies where it was reported and so we were unable to produce a network diagram, network relative effects and a rankogram. Direct meta-analysis was also not possible and so results are presented narratively. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Twenty-three trials reported women's views or satisfaction using varying different methods. Four trials (Bagratee 2004; Moodliar 2005; Nielsen 1999; Phusaanantakul 2010) used a visual analogue scale. Eight trials used a five-point descriptive scale (very satisfied, satisfied, neutral, dissatisfied and very dissatisfied) (Bique 2007; Chigbu 2012; Dabash 2010; Dao 2007; Montesinos 2011; Shwekerela 2007; Taylor 2011; Weeks 2005), and seven trials used a three-point descriptive scale (satisfied, neutral and dissatisfied) (Chipchase 1997; Dangalla 2012; Demetroulis 2001; Ibiyemi 2018; Lister 2005; Niinimaki 2006; Shuaib 2013.

Overall, all methods of managing a miscarriage were found to be acceptable. The most commonly investigated method of miscarriage management was misoprostol with 18 trials, followed by suction aspiration with 17 trials. The most common comparison was misoprostol versus suction aspiration with 12 trials. Of these 12 trials, Arellano 2009 examined only the side effects of the treatment options with 95% describing the side effects of misoprostol as tolerable, whereas 91% described the side effects of suction aspiration as tolerable. Sahin 2001 described women's dissatisfaction with only one woman out of 40 being dissatisfied with misoprostol, whereas 14 women out of 40 were dissatisfied with suction aspiration. The remaining 10 trials used either a five- or three-point scale of satisfaction. In total, 1389 women out of 1443 (96.3%) were either satisfied or very satisfied with misoprostol and 1350 women out of 1400 (96.4%) were either satisfied or very satisfied with suction aspiration.

Suction aspiration versus expectant management or placebo was the next most common comparison with three trials. Chipchase 1997; and Dangalla 2012 found 92 out of 96 women (98.5%) were satisfied with suction aspiration compared to 97 out of 99 women (98.0%) were satisfied with expectant management or placebo (*moderate-certainty evidence*). Nadarajah 2014 used a 10-point numerical scale and similarly found suction aspiration had a satisfaction score of 7.57 from 175 women and expectant management or placebo also had a 7.57 score from 177 women (*moderate-certainty evidence*). Two trials compared misoprostol versus expectant/placebo and misoprostol versus dilatation and curettage respectively (Summary of findings 9).

Mean duration of hospital stay (days)

The network diagram for the outcome of mean duration of hospital stay (days) is presented in Figure 25. Six trials contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 25. Network diagram for outcome of mean duration of hospital stay (days). The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. Multi-arm trials contribute to more than one comparison.

Due to the small number of trials reporting this outcome, network meta-analysis was not possible for this outcome, and so we were unable to produce a network diagram, network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis.

Pairwise meta-analysis of three trials suggests women having suction aspiration probably have a shorter mean duration of hospital stay when compared to dilatation and curettage (MD -0.56, 95% CI -0.89 to -0.23) (Analysis 3.9). One trial shows women having suction aspiration probably have a shorter mean duration of hospital stay when compared to misoprostol (MD -0.40, 95% CI -0.68 to -0.12) (Analysis 1.9). Misoprostol may have a shorter mean

duration of hospital stay compared to expectant management or placebo (MD -0.10, 95% CI -0.19 to -0.01) (Analysis 8.8). However, we cannot rule out an important benefit or harm for this outcome for the comparison between suction aspiration versus expectant management or placebo (MD 0.99, 95% CI 0.74 to 1.24) (Analysis 4.9).

Readmission to hospital

The network diagram for the outcome of readmission to hospital is presented in Figure 26. Twelve trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 26. Network diagram for outcome of readmission to hospital. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
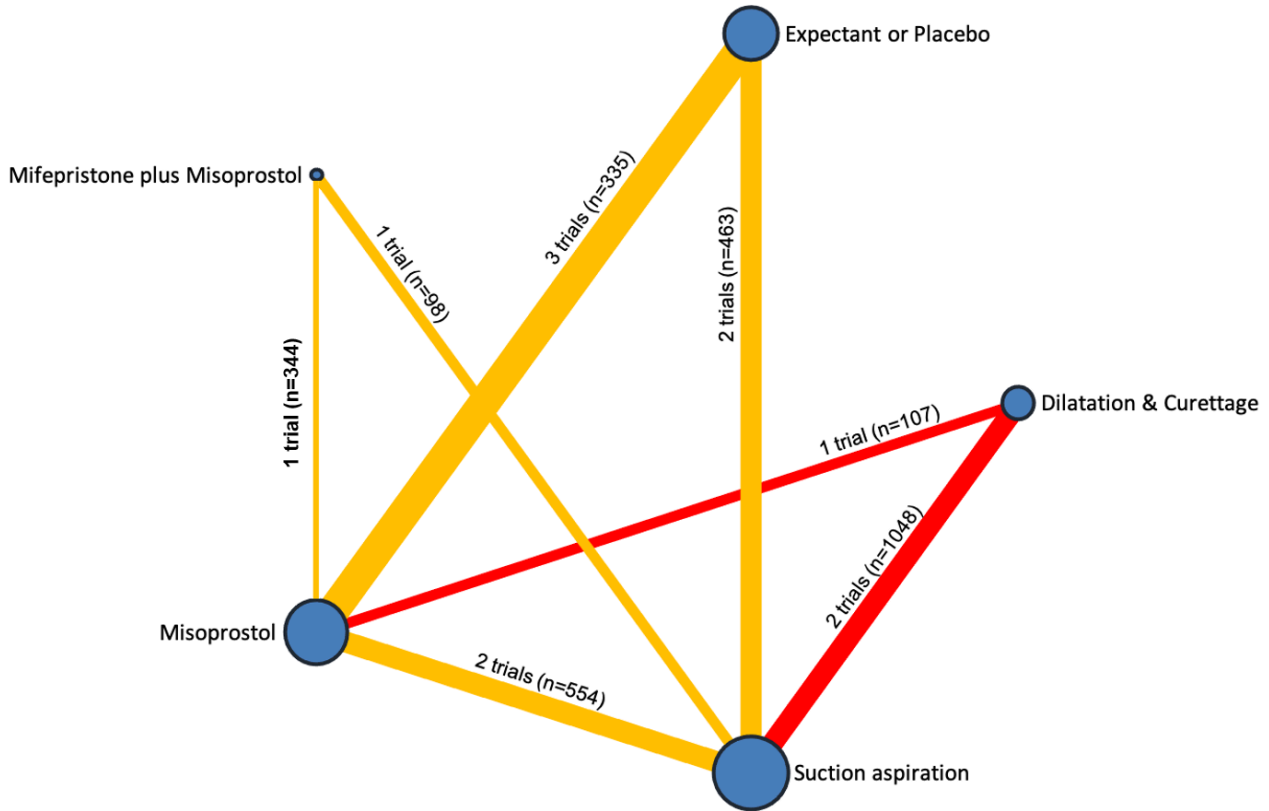
Relative effects from the network meta-analysis of 10 trials suggest that for suction aspiration (RR 0.50, 95% CI 0.21 to 1.15, *low-certainty evidence*), mifepristone plus misoprostol (RR 0.56, 95% CI 0.13 to 2.48, *low-certainty evidence*), dilatation and curettage (RR 0.32, 95% CI 0.08 to 1.24, *very low-certainty evidence*), and misoprostol (RR 1.08, 95% CI 0.40 to 2.96, *very low-certainty evidence*) were compatible with a wide range of treatment effects for readmission to hospital when compared to expectant management or placebo ([Figure 27](#)).

Figure 27. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of readmission to hospital.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	0.72 (0.15, 3.41)
Indirect	0.14 (0.01, 1.67)
Network	0.50 (0.21, 1.15)
Misoprostol vs Expectant or placebo	
Direct	1.25 (0.46, 3.35)
Indirect	1.27 (0.10, 15.91)
Network	1.08 (0.40, 2.96)
Mifepristone plus misoprostol vs Expectant or placebo	
Network	0.56 (0.13, 2.48)
Dilatation & curettage vs Expectant or placebo	
Network	0.32 (0.08, 1.24)
Suction aspiration vs Misoprostol	
Direct	0.77 (0.27, 2.21)
Indirect	0.26 (0.07, 0.98)
Network	0.46 (0.18, 1.19)
Suction aspiration vs Mifepristone plus misoprostol	
Direct	0.14 (0.01, 2.69)
Indirect	1.28 (0.35, 4.72)
Network	0.89 (0.23, 3.47)
Suction aspiration vs Dilatation & curettage	
Direct	1.61 (0.62, 4.16)
Indirect	1.44 (0.04, 46.11)
Network	1.55 (0.53, 4.53)
Misoprostol vs Mifepristone plus misoprostol	
Direct	2.30 (1.48, 3.58)
Indirect	0.26 (0.01, 6.19)
Network	1.94 (0.71, 5.31)
Misoprostol vs Dilatation & curettage	
Direct	3.17 (0.13, 76.11)
Indirect	3.43 (0.72, 16.26)
Network	3.38 (0.87, 13.20)
Dilatation & curettage vs Mifepristone plus misoprostol	

Figure 27. (Continued)

Dilatation & curettage vs
Mifepristone plus misoprostol
Network   0.57 (0.11, 2.99)

.1   1   10

Favours intervention   Favours comparator

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of readmission to hospital are shown in Figure 28. The highest ranked method for managing a miscarriage for the outcome of readmission to hospital was dilatation and curettage (SUCRA 85.1%),

followed by suction aspiration (SUCRA 66.5%), mifepristone plus misoprostol (SUCRA 60.7%) ranked third, expectant management or placebo (SUCRA 21.2%) ranked fourth and misoprostol (SUCRA 16.5%) last.

Figure 28. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of readmission to hospital. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
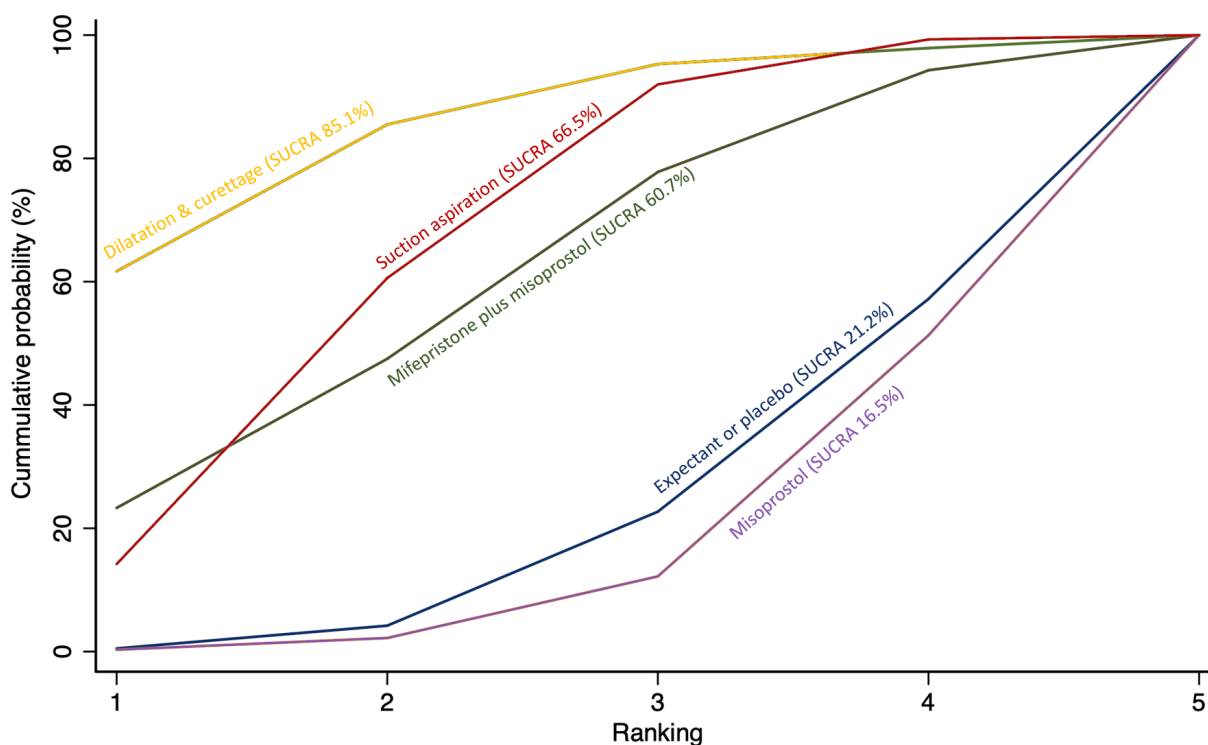
Nausea

The network diagram for the outcome of nausea is presented in Figure 29. Twenty-one trials contributed towards this outcome.

This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 29. Network diagram for outcome of nausea. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
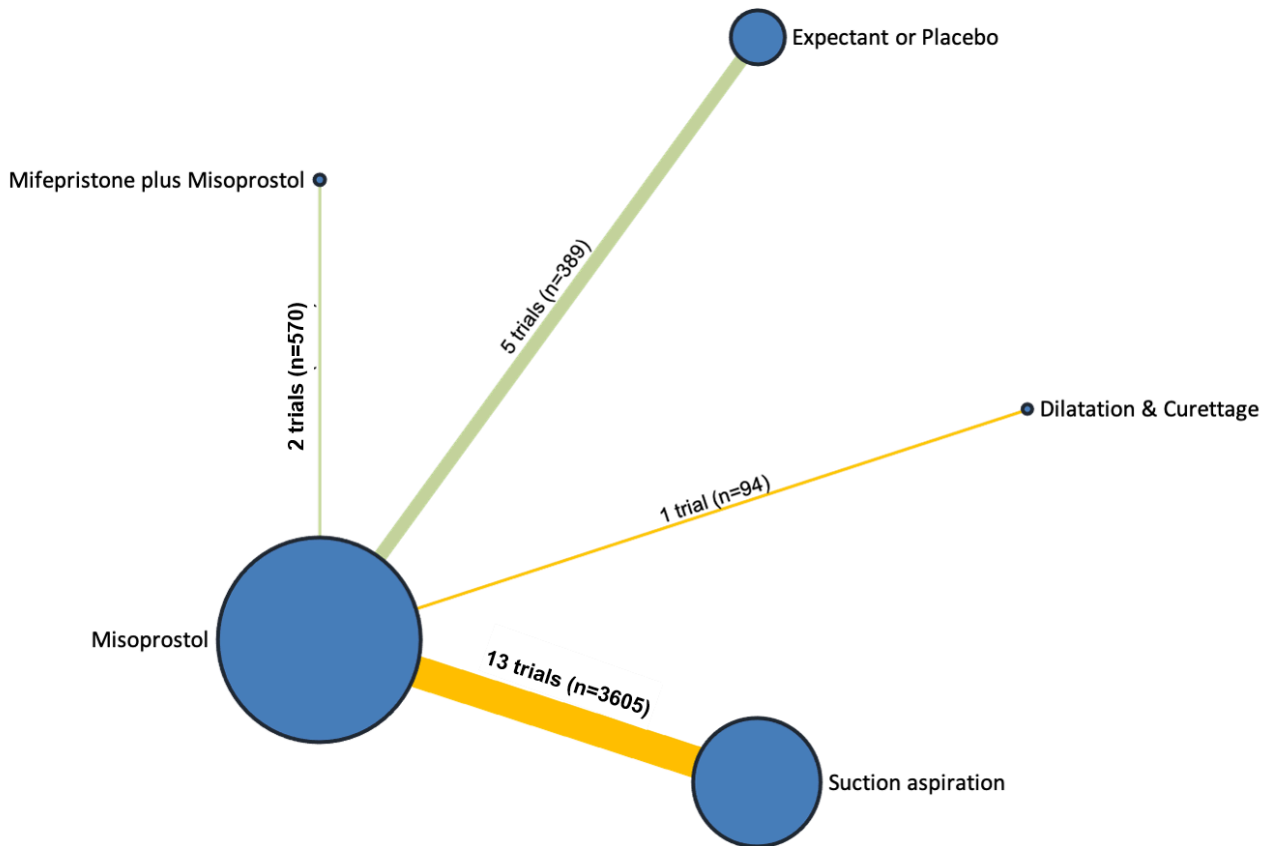
Relative effects from the network meta-analysis of 21 trials suggests that for misoprostol (RR 1.37, 95% CI 0.70 to 2.69, *moderate-certainty evidence*), mifepristone plus misoprostol (RR 1.89, 95% CI 0.62 to 5.72, *moderate-certainty evidence*) and dilatation and curettage (RR 4.12, 95% CI 0.13 to 129.62, *low-certainty evidence*), suction aspiration (RR 0.68, 95% CI 0.31 to 1.52, *very low-certainty evidence*) were compatible with a wide range of treatment effects for nausea when compared to expectant management or placebo (Figure 30).

Figure 30.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of nausea.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Network	0.68 (0.31, 1.52)
Misoprostol vs Expectant or placebo	
Direct	1.15 (0.93, 1.42)
Network	1.37 (0.70, 2.69)
Mifepristone plus misoprostol vs Expectant or placebo	
Network	1.89 (0.62, 5.72)
Dilatation & curettage vs Expectant or placebo	
Network	4.12 (0.13, 129.62)
Suction aspiration vs Misoprostol	
Direct	0.52 (0.35, 0.76)
Network	0.50 (0.31, 0.79)
Suction aspiration vs Mifepristone plus misoprostol	
Network	0.36 (0.13, 0.97)
Suction aspiration vs Dilatation & curettage	
Network	0.17 (0.01, 5.03)
Misoprostol vs Mifepristone plus misoprostol	
Direct	0.74 (0.39, 1.39)
Network	0.73 (0.30, 1.74)
Misoprostol vs Dilatation & curettage	
Direct	0.33 (0.01, 7.98)
Network	0.33 (0.01, 9.82)
Dilatation & curettage vs Mifepristone plus misoprostol	
Network	2.18 (0.07, 71.79)

.1   1   10

Favours intervention   Favours comparator

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of nausea are shown in Figure 31. The highest ranked method for managing a miscarriage for the outcome of nausea was suction aspiration (SUCRA 91.6%), followed by expectant management or placebo (SUCRA 65.9%), misoprostol (SUCRA 42.0%) with mifepristone plus misoprostol (SUCRA 27.4%) ranked fourth and dilatation and curettage (SUCRA 23.1%) last.

Figure 31. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of nausea. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
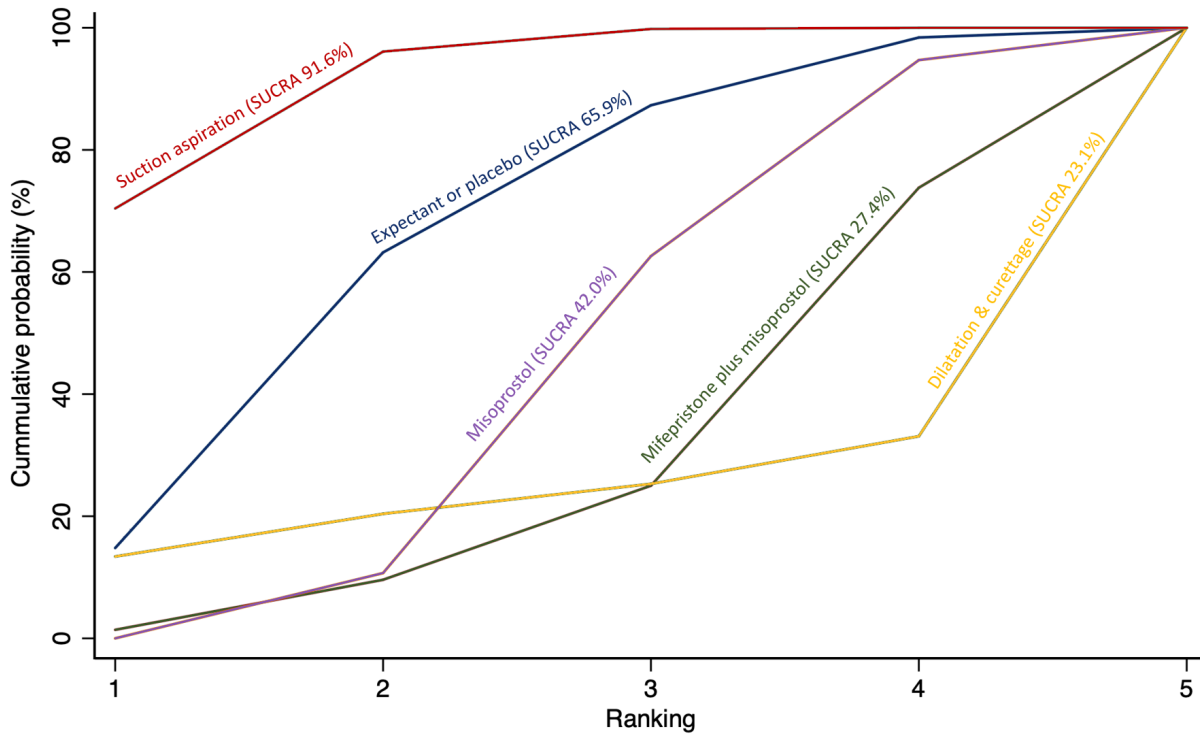
Following assessment using funnel plots, we identified publication bias for the comparison of suction aspiration versus misoprostol for this outcome of nausea. Funnel plots are not included but can be obtained from the author on request.

Vomiting

The network diagram for the outcome of vomiting is presented in Figure 32. 23 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 32.   Network diagram for outcome of vomiting. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
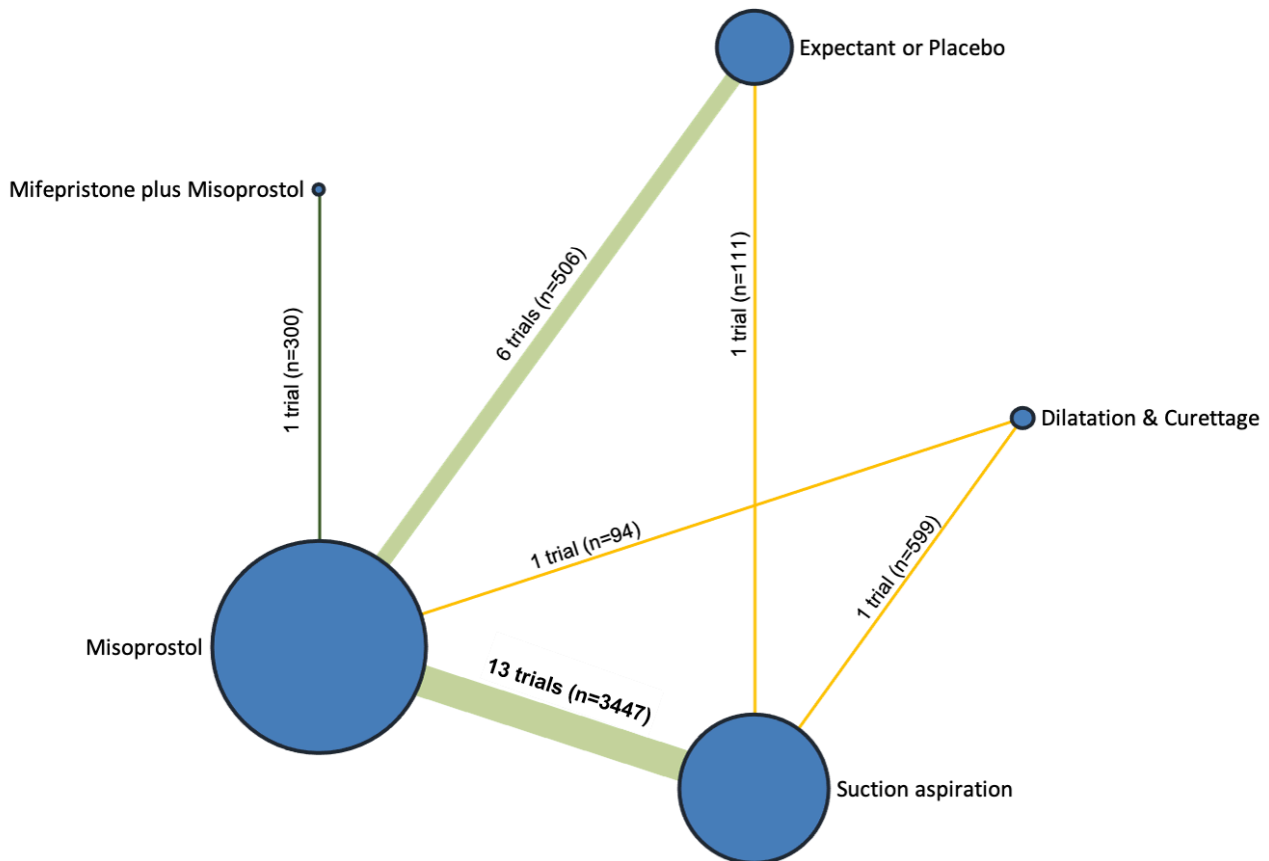
Relative effects from the network meta-analysis of 21 trials suggest that for suction aspiration (RR 0.71, 95% CI 0.37 to 1.39, *low-certainty evidence*), misoprostol (RR 1.32, 95% CI 0.76 to 2.30, *low-certainty evidence*), dilatation and curettage (RR 0.48, 95% CI 0.11 to 2.13, *low-certainty evidence*) and mifepristone plus misoprostol (RR 2.32, 95% CI 0.91 to 5.91, *low-certainty evidence*) were compatible with a wide range of treatment effects for this outcome when compared with expectant management or placebo (Figure 33).

Figure 33. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of vomiting.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	0.82 (0.19, 3.50)
Indirect	0.67 (0.32, 1.43)
Network	0.71 (0.37, 1.39)
Misoprostol vs Expectant or placebo	
Direct	1.37 (0.75, 2.52)
Indirect	0.39 (0.03, 5.84)
Network	1.32 (0.76, 2.30)
Mifepristone plus misoprostol vs Expectant or placebo	
Network	2.32 (0.91, 5.91)
Dilatation & curettage vs Expectant or placebo	
Network	0.48 (0.11, 2.13)
Suction aspiration vs Misoprostol	
Direct	0.50 (0.38, 0.68)
Indirect	5.21 (0.75, 36.34)
Network	0.54 (0.37, 0.79)
Suction aspiration vs Mifepristone plus misoprostol	
Network	0.31 (0.13, 0.71)
Suction aspiration vs Dilatation & curettage	
Direct	2.31 (0.60, 8.85)
Indirect	0.18 (0.01, 4.49)
Network	1.49 (0.39, 5.72)
Misoprostol vs Mifepristone plus misoprostol	
Direct	0.57 (0.36, 0.90)
Network	0.57 (0.27, 1.20)
Misoprostol vs Dilatation & curettage	
Direct	0.33 (0.01, 7.98)
Indirect	4.40 (0.98, 19.69)
Network	2.76 (0.69, 11.04)
Dilatation & curettage vs Mifepristone plus misoprostol	
Network	0.21 (0.04, 0.99)

Figure 33. (Continued)

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of vomiting are shown in Figure 34. The highest ranked method for managing a miscarriage for the outcome of vomiting was dilatation and curettage (SUCRA 85.6%), followed by suction aspiration (SUCRA 78.3%), expectant management or placebo (SUCRA 53.1%) with misoprostol (SUCRA 29.3%) ranked fourth and mifepristone plus misoprostol (SUCRA 3.7%) last.

Figure 34. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of vomiting. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
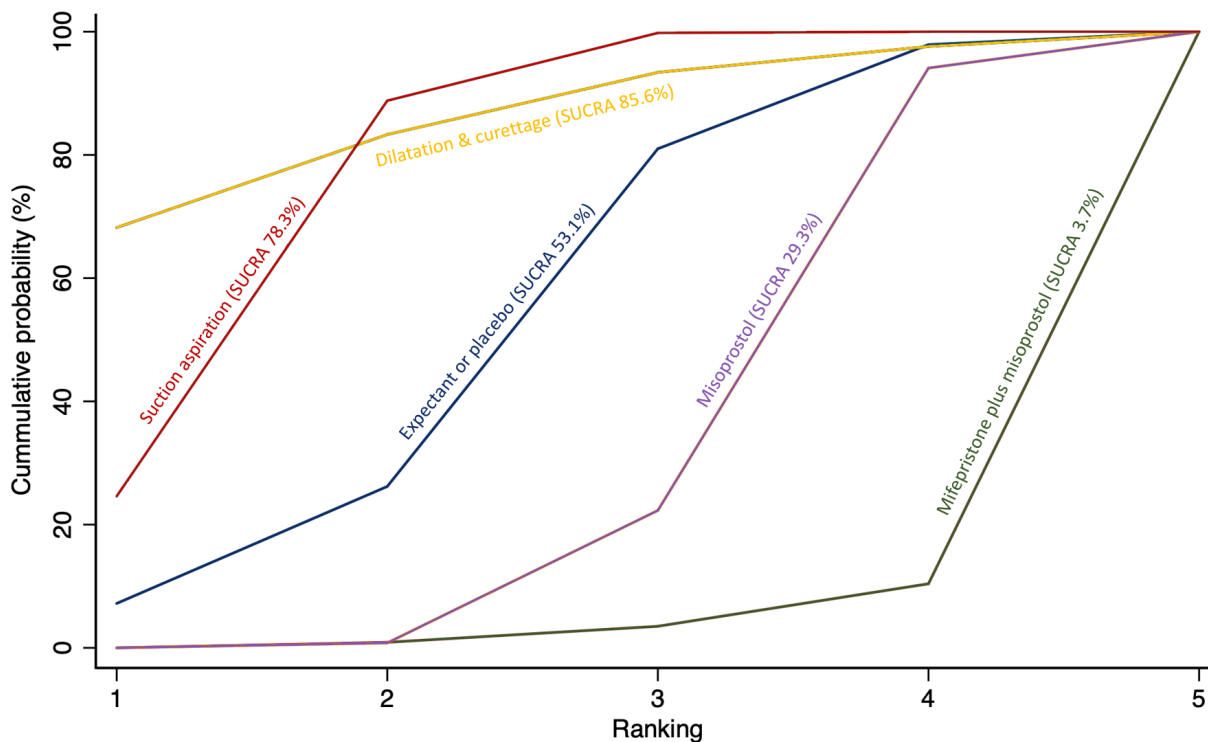
Following assessment using funnel plots, we identified publication bias for the comparison of suction aspiration versus misoprostol for this outcome of vomiting. Funnel plots are not included but can be obtained from the author on request.

Diarrhoea

The network diagram for the outcome of diarrhoea is presented in Figure 35. 20 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 35.   Network diagram for outcome of diarrhoea. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 18 trials, suggest that for suction aspiration (RR 0.69, 95% CI 0.42 to 1.12, *low-certainty evidence*), misoprostol (RR 1.61, 95% CI 1.11 to 2.32, *low-certainty evidence*), mifepristone plus misoprostol (RR 1.47, 95% CI 0.93 to 2.33, *low-certainty evidence*), and dilatation and curettage (RR 0.54, 95% CI 0.02 to 13.10, *very low-certainty evidence*) are compatible with a wide range of treatment effects for diarrhoea when compared with expectant management or placebo (Figure 36).

Figure 36.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of diarrhoea.
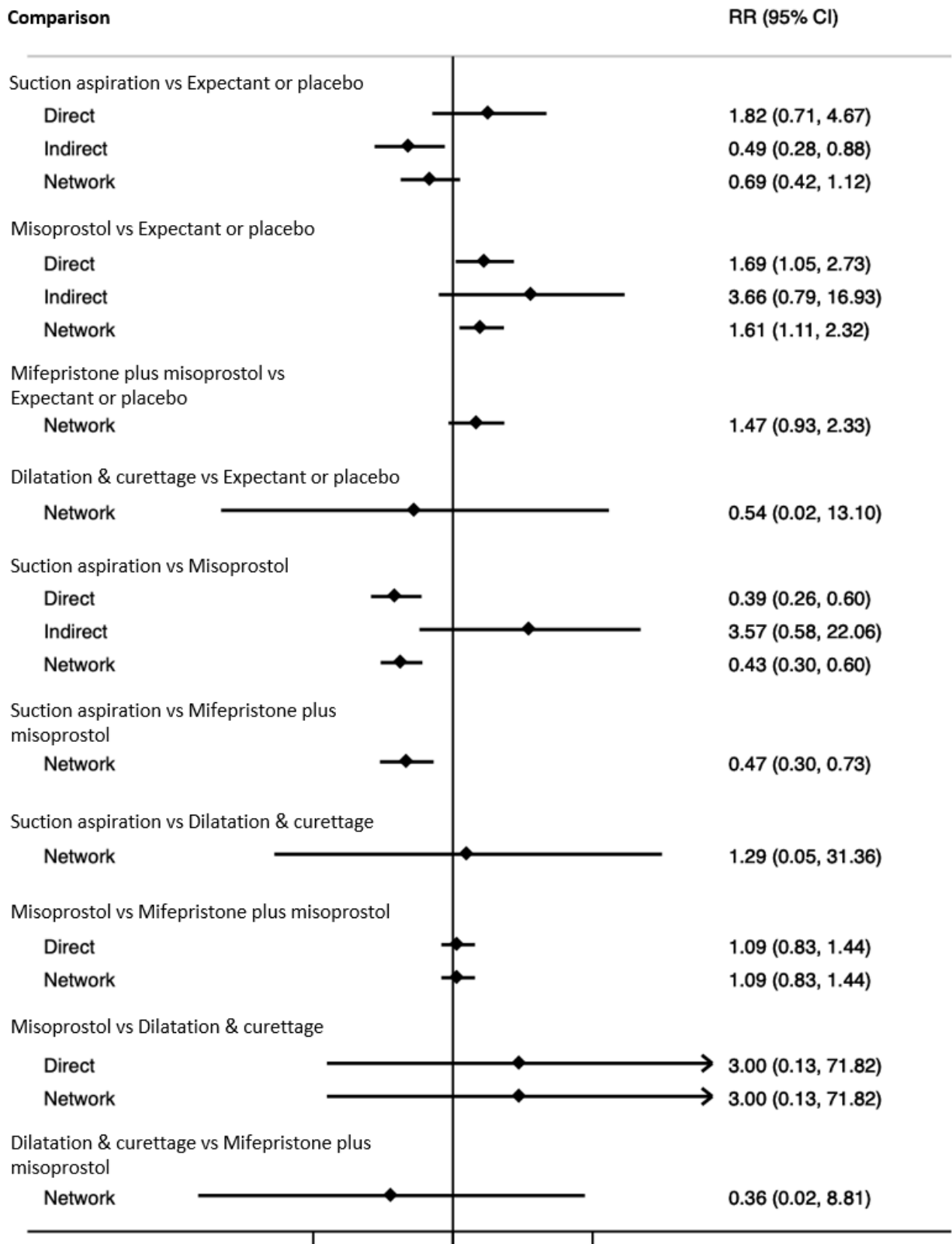
Figure 36.   (Continued)
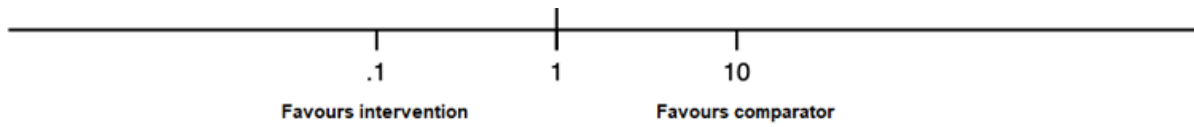
The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of diarrhoea are shown in Figure 37. The highest ranked method for managing a miscarriage for the outcome of diarrhoea was suction aspiration (SUCRA 85.3%), followed by dilatation and curettage (SUCRA 65.0%), expectant management or placebo (SUCRA 59.6%) with mifepristone plus misoprostol (SUCRA 26.8%) ranked fourth and misoprostol (SUCRA 13.3%) last.

Figure 37.   Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of diarrhoea. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
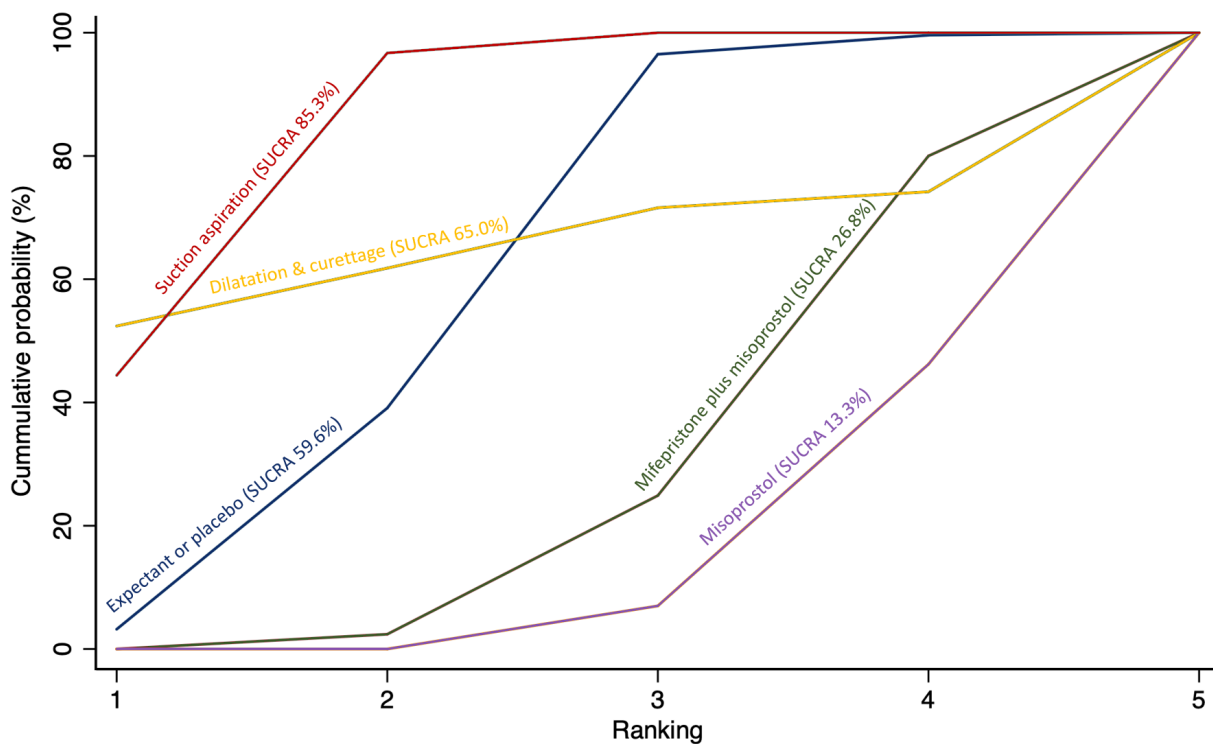
Following assessment using funnel plots, we identified publication bias for the comparison of suction aspiration versus misoprostol for this outcome of diarrhoea. Funnel plots are not included but can be obtained from the author on request.

