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# Medical methods for mid-trimester termination of pregnancy (Review)

Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N

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#### [Intervention Review]

### Medical methods for mid-trimester termination of pregnancy

Hajo Wildschut<sup>1</sup>, Marieke I Both<sup>1</sup>, Suzanne Medema<sup>2</sup>, Eeke Thomee<sup>3</sup>, Mark F Wildhagen<sup>4</sup>, Nathalie Kapp<sup>5</sup>

<sup>1</sup>Department of Obstetrics and Gynaecology, Erasmus Medical Center, Rotterdam, Netherlands. <sup>2</sup>Bouman GGZ, Rotterdam, Netherlands. <sup>3</sup>The Royal Marsden Hospital, London, UK. <sup>4</sup>Department of Urology and Obstetrics and Gynecology, Erasmus Medical Center, Rotterdam, Netherlands. <sup>5</sup>Department of Reproductive Health and Research, World Health Organization, Geneva 27, Switzerland

**Contact:** Hajo Wildschut, Department of Obstetrics and Gynaecology, Erasmus Medical Center, PO Box 2040, Rotterdam, 3000 CA, Netherlands. h.wildschut@erasmusmc.nl.

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#### ABSTRACT

#### Background

With the improvement of ultrasound technology, the likelihood of detection of major fetal structural anomalies in mid-pregnancy has increased considerably. Upon the detection of serious anomalies, women typically are offered the option of pregnancy termination. Additionally, there are still many reasons other than fetal anomalies why women seek abortion in the mid-trimester.

#### Objectives

To compare different methods of second trimester medical termination of pregnancy for their efficacy and side-effects.

#### Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*), MEDLINE, Popline and reference lists of retrieved papers and other sources.

#### **Selection criteria**

All randomised controlled trials (RCTs) examining medical regimens for termination of pregnancy of a singleton living fetus between 12-28 weeks' gestation were analysed. The outcome measures were the induction to abortion interval, abortion rate within 24 hours, need for surgical evacuation, blood loss, uterine rupture, pain, and side-effects.Trials including >20% fetal death, multiple pregnancies, previous uterine scars and regimens which involved cervical preparation were excluded.

#### Data collection and analysis

Two authors selected the trials and three authors extracted data.

#### **Main results**

Fourty RCTs were included, addressing various agents for pregnancy termination and methods of administration. When used alone, misoprostol was an effective inductive agent, though it appeared to be more effective in combination with mifepristone. However, the evidence from RCTs is limited.

Misoprostol was preferably administered vaginally, although among multiparous women sublingual administration appeared equally effective. A range of doses of vaginally administered misoprostol has been used. No randomised trials comparing doses of misoprostol were identified; however low doses of misoprostol appear to be associated with fewer side-effects while moderate doses appear to be more efficient in completing abortion. Four RCTs showed that the induction to abortion interval with 3-hourly vaginal administration of prostaglandins is shorter than 6-hourly administration without an increase in side-effects.



Many studies reported the need for surgical evacuation. Indications for surgical evacuation include retained products of the placenta and heavy vaginal bleeding. Fewer women required surgical evacuation when misoprostol was administrated vaginally compared with women receiving intra-amniotical PGF<sub>2a</sub>. Mild, self-limiting diarrhoea was more common among women who received misoprostol compared to other agents.

#### **Authors' conclusions**

Medical abortion in the second trimester using the combination of mifepristone and misoprostol appeared to have the highest efficacy and shortest abortion time interval. Where mifepristone is not available, misoprostol alone is a reasonable alternative. The optimal route for administering misoprostol is vaginally, preferably using tablets at 3-hourly intervals. Apart from pain, the side-effects of vaginal misoprostol are usually mild and self limiting. Conclusions from this review are limited by the gestational age ranges and variable medical regimens, including dosing, administrative routes and intervals of medication, of the included trials.

#### PLAIN LANGUAGE SUMMARY

# Planned abortion after three months of pregnancy can be done using several medicines. This review looked at which medical procedure is the best.

There are many medical methods for planned termination of pregnancy in the second trimester of pregnancy (abortion after three months). We did a search of the scientific literature to find out which is the best method. We identified 38 studies and came to the conclusion that misoprostol is the drug of choice for medical pregnancy termination, preferably in combination with mifepristone which facilitates the effectiveness of misoprostol. Misoprostol works best when it is administered into the vagina. Women who had previously given birth could take misoprostol by mouth (under the tongue). Irrespective of the medication used for second trimester termination there is a considerable risk of surgical intervention because of vaginal bleeding or incomplete abortion.



#### BACKGROUND

With the wide-scale introduction of prenatal screening programmes the issue of second trimester abortion has become increasingly relevant, in particular for women whose pregnancies are complicated by a serious fetal anomaly (Asch 1999; Ballantyne 2009; Boyd 2008). Additionally, there are many reasons other than fetal anomalies for which women seek abortion in the midtrimester (Drey 2006; Grimes 1998; Ingham 2008). Second trimester abortion for fetal structural anomalies may have advantages over surgical abortion as it is operator independent and the intact fetus may be preferable for feto-pathological examination (Akgun 2007; Isaksen 1998; Isaksen 1999; Kaasen 2006). Medical abortion, however, also has several limitations including the need for the hospitalisation, the need for surgical removal of (the retained products of) the placenta when indicated, and the emotional impact of the process of labor and delivery on women who choose to end a pregnancy.

Medical abortion in the first trimester of pregnancy is considered successful if complete expulsion of the conceptus occurs without the need for surgical intervention (Christin-Maitre 2000). Beyond the first trimester, definitions differ but generally consider expulsion of the fetus separate from management of the placenta.

Several regimens for second trimester abortion have been published. Most of these are based on misoprostol or gemeprost, which are synthetic prostaglandin  $E_1$  analogues (PGE<sub>1</sub>), and used alone or misoprostol combined with mifepristone. Comparison of medical methods with surgical evacuation for mid-trimester termination of pregnancy is the subject of another review (Lohr 2008).

#### Agents used for medical abortion

#### Prostaglandins

Prostaglandins and their analogues are widely used for medical termination of pregnancy. Prostaglandins are produced by almost every tissue in the body and play a major role in human reproduction and in many other vital processes. To date, nine groups (A, B, C, D, E, F, G, H, I) and three types (PG1, PG2, PG3) of prostaglandins have been identified. Prostaglandins of the F and E series are the most important prostaglandins involved in pregnancy, labor, delivery and puerperium. PG receptors are always present in myometrial tissue.

Misoprostol (PGE<sub>1</sub>) is increasingly used for second trimester termination of pregnancy (Friedman 2001; Goldberg 2001; Wagner 2005; Weeks 2005). Misoprostol is marketed for use in the prevention and treatment of peptic ulcer disease, and it is registered for obstetric indications, including abortion, in a few countries. It is inexpensive, stable at room temperature and it is rapidly absorbed by vaginal, sublingual, buccal and oral routes (Tang 2002; Zieman 1997). Moreover, misoprostol is reportedly associated with few, relatively minor side-effects. Serious complications such as uterine rupture are rare.

Gemeprost ( $PGE_1$ ) is formulated as a vaginal suppository which requires refrigeration, and is not as widely available as misoprostol. Like other prostaglandins, it induces uterine contractions and cervical softening. Dinoprost  $(PGF_{2\alpha})$  and dinoprostone  $(PGE_2)$  are natural prostaglandins which induce uterine activity and are available for intravenous, intra-amniotic and extra-amniotic use.

Carboprost (15 methyl  $PGF_{2\alpha}$ ) can be given by intramuscular or intra-amniotic injection and its methyl ester can be given as vaginal suppository. Carboprost and its methyl ester are both effective in inducing uterine contractions.

Sulprostone ( $PGE_2$ ) is used intravenously. The intramuscular preparation of sulprostone is no longer available because it was associated with cardiovascular complications, such as acute myocardial infarction and hypotension (Ulmann 1992).

#### Uterotonic agents other than prostaglandins

Mifepristone, also known as RU 486 or RU 38486, is a 19-norsteroid that specifically blocks the receptors for progesterone and glucosteroids. It is used as pretreatment 24 to 48 hours prior to the induction of first trimester abortion with a prostaglandin analogue. It sensitizes the myometrium of the uterus to prostaglandin (Belanger 1981; Bygdeman 1985; Norman 1992; Swahn 1988).