Pyrexia

The network diagram for the outcome of pyrexia is presented in Figure 38. 28 trial arms contributed towards this outcome. This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 38.   Network diagram for outcome of pyrexia. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.
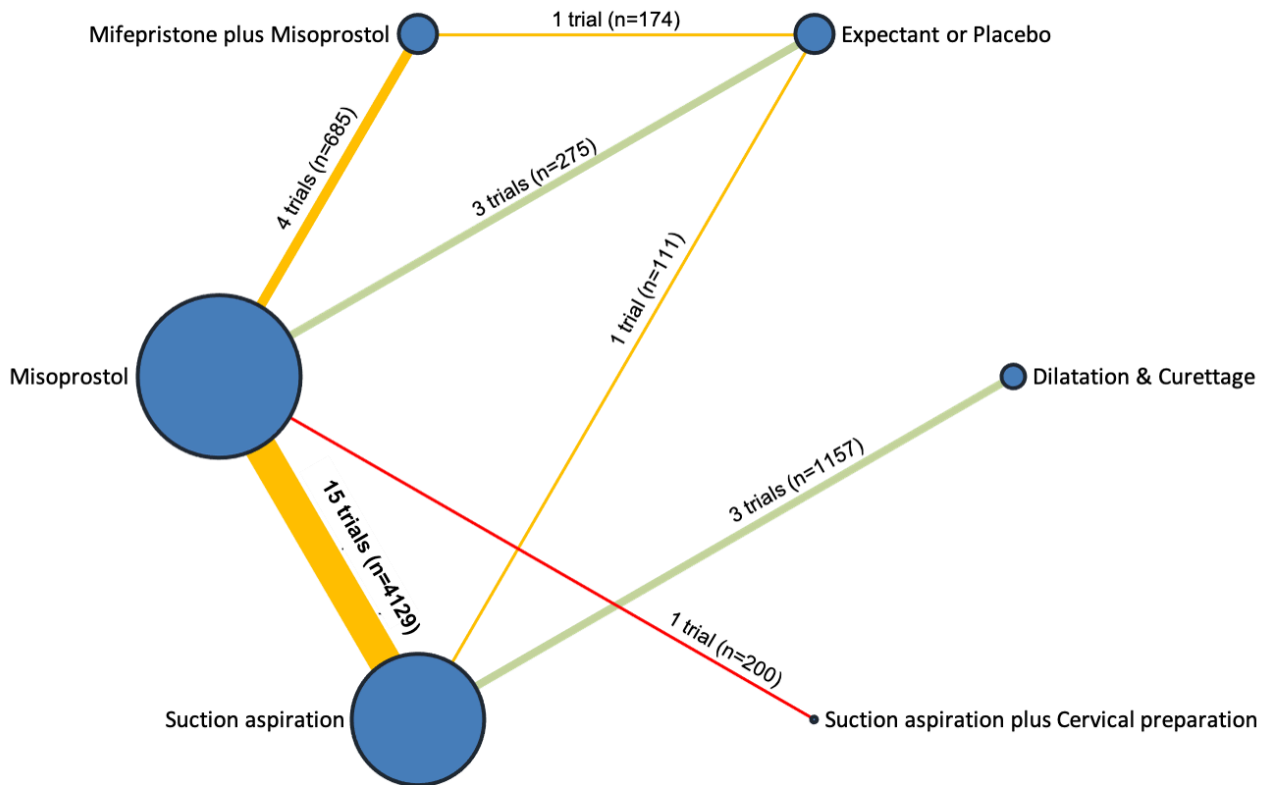
Relative effects from the network meta-analysis of 26 trials suggest that for misoprostol (RR 3.51, 95% CI 0.98 to 12.53, *moderate-certainty evidence*) and dilatation and curettage (RR 1.10, 95% CI 0.23 to 5.19, *low-certainty evidence*), suction aspiration (RR 1.36, 95% CI 0.37 to 5.06, *very low-certainty evidence*), suction aspiration plus cervical preparation (RR 1.40, 95% CI 0.19 to 10.18, *very low-certainty evidence*), and mifepristone plus misoprostol (RR 4.15, 95% CI 0.88 to 19.59, *very low-certainty evidence*) were compatible with a wide range of treatment effects for pyrexia when compared with expectant management or placebo (Figure 39).

Figure 39.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for outcome of pyrexia.
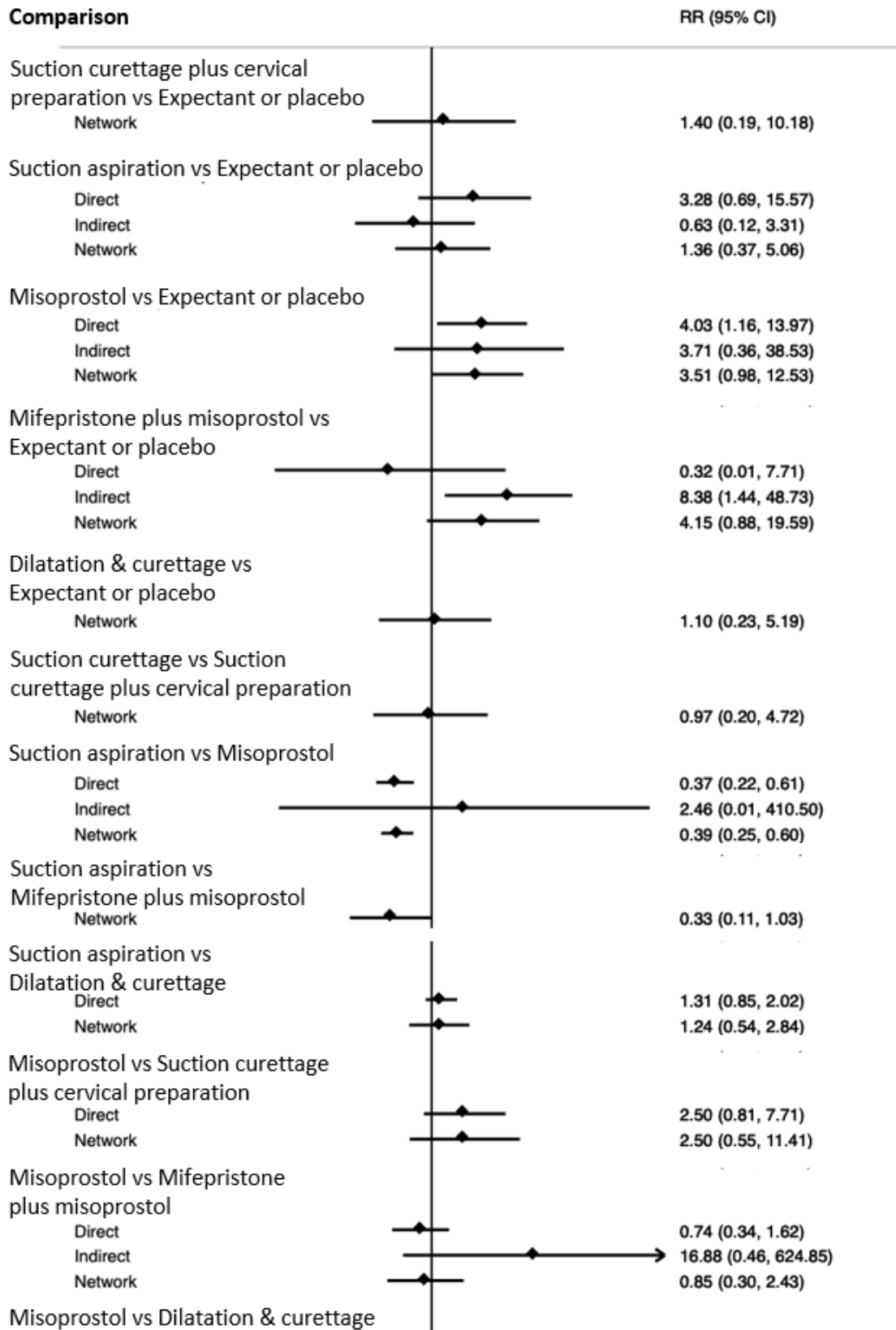
Figure 39. (Continued)
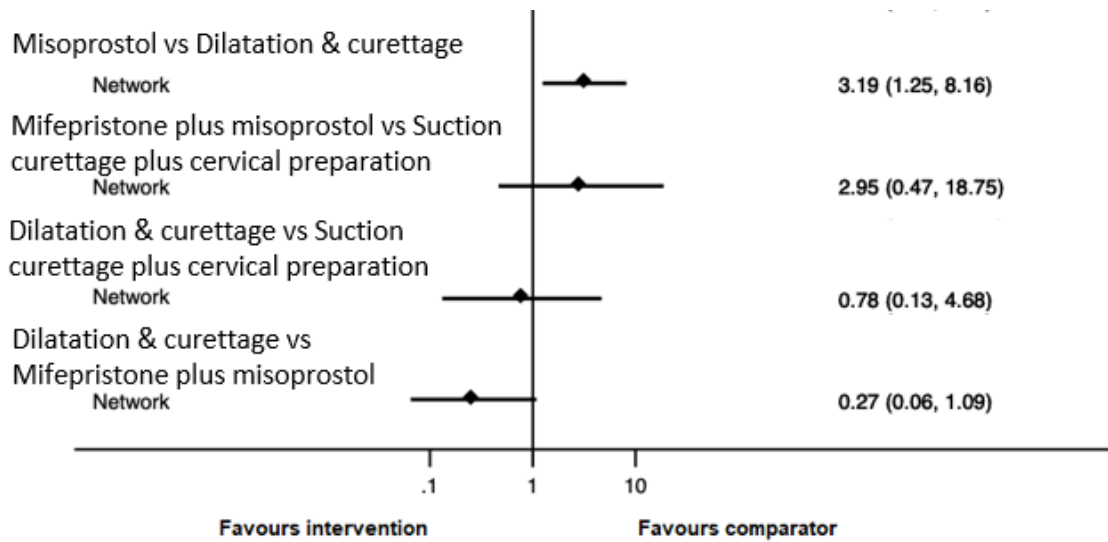
The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of pyrexia are shown in Figure 40. The highest ranked method for managing a miscarriage for the outcome of pyrexia was expectant management or placebo (SUCRA 75.8%), followed by dilatation and curettage (SUCRA 74.0%), with suction aspiration (SUCRA 62.8%) and suction aspiration plus cervical preparation (SUCRA 60.3%) ranked joint third. Misoprostol (SUCRA 14.8%) ranked fifth with mifepristone plus misoprostol (SUCRA 12.3%) last.

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Figure 40. Cumulative rankogram comparing each of the methods of management of a miscarriage for the outcome of pyrexia. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
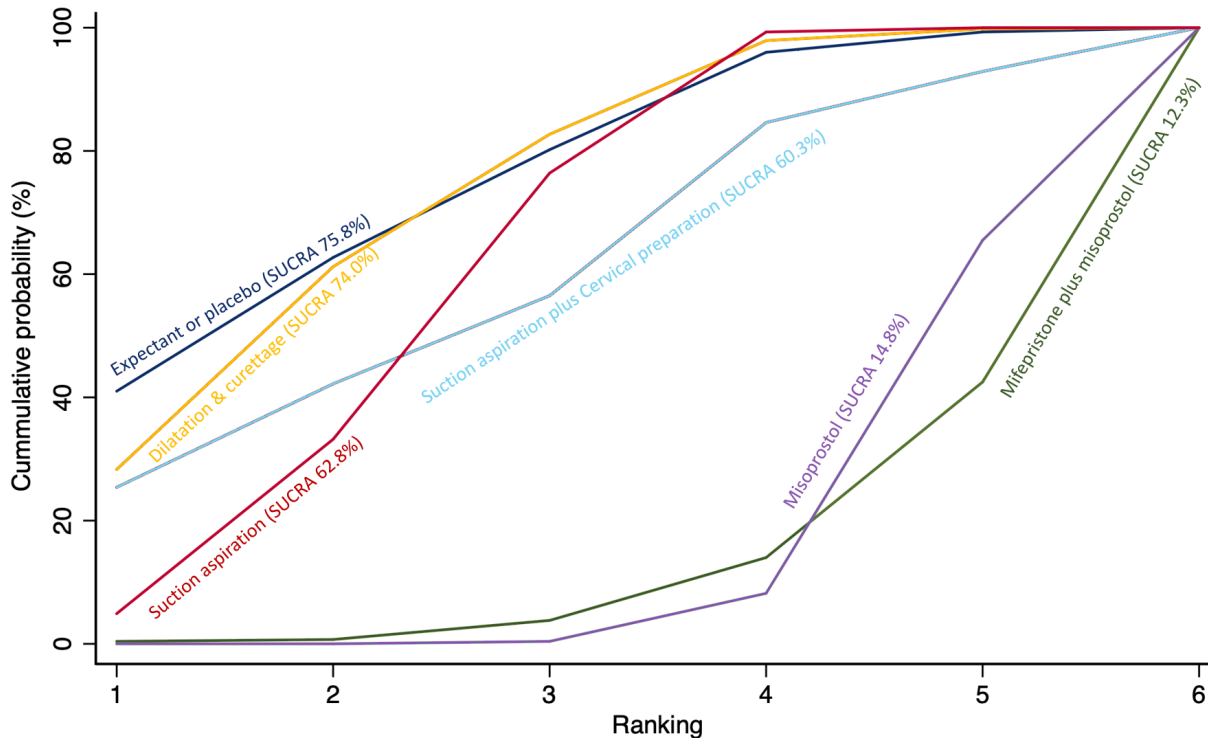
Anxiety score

There were two trials which reported anxiety score. Network meta-analysis was therefore not possible, and so we were unable to produce a network diagram, network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis. Both trials (Harwood 2008; Kong 2013) looked at the comparison of suction aspiration versus misoprostol (SMD -0.08, 95% CI -0.24 to 0.09) (Analysis 1.15), with no difference shown.

Depression Score

There were three trials which reported depression score. Network meta-analysis was therefore not possible, so we were unable to produce a network diagram, network relative effects and a rankogram. Direct evidence is presented only from pairwise meta-analysis. Two of the trials were also those that reported anxiety score (Harwood 2008; Kong 2013), and therefore suction aspiration versus misoprostol was the only comparison with more than one trial (SMD -0.17, 95% CI -0.46 to 0.12) (Analysis 1.16), and no difference was shown. The third trial compared misoprostol versus dilatation and curettage.

Subgroup and sensitivity analysis

Statistical inconsistency

We assessed the global statistical inconsistency for the network meta-analyses, which are provided in Appendix 2. A significant inconsistency was observed for the outcomes of complete miscarriage (P = 0.00) and days of bleeding (P = 0.017), and therefore the interpretation of these findings require a high degree of caution. The pairwise meta-analyses also revealed high levels of heterogeneity for the outcome of complete miscarriage which was derived from the type of miscarriage (I² range 63% to 94%) (Analysis 1.1; Analysis 1.7; Analysis 2.1; Analysis 3.1; Analysis 3.7; Analysis 4.1; Analysis 4.7; Analysis 5.1; Analysis 5.6; Analysis 6.1; Analysis 6.7; Analysis 8.1; Analysis 8.7; Analysis 9.1; Analysis 9.3; Analysis 10.1). For this reason, a subgroup analysis for missed miscarriage and incomplete miscarriage, which have been identified as the major source of inconsistency and heterogeneity, were conducted for the complete miscarriage outcome.

Type of miscarriage

We carried out subgroup analyses for the primary outcome of complete miscarriage and also days of bleeding by type of miscarriage (incomplete miscarriage versus missed miscarriage).

Missed miscarriage subgroup

Complete miscarriage

The network diagram for the missed miscarriage subgroup analysis for the outcome of complete miscarriage is presented in Figure 41. Misoprostol was the most frequently investigated method of miscarriage management (12 of 16 trials [75%]) for this subgroup analysis for the outcome of complete miscarriage (Figure 41). This

outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 41. Network diagram for missed miscarriage subgroup analysis of outcome of complete miscarriage. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 16 trials, suggest that dilatation and curettage (RR 2.07, 95% CI 1.19 to 3.59, *high-certainty evidence*) is more effective in achieving a complete miscarriage compared with expectant management or placebo. Misoprostol (RR 1.67, 95% CI 1.18 to 2.37, *low-certainty evidence*), mifepristone plus misoprostol (RR 1.82, 95% CI 1.28 to 2.58, *moderate-certainty evidence*) and suction aspiration (RR 2.43, 95% CI 1.69 to 3.49, *moderate-certainty evidence*) were probably also more effective in achieving a complete miscarriage compared with expectant management or placebo (Figure 42, Summary of findings 2).

Figure 42. Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for missed miscarriage subgroup of complete miscarriage outcome.
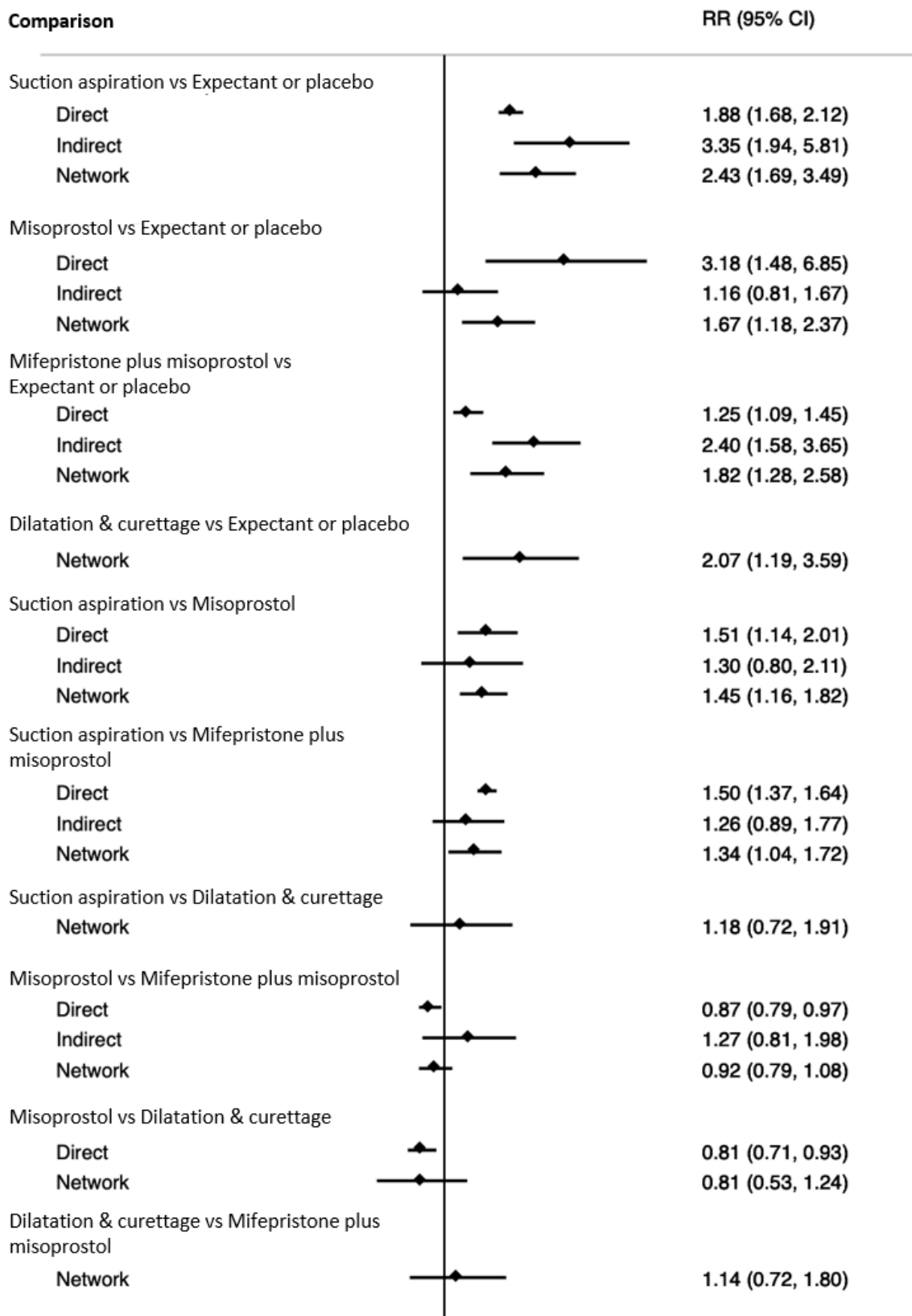
Figure 42. (Continued)
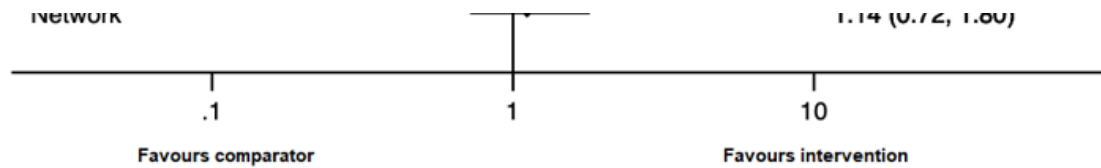
The cumulative probabilities for each method of managing a miscarriage being at each possible rank for completing a miscarriage are shown in Figure 43. The highest ranked method for managing a miscarriage for the outcome of complete miscarriage in the missed miscarriage subgroup was suction curettage (SUCRA 92.7%), followed by dilatation and curettage (SUCRA 70.8%), mifepristone plus misoprostol (SUCRA 53.1%) with misoprostol (SUCRA 33.3%) ranked fourth and expectant management or placebo (SUCRA 0.2%) last.

Figure 43. Cumulative rankogram comparing each of the methods of management of a miscarriage for missed miscarriage subgroup analysis for the outcome of complete miscarriage. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.

Days of bleeding

The network diagram for the missed miscarriage subgroup analysis for the outcome of days of bleeding is presented in Figure 44.

Figure 44.   Network diagram for missed miscarriage subgroup analysis of outcome of days of bleeding. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 12 trials, suggest that suction aspiration (RR -4.00, 95% CI -6.84 to -1.16, *very low-certainty evidence*), mifepristone plus misoprostol (RR -2.32, 95% CI -4.60 to -0.04, *very* low-*certainty evidence*) and misoprostol (RR -2.30, 95% CI -4.58 to -0.02, *very low-certainty evidence*) may cause less days of bleeding when compared to expectant management or placebo, but the evidence is very uncertain (Figure 45).

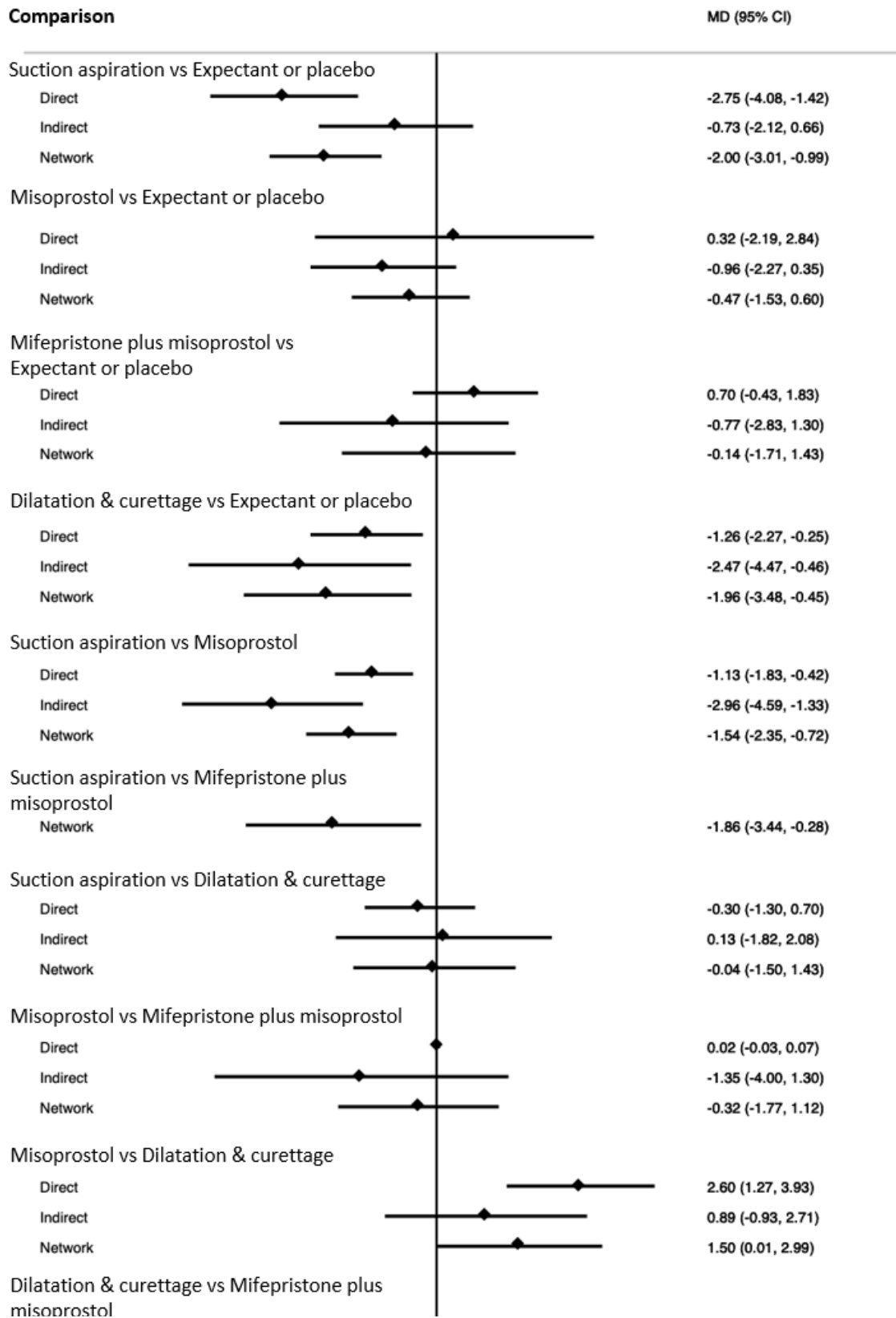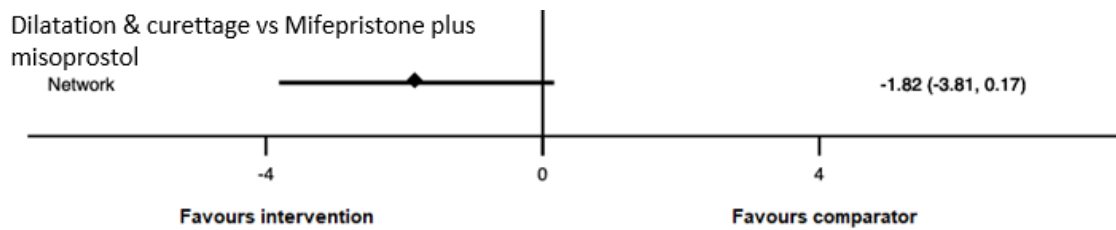**Figure 45.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for missed miscarriage subgroup of the days of bleeding outcome.**
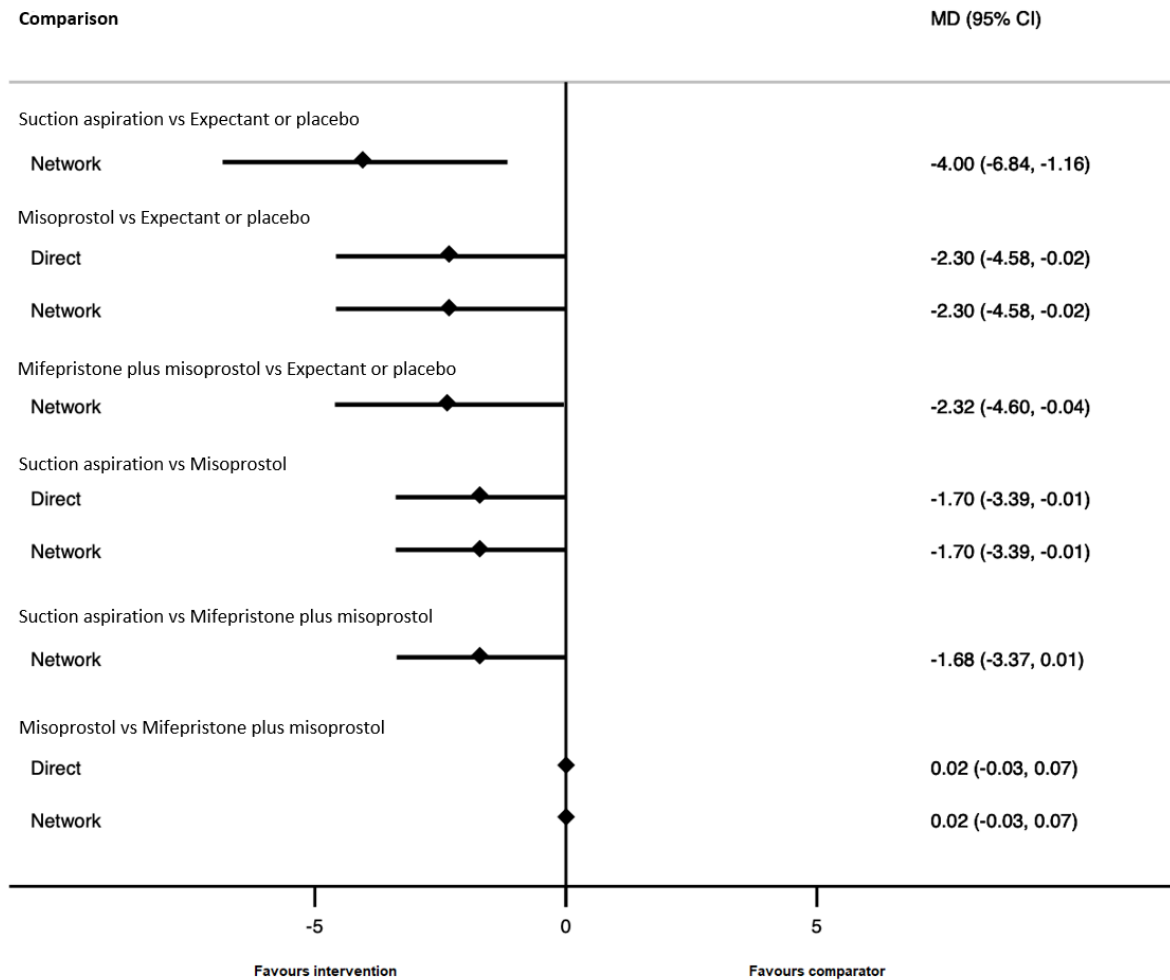
The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of days of bleeding are shown in Figure 46. The highest ranked method for managing a miscarriage for the outcome of days of bleeding was suction aspiration (SUCRA 97.6%), followed by mifepristone plus misoprostol (SUCRA 60.7%), misoprostol (SUCRA 39.9%) with expectant management or placebo (SUCRA 1.7%) last.

Figure 46. Cumulative rankogram comparing each of the methods of management of a miscarriage for missed miscarriage subgroup analysis for the outcome of days of bleeding. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
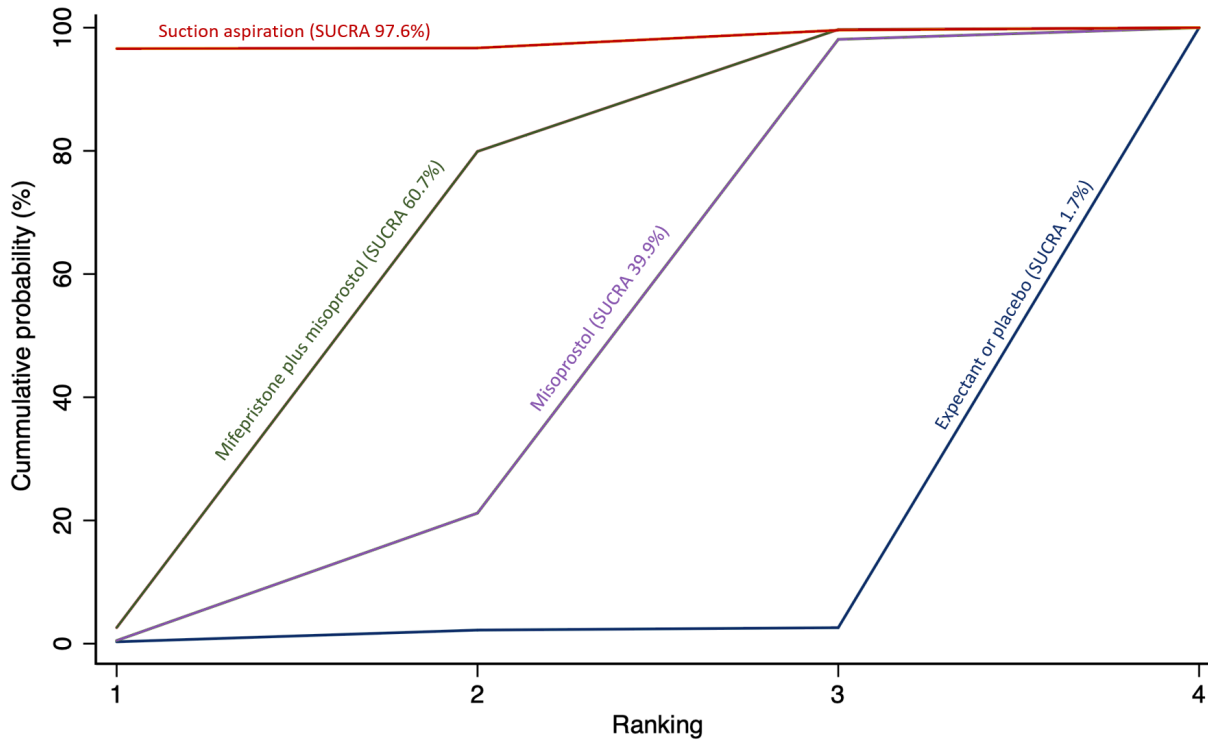
Incomplete miscarriage subgroup

Compete miscarriage

The network diagram for the incomplete miscarriage subgroup analysis for the outcome of complete miscarriage is presented in Figure 47. Suction curettage was the most frequently investigated method of miscarriage management (18 of 26 trials [69%]) for this subgroup analysis for the outcome of complete miscarriage (Figure 47). This outcome was not reported for any trial involving suction aspiration plus cervical preparation.

Figure 47. Network diagram for incomplete miscarriage subgroup analysis of outcome of complete miscarriage. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 26 trials suggest that misoprostol (RR 1.14, 95% CI 1.03 to 1.25, *moderate-certainty evidence*), dilatation and curettage (RR 1.19, 95% CI 1.08 to 1.31, *moderate-certainty evidence*) and suction aspiration (RR 1.19, 95% CI 1.09 to 1.31, *moderate-certainty evidence*) were probably more effective in achieving a complete miscarriage compared with expectant management or placebo. Mifepristone plus misoprostol (RR 1.08, 95% CI 0.87 to 1.34, *very low-certainty evidence*) was compatible with a wide range of treatment effects for the outcome of complete miscarriage compared with expectant management or placebo (Figure 48, Summary of findings 3).

Figure 48.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for incomplete miscarriage subgroup of complete miscarriage outcome.

Comparison	RR (95% CI)
Suction aspiration vs Expectant or placebo	
Direct	1.20 (0.85, 1.69)
Indirect	1.28 (1.11, 1.48)
Network	1.19 (1.09, 1.31)
Misoprostol vs Expectant or placebo	
Direct	1.91 (0.44, 8.20)
Indirect	1.12 (1.02, 1.24)
Network	1.14 (1.03, 1.25)
Mifepristone plus misoprostol vs Expectant or placebo	
Direct	1.08 (0.90, 1.30)
Network	1.08 (0.87, 1.34)
Dilatation & curettage vs Expectant or placebo	
Direct	1.25 (1.12, 1.39)
Indirect	1.15 (1.02, 1.30)
Network	1.19 (1.08, 1.31)
Suction aspiration vs Misoprostol	
Direct	1.03 (1.01, 1.05)
Indirect	1.10 (0.95, 1.28)
Network	1.05 (1.01, 1.08)
Suction aspiration vs Mifepristone plus misoprostol	
Network	1.11 (0.87, 1.40)
Suction aspiration vs Dilatation & curettage	
Direct	1.02 (0.98, 1.06)
Indirect	0.92 (0.83, 1.04)
Network	1.00 (0.95, 1.06)
Misoprostol vs Mifepristone plus misoprostol	
Network	1.06 (0.83, 1.34)
Misoprostol vs Dilatation & curettage	
Direct	0.38 (0.06, 2.46)
Indirect	0.97 (0.91, 1.04)
Network	0.96 (0.90, 1.02)
Dilatation & curettage vs Mifepristone plus misoprostol	
Network	1.10 (0.87, 1.40)

Figure 48.   (Continued)

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for completing a miscarriage are shown in Figure 5. The highest ranked method for managing a miscarriage for the outcome of complete miscarriage in the incomplete miscarriage subgroup was suction aspiration (SUCRA 83.6%), followed by dilatation and curettage (SUCRA 79.4%), misoprostol (SUCRA 44.2%) with mifepristone

plus misoprostol ranked fourth (SUCRA 36.1%) and expectant management or placebo (SUCRA 6.7%) last.

Days of bleeding

The network diagram for the missed miscarriage subgroup analysis for the outcome of days of bleeding is presented in Figure 49.

Figure 49.   Network diagram for incomplete miscarriage subgroup analysis of outcome of days of bleeding. The nodes represent an intervention and their size is proportional to the number of trials comparing this intervention to any other in the network. The lines connecting each pair of interventions represent a direct comparison and are drawn proportional to the number of trials making each direct comparison. Numbers on the lines represent the number of trials and participants for each comparison. The colour of the line is green for high-certainty evidence; light green for moderate-certainty evidence; orange for low-certainty evidence and red for very low-certainty evidence. Multi-arm trials contribute to more than one comparison.

Relative effects from the network meta-analysis of 11 trials, suggest that suction aspiration (RR -0.86, 95% CI -2.51 to 0.79, very *low-certainty evidence*), mifepristone plus misoprostol (RR 0.70, 95% CI -0.69 to 2.09, *very* low-*certainty evidence*), misoprostol (RR 0.31,

95% CI -1.38 to 1.99, *very* low-*certainty evidence*) and dilatation and curettage (RR -1.26, 95% CI -2.56 to 0.04, *very* low-*certainty evidence*) were compatible with a wide range of treatment effects for days of bleeding when compared with expectant management or placebo, and the evidence is very uncertain (Figure 50).