Oxytocin is released physiologically by the posterior pituitary and stimulates uterine contractions. The sensitivity of the uterus to oxytocin increases with gestational age.

#### **Injection techniques**

#### Intra-amniotic instillation

Several chemical solutions for intra-amniotic injection techniques have been used, including formalin, glucose, hypertonic saline, urea and  $PGF_{2\alpha}$ . When using hypertonic saline, a spinal needle is passed through the abdominal wall into the amniotic cavity. A variable amount of the amniotic fluid surrounding the fetus is removed and replaced by 150 to 250 ml of 20% saline chloride solution that will induce abortion (Bygdeman and Gemzell-Danielsson 2008).

#### Extra-amniotic instillation

Instead of passing a spinal needle directly into the amniotic sac, effective irritants, such as ethacridine lactate or  $PGF_{2\alpha}$ , can be introduced through the cervix into the extra-amniotic space, that is, the space between the uterine wall and the fetal membranes. Ethacridine lactate is an organic compound based on acridine. Its primary use is as an antiseptic in solutions of 0.1%. When used as an agent for second trimester abortion, it is thought to stimulate endogenous prostaglandin production and subsequent uterine contractions. Up to 150 ml of 0.1% ethacridine is instilled into the extra-amniotic space using a Foley catheter. Oxytocin intravenous administration is often used concomitantly to expedite fetal expulsion (Bygdeman and Gemzell-Danielsson 2008).

#### Description of the problem or issue

Second trimester abortions constitute 10% to 15% of all induced abortions worldwide but are responsible for two-thirds of major abortion-related complications (Drey 2006; Grimes 1998). Medical methods for second trimester induced abortion have improved considerably during the last decades in terms of efficacy and safety; however, a variety of regimens remain in use.

Medical methods for mid-trimester termination of pregnancy (Review) Copyright © 2011 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



#### Why it is important to do this review

Because of improved ultrasound technology, the prenatal detection of fetal structural anomalies during the second trimester of pregnancy has improved substantially. For this reason, the demand for medical methods to terminate pregnancy during the second trimester has also increased (Grimes 1998). Additionally, there are a number of other reasons why women seek abortion in the mid-trimester. There are many medical regimens for mid-trimester termination of pregnancy. This review aims to identify the most effective medical regimens for mid-trimester abortion with the fewest side-effects.

#### OBJECTIVES

To evaluate the medical regimens for second trimester medical abortion in terms of efficacy and side-effects.

#### METHODS

#### Criteria for considering studies for this review

#### **Types of studies**

Randomised controlled trials were considered for inclusion if different medical methods, routes of application or doses used for second trimester medical abortion were compared.

#### **Types of participants**

Studies which included healthy women undergoing a second trimester abortion were eligible if carrying a singleton, living fetus between 12 to 28 weeks gestation. Studies including women with multiple pregnancies, or those who had cervical preparation prior to the abortion procedure were excluded.

#### **Types of interventions**

Different medical methods, administration routes or doses of medication used for second trimester medical abortion.

#### Types of outcome measures

The main outcome measures were the induction to abortion interval and the number of complete abortions within 24 hours. The primary endpoint for the abortion interval is expulsion of the fetus. The secondary endpoint for the abortion interval is the expulsion of the placenta. In addition, other secondary outcome measures included the need for surgical evacuation (non-emergency procedure, emergency procedure, or not specified, including manual removal of the placenta), blood loss (measured, need for blood transfusion or clinically relevant drop in haemoglobin), uterine rupture, pain resulting from the procedure (reported by the women or measured by use of analgesics), nausea, vomiting and diarrhoea. The table Characteristics of included studies includes whether a surgical intervention was performed routinely in the study.

#### Potential confounding

The sensitivity of the myometrium for uterotonic drugs increases with gestational age. Hence, the longer the gestation, the less uterotonic drugs are needed. Apart from gestational age, parity could also be viewed as a potential confounder as multiparous women appear to have a shorter time interval to abortion. Differential treatment effects could theoretically be ascribed by differences in gestational age or parity. Parity and gestational age of study participants are listed under Characteristics of included studies.

#### Search methods for identification of studies

See:Collaborative Review Group search strategy.

The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*), MEDLINE and Popline were systematically searched. Reference lists of retrieved papers were searched. Electronic literature search was conducted using the following key words: (induced abortion) AND (second trimester) AND (mifepristone OR misoprostol OR methotrexate OR dinoprost OR dinoprostone OR carboprost OR sulprostone OR gemeprost OR meteneprost OR epostane OR oxytocin OR RU 486 OR mifegyne) OR ethacridine lactate AND ((randomised controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR singleblind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw] ) OR ((singl\* [tw] OR doubl\* [tw] OR tripl\* [tw] ) AND (mask\* [tw] OR blind\* [tw] )) OR ("latin square" [tw] ) OR placebos [mh] OR placebo\* [tw] OR random\* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control\* [tw] OR prospectiv\* [tw] OR volunteer\* [tw] ) NOT (animal [mh] NOT human [mh]) )

#### Data collection and analysis

#### **Selection of studies**

The selection of trials for inclusion was performed independently by two review authors after employing the research strategy described previously. Trials under consideration were evaluated for inclusion and methodological quality without consideration of the results. This review is limited to randomised controlled trials, thereby focusing on four types of medical interventions for second trimester termination of pregnancy, that is (1) mifepristone and prostaglandin, (2) misoprostol, (3) other prostaglandins and (4) hyperosmolar agents (hypertonic saline, ethacridine lactate).

A form was designed to facilitate the process of data extraction which was performed by two of the reviewers independently. There were no discrepancies between the reviewers in either decision of inclusion/exclusion of studies or in data extraction.

Trials were not excluded based on an arbitrary cut-off limit regarding losses to follow up. Subgroup analyses were planned for early and late second trimester abortions as the performance of methods may differ with gestational age.

Trials describing the use of quinine were excluded. Trials including more than 20% fetal death at the onset of treatment (unless separate analysis was available), multiple pregnancies, women with uterine scars (if reportedly included in the trial) and regimens which included cervical preparation prior to the abortion procedure were excluded.

#### **Data extraction and management**

Data were extracted by two authors from eligible studies. Study characteristics (type of study, allocation, blinding), participants characteristics (number, gestational age), interventions, main

outcome measures and results were recorded. An attempt was made to obtain additional information from authors if required.

#### Assessment of risk of bias in included studies

The quality of studies was assessed without blinding to authorship or journal. Bias was assessed using the following.

1. Allocation concealment. The quality score for concealment of allocation was assigned to each trial using the criteria in the Cochrane Handbook:

A adequate concealment of allocation;

B unclear whether adequate concealment of allocation;

C inadequate concealment of allocation (includes quasirandomised studies.

Only trials scoring A or B were included in the review.

2. Blinding of participants, clinicians and investigators.

3. Protection against exclusion bias.

4. Appropriate analysis of data.

#### Assessment of heterogeneity

Heterogeneity was analysed using the  $\mathsf{I}^2$  statistic (Higgins 2003).  $\mathsf{I}^2$  values of 25%, 50%, and 75% correspond to low, medium and high levels of heterogeneity.

#### Data synthesis

Data analyses was performed by using Revman 5 software.

Trials that were conducted within the subject of this review included the comparison of different medical methods, application methods and dose regimens. For this reason, the trials were considered by medical regimen comparing the outcome measures for each regimen as described earlier. The different comparisons are as follows.

Comparison 1: mifepristone + misoprostol versus mifepristone + gemeprost.

Comparison 2: mifepristone + misoprostol versus misoprostol alone.

Comparisons 3 to 5: routes of administration of misoprostol combined with mifepristone:

- Comparison 3: vaginal use versus the oral use of misoprostol;
- Comparison 4: vaginal use versus the sublingual use of misoprostol;
- Comparison 5: oral use versus the sublingual use of misoprostol.

Comparison 6: dosing interval of misoprostol following mifepristone.

Comparison 7: dosing of mifepristone previous to misoprostol.

Comparison 8: combined regimen of mifepristone + gemeprost.

Comparisons 9 to 11: misoprostol versus another prostaglandin:

- Comparison 9: misoprostol versus intra-amniotic PGF<sub>2</sub>;
- Comparison 10: misoprostol versus gemeprost;
- Comparison 11: misoprostol versus dinoprostone.