Figure 50.   Forest plot with relative risk ratios and 95% CIs from pairwise, indirect and network (combining direct and indirect) analyses for incomplete miscarriage subgroup of the days of bleeding outcome.
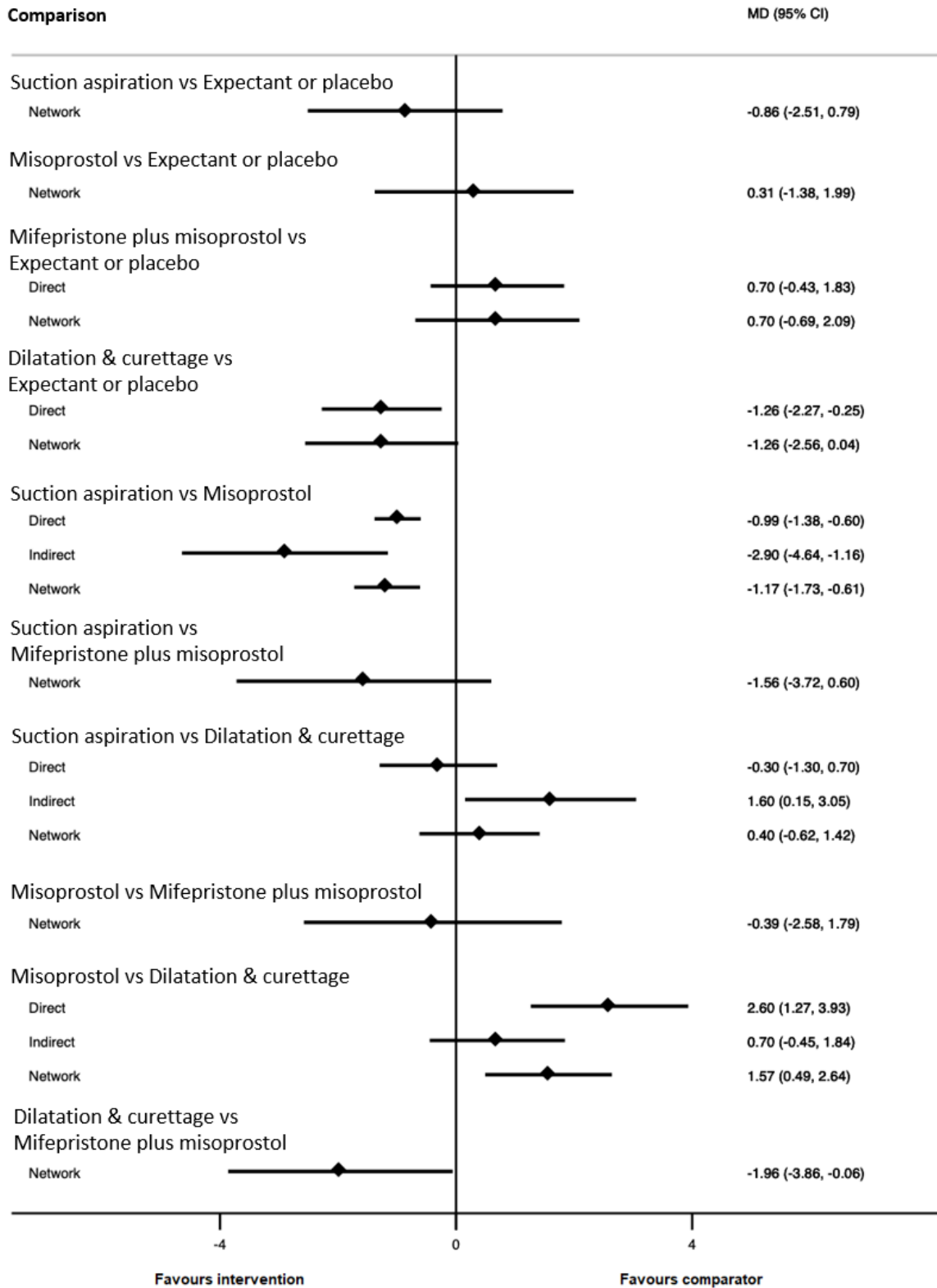
Figure 50.   (Continued)

The cumulative probabilities for each method of managing a miscarriage being at each possible rank for the outcome of days of bleeding are shown in Figure 51. The highest ranked method for managing a miscarriage for the outcome of days of bleeding in the missed miscarriage subgroup was dilatation and curettage (SUCRA 92.9%), followed by suction aspiration (SUCRA 75.2%), followed by expectant or placebo (SUCRA 40.6%), misoprostol (SUCRA 25.4%) ranked fourth and mifepristone plus misoprostol (SUCRA 16.0%) last.

Figure 51.   Cumulative rankogram comparing each of the methods of management of a miscarriage for incomplete miscarriage subgroup analysis for the outcome of days of bleeding. Ranking indicates the cumulative probability of being the best method, the second best, the third best, etc. The x axis shows the relative ranking and the y-axis the cumulative probability of each ranking. We estimate the SUrface underneath this Cumulative RAnking line (SUCRA); the larger the SUCRA the higher its rank among all available methods.
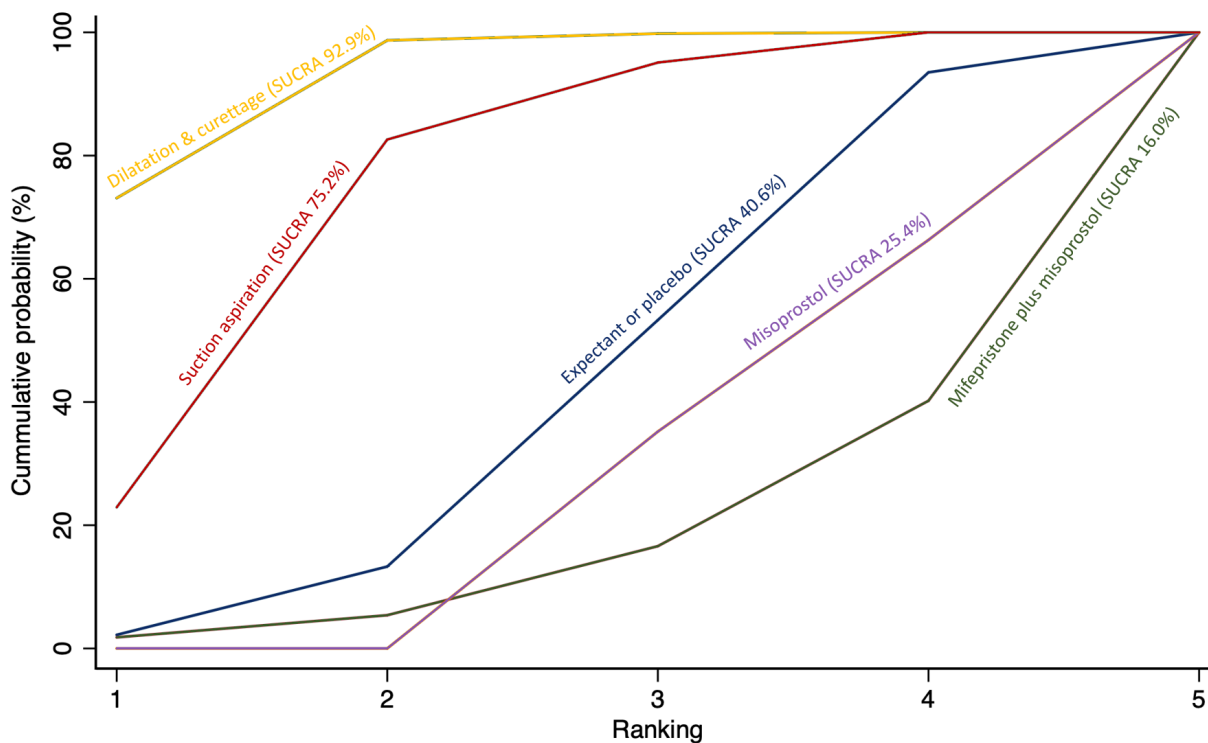
Other subgroup analyses

We had planned on performing a subgroup analyses based on gestation of miscarriage, however, only five trials (Machtinger 2002; Machtinger 2004; Nasreen 2009; Sahin 2001; Stockheim 2006) specified a gestational age of less than or equal to nine weeks. The remaining trials did not differentiate between miscarriages of less than or equal to nine weeks or greater than nine weeks but less than or equal to 14 weeks of gestation. Therefore, this analysis was not possible. We had also planned to perform a subgroup analysis of electric versus manual vacuum aspiration for the suction aspiration intervention, however, 12 trials did not explicitly state the method of suction aspiration, one trial (Zhang 2005) included both electric and manual aspiration in their suction aspiration group depending upon which site the patient was treated at and did not differentiate between them. Therefore this left only four trials (Chung 1999; Dangalla 2012; Demetroulis 2001; Kittiwatanakul 2012), which explicitly used electric vacuum aspiration and 15 trials which explicitly used manual vacuum aspiration and network meta-analysis was not possible. We had also planned to perform a subgroup analysis based on type of healthcare setting (inpatient versus outpatient). This was not performed as the healthcare setting was not explicitly stated in the vast majority of trials and many of the interventions appeared to have presented the results combining inpatient and

outpatient patients. When describing the interventions, authors made judgements on the healthcare settings for the table of characteristics based on the available descriptions in the trials, but a meaningful subgroup analysis was not possible. We had also planned a subgroup analysis based on the dosage, regimen and route of drug administration for the medical interventions. Whilst most of the trials used mifepristone at a similar dose and a similar route of administration, there was significant heterogeneity in terms of the way misoprostol was used for route, dosage and regimen. For this reason, a network meta-analysis according to the different routes, dosages and regimens of misoprostol was not considered meaningful and was not performed. Finally, we considered performing subgroup analysis for the composite outcome of death and serious complications for the subgroups of missed miscarriage and incomplete miscarriage but only ten and 14 trials, respectively reported the type of miscarriage for this composite outcome and therefore any meaningful network meta-analysis was judged by the authors not to be possible or relevant.

Sensitivity analysis

We carried out pre-specified sensitivity analyses by restricting our analyses to studies at low risk of bias and studies that were placebo-controlled. Sensitivity analyses were also performed according to the choice of relative effect measure (risk ratio (RR) versus odds ratio (OR)) and the statistical model (fixed-effect versus random-effects model). The sensitivity analyses show that the overall results are not affected by the above mentioned criteria or decisions.

DISCUSSION

Summary of main results

This review includes 78 randomised trials involving 17,795 women. Most trials were conducted in hospital settings and included women with missed or incomplete miscarriage. Of the 78 included studies, 92% contributed data to the analysis, 8% did not present the data in a usable form for meta-analysis. Across the 71 trials (158 trial arms), the following methods were used: 33% used misoprostol; 32% used suction aspiration; 16% used expectant management or placebo; 11% used dilatation and curettage; 6% used mifepristone plus misoprostol; and 2% used suction aspiration plus cervical preparation.

Based on relative effects from network meta-analysis of 59 trials (12,591 women), we found that suction aspiration plus cervical preparation, dilatation and curettage, suction aspiration, mifepristone plus misoprostol and misoprostol may be more effective than expectant management or placebo for achieving a complete miscarriage. The highest ranked surgical method was suction aspiration plus cervical preparation. The highest ranked non-surgical method was mifepristone plus misoprostol. All surgical methods were ranked higher than medical methods, which in turn were ranked higher than expectant management or placebo.

Based on relative effects from network meta-analysis of 35 trials (8161 participants), we found that dilatation and curettage, suction aspiration, misoprostol and mifepristone plus misoprostol are compatible with a wide range of treatment effects for death and serious complications when compared with expectant management or placebo. No deaths were reported in the trials that contributed towards this outcome, therefore it was entirely composed of serious complications. The most common serious

complications included blood transfusions, uterine perforations, hysterectomies, and intensive care unit admissions. The ranking for most methods was not clear for this outcome due to limited data. However, expectant management or placebo ranked bottom amongst all available methods.

Subgroup analyses revealed important differences for the effectiveness of the available methods for managing the miscarriage according to the type of miscarriage. Specifically, for women with missed miscarriage, relative effects from the network meta-analysis of 16 trials, suggest that dilatation and curettage is more effective in achieving a complete miscarriage compared with expectant management or placebo. Misoprostol, mifepristone plus misoprostol and suction aspiration are probably also more effective in achieving a complete miscarriage compared with expectant management or placebo. For women with incomplete miscarriage, relative effects from the network meta-analysis of 26 trials suggest that misoprostol, dilatation and curettage and suction aspiration are probably more effective in achieving a complete miscarriage compared with expectant management or placebo. Mifepristone plus misoprostol is compatible with a wide range of treatment affects for the outcome of complete miscarriage, when compared with expectant management or placebo. The network meta-analyses for incomplete and missed miscarriages agreed with the overall analysis in that surgical methods were better for providing a definitive treatment for a miscarriage than medical methods, which in turn were better than expectant management/ placebo. However, the relative effects were substantially lessened in women with incomplete miscarriage compared to women with missed miscarriage. Since type of miscarriage (missed and incomplete) appears to be a source of inconsistency and heterogeneity within these data, we acknowledge that the main network meta-analysis may be unreliable. However, we plan to explore this further in future updates and consider the primary analysis as separate networks for missed and incomplete miscarriage.

Overall completeness and applicability of evidence

This network meta-analysis provides the relative effectiveness of all methods used in the management of a miscarriage in a coherent and methodologically robust way across important clinical outcomes by combining both direct and indirect evidence, thus increasing the statistical power and confidence in the results. We found that most of the included trials reported our primary outcome of complete miscarriage and provided enough information to allow us to extract a composite outcome of death and serious complications. Most of our secondary outcomes were also reported in enough trials to perform network meta-analysis. This increased the power across most of our analyses and contributed to the consistency in the rankings across all outcomes related to complete miscarriage such as need for unplanned or emergency surgical procedures, readmissions to hospital and days of bleeding.

We were able to evaluate the impact of the type of miscarriage on the rankings and relative effectiveness of each method of miscarriage management. A high level of statistical inconsistency and heterogeneity was identified within the evidence, therefore subgroup analyses were performed for incomplete and missed miscarriage. Rankings within the subgroups were comparable to the overall rankings. For both incomplete and missed miscarriages, the surgical methods were ranked higher than the medical methods, which in turn were ranked higher than the expectant

management or placebo. However, we did find important differences in the effectiveness of the surgical and medical options amongst the two subgroups of women. The relative benefits for women with missed miscarriages undergoing any management method other than expectant management or placebo were far greater compared to women with incomplete miscarriages. This is probably because expectant management or placebo is more likely to be a more effective management option when the process of miscarriage has already started.

Unfortunately, not enough of the included trials differentiated between other effect modifiers such as gestational age of the miscarriage, healthcare setting of the intervention was not clearly stated in most trials and there was too much heterogeneity with regard to different dosages, regimens and routes of drug administration for meaningful results from network meta-analysis. This was particularly the case with misoprostol and the misoprostol component of mifepristone and misoprostol. Misoprostol depending on the trial was administered orally, vaginally or sublingually, at a dose of 400 mcg or 600 mcg or 800 mcg as a one-off dose, every four hours or six hours or on a following day (see Characteristics of included studies).

All the trials had wide inclusion criteria, none of the trials had restrictions on age or body mass index or ethnicity. Trials were also conducted across 37 countries, in a mix of high-, middle- and low-income countries from North America, South America, Europe, Africa and all over Asia. Trials were performed in a wide variety of settings from local clinics to district hospitals and in large tertiary and university hospitals. Many of the trials conducted in low- and middle-income countries also included women who may have had incomplete termination care who presented at inclusion as incomplete miscarriage (Characteristics of included studies). All of this ensures applicability of the evidence worldwide, to any women seeking treatment for a miscarriage of less than or equal to 14 weeks gestation in any healthcare setting including women whose miscarriage may have been induced medically. Both mifepristone and misoprostol are listed in the WHO Model list of essential medicines 2019 (WHO 2019). A vaginal speculum and surgical suction pump (manual or electric) with catheter (which is the basis of suction aspiration) are on the WHO generic essential emergency equipment list (WHO 2012) ensuring they are available around the world for most healthcare settings.

Quality of the evidence

We recognise that there is no single established approach for assessing the certainty of the effect estimates generated by the network meta-analysis. We applied the rigorous method for appraising the certainty of network evidence as proposed by the GRADE Working group. Overall, the evidence presented varied widely in certainty, and our confidence in the effect estimates ranged from very low to moderate certainty. When we compared the five other methods of miscarriage management versus expectant management or placebo, the certainty of network level evidence for the outcome of complete miscarriage, was either moderate or low. For suction aspiration plus cervical preparation being ranked first, the certainty was low due to downgrading of the indirect evidence for limitations in study design. For dilatation and curettage, suction aspiration and misoprostol being ranked second, third and fifth, the certainty of network level evidence was low due to moderate certainty direct evidence and inconsistency between direct and indirect estimates. The certainty of network

level evidence was moderate for mifepristone plus misoprostol (Summary of findings 1). Evidence for suction aspiration versus misoprostol for the outcomes of nausea, vomiting and diarrhoea were downgraded for publication bias. The certainty of evidence is also affected by inconsistencies between how different studies have reported outcomes.

The GRADE certainty of evidence assessment for the network meta-analysis for the composite outcome of death and serious complications when comparing the five other methods to expectant management or placebo was low. There was downgrading either due to low certainty direct evidence (no intransitivity or incoherence) or due to low certainty indirect evidence (no intransitivity or incoherence) (Summary of findings 4).

The risk of bias of the individual studies which contributed to this network meta-analysis varied, but the majority were judged to be at low risk of bias which included large, well-conducted and methodologically robust trials (Figure 3). Overall therefore, we feel the risk of bias was low and the sensitivity analysis removing high risk of bias trials, confirmed our conclusion.

Potential biases in the review process

Four of the review authors (AC, AJD, IDG and LB) were involved with the MifeMiso trial (Chu 2020). None of these authors participated in any decisions regarding this trial (i.e. assessment for inclusion/ exclusion, trial quality, data extraction) for the purposes of this review or for future updates – these tasks have been carried out by other members of the team who were not directly involved in the trial. The certainty of the evidence was assessed by a team of authors based in different countries. Before we could GRADE the network meta-analysis evidence, we had to determine the methodology for this process because there is no well-established approach or accompanying tools such as software. All GRADE assessments were undertaken independently by two individuals (JG and AP) and then re-assessed independently by a third review author (IDG) who was the arbiter of any disagreements.

The included studies did vary according to when they were conducted. The earliest was in 1979 (Caceres 1979), with a further study conducted in 1981 by the same author (Caceres 1981); nine studies were published in the decade beginning 1990; 32 were published in the decade beginning 2000; and 27 were published in the decade beginning 2010. The actual interventions are unlikely to have changed significantly during this time, however, the general care women receive may well have done, with improvements to efforts used to control side effects such as pain, nausea and vomiting. However, overall 59 out of 70 trials were conducted since 2000 and therefore we believe that there is minimal impact on the network meta-analysis from this.

A source of heterogeneity and inconsistency was the type of miscarriage as discussed before that we plan to explore this further in future updates and consider the primary analysis as separate networks for missed and incomplete miscarriage.

A further source of heterogeneity was differences in how the primary outcome of complete miscarriage was assessed with some trials assessing the complete miscarriage outcome clinically based on history and examination, whilst others used a combination of ultrasonography to check for an empty uterine cavity and clinical assessment. Another source of heterogeneity was the time

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point used to assess complete miscarriage. Removing trials which only used clinical examination or ultrasonography, or limiting the analysis to studies that used a specific time point to assess complete miscarriage would have greatly reduced the number of trials available for the network meta-analysis and hence reduced the strength of our overall findings. Lastly, not all trials reported data on side effects and severity of side effects, hence these analyses were often underpowered or network meta-analysis was not possible.

Agreements and disagreements with other studies or reviews

There are four Cochrane Reviews listed in the treatment of miscarriage section for the Pregnancy and Childbirth group which are comparable to this review, (Lemmers 2019; Kim 2017; Nanda 2012; Tuncalp 2010). Lemmers 2019 compared misoprostol (with various routes of administration), mifepristone and vaginal gemeprost with surgical management, expectant management, placebo or other different types of medical intervention for miscarriages up to 24 weeks of gestation. Our results agreed that misoprostol was better than placebo and expectant management in accomplishing a complete miscarriage, but less effective when compared to surgical management. Kim 2017 compared vaginal misoprostol with expectant management and misoprostol via any route of administration with surgical evacuation for incomplete miscarriage. Our results agreed that misoprostol was less effective at completing a miscarriage compared to surgical methods. Kim 2017 found no difference when comparing misoprostol with expectant care (based on two studies, 150 women) whereas we found a difference when comparing misoprostol with expectant management or placebo (based on nine studies, 755 women). Nanda 2012 compared expectant management with surgical management for management of a miscarriage. Our results agreed with this review that expectant management was more likely to result in an incomplete miscarriage and that there was a higher need for unplanned surgical treatment with expectant management when compared to surgical management. Tuncalp 2010 compared suction aspiration with dilatation and curettage. Our results agreed with this review that suction aspiration was associated with decreased blood loss when compared with dilatation and curettage. A similar network meta-analysis on this has previously been conducted (Al Wattar 2019), which concluded that medical treatments for first-trimester miscarriage have similar effectiveness and side effects compared to surgery. The scope of this review was much smaller, with only 46 trials included, which resulted in lower power and may account for the different conclusion reached.

AUTHORS' CONCLUSIONS

Implications for practice

This review shows that all medical and surgical methods for managing a miscarriage were more effective than when compared with expectant management, based on moderate- and low-certainty evidence. Expectant management has the lowest chance of successfully managing a miscarriage and has the highest chance of serious complications and the need for unplanned or emergency surgery. This review adds to the evidence base that surgical and medical methods for managing miscarriage appear to be more beneficial in women with missed miscarriage compared to women with incomplete miscarriage. However, the

evidence suggests that surgical treatment of a miscarriage does carry higher risks of pelvic infection compared to medical and expectant options and that medical options are probably the worst for side effects such as nausea, vomiting, diarrhoea and pyrexia. Policy makers should take into account the various options when considering implementation strategies, building or supporting health service delivery and healthcare providers should take into account the type of miscarriage when making decisions about the management of miscarriage. Healthcare providers should inform women about the risks and benefits for each method according to the type of miscarriage, and take into account their preferences for management options with similar risks and benefits.

Implications for research

The majority of the evidence presented in this review are of low certainty. Further high-quality trials are required to improve the certainty of the evidence. Many of the outcomes of this review are not routinely reported and future trials should report serious complications such as blood transfusions, infection, mean volumes of blood loss, changes in haemoglobin measurement before and after the miscarriage, mean durations of hospital stay, readmission to hospital consistently. This is especially the case for patient-reported outcomes such as pain scores, days of bleeding, women's views or satisfaction, nausea, vomiting, diarrhoea, anxiety and depression scores.

Future trials should examine the effectiveness of the methods of miscarriage separate for the subgroups of women according to their type of miscarriage. Trials could have broad inclusion criteria, including women both with missed or incomplete miscarriage, but effectiveness results should be presented separately for type of miscarriage. There is likely to be wider availability of the medical management of miscarriage options due to the nature of the surgical interventions requiring specialist equipment and training and therefore further work is needed to establish the most effective doses, routes and regimens of misoprostol and the misoprostol component for mifepristone plus misoprostol as this current network meta-analysis does not establish this. There is paucity of data regarding cervical preparation before surgical management, and the combination of mifepristone plus misoprostol so future trials should try to address this.

Future trials should also examine the impact of longer-term sequelae of methods of miscarriage management such as time to return to normal menstruation and future fertility rates to provide additional information to women when counselling about treatment options as this information is often a priority for women. This information was not widely available in the included papers for this current review, but should be considered for inclusion in a future update if and when sufficient evidence becomes available. A uniform core outcome set for miscarriage would also aid any future evidence synthesis.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abdelaleem 2020

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	84 women attending a university hospital in Egypt between July 2017 and July 2019 with a first trimester miscarriage (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage
Notes	Conference abstract only, source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being expectant management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	>10% of women lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Al-Maani 2014

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial

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Al-Maani 2014 *(Continued)*

Participants	234 women attending a university hospital in Germany between February 2011 and April 2012 with a miscarriage of ≤13 weeks of gestation (both incomplete and missed miscarriage)
Interventions	Suction aspiration as an inpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; days of bleeding
Notes	Corresponding author emailed on 01-Apr-2019 to clarify nature of surgical treatment, however, no response was received from the corresponding author after 2 emails. It is the judgement of the authors the surgical intervention was most likely suction aspiration. Source of funding not stated, no declarations of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated list of random numbers
Allocation concealment (selection bias)	Low risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% of participants lost to follow-up
Selective reporting (reporting bias)	Low risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other significant sources of bias noted

Ara 2009

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	600 women attending a university hospital in Bangladesh between January 2007 and December 2008 with a miscarriage of ≤12 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol given vaginally (exact dose and regimen not specified) versus suction aspiration
Outcomes	Data presented in an unusable form

Ara 2009 *(Continued)*

Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera-tion (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (perfor-mance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome as-sessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (re-porting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Arellano 2009

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	242 women attending a tertiary maternity hospital or a small private family planning clinic in Ecuador between unspecified dates with a miscarriage (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; women's views/satisfaction
Notes	Abstract only, no corresponding author details available. Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera-tion (selection bias)	Unclear risk	Method of randomisation not stated

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Arellano 2009 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	>10% of women lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Arif 2018

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	90 women attending a teaching hospital in Pakistan between August 2017 and February 2018, with a miscarriage of <12 weeks gestation (type of miscarriage unspecified)
Interventions	Suction aspiration as an outpatient manual procedure versus dilatation and curettage as an inpatient
Outcomes	Complete miscarriage; mean duration of hospital stay
Notes	Corresponding author emailed on 04-Jul-2019 to clarify type of miscarriage but no response was received from the corresponding author after 2 emails. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Draw method of randomisation used
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to both arms being surgical and one arm being under local anaesthetic and other arm being under general anaesthetic surgical
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated if outcome assessors were blinded

Arif 2018 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other significant sources of bias noted

Bagratee 2004

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, randomised, placebo-controlled trial
Participants	104 women presenting to a university hospital in the UK between August 2001 and March 2002 with a miscarriage of <13 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 600 micrograms given vaginally (as a single dose on day 1 and if needed day 2) as an outpatient versus placebo given vaginally (as a single dose on day 1 and if needed day 2) as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; pain scores; pelvic inflammatory disease, endometritis or sepsis; women's views/satisfaction; duration of bleeding; nausea; vomiting; diarrhoea; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer based allocation to either arm
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, sealed envelopes created by a third party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both participants and personnel blinded to intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting

Bagratee 2004 *(Continued)*

Other bias	Low risk	No other significant sources of bias noted

Bique 2007

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	247 women attending a tertiary hospital in Mozambique between December 2004 and January 2006, with a miscarriage of $\leq$ 12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pain scores; pelvic inflammatory disease, endometritis or sepsis; women's views/ satisfaction; nausea; vomiting; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-based randomisation
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	>10% lost at follow-up with nearly double lost from the suction curettage arm compared to the misoprostol arm
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Blohm 2005

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, randomised, placebo-controlled trial

Blohm 2005 *(Continued)*

Participants	126 women attending a university hospital in Sweden between unspecified dates, with a miscarriage in the first trimester (exact gestation unspecified) (type of miscarriage unspecified)
Interventions	Misoprostol 400 micrograms given vaginally as an outpatient versus placebo given vaginally as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; pain scores; pelvic inflammatory disease, sepsis or endometritis
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table used for sequence generation
Allocation concealment (selection bias)	Low risk	Sealed numbered enveloped created by a third party used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both participants and personnel blinded to intervention. Placebo and misoprostol identical looking
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Randomisation list not kept by trial team and not broken until after completion of study
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Braham 2016

Study characteristics

Methods	Single-centre, 2 arm, unblinded, randomised controlled trial
Participants	60 women attending a tertiary hospital in the Bahamas between April 2007 and October 2007, with a miscarriage in the first trimester (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given orally (every 4 hours for 3 doses in total) as an outpatient versus suction aspiration
Outcomes	Days of bleeding
Notes	Abstract only available, no corresponding author details or full text available. Source of funding not stated, declarations of interest not stated.

Braham 2016 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of patients in surgical group not clearly stated.
Selective reporting (reporting bias)	Unclear risk	No protocol or full text available, complete miscarriage rate only reported for one intervention
Other bias	Low risk	No other sources of bias noted

Caceres 1979

Study characteristics

Methods	Single-centre, 4-arm, unblinded, randomised controlled trial
Participants	600 women attending a tertiary hospital in El Salvador between April 1978 and May 1979 with a miscarriage of $\leq$ 14 weeks gestation (incomplete miscarriage only)
Interventions	Dilatation and curettage versus suction aspiration
Outcomes	Complete miscarriage; composite outcome of death of serious complication; pelvic inflammatory disease, endometritis or sepsis; cervical tear; mean duration of hospital stay; readmission to hospital; pyrexia
Notes	Study performed with 4 arms with randomisation between inpatient and outpatient settings as well as the two different intervention but these groups were combined for purposes of this review into the interventions above. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated

Caceres 1979 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to both arms being surgical
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor was blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	24% lost to analysis due to reassignment between study groups
Selective reporting (reporting bias)	Unclear risk	No protocol available for inspection but protocol is mentioned in text, no specific evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Caceres 1981

Study characteristics

Methods	Single-centre, 4-arm, unblinded, randomised controlled trial
Participants	599 women attending a university maternity hospital in Columbia between April 1978 to September 1978, with a miscarriage of $\leq$ 15 weeks gestation (incomplete miscarriage only)
Interventions	Dilatation and curettage versus suction aspiration
Outcomes	Composite outcome of death or serious complication; re-admission to hospital; vomiting; pyrexia
Notes	It was noted by the authors that 98.7% of participants were $\leq$ 12 weeks of gestation therefore it was felt that as only a very small proportion of participants would be > 14 weeks and that the study should be included. Study performed with 4 arms with randomisation between inpatient and outpatient settings as well as the two different interventions but these groups were combined for purposes of this review into the interventions above. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Shuffled cards in sealed envelopes
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to surgical nature of both intervention arms

Caceres 1981 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Chigbu 2012

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	320 women attending a private clinic in Nigeria between January 2010 and December 2011 with a miscarriage of gestation ≤ 12 weeks (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; pain scores; women's views/ satisfaction; nausea; vomiting; diarrhoea; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Low risk	Sequentially-numbered envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting

Chigbu 2012 *(Continued)*

Other bias	Low risk	No other sources of bias noted

Chipchase 1997

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	35 women attending a university hospital in the UK between unspecified dates, with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Suction aspiration as an inpatient electric procedure versus expectant management as an outpatient
Outcomes	Pelvic inflammatory disease, endometritis or sepsis; women's views/ satisfaction
Notes	Published short communication only, no up-to-date corresponding author details or full paper found. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Chu 2020

Study characteristics

Methods	Multi-centre, 2-arm, blinded, placebo-controlled randomised controlled trial

Chu 2020 *(Continued)*

Participants	711 women attending hospitals in the UK between Oct 2017 and July 2019 with a miscarriage of <12 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 200 mg given orally or an oral placebo tablet, both followed by a single dose of vaginal, oral, or sublingual misoprostol 800 micrograms 2 days later.
Outcomes	Complete miscarriage; composite outcome of death or serious complication; infection; need for emergency surgery; days of bleeding.
Notes	Funded by the UK NIHR Health Technology Assessment program (project number HTA 15/160/02). Authors declare no relevant conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated in 1:1 ratio with the use of minimization.
Allocation concealment (selection bias)	Low risk	Through a secure, centralised Internet facility.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Study participants and caregivers were blinded to treatment allocations.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded to treatment allocations.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition bias was <10% and balanced across study arms.
Selective reporting (reporting bias)	Low risk	The study report matches the study protocol (ISRCTN17405024) that was registered prospectively.
Other bias	Low risk	Funded by the UK NIHR Health Technology Assessment programme (project number HTA 15/160/02).

Chung 1997

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	350 women attending a university hospital in Hong Kong between unspecified dates, with a miscarriage (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Suction aspiration versus expectant management
Outcomes	Data presented in an unusable form

Chung 1997 *(Continued)*

Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Chung 1999

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	635 women attending a university hospital in Hong Kong between October 1995 and January 1998, with a miscarriage (exact gestation unspecified but the mean gestation of each arm was < 11 weeks with a standard deviation of 2.6 for the suction aspiration group and 2.5 for the misoprostol group) (both incomplete and missed miscarriage)
Interventions	Misoprostol 400 micrograms given orally (every 4 hours for 3 doses in total) as an inpatient versus suction aspiration as an inpatient electric procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; pelvic inflammatory disease, endometritis or sepsis; change in haemoglobin measurements before and after the miscarriage; days of bleeding; cervical tear; mean duration of hospital stay
Notes	Authored confirmed via email on 02-May-2019 that surgical arm was electric suction curettage +/- possible check curettage. Trial funded by Health Services Research Fund of Hong Kong. Declarations of interest not stated.

Risk of bias

Chung 1999 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated set of random numbers
Allocation concealment (selection bias)	Low risk	Serially-numbered, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up at 2 weeks
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Dabash 2010

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	697 women attending 2 tertiary hospitals in Egypt between 7th February 2007 and 28th October 2008, with a miscarriage of ≤12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given sublingually as an outpatient versus suction aspiration as an outpatient or inpatient manual procedure
Outcomes	Complete miscarriage; change in haemoglobin measurements before and after the miscarriage; women's views/ satisfaction; nausea; vomiting; pyrexia
Notes	Study was funded by the David and Lucille Packard Foundation. The authors declare no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Remote, third party, computer-generated randomisation in blocks of 10
Allocation concealment (selection bias)	Low risk	Remotely created by a third party, sequentially-numbered envelopes

Dabash 2010 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Dangalla 2012

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	160 women attending a university hospital in Sri Lanka between 1st January 2009 to 15th July 2009 with a miscarriage of < 14 weeks gestation (incomplete miscarriage only)
Interventions	Expectant care as an inpatient versus suction aspiration as an inpatient electric procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; women's views/ satisfaction
Notes	Clinical Trials Register, Sri Lanka (SLCTR/2008/011). Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation used
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded

Dangalla 2012 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Some results were only reported as a difference with a P-value not the actual results themselves.
Other bias	Low risk	No other sources of bias notes

Dao 2007

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	460 women attending 2 university hospitals in Burkina Faso between April 2004 and October 2004 with a miscarriage of < 12 weeks of gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; pain score; pelvic inflammatory disease, endometritis or sepsis; women's views/ satisfaction; re-admission to hospital; nausea; vomiting; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, computer-generated random sequence
Allocation concealment (selection bias)	Low risk	Third-party, sequentially-ordered, opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if all outcome assessors were blinded, only stated sonographers performing scans were not members of the study team
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	Funded by the Packard Foundation

Das 2014

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	222 women attending a university hospital in Pakistan between May 2011 and April 2012 with a miscarriage of <12 weeks of gestation (incomplete miscarriage only)
Interventions	Manual vacuum aspiration versus misoprostol 600 micrograms given orally as an outpatient
Outcomes	Complete miscarriage; pyrexia
Notes	Source of funding not stated, declarations of interest not stated; no evidence of prospective trial registration

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation using computer-generated random sequence,
Allocation concealment (selection bias)	Low risk	Treatment was printed on a card and that card was closed in a envelop. Envelopes were then sealed and were mixed randomly
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being surgical management and other arm being medical management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% of women lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Low risk	No other sources of bias noted

Davis 2007

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	652 women attending 4 university medical centres in the USA between March 2002 and March 2004 with a miscarriage of ≤13 weeks gestation (both incomplete and missed miscarriage)

Davis 2007 *(Continued)*

Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed day 3) as an out-patient versus suction aspiration either as an outpatient manual or inpatient electric procedure in a 3:1 ratio
Outcomes	Changes in haemoglobin measurements before and after the miscarriage
Notes	Is a secondary analysis of Zhang 2005. Funded by contracts (N01-HD-1-3321, N01- HD-3322, N01-HD-3323, N01-HD-3324, and N01-HD-3325) with the National Institute of Child Health and Human Development, National Institutes of Health. No declarations of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centralised, remote, computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Centralised, remote, computer-generated allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not clear if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias notes

de Holanda 2003

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	102 women attending a university hospital in Brazil between Jan 1998 and July 2001 with a miscarriage of ≤12 weeks gestation (type of miscarriage not specified)
Interventions	Suction curettage versus manual vacuum aspiration
Outcomes	Pain control, need of mechanical cervical dilation, time of evacuation of the uterus, rate of complications and hospital stay
Notes	Source of funding not stated, declarations of interest not stated. None of the reported outcomes were eligible for inclusion in the review.

de Holanda 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to the two groups being surgical management
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol or full text available
Other bias	Unclear risk	No other sources of bias noted

de Jonge 1995

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	50 women attending a university hospital in South Africa between unspecified dates with a miscarriage of ≤ 14 weeks of gestation (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given orally as an inpatient versus dilatation and curettage as an inpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication
Notes	Short communication only available, no corresponding author contact details or full paper available. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random numbers
Allocation concealment (selection bias)	Low risk	Opaque, sealed envelopes used

Cochrane
Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

de Jonge 1995 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol mentioned but not available for review. No evidence of selective reporting.
Other bias	Low risk	No other sources of bias noted

Demetroulis 2001

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	80 women attending a secondary hospital in the UK between unspecified dates, with a miscarriage of <13 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 800 micrograms given vaginally as an inpatient versus suction aspiration as an inpatient electric procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; women's views/satisfaction; nausea; vomiting; diarrhoea
Notes	Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random numbers
Allocation concealment (selection bias)	Low risk	Opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if all outcome assessors were blinded

Demetroulis 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Fernlund 2018

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	189 women attending a university hospital in Sweden between September 2008 and December 2015, with a miscarriage of 6 to 16 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death of serious complication; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; days of bleeding; mean duration of hospital stay; re-admission to hospital; nausea; vomiting; diarrhoea
Notes	Clinicaltrials.gov identifier NCT01033903. Study terminated prematurely due to slower than anticipated recruitment despite a prolonged recruitment period. It was noted the maximum gestation age of the study was 16 weeks, however, the mean gestational age in weeks of the misoprostol arm was 10.9 with a standard deviation of 2.0 and the mean gestational age in weeks of the expectant arm was 10.8 with a standard deviation of 1.8 and so it was felt by the authors that the vast majority of patients would have been ≤ 14 weeks gestation and therefore the paper was included. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, computer-generated, randomisation in blocks of 6
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed, opaque envelopes prepared by a third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessor was unblinded
Incomplete outcome data (attrition bias)	Low risk	< 10% lost to follow-up

Fernlund 2018 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Low risk	Outcomes listed in protocol have been reported
Other bias	Low risk	No other sources of bias noted

Fonseca 1997

Study characteristics

Methods	Single-centre, 2-arm, randomised controlled trial
Participants	30 women attending an unspecified healthcare facility in Brazil between 11th December 1995 and 4th January 1996 with a miscarriage of <12 weeks gestation (incomplete miscarriage only)
Interventions	Dilatation and sharp curettage as an inpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Mean duration of hospital stay
Notes	Translation only available at time of data extraction. Cochrane translation by r.reisdasilva@gmail.com. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation sequence was concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated if participants and personnel were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if all outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available
Other bias	Low risk	No other sources of bias noted

Ganguly 2010

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	180 women attending a university hospital in India between 1st May 2007 and 30th April 2008, with a miscarriage of <12 weeks gestation (both incomplete and missed miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed on day 3) as an outpatient versus suction aspiration as an inpatient manual procedure in a 2:1 ratio
Outcomes	Complete miscarriage; composite outcome of death or serious complication; cervical tear; nausea; diarrhoea; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random number list
Allocation concealment (selection bias)	Low risk	Opaque, sealed envelopes used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Gazvani 2000

Study characteristics

Methods	Single centre, 3-arm, unblinded, randomised controlled trial
Participants	22 women attending a maternity hospital in the UK between November 1998 and April 1999, with a miscarriage in the 1st trimester (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Suction aspiration as a manual procedure versus expectant management
Outcomes	Data presented in an unusable form

Gazvani 2000 *(Continued)*

Notes	Abstract only, no corresponding author details available, medical management arm was also present for patients with missed miscarriage but medical management was not qualified and therefore this side of trial not included, results given for incomplete miscarriage side of trial do not make mathematical sense. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Graziosi 2004

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	154 women attending three hospitals in the Netherlands between November 2001 and June 2003 with a miscarriage of between 6 and 14 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 200 micrograms given vaginally, followed by misoprostol 800 micrograms given vaginally if needed versus suction aspiration
Outcomes	Complete miscarriage; need for emergency surgery; pain score; days of bleeding; nausea; diarrhoea
Notes	Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed using a computer program with a block randomisation sequence

Graziosi 2004 *(Continued)*

Allocation concealment (selection bias)	Low risk	A computer-based block randomisation sequence guaranteed the concealment of allocation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Unclear risk	No other sources of bias noted

Hamel 2021

Study characteristics

Methods	Multi-centre, 2-arm, blinded, placebo-controlled randomised controlled trial
Participants	351 women attending hospitals in the Netherlands between June 2018 and January 2020 with a miscarriage of ≤14 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 200 mg given orally or an oral placebo tablet, both followed by misoprostol 800 micrograms given orally 36 to 48 hours later.
Outcomes	Complete miscarriage; composite outcome of death or serious complication; infection; need for emergency surgery; diarrhoea; nausea
Notes	Funded by the (project number: 3080 B15191). In addition, departmental funds from the Department of Obstetrics and Gynaecology from both Radboud university medical centre and Canisius Wilhelmina Hospital, both Nijmegen, the Netherlands, were used. Dr. Hamel reports grants from Healthcare Insurers Innovation Foundation, during the conduct of the study; meant to cover costs of performing the trial, no involvement in any other aspect of the trial such as study design, data gathering/analysis, manuscript preparation. All other authors have nothing to declare.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was conducted by block randomisation, with a block size of eight, stratified by hospital. The randomisation tables were generated by two independent physicians, who had no further role in the execution of the trial.
Allocation concealment (selection bias)	Low risk	Through a secure, computerised system.

Hamel 2021 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Study participants and caregivers were blinded to treatment allocations.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blinded to treatment allocations.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition bias was <10% and balanced across study arms.
Selective reporting (reporting bias)	Low risk	The study report matches the study protocol (ISRCTN17405024) that was registered prospectively.
Other bias	Low risk	Funded by the Healthcare Insurers Innovation Foundation (project number: 3080 B15191). In addition, departmental funds from the Department of Obstetrics and Gynaecology from both Radboud university medical centre and Canisius Wilhelmina Hospital, both Nijmegen, the Netherlands, were used.

Harwood 2008

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	652 women attending 4 university hospitals in the USA between March 2002 and March 2004 with a miscarriage of <12 weeks of gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed day 3) as an outpatient versus suction aspiration either as an outpatient manual or inpatient electric procedure in a 3:1 ratio
Outcomes	Pain scores; depression; anxiety
Notes	this is a secondary analysis of Zhang 2005. NICHD, National Institutes of Health (NIH), under contract numbers N01-HD-1-3321 through 3325 and by NIH General Clinic Research Center Grant MOIRR000056. Declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centralised, remote, computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Centralised, remote, computer-generated allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical

Harwood 2008 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not clear if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias notes

Ibiyemi 2018

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	200 women attending a teaching hospital in Nigeria between April 2014 and November 2015 with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an inpatient versus suction aspiration as an inpatient manual procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; women's views/ satisfaction; nausea; vomiting; diarrhoea; pyrexia
Notes	PACTR201803003087264. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Low risk	Allocation concealed, statistician not involved in care
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol not able to be found but no obvious selective reporting

Ibiyemi 2018 *(Continued)*

Other bias	Low risk	No other sources of bias noted

Igogo 2015

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	260 women attending a district general hospital and a tertiary hospital in Kenya between unspecified dates, with a miscarriage (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Suction aspiration as an outpatient manual procedure versus misoprostol 400 micrograms given sub-lingually as an outpatient
Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Kaluaarachchi 2015

Study characteristics

Methods	Single-centre, 3-arm, unblinded, randomised controlled trial

Kaluaarachchi 2015 *(Continued)*

Participants	180 women attending a university hospital in Sri Lanka between unspecified dates, with a miscarriage in the first trimester (both incomplete and missed miscarriage)
Interventions	Suction aspiration versus medical management versus expectant management
Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, medical management not qualified, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical, one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available
Other bias	Low risk	No other sources of bias noted

Karlsen 2001

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	97 women attending a women's Clinic in Norway between unspecified dates, with a miscarriage of ≤ 12 weeks gestation (type of miscarriage unspecified)
Interventions	Suction aspiration as an inpatient procedure versus expectant management as an outpatient
Outcomes	Complete miscarriage; pelvic inflammatory disease, endometritis or sepsis; days of bleeding
Notes	Email of corresponding author not in use anymore, article translated to English for data extraction from Norwegian. Source of funding not stated, declarations of interest not stated.

Risk of bias

Cochrane
Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence of envelopes was achieved
Allocation concealment (selection bias)	Low risk	Closed envelopes were used to conceal allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being surgical and other arm being expectant
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Kashif 2020

Study characteristics	
Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	60 women attending a university hospital in Pakistan between August 2011 and August 2012 with a miscarriage of <12 weeks of gestation (incomplete and missed miscarriage)
Interventions	Misoprostol 800 micrograms given vaginally as an outpatient versus suction aspiration as an inpatient
Outcomes	Complete miscarriage; need for emergency surgery; infection; pyrexia; vomiting; diarrhoea
Notes	Source of funding not stated, declarations of interest not stated; no evidence of prospective trial registration

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation achieved using block method, however block size not stated
Allocation concealment (selection bias)	Unclear risk	Details of allocation concealment not stated
Blinding of participants and personnel (performance bias)	High risk	Not possible due to one arm being medical management and other arm being expectant management

Kashif 2020 *(Continued)*

All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% of women lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No registered protocol or prospective trial registration available
Other bias	Low risk	No other sources of bias noted

Kittiwatanakul 2012

Study characteristics

Methods	Single-centre, 2 arm, unblinded, randomised controlled trial
Participants	94 women attending a hospital in Thailand between 1st March 2005 and 15th December 2009 with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Suction aspiration as an outpatient electric procedure versus dilatation and curettage as an outpatient procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; mean volume of blood loss
Notes	Source of funding not stated, the authors declare no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random number list used
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, opaque, sealed envelopes used
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to both arms being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up

Kittiwatanakul 2012 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Kong 2013

Study characteristics

Methods	Single-centre, 3-arm, unblinded, randomised controlled trial
Participants	180 women attending a university-affiliated, tertiary hospital in Hong Kong between September 2008 and July 2010 with a miscarriage in the first trimester (exact gestation not specified) (both incomplete and missed miscarriage)
Interventions	Suction aspiration as an inpatient procedure versus misoprostol 800 micrograms given vaginally as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; change in haemoglobin measurements before and after the miscarriage; days of bleeding; readmission to hospital; vomiting; diarrhoea; pyrexia; anxiety score; depression score
Notes	Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random numbers used
Allocation concealment (selection bias)	Low risk	Personnel were unaware of randomisation schedule
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical, another being surgical and another being expectant
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol mentioned in text but not available for inspection. No obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Kovavisarach 2002

Study characteristics

Methods	Single-centre, 2-arm, single-blinded, randomised placebo-controlled trial
Participants	54 women attending a tertiary hospital in Thailand between 1st July 1998 and 31st January 1999 with a miscarriage of ≤12 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 400 micrograms given vaginally as an outpatient versus placebo given vaginally as an outpatient
Outcomes	Complete miscarriage; diarrhoea; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how patients were randomly allocated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated if study personnel were blinded, it is assumed participants were blinded due to the use of a placebo
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Kyaw 2015

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	108 women attending a teaching hospital in Myanmar between unspecified dates with a miscarriage (exact gestation not specified) (type of miscarriage not specified)
Interventions	Misoprostol 800 micrograms given vaginally as an inpatient versus dilatation and curettage as an inpatient
Outcomes	Complete miscarriage; mean volume of blood loss

Kyaw 2015 *(Continued)*

Notes	Abstract only, corresponding author details not available. The abstract states 800mg of misoprostol was used. It is assumed that the authors mean Mg to mean micrograms. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Lottery method used for randomisation
Allocation concealment (selection bias)	Unclear risk	Allocation sequence unlikely to have been concealed due to lottery method
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% of participants lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol or full paper available but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Lee 2001

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	218 women attending a university teaching hospital in Hong Kong between October 1995 and June 1996 with a miscarriage (exact gestation not specified) (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given orally (every 4 hours for 3 doses in total) as an inpatient versus dilatation and curettage as an inpatient
Outcomes	Depression score
Notes	It is assumed that when describing the medical arm in the full text the unit of measurement of pg was written in error and it was supposed to be micrograms, not picograms. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement

Lee 2001 *(Continued)*

Random sequence genera- tion (selection bias)	Low risk	Computer-generated, set of random numbers used
Allocation concealment (selection bias)	Low risk	Opaque, sequentially-numbered envelopes
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome as- sessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	>10% lost to follow-up in each arm
Selective reporting (re- porting bias)	High risk	No protocol available. Complete miscarriage not and other clinical outcomes not reported to give context for depression scores.
Other bias	Low risk	No other sources of bias noted

Lister 2005

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, randomised placebo-controlled trial
Participants	36 women attending a teaching hospital in the USA| between 15th February 2002 and 19th March 2003 with a miscarriage (exact gestation not stated) (missed miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed day 2) as an outpa- tient versus placebo given vaginally (as a single dose on day 1 and if needed day 2)
Outcomes	Complete miscarriage; pain scores; women's views/ satisfaction; re-admission to hospital; nausea; vomiting; diarrhoea
Notes	Supported by the Riverside Methodist Hospital Medical Research Foundation, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence genera- tion (selection bias)	Low risk	Random sequence generated by the study epidemiologist in blocks
Allocation concealment (selection bias)	Low risk	Opaque randomisation packets used and both interventions similar in appear- ance
Blinding of participants and personnel (perfor- mance bias)	Low risk	Study personnel and participants blinded to intervention and placebo similar in appearance to misoprostol

Lister 2005 (Continued)

All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol or full text available but no obvious selective reporting
Other bias	Low risk	No other sources of bias noted

Machtinger 2002

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	66 women attending a medical centre in Israel between unspecified dates with a miscarriage of ≤ 9 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 600 milligrams given orally + misoprostol 400 micrograms given orally 48 hours later and if needed repeat of misoprostol dose 3 hours later versus misoprostol 400 micrograms given orally + misoprostol 400 micrograms given orally 48 hours later and if needed repeat of misoprostol dose 3 hours later
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; pyrexia
Notes	Abstract only, no corresponding author details, It is assumed that the units of measurement for mifepristone (mcg) and misoprostol (mg) were written incorrectly in the abstract and therefore the units of measurement of milligrams and micrograms respectively were used as written above. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated methods of randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was unblinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded

Machtinger 2002 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	1 patient unaccounted, it is unclear from which study group they were lost
Selective reporting (reporting bias)	Unclear risk	No protocol or full text available but no obvious selective reporting
Other bias	Low risk	Mifepristone provided as a non-limited gift by A. Lapidot

Machtinger 2004

Study characteristics

Methods	Single-centre, 4-arm, unblinded, randomised controlled trial
Participants	205 women attending a medical centre in Israel between unspecified dates with a miscarriage of < 9 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 600 milligrams given orally + misoprostol 400 micrograms given orally 48 hours later and if needed repeat of misoprostol dose 3 hours later versus mifepristone 600 milligrams given orally + misoprostol 800 micrograms given vaginally 48 hours later versus misoprostol 400 micrograms given orally + misoprostol 400 micrograms given orally 48 hours later and if needed repeat of misoprostol dose 3 hours later versus misoprostol 800 micrograms given vaginally + misoprostol 800 micrograms given vaginally 48 hours later all as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; pyrexia
Notes	Abstract only, no corresponding author details, for purposes of this review, the two arms both containing mifepristone and misoprostol and the two arms both containing misoprostol only were combined. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated method of randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was unblinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up

Machtinger 2004 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol or full text available but no obvious selective reporting
Other bias	Unclear risk	Group 2 > 50% smaller than Group 1, Mifepristone provided as a non limited gift by A. Lapidot.

Montesinos 2011

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	242 women attending a tertiary maternity hospital or a small private secondary level family planning clinic in Ecuador between 6th November 2006 and 28th November 2007 with a miscarriage of $\leq$ 12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration either as an outpatient or inpatient manual procedure
Outcomes	Complete miscarriage; days of bleeding; women's views/satisfaction; nausea; vomiting; pyrexia
Notes	Clinicaltrials.gov trial registration number NCT00674232. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Remotely created, stratified, computer-generated random sequence in blocks of 10
Allocation concealment (selection bias)	Low risk	Remotely created, sequentially-numbered, sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	16% lost to follow-up
Selective reporting (reporting bias)	High risk	Secondary outcomes reported in paper were not pre-specified in the original protocol that was registered.
Other bias	Unclear risk	The method of outcome assessment varied between sites with some being assessed clinically and others using ultrasound, funded by Packard Foundation

Moodliar 2005

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	94 women attending a tertiary university teaching hospital in South Africa between October 2003 and April 2004 with a miscarriage of ≤13 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given vaginally (as a single dose on day 1 and if needed on day 2) as an in-patient versus dilatation and curettage as an inpatient procedure
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pain scores; pelvic inflammatory disease, endometritis or sepsis; days of bleeding; women's views/ satisfaction; nausea; vomiting; diarrhoea
Notes	Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated patient number allocation
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, sealed, envelopes created by a third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Muffley 2002

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	50 women attending a naval military medical centre in the USA between June 1999 and March 2000 with a miscarriage of < 12 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed on day 2) as an outpatient versus suction aspiration either as an inpatient or an outpatient

Muffley 2002 *(Continued)*

Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; nausea; vomiting; diarrhoea
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation via computer-generated, random number table
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed, opaque envelopes created by a third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Unclear risk	The study authors noted that some medical patients had misoprostol co-administered with a vaginal lubricant which could have introduced non-uniformity of dosing or a variable absorption pattern. Authors acknowledge this study maybe subject to a type 2 statistical error due to overestimation of the success of misoprostol.

Nadarajah 2014

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	360 women attending a tertiary hospital in Malaysia between 1st January 2009 and 31st December 2009 with a miscarriage of ≤ 14 weeks gestation (both incomplete and missed miscarriage)
Interventions	Suction aspiration as an inpatient procedure versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; mean volumes of blood loss; change in haemoglobin measurements before and after the miscarriage; days of bleeding; cervical tears; women's views/satisfaction; readmission to hospital
Notes	Source of funding not stated, declarations of interest not stated.

Nadarajah 2014 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence prepared in blocks of 10
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded to the interventions
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Nasreen 2009

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	216 women attending a university hospital in Bangladesh between January 2006 and January 2008 with a miscarriage of <10 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 400 micrograms given orally (every 4 hours for 3 doses in total) + if needed misoprostol 200 micrograms given orally 48 hours later versus suction aspiration with cervical priming using misoprostol 400 micrograms given orally as an outpatient manual procedure
Outcomes	Complete miscarriage; women's views/ satisfaction; pyrexia
Notes	Abstract only available, no corresponding author details. It is stated 216 women were randomised but only 100 in each arm. It is not explained what happened to these 16 patients. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated

Nasreen 2009 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	16 patients not accounted for in each arm compared to initial randomisation
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Ngai 2001

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	60 women attending a university tertiary hospital in Hong Kong between 1998 and 1999 (exact dates not specified) with a miscarriage of ≤ 12 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 400 micrograms given vaginally (as a single dose on day 1 and if needed on day 3 and day 5) as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; nausea; vomiting; diarrhoea
Notes	It is not stated in the paper what the type of infection was but it is the judgment of the authors the cases of infection would be of gynaecological origin or sepsis. Study was supported by the Committee on Research and Conference Grants, the University of Hong Kong; declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Validated randomisation table
Allocation concealment (selection bias)	Low risk	Serially-labelled, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being expectant

Methods for managing miscarriage: a network meta-analysis (Review)

Ngai 2001 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Nielsen 1995

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	155 attending a university hospital in Sweden between December 1992 and March 1994 with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Expectant management as an outpatient versus dilatation and curettage as an inpatient in a 2:1 ratio
Outcomes	Complete miscarriage; pelvic inflammatory disease, endometritis or sepsis; days of bleeding
Notes	Supported by grants from the Swedish Medical Research Council (B95-17X-11237-01A); declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation via drawing pre-prepared sealed envelopes
Allocation concealment (selection bias)	Low risk	Allocation via drawing sealed envelopes from a box
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being surgical and other being expectant
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting

Nielsen 1995 *(Continued)*

Other bias	Low risk	No other sources of bias noted

Nielsen 1999

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	122 women attending a university hospital in Sweden between unspecified dates with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Mifepristone 400milligrams given orally + misoprostol 400 micrograms given orally 48 hours later as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pain score; pelvic inflammatory disease, endometritis or sepsis; days of bleeding; women's views/ satisfaction
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being expectant
Blinding of outcome assessment (detection bias) All outcomes	High risk	It is stated the study was not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Niinimaki 2006

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial

Niinimaki 2006 *(Continued)*

Participants	98 women attending a university hospital in Finland between 4th February 2003 and 8th December 2004 with a miscarriage in the first trimester (exact gestation unspecified) (both incomplete and missed miscarriage)
Interventions	Mifepristone 200 milligrams given orally + misoprostol 800 micrograms given vaginally 24 to 72 hours later as an outpatient versus suction aspiration as an inpatient procedure
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; women's views/ satisfaction; re-admission to hospital
Notes	Some of the surgical arm may have received cervical priming with 400 micrograms of misoprostol given vaginally, however, it is the judgment of the authors the majority would not have been, as cervical priming was mainly given to nulliparous patients and the mean parity of the surgical arm was 1.7. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third party, computer randomisation was used in blocks of 6
Allocation concealment (selection bias)	Low risk	Numbered, opaque, envelopes created by a third party
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Nwafor 2020

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	100 women attending a university hospital in Nigeria between February 2018 and August 2018 with a miscarriage of <13 weeks of gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus manual vacuum aspiration as an inpatient

Nwafor 2020 *(Continued)*

Outcomes	Complete miscarriage, need for emergency surgery, infection, cervical tear
Notes	No external funding obtained to conduct the study, authors declare no conflicts of interest.; no evidence of prospective trial registration

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A statistician blinded to the study's objectives generated the allocation sequence by simple randomisation using `computer-generated` random numbers.
Allocation concealment (selection bias)	Low risk	The allocation concealment was achieved by placing the allocation in sequentially numbered, opaque, sealed identical envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical managment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors not blinded to the intervention allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% of women lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No registered protocol or prospective trial registration available
Other bias	Low risk	No other sources of bias noted

Patua 2013

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	100 women attending a university hospital in India in 2009 (exact dates unspecified), with a miscarriage of ≤ 12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given vaginally (every 3 hours for 3 doses in total) as an inpatient versus suction aspiration as an inpatient
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; change in haemoglobin measurements before and after the miscarriage; pyrexia
Notes	Source of funding not stated, the authors declare no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement

Patua 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table used for randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were unblinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Pereira 2006

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	100 women attending a University hospital in Brasil between 1st January 2003 and 17th March 2004, with a miscarriage of <13 weeks gestation (incomplete miscarriage only)
Interventions	Dilatation and curettage as an inpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Composite outcome of death or serious complications; change in haemoglobin measurement before and after the miscarriage; cervical tear; mean duration of hospital stay; pyrexia
Notes	Paper available in Portuguese only. Translation used for data extraction. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm using general anaesthesia and other not using anaesthetic

Pereira 2006 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available, figures reported in results text not reported
Other bias	Low risk	No other sources of bias noted

Phusaanantakul 2010

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, placebo-controlled randomised trial
Participants	48 women attending a university hospital in Thailand between October 2008 and June 2009 with a miscarriage of < 12 weeks gestation (missed miscarriage only)
Interventions	Isosorbide mononitrate 20 milligrams given vaginally 4 hours before suction aspiration as an inpatient versus placebo given vaginally 4 hours before suction aspiration as an inpatient
Outcomes	Women's views/ satisfaction
Notes	Source of funding not stated, the authors declare no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed, opaque envelopes used
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Study was double blinded, placebo was identical-looking to intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors blinded to intervention versus placebo
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	High risk	No protocol available and no results given for outcomes such as nausea, vomiting, headache, palpitations and vaginal bleeding which were discussed in the materials and methods section

Phusaanantakul 2010 *(Continued)*

Other bias	Low risk	No other sources of bias noted

Sahin 2001

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	80 women attending a university hospital in Turkey between unspecified dates, with a miscarriage of ≤ 10 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 200 micrograms given vaginally + misoprostol 200 micrograms given via an unspecified route 4-6 hourly for 5 days as an outpatient versus suction aspiration as either an inpatient or outpatient procedure
Outcomes	Complete miscarriage; pelvic inflammatory disease, endometritis or sepsis; change in haemoglobin measurement before and after the miscarriage; days of bleeding; women's views/ satisfaction
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation process not stated
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Salam 2016

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial

Salam 2016 *(Continued)*

Participants	610 women attending a university hospital in Pakistan between July 2014 and July 2015 with a miscarriage of < 12 weeks gestation (incomplete miscarriage only)
Interventions	Suction aspiration as a outpatient manual procedure versus dilatation and curettage as an outpatient
Outcomes	Complete miscarriage
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation process not stated
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants or personnel not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available and no other outcomes available
Other bias	Low risk	No other sources of bias noted

Schreiber 2018

Study characteristics

Methods	Multi-centre, 2-arm, single-blinded, randomised controlled trial
Participants	300 women attending 2 university hospitals in the USA between May 2014 and April 2017, with a miscarriage of <13 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 200 milligrams given orally + misoprostol 800 micrograms given vaginally 24 hours later (and if needed repeated 48 to 72 hours later) as an outpatient versus misoprostol 800 micrograms given vaginally (and if needed repeated 48 to 72 hours later) as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complications; pelvic inflammatory disease, sepsis or endometritis; nausea, vomiting, diarrhoea, pyrexia

Schreiber 2018 *(Continued)*

Notes	PreFaiR trial Clinicaltrials.gov NCT02012491. Funded by the National Institute of Child Health and Human Development. Dr. Creinin reports receiving consulting fees from Danco Laboratories. No other potential conflict of interest relevant to this article were reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, blocked and stratified randomisation
Allocation concealment (selection bias)	Low risk	Computer-generated randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were unblinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Low risk	Outcomes relevant to this review stated in protocol are reported
Other bias	Low risk	No other sources of bias noted

Schwarzler 2003

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	104 women attending a university hospital in Austria between unspecified dates, with a miscarriage in the 1st trimester (exact gestation unspecified) (type of miscarriage unspecified)
Interventions	Dilatation and curettage as an inpatient procedure versus expectant management as an outpatient
Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated

Schwarzler 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Shaheen 2017

Study characteristics		
Methods	Single-centre, 2-arm, unblinded, randomised controlled trial	
Participants	104 women attending a university hospital in Pakistan between January 2016 and June 2016, with a miscarriage of < 12 weeks gestation (missed miscarriage only)	
Interventions	Suction aspiration as an outpatient manual procedure versus misoprostol 800 micrograms given vaginally (and misoprostol 400 micrograms given vaginally every 6 hours for 2 doses in total)	
Outcomes	Complete miscarriage	
Notes	Source of funding not stated, declarations of interest not stated	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated how random sequence was achieved
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were not blinded

Shaheen 2017 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available, only complete miscarriage outcome reported
Other bias	Low risk	No other sources of bias noted

Shaikh 2008

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	200 women attending a university hospital in Bangladesh between unspecified dates, with a miscarriage of <10 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 400 micrograms given orally every 4 hours for 3 doses in total (and if needed entire regimen repeated) as an inpatient versus misoprostol 400 micrograms given orally + suction aspiration as an outpatient manual procedure
Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Shelley 2005

Study characteristics

Methods	Multi-centre, 3-arm, unblinded, randomised controlled trial
Participants	27 women attending 3 district general hospitals, 1 tertiary hospital and 1 specialist women's hospital in Australia between June 1999 and December 2000 with a miscarriage of ≤ 13 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 400 micrograms given vaginally (and repeated 4-6 hours later if needed) as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/emergency surgical procedure; pelvic inflammatory disease, endometritis or sepsis; nausea; vomiting; diarrhoea
Notes	An additional surgical arm was reported, however, it was combined suction aspiration and dilatation and curettage and therefore data were not able to extracted separately, author contacted on 31-Mar-2019 but email address no longer in use, therefore surgical arm excluded for purposed of this review. VICMIST trial terminated early due to poor recruitment from eligible population.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, remote, stratified, computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Third-party, remote, computer-generated randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being expectant
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	Funding by Department of Human Services, Victoria, Best Practice Initiatives Grant and an MBF Medical Research Award.

Shuaib 2013

Study characteristics

Shuaib 2013 *(Continued)*

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	107 women attending a district general hospital in Yemen between 1st December 2010 and 31st November 2011, with a miscarriage of ≤ 12 weeks (missed miscarriage only)
Interventions	Dilatation and curettage as an inpatient versus misoprostol 400 micrograms given vaginally (and misoprostol 200 micrograms given vaginally every 4 hours for 11 doses in total if needed) as an inpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; pelvic inflammatory disease, endometritis or sepsis; cervical tear; women's views/ satisfaction; re-admission to hospital
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation process not stated
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Shwekerela 2007

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	300 women attending a tertiary hospital in Tanzania between July 2004 and April 2005 with a miscarriage of < 12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; pelvic inflammatory disease, endometritis or sepsis; pain scores; women's views/ satisfaction; nausea; vomiting; pyrexia

Shwekerela 2007 *(Continued)*

Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, remote, computer-generated, randomisation in blocks of 10
Allocation concealment (selection bias)	Low risk	Consecutively numbered, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol mentioned in text but not available for review, no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Sinha 2018

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, randomised placebo-controlled trial
Participants	92 women attending a university hospital in India between October 2011 and April 2013 with a miscarriage of ≤12 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 200mg given orally + misoprostol 800 micrograms given vaginally 48 hours later (and+ 4 hours later if needed misoprostol 400 micrograms given orally + 3 hours later if needed misoprostol 400 micrograms given orally and repeated every 3 hours for a maximum of 2 doses in women ≤9 weeks of gestation or 4 doses in women >9 weeks of gestation versus placebo given orally + misoprostol 800 micrograms given vaginally 48 hours later + 4 hours later if needed misoprostol 400 micrograms given orally + 3 hours later if needed misoprostol 400 micrograms given orally and repeated every 3 hours for a maximum of 2 doses in women ≤9 weeks of gestation or 4 doses in women >9 weeks of gestation
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/emergency surgical procedure; change in haemoglobin measurements before and after the miscarriage; days of bleeding
Notes	Clinical Trial Registry of India (CTRI 2013/03/003492). Source of funding not stated, declarations of interest not stated.

Risk of bias

Sinha 2018 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, computer-generated, random number tables used
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, sealed envelopes created by a third party used
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Similar looking placebo and mifepristone tablets were used for blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Decoding of sealed envelopes only done at time of analysis and so outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% of patients lost to follow-up
Selective reporting (reporting bias)	Low risk	Outcomes stated in trial registry were reported
Other bias	Low risk	No other sources of bias noted

Stockheim 2006

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	115 women a university tertiary hospital in Israel between July 2001 and December 2002 with a miscarriage of < 9 weeks gestation (missed miscarriage only)
Interventions	Mifepristone 600 milligrams given orally + misoprostol 400 micrograms given orally 48 hours later (and repeated 3 hours later if needed) as an outpatient versus misoprostol 400 micrograms given orally (and repeated 3 hours later if needed and repeated again for 2 further doses 48 hours later if needed) as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/emergency surgical procedure; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, sealed, opaque envelopes used

Stockheim 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	The participants and personnel were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Tationo 2012

Study characteristics

Methods	Single-centre, 2-arm, randomised controlled trial
Participants	186 women attending a tertiary hospital in Malaysia between unspecified dates, with a miscarriage in the 1st trimester (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Suction aspiration as a manual procedure versus dilatation and curettage
Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated if participants and personnel were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	No patients lost to follow-up

Tationo 2012 *(Continued)*

All outcomes

Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Taylor 2011

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	230 women attending a tertiary hospital in Ghana between 16th June 2004 and 20th July 2005, with a miscarriage of < 12 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/ emergency surgical procedure; pain score; days of bleeding; women's views/ satisfaction; nausea; vomiting; pyrexia
Notes	Funding was provided by the Fred H. Bixby Foundation and the David and Lucile Packard Foundation. The authors declare no conflicts of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, computer-generated randomisation in blocks of 10
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	<10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol or full text available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Torre 2012

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	182 women attending a teaching hospital in France between April 2003 and April 2006, with a miscarriage of <14 weeks gestation (both incomplete and missed miscarriage)
Interventions	Mifepristone 200 milligrams given orally + misoprostol 400 micrograms given vaginally 48 hours later as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complications; need for unplanned/emergency surgical procedure; pyrexia
Notes	Clinicaltrials.gov identifier NCT00190294
	Expectant arm in trial was delayed mifepristone 200 milligrams given orally + 48 hours later misoprostol 400 micrograms given vaginally 7 days after randomisation. For purposes of this review data were extracted at day 7 before this arm received intervention but after expectant treatment was given for 7 days. Funding was provided by Assistance Publique Hôpitaux de Paris. The authors report no conflict of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, computer-generated randomisation in blocks of 4
Allocation concealment (selection bias)	Low risk	Third-party, remote, computer-generated randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Neither participants or personnel were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were unblinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Low risk	Outcomes listed in protocol have been reported
Other bias	Low risk	No other sources of bias noted

Trinder 2006

Study characteristics

Methods	Multi-centre, 3-arm, unblinded, randomised controlled trial

Trinder 2006 *(Continued)*

Participants	926 women attending 7 hospitals in the UK between May 1997 and December 2001, with a miscarriage of < 13 weeks gestation (both incomplete and missed miscarriage)
Interventions	Suction aspiration as an inpatient procedure versus expectant management as an outpatient versus mifepristone 200 milligrams given orally + misoprostol 800 micrograms given vaginally 24 to 48 hours later as an inpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complications; pelvic inflammatory disease, endometritis or sepsis
Notes	272 patients with incomplete miscarriage are not reported as part of this review as the medical arm would have included those treated with purely misoprostol and those given mifepristone before misoprostol. Therefore the data for incomplete miscarriage are excluded as it would have been contaminated. Funded by a South and West NHS Executive research and development grant. The MIST trial group accepted a donation of £20,000 from Exelgyn, the manufacturers of mifepristone, which is declared as a conflict of interest.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Third-party, remote randomisation
Allocation concealment (selection bias)	Low risk	Centralised, third-party, randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical, one arm being surgical and other being expectant
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Ulstrup 1997

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	An unspecified number of women attending a district general hospital in Denmark between unspecified dates, with a miscarriage <13 weeks of gestation (incomplete miscarriage only)
Interventions	Dilatation and curettage as an inpatient procedure versus expectant management as an outpatient

Ulstrup 1997 *(Continued)*

Outcomes	Data presented in an unusable form
Notes	Abstract only, no corresponding author details available, data presented in an unusable form. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not stated
Allocation concealment (selection bias)	Unclear risk	Not stated if allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other arm being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available or full text paper available. No contact details available.
Other bias	Low risk	No other sources of bias noted

Verkuyl 1993

Study characteristics

Methods	Single-centre, 2-arm, randomised-controlled trial (blinding not mentioned)
Participants	357 women attending a tertiary hospital in Zimbabwe between unspecified dates, with a miscarriage of $\leq$ 18 weeks gestation (incomplete miscarriage only)
Interventions	Suction aspiration as an outpatient procedure versus dilatation and curettage as an outpatient procedure
Outcomes	Complete miscarriage; composite outcome of death of serious complication; pelvic inflammatory disease, endometritis or sepsis; mean volumes of blood loss; change in haemoglobin measurements before and after the miscarriage; days of bleeding
Notes	It was noted the maximum gestation age of the study was 18 weeks, however, the mean gestational age in weeks of the suction aspiration arm was 8.7 with a standard deviation of 3.1 and the mean gestational age in weeks of the dilatation and curettage arm was 9.7 with a standard deviation of 3.1 and so it was felt that the vast majority of patients would have been $\leq$ 14 weeks gestation and therefore the paper was included. Source of funding not stated, declarations of interest not stated.