Comparisons 12 to 13: routes of administration of misoprostol:

- Comparison 12: vaginal use versus the oral use of misoprostol;
- Comparison 13: vaginal use versus the sublingual use of misoprostol.

Comparison 14: misoprostol tablet insertion versus gel insertion.

Comparisons 15 to 16: time interval for repeat dosing of misoprostol or gemeprost:

- Comparison 15: Time interval of misoprostol;
- Comparison 16: Time interval of gemeprost.

Comparison 17: low dose versus a higher dose of misoprostol.

Comparisons 18 to 19: prostaglandin  $E_2$  versus prostaglandin  $F_{2\alpha}$ :

- Comparison 18: prostaglandin E<sub>2</sub> versus prostaglandin F<sub>2α</sub>;
- Comparison 19: prostaglandin  $E_2$  versus prostaglandin  $F_{2\alpha}$  + oxytocin.

Comparison 20: intra-amniotic instillation of prostaglandin  $F_{2\alpha}$  versus intra-amniotic instillation of hypertonic saline (20%).

Comparison 21: combined regimen intra-amniotic prostaglandin  $F_{2\alpha}$  + hypertonic saline.

Comparison 22: prostaglandin  $E_1$  vaginally versus the intraamniotic instillation of prostaglandin  $F_{2\alpha}$  + hypertonic saline.

Comparison 23: prostaglandins versus ethacridine lactate.

Comparison 24: ethacridine lactate versus normal saline.

#### RESULTS

#### **Description of studies**

See: Characteristics of included studies; Characteristics of excluded studies

#### **Results of the search**

Eighty-eight studies underwent full review. Full text review excluded 52 studies as they were not randomised; used inadequate concealment (score C); included over 20% fetal demise, multiple pregnancies, patients with uterine scarring; a pre-treatment trial, including medical or mechanical dilatation of the cervix. See Characteristics of excluded studies.

Forty studies were included in this review. Due to the diversity of the interventions, the review concerns the comparison of 24 regimens. Three trials compared more than two different groups and the interventions are therefore listed as different comparisons (Mehta 1975 a; Mehta 1975 b; Muzsnai 1979 a; Muzsnai 1979 b; Muzsnai 1979 c; Muzsnai 1979 d; Nuutila 1997 a; Nuutila 1997 b; Nuutila 1997 c). The main outcomes considered were induction to abortion interval or completed abortion within 24 hours.

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#### **Included studies**

Four studies (Borgida 1995; Ho 1996; Nielsen 1975; Steyn 1993) each enrolled 50 patients or less.

Four separate interventions were used.

1. Mifepristone and prostaglandin

- Three studies (210 patients) compared a regimen of mifepristone and misoprostol to mifepristone and gemeprost (Bartley 2002; el-Refaey 1993; Ho 1996).
- One study (64 patients) compared mifepristone to a placebo prior to misoprostol induced abortion (Kapp 2007).
- Five studies (500 patients) compared different routes of administration of misoprostol combined with mifepristone:
  - vaginal use compared to oral use (306 patients) (El-Refaey 1995; Ho 1997; Ngai 2000);
  - vaginal use compared to sublingual use (76 patients) (Hamoda 2005);
  - oral use compared to sublingual use (118 patients) (Tang 2005).
- One study (141 patients) compared the dosing interval of misoprostol following mifepristone administration (Chai 2009).
- One study (70 patients) compared the dosage of mifepristone before misoprostol was administered (Webster 1996).
- One study (100 patients) compared 0.5mg and 1.0 mg gemeprost combined with mifepristone (Thong 1996).

#### 2. Misoprostol

- Five studies (693 patients) compared misoprostol to another prostaglandin:
  - one studies (125 patients) compared the vaginal use of misoprostol to PGF2α (Su 2005);
  - two studies (221 patients) compared the vaginal use of misoprostol to gemeprost (Nuutila 1997 a; Nuutila 1997 b; Wong 1998);
  - one study (130 patients) compared the vaginal use of misoprostol to dinoprostone (Makhlouf 2003).
- Five studies (812 patients) compared different routes of administration of misoprostol:
  - vaginal use compared to oral use (310 patients) (Akoury 2004; Bebbington 2002; Behrashi 2008);
  - vaginal use compared to sublingual use (502 patients) (Bhattacharjee 2008; Tang 2004; von Hertzen 2009).
- One study (148 patients) compared misoprostol tablets to gel insertion (Pongsatha 2008).
- Three studies (427 patients) compared different time intervals of misoprostol or gemeprost (Armatage 1996; Herabutya 2005; Wong 2000).
- Two studies (133 patients) compared different doses of misoprostol (Nuutila 1997 c; Ozerkan 2009).
- 2. Other prostaglandins
- Three studies (143 patients) compared prostaglandin E<sub>2</sub> to prostaglandin F<sub>2α</sub> (Borgida 1995; Sorensen 1984; Steyn 1993).
- 3. Hyperosmolar agents

- Four studies (1670 patients) compared hypertonic saline and prostaglandin  $F_{2\alpha}$  (Faktor 1988; Mehta 1975 a; Mehta 1975 b; Nielsen 1975; WHO 1976).
- One study (385 patients) compared different regimens of prostaglandin  $F_{2\alpha}$  and hypertonic saline (Muzsnai 1979 a; Muzsnai 1979 b; Muzsnai 1979 c; Muzsnai 1979 d).
- One study (58 patients) compared gemeprost to prostaglandin  $F_{2\alpha}$  and hypertonic saline (Waldron 1990).
- Three studies (302 patients) compared prostaglandins to ethacridine lactate (Inan 1997; Kelekci 2006; Olund 1978).
- One study (37 patients) compared ethacridine lactate to normal saline (Zauva 1989).

#### **Risk of bias in included studies**

Only randomised controlled trials were included in this review. Thirty-two studies reported the method of randomisation (Akoury 2004; Armatage 1996; Bartley 2002; Bebbington 2002; Bhattacharjee 2008; Borgida 1995; Chai 2009; el-Refaey 1993; Elrefaey 1995; Hamoda 2005; Herabutya 2005; Ho 1996; Ho 1997; Kapp 2007; Kelekci 2006; Makhlouf 2003; Mehta 1975 a; Mehta 1975 b; Ngai 2000; Nuutila 1997 a; Nuutila 1997 b; Nuutila 1997 c; Ozerkan 2009; Pongsatha 2008; Sorensen 1984; Steyn 1993; Su 2005; Tang 2004; Tang 2005; Thong 1996; von Hertzen 2009; Webster 1996; WHO 1976; Wong 1998; Wong 2000). For more detailed information, see the section Included studies. Eleven studies did not state the inclusion or exclusion criteria (Bartley 2002; el-Refaey 1993; Elrefaey 1995; Faktor 1988; Inan 1997; Mehta 1975 a; Mehta 1975 b; Nielsen 1975; Nuutila 1997 a; Nuutila 1997 b; Nuutila 1997 c; Olund 1978; Ozerkan 2009; Webster 1996).

#### Allocation

Allocation concealment was adequately reported in 28 studies (Akoury 2004; Armatage 1996; Bartley 2002; Bebbington 2002; Bhattacharjee 2008; Borgida 1995; Chai 2009; el-Refaey 1993; Elrefaey 1995; Hamoda 2005; Herabutya 2005; Ho 1996; Ho 1997; Kapp 2007; Makhlouf 2003; Mehta 1975 a; Mehta 1975 b; Ngai 2000; Nuutila 1997 a; Nuutila 1997 b; Nuutila 1997 c; Steyn 1993; Su 2005; Tang 2004; Tang 2005; Thong 1996; von Hertzen 2009; Webster 1996; WHO 1976; Wong 1998; Wong 2000).

#### Blinding

Blinding (no further explanation was given) was reported in one study (von Hertzen 2009). Blinding of participants was reported in one study (Ngai 2000). Blinding of participants and clinicians was reported in two studies (Ho 1997; Tang 2005). Blinding of participants, clinicians and researchers was reported in one study (Kapp 2007).

#### **Effects of interventions**

For outcomes using a continuous scale, the mean difference (MD) with 95% confidence intervals (95% Cl) were used to asses the effects of the intervention. For dichotomous outcomes the results were expressed using odds ratio (OR) with 95% confidence intervals (95% Cl).

# Comparison 1: combined regimen mifepristone + misoprostol versus mifepristone + gemeprost

Three trials (Bartley 2002; el-Refaey 1993; Ho 1996) were included in this comparison. In total, 210 women were eligible for analysis.

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In regards to the induction to abortion interval, el-Refaey 1993 did not provide standard deviations, and thus precluded inclusion of these data in the meta-analysis. The median induction to abortion interval was 8 hrs (range 1 to 60) and 9.1 hrs (range 3 to 22) for the oral use of 400 µg misoprostol and the 1 mg gemeprost pessaries group respectively (not significant). There were no significant differences in the induction-to-abortion interval (Analysis 1.1), abortion rate within 24 hours (Analysis 1.2), need for surgical evacuation (Analysis 1.3) or side-effects (pain, Analysis 1.4; nausea, Analysis 1.5; vomiting, Analysis 1.6; diarrhoea, Analysis 1.7) between regimens using mifepristone with either misoprostol or gemeprost.

#### Comparison 2: misoprostol versus mifepristone + misoprostol

One trial (Kapp 2007) was included in this comparison. In this regimen, 64 women were eligible for analysis. Women who received mifepristone + misoprostol aborted more rapidly than women who had misoprostol alone (Analysis 2.1) (MD 12.13, 95% CI 1.43 to 102.61). No difference was found in terms of the need for surgical evacuation (Analysis 2.2), pain (Analysis 2.3), vomiting (Analysis 2.5) or nausea (Analysis 2.4).

# Comparisons 3 to 5: routes of administration of misoprostol combined with mifepristone

In this comparison, five trials with three comparisons (El-refaey 1995; Hamoda 2005; Ho 1997; Ngai 2000; Tang 2005) were included.

#### Comparison 3: vaginal use compared to oral use of misoprostol

In this comparison, three trials (El-refaey 1995; Ho 1997; Ngai 2000) were included. In total, 306 women were eligible for analysis. The largest trial in this analysis was conducted by Ngai, comparing the oral use of 400 µg and the vaginal use of 200 µg of misoprostol, both combined with 200 mg mifepristone administered orally 36 to 48 hours in advance. In addition to this comparison, both groups received either vaginal or oral placebo tablets. Ho 1997 conducted a randomised controlled trial comparing the use of 200  $\mu g$  of misoprostol orally combined with a vaginal placebo to the vaginal use of 200 µg misoprostol combined with an oral placebo, each arm combined with 200 mg mifepristone. The vaginal use of 200 µg misoprostol was superior (MD 13.00, 95% CI 2.77 to 23.23) to the oral use of 200 µg misoprostol (Analysis 3.1). When both oral and vaginal misoprostol was administered in a low dose (200  $\mu$ g), the vaginal use was superior to the oral use regarding the abortion rate within 24 hours (Analysis 3.2) (OR 0.26, 95% CI 0.09 to 0.78). In regards to the induction-to-abortion interval, El Refaey 1995 did not provide a standard deviation in addition to estimates which precluded the inclusion of these data in the meta-analysis. The mean induction to abortion interval was 6.0 hrs (95% CI 5.0 to 7.2) and 6.7 hrs (95% CI 5.8 to 7.6) for the oral and the vaginal groups respectively (not significant). No significant difference was found between the oral and vaginal use of misoprostol in terms of induction-to-abortion interval. In addition, no difference was found between the need for surgical evacuation (Analysis 3.3), amount of pain (Analysis 3.4), nausea (Analysis 3.5) or vomiting (Analysis 3.6). However, fewer episodes of diarrhoea occurred (Analysis 3.7) (OR 2.21, 95% CI 1.06 to 4.61) when 200  $\mu$ g misoprostol was administered vaginally compared to 400 µg misoprostol, orally.

# Comparison 4: vaginal use compared to sublingual use of misoprostol

In this comparison, one trial (Hamoda 2005) was included. In total, 69 women were eligible for analyses. The comparison was made between the sublingual use of 600  $\mu$ g of misoprostol and the vaginal use of 800  $\mu$ g, both combined with 200 mg mifepristone. In regards to the induction-to-the abortion interval, no mean or SD was provided and thus precluded inclusion of these data in a meta-analysis. The median and range of the sublingual group (median 5.27, range 0.55 to 29.35) and of the vaginal group (median 5.40, range 2.10 to 13.00) showed no significant difference (P = 0.95) for the abortion interval. In addition, no difference between the sublingual and vaginal use was found in terms of the need for surgical evacuation (Analysis 4.1) or side-effects such as pain (Analysis 4.2), nausea (Analysis 4.3), vomiting (Analysis 4.4) or diarrhoea (Analysis 4.5).

### Comparison 5: oral use compared to sublingual use of misoprostol

In this comparison, one trial (Tang 2005) was included. In total, 118 women were eligible for analysis. Tang 2005 compared the oral and sublingual use of 400  $\mu$ g of misoprostol in combination with 200 mg of mifepristone. Both groups received oral or sublingual placebo tablets. In regards to the induction-to-the abortion interval, no mean or SD was provided and thus precluded inclusion of these data in a meta-analysis. The sublingual group (median 5.5, range 1.4 to 43.2) aborted in a shorter time interval when compared to the oral group (median 7.5, range 2.4 to 38.8) (P = 0.009). No difference was found in regards to the abortion rate within 24 hours (Analysis 5.1) or side-effects such as pain (Analysis 5.2), nausea (Analysis 5.3) or diarrhoea (Analysis 5.4).

### Comparison 6: dosing interval of misoprostol following mifepristone administration

One trial (Chai 2009) was included in this comparison. There were 141 women eligible for analyses. No difference was found in the abortion rate within 24 hours (Analysis 6.1), need of surgical evacuations (Analysis 6.2), or side-effects of pain (Analysis 6.3), nausea (Analysis 6.4) and diarrhoea (Analysis 6.5). All patients from one centre had dilatation and curettage the day following abortion, as it was the routine practice in that hospital. These patients were not included in Analysis 6.2.

### Comparison 7: dose of mifepristone before the administration of misoprostol

One trial (Webster 1996) was included in this comparison. In total, 70 women were eligible for analyses. No difference was found in the induction of the abortion interval (Analysis 7.1), abortion rate within 24 hours (Analysis 7.2), need of surgical evacuation (Analysis 7.3) or side-effects of pain (Analysis 7.4), vomiting (Analysis 7.5) or diarrhoea (Analysis 7.6).

# Comparison 8: regimen mifepristone + gemeprost 1.0 mg versus mifepristone + gemeprost 0.5 mg

One trial (Thong 1996) was included in this comparison. There were 100 women eligible for analysis. No difference was found in the abortion rate within 24 hours (Analysis 8.1), excessive blood loss (Analysis 8.2), need for surgical evacuation (Analysis 8.3) or episodes of diarrhoea (Analysis 8.5). When patients were given 0.5

mg gemeprost rather than 1 mg, they experienced fewer episodes of vomiting (Analysis 8.4) (OR 2.83, 95% CI 1.04 to 7.66).

# Comparisons 9 to 11: misoprostol versus another prostaglandin

Four trials with seven comparisons (Makhlouf 2003; Nuutila 1997 a; Nuutila 1997 b; Su 2005; Wong 1998) were included. Nuutila compared three interventions, that is, two doses of vaginal misoprostol and vaginal gemeprost. For this reason, this trial was considered for each of the different comparisons (see Characteristics of included studies).

#### Comparison 9: misoprostol versus intra-amniotic $PGF_{2\alpha}$

In this comparison, one trial was included (Su 2005). In total, 125 women were eligible for analysis. Su 2005 compared the use of vaginal misoprostol with the use of intra-amniotic PGF<sub>2</sub> $\alpha$ . Vaginal misoprostol was superior to intra-amniotic PGF<sub>2</sub> $\alpha$  (MD -4.60, 95% CI -7.74 to -1.46) (Analysis 9.1) regarding the induction to the abortion interval. No difference was found between the groups in relation to the abortion completion rate (Analysis 9.2), need for surgical evacuations (Analysis 9.3), nausea (Analysis 9.4), vomiting (Analysis 9.5) or diarrhoea (Analysis 9.6).