Verkuyl 1993 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table was used
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding of participants not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor was blinded to intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	>20% lost to follow-up in both arms
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Weeks 2005

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	317 women attending a university hospital in Uganda between August 2001 and October 2002, with a miscarriage of < 13 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally as an outpatient versus suction aspiration as an outpatient manual procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complications; pelvic inflammatory disease, endometritis or sepsis; cervical tear; women's views/ satisfaction; pyrexia
Notes	Source of funding not stated, declarations of interest not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers were used
Allocation concealment (selection bias)	Low risk	Consecutively-numbered, opaque, sealed envelopes

Weeks 2005 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were unblinded
Incomplete outcome data (attrition bias) All outcomes	High risk	>30% lost to follow-up in both arms, >10% difference between arms in terms of numbers lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Wijesinghe 2011

Study characteristics

Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	140 women attending a university hospital in Sri Lanka between December 2007 and July 2009, with a miscarriage of < 14 weeks gestation (incomplete miscarriage only)
Interventions	Expectant management as an inpatient versus suction aspiration as an inpatient
Outcomes	Complete miscarriage by day 14 post intervention; composite outcome of death or serious complication; pelvic inflammatory disease, endometritis or sepsis; change in haemoglobin before and after the miscarriage; cervical tear; mean duration of hospital stay
Notes	Sri Lankan clinical trials registry identifier SLCTR/2008/012, Protocol was retrospectively registered. Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, random numbers were used
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not mentioned
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being expectant and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded

Wijesinghe 2011 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Low risk	Outcomes stated in protocol have been reported
Other bias	Low risk	No other sources of bias noted

Wood 2002

Study characteristics

Methods	Single-centre, 2-arm, double-blinded, placebo-controlled, randomised trial
Participants	50 women attending a university hospital in Canada between February 1999 and April 2000 with a miscarriage of ≤ 12 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally (and repeated 24 hours later if needed) as an outpatient versus placebo given vaginally (and repeated 24 hours later if needed) as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/ emergency surgical procedure; change in haemoglobin measurements before and after the miscarriage
Notes	Source of funding not stated, declarations of interest not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation in blocks of between 4 and 8
Allocation concealment (selection bias)	Low risk	Numbered envelopes created by a third party
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Both participants and personnel were blinded to the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Personnel were blinded to the intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Zhang 2005

Study characteristics

Methods	Multi-centre, 2-arm, unblinded, randomised controlled trial
Participants	652 women attending 4 university medical centres in theUSA between March 2002 and March 2004, with a miscarriage of <13 weeks gestation (both incomplete and missed miscarriage)
Interventions	Misoprostol 800 micrograms given vaginally (as a single dose on day 1 and if needed day 3) as an outpatient versus suction aspiration either as an outpatient manual or inpatient electric procedure
Outcomes	Complete miscarriage; pain scores; pelvic inflammatory disease, endometritis or sepsis; change in haemoglobin measurements before and after the miscarriage; nausea; vomiting; diarrhoea; pyrexia
Notes	Funded by contracts (N01-HD-1-3321, N01-HD-3322, N01-HD3323, N01-HD-3324, and N01-HD-3325) with the National Institute of Child Health and Human Development, National Institutes of Health. Drs. Creinin and Westhoff report having served as consultants to Pfizer, which now owns Searle. Dr. Westhoff reports having received grant support from Pfizer.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centralised, computer-generated randomisation in a 3:1 randomisation
Allocation concealment (selection bias)	Low risk	Centralised, computer-automated, telephone response system,
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not possible due to one arm being medical and other being surgical
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated if outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available but no evidence of selective reporting
Other bias	Low risk	No other sources of bias noted

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abbasalizadeh 2018	Wrong intervention - letrozole + misoprostol versus misoprostol
Abdel Fattah 1997	Wrong patient population - women with a 2nd trimester miscarriage and intrauterine fetal death

Study	Reason for exclusion
Abd-El-Maeboud 2012	Wrong patient population - women with a pregnancy of 14-26 weeks of gestation
Abdelshafy 2019a	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus sublingual misoprostol
Abediasl 2016	Wrong patient population - women with a 2nd trimester miscarriage and intrauterine fetal death
Abeysundara 2012	Wrong study design - qualitative work on patient perceptions
Ajand 2017	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus sublingual misoprostol
Al 2003	Wrong intervention - misoprostol versus dinoprostone
Al-Bdour 2007	Wrong patient population - women with a missed miscarriage between 9 and 22 weeks gestation. Unable to extract data for women with a miscarriage < 14 weeks gestation.
Ali 2015	Wrong intervention - misoprostol + isosorbide mononitrate versus misoprostol + placebo
Ali 2017	Wrong intervention - comparator is same as intervention, outpatient extended low dose buccal misoprostol versus inpatient standard dose vaginal misoprostol
Allameh 2020	Ineligible interventions for this review
Almog 2005	Wrong patient population - women undergoing mid-trimester terminations
Altaf 2006	Wrong patient population - women undergoing termination of pregnancy from 10 to 28 weeks of gestation
Ameen 2009	Trial compared different routes of administration of the same treatment, which are excluded from this review
Amjad 1999	Wrong patient population - women with a miscarriage greater than 14 weeks of gestation
Anderman 2000	Wrong patient population - women with a mid-trimester miscarriage
Anderson 2009	Wrong intervention - Comparator is same as intervention, oral mifepristone + oral misoprostol versus oral mifepristone + vaginal misoprostol
Aramide 2014	Ineligible interventions for this review
Arteaga-Troncoso 2005	Wrong interventions - each arm has been combined for different types of surgical management and therefore contains patients who have had either sharp curettage or suction curettage. It is not possible to extract data for each intervention separately within each arm.
Autry 1999	Wrong intervention - misoprostol versus intramuscular methotrexate + misoprostol
Avila-Vergara 1997	Wrong patient population - women with fetal death undergoing induction of labour (exact gestations not stated)
Avila VergaraMa 1997	Wrong patient population - women with intrauterine fetal death of 20 weeks of gestation or more
Aye 2017	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus sublingual misoprostol

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Study	Reason for exclusion
Ayudhaya 2006	Wrong intervention - comparator is same as intervention, oral misoprostol versus sublingual misoprostol
Azra 2007	Wrong patient population - women having second trimester terminations
Bagratee 2009	Abstract only, numbers reported in each group not provided and no corresponding author details
Bani-Irshaid 2006	Wrong patient population - women having second trimester and early third trimester terminations
Barnhart 2004	Ineligible intervention for this review
Bartz 2013	Wrong intervention - comparator is same as intervention, buccal misoprostol + suction curettage versus osmotic dilator + suction curettage
Bebbington 2002	Wrong patient population - women having mid-trimester terminations
Behrashi 2008	Wrong patient population - women having second trimester terminations
Ben-Meir 2009	Wrong patient population - women having terminations between 14 and 25 weeks of gestation
Betstadt 2008	Trial registration document only. Author emailed who confirmed study was terminated and no data published. Original data no longer available
Biswas 2007	Wrong patient population - women having terminations between 13 and 20 weeks of gestation
Blanchard 2004	Wrong intervention - comparator is same as intervention, 600 mcg misoprostol versus 2 x doses of 600 mcg misoprostol
Blohm 1997	Wrong study design - questionnaire based qualitative study
Bracken 2014	Wrong patient population - women with intrauterine fetal death between 14 and 28 weeks of gestation
Bracken 2019	Conference abstract only and does not state gestational age of participants. No author contact details available
Brouns 2010	Wrong patient population - women with intrauterine fetal death between 14 and 24 weeks of gestation
Cabrol 1990	Wrong patient population - women with intrauterine fetal death after 16 weeks of gestation
Caliskan 2005	Wrong patient population - women with a miscarriage between 13 and 20 weeks of gestation
Caliskan 2009	Wrong patient population - women with a miscarriage between 15 and 22 weeks of gestation
Chen 2008a	Wrong intervention - cervical priming before dilatation plus curettage
Chittacharoen 2003	Wrong patient population - women with intrauterine fetal death between 16 and 41 weeks of gestation
Chowdhury 2012	Wrong patient population - women with a second trimester miscarriage
Cleeve 2016	Wrong intervention - physician administration of misoprostol versus midwife administration of misoprostol

Study	Reason for exclusion
Clevin 2001	Wrong intervention - gemeprost versus dilatation and curettage
Creinin 1997	Wrong intervention - comparator is same as intervention, oral misoprostol versus vaginal misoprostol
Creinin 2004	Wrong study design - not randomised
Cruz 2017	Trial compared different methods of administration of the same treatment, which are excluded from this review.
Danielsson 2012	Wrong intervention - comparator is same as intervention, misoprostol 800 mcg given vaginally versus misoprostol 800 mcg given vaginally with repeated doses of misoprostol 400 mcg given orally 3, 5, 7 and 9 hours later
David 2003	Ineligible intervention for this review
David 2005	Ineligible intervention for this review
Davis 2004	Wrong study design - not randomised
Dee 2009	Wrong intervention - comparator is same as intervention, intrauterine misoprostol versus vaginal misoprostol
Dehbashi 2016	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Devall 2019	Wrong Intervention - feasibility study for the use of ultrasonography during surgical evacuation
Dhillon 2015	Wrong intervention - comparator is same as intervention, isosorbide mononitrate + suction curettage versus misoprostol + suction curettage
Dickinson 1998	Wrong patient population - women with intrauterine fetal death between 14 and 28 weeks of gestation
Dickinson 2002	Wrong patient population - women having a termination between 14 and 30 weeks of gestation
Dickinson 2003	Wrong patient population - women having a termination between 14 and 26 weeks of gestation
Diop 2009	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus oral misoprostol
Dunford 2012	Study terminated 23rd August 2019 due to a lack of funding/ staff/facilities
Dunn 2008	Ineligible intervention for this review
Egarter 1995	Wrong intervention - gemeprostol versus dilatation and curettage
Elami-Suzin 2013	Wrong patient population - women either having a termination or with a missed miscarriage between 14 and 24 weeks of gestation
Elbareg 2018	Wrong intervention - letrozole + misoprostol versus misoprostol
Elhassan 2008	Wrong patient population - women with intrauterine fetal death between 13 and 28 weeks of gestation

Study	Reason for exclusion
El Sokkary 2016	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Eng 1997	Wrong patient population - women with intrauterine fetal death between 13 and 26 weeks of gestation
Eppel 2005	Wrong patient population - women having a termination between 13 and 23 weeks of gestation
Eslamian 2007	Wrong patient population - women having a termination between 14 and 24 weeks of gestation
EUCTR2011-001505-26-SE	Wrong intervention - comparator is same as intervention, repeated doses of vaginal misoprostol versus repeated doses of vaginal misoprostol of a difference dose
Ezzatosadat 2012	Wrong intervention - hyoscine + misoprostol versus placebo + misoprostol
Facchinetti 2001	Ineligible intervention for this review
Fadalla 2004	Wrong patient population - women with intrauterine fetal death between 13 and 28 weeks of gestation
Farooq 2018	Wrong study design - outcomes not reported separately for missed miscarriage which received cervical priming versus incomplete miscarriage which did not before vacuum aspiration, therefore data useful for this review cannot be extracted
Faxelid 2012	Wrong intervention - physician administration of misoprostol versus midwife administration of misoprostol
Feldman 2003	Wrong patient population - women having a termination between 14 and 23 weeks of gestation
Fiala 2005	Wrong patient population - women having a termination between 13 and 22 weeks of gestation
Firouzabadi 2012	Wrong intervention - Laminaria tents + suction dilatation and curettage versus misoprostol + suction dilatation and curettage
Freeman 2016	Wrong patient population - women between 14 and 24 weeks of gestation having either a termination or treatment of miscarriage
Ghorab 1998	Wrong patient population - women between 16 and 24 weeks of gestation having either a termination or treatment for intrauterine fetal death
Gilles 2004	Wrong intervention - comparator is same as intervention, vaginal misoprostol mixed with normal saline versus vaginal misoprostol
Gonzalez 2001	Wrong patient population - women between 12 and 28 weeks of gestation having either a termination or treatment for intrauterine fetal death
Graziosi 2005	Wrong study design - this is a letter to an editor about a telephone survey about fertility outcomes
Grimes 2005	Wrong patient population - women having a termination between 14 and 19 weeks of gestation
Gronlund 2002	Wrong study design - cross-over study
Guix 2005	Wrong patient population - women having a termination between 13 and 22 weeks of gestation
Halimi 2004	Wrong patient population - women between 14 and 28 weeks of gestation having either a termination or treatment for intrauterine fetal death

Study	Reason for exclusion
Harrington 2004	Wrong intervention - transcervical amniotic puncture + misoprostol versus misoprostol
Hassan 2007	Wrong intervention - comparator is same as intervention, oral misoprostol versus rectal misoprostol
Hausler 1997	Wrong outcomes - HCG clearance tine, endometrial thickness, secondary bleeding. Original paper in German, full literal translation used.
Heard 2002	Wrong intervention - comparator is same as intervention, 400 mcg misoprostol versus 800 mcg misoprostol
Henshaw 1995	Wrong trial design - only party randomised. Abstract only available. No corresponding author details. Randomised data not able to be extracted.
Herabutya 1997	Wrong patient population - women with an intrauterine fetal death between 14 and 39 weeks of gestation
Herabutya 1997a	Wrong intervention - both arms are treated with suction curettage and sharp curettage after cervical priming. Not possible to separate out data needed for this review as suction curettage and dilatation and sharp curettage are two separate interventions in this review.
Herabutya 2005	Wrong patient population - women having a termination between 14 and 26 weeks of gestation
Herman 2017	Trial compared different routes of administration of the same treatment, which are excluded from this review.
Hernandez-Valencia 2003	Wrong intervention - comparison is ambulatory versus inpatient care
Hidalgo 2010	Ineligible intervention for this review
Hidar 2001	Wrong patient population - women having a termination between 13 and 29 weeks of gestation
Hidar 2005	Wrong patient population - women having a termination between 13 and 29 weeks of gestation
Hill 1991	Wrong patient population - women with an intrauterine fetal death in the second or third trimester
Hinshaw 1995	Wrong study design - only partly randomised. Abstract only available, no corresponding author details, unclear from abstract what exact nature of intervention is, whole data set not from only randomised patients, not able to extract data that is just from randomised patients
Hogg 2000	Wrong patient population - women having a termination between 16 and 24 weeks of gestation
Hombalegowda 2015	Wrong intervention - comparator is same as intervention, 400 mcg misoprostol versus 800 mcg misoprostol
Hooker 2016	Wrong intervention - application of hyalobarrier gel after dilatation and curettage for miscarriage
Huchon 2015	Wrong intervention - operative hysteroscopy versus suction aspiration
Hughes 1996	Non-randomised trial of treatment cost-effectiveness
Ibrahim 2019	Ineligible intervention for this review
Imran 2010	Wrong patient population - women between 14 and 28 weeks of gestation having either a termination or treatment for intrauterine fetal death

Study	Reason for exclusion
IRCT2015112421506N3 2016	Wrong intervention - Isonicotinic acid hydrazide + misoprostol versus misoprostol
IRCT2016122729062N1 2016	Wrong intervention - *Sesamum indicum* + misoprostol versus misoprostol
Islam 2006	Wrong patient population - women in the second trimester having either a termination or treatment for intrauterine fetal death
Jabir 2009a	Wrong intervention - comparator is same as intervention, oral misoprostol + surgery versus vaginal misoprostol + surgery versus oral placebo + surgery versus vaginal placebo + surgery. Surgery undefined and contact details no longer in use.
Jain 1994	Wrong patient population - women between 12 and 22 weeks of gestation having either a termination or treatment for intrauterine fetal death
Jain 1996	Wrong patient population - women between 12 and 22 weeks of gestation having either a termination or treatment for intrauterine fetal death
Jain 1999	Wrong patient population - women between 12 and 22 weeks of gestation having either a termination or treatment for intrauterine fetal death
Jamilian 2014	Wrong intervention - castor oil + misoprostol versus misoprostol
Javadi 2015	Wrong intervention - misoprostol versus letrozole + misoprostol
Johnson 1997	Wrong intervention - mifepristone + gemeprostol versus dilatation and curettage
Kakinuma 2020	Retrospective cohort study comparing treatment regimens administered between defined date ranges
Kamal 2005	Wrong patient population - women having a termination between 13 and 28 weeks of gestation
Kanhai 1988	Wrong patient population - women with intrauterine fetal death between 14 and 42 weeks of gestation
Kanhai 1989	Wrong patient population - women with intrauterine fetal death between 14 and 42 weeks of gestation
Kapp 2007	Wrong patient population - women in the second trimester having a termination
Kara 1999	Wrong patient population - women in the second trimester having treatment for intrauterine fetal death
Khanam 2019	Trial compares different dosages of the same treatment, which are excluded from this review
Khoosideh 2017	Ineligible intervention for this review
Khosravi 2017	Wrong patient population - women less than 14 weeks gestation having a termination of pregnancy
Klingberg-Allvin 2015	Wrong intervention - clinical assessment by a physician versus a midwife
Kovavisarach 2005	Wrong intervention - comparator is same as intervention, 600 mcg misoprostol versus 800 mcg misoprostol
Kurshid 2010	Wrong patient population - women having a termination between 19 and 23 weeks of gestation

Study	Reason for exclusion
Kushwah 2009	Wrong intervention - comparator is same as intervention, mifepristone + sublingual misoprostol versus mifepristone + oral misoprostol
Lei 2015	Wrong intervention - mifepristone + misoprostol versus ultrasound guided surgical curettage
Lelaidier 1993	Wrong intervention - mifepristone versus placebo
Lemmers 2016	Wrong patient population - women having treatment for miscarriage after failed medical management of miscarriage with misoprostol
Leung 2004	Wrong patient population - women having treatment for miscarriage after failed medical management of miscarriage with misoprostol
Li 2018	Ineligible intervention for this review
Linn 2015	Wrong patient population - women with intrauterine fetal death greater than or including 20 weeks of gestation
Lippert 1978	Wrong patient population - women with intrauterine fetal death between 18 and 32 weeks of gestation
Louey 2000	This is a trial registration document. Email address listed no longer in use. No resulting published papers or data found.
Lu 2014	Wrong intervention - comparator is same as intervention, mifepristone + vaginal misoprostol versus mifepristone + oral misoprostol
Lughmani 2007	Wrong intervention - misoprostol versus PGE2
Mahjabeen, 2009	Wrong patient population - women in the second trimester having a termination of pregnancy
Makenzius 2017	Wrong intervention - physician administration of misoprostol versus midwife administration of misoprostol
Makhlouf 2003	Wrong patient population - women having a termination of pregnancy between 13 and 28 weeks of gestation
Marfou 2012	Ineligible intervention for this review
Martin 1955	Wrong patient population - majority of cases were greater than 28 weeks of gestation
Marwah 2016	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus oral misoprostol
Mitwaly 2016	Wrong patient population - women with intrauterine fetal death between 13 and 24 weeks of gestation
Mizrachi 2017	Wrong intervention - comparator is same as intervention, 800 mcg misoprostol versus 2 x doses of 800 mcg misoprostol
Moran 2005	Wrong patient population - women with a pregnancy of unknown location
Mostafa-Gharebaghi 2010	Wrong patient population - includes women having a termination of pregnancy under 20 weeks of gestation. Data for women not having a termination and under 14 weeks of gestation not able to be extracted.

Study	Reason for exclusion
Mulayim 2009	Wrong patient population - includes women having a termination of pregnancy. Data for women with a miscarriage not presented separately.
Nakintu 2001	Wrong patient population - women with intrauterine fetal death above 18 weeks of gestation
Nasrollahi 2008	Wrong intervention - PGE2 (dinoprostone) administered intravenously versus intramuscularly in the management of missed miscarriage
Nassar 2005	Wrong patient population - women with intrauterine fetal death between 14 and 24 weeks of gestation
Nauman 2016	Wrong intervention - comparator is same as intervention, electric suction curettage versus manual suction curettage
NCT00426491 2007	Wrong intervention - letrozole + misoprostol versus placebo + misoprostol
NCT00670761 2008	Wrong study design - not randomised
NCT00797693 2008	Trial compared different routes of administration of the same treatment, which are excluded from this review.
NCT02141555 2014	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus buccal misoprostol
NCT02342002 2015	Study terminated due to lack of funding. No contact details on trial registry.
NCT02580175 2015	Wrong intervention - blinded suction evacuation versus ultrasound guided suction evacuation
NCT02957305 2016	Trial compares different dosages of the same treatment, which are excluded from this review.
NCT03148314 2017	Wrong interventions - misoprostol in a low dose given sublingually or buccally as outpatient versus misoprostol at a standard dose as an inpatient
NCT03148561 2017	Wrong patient population - women having treatment for miscarriage after failed medical management of miscarriage with misoprostol
NCT03230825 2017	Wrong patient population - includes women having a termination of pregnancy in the first trimester
NCT03628625 2018	Wrong intervention - letrozole + misoprostol versus placebo + misoprostol
Ng 2015	Wrong intervention - inpatient versus outpatient misoprostol treatment
Ngoc 2004	Wrong comparator - both arms are misoprostol
Nguyen 2005	Wrong intervention - comparator is same as intervention, 600 mcg misoprostol versus 2 x doses of 600 mcg misoprostol
Niederauer 2018	Trial compares different dosages of the same treatment, which are excluded from this review.
Niromanesh 2005	Wrong patient population - women with intrauterine fetal death between 14 and 25 weeks of gestation
Nor 2006	Wrong patient population - women having a termination of pregnancy between 14 and 26 weeks of gestation

Study	Reason for exclusion
Nuthalapaty 2005	Wrong patient population - women having a termination of pregnancy between 14 and 24 weeks of gestation
Nuutila 1997	Wrong patient population - women having a termination of pregnancy between 12 and 24 weeks of gestation
Ogden 2004	Wrong study design - qualitative study protocol
Owen 1999	Wrong patient population - women between 16 and 24 weeks of gestation having either a termination of pregnancy or treatment for intrauterine fetal death
Pang 2001	Wrong intervention - comparator is same as intervention, vaginal misoprostol versus oral misoprostol
Pansky 2011	Wrong intervention - women having their uterine cavity filled with Oxiplex/ AP gel versus no intervention after blunt hysteroscopic dissection for suspected retained products of conception
Paraskevaides 1992	Wrong intervention - dilatation and curettage versus prostaglandin F2 alpha versus trilostane
Paritakul 2010	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus oral misoprostol
Perry 1999	Wrong patient population - women having a termination of pregnancy between 17 and 24 weeks of gestation
Petersen 2013	Wrong intervention - comparator is same as intervention, 400 mcg misoprostol versus 800 mcg misoprostol
Phupong 2004	Wrong patient population - women with a miscarriage < 20 weeks of gestation. Data for women with < 14 weeks gestation not analysed separately to >14 weeks gestation.
Piotrowski 1979	Wrong intervention - pretreatment with indomethacin versus no pretreatment before intravenous PGE2 (dinoprostone) for treatment of intrauterine fetal death
Pomeranz 2016	Wrong patient population - women having treatment for miscarriage after failed medical management of miscarriage with misoprostol
Pongsatha 2004	Wrong patient population - women having a termination of pregnancy between 14 and 28 weeks of gestation
Prasartsakulchai 2004	Wrong intervention - comparator is same as intervention, 400 mcg misoprostol versus 800 mcg misoprostol
Promwangkwa 2017	Wrong patient population - women having a termination of pregnancy in the 2nd trimester
Ragusa 1994	Ineligible intervention for this review
Rahimi-Sharbaf 2015	Wrong patient population - women having a termination of pregnancy between 13 and 24 weeks of gestation
Ramsey 2004	Wrong patient population - women in the second trimester having a termination of pregnancy
Rita 2006	Wrong intervention - comparator is same as intervention, oral misoprostol versus vaginal misoprostol

Study	Reason for exclusion
Rivero-Lopez 1998	Wrong intervention - comparator is same as intervention, misoprostol + suction curettage versus laminaria stems + suction curettage
Robledo 2007	Wrong study design - not randomised
Roy 2003	Wrong patient population - women in the second trimester having a termination of pregnancy
Ruangchainikhom 2006	Wrong patient population - women having a termination of pregnancy less than 20 weeks of gestation
Saciloto 2011	Wrong study design - not randomised
Saeed 2018	Wrong intervention - comparator is same as intervention, oral misoprostol versus vaginal misoprostol
Saichua 2009	Wrong intervention - comparator is same as intervention, sublingual powered misoprostol versus sublingual tablet misoprostol
Salamalekis 1990	Wrong patient population - women with an intrauterine fetal death in the second trimester
	Wrong intervention - Prostaglandin F2 Alpha versus prostaglandin E2 (dinoprostone)
Sewzie 2014	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol versus oral misoprostol
Shaamash 2019	Trial compares different dosages of the same treatment, which are excluded from this review.
Shah 2010	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Sharifzadeh 2015	Ineligible intervention for this review
Shobeira 2007	Wrong patient population - women in the second trimester having a termination
Shochet 2012	Wrong intervention - misoprostol versus surgical evacuation (which includes both suction curettage and dilatation and curettage), corresponding author emailed to see if breakdown of data available but no response received
Shokry 2009	Wrong intervention - surgical evacuation followed by either misoprostol versus no misoprostol
Sonsanoh 2014	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Souizi 2020	Trial compares different dosages of the same treatment, which are excluded from this review
Srikhao 2005	Wrong intervention - comparator is same as intervention, 400 mcg misoprostol versus 800 mcg misoprostol
Sripramote 2000	Wrong intervention - cervical priming + dilatation and curettage
Su 2005	Wrong patient population - women having a termination of pregnancy between 12 and 24 weeks of gestation
Suchonwanit 1999	Wrong intervention - comparator is same as intervention, 200 mcg misoprostol versus 400 mcg misoprostol

Study	Reason for exclusion
Surita 1997	Wrong patient population - Women with intrauterine fetal death greater than 15 weeks of gestation
Sweed 2015	Wrong intervention - placebo + misoprostol versus letrozole + misoprostol
Sweed 2018	Wrong intervention - misoprostol single dose versus misoprostol repeated doses
Tam 2002	Wrong study design - non interventional follow-up study to previous randomised trial
Tam 2005	Wrong study design - qualitative telephone interviews after previous randomised trial
Tan 1969	Wrong study design - case series
Tang 2003	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Tang 2006	Wrong intervention -cComparator is same as intervention, misoprostol for 3 doses versus misoprostol for 3 doses + misoprostol once a day for seven further days
Tanha 2010	Wrong patient population - women in the second trimester having a termination
Tanha 2010a	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol
Tanha 2013	Wrong patient population - women having a termination between 13 and 24 weeks of gestation
Tasnim 2011	Wrong intervention - comparator is same as intervention, electric suction curettage versus manual suction curettage
Tasnim 2014	Wrong intervention - inpatient versus outpatient suction curettage treatment
Teymouri 2017	Wrong intervention - misoprostol versus misoprostol + oestrogen valerate
Thavarasah 1986	Wrong intervention - Prostaglandin F2 alpha administered either intravenously, extramniotic or intramuscularly
Thida 2015	Wrong intervention - comparator is same as intervention, sublingual misoprostol versus vaginal misoprostol versus oral misoprostol
Thong 2005	Insufficient information to determine whether the trial data should be included in the review, and there are no corresponding author contact details.
Toppozada 1994	Wrong patient population - women with intrauterine fetal death greater than 20 weeks of gestation
Toptas 2011	Wrong patient population - women between 13 and 26 weeks of gestation having either a termination or treatment for intrauterine fetal death
Torky 2018	Wrong intervention - placebo + misoprostol versus letrozole + misoprostol
Vafaei 2019	Wrong intervention - herbal medicine myrrh versus expectant management
Van Mensel 2009	Wrong patient population - women with intrauterine fetal death between 14 and 42 weeks of gestation
Wieringa-de 2002	Wrong patient population - women having treatment for a miscarriage <16 weeks of gestation. Data of patients between 14-16 weeks of gestation unable to be extracted and 23.4% of patients in the expectant group and 31% of patients in the curettage group were between 12 and 16 weeks so

Study	Reason for exclusion
	it was the judgement of the authors that there would be too much contamination by patients >14 weeks of gestation to be included.
Wijesinghe 2012	Wrong study design - qualitative interviews on patient perceptions of expectant management of miscarriage
Yapar 1996	Wrong patient population - women having a termination between 14 and 28 weeks of gestation
Yilmaz 2005	Wrong patient population - women in the second trimester having either a termination of pregnancy or treatment for intrauterine fetal death
Yilmaz 2007	Wrong patient population - women in the second trimester having either a termination or treatment for intrauterine fetal death
Zanganeh 2010	Wrong patient population - women having a termination in the second trimester
Zhang 2000	Wrong patient population - women having a termination between 16 and 24 weeks of gestation

Characteristics of studies awaiting classification *[ordered by study ID]*

Fang 2009

Methods	Single-centre, 3-arm, unblinded, randomised controlled trial
Participants	90 women attending a university hospital in China between 1st September 2005 and 28th February 2007, with a miscarriage of ≤12 weeks gestation (missed miscarriage only)
Interventions	Misoprostol 400 micrograms given vaginally + suction aspiration (not stated if manual or electric) as an inpatient procedure versus misoprostol 400 micrograms given vaginally + repeated every 3 hours for 5 doses if needed as an inpatient versus mifepristone 200 mg given orally + misoprostol 400 micrograms given vaginally every 3 hours for 5 doses if needed 36-48 hours later as an inpatient
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; women's views/ satisfaction
Notes	Awaiting clarification from authors re outcome data. Authors last contacted on 17-Feb-2021.

HCG: human chorionic gonadotropin; **mcg:** microgram; **PGE2:** prostaglandin E2.

Characteristics of ongoing studies *[ordered by study ID]*

ChiCTR1900023198 2019

Study name	The incidence of intrauterine adhesion after ultrasound-guided manual vacuum aspiration (USG-MVA): A prospective randomized controlled trial
Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	1. Women 18 years old or above; 2. Women with miscarriage who are suitable candidates for USG-MVA; 3. first-trimester delayed miscarriage≤ 10 weeks of gestation; 4. incomplete miscarriage With POG ≤ 5cm; 5. haemodynamically stable; 6. tolerates well with speculum examination.
Interventions	Ultrasound guided manual vacuum evacuation vs traditional surgical evacuation

ChiCTR1900023198 2019 *(Continued)*

Outcomes	The incidence of intrauterine adhesion
Starting date	12-Feb-2019
Contact information	margaretlee@cuhk.edu.hk
Notes	None

ChiCTR-TRC-08000725 2008

Study name	The and psychological outcomes of expectant management, surgical evacuation or medical evacuation with single dose 800 mcg vaginal misoprostol for women with first trimester miscarriage in a randomized controlled trial
Methods	A randomised, parallel group, three-arm, single-blinded study
Participants	180 women attending a university hospital in Hong Kong between 1st September 2008 to 5th September 2012 with a miscarriage of < 13 weeks gestation (both incomplete and missed miscarriage)
Interventions	Expectant management versus surgical evacuation versus misoprostol 800 micrograms
Outcomes	Complete miscarriage; women's views/satisfaction
Starting date	1st September 2008
Contact information	gracekong@cuhk.edu.hk
Notes	Last updated 4th June 2015, no link to published record

Economides 2004

Study name	Non-surgical management of delayed miscarriage: a randomised trial
Methods	Randomised controlled trial
Participants	100 women attending a university hospital in the UK between unspecified dates with a miscarriage (exact gestation not specified)(missed miscarriage only)
Interventions	Misoprostol given orally or vaginally as an outpatient versus expectant management as an outpatient
Outcomes	Complete miscarriage; need for unplanned/emergency surgical procedure
Starting date	9th July 2003
Contact information	Not provided
Notes	Publication status listed as "Results overdue"

Ethayarooban 2017

Study name	Safety and effectiveness of vacuum aspiration, compared to curettage for management of patients with first trimester miscarriage in a limited resource setting in Sri Lanka.
Methods	A randomised, parallel group, two-arm, single-blinded study
Participants	136 women attending a maternity Hospital in Sri Lanka between unspecified dates with a miscarriage of < 13 weeks of gestation (type of miscarriage not specified)
Interventions	Suction aspiration as an inpatient manual procedure versus dilatation and curettage as an inpatient procedure
Outcomes	Composite outcome of death or serious complication; need for unplanned/emergency surgical procedure; pain scores (visual analogue scale); cervical tear; mean duration of hospital stay (days)
Starting date	24th July 2017
Contact information	roobanethayan@gmail.com
Notes	Recruitment status listed as "Recruiting", last updated 3rd March 2019

EUCTR2007-007661-20-SE

Study name	Which is the optimal treatment for miscarriage with a gestational sac in the uterus and which factors can predict if the treatment will be successful?
Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	240 women attending a university hospital in Sweden between unspecified dates with a miscarriage of <14 weeks gestation (incomplete miscarriage only)
Interventions	Misoprostol 800 micrograms given vaginally versus expectant management
Outcomes	Complete miscarriage; need for unplanned/ emergency surgical procedure; pelvic inflammatory disease, sepsis or endometritis; change in haemoglobin measurements before and after the miscarriage; re-admission to hospital; anxiety score; depression score
Starting date	21st April 2008
Contact information	Not stated in trial registry
Notes	Trial status listed as "Ongoing"

ISRCTN11046192 2020

Study name	Efficacy of mifepristone followed by misoprostol compared to misoprostol alone in first-trimester miscarriage treatment
Methods	Single centre 2-arm, blinded, placebo-controlled randomised controlled trial
Participants	Women diagnosed with first-trimester miscarriage (up to 9 weeks of gestation)

ISRCTN11046192 2020 *(Continued)*

Interventions	Mifepristone 200 mg or placebo given orally, both followed by misoprostol 800 micrograms given vaginally 36 to 48 hours after the oral pill.
Outcomes	Complete miscarriage; complications; adverse effects; acceptability of the treatment
Starting date	10-Apr-2019
Contact information	beatrizbettsilva@gmail.com
Notes	Retrospectively registered

Kopalakrishnan 2014

Study name	Surgical, medical or expectant management of first trimester miscarriage and its implications on clinical and psychological outcomes - a randomized controlled trial
Methods	A randomised, parallel group, three-arm, unblinded study
Participants	180 women attending an unspecified healthcare facility with a miscarriage of < 14 weeks gestation
Interventions	Suction aspiration as an inpatient versus misoprostol 800 micrograms given vaginally + repeated 4-6 hours later if needed versus expectant management
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for un-planned/emergency surgical procedure; pelvic inflammatory disease, sepsis or endometritis; change in haemoglobin measurements before and after the miscarriage; days of bleeding; cervi-cal tear; women's views/satisfaction; mean duration of hospital stay (days); nausea; vomiting; diar-rhoea
Starting date	Anticipated start date 5th November 2014
Contact information	kopalakrishnan14@yahoo.com
Notes	Recruitment status listed as "pending", last updated 3rd March 2019

Otieno 2018

Study name	Outcomes of medical versus surgical management of first trimester incomplete abortion on among women admitted at Kampala International University Teaching Hospital (KIU -TH)
Methods	A randomised, parallel group, two-arm, unblinded study
Participants	100 women attending a university hospital in Uganda with a miscarriage of gestation ≤ 12 weeks of gestation (incomplete miscarriage only)
Interventions	Misoprostol versus suction aspiration as an inpatient manual procedure
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for un-planned/emergency surgical procedure; pain scores (visual analogue scale); pelvic inflammatory disease, sepsis or endometritis; women's views/satisfaction; mean duration of hospital stay (days); re-admission to hospital

Otieno 2018 *(Continued)*

Starting date	1st November 2018
Contact information	pwaveno.bamaiyi@kiu.ac.ug
Notes	Recruitment status listed as "pending", last updated 17th August 2020

PACTR202009610896579 2020

Study name	Misoprostol versus manual vacuum aspiration for the treatment of first trimester incomplete miscarriage at university of Maiduguri teaching hospital. a randomized controlled study
Methods	Single-centre, 2-arm, unblinded, randomised controlled trial
Participants	Women with an incomplete miscarriage
Interventions	Misoprostol (dose and route not stated) versus manual vacuum aspiration
Outcomes	Complete miscarriage
Starting date	Not stated
Contact information	Not stated
Notes	None

PACTR202009857889210 2020

Study name	Sublingual misoprostol versus manual vacuum aspiration for treatment of incomplete abortion in Nigeria: a randomized control study
Methods	2-arm, unblinded, randomised controlled trial
Participants	Women with a first-trimester incomplete abortion, confirmed by a trans-abdominal ultrasound scan of the uterus
Interventions	Single-dose sublingual misoprostol 400 micrograms versus manual vacuum aspiration
Outcomes	Complete miscarriage; side effects and tolerability
Starting date	Not stated
Contact information	Not stated
Notes	None

Sutharshan 2017

Study name	Effectiveness of manual vacuum aspiration when compared to expectant care in achieving complete miscarriage in women with first trimester pregnancy loss- a randomized controlled trial

Sutharshan 2017 *(Continued)*

Methods	A randomised, parallel group, two-arm, unblinded study
Participants	134 women attending a teaching hospital in Sri Lanka with a miscarriage ≤ 12 weeks of gestation
Interventions	Suction aspiration as an inpatient manual procedure versus expectant management as an outpatient
Outcomes	Complete miscarriage; composite outcome of death or serious complication; need for unplanned/emergency surgical procedure; pain scores (visual analogue scale); pelvic inflammatory disease, sepsis or endometritis; change in haemoglobin measurements before and after the miscarriage; cervical tear; women's views/satisfaction; mean duration of hospital stay (days)
Starting date	10th June 2017
Contact information	sutharshan11@gmail.com
Notes	Recruitment status listed as "recruiting", last updated 3rd March 2019

Unkels 2008

Study name	Is misoprostol a safe alternative to manual vacuum aspiration in women with incomplete abortions in developing countries?
Methods	Evaluator-blinded, single-centre, randomised controlled non-inferiority trial
Participants	180 women attending an unspecified healthcare facility in Tanzania with a miscarriage in the first trimester (exact gestation unspecified) (incomplete miscarriage only)
Interventions	Misoprostol 600 micrograms given orally every 4 hours for 3 doses versus suction aspiration as a manual procedure
Outcomes	Composite outcome of death or serious complication; pain scores (visual analogue scale); change in haemoglobin measurements before and after the miscarriage; women's views/satisfaction; nausea; vomiting; diarrhoea;
Starting date	11th February 2008
Contact information	PO box 228, Lindi, Tanzania
Notes	Overall trial status listed as "completed", recruitment status listed as "no longer recruiting", publication status listed as "results overdue", last updated 22nd Feb 2008

USG-MVA: ultrasound-guided manual vacuum aspiration.