#### Comparison 10: misoprostol versus PGE<sub>1</sub> (gemeprost)

In this comparison, two trials with three comparisons were included (Nuutila 1997 a; Nuutila 1997 b; Wong 1998). In total, 249 women were eligible for analysis. The largest trial in this analysis was conducted by Wong 1998, comparing the vaginal use of misoprostol, 400 µg every 4 hours, to the vaginal use of gemeprost. When misoprostol was used at very low doses (100 μg) (MD 8.60, 95% CI 3.11 to 14.09) or 200 μg (MD 13.30, 95% CI 7.90 to 18.70) every 6 or 12 hours, respectively, gemeprost was superior (Analysis 10.1). In contrast, when misoprostol was used at a higher dose (400 µg) (OR 2.83, 95% CI 1.33 to 6.02) every 3 or 6 hours, more women aborted within 24 hours in comparison to gemeprost (Analysis 10.2). In regards to the side-effects, women who received misoprostol experienced less pain (100  $\mu$ g) (OR 0.22, 95% CI 0.07 to 0.71) or 200 µg (OR 0.23, 95% CI 0.07 to 0.77), vomiting (misoprostol 200  $\mu$ g, OR 0.15, 95% CI 0.04 to 0.62) and diarrhoea (100 µg, OR 0.04, 95% CI 0.00 to 0.68) or 200 µg (OR 0.18, 95% CI 0.03 to 0.91) (Analysis 10.5; Analysis 10.7; Analysis 10.8). Moreover, the amount of blood loss was decreased when women received 200 μg misoprostol when compared to gemeprost (Analysis 10.3) (OR -146.00, 95% CI -219.02 to -72.98). No difference was found between the groups in relation to the need for surgical evacuation (Analysis 10.4) or nausea (Analysis 10.6).

#### Comparison 11: misoprostol versus PGE<sub>2</sub> (dinoprostone)

In this comparison, one trial was included (Makhlouf 2003). In total, 80 women were eligible for analysis. More women who were given misoprostol, 100  $\mu$ g every four hours, aborted within 24 hours when compared to PGE<sub>2</sub>, 6 mg every six hours (Analysis 11.1) (OR 51.73, 95% CI 2.89 to 924.42). There was no difference regarding blood loss (Analysis 11.2), need for surgical evacuation (Analysis 11.3) or sideeffects of pain (Analysis 11.4), vomiting (Analysis 11.5) or diarrhoea (Analysis 11.6) between the groups.

# Comparisons 12 to 13: routes of misoprostol for misoprostol used alone

In this comparison, six trials with two comparisons (Akoury 2004; Bebbington 2002; Behrashi 2008; Bhattacharjee 2008; Tang 2004; von Hertzen 2009) were included.

# Comparison 12: vaginal use of misoprostol versus the oral use of misoprostol

In this comparison, three trials were included (Akoury 2004; Bebbington 2002; Behrashi 2008). In total, 310 women were eligible for analysis. The largest trial was conducted by Akoury, comparing the oral and vaginal use of misoprostol and the intra-amniotic use of PGF $_{2\alpha}$ . The vaginal administration of misoprostol was superior to the oral route (Analysis 12.1), at both a lower dose (200  $\mu$ g) (mean difference (MD) -14.90, 95% CI -23.33 to -6.47) and a higher dose (400 µg) (MD -6.04, 95% CI -8.51 to -3.58). The abortion rate after 24 hours with vaginal use was also superior to the oral use of 200 μg of misoprostol (OR 9.60, 95% CI 3.74 to 24.66) (Analysis 12.2). Fewer women experienced nausea when the misoprostol was given vaginally when compared to the oral use of 400 µg of misoprostol (Analysis 12.6) (OR 0.41, 95% CI 0.18 to 0.93). No difference was found between the groups in regard to the amount of blood loss (Analysis 12.3), pain (Analysis 12.4), need for surgical evacuation (Analysis 12.5), vomiting (Analysis 12.7) or diarrhoea (Analysis 12.8).

# Comparison 13: vaginal use of misoprostol versus the sublingual use of misoprostol

In this comparison, three trials were included (Bhattacharjee 2008; Tang 2004; von Hertzen 2009). In total, 1178 women were eligible for analysis. The largest trial was conducted by von Hertzen, comparing the vaginal use of 400 µg misoprostol to the sublingual use of 400 µg misoprostol with the use of placebo tablets. No difference was found between the vaginal or the sublingual use of misoprostol for the induction to abortion interval in one smaller study (Analysis 13.1). Von Hertzen was not included in this analyses, because no mean (SD) was provided. However, authors did provide median (range). In the vaginal group, the induction to abortion interval was longer (median 12.3, range 3.2 to 48.0) than the sublingual group (median 12.0, range 4.1 to 61.8). However, this difference was not significant. The abortion rate after 24 hours with vaginal use was superior to the sublingual use (Analysis 13.2) (OR 1.39, 95% CI 1.05 to 1.83). However, the significant heterogeneity for the analysis (Analysis 13.2) (I<sup>2</sup> = 63%) must be noted despite use of identical regimens precludes confidence in these combined estimates. The heterogeneity between these data could potentially be explained by the difference in included numbers of multigravidas between both trials; Tang included 36% to 39%, while Bhattacharjee included 80% of women studied. Because of the possibility that among nulliparous women, vaginal misoprostol is associated with higher rates of complete abortion within 24 hours, the analysis were separated. Vaginal misoprostol is associated with significantly higher rates of complete abortion within 24 hours among nulliparous women (OR 2.31, 95% CI 1.17 to 4.54), while among multiparous women, there is no difference between vaginal or sublingual administration (OR 0.90, 95% CI 0.55 to 1.47). Von Hertzen conducted a stratified analysis by parity because there was a highly significant interaction of treatment by parity. When success rates at 24 h were analysed according to parity, vaginal administration was clearly superior to sublingual administration in nulliparous women (87.3% versus 68.5%) but

the difference between treatments was not present among parous women: 84.7% (vaginal) versus 88.5% (sublingual).

No differences were noted in the meta-analysis for the occurrence of complications of blood loss (Analysis 13.3) or surgical evacuations (Analysis 13.5) or side-effects of pain (Analysis 13.4), nausea (Analysis 13.6), vomiting (Analysis 13.7) or diarrhoea (Analysis 13.8).

# Comparison 14: misoprostol tablet insertion versus gel insertion

One trial (Pongsatha 2008) was included in this comparison. For analysis, 148 women were eligible for analysis. In terms of adverse outcomes, women who had misoprostol inserted with gel experienced more diarrhoea (Analysis 14.7) (OR 0.15, 95% CI 0.03 to 0.71). No significant difference was observed between the two groups in terms of abortion within 24 hours (Analysis 14.1), excessive blood loss (Analysis 14.2), need for surgical evacuation (Analysis 14.3), pain (Analysis 14.4), nausea (Analysis 14.5) or vomiting (Analysis 14.6).

# Comparisons 15 to 16: time interval and dose of misoprostol or gemeprost

Four trials with two comparisons (Armatage 1996; Herabutya 2005; Wong 2000) were included.

#### Comparison 15: time interval of misoprostol

Two trials (Herabutya 2005; Wong 2000) were included in this comparison. In total, 427 women were eligible for analysis. The largest trial in this analysis was conducted by Wong 2000 who examined the optimal time interval for the vaginal use of 400  $\mu$ g misoprostol, either administered every three or every six hours. When the time interval was shorter, the interval to abortion was shorter (three hours) (Analysis 15.1) (MD -19.20, 95% CI -36.02 to -2.38) compared to the longer time interval (six hours). In regards to the induction to abortion interval, no mean or SD was provided by Herabutya 2005 and thus precluded inclusion of these data in the meta-analysis. The median induction-to-abortion interval was 15.8 hrs (25, 75 centiles: 12, 26) and 16.0 hrs (25, 75 centiles: 12, 30) for the group given misoprostol with a shorter time interval and the group with a longer time interval respectively (P =0.80). No effect was found for the time interval in relation to the abortion rate within 24 hours (Analysis 15.2), excessive blood loss (Analysis 15.3; Analysis 15.4), need for surgical evacuation (Analysis 15.5), or side-effects of pain (Analysis 15.6), nausea (Analysis 15.7), vomiting (Analysis 15.8) or diarrhoea (Analysis 15.9).

#### Comparison 16: time interval of gemeprost

One trial (Armatage 1996) was included in this comparison. In total, 99 women were eligible for analysis. In regards to the induction to abortion interval, no mean or SD was given, and thus precluded inclusion of these data in a meta-analysis. The median induction-to-abortion interval was 16 hrs (25, 75 centiles: 12, 26) and 15 hrs (25, 75 centiles: 11.4, 28.5) for the group given gemeprost with a shorter time interval compared with the longer time interval, respectively (not significant). In addition, no significant difference was found between both groups in the abortion rate after 24 hours (Analysis 16.1), need for surgical evacuation (Analysis 16.2) or pain (Analysis 16.3).

#### Comparison 17: low dose versus a higher dose of misoprostol

Two trials (Nuutila 1997 c; Ozerkan 2009) were included in this comparison. In total, 133 women were eligible for analyses. Ozerkan 2009 compared the use of 600  $\mu$ g with the use of 400  $\mu$ g of misoprostol. An initial first dose of 600 µg of misoprostol was found to be more effective than 400  $\mu g$  (Analysis 17.1) (MD 6.40, 95% CI 0.40 to 12.40). While gestational age or parity were not found to be related to the duration of the termination procedure, a higher parity was shown to be correlated with a shorter induction to fetal-expulsion period in the low dose, but not in the high dose group. Nuutila 1997 c compared the use of 100 µg of misoprostol to the use of 200  $\mu g$  of misoprostol. The study found no difference between these groups in terms of the induction of the abortion interval (Analysis 17.1). The significant heterogeneity for the analysis (Analysis 17.1) ( $I^2 = 84\%$ ) must be noted. This is most likely do to the different misoprostol doses the trials used. Both studies found no difference in the amount of pain (Analysis 17.2), and side effects such as vomiting (Analysis 17.4) and diarrhoea (Analysis 17.5).

# Comparisons 18 to 19: prostaglandin $E_2$ versus prostaglandin $F_{2\alpha}$

Three trials with two comparisons (Borgida 1995; Sorensen 1984; Steyn 1993) were included.

#### Comparison 18: prostaglandin $E_2$ versus prostaglandin $F_{2\alpha}$

One trial (Borgida 1995) was included in this comparison. In total, 50 women were eligible for analysis. When women were given prostaglandin E<sub>2</sub>intravaginally, the interval to abortion was shorter (Analysis 18.1) (MD -9.10, 95% CI -13.68 to -4.52) when compared to the women receiving prostaglandin F<sub>2α</sub> intramuscularly. In addition, more women given prostaglandin E<sub>2</sub> aborted within 24 hours (Analysis 18.2) (OR 11.29, 95% CI 1.29 to 98.89). No difference was found between the occurrence of side-effects of pain (Analysis 18.3), nausea (Analysis 18.4), vomiting (Analysis 18.5) or diarrhoea (Analysis 18.6).

# Comparison 19: prostaglandin $E_2$ versus prostaglandin $F_{2\alpha}^{2}$ + oxytocin

Two trials (Sorensen 1984; Steyn 1993) were included in this comparison. In total, 59 women were eligible for analysis. In regards to the induction-to-abortion interval, Steyn 1993 did not provide SDs, and thus precluded inclusion of these data in a meta-analysis. The median induction to abortion interval was 38 hrs (range 19 to 61) and 23 hrs (range 11 to 54.5) for the intra-amniotic prostaglandin  $F_{2\alpha}$  and the extra-amniotic prostaglandin  $E_2$  group, respectively (not significant). When women were given prostaglandin  $E_2$  + oxytocin, the interval to abortion was longer (Analysis 19.1) (MD 2.00, 95% CI 0.90 to 3.10) compared to the women receiving prostaglandin  $F_{2\alpha}$  + oxytocin. Fewer surgical evacuations were performed in the prostaglandin E<sub>2</sub> + oxytocin group (Analysis 19.2) (OR 0.25, 95% CI 0.07 to 0.90) and fewer women experienced pain (Analysis 19.3) (OR 0.03, 95% CI 0.00 to 0.72) when compared to the use of prostaglandin  $F_{2\alpha}$  + oxytocin. No difference was found regarding the episodes of vomiting or diarrhoea (Analysis 19.4; Analysis 19.5).



# Comparison 20: intra-amniotic instillation of prostaglandin $F_{2\alpha}$ versus intra-amniotic instillation of hypertonic saline (20%)

Four trials (Faktor 1988; Mehta 1975 a; Mehta 1975 b; Nielsen 1975; WHO 1976) were included for analysis. In total, 1703 women were eligible for analysis. The largest trial in this analysis was conducted by the WHO 1976, comparing the intra-amniotic use of 25 mg of prostaglandin  $F_{2\alpha}$  to the intra-amniotic instillation of 20% saline. In regards to the induction to abortion interval, Nielsen 1975. and the WHO trials did not provide standard deviations, and thus precluded inclusion of these data in a meta-analysis. The median induction to abortion interval in the study by Nielsen 1975 was 21.5 hrs (ranges not given) and 14.2 hrs (ranges not given) for the hypertonic saline and the  $\mathsf{PGF}_{2\alpha}$  group, respectively (P < 0.01). The median inductionto-abortion interval in the study by the WHO was 30.4 hrs (ranges not given) and 19.7 hrs (ranges not given) for the hypertonic saline and the  $PGF_{2\alpha}$  group respectively (P <0.001). Based on analysis of only 25 women, a single dose of 40 mg prostaglandin  $F_{2\alpha}$  proved to be more effective than 20% hypertonic saline in terms of inductionto-abortion interval (Analysis 20.1) (MD -5.30, 95% CI -6.67 to -3.93). The analysis of the abortion rate within 24 hours included 1678 women. Multiple doses of  $PGF_{2\alpha}$  proved to be more effective than 20% hypertonic saline (Analysis 20.2) (OR 6.14, 95% CI 4.91 to 7.68). On the other hand, women who received hypertonic saline experienced fewer complications, such as the need for surgical evacuation (Analysis 20.8) (single dose of 50 mg PGF<sub>2 $\alpha$ </sub> OR 7.89, 95% CI 2.01 to 30.95; multiple doses of 25 mg PGF  $_{2\alpha}$  OR 1.52, 95% CI 1.24 to 1.87) episodes of nausea (Analysis 20.5) (OR 3.01, 95% CI 1.17 to 7.72), vomiting (Analysis 20.6) (single dose of 50 mg PGF $_{2\alpha}$  OR 22.40, 95% CI 2.73 to 183.71; and multiple doses of 25 mg PGF OR 5.01, 95% CI 3.99 to 6.28) and diarrhoea (Analysis 20.7) (multiple doses of  $25 mg\,PGF_{2\alpha}$  OR 12.47, 95% CI 6.81 to 22.82). The WHO trial reported more episodes of excessive blood loss in women receiving  $PGF_{2\alpha}$ (Analysis 20.4) (OR 3.05, 95% CI 1.56 to 5.97).

# Comparison 21: combined regimen prostaglandin $F_{2\alpha}$ and hypertonic saline

One trial (Muzsnai 1979 a; Muzsnai 1979 b; Muzsnai 1979 c; Muzsnai 1979 d) was included for analysis. In total, 770 women were eligible for analysis. The instillation of 25 ml 20% NaCl (5 g) + PGF<sub>2α</sub> (20 mg) was superior to the instillation of 100 ml 10% NaCl (10 g) + PGF<sub>2α</sub> (20 mg) (Analysis 21.1) in terms of the induction to the abortion interval (MD -2.96, 95% Cl -5.29 to -0.64), but also in terms of the 24 hour abortion rate (OR 2.30, 95% Cl 1.38 to 3.86) (Analysis 21.2). No significant difference was found between those who received 5 g of hypertonic saline versus 10 g in terms of excessive blood loss (Analysis 21.3), need for surgical evacuation (Analysis 21.4), vomiting (Analysis 21.6) and diarrhoea (Analysis 21.7). When given 25 ml of 20% hypertonic saline, women experienced less nausea (Analysis 21.5) (OR 0.33, 95% Cl 0.17 to 0.62) than those who received 100 ml of 10% hypertonic saline.