D A T A   A N D   A N A L Y S E S

Comparison 1.   Suction aspiration vs Misoprostol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Complete Miscarriage	23		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1.1 Missed miscarriage	3	308	Risk Ratio (IV, Random, 95% CI)	1.51 [1.14, 2.01]
1.1.2 Incomplete miscarriage	14	3474	Risk Ratio (IV, Random, 95% CI)	1.03 [1.01, 1.05]
1.1.3 Mixed population	6	1706	Risk Ratio (IV, Random, 95% CI)	1.19 [1.06, 1.32]
1.2 Composite outcome of death or serious complication	9	2146	Risk Ratio (IV, Random, 95% CI)	1.53 [0.45, 5.16]
1.3 Need for unplanned/emergency surgical procedure	9	1078	Risk Ratio (IV, Random, 95% CI)	0.19 [0.10, 0.37]
1.4 Pain score	8	2857	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.35, 0.51]
1.5 Pelvic inflammatory disease, sepsis or endometritis	12	2989	Risk Ratio (IV, Random, 95% CI)	1.27 [0.67, 2.41]
1.6 Change in haemoglobin measurements before and after the miscarriage	7	2706	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.29, -0.05]
1.7 Days of bleeding	7		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.8 Cervical tear	5	1252	Risk Ratio (IV, Random, 95% CI)	7.18 [0.84, 61.00]
1.9 Mean duration of hospital stay (days)	1	635	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.68, -0.12]
1.10 Re-admission to hospital	2	554	Risk Ratio (IV, Random, 95% CI)	0.77 [0.27, 2.21]
1.11 Nausea	13	3605	Risk Ratio (IV, Random, 95% CI)	0.52 [0.35, 0.76]
1.12 Vomiting	13	3447	Risk Ratio (IV, Random, 95% CI)	0.50 [0.38, 0.68]
1.13 Diarrhoea	9	1769	Risk Ratio (IV, Random, 95% CI)	0.39 [0.26, 0.60]
1.14 Pyrexia	15	4129	Risk Ratio (IV, Random, 95% CI)	0.37 [0.22, 0.61]
1.15 Anxiety score	2	719	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.24, 0.09]
1.16 Depression score	2	719	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.46, 0.12]

Analysis 1.1. Comparison 1: Suction aspiration vs Misoprostol, Outcome 1: Complete Miscarriage

Study or Subgroup	Suction aspiration Events	Total	Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
1.1.1 Missed miscarriage							
Graziosi 2004	72	75	42	79	34.7%	1.81 [1.46 , 2.23]	
Muffley 2002	25	25	15	25	27.8%	1.65 [1.19 , 2.27]	
Shaheen 2017	48	52	40	52	37.4%	1.20 [1.01 , 1.42]	
Subtotal (95% CI)		**152**		**156**	**100.0%**	**1.51 [1.14 , 2.01]**	
Total events:	145		97				
Heterogeneity: Tau² = 0.05; Chi² = 9.55, df = 2 (P = 0.008); I² = 79%							
Test for overall effect: Z = 2.83 (P = 0.005)							
1.1.2 Incomplete miscarriage							
Arellano 2009	97	97	100	106	6.8%	1.06 [1.01 , 1.11]	
Bique 2007	101	101	101	111	5.4%	1.10 [1.03 , 1.17]	
Chigbu 2012	160	160	158	160	12.4%	1.01 [0.99 , 1.03]	
Dabash 2010	346	347	342	348	13.6%	1.01 [1.00 , 1.03]	
Dao 2007	222	224	206	218	9.6%	1.05 [1.01 , 1.09]	
Das 2014	109	111	108	111	8.5%	1.01 [0.97 , 1.05]	
Ibiyemi 2018	97	98	83	100	3.0%	1.19 [1.09 , 1.31]	
Montesinos 2011	97	97	100	106	6.8%	1.06 [1.01 , 1.11]	
Nwafor 2020	44	46	39	48	1.3%	1.18 [1.01 , 1.37]	
Patua 2013	48	50	42	48	1.9%	1.10 [0.97 , 1.24]	
Sahin 2001	40	40	38	40	3.4%	1.05 [0.97 , 1.15]	
Shwekerela 2007	150	150	149	150	13.0%	1.01 [0.99 , 1.03]	
Taylor 2011	109	110	106	108	10.2%	1.01 [0.98 , 1.04]	
Weeks 2005	75	82	103	107	4.0%	0.95 [0.88 , 1.03]	
Subtotal (95% CI)		**1713**		**1761**	**100.0%**	**1.03 [1.01 , 1.05]**	
Total events:	1695		1675				
Heterogeneity: Tau² = 0.00; Chi² = 36.15, df = 13 (P = 0.0006); I² = 64%							
Test for overall effect: Z = 3.59 (P = 0.0003)							
1.1.3 Mixed population							
Chung 1999	308	314	318	321	20.9%	0.99 [0.97 , 1.01]	
Demetroulis 2001	40	40	33	40	15.2%	1.21 [1.04 , 1.40]	
Ganguly 2010	59	60	98	120	18.4%	1.20 [1.10 , 1.32]	
Kashif 2020	30	30	22	30	11.4%	1.36 [1.09 , 1.69]	
Kong 2013	54	55	42	60	14.0%	1.40 [1.18 , 1.66]	
Zhang 2005	143	148	412	488	20.2%	1.14 [1.09 , 1.20]	
Subtotal (95% CI)		**647**		**1059**	**100.0%**	**1.19 [1.06 , 1.32]**	
Total events:	634		925				
Heterogeneity: Tau² = 0.01; Chi² = 68.86, df = 5 (P < 0.00001); I² = 93%							
Test for overall effect: Z = 3.04 (P = 0.002)							
Test for subgroup differences: Chi² = 12.54, df = 2 (P = 0.002), I² = 84.0%							

0.5 0.7 1 1.5 2
Favours Misoprostol   Favours Suction aspiration

Analysis 1.2. Comparison 1: Suction aspiration vs Misoprostol, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Suction aspiration Events	Total	Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Chung 1999	6	314	0	321	16.8%	13.29 [0.75 , 234.90]	
Dao 2007	0	224	1	218	13.7%	0.32 [0.01 , 7.92]	
Demetroulis 2001	0	40	0	40		Not estimable	
Ganguly 2010	1	60	3	120	26.5%	0.67 [0.07 , 6.27]	
Graziosi 2004	2	75	0	79	15.3%	5.26 [0.26 , 107.86]	
Ibiyemi 2018	0	98	0	100		Not estimable	
Muffley 2002	1	25	0	25	14.1%	3.00 [0.13 , 70.30]	
Taylor 2011	0	110	1	108	13.8%	0.33 [0.01 , 7.95]	
Weeks 2005	0	82	0	107		Not estimable	
Total (95% CI)		**1028**		**1118**	**100.0%**	**1.53 [0.45 , 5.16]**	
Total events:	10		5				

Heterogeneity: Tau² = 0.14; Chi² = 5.32, df = 5 (P = 0.38); I² = 6%

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

0.005 0.1 1 10 200
Favours Suction aspiration   Favours Misoprostol

Analysis 1.3. Comparison 1: Suction aspiration vs Misoprostol, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Suction aspiration Events	Total	Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bique 2007	0	101	4	111	5.1%	0.12 [0.01 , 2.24]	
Demetroulis 2001	0	40	0	40		Not estimable	
Graziosi 2004	5	75	37	79	55.9%	0.14 [0.06 , 0.34]	
Kashif 2020	0	30	2	30	4.8%	0.20 [0.01 , 4.00]	
Kong 2013	0	55	0	59		Not estimable	
Muffley 2002	1	25	1	25	5.9%	1.00 [0.07 , 15.12]	
Nwafor 2020	2	46	9	48	19.8%	0.23 [0.05 , 1.02]	
Patua 2013	0	50	1	46	4.3%	0.31 [0.01 , 7.36]	
Taylor 2011	0	110	1	108	4.2%	0.33 [0.01 , 7.95]	
Total (95% CI)		**532**		**546**	**100.0%**	**0.19 [0.10 , 0.37]**	
Total events:	8		55				

Heterogeneity: Tau² = 0.00; Chi² = 2.21, df = 6 (P = 0.90); I² = 0%

Test for overall effect: Z = 4.96 (P < 0.00001)

Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Suction aspiration   Favours Misoprostol

Analysis 1.4. Comparison 1: Suction aspiration vs Misoprostol, Outcome 4: Pain score

Study or Subgroup	Suction aspiration Mean	SD	Total	Misoprostol Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Bique 2007	4.21	3.44	101	2.63	3.44	111	12.4%	0.46 [0.18 , 0.73]	
Chigbu 2012	4.5	4.04	160	3	4.04	160	12.6%	0.37 [0.15 , 0.59]	
Dao 2007	2.73	2.18	224	2.32	2.18	218	12.7%	0.19 [0.00 , 0.37]	
Graziosi 2004	3	2.4	75	5	3	79	12.1%	-0.73 [-1.06 , -0.40]	
Harwood 2008	45.84	10.95	150	40.04	10.31	457	12.7%	0.55 [0.37 , 0.74]	
Shwekerela 2007	3.5	1.3	150	3	1.3	150	12.6%	0.38 [0.16 , 0.61]	
Taylor 2011	4.6	2.99	112	3.2	2.99	93	12.3%	0.47 [0.19 , 0.75]	
Zhang 2005	3.2	2.4	141	5.7	2.4	476	12.7%	-1.04 [-1.24 , -0.84]	
Total (95% CI)			**1113**			**1744**	**100.0%**	**0.08 [-0.35 , 0.51]**	

Heterogeneity: Tau² = 0.37; Chi² = 202.17, df = 7 (P < 0.00001); I² = 97%
Test for overall effect: Z = 0.38 (P = 0.71)
Test for subgroup differences: Not applicable

Favours Suction aspiration Favours Misoprostol

Analysis 1.5. Comparison 1: Suction aspiration vs Misoprostol, Outcome 5: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Suction aspiration Events	Total	Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bique 2007	0	101	4	111	4.8%	0.12 [0.01 , 2.24]	
Chung 1999	10	314	9	321	51.7%	1.14 [0.47 , 2.76]	
Dao 2007	0	224	1	218	4.0%	0.32 [0.01 , 7.92]	
Demetroulis 2001	4	38	2	37	15.2%	1.95 [0.38 , 10.00]	
Graziosi 2004	0	75	0	79		Not estimable	
Kashif 2020	0	30	0	30		Not estimable	
Kong 2013	2	53	0	59	4.5%	5.56 [0.27 , 113.16]	
Nwafor 2020	0	46	0	48		Not estimable	
Sahin 2001	2	40	1	40	7.3%	2.00 [0.19 , 21.18]	
Shwekerela 2007	0	150	0	150		Not estimable	
Weeks 2005	3	82	1	107	8.1%	3.91 [0.41 , 36.95]	
Zhang 2005	0	148	2	488	4.4%	0.66 [0.03 , 13.60]	
Total (95% CI)		**1301**		**1688**	**100.0%**	**1.27 [0.67 , 2.41]**	
Total events:	21		20				

Heterogeneity: Tau² = 0.00; Chi² = 5.73, df = 7 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.74 (P = 0.46)
Test for subgroup differences: Not applicable

Favours Suction aspiration Favours Misoprostol

Analysis 1.6. Comparison 1: Suction aspiration vs Misoprostol, Outcome 6: Change in haemoglobin measurements before and after the miscarriage

Study or Subgroup	Suction aspiration			Misoprostol			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Chung 1999	0.28	0.7	314	0.34	1.1	321	14.9%	-0.06 [-0.20 , 0.08]	
Dabash 2010	0.4	0.55	337	0.5	0.55	335	17.3%	-0.10 [-0.18 , -0.02]	
Davis 2007	0.2	0.9	134	0.7	1.1	422	13.1%	-0.50 [-0.69 , -0.31]	
Kong 2013	0.12	0.84	53	0.19	1.03	59	7.4%	-0.07 [-0.42 , 0.28]	
Patua 2013	0.19	0.12	50	0.22	0.13	46	18.3%	-0.03 [-0.08 , 0.02]	
Sahin 2001	0.38	0.26	40	0.41	0.29	40	15.9%	-0.03 [-0.15 , 0.09]	
Zhang 2005	0.18	0.89	134	0.65	1.1	421	13.1%	-0.47 [-0.65 , -0.29]	
Total (95% CI)			1062			1644	100.0%	-0.17 [-0.29 , -0.05]	

Heterogeneity: Tau² = 0.02; Chi² = 41.85, df = 6 (P < 0.00001); I² = 86%
Test for overall effect: Z = 2.75 (P = 0.006)
Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1: Suction aspiration vs Misoprostol, Outcome 7: Days of bleeding

Study or Subgroup	Suction aspiration			Misoprostol			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Braham 2016	2.67	1.2	30	3.68	1.8	30	-1.01 [-1.78 , -0.24]	
Chung 1999	9.3	3.57	314	9.1	3.57	321	0.20 [-0.36 , 0.76]	
Graziosi 2004	8.7	5.1	75	10.4	5.6	79	-1.70 [-3.39 , -0.01]	
Kong 2013	10.73	5.92	53	15.38	6.63	59	-4.65 [-6.97 , -2.33]	
Montesinos 2011	3.1	2.06	97	3.7	2.06	106	-0.60 [-1.17 , -0.03]	
Sahin 2001	4.9	2.19	40	6.45	2.23	40	-1.55 [-2.52 , -0.58]	
Taylor 2011	1.64	2.6	112	2.86	2.6	93	-1.22 [-1.93 , -0.51]	

Test for subgroup differences: Not applicable

Analysis 1.8. Comparison 1: Suction aspiration vs Misoprostol, Outcome 8: Cervical tear

Study or Subgroup	Suction aspiration		Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Chung 1999	1	314	0	321	44.8%	3.07 [0.13 , 75.00]	
Ganguly 2010	0	60	0	120		Not estimable	
Graziosi 2004	0	75	0	79		Not estimable	
Nwafor 2020	0	46	0	48		Not estimable	
Weeks 2005	5	82	0	107	55.2%	14.31 [0.80 , 255.21]	
Total (95% CI)		577		675	100.0%	7.18 [0.84 , 61.00]	
Total events:	6		0				

Heterogeneity: Tau² = 0.00; Chi² = 0.49, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.80 (P = 0.07)
Test for subgroup differences: Not applicable

Analysis 1.9. Comparison 1: Suction aspiration vs Misoprostol, Outcome 9: Mean duration of hospital stay (days)

Study or Subgroup	Suction aspiration			Misoprostol			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Chung 1999	1.78	1.79	314	2.18	1.79	321	100.0%	-0.40 [-0.68 , -0.12]	
Total (95% CI)			**314**			**321**	**100.0%**	**-0.40 [-0.68 , -0.12]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.82 (P = 0.005)
Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Suction aspiration   Favours Misoprostol

Analysis 1.10. Comparison 1: Suction aspiration vs Misoprostol, Outcome 10: Re-admission to hospital

Study or Subgroup	Suction aspiration		Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Dao 2007	0	224	2	218	12.2%	0.19 [0.01 , 4.03]	
Kong 2013	5	53	6	59	87.8%	0.93 [0.30 , 2.86]	
Total (95% CI)		**277**		**277**	**100.0%**	**0.77 [0.27 , 2.21]**	
Total events:	5		8				

Heterogeneity: Tau² = 0.00; Chi² = 0.90, df = 1 (P = 0.34); I² = 0%
Test for overall effect: Z = 0.49 (P = 0.62)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Suction aspiration   Favours Misoprostol

Analysis 1.11. Comparison 1: Suction aspiration vs Misoprostol, Outcome 11: Nausea

Study or Subgroup	Suction aspiration		Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Bique 2007	2	101	13	111	4.8%	0.17 [0.04 , 0.73]	
Chigbu 2012	7	160	8	160	7.7%	0.88 [0.32 , 2.36]	
Dabash 2010	83	316	132	327	15.0%	0.65 [0.52 , 0.82]	
Dao 2007	2	224	12	223	4.7%	0.17 [0.04 , 0.73]	
Demetroulis 2001	22	40	6	40	9.5%	3.67 [1.67 , 8.07]	
Ganguly 2010	17	60	63	120	13.1%	0.54 [0.35 , 0.84]	
Graziosi 2004	0	75	11	79	1.7%	0.05 [0.00 , 0.76]	
Ibiyemi 2018	7	98	12	100	8.5%	0.60 [0.24 , 1.45]	
Montesinos 2011	0	97	5	106	1.6%	0.10 [0.01 , 1.77]	
Muffley 2002	0	25	12	25	1.7%	0.04 [0.00 , 0.64]	
Shwekerela 2007	9	150	38	150	10.4%	0.24 [0.12 , 0.47]	
Taylor 2011	5	112	7	93	6.8%	0.59 [0.19 , 1.81]	
Zhang 2005	41	141	250	472	14.7%	0.55 [0.42 , 0.72]	
Total (95% CI)		**1599**		**2006**	**100.0%**	**0.52 [0.35 , 0.76]**	
Total events:	195		569				

Heterogeneity: Tau² = 0.24; Chi² = 42.91, df = 12 (P < 0.0001); I² = 72%
Test for overall effect: Z = 3.39 (P = 0.0007)
Test for subgroup differences: Not applicable

0.001 0.1 1 10 1000
Favours Suction aspiration   Favours Misoprostol

Analysis 1.12. Comparison 1: Suction aspiration vs Misoprostol, Outcome 12: Vomiting

Study or Subgroup	Suction aspiration Events	Suction aspiration Total	Misoprostol Events	Misoprostol Total	Weight	Risk Ratio IV, Random, 95% CI
Bique 2007	0	101	5	111	1.1%	0.10 [0.01 , 1.78]
Chigbu 2012	6	160	6	160	7.1%	1.00 [0.33 , 3.03]
Dabash 2010	17	316	32	327	27.3%	0.55 [0.31 , 0.97]
Dao 2007	4	224	5	223	5.2%	0.80 [0.22 , 2.93]
Demetroulis 2001	6	40	3	40	5.1%	2.00 [0.54 , 7.45]
Ibiyemi 2018	4	98	6	100	5.8%	0.68 [0.20 , 2.34]
Kashif 2020	1	30	2	30	1.6%	0.50 [0.05 , 5.22]
Kong 2013	3	53	14	59	6.2%	0.24 [0.07 , 0.78]
Montesinos 2011	0	97	2	106	1.0%	0.22 [0.01 , 4.49]
Muffley 2002	0	25	1	25	0.9%	0.33 [0.01 , 7.81]
Shwekerela 2007	6	150	17	150	10.8%	0.35 [0.14 , 0.87]
Taylor 2011	4	112	5	93	5.3%	0.66 [0.18 , 2.40]
Zhang 2005	10	142	96	475	22.6%	0.35 [0.19 , 0.65]
Total (95% CI)		**1548**		**1899**	**100.0%**	**0.50 [0.38 , 0.68]**
Total events:	61		194			

Heterogeneity: Tau² = 0.00; Chi² = 11.69, df = 12 (P = 0.47); I² = 0%
Test for overall effect: Z = 4.52 (P < 0.00001)
Test for subgroup differences: Not applicable

Risk Ratio IV, Random, 95% CI
0.005   0.1   1   10   200
Favours Suction aspiration   Favours Misoprostol

Analysis 1.13. Comparison 1: Suction aspiration vs Misoprostol, Outcome 13: Diarrhoea

Study or Subgroup	Suction aspiration Events	Suction aspiration Total	Misoprostol Events	Misoprostol Total	Weight	Risk Ratio IV, Random, 95% CI
Chigbu 2012	0	160	3	160	1.9%	0.14 [0.01 , 2.74]
Demetroulis 2001	0	40	1	40	1.7%	0.33 [0.01 , 7.95]
Ganguly 2010	7	60	28	120	22.6%	0.50 [0.23 , 1.08]
Graziosi 2004	0	75	21	79	2.2%	0.02 [0.00 , 0.40]
Ibiyemi 2018	0	98	2	100	1.9%	0.20 [0.01 , 4.20]
Kashif 2020	0	30	0	30		Not estimable
Kong 2013	10	53	22	59	29.0%	0.51 [0.26 , 0.97]
Muffley 2002	0	25	12	25	2.2%	0.04 [0.00 , 0.64]
Zhang 2005	14	142	113	473	38.5%	0.41 [0.24 , 0.70]
Total (95% CI)		**683**		**1086**	**100.0%**	**0.39 [0.26 , 0.60]**
Total events:	31		202			

Heterogeneity: Tau² = 0.05; Chi² = 8.00, df = 7 (P = 0.33); I² = 13%
Test for overall effect: Z = 4.39 (P < 0.0001)
Test for subgroup differences: Not applicable

Risk Ratio IV, Random, 95% CI
0.001   0.1   1   10   1000
Favours Suction aspiration   Favours Misoprostol

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Analysis 1.14. Comparison 1: Suction aspiration vs Misoprostol, Outcome 14: Pyrexia

Study or Subgroup	Suction aspiration Events	Total	Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bique 2007	0	101	28	111	2.8%	0.02 [0.00 , 0.31]	
Chigbu 2012	9	160	15	160	10.5%	0.60 [0.27 , 1.33]	
Dabash 2010	16	316	93	327	12.3%	0.18 [0.11 , 0.30]	
Dao 2007	4	224	11	223	8.4%	0.36 [0.12 , 1.12]	
Das 2014	0	111	5	111	2.6%	0.09 [0.01 , 1.62]	
Ganguly 2010	2	60	5	120	5.9%	0.80 [0.16 , 4.00]	
Ibiyemi 2018	0	98	39	100	2.8%	0.01 [0.00 , 0.21]	
Kashif 2020	0	30	3	30	2.6%	0.14 [0.01 , 2.65]	
Kong 2013	6	53	7	59	9.0%	0.95 [0.34 , 2.66]	
Montesinos 2011	1	97	3	106	3.9%	0.36 [0.04 , 3.44]	
Patua 2013	3	50	9	46	7.7%	0.31 [0.09 , 1.06]	
Shwekerela 2007	1	150	6	150	4.2%	0.17 [0.02 , 1.37]	
Taylor 2011	9	112	16	93	10.7%	0.47 [0.22 , 1.01]	
Weeks 2005	3	147	6	159	7.1%	0.54 [0.14 , 2.12]	
Zhang 2005	6	148	13	477	9.5%	1.49 [0.58 , 3.84]	
Total (95% CI)		**1857**		**2272**	**100.0%**	**0.37 [0.22 , 0.61]**	
Total events:	60		259				

Heterogeneity: Tau² = 0.50; Chi² = 34.35, df = 14 (P = 0.002); I² = 59%

Test for overall effect: Z = 3.80 (P = 0.0001)

Test for subgroup differences: Not applicable

0.01   0.1   1   10   100
Favours Suction aspiration   Favours Misoprostol

Analysis 1.15. Comparison 1: Suction aspiration vs Misoprostol, Outcome 15: Anxiety score

Study or Subgroup	Suction aspiration Mean	SD	Total	Misoprostol Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Harwood 2008	2.33	1.04	150	2.45	1.15	457	80.2%	-0.11 [-0.29 , 0.08]	
Kong 2013	58.62	10.56	53	58.08	13.57	59	19.8%	0.04 [-0.33 , 0.41]	
Total (95% CI)			**203**			**516**	**100.0%**	**-0.08 [-0.24 , 0.09]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.48); I² = 0%

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Not applicable

-0.2 -0.1   0   0.1 0.2
Favours Suction aspiration   Favours Misoprostol

Analysis 1.16. Comparison 1: Suction aspiration vs Misoprostol, Outcome 16: Depression score
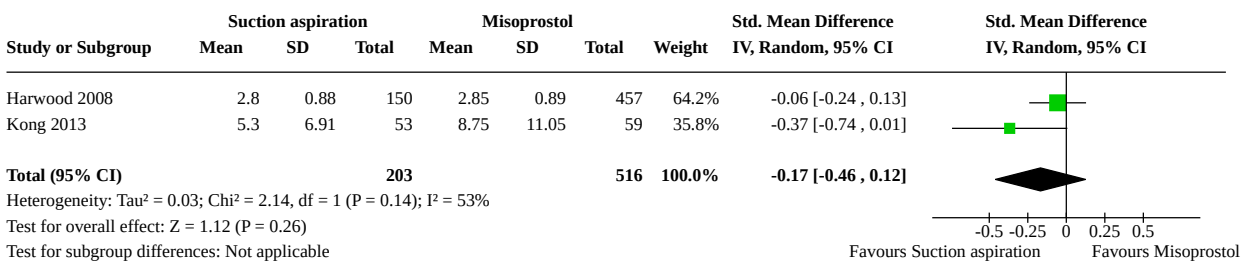
Study or Subgroup	Suction aspiration Mean	SD	Total	Misoprostol Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Harwood 2008	2.8	0.88	150	2.85	0.89	457	64.2%	-0.06 [-0.24 , 0.13]	
Kong 2013	5.3	6.91	53	8.75	11.05	59	35.8%	-0.37 [-0.74 , 0.01]	
Total (95% CI)			**203**			**516**	**100.0%**	**-0.17 [-0.46 , 0.12]**	

Heterogeneity: Tau² = 0.03; Chi² = 2.14, df = 1 (P = 0.14); I² = 53%

Test for overall effect: Z = 1.12 (P = 0.26)

Test for subgroup differences: Not applicable

-0.5 -0.25   0   0.25 0.5
Favours Suction aspiration   Favours Misoprostol

Comparison 2.   Suction aspiration vs Mifepristone + Misoprostol

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2.1 Complete Miscarriage	2		Risk Ratio (IV, Random, 95% CI)	Subtotals only
2.1.1 Missed miscarriage	1	618	Risk Ratio (IV, Random, 95% CI)	1.50 [1.37, 1.64]
2.1.2 Mixed population	1	98	Risk Ratio (IV, Random, 95% CI)	1.11 [1.01, 1.23]
2.2 Composite outcome of death or serious complication	1	618	Risk Ratio (IV, Random, 95% CI)	0.14 [0.01, 2.74]
2.3 Need for unplanned/emergency surgical procedure	1	98	Risk Ratio (IV, Random, 95% CI)	1.00 [0.06, 15.54]
2.4 Pelvic inflammatory disease, sepsis or endometritis	2	716	Risk Ratio (IV, Random, 95% CI)	2.33 [0.47, 11.44]
2.5 Re-admission to hospital	1	98	Risk Ratio (IV, Random, 95% CI)	0.14 [0.01, 2.69]

Analysis 2.1. Comparison 2: Suction aspiration vs Mifepristone + Misoprostol, Outcome 1: Complete Miscarriage

Study or Subgroup	Suction aspiration Events	Total	Mifepristone+Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
2.1.1 Missed miscarriage							
Trinder 2006	290	310	192	308	100.0%	1.50 [1.37 , 1.64]	
Subtotal (95% CI)		**310**		**308**	**100.0%**	**1.50 [1.37 , 1.64]**	
Total events:	290		192				
Heterogeneity: Not applicable							
Test for overall effect: Z = 8.69 (P < 0.00001)							
2.1.2 Mixed population							
Niinimaki 2006	49	49	44	49	100.0%	1.11 [1.01 , 1.23]	
Subtotal (95% CI)		**49**		**49**	**100.0%**	**1.11 [1.01 , 1.23]**	
Total events:	49		44				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.06 (P = 0.04)							

0.5   0.7   1   1.5   2
Favours Mifepristone+Misoprostol   Favours Suction aspiration

Analysis 2.2. Comparison 2: Suction aspiration vs Mifepristone + Misoprostol, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Suction aspiration		Mifepristone+Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Trinder 2006	0	310	3	308	100.0%	0.14 [0.01 , 2.74]	
Total (95% CI)		**310**		**308**	**100.0%**	**0.14 [0.01 , 2.74]**	
Total events:	0		3				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.29 (P = 0.20)							
Test for subgroup differences: Not applicable							

0.001　0.1　1　10　1000
Favours Suction aspiration　　Favours Mifepristone+Misoprostol
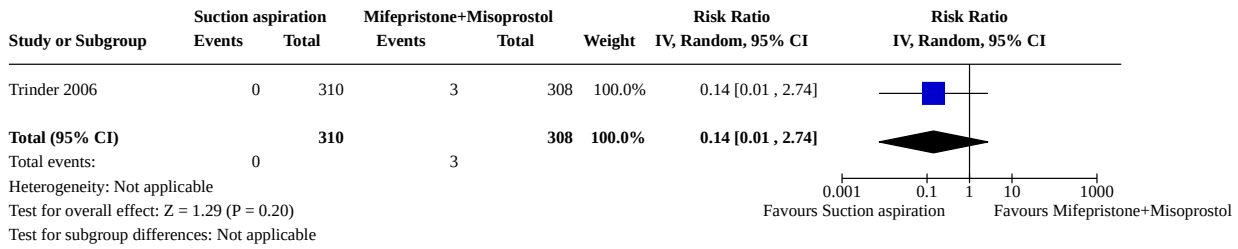
Analysis 2.3. Comparison 2: Suction aspiration vs Mifepristone + Misoprostol, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Suction aspiration		Mifepristone+Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Niinimaki 2006	1	49	1	49	100.0%	1.00 [0.06 , 15.54]	
Total (95% CI)		**49**		**49**	**100.0%**	**1.00 [0.06 , 15.54]**	
Total events:	1		1				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.00 (P = 1.00)							
Test for subgroup differences: Not applicable							

0.05　0.2　1　5　20
Favours Suction aspiration　　Favours Mifepristone+Misoprostol
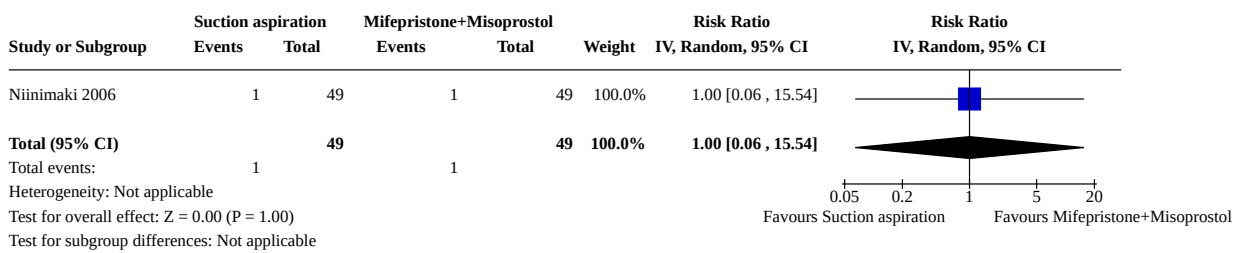
Analysis 2.4. Comparison 2: Suction aspiration vs Mifepristone + Misoprostol, Outcome 4: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Suction aspiration		Mifepristone+Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Niinimaki 2006	7	49	1	49	35.2%	7.00 [0.89 , 54.79]	
Trinder 2006	9	310	7	308	64.8%	1.28 [0.48 , 3.39]	
Total (95% CI)		**359**		**357**	**100.0%**	**2.33 [0.47 , 11.44]**	
Total events:	16		8				
Heterogeneity: Tau² = 0.77; Chi² = 2.14, df = 1 (P = 0.14); I² = 53%							
Test for overall effect: Z = 1.04 (P = 0.30)							
Test for subgroup differences: Not applicable							

0.01　0.1　1　10　100
Favours Suction aspiration　　Favours Mifepristone+Misoprostol

Analysis 2.5. Comparison 2: Suction aspiration vs Mifepristone + Misoprostol, Outcome 5: Re-admission to hospital
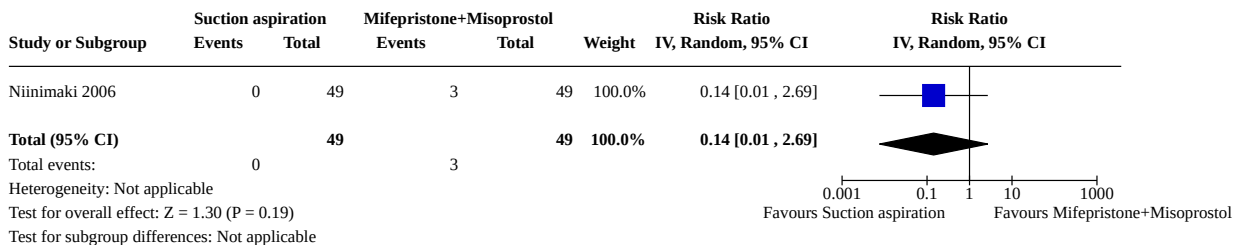
Study or Subgroup	Suction aspiration		Mifepristone+Misoprostol		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Niinimaki 2006	0	49	3	49	100.0%	0.14 [0.01 , 2.69]	
Total (95% CI)		**49**		**49**	**100.0%**	**0.14 [0.01 , 2.69]**	
Total events:	0		3				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.30 (P = 0.19)							
Test for subgroup differences: Not applicable							

0.001　0.1　1　10　1000
Favours Suction aspiration　　Favours Mifepristone+Misoprostol

Comparison 3.   Suction aspiration vs Dilatation & Curettage

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.1 Complete Miscarriage	5		Risk Ratio (IV, Random, 95% CI)	Subtotals only
3.1.1 Incomplete miscarriage	4	1432	Risk Ratio (IV, Random, 95% CI)	1.02 [0.98, 1.06]
3.1.2 Mixed population	1	90	Risk Ratio (IV, Random, 95% CI)	1.05 [0.94, 1.17]
3.2 Composite outcome of death or serious complication	5	1521	Risk Ratio (IV, Random, 95% CI)	1.27 [0.80, 2.02]
3.3 Need for unplanned/emergency surgical procedure	2	693	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 8.07]
3.4 Pelvic inflammatory disease, sepsis or endometritis	3	822	Risk Ratio (IV, Random, 95% CI)	0.77 [0.53, 1.11]
3.5 Mean volumes of blood loss (millilitres)	2	451	Mean Difference (IV, Random, 95% CI)	-11.44 [-21.49, -1.40]
3.6 Change in haemoglobin measurements before and after the miscarriage	2	370	Mean Difference (IV, Random, 95% CI)	-0.41 [-0.68, -0.14]
3.7 Days of bleeding	1	270	Mean Difference (IV, Random, 95% CI)	-0.30 [-1.30, 0.70]
3.8 Cervical tear	2	558	Risk Ratio (IV, Random, 95% CI)	0.49 [0.20, 1.18]
3.9 Mean duration of hospital stay (days)	3	220	Mean Difference (IV, Random, 95% CI)	-0.56 [-0.89, -0.23]
3.10 Re-admission to hospital	2	1042	Risk Ratio (IV, Random, 95% CI)	1.61 [0.62, 4.16]
3.11 Vomiting	1	599	Risk Ratio (IV, Random, 95% CI)	2.31 [0.60, 8.85]
3.12 Pyrexia	3	1157	Risk Ratio (IV, Random, 95% CI)	1.31 [0.85, 2.02]

Analysis 3.1. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 1: Complete Miscarriage

Study or Subgroup	Suction aspiration Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
3.1.1 Incomplete miscarriage							
Caceres 1979	223	223	234	235	29.0%	1.00 [0.99 , 1.02]	
Kittiwatanakul 2012	47	47	47	47	22.4%	1.00 [0.96 , 1.04]	
Salam 2016	301	305	270	305	22.0%	1.11 [1.07 , 1.16]	
Verkuyl 1993	136	138	132	132	26.6%	0.99 [0.96 , 1.01]	
Subtotal (95% CI)		**713**		**719**	**100.0%**	**1.02 [0.98 , 1.06]**	
Total events:	707		683				
Heterogeneity: Tau² = 0.00; Chi² = 25.25, df = 3 (P < 0.0001); I² = 88%							
Test for overall effect: Z = 1.08 (P = 0.28)							
3.1.2 Mixed population							
Arif 2018	43	45	41	45	100.0%	1.05 [0.94 , 1.17]	
Subtotal (95% CI)		**45**		**45**	**100.0%**	**1.05 [0.94 , 1.17]**	
Total events:	43		41				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.84 (P = 0.40)							
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² = 0%							

0.85   0.9   1   1.1   1.2
Favours Dilatation & Curettage   Favours Suction aspiration

Analysis 3.2. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Suction aspiration Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Caceres 1979	1	223	1	235	2.8%	1.05 [0.07 , 16.75]	
Caceres 1981	36	301	27	298	95.1%	1.32 [0.82 , 2.12]	
Kittiwatanakul 2012	0	47	0	47		Not estimable	
Pereira 2006	0	50	0	50		Not estimable	
Verkuyl 1993	0	138	1	132	2.1%	0.32 [0.01 , 7.76]	
Total (95% CI)		**759**		**762**	**100.0%**	**1.27 [0.80 , 2.02]**	
Total events:	37		29				
Heterogeneity: Tau² = 0.00; Chi² = 0.76, df = 2 (P = 0.68); I² = 0%							
Test for overall effect: Z = 1.03 (P = 0.30)							
Test for subgroup differences: Not applicable							

0.02   0.1   1   10   50
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.3. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Suction aspiration Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Caceres 1981	0	301	1	298	100.0%	0.33 [0.01 , 8.07]	
Kittiwatanakul 2012	0	47	0	47		Not estimable	
Total (95% CI)		**348**		**345**	**100.0%**	**0.33 [0.01 , 8.07]**	
Total events:	0		1				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.68 (P = 0.50)							
Test for subgroup differences: Not applicable							

0.01   0.1   1   10   100
Favours Suction aspiration   Favours Dilatation & Curettage

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Analysis 3.4. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 4: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Suction aspiration Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Caceres 1979	37	223	48	235	90.6%	0.81 [0.55 , 1.20]	
Kittiwatanakul 2012	2	47	2	47	3.7%	1.00 [0.15 , 6.81]	
Verkuyl 1993	2	138	7	132	5.6%	0.27 [0.06 , 1.29]	
Total (95% CI)		**408**		**414**	**100.0%**	**0.77 [0.53 , 1.11]**	
Total events:	41		57				

Heterogeneity: Tau² = 0.00; Chi² = 1.85, df = 2 (P = 0.40); I² = 0%
Test for overall effect: Z = 1.39 (P = 0.16)
Test for subgroup differences: Not applicable

0.1 0.2 0.5 1 2 5 10
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.5. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 5: Mean volumes of blood loss (millilitres)

Study or Subgroup	Suction aspiration Mean	SD	Total	Dilatation & Curettage Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Kittiwatanakul 2012	30.4	7.3	47	37.2	6.8	47	54.9%	-6.80 [-9.65 , -3.95]	
Verkuyl 1993	19.2	25.6	179	36.3	39.8	178	45.1%	-17.10 [-24.05 , -10.15]	
Total (95% CI)			**226**			**225**	**100.0%**	**-11.44 [-21.49 , -1.40]**	

Heterogeneity: Tau² = 45.71; Chi² = 7.23, df = 1 (P = 0.007); I² = 86%
Test for overall effect: Z = 2.23 (P = 0.03)
Test for subgroup differences: Not applicable

-20 -10 0 10 20
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.6. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 6: Change in haemoglobin measurements before and after the miscarriage

Study or Subgroup	Suction aspiration Mean	SD	Total	Dilatation & Curettage Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Pereira 2006	0.63	0.89	50	1.05	0.89	50	60.4%	-0.42 [-0.77 , -0.07]	
Verkuyl 1993	0.3	1.7	138	0.7	1.9	132	39.6%	-0.40 [-0.83 , 0.03]	
Total (95% CI)			**188**			**182**	**100.0%**	**-0.41 [-0.68 , -0.14]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)
Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.7. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 7: Days of bleeding

Study or Subgroup	Suction aspiration Mean	SD	Total	Dilatation & Curettage Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Verkuyl 1993	4.9	3.8	138	5.2	4.5	132	100.0%	-0.30 [-1.30 , 0.70]	
Total (95% CI)			**138**			**132**	**100.0%**	**-0.30 [-1.30 , 0.70]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)
Test for subgroup differences: Not applicable

-1 -0.5 0 0.5 1
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.8.   Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 8: Cervical tear

Study or Subgroup	Suction aspiration		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Caceres 1979	7	223	15	235	100.0%	0.49 [0.20 , 1.18]	
Pereira 2006	0	50	0	50		Not estimable	
Total (95% CI)		273		285	100.0%	0.49 [0.20 , 1.18]	
Total events:	7		15				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.58 (P = 0.11)
Test for subgroup differences: Not applicable

0.2   0.5   1   2   5
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.9.   Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 9: Mean duration of hospital stay (days)

Study or Subgroup	Suction aspiration			Dilatation & Curettage			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Arif 2018	0.24	0.54	45	0.7	0.54	45	45.3%	-0.46 [-0.68 , -0.24]	
Fonseca 1997	0.35	0.88	15	1.52	0.88	15	18.4%	-1.17 [-1.80 , -0.54]	
Pereira 2006	0.59	0.84	50	0.96	0.84	50	36.3%	-0.37 [-0.70 , -0.04]	
Total (95% CI)			110			110	100.0%	-0.56 [-0.89 , -0.23]	

Heterogeneity: Tau² = 0.05; Chi² = 5.06, df = 2 (P = 0.08); I² = 60%
Test for overall effect: Z = 3.33 (P = 0.0009)
Test for subgroup differences: Not applicable

-1   -0.5   0   0.5   1
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.10.   Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 10: Re-admission to hospital

Study or Subgroup	Suction aspiration		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Caceres 1979	8	216	4	227	64.3%	2.10 [0.64 , 6.88]	
Caceres 1981	3	301	3	298	35.7%	0.99 [0.20 , 4.87]	
Total (95% CI)		517		525	100.0%	1.61 [0.62 , 4.16]	
Total events:	11		7				

Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 1 (P = 0.46); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)
Test for subgroup differences: Not applicable

0.2   0.5   1   2   5
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.11.   Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 11: Vomiting

Study or Subgroup	Suction aspiration		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Caceres 1981	7	301	3	298	100.0%	2.31 [0.60 , 8.85]	
Total (95% CI)		301		298	100.0%	2.31 [0.60 , 8.85]	
Total events:	7		3				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)
Test for subgroup differences: Not applicable

0.1   0.2   0.5   1   2   5   10
Favours Suction aspiration   Favours Dilatation & Curettage

Analysis 3.12. Comparison 3: Suction aspiration vs Dilatation & Curettage, Outcome 12: Pyrexia

Study or Subgroup	Suction aspiration Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Caceres 1979	13	223	14	235	35.1%	0.98 [0.47 , 2.04]	
Caceres 1981	31	301	20	298	64.9%	1.53 [0.90 , 2.63]	
Pereira 2006	0	50	0	50		Not estimable	
Total (95% CI)		**574**		**583**	**100.0%**	**1.31 [0.85 , 2.02]**	
Total events:	44		34				

Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 1 (P = 0.33); I² = 0%
Test for overall effect: Z = 1.22 (P = 0.22)
Test for subgroup differences: Not applicable