# Comparison 22: prostaglandin E1 (gemeprost) vaginally versus intra-amniotic instillation of prostaglandin $F_{2\alpha}$ + hypertonic saline

One trial (Waldron 1990) was included in this comparison. In total, 58 women were eligible for analysis. Women who had intra-amniotic instillation of prostaglandin  $F_{2\alpha}$  + hypertonic

saline aborted more rapidly than women who received vaginally administered gemeprost (Analysis 22.1) (MD 0.90, 95% CI 0.10 to 0.70) and the 24 hour abortion rate was significantly higher (Analysis 22.2) (OR 0.16, 95% CI 0.04 to 0.67). In addition, women who received gemeprost experienced more episodes of vomiting (Analysis 22.6) (OR 3.11, 95% CI 1.06 to 9.08) and diarrhoea (Analysis 22.7) (OR 19.13, 95% CI 3.80 to 96.18). No significant difference was found in terms of excessive blood loss (Analysis 22.3), need for surgical evacuation (Analysis 22.4) or pain (Analysis 22.5).

#### Comparison 23: prostaglandins versus ethacridine lactate

Three trials (Inan 1997; Kelekci 2006; Olund 1978) were included in this comparison. For analyses, 302 women were eligible. No significant difference in induction to abortion interval was found (Analysis 23.1). Olund 1978 provided no standard deviation and could therefore not enter our analysis. The mean and range of the abortion interval of the ethacridine lactate group (29.9, 23.9 to 47.2) and of the prostaglandin  $F_{2\alpha}$  group (26.7, 8.9 to 63.0) showed no significant difference. More women in the ethacridine lactate group aborted within 24 hours (Analysis 23.2) (OR 0.18, 95% CI 0.06 to 0.48) in comparison to prostaglandin E2, but not in comparison to misoprostol. No differences were found in regard to the amount of blood loss (Analysis 23.3) or side-effects, such as nausea (Analysis 23.4), vomiting (Analysis 23.5) or diarrhoea (Analysis 23.6). Kelekci 2006 provided no information about the side-effects of each group, but found similar occurrences in both groups. Other side-effects described by Inan 1997 included endometritis (ethacridine lactate group 4.1%, PGE2 group 3.3%; difference not significant).

#### Comparison 24: ethacridine lactate versus normal saline

One trial (Zauva 1989) was included in this comparison. In total, 37 women were eligible for analysis. No differential effect was found between extra-amniotic ethacridine lactate and extra-amniotic normal saline regarding the induction-to-abortion interval (Analysis 24.1), excessive blood loss (Analysis 24.2), pain (Analysis 24.3), vomiting (Analysis 24.4) or rate of uterine rupture (Analysis 24.5).

#### DISCUSSION

Second trimester medical abortion regimens have evolved greatly over the past 20 years with increasing availability of prostaglandin analogues and anti-progesterone agents such as mifepristone. Older regimens such as instillation of hypertonic saline or prostaglandin  $F_{2\alpha}$  although effective in provoking abortion, were associated with higher rates of serious adverse events than are modern methods (Bygdeman and Gemzell-Danielsson 2008).

Randomised comparisons included in this review demonstrate that misoprostol is the prostaglandin analogue of choice: it is as effective or more effective than other studied prostaglandins and has the preferable characteristics of heat stability and multiple administrative routes. However, in settings where prostaglandins are not available for second trimester medical abortion, extraamniotic instillation of ethacridine lactate may be an alternative (Comparisons 23, 24) (Hou 2010). However, limited information is available percentage of women needing a surgical intervention for incomplete abortion and the safety outcomes of ethacridine lactate, given the small number of subjects studied. When using extra-amniotic instillation of drugs, the catheter tends to be expelled as the cervix dilates, before the abortion process is self-

sustaining. For this reason, supplementary infusions of oxytocin are commonly used (Kelekci 2006; WHO technical report series) which also increases the associated costs. Furthermore, intra-amniotic injection of drugs is potentially dangerous as accidental injection into maternal tissue or placenta can result in local tissue damage or harmful absorption into the maternal circulation (WHO technical report series). For this reason, the drugs should only be given by skilled operators. Intra-amniotic injection of drugs may also induce infection into the amniotic cavity (WHO technical report series).

Misoprostol when used alone is an effective inductive agent; however, it appears more efficient when combined with mifepristone, although the evidence from randomised trials is limited. In fact, there is only one relatively small randomised study (Kapp 2007) comparing the effect of misoprostol + mifepristone with misoprostol only (Comparison 2). This study demonstrated that the addition of mifepristone in second trimester abortion reduces the induction to abortion interval from 18 hours (95% CI 1 to 22) to 10 hours (95% CI 8 to12), while the occurrence of side-effects in both groups was similar. Indirect evidence, however, suggests a beneficial effect of adding mifepristone to prostaglandin tablets or gel since the induction-to-abortion interval is generally shorter in regimens using mifepristone + prostaglandins (Comparisons 1, 3, 4, 5 and 7) than those using prostaglandins alone (Comparisons 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 19). Additionally, mifepristone is known to potentiate the uterine effect of misoprostol and is superior to misoprostol alone in first trimester abortion.

Misoprostol may be administered by different routes, the oral route being the least effective (Comparisons 3, 4 and 5). For regimens using misoprostol, vaginal dosing appears to be the most efficient when compared to both oral and sublingual regimens. Among multiparous women undergoing medical abortion with misoprostol alone, sublingual administration appears equally effective as vaginal administration. No study of second trimester medical abortion has compared vaginal with buccal administration of misoprostol.

The optimal dose of vaginally administered misoprostol is difficult to ascertain since there are no randomised studies comparing various dosing schemes for vaginal administration. Four randomised clinical trials showed that the induction to abortion interval with 3-hourly vaginal administration of prostaglandins was significantly shorter than 6-hourly administration without significant increase in side-effects (Comparisons 15 and 16).

There is insufficient data to make any gestational, age-specific recommendations on the dosage and regimen for abortion. Since the uterus becomes more sensitive to prostaglandins with increasing gestational age, reducing the dosage or frequency of administration should be considered at later gestational ages (Ho 2007). The age range considered in this review includes 12 through 28 weeks of gestation. Overall, from the design of the included studies, there is no indication for confounding by gestational age.

Other considerations for second trimester medical abortion regimens which could not be addressed in this review include the effect on the abortion process of the use of pre-procedure feticide to avoid the occurrence of a fetus with signs of life at abortion, and therapeutic strategies for women who have not aborted after 24 hours of treatment. There are considerable differences in practices regarding the management of the placenta following the expulsion of the fetus. We considered surgical evacuation any procedure where an instrument was introduced into the uterine cavity. Indications for surgical evacuation include the removal of retained products of the placenta and heavy vaginal bleeding, where reported. Fewer women required surgical evacuation when misoprostol was administrated vaginally when compared to women having mid-trimester abortion by intra-amniotic instillation of  $PGF_{2\alpha}$  (OR 0.52, 95% CI 0.31 to 0.87) (Comparison 9). Apart from the latter finding, there were no statistically significant differences in reported frequencies of surgical removal of the placenta among women undergoing misoprostol-induced abortions when compared to other regimens.

Diarrhoea is the most common adverse reaction that has been reported consistently with misoprostol, but it is usually mild and self limiting. Nausea and vomiting may also occur and generally resolves in two to six hours (Tang 2007). Uterine rupture is a rare but serious complication of abortion in the second trimester of pregnancy, especially in women with a previous uterine scar (Berghella 2009). Uterine rupture is uncommon and did not occur during any of the included trials; thus, its relative risk with differing medical regimens are not informed by this review.

#### Summary of main results

Thirty-six randomised controlled trials were included in the review. The included studies addressed the various agents for pregnancy termination and methods of administration which were grouped into 28 comparisons. When used alone, misoprostol is an effective inductive agent, though it appears to be more effective in combination with mifepristone.

Misoprostol is preferably administered vaginally, although among multiparous women sublingual administration appears equally effective. The optimal dose of vaginally administered misoprostol could not be determined, as no randomised studies could be identified. Low doses of misoprostol are associated with fewer side-effects, while moderate doses are more efficient in completing abortion. Four randomised controlled trials showed that the induction to abortion interval with 3-hourly vaginal administration of prostaglandins is significantly shorter than 6hourly administration without a significant increase in side-effects.