0.5 0.7 1 1.5 2
Favours Suction aspiration   Favours Dilatation & Curettage

Comparison 4. Suction aspiration vs Expectant/ Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Complete Miscarriage	7		Risk Ratio (IV, Random, 95% CI)	Subtotals only
4.1.1 Missed miscarriage	1	616	Risk Ratio (IV, Random, 95% CI)	1.88 [1.68, 2.12]
4.1.2 Incomplete miscarriage	2	300	Risk Ratio (IV, Random, 95% CI)	1.20 [0.85, 1.69]
4.1.3 Mixed population	4	776	Risk Ratio (IV, Random, 95% CI)	1.18 [1.11, 1.25]
4.2 Composite outcome of death or serious complication	5	1485	Risk Ratio (IV, Random, 95% CI)	0.43 [0.12, 1.53]
4.3 Need for unplanned/emergency surgical procedure	4	842	Risk Ratio (IV, Random, 95% CI)	0.51 [0.30, 0.87]
4.4 Pelvic inflammatory disease, sepsis or endometritis	8	1725	Risk Ratio (IV, Random, 95% CI)	1.35 [0.76, 2.41]
4.5 Mean volumes of blood loss (millilitres)	1	352	Mean Difference (IV, Random, 95% CI)	-23.00 [-40.41, -5.59]
4.6 Change in haemoglobin measurements before and after the miscarriage	3	603	Mean Difference (IV, Random, 95% CI)	0.18 [0.10, 0.25]
4.7 Days of bleeding	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
4.8 Cervical tear	2	492	Risk Ratio (IV, Random, 95% CI)	Not estimable
4.9 Mean duration of hospital stay (days)	1	140	Mean Difference (IV, Random, 95% CI)	0.99 [0.74, 1.24]
4.10 Re-admission to hospital	2	463	Risk Ratio (IV, Random, 95% CI)	0.72 [0.15, 3.41]
4.11 Vomiting	1	111	Risk Ratio (IV, Random, 95% CI)	0.82 [0.19, 3.50]
4.12 Diarrhoea	1	111	Risk Ratio (IV, Random, 95% CI)	1.82 [0.71, 4.67]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.13 Pyrexia	1	111	Risk Ratio (IV, Random, 95% CI)	3.28 [0.69, 15.57]
4.14 Anxiety score	1	111	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.49, 0.26]
4.15 Depression score	1	111	Std. Mean Difference (IV, Random, 95% CI)	-0.29 [-0.67, 0.08]

Analysis 4.1. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 1: Complete Miscarriage

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
4.1.1 Missed miscarriage							
Trinder 2006	290	310	152	306	100.0%	1.88 [1.68 , 2.12]	
Subtotal (95% CI)		310		306	100.0%	**1.88 [1.68 , 2.12]**	
Total events:	290		152				
Heterogeneity: Not applicable							
Test for overall effect: Z = 10.65 (P < 0.00001)							
4.1.2 Incomplete miscarriage							
Dangalla 2012	79	80	55	80	48.2%	1.44 [1.24 , 1.67]	
Wijesinghe 2011	66	69	67	71	51.8%	1.01 [0.94 , 1.09]	
Subtotal (95% CI)		149		151	100.0%	**1.20 [0.85 , 1.69]**	
Total events:	145		122				
Heterogeneity: Tau² = 0.06; Chi² = 16.55, df = 1 (P < 0.0001); I² = 94%							
Test for overall effect: Z = 1.04 (P = 0.30)							
4.1.3 Mixed population							
Al-Maani 2014	110	115	83	102	33.0%	1.18 [1.06 , 1.30]	
Karlsen 2001	48	48	39	46	20.5%	1.18 [1.04 , 1.34]	
Kong 2013	54	55	46	58	18.0%	1.24 [1.08 , 1.42]	
Nadarajah 2014	147	175	131	177	28.4%	1.13 [1.02 , 1.27]	
Subtotal (95% CI)		393		383	100.0%	**1.18 [1.11 , 1.25]**	
Total events:	359		299				
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 3 (P = 0.81); I² = 0%							
Test for overall effect: Z = 5.47 (P < 0.00001)							
Test for subgroup differences: Chi² = 50.65, df = 2 (P < 0.00001), I² = 96.1%							

0.5   0.7   1   1.5   2
Favours Expectant/ Placebo   Favours Suction aspiration

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Analysis 4.2. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Al-Maani 2014	1	115	2	102	26.1%	0.44 [0.04 , 4.82]	
Dangalla 2012	2	80	1	80	26.2%	2.00 [0.19 , 21.62]	
Nadarajah 2014	1	175	3	177	28.9%	0.34 [0.04 , 3.21]	
Trinder 2006	0	310	7	306	18.7%	0.07 [0.00 , 1.15]	
Wijesinghe 2011	0	69	0	71		Not estimable	
Total (95% CI)		**749**		**736**	**100.0%**	**0.43 [0.12 , 1.53]**	
Total events:	4		13				

Heterogeneity: Tau² = 0.16; Chi² = 3.30, df = 3 (P = 0.35); I² = 9%
Test for overall effect: Z = 1.31 (P = 0.19)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.3. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Al-Maani 2014	6	115	5	102	21.3%	1.06 [0.33 , 3.38]	
Dangalla 2012	0	80	1	80	2.8%	0.33 [0.01 , 8.06]	
Kong 2013	0	55	0	58		Not estimable	
Nadarajah 2014	13	175	31	177	75.9%	0.42 [0.23 , 0.78]	
Total (95% CI)		**425**		**417**	**100.0%**	**0.51 [0.30 , 0.87]**	
Total events:	19		37				

Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 2.45 (P = 0.01)
Test for subgroup differences: Not applicable

0.02 0.1 1 10 50
Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.4. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 4: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Al-Maani 2014	4	115	2	102	11.8%	1.77 [0.33 , 9.48]	
Chipchase 1997	1	16	1	19	4.6%	1.19 [0.08 , 17.51]	
Dangalla 2012	3	80	2	80	10.7%	1.50 [0.26 , 8.74]	
Karlsen 2001	0	48	0	46		Not estimable	
Kong 2013	2	53	0	58	3.6%	5.46 [0.27 , 111.26]	
Nadarajah 2014	7	175	5	177	26.0%	1.42 [0.46 , 4.38]	
Trinder 2006	9	310	9	306	40.0%	0.99 [0.40 , 2.45]	
Wijesinghe 2011	1	69	0	71	3.3%	3.09 [0.13 , 74.47]	
Total (95% CI)		**866**		**859**	**100.0%**	**1.35 [0.76 , 2.41]**	
Total events:	27		19				

Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 6 (P = 0.95); I² = 0%
Test for overall effect: Z = 1.03 (P = 0.30)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.5. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 5: Mean volumes of blood loss (millilitres)

Study or Subgroup	Suction aspiration			Expectant/ Placebo			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Nadarajah 2014	148	83.31	175	171	83.31	177	100.0%	-23.00 [-40.41 , -5.59]	
Total (95% CI)			**175**			**177**	**100.0%**	**-23.00 [-40.41 , -5.59]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.59 (P = 0.010)									
Test for subgroup differences: Not applicable									

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.6. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 6: Change in haemoglobin measurements before and after the miscarriage

Study or Subgroup	Suction aspiration			Expectant/ Placebo			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Kong 2013	0.12	0.84	53	0.03	0.98	58	5.0%	0.09 [-0.25 , 0.43]	
Nadarajah 2014	0.8	2.01	175	0.9	2.01	177	3.3%	-0.10 [-0.52 , 0.32]	
Wijesinghe 2011	0.91	0.12	69	0.72	0.2	71	91.7%	0.19 [0.14 , 0.24]	
Total (95% CI)			**297**			**306**	**100.0%**	**0.18 [0.10 , 0.25]**	
Heterogeneity: Tau² = 0.00; Chi² = 2.10, df = 2 (P = 0.35); I² = 5%									
Test for overall effect: Z = 4.47 (P < 0.00001)									
Test for subgroup differences: Not applicable									

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.7. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 7: Days of bleeding

Study or Subgroup	Suction aspiration			Expectant/ Placebo			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Al-Maani 2014	7	2.1	115	11	2.3	102	-4.00 [-4.59 , -3.41]	
Karlsen 2001	4.8	4.42	48	7.2	4.42	46	-2.40 [-4.19 , -0.61]	
Kong 2013	10.73	5.92	53	12.95	5.73	58	-2.22 [-4.39 , -0.05]	
Nadarajah 2014	3.5	6.52	175	5.3	6.52	177	-1.80 [-3.16 , -0.44]	
Test for subgroup differences: Not applicable								

Favours Suction aspiration   Favours Expectant/ Placebo
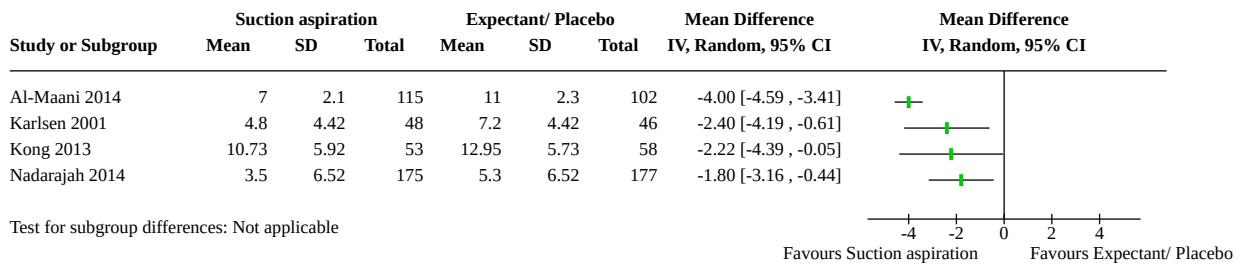
Analysis 4.8. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 8: Cervical tear

Study or Subgroup	Suction aspiration		Expectant/ Placebo		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Nadarajah 2014	0	175	0	177		Not estimable	
Wijesinghe 2011	0	69	0	71		Not estimable	
Total (95% CI)		**244**		**248**		**Not estimable**	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.9. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 9: Mean duration of hospital stay (days)

Study or Subgroup	Suction aspiration Mean	SD	Total	Expectant/ Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Wijesinghe 2011	2.57	0.82	69	1.58	0.66	71	100.0%	0.99 [0.74 , 1.24]	
Total (95% CI)			**69**			**71**	**100.0%**	**0.99 [0.74 , 1.24]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 7.86 (P < 0.00001)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.10. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 10: Re-admission to hospital

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Kong 2013	5	53	3	58	42.2%	1.82 [0.46 , 7.26]	
Nadarajah 2014	13	175	36	177	57.8%	0.37 [0.20 , 0.66]	
Total (95% CI)		**228**		**235**	**100.0%**	**0.72 [0.15 , 3.41]**	
Total events:	18		39				

Heterogeneity: Tau² = 1.00; Chi² = 4.38, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.41 (P = 0.68)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.11. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 11: Vomiting

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Kong 2013	3	53	4	58	100.0%	0.82 [0.19 , 3.50]	
Total (95% CI)		**53**		**58**	**100.0%**	**0.82 [0.19 , 3.50]**	
Total events:	3		4				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.79)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo
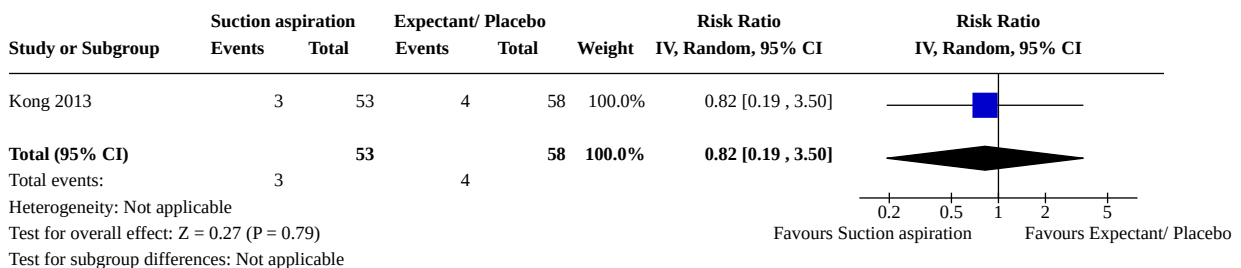
Analysis 4.12. Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 12: Diarrhoea

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Kong 2013	10	53	6	58	100.0%	1.82 [0.71 , 4.67]	
Total (95% CI)		**53**		**58**	**100.0%**	**1.82 [0.71 , 4.67]**	
Total events:	10		6				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.13.   Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 13: Pyrexia

Study or Subgroup	Suction aspiration Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Kong 2013	6	53	2	58	100.0%	3.28 [0.69 , 15.57]	
Total (95% CI)		53		58	100.0%	**3.28 [0.69 , 15.57]**	
Total events:	6		2				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.50 (P = 0.13)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.14.   Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 14: Anxiety score

Study or Subgroup	Suction aspiration Mean	SD	Total	Expectant/ Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Kong 2013	58.62	10.56	53	60.05	13.74	58	100.0%	-0.12 [-0.49 , 0.26]	
Total (95% CI)			53			58	100.0%	**-0.12 [-0.49 , 0.26]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Analysis 4.15.   Comparison 4: Suction aspiration vs Expectant/ Placebo, Outcome 15: Depression score

Study or Subgroup	Suction aspiration Mean	SD	Total	Expectant/ Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Kong 2013	5.3	6.91	53	7.93	10.41	58	100.0%	-0.29 [-0.67 , 0.08]	
Total (95% CI)			53			58	100.0%	**-0.29 [-0.67 , 0.08]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)
Test for subgroup differences: Not applicable

Favours Suction aspiration   Favours Expectant/ Placebo

Comparison 5.   Misoprostol vs Mifepristone + Misoprostol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Complete Miscarriage	7		Risk Ratio (IV, Random, 95% CI)	Subtotals only
5.1.1 Missed miscarriage	7	1812	Risk Ratio (IV, Random, 95% CI)	0.87 [0.79, 0.97]
5.2 Composite outcome of death or serious complication	7	1822	Risk Ratio (IV, Random, 95% CI)	0.50 [0.20, 1.25]
5.3 Need for unplanned/emergency surgical procedure	6	1527	Risk Ratio (IV, Random, 95% CI)	1.55 [1.22, 1.96]
5.4 Pelvic inflammatory disease, sepsis or endometritis	5	1617	Risk Ratio (IV, Random, 95% CI)	1.02 [0.54, 1.92]
5.5 Change in haemoglobin measurements before and after the miscarriage	1	90	Mean Difference (IV, Random, 95% CI)	0.02 [-0.18, 0.22]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.6 Days of bleeding	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.7 Re-admission to hospital	1	344	Risk Ratio (IV, Random, 95% CI)	2.30 [1.48, 3.58]
5.8 Nausea	2	570	Risk Ratio (IV, Random, 95% CI)	0.74 [0.39, 1.39]
5.9 Vomiting	1	300	Risk Ratio (IV, Random, 95% CI)	0.57 [0.36, 0.90]
5.10 Diarrhoea	2	570	Risk Ratio (IV, Random, 95% CI)	1.09 [0.83, 1.44]
5.11 Pyrexia	4	685	Risk Ratio (IV, Random, 95% CI)	0.74 [0.34, 1.62]

Analysis 5.1. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 1: Complete Miscarriage

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
5.1.1 Missed miscarriage							
Chu 2020	266	348	289	348	21.0%	0.92 [0.85 , 0.99]	
Hamel 2021	101	172	136	172	16.3%	0.74 [0.64 , 0.86]	
Machtinger 2002	25	31	27	34	10.6%	1.02 [0.80 , 1.29]	
Machtinger 2004	79	111	70	94	14.9%	0.96 [0.81 , 1.13]	
Schreiber 2018	100	149	124	148	17.2%	0.80 [0.70 , 0.91]	
Sinha 2018	26	45	39	45	9.2%	0.67 [0.51 , 0.88]	
Stockheim 2006	42	57	38	58	10.6%	1.12 [0.88 , 1.43]	
Subtotal (95% CI)		913		899	100.0%	**0.87 [0.79 , 0.97]**	
Total events:	639		723				

Heterogeneity: Tau² = 0.01; Chi² = 18.52, df = 6 (P = 0.005); I² = 68%

Test for overall effect: Z = 2.45 (P = 0.01)

Test for subgroup differences: Not applicable

0.5 0.7 1 1.5 2
Favours Mifepristone + Misoprostol   Favours Misoprostol

Analysis 5.2.   Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Chu 2020	5	351	11	352	75.6%	0.46 [0.16 , 1.30]	
Hamel 2021	1	172	0	172	8.1%	3.00 [0.12 , 73.13]	
Machtinger 2002	0	31	0	34		Not estimable	
Machtinger 2004	0	111	0	94		Not estimable	
Schreiber 2018	1	151	3	149	16.3%	0.33 [0.03 , 3.13]	
Sinha 2018	0	45	0	45		Not estimable	
Stockheim 2006	0	57	0	58		Not estimable	
Total (95% CI)		918		904	100.0%	**0.50 [0.20 , 1.25]**	
Total events:	7		14				

Heterogeneity: Tau² = 0.00; Chi² = 1.37, df = 2 (P = 0.50); I² = 0%

Test for overall effect: Z = 1.48 (P = 0.14)

Test for subgroup differences: Not applicable

0.001 0.1 1 10 1000
Favours Misoprostol   Favours Mifepristone + Misoprostol

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Analysis 5.3. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Chu 2020	87	353	62	355	60.1%	1.41 [1.06 , 1.89]	
Hamel 2021	60	172	30	172	35.8%	2.00 [1.36 , 2.94]	
Machtinger 2002	1	31	1	34	0.7%	1.10 [0.07 , 16.80]	
Machtinger 2004	0	111	1	94	0.5%	0.28 [0.01 , 6.86]	
Sinha 2018	1	45	1	45	0.7%	1.00 [0.06 , 15.50]	
Stockheim 2006	2	57	4	58	2.0%	0.51 [0.10 , 2.67]	
Total (95% CI)		**769**		**758**	**100.0%**	**1.55 [1.22 , 1.96]**	
Total events:	151		99				

Heterogeneity: Tau² = 0.00; Chi² = 5.08, df = 5 (P = 0.41); I² = 2%
Test for overall effect: Z = 3.61 (P = 0.0003)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Misoprostol Favours Mifepristone + Misoprostol

Analysis 5.4. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 4: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Chu 2020	15	351	13	352	76.1%	1.16 [0.56 , 2.40]	
Hamel 2021	1	172	1	172	5.3%	1.00 [0.06 , 15.86]	
Machtinger 2002	0	31	1	34	4.0%	0.36 [0.02 , 8.63]	
Machtinger 2004	0	111	1	94	4.0%	0.28 [0.01 , 6.86]	
Schreiber 2018	2	151	2	149	10.6%	0.99 [0.14 , 6.91]	
Total (95% CI)		**816**		**801**	**100.0%**	**1.02 [0.54 , 1.92]**	
Total events:	18		18				

Heterogeneity: Tau² = 0.00; Chi² = 1.14, df = 4 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.06 (P = 0.95)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Misoprostol Favours Mifepristone + Misoprostol

Analysis 5.5. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 5: Change in haemoglobin measurements before and after the miscarriage

Study or Subgroup	Misoprostol Mean	SD	Total	Mifepristone + Misoprostol Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Sinha 2018	0.62	0.49	45	0.6	0.49	45	100.0%	0.02 [-0.18 , 0.22]	
Total (95% CI)			**45**			**45**	**100.0%**	**0.02 [-0.18 , 0.22]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.19 (P = 0.85)
Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Misoprostol Favours Mifepristone + Misoprostol
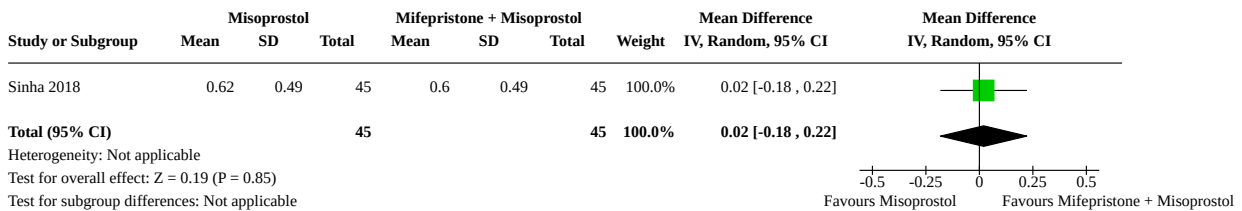
Analysis 5.6. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 6: Days of bleeding

Study or Subgroup	Misoprostol Mean	SD	Total	Mifepristone + Misoprostol Mean	SD	Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Chu 2020	16	12.6	326	16.3	15.2	330	-0.30 [-2.44 , 1.84]	
Sinha 2018	6.22	0.11	45	6.2	0.11	45	0.02 [-0.03 , 0.07]	

Test for subgroup differences: Not applicable

-2 -1 0 1 2
Favours Misoprostol Favours Mifepristone + Misoprostol
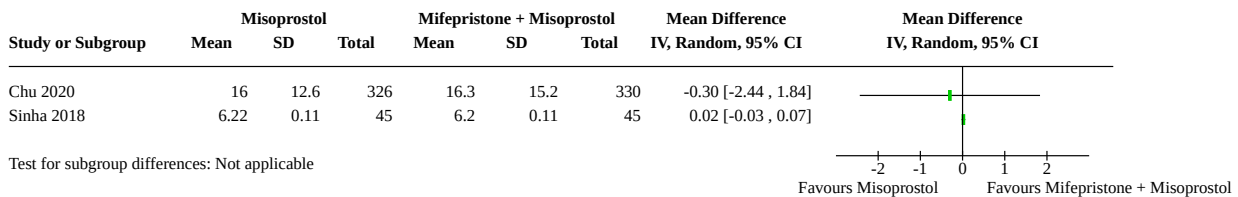
Analysis 5.7. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 7: Re-admission to hospital

Study or Subgroup	Misoprostol Events	Total	Mifepristone + misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Hamel 2021	53	172	23	172	100.0%	2.30 [1.48 , 3.58]	
Total (95% CI)		**172**		**172**	**100.0%**	**2.30 [1.48 , 3.58]**	
Total events:	53		23				
Heterogeneity: Not applicable							
Test for overall effect: Z = 3.71 (P = 0.0002)							
Test for subgroup differences: Not applicable							

0.02 0.1 1 10 50
Favours Misoprostol — Favours mifepristone + misoprostol

Analysis 5.8. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 8: Nausea

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Hamel 2021	18	137	34	133	44.4%	0.51 [0.31 , 0.86]	
Schreiber 2018	56	151	56	149	55.6%	0.99 [0.74 , 1.32]	
Total (95% CI)		**288**		**282**	**100.0%**	**0.74 [0.39 , 1.39]**	
Total events:	74		90				
Heterogeneity: Tau² = 0.17; Chi² = 4.60, df = 1 (P = 0.03); I² = 78%							
Test for overall effect: Z = 0.93 (P = 0.35)							
Test for subgroup differences: Not applicable							

0.2 0.5 1 2 5
Favours Misoprostol — Favours Mifepristone + Misoprostol

Analysis 5.9. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 9: Vomiting

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Schreiber 2018	23	151	40	149	100.0%	0.57 [0.36 , 0.90]	
Total (95% CI)		**151**		**149**	**100.0%**	**0.57 [0.36 , 0.90]**	
Total events:	23		40				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.41 (P = 0.02)							
Test for subgroup differences: Not applicable							

0.2 0.5 1 2 5
Favours Misoprostol — Favours Mifepristone + Misoprostol

Analysis 5.10. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 10: Diarrhoea

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Hamel 2021	34	137	29	133	40.8%	1.14 [0.74 , 1.76]	
Schreiber 2018	44	151	41	149	59.2%	1.06 [0.74 , 1.52]	
Total (95% CI)		**288**		**282**	**100.0%**	**1.09 [0.83 , 1.44]**	
Total events:	78		70				
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%							
Test for overall effect: Z = 0.61 (P = 0.54)							
Test for subgroup differences: Not applicable							

0.5 0.7 1 1.5 2
Favours Misoprostol — Favours Mifepristone + Misoprostol

Analysis 5.11. Comparison 5: Misoprostol vs Mifepristone + Misoprostol, Outcome 11: Pyrexia

Study or Subgroup	Misoprostol Events	Total	Mifepristone + Misoprostol Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Machtinger 2002	0	31	1	34	6.2%	0.36 [0.02 , 8.63]	
Machtinger 2004	0	111	1	94	6.1%	0.28 [0.01 , 6.86]	
Schreiber 2018	9	151	10	149	81.6%	0.89 [0.37 , 2.12]	
Stockheim 2006	0	57	1	58	6.1%	0.34 [0.01 , 8.15]	
Total (95% CI)		**350**		**335**	**100.0%**	**0.74 [0.34 , 1.62]**	
Total events:	9		13				

Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 3 (P = 0.82); I² = 0%
Test for overall effect: Z = 0.75 (P = 0.45)
Test for subgroup differences: Not applicable

0.02 0.1 1 10 50
Favours Misoprostol   Favours Mifepristone + Misoprostol

Comparison 6. Misoprostol vs Dilatation & Curettage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Complete Miscarriage	4		Risk Ratio (IV, Random, 95% CI)	Subtotals only
6.1.1 Missed miscarriage	1	107	Risk Ratio (IV, Random, 95% CI)	0.81 [0.71, 0.93]
6.1.2 Incomplete miscarriage	1	94	Risk Ratio (IV, Random, 95% CI)	0.92 [0.83, 1.01]
6.1.3 Mixed population	2	154	Risk Ratio (IV, Random, 95% CI)	0.32 [0.07, 1.47]
6.2 Composite outcome of death or serious complication	2	157	Risk Ratio (IV, Random, 95% CI)	1.26 [0.54, 2.97]
6.3 Need for unplanned/emergency surgical procedure	1	94	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.4 Pain score	1	94	Std. Mean Difference (IV, Random, 95% CI)	0.51 [0.10, 0.92]
6.5 Pelvic inflammatory disease, sepsis or endometritis	2	201	Risk Ratio (IV, Random, 95% CI)	2.12 [0.20, 22.64]
6.6 Mean volumes of blood loss (millilitres)	1	104	Mean Difference (IV, Random, 95% CI)	22.30 [4.45, 40.15]
6.7 Days of bleeding	1	94	Mean Difference (IV, Random, 95% CI)	2.60 [1.27, 3.93]
6.8 Cervical tear	1	107	Risk Ratio (IV, Random, 95% CI)	Not estimable
6.9 Re-admission to hospital	1	107	Risk Ratio (IV, Random, 95% CI)	3.17 [0.13, 76.11]
6.10 Vomiting	1	94	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.98]
6.11 Nausea	1	94	Risk Ratio (IV, Random, 95% CI)	0.33 [0.01, 7.98]
6.12 Diarrhoea	1	94	Risk Ratio (IV, Random, 95% CI)	3.00 [0.13, 71.82]

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
6.13 Depression score	1	215	Std. Mean Difference (IV, Random, 95% CI)	-0.09 [-0.36, 0.18]

Analysis 6.1. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 1: Complete Miscarriage

Study or Subgroup	Misoprostol Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
6.1.1 Missed miscarriage							
Shuaib 2013	42	52	55	55	100.0%	0.81 [0.71 , 0.93]	
Subtotal (95% CI)		**52**		**55**	**100.0%**	**0.81 [0.71 , 0.93]**	
Total events:	42		55				
Heterogeneity: Not applicable							
Test for overall effect: Z = 3.05 (P = 0.002)							
6.1.2 Incomplete miscarriage							
Moodliar 2005	43	47	47	47	100.0%	0.92 [0.83 , 1.01]	
Subtotal (95% CI)		**47**		**47**	**100.0%**	**0.92 [0.83 , 1.01]**	
Total events:	43		47				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.81 (P = 0.07)							
6.1.3 Mixed population							
de Jonge 1995	3	23	26	27	44.2%	0.14 [0.05 , 0.39]	
Kyaw 2015	32	50	54	54	55.8%	0.64 [0.52 , 0.79]	
Subtotal (95% CI)		**73**		**81**	**100.0%**	**0.32 [0.07 , 1.47]**	
Total events:	35		80				
Heterogeneity: Tau² = 1.06; Chi² = 8.02, df = 1 (P = 0.005); I² = 88%							
Test for overall effect: Z = 1.46 (P = 0.14)							
Test for subgroup differences: Chi² = 3.80, df = 2 (P = 0.15), I² = 47.4%							

0.05 0.2 1 5 20
Favours Dilatation & Curettage   Favours Misoprostol

Analysis 6.2. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Misoprostol Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
de Jonge 1995	7	23	7	27	92.8%	1.17 [0.48 , 2.85]	
Shuaib 2013	1	52	0	55	7.2%	3.17 [0.13 , 76.11]	
Total (95% CI)		**75**		**82**	**100.0%**	**1.26 [0.54 , 2.97]**	
Total events:	8		7				
Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 1 (P = 0.56); I² = 0%							
Test for overall effect: Z = 0.53 (P = 0.59)							
Test for subgroup differences: Not applicable							

0.001 0.1 1 10 1000
Favours Misoprostol   Favours Dilatation & Curettage
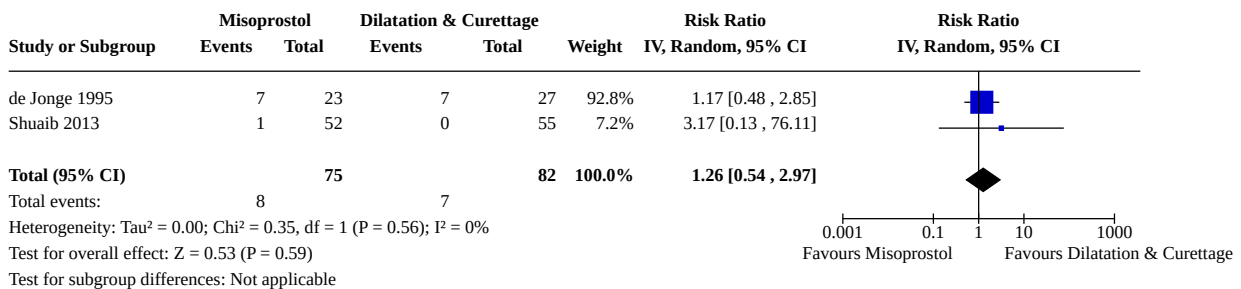
Analysis 6.3. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Misoprostol Events	Misoprostol Total	Dilatation & Curettage Events	Dilatation & Curettage Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Moodliar 2005	0	47	0	47		Not estimable	
Total (95% CI)		**47**		**47**		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

0.001 0.1 1 10 1000
Favours Misoprostol   Favours Dilatation & Curettage
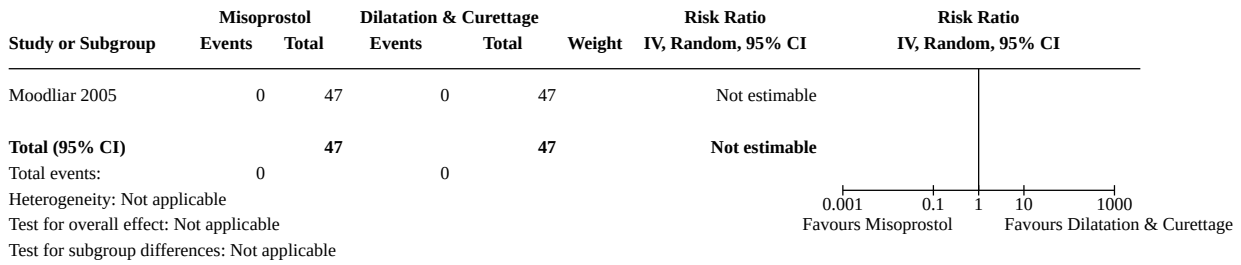
Analysis 6.4. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 4: Pain score

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Dilatation & Curettage Mean	Dilatation & Curettage SD	Dilatation & Curettage Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Moodliar 2005	5.6	2.7	47	4.1	3.1	47	100.0%	0.51 [0.10 , 0.92]	
Total (95% CI)			**47**			**47**	**100.0%**	**0.51 [0.10 , 0.92]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.44 (P = 0.01)
Test for subgroup differences: Not applicable

-1 -0.5 0 0.5 1
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.5. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 5: Pelvic inflammatory disease, sepsis or endometritis

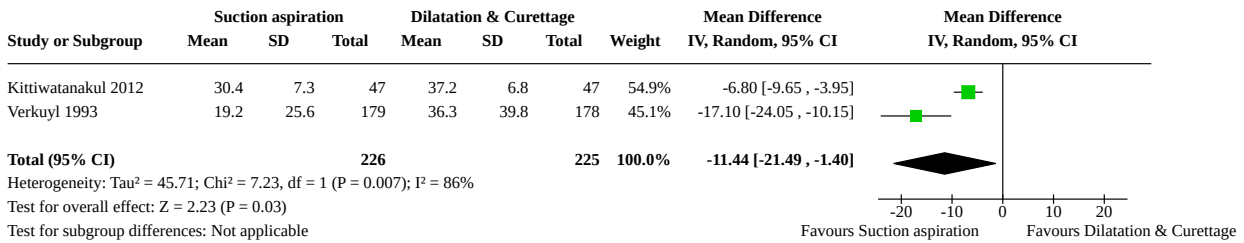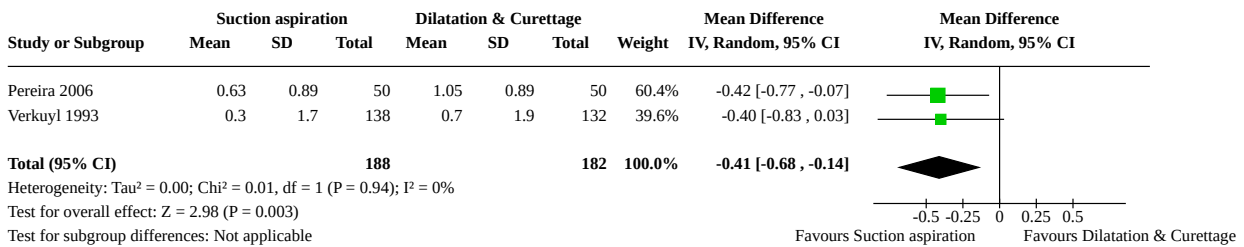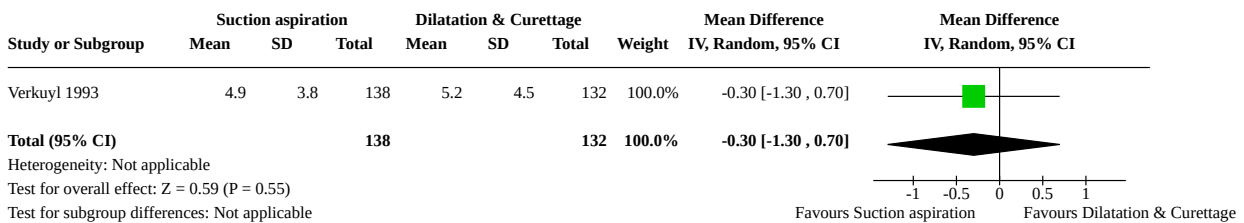| Study or Subgroup	Misoprostol Events	Misoprostol Total	Dilatation & Curettage Events	Dilatation & Curettage Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Moodliar 2005	0	47	0	47		Not estimable	
Shuaib 2013	2	52	1	55	100.0%	2.12 [0.20 , 22.64]	
Total (95% CI)		**99**		**102**	**100.0%**	**2.12 [0.20 , 22.64]**	
Total events:	2		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.62 (P = 0.54)
Test for subgroup differences: Not applicable

0.05 0.2 1 5 20
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.6. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 6: Mean volumes of blood loss (millilitres)

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Dilatation & Curettage Mean	Dilatation & Curettage SD	Dilatation & Curettage Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Kyaw 2015	77.5	46.4	50	55.2	46.4	54	100.0%	22.30 [4.45 , 40.15]	
Total (95% CI)			**50**			**54**	**100.0%**	**22.30 [4.45 , 40.15]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.45 (P = 0.01)
Test for subgroup differences: Not applicable

-100 -50 0 50 100
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.7. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 7: Days of bleeding

Study or Subgroup	Misoprostol			Dilatation & Curettage			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Moodliar 2005	7	3.4	47	4.4	3.2	47	100.0%	2.60 [1.27 , 3.93]	
Total (95% CI)			47			47	100.0%	**2.60 [1.27 , 3.93]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.82 (P = 0.0001)
Test for subgroup differences: Not applicable

-4 -2 0 2 4
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.8. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 8: Cervical tear

Study or Subgroup	Misoprostol		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Shuaib 2013	0	52	0	55		Not estimable	
Total (95% CI)		52		55		**Not estimable**	
Total events:	0		0				

Heterogeneity: Not applicable
Test for overall effect: Not applicable
Test for subgroup differences: Not applicable

0.005 0.1 1 10 200
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.9. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 9: Re-admission to hospital

Study or Subgroup	Misoprostol		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Shuaib 2013	1	52	0	55	100.0%	3.17 [0.13 , 76.11]	
Total (95% CI)		52		55	100.0%	**3.17 [0.13 , 76.11]**	
Total events:	1		0				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)
Test for subgroup differences: Not applicable

0.02 0.1 1 10 50
Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.10. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 10: Vomiting

Study or Subgroup	Misoprostol		Dilatation & Curettage		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Moodliar 2005	0	47	1	47	100.0%	0.33 [0.01 , 7.98]	
Total (95% CI)		47		47	100.0%	**0.33 [0.01 , 7.98]**	
Total events:	0		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Misoprostol   Favours Dilatation & Curettage

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Analysis 6.11. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 11: Nausea

Study or Subgroup	Misoprostol Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Moodliar 2005	0	47	1	47	100.0%	0.33 [0.01 , 7.98]	
Total (95% CI)		47		47	100.0%	**0.33 [0.01 , 7.98]**	
Total events:	0		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.12. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 12: Diarrhoea

Study or Subgroup	Misoprostol Events	Total	Dilatation & Curettage Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Moodliar 2005	1	47	0	47	100.0%	3.00 [0.13 , 71.82]	
Total (95% CI)		47		47	100.0%	**3.00 [0.13 , 71.82]**	
Total events:	1		0				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Dilatation & Curettage

Analysis 6.13. Comparison 6: Misoprostol vs Dilatation & Curettage, Outcome 13: Depression score

Study or Subgroup	Misoprostol Mean	SD	Total	Dilatation & Curettage Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Lee 2001	5.5	7.2	104	6.1	6.4	111	100.0%	-0.09 [-0.36 , 0.18]	
Total (95% CI)			104			111	100.0%	**-0.09 [-0.36 , 0.18]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Dilatation & Curettage
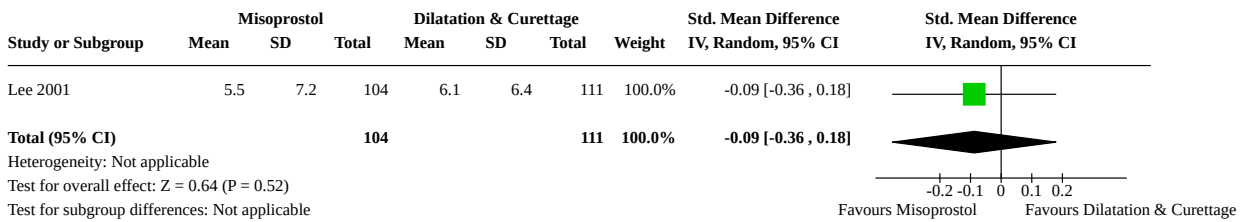
Comparison 7. Misoprostol vs Suction aspiration + Cervical preparation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Complete Miscarriage	1		Risk Ratio (IV, Random, 95% CI)	Subtotals only
7.2 Pyrexia	1	200	Risk Ratio (IV, Random, 95% CI)	2.50 [0.81, 7.71]

Analysis 7.1. Comparison 7: Misoprostol vs Suction aspiration + Cervical preparation, Outcome 1: Complete Miscarriage

Study or Subgroup	Misoprostol Events	Total	Suction aspiration + Cx prep Events	Total	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Nasreen 2009	61	100	100	100	0.61 [0.52 , 0.72]	

Test for subgroup differences: Not applicable

0.7 0.85 1 1.2 1.5
Favours Suction aspiration + Cx prep   Favours Misoprostol
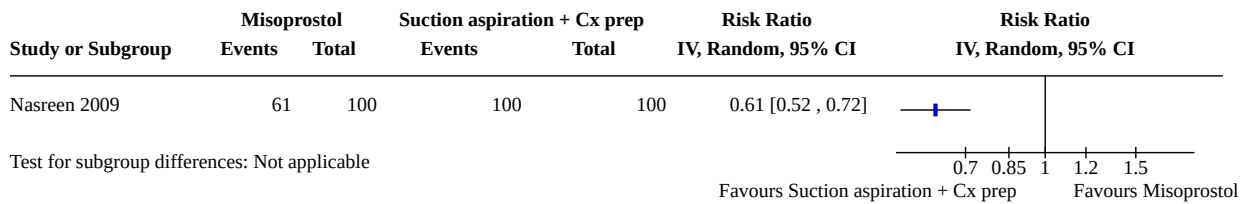
Analysis 7.2. Comparison 7: Misoprostol vs Suction aspiration + Cervical preparation, Outcome 2: Pyrexia
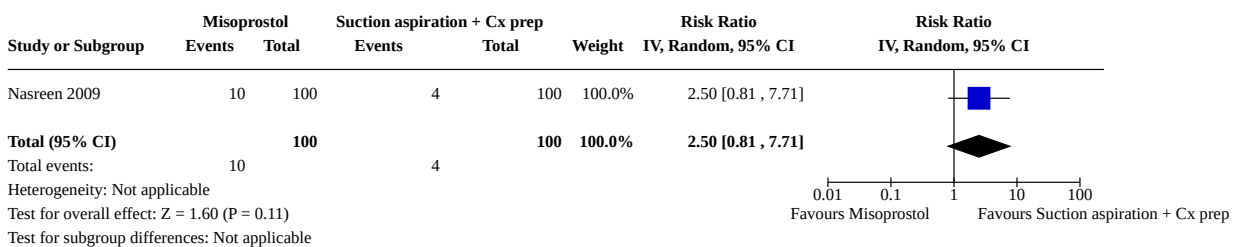
Study or Subgroup	Misoprostol Events	Total	Suction aspiration + Cx prep Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Nasreen 2009	10	100	4	100	100.0%	2.50 [0.81 , 7.71]	
Total (95% CI)		**100**		**100**	**100.0%**	**2.50 [0.81 , 7.71]**	
Total events:	10		4				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)
Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Misoprostol   Favours Suction aspiration + Cx prep

Comparison 8. Misoprostol vs Expectant/ Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Complete Miscarriage	10		Risk Ratio (IV, Random, 95% CI)	Subtotals only
8.1.1 Missed miscarriage	4	322	Risk Ratio (IV, Random, 95% CI)	3.18 [1.48, 6.85]
8.1.2 Incomplete miscarriage	2	108	Risk Ratio (IV, Random, 95% CI)	1.91 [0.44, 8.20]
8.1.3 Mixed population	4	408	Risk Ratio (IV, Random, 95% CI)	1.45 [0.97, 2.16]
8.2 Composite outcome of death or serious complication	6	548	Risk Ratio (IV, Random, 95% CI)	0.96 [0.06, 15.08]
8.3 Need for unplanned/emergency surgical procedure	5	437	Risk Ratio (IV, Random, 95% CI)	0.67 [0.23, 1.95]
8.4 Pain score	3	262	Std. Mean Difference (IV, Random, 95% CI)	0.33 [0.08, 0.57]
8.5 Pelvic inflammatory disease, sepsis or endometritis	6	615	Risk Ratio (IV, Random, 95% CI)	1.84 [0.35, 9.68]
8.6 Change in haemoglobin measurements before and after the miscarriage	2	167	Mean Difference (IV, Random, 95% CI)	0.15 [-0.21, 0.52]
8.7 Days of bleeding	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.8 Mean duration of hospital stay (days)	1	184	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.19, -0.01]
8.9 Re-admission to hospital	3	335	Risk Ratio (IV, Random, 95% CI)	1.25 [0.46, 3.35]
8.10 Nausea	5	389	Risk Ratio (IV, Random, 95% CI)	1.15 [0.93, 1.42]
8.11 Vomiting	6	506	Risk Ratio (IV, Random, 95% CI)	1.37 [0.75, 2.52]
8.12 Diarrhoea	7	560	Risk Ratio (IV, Random, 95% CI)	1.69 [1.05, 2.73]
8.13 Pyrexia	3	275	Risk Ratio (IV, Random, 95% CI)	4.03 [1.16, 13.97]
8.14 Anxiety score	1	117	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.51, 0.22]
8.15 Depression score	1	117	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.29, 0.44]

Analysis 8.1. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 1: Complete Miscarriage

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
8.1.1 Missed miscarriage							
Fernlund 2018	62	94	39	90	34.1%	1.52 [1.15 , 2.01]	
Kovavisarach 2002	17	27	5	27	24.9%	3.40 [1.46 , 7.89]	
Lister 2005	15	18	2	16	17.4%	6.67 [1.79 , 24.78]	
Wood 2002	20	25	4	25	23.6%	5.00 [1.99 , 12.54]	
Subtotal (95% CI)		164		158	100.0%	3.18 [1.48 , 6.85]	
Total events:	114		50				
Heterogeneity: Tau² = 0.43; Chi² = 12.05, df = 3 (P = 0.007); I² = 75%							
Test for overall effect: Z = 2.96 (P = 0.003)							
8.1.2 Incomplete miscarriage							
Abdelaleem 2020	29	42	7	42	47.9%	4.14 [2.05 , 8.39]	
Shelley 2005	8	10	12	14	52.1%	0.93 [0.64 , 1.36]	
Subtotal (95% CI)		52		56	100.0%	1.91 [0.44 , 8.20]	
Total events:	37		19				
Heterogeneity: Tau² = 1.03; Chi² = 13.33, df = 1 (P = 0.0003); I² = 92%							
Test for overall effect: Z = 0.87 (P = 0.39)							
8.1.3 Mixed population							
Bagratee 2004	46	52	23	52	24.5%	2.00 [1.45 , 2.76]	
Blohm 2005	52	64	32	62	25.8%	1.57 [1.20 , 2.06]	
Kong 2013	42	60	46	58	26.9%	0.88 [0.71 , 1.09]	
Ngai 2001	25	30	15	30	22.8%	1.67 [1.13 , 2.47]	
Subtotal (95% CI)		206		202	100.0%	1.45 [0.97 , 2.16]	
Total events:	165		116				
Heterogeneity: Tau² = 0.14; Chi² = 23.31, df = 3 (P < 0.0001); I² = 87%							
Test for overall effect: Z = 1.81 (P = 0.07)							
Test for subgroup differences: Chi² = 3.21, df = 2 (P = 0.20), I² = 37.7%							

0.05 0.2 1 5 20
Favours Expectant/ Placebo — Favours Misoprostol

Analysis 8.2. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	0	52	0	52		Not estimable	
Blohm 2005	0	64	0	62		Not estimable	
Fernlund 2018	1	94	1	90	100.0%	0.96 [0.06 , 15.08]	
Ngai 2001	0	30	0	30		Not estimable	
Shelley 2005	0	10	0	14		Not estimable	
Wood 2002	0	25	0	25		Not estimable	
Total (95% CI)		**275**		**273**	**100.0%**	**0.96 [0.06 , 15.08]**	
Total events:	1		1				

Heterogeneity: Not applicable

Test for overall effect: Z = 0.03 (P = 0.98)

Test for subgroup differences: Not applicable

0.02 0.1 1 10 50
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.3. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Fernlund 2018	3	94	4	90	53.1%	0.72 [0.17 , 3.12]	
Kong 2013	0	59	0	58		Not estimable	
Ngai 2001	1	30	3	30	23.5%	0.33 [0.04 , 3.03]	
Shelley 2005	0	11	1	15	11.8%	0.44 [0.02 , 9.98]	
Wood 2002	1	25	0	25	11.5%	3.00 [0.13 , 70.30]	
Total (95% CI)		**219**		**218**	**100.0%**	**0.67 [0.23 , 1.95]**	
Total events:	5		8				

Heterogeneity: Tau² = 0.00; Chi² = 1.33, df = 3 (P = 0.72); I² = 0%

Test for overall effect: Z = 0.74 (P = 0.46)

Test for subgroup differences: Not applicable

0.001 0.1 1 10 1000
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.4. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 4: Pain score

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Bagratee 2004	6	2.7	52	5.4	2.7	52	40.1%	0.22 [-0.17 , 0.61]	
Blohm 2005	60.4	31	64	43.8	37.1	62	47.5%	0.48 [0.13 , 0.84]	
Lister 2005	5.6	4.57	16	5.2	4.57	16	12.4%	0.09 [-0.61 , 0.78]	
Total (95% CI)			**132**			**130**	**100.0%**	**0.33 [0.08 , 0.57]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.51, df = 2 (P = 0.47); I² = 0%

Test for overall effect: Z = 2.64 (P = 0.008)

Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.5. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 5: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	1	52	0	52	18.3%	3.00 [0.13 , 71.99]	
Blohm 2005	3	64	0	62	20.2%	6.78 [0.36 , 128.70]	
Fernlund 2018	3	94	7	90	41.2%	0.41 [0.11 , 1.54]	
Kong 2013	0	59	0	58		Not estimable	
Ngai 2001	0	30	0	30		Not estimable	
Shelley 2005	2	10	0	14	20.3%	6.82 [0.36 , 128.33]	
Total (95% CI)		309		306	100.0%	1.84 [0.35 , 9.68]	
Total events:	9		7				

Heterogeneity: Tau² = 1.29; Chi² = 5.47, df = 3 (P = 0.14); I² = 45%

Test for overall effect: Z = 0.72 (P = 0.47)

Test for subgroup differences: Not applicable

0.005 0.1 1 10 200
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.6. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 6: Change in haemoglobin measurements before and after the miscarriage

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Kong 2013	0.19	1.03	59	0.03	0.98	58	99.5%	0.16 [-0.20 , 0.52]	
Wood 2002	3.2	7.9	25	4.3	10.1	25	0.5%	-1.10 [-6.13 , 3.93]	
Total (95% CI)			84			83	100.0%	0.15 [-0.21 , 0.52]	

Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.62); I² = 0%

Test for overall effect: Z = 0.83 (P = 0.41)

Test for subgroup differences: Not applicable

-4 -2 0 2 4
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.7. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 7: Days of bleeding

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Bagratee 2004	11.65	4.4	52	10.88	4.78	52	0.77 [-1.00 , 2.54]	
Fernlund 2018	12.7	6.6	91	15	8.2	77	-2.30 [-4.58 , -0.02]	
Kong 2013	15.38	6.63	59	12.95	5.73	58	2.43 [0.19 , 4.67]	

Test for subgroup differences: Not applicable

-4 -2 0 2 4
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.8. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 8: Mean duration of hospital stay (days)

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Fernlund 2018	0	0.2	94	0.1	0.4	90	100.0%	-0.10 [-0.19 , -0.01]	
Total (95% CI)			94			90	100.0%	-0.10 [-0.19 , -0.01]	

Heterogeneity: Not applicable

Test for overall effect: Z = 2.13 (P = 0.03)

Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.9. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 9: Re-admission to hospital

Study or Subgroup	Misoprostol Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Fernlund 2018	3	94	4	90	45.3%	0.72 [0.17 , 3.12]	
Kong 2013	6	59	3	58	54.7%	1.97 [0.52 , 7.49]	
Lister 2005	0	18	0	16		Not estimable	
Total (95% CI)		171		164	100.0%	1.25 [0.46 , 3.35]	
Total events:	9		7				

Heterogeneity: Tau² = 0.00; Chi² = 0.99, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 0.43 (P = 0.66)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.10. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 10: Nausea

Study or Subgroup	Misoprostol Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	18	52	16	52	14.7%	1.13 [0.65 , 1.96]	
Fernlund 2018	57	91	45	77	74.2%	1.07 [0.84 , 1.37]	
Lister 2005	4	18	3	16	2.5%	1.19 [0.31 , 4.51]	
Ngai 2001	14	30	7	29	8.0%	1.93 [0.91 , 4.09]	
Shelley 2005	2	10	0	14	0.5%	6.82 [0.36 , 128.33]	
Total (95% CI)		201		188	100.0%	1.15 [0.93 , 1.42]	
Total events:	95		71				

Heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 4 (P = 0.47); I² = 0%
Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.11. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 11: Vomiting

Study or Subgroup	Misoprostol Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	8	52	7	52	24.8%	1.14 [0.45 , 2.92]	
Fernlund 2018	7	91	10	77	25.5%	0.59 [0.24 , 1.48]	
Kong 2013	14	59	4	58	21.6%	3.44 [1.20 , 9.84]	
Lister 2005	1	18	1	16	4.7%	0.89 [0.06 , 13.08]	
Ngai 2001	7	30	4	29	19.9%	1.69 [0.55 , 5.17]	
Shelley 2005	1	10	0	14	3.6%	4.09 [0.18 , 91.23]	
Total (95% CI)		260		246	100.0%	1.37 [0.75 , 2.52]	
Total events:	38		26				

Heterogeneity: Tau² = 0.16; Chi² = 7.00, df = 5 (P = 0.22); I² = 29%
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Not applicable

Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.12. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 12: Diarrhoea

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	11	52	11	52	26.4%	1.00 [0.48 , 2.10]	
Fernlund 2018	26	91	17	77	38.1%	1.29 [0.76 , 2.20]	
Kong 2013	22	59	6	58	22.9%	3.60 [1.58 , 8.24]	
Kovavisarach 2002	2	27	0	27	2.5%	5.00 [0.25 , 99.51]	
Lister 2005	1	18	1	16	3.1%	0.89 [0.06 , 13.08]	
Ngai 2001	4	30	1	29	4.7%	3.87 [0.46 , 32.57]	
Shelley 2005	1	10	0	14	2.3%	4.09 [0.18 , 91.23]	
Total (95% CI)		**287**		**273**	**100.0%**	**1.69 [1.05 , 2.73]**	
Total events:	67		36				

Heterogeneity: Tau² = 0.08; Chi² = 7.61, df = 6 (P = 0.27); I² = 21%

Test for overall effect: Z = 2.14 (P = 0.03)

Test for subgroup differences: Not applicable

0.01 0.1 1 10 100
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.13. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 13: Pyrexia

Study or Subgroup	Misoprostol Events	Misoprostol Total	Expectant/ Placebo Events	Expectant/ Placebo Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Bagratee 2004	1	52	0	52	15.3%	3.00 [0.13 , 71.99]	
Kong 2013	7	59	2	58	66.0%	3.44 [0.75 , 15.88]	
Kovavisarach 2002	4	27	0	27	18.7%	9.00 [0.51 , 159.43]	
Total (95% CI)		**138**		**137**	**100.0%**	**4.03 [1.16 , 13.97]**	
Total events:	12		2				

Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 2 (P = 0.83); I² = 0%

Test for overall effect: Z = 2.20 (P = 0.03)

Test for subgroup differences: Not applicable

0.005 0.1 1 10 200
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.14. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 14: Anxiety score

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Kong 2013	58.08	13.57	59	60.05	13.74	58	100.0%	-0.14 [-0.51 , 0.22]	
Total (95% CI)			**59**			**58**	**100.0%**	**-0.14 [-0.51 , 0.22]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.77 (P = 0.44)

Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Misoprostol   Favours Expectant/ Placebo

Analysis 8.15. Comparison 8: Misoprostol vs Expectant/ Placebo, Outcome 15: Depression score

Study or Subgroup	Misoprostol Mean	Misoprostol SD	Misoprostol Total	Expectant/ Placebo Mean	Expectant/ Placebo SD	Expectant/ Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Kong 2013	8.75	11.05	59	7.93	10.41	58	100.0%	0.08 [-0.29 , 0.44]	
Total (95% CI)			**59**			**58**	**100.0%**	**0.08 [-0.29 , 0.44]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 0.41 (P = 0.68)

Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Misoprostol   Favours Expectant/ Placebo

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Comparison 9. Dilatation & Curettage vs Expectant/ Placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Complete Miscarriage	1		Risk Ratio (IV, Random, 95% CI)	Subtotals only
9.1.1 Incomplete miscarriage	1	155	Risk Ratio (IV, Random, 95% CI)	1.25 [1.12, 1.39]
9.2 Pelvic inflammatory disease, sepsis or endometritis	1	155	Risk Ratio (IV, Random, 95% CI)	3.30 [0.82, 13.28]
9.3 Days of bleeding	1	155	Mean Difference (IV, Random, 95% CI)	-1.26 [-2.27, -0.25]

Analysis 9.1. Comparison 9: Dilatation & Curettage vs Expectant/ Placebo, Outcome 1: Complete Miscarriage

Study or Subgroup	Dilatation & Curettage Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
9.1.1 Incomplete miscarriage							
Nielsen 1995	51	52	81	103	100.0%	1.25 [1.12 , 1.39]	
Subtotal (95% CI)		52		103	100.0%	**1.25 [1.12 , 1.39]**	
Total events:	51		81				

Heterogeneity: Not applicable

Test for overall effect: Z = 4.02 (P < 0.0001)

Test for subgroup differences: Not applicable

Favours Expectant/ Placebo 0.7 0.85 1 1.2 1.5 Favours Dilatation & Curettage

Analysis 9.2. Comparison 9: Dilatation & Curettage vs Expectant/ Placebo, Outcome 2: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Dilatation & Curettage Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
Nielsen 1995	5	52	3	103	100.0%	3.30 [0.82 , 13.28]	
Total (95% CI)		52		103	100.0%	**3.30 [0.82 , 13.28]**	
Total events:	5		3				

Heterogeneity: Not applicable

Test for overall effect: Z = 1.68 (P = 0.09)

Test for subgroup differences: Not applicable

Favours Dilatation & Curettage 0.01 0.1 1 10 100 Favours Expectant/ Placebo

Analysis 9.3. Comparison 9: Dilatation & Curettage vs Expectant/ Placebo, Outcome 3: Days of bleeding
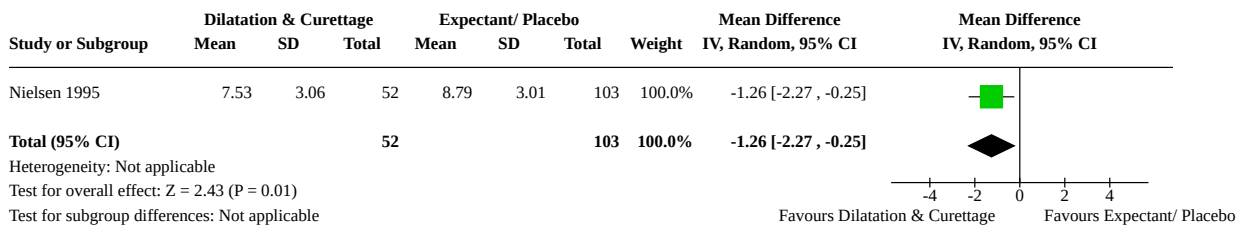
Study or Subgroup	Dilatation & Curettage Mean	SD	Total	Expectant/ Placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Nielsen 1995	7.53	3.06	52	8.79	3.01	103	100.0%	-1.26 [-2.27 , -0.25]	
Total (95% CI)			52			103	100.0%	**-1.26 [-2.27 , -0.25]**	

Heterogeneity: Not applicable

Test for overall effect: Z = 2.43 (P = 0.01)

Test for subgroup differences: Not applicable

Favours Dilatation & Curettage -4 -2 0 2 4 Favours Expectant/ Placebo

Comparison 10. Mifepristone + Misoprostol vs Expectant/ Placebo

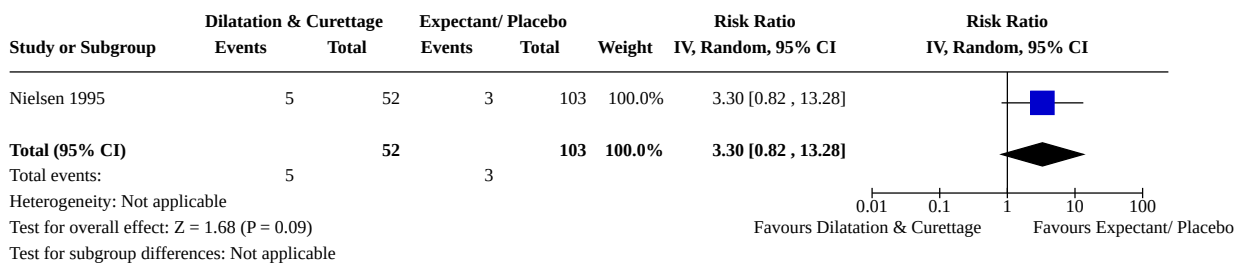| Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Complete Miscarriage	3		Risk Ratio (IV, Random, 95% CI)	Subtotals only
10.1.1 Missed miscarriage	1	614	Risk Ratio (IV, Random, 95% CI)	1.25 [1.09, 1.45]
10.1.2 Incomplete miscarriage	1	122	Risk Ratio (IV, Random, 95% CI)	1.08 [0.90, 1.30]
10.1.3 Mixed population	1	174	Risk Ratio (IV, Random, 95% CI)	3.44 [2.31, 5.11]
10.2 Composite outcome of death or serious complication	2	788	Risk Ratio (IV, Random, 95% CI)	0.43 [0.11, 1.63]
10.3 Need for unplanned/emergency surgical procedure	2	296	Risk Ratio (IV, Random, 95% CI)	0.32 [0.11, 0.90]
10.4 Pain score	1	122	Std. Mean Difference (IV, Random, 95% CI)	0.14 [-0.21, 0.50]
10.5 Pelvic inflammatory disease, sepsis or endometritis	2	736	Risk Ratio (IV, Random, 95% CI)	0.73 [0.30, 1.80]
10.6 Days of bleeding	1	122	Mean Difference (IV, Random, 95% CI)	0.70 [-0.43, 1.83]
10.7 Pyrexia	1	174	Risk Ratio (IV, Random, 95% CI)	0.32 [0.01, 7.71]

Analysis 10.1.   Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 1: Complete Miscarriage

Study or Subgroup	Mifepristone + Misoprostol Events	Total	Expectant/ Placebo Events	Total	Weight	Risk Ratio IV, Random, 95% CI
10.1.1 Missed miscarriage						
Trinder 2006	192	308	152	306	100.0%	1.25 [1.09 , 1.45]
Subtotal (95% CI)		**308**		**306**	**100.0%**	**1.25 [1.09 , 1.45]**
Total events:	192		152			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.13 (P = 0.002)						
10.1.2 Incomplete miscarriage						
Nielsen 1999	49	60	47	62	100.0%	1.08 [0.90 , 1.30]
Subtotal (95% CI)		**60**		**62**	**100.0%**	**1.08 [0.90 , 1.30]**
Total events:	49		47			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						
10.1.3 Mixed population						
Torre 2012	72	89	20	85	100.0%	3.44 [2.31 , 5.11]
Subtotal (95% CI)		**89**		**85**	**100.0%**	**3.44 [2.31 , 5.11]**
Total events:	72		20			
Heterogeneity: Not applicable						
Test for overall effect: Z = 6.11 (P < 0.00001)						

Test for subgroup differences: Chi² = 27.29, df = 2 (P < 0.00001), I² = 92.7%

Favours Expectant/ Placebo   Favours Mifepristone + Misoprostol

Analysis 10.2. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 2: Composite outcome of death or serious complication

Study or Subgroup	Mifepristone + Misoprostol		Expectant/ Placebo		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Torre 2012	0	89	0	85		Not estimable	
Trinder 2006	3	308	7	306	100.0%	0.43 [0.11 , 1.63]	
Total (95% CI)		**397**		**391**	**100.0%**	**0.43 [0.11 , 1.63]**	
Total events:	3		7				

Heterogeneity: Not applicable
Test for overall effect: Z = 1.25 (P = 0.21)
Test for subgroup differences: Not applicable

0.1 0.2 0.5 1 2 5 10
Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

Analysis 10.3. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 3: Need for unplanned/emergency surgical procedure

Study or Subgroup	Mifepristone + Misoprostol		Expectant/ Placebo		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Nielsen 1999	0	60	1	62	10.5%	0.34 [0.01 , 8.29]	
Torre 2012	4	89	12	85	89.5%	0.32 [0.11 , 0.95]	
Total (95% CI)		**149**		**147**	**100.0%**	**0.32 [0.11 , 0.90]**	
Total events:	4		13				

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 2.16 (P = 0.03)
Test for subgroup differences: Not applicable

0.02 0.1 1 10 50
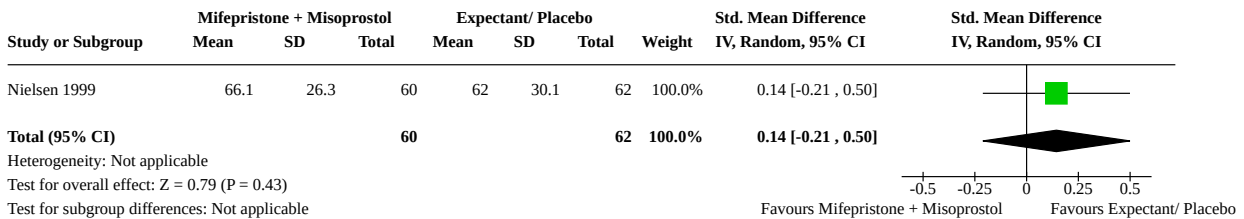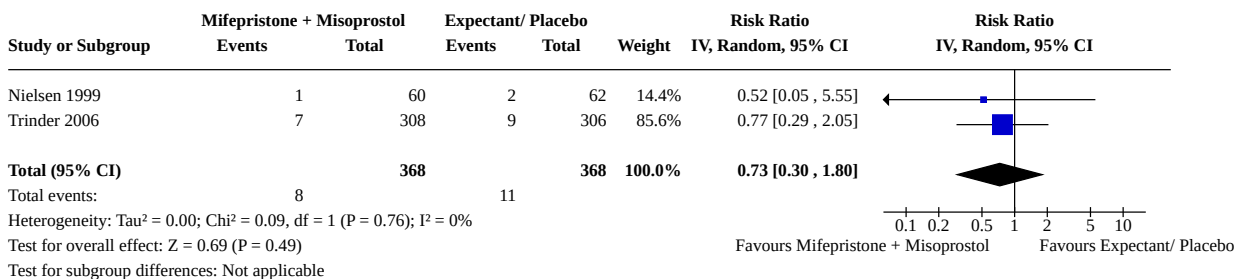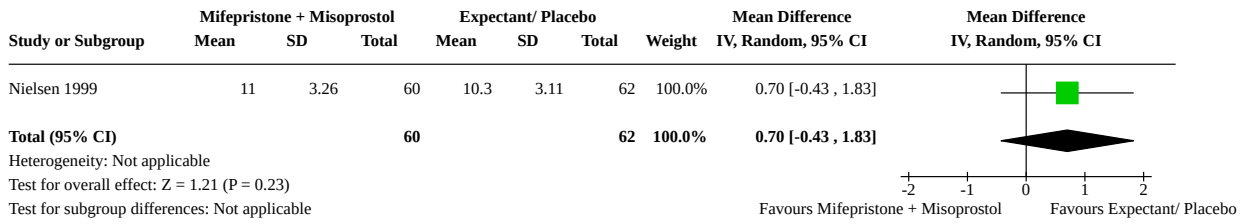Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

Analysis 10.4. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 4: Pain score

Study or Subgroup	Mifepristone + Misoprostol			Expectant/ Placebo			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Nielsen 1999	66.1	26.3	60	62	30.1	62	100.0%	0.14 [-0.21 , 0.50]	
Total (95% CI)			**60**			**62**	**100.0%**	**0.14 [-0.21 , 0.50]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)
Test for subgroup differences: Not applicable

-0.5 -0.25 0 0.25 0.5
Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

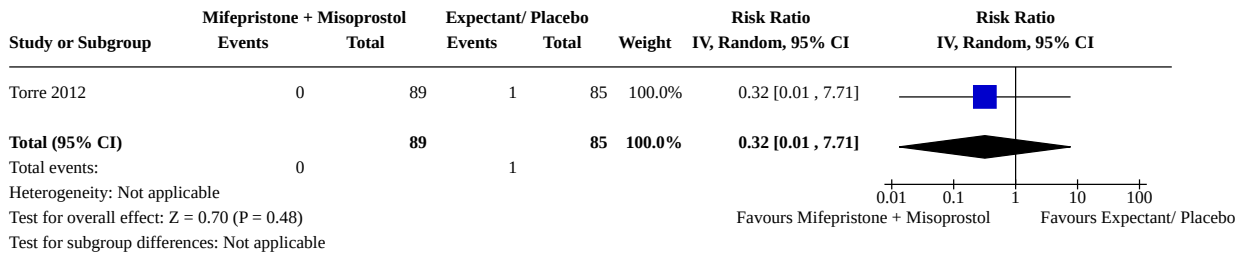### Analysis 10.5. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 5: Pelvic inflammatory disease, sepsis or endometritis

Study or Subgroup	Mifepristone + Misoprostol		Expectant/ Placebo		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Nielsen 1999	1	60	2	62	14.4%	0.52 [0.05 , 5.55]	
Trinder 2006	7	308	9	306	85.6%	0.77 [0.29 , 2.05]	
Total (95% CI)		**368**		**368**	**100.0%**	**0.73 [0.30 , 1.80]**	
Total events:	8		11				

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 0.69 (P = 0.49)
Test for subgroup differences: Not applicable

0.1 0.2 0.5 1 2 5 10
Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

Analysis 10.6. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 6: Days of bleeding

Study or Subgroup	Mifepristone + Misoprostol			Expectant/ Placebo			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Nielsen 1999	11	3.26	60	10.3	3.11	62	100.0%	0.70 [-0.43 , 1.83]	
Total (95% CI)			**60**			**62**	**100.0%**	**0.70 [-0.43 , 1.83]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.21 (P = 0.23)
Test for subgroup differences: Not applicable

Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

Analysis 10.7. Comparison 10: Mifepristone + Misoprostol vs Expectant/ Placebo, Outcome 7: Pyrexia

Study or Subgroup	Mifepristone + Misoprostol		Expectant/ Placebo		Weight	Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total			
Torre 2012	0	89	1	85	100.0%	0.32 [0.01 , 7.71]	
Total (95% CI)		**89**		**85**	**100.0%**	**0.32 [0.01 , 7.71]**	
Total events:	0		1				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.48)
Test for subgroup differences: Not applicable

Favours Mifepristone + Misoprostol   Favours Expectant/ Placebo

A P P E N D I C E S

Appendix 1. Search terms for WHO ICTRP and ClinicalTrials.gov

curettage AND miscarriage

misoprostol AND miscarriage

mifepristone AND miscarriage

vacuum AND miscarriage

expectant AND miscarriage

management AND miscarriage

surgical AND miscarriage

Appendix 2. Global statistical inconsistencies for network meta-analyses

Outcome	P value for global inconsistency
Complete miscarriage	0.000
Complete miscarriage (incomplete miscarriage only)	0.208
Complete miscarriage (missed miscarriage only)	0.105
Composite outcome of death or serious complication	0.570
Need for unplanned/emergency surgical procedure	0.819

(Continued)

Pain scores (visual analogue scale)	0.696
Re-admission to hospital	0.301
Nausea	-
Vomiting	0.073
Diarrhoea	0.061
Pyrexia	0.208
Change in haemoglobin measurements before and after the miscarriage	0.927
Days of bleeding	0.017
Days of bleeding (incomplete miscarriage only)	0.038
Days of bleeding (missed miscarriage only)	-

HISTORY

Protocol first published: Issue 3, 2017

CONTRIBUTIONS OF AUTHORS

Ioannis D Gallos (IDG) and Arri Coomarasamy (AC) conceived the idea for this review. IDG, AC, Malcolm J Price (MP), Aurelio Tobias (AT), Özge Tunçalp (OT), Antonella Lavelanet (AL) and A Metin Gülmezoglu (AMG) designed the meta-analysis. Jayasish Ghosh (JG) designed the electronic data collection forms. JG, Hannah Jeffery (HJ) and IDG performed study selection. JG, Argyro Papadopoulou (AP), HJ, Adam Devall (AJD), Leanne Beeson (LB) and Vivian Do (VD) performed data extraction. JG performed the pairwise meta-analysis. AT performed the network analysis. JG, AJD, AP and IDG graded the evidence and AP created the "summary of findings table". IDG created the protocol. JG and AJD drafted this review. IDG, AJD and AC edited and revised the review. All authors reviewed the manuscript prior to submission. AJD and IDG are the guarantors for this review.

DECLARATIONS OF INTEREST

Jay Ghosh: Grants and contracts - this work is supported by Tommy's Charity who fund the Tommy's National Centre for Miscarriage Research, which is held by Prof Arri Coomarasamy. Work related to the topic of the review as health professional - O&G Medical Doctor.

Argyro Papadopoulou: I am currently a PhD student at the University of Birmingham, UK. My tuition fees are paid by Tommy's charity.

Adam J Devall: co-investigator for the MifeMiso trial now published in the Lancet, which was funded by the NIHR HTA programme. AJD did not participate in any decisions regarding this trial (i.e. assessment for inclusion/exclusion, trial quality, data extraction) for the purposes of this review or future updates, these tasks have been carried out by other members of the team who were not directly involved in the trial.

Hannah C Jeffery: none known.

Leanne E Beeson: co-investigator for the MifeMiso trial now published in the Lancet, which was funded by the NIHR HTA programme. LEB did not participate in any decisions regarding this trial (i.e. assessment for inclusion/exclusion, trial quality, data extraction) for the purposes of this review or future updates, these tasks have been carried out by other members of the team who were not directly involved in the trial.

Vivian Do: none known.

Malcolm J Price: none known.

Aurelio Tobias: none known.

Özge Tunçalp: none known.

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Antonella Lavelanet: I published work as a freelance writer. I am a board certified OBGYN, but I am currently not practicing and have not practiced for the last 4 years.

Ahmet Metin Gülmezoglu: none known.

Arri Coomarasamy: chief-investigator for the MifeMiso trial now published in the Lancet, which was funded by the NIHR HTA programme. AC did not participate in any decisions regarding this trial (i.e. assessment for inclusion/exclusion, trial quality, data extraction) for the purposes of this review or future updates, these tasks have been carried out by other members of the team who were not directly involved in the trial.

Ioannis D Gallos: co-investigator for the MifeMiso trial now published in the Lancet, which was funded by the NIHR HTA programme. IDG did not participate in any decisions regarding this trial (i.e. assessment for inclusion/exclusion, trial quality, data extraction) for the purposes of this review or future updates, these tasks have been carried out by other members of the team who were not directly involved in the trial.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There are some differences between the published protocol for this review (Gallos 2017) and the full review, these are listed below.

Methods/ criteria for considering studies for this review/ types of interventions

The protocol stated the following methods.

We will include the following interventions: dilatation plus sharp curettage, suction curettage, suction curettage with cervical preparation, misoprostol alone, and mifepristone plus misoprostol versus expectant management or placebo.

Instead of dilatation plus sharp curettage we have named this intervention dilatation and curettage. Instead of suction curettage we have named this intervention suction aspiration. Instead of suction curettage with cervical preparation we have named this intervention suction aspiration plus cervical preparation.

We had also planned to include comparisons between different routes of administration of medical treatment (e.g. oral versus vaginal), or between different drugs or doses of drug, or duration or timing of treatment which would have been part of a subgroup analysis. This was not performed as there was significant heterogeneity between the different misoprostol arms present in the trials however this may be examined in a future separate review. We had planned to include a sensitivity analysis to assess different effect measures (risk ratio versus odds ratio), however this was not done because different effect measures cannot be combined in one analysis. We had planned to include a sensitivity analysis to assess use of fixed-effect versus random-effects model, however since fixed effects should only be used in the absence of heterogeneity, this was not done. We have added 'exclusion of quasi-randomised trials' to the planned sensitivity analysis in the methods section. We had also aimed to compare cervical preparation drugs with each other and compare different doses, routes and regimens of the same drug with each other in a subgroup analysis however sufficient data did not exist.

Methods/ data synthesis/ methods for direct treatment comparisons

The protocol stated the following.

We will perform standard pairwise meta-analyses using a random-effects model in the presence of substantial heterogeneity or fixed-effect model in STATA for every treatment comparison.

We performed standard pairwise meta-analyses in Review Manager 5.4 and STATA.

Methods/ subgroup analysis and investigation of heterogeneity

The protocol in this section stated the following.

If we find important heterogeneity or inconsistency, or both, we will explore the possible sources. If sufficient studies are available, we will perform subgroup analyses by using the following effect modifiers:

- gestational age (nine weeks versus > nine weeks of gestation);
- type of miscarriage (incomplete versus missed miscarriage);
- type of vacuum aspiration device used (electrical versus manual vacuum aspiration);
- type of healthcare setting (inpatient versus outpatient);
- dosage, regimen, and route of drug administration (sublingual, rectal, oral).

We will assess subgroup differences by evaluating the relative effects and assessment of model fit for the primary outcomes.

Sufficient studies were not available for subgroup analysis of gestational age, type of vacuum aspiration device used and dosage, regimen, and route of drug administration (sublingual, rectal, oral). The detail in the study characteristics of included studies was not sufficient enough, in order to perform the subgroup analysis of type of healthcare setting.

Methods/ sensitivity analysis

The protocol in this section stated the following.

For the primary outcomes we will perform sensitivity analysis for the following:

- overall risk of bias of the studies (low versus high risk of overall bias);
- randomisation unit (cluster versus individual);
- different effect measures (risk ratio versus odds ratio);
- use of fixed-effect versus random-effects model;
- use of placebo versus expectant management

We will assess differences by evaluating the relative effects and assessment of model fit.

There were no cluster-randomised trials included to allow us to perform a sensitivity analysis based on randomisation unit. Other planned sensitivity analyses were performed but no differences were detected in terms of the overall results.