Many studies reported the need for surgical evacuation in a considerable number of women undergoing mid-trimester termination. Indications for surgical evacuation include the removal of retained products of the placenta and heavy vaginal bleeding. Fewer women required surgical evacuation when misoprostol was administrated vaginally when compared with those having intra-amniotic instillation of PGF<sub>2a</sub>. Apart from the latter finding, there were no statistically significant differences in reported frequencies of surgical removal of the placenta among women undergoing misoprostol-induced abortions when compared to other regimens. Diarrhoea was more common among women having misoprostol when compared to other agents. However, diarrhoea is reportedly mild and self limiting.

#### Overall completeness and applicability of evidence

The results of this review fit well into the current practices of midtrimester termination of pregnancy.

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#### Quality of the evidence

All randomised controlled trials, most of these being unblinded. Given the heterogeneity of the some studies included in the review, the internal validity of the findings is limited.

#### Potential biases in the review process

None.

# Agreements and disagreements with other studies or reviews

Agree with recent Society for Family Planning Guidelines, in press.

#### AUTHORS' CONCLUSIONS

#### **Implications for practice**

The results of this review suggest that the most efficient regimen for medical abortion in the second trimester is the combination of mifepristone and misoprostol. If mifepristone is not available, misoprostol alone is a reasonable alternative. The available data suggest that vaginal administration is the most efficient route of administration, and 3-hourly intervals of administration are more effective than 6-hourly intervals. Meta-analysis of the various randomised controlled trials on misoprostol was hampered by the heterogeneity in medical regimens used among the included trials. Included studies indicate that adverse effects of misoprostol are usually mild and dose dependant. Apart from pain resulting from uterine contractions, diarrhoea is the most common side-effect that has been reported consistently with misoprostol. There are considerable differences in practices regarding the management of the placenta following the expulsion of the fetus.

#### **Implications for research**

This review highlights the importance of developing a standardised medical method for women requesting mid-trimester abortion. Further research is needed to evaluate the gestational-age-specific dosage of misoprostol for mid-trimester abortion. In addition, more data are needed to guide medical and/or surgical strategies for women with a uterine scar resulting from prior hysterotomy (see Berghella 2009) and for those who failed to abort within 24 hours or five doses of misoprostol. Finally, more research is needed to evaluate the additional value, optimal dose and timing of mifepristone when used in combination with misoprostol.

#### ACKNOWLEDGEMENTS

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#### CHARACTERISTICS OF STUDIES

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

#### Akour

koury 2004	
Methods	Computer-generated randomisation sequence with stratification for participating centre and gesta- tional age (≥20 weeks versus < 20 weeks) using blocks of 6. A central office allocated study patients to groups using sealed opaque envelopes. Women were randomly assigned.
Participants	136 pregnant women (group I: 84, group II: 52)
	Inclusion criteria: singleton, live fetus at 15 to 24 weeks' gestation with a complex fetal anomaly and/or abnormal fetal karyotype were included.
	Exclusion criteria: allergy to prostaglandins, a previous classic cesarean section or hysterotomy, active bleeding, severe asthma, severe oligohydramnios, pre-labor rupture of membranes.
Interventions	Group I: 400 mg of misoprostol in the posterior fornix of the vagina every 4 hours for a total of 6 doses or until delivery occurred. If after 24 hours no labor commenced, an intravenous solution of oxytocin, 100 U/of L Ringer's lactate at 100 mL per hour, was commenced.
	Group II: 400 μg misoprostol orally every 4 hours for a total of 6 doses or until delivery occurred. If after 24 hours no labor commenced, an intravenous solution of oxytocin, 100 U/of L Ringer's lactate at 100 mL per hour, was commenced.
Outcomes	Primary outcome: time from the start of the procedure to placental delivery.
	Secondary outcomes: incidence of major and minor maternal complications, women's views of the method and the success rate for culture of fetal umbilical cord.
Notes	In this study, women were randomly assigned to 1 of 3 groups: intra-amniotic PGF2a, vaginal misopros- tol, or oral misoprostol. (n=217). The women receiving PGF2a were excluded from our analyses, be- cause of the use of laminaria.
	Definition of abortion: expulsion of the fetus and placenta.
	No clear information was provided regarding the policy of evacuation of the uterus.
	No major complications occurred.

Zieman 1997

**Risk of bias** 

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.



#### Armatage 1996

Methods	Patients were randomised into 2 groups using sealed sequentially numbered envelopes.		
Participants	99 pregnant women (group I: 50, group II: 49)		
	Inclusion criteria: uncomplicated pregnancies, between 12-20 weeks gestation.		
	Exclusion criteria: multiple pregnancy, known fetal abnormality, significant maternal illness.		
Interventions	Group I: gemeprost pessaries at 3-hourly intervals up to a maximum of 5 in 24 hours, until fetal expulsion.		
	Group II: gemeprost pessaries at 6-hourly intervals until fetal expulsion.		
	Where abortion did not occur within 48 hours, an intravenous oxytocin infusion was commenced un- less delivery was deemed imminent.		
Outcomes	Primary outcome: abortion interval, abortion rates.		
	Secondary outcomes: analgesia, side-effects, surgical evacuations.		
Notes	Definition of abortion: expulsion of the fetus.		
	Following delivery of the fetus, intramuscular Syntometrine (ergometrine maleate 500 μg and oxytocin 5 iu, Sandez Products Limited) was given.		
	One women received a blood transfusion (group 1).		
	Women underwent surgical evacuation if the placenta was retained or did not appear intact.		

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

#### Bartley 2002

Methods	Randomisation was carried out using opaque envelopes. These envelopes were sealed, then shuffled and numbered consecutively in two batches of 50.	
Participants	100 pregnant women (group I: 50, group II: 50).	
	Inclusion criteria: gestation 12 to 20 weeks.	
	No exclusion criteria were reported. A history of previous caesarean section was not considered a rea- son for exclusion.	
	A history of previous caesarean section was not considered a reason for exclusion.	
Interventions	All: 200 mg mifepristone and admission followed approximately 36 hours later:	

Medical methods for mid-trimester termination of pregnancy (Review)

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Bartlev 2002 (Continued)			
Group I: 800 μg misoprostol tablets inserted in the posterior vaginal fornix followed by 400 μg mi prostol tablets orally every 3 hours for a maximum of four doses over the first 24 hours;			
	Group II: 1 mg gemeprost inserted in the posterior vaginal fornix every 6 hours for a maximum of fo doses over the first 24 hours.		
	If abortion did not occu maximum of five doses the abortion was comp evacuation.	ur within 24 hours, 1 mg vaginal gemeprost was administered every 3 hours to a s over the next 12 hours. If abortion did not occur after this course of gemeprost, oleted by intravenous oxytocin, repeated course of gemeprost or dilatation and	
Outcomes	Primary outcome: prostaglandin to abortion interval.		
	Secondary outcomes: differences in percentage of women delivered by 24 hours, incidence in side effects and adverse events.		
Notes	No clear definition of abortion.		
	One woman required a blood transfusion and an emergency evacuation of the uterus due to severe haemorrhage.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal	

age, gestational age and parity.

Bebbington 2002		
Methods	Randomization was performed with a series of sequentially numbered opaque envelopes that con- tained allocations determined through the use of a random number table.	
Participants	114 pregnant women (group I: 49, group II: 65)	
	Inclusion criteria: midtrimester abortion.	
	Exclusion criteria: hypersensitivity to prostaglandins, inability to understand English to ensure in- formed consent.	
Interventions	Group I: misoprostol 400 μg in the posterior vaginal fornix every 4 hours.	
	Group II: misoprostol 200 $\mu g$ orally every hour for 3 hours and then 400 $\mu g$ orally every 4 hours.	
	If the patient was undelivered after 24 hours, the attending physician determined further management. The options available were to increase the dosage of misoprostol using the same route of administra- tion, to change the route of administration of the misoprostol, to proceed with a high-dose oxytocin in- fusion, or to proceed with surgical evacuation of the uterus.	
Outcomes	Primairy outcomes: induction to abortion interval.	
	Secondary outcomes: maternal fever >38°C; maternal infection defined as maternal fever, elevated white blood cell count, and the need for antibiotics in the postabortion period; maternal side effects	

<b>Bebbington 2002</b> (Continued) from the medication including nausea or diarrhoea, blood loss, the need for additional oper vention; and the failure to achieve a medical termination of pregnancy.			
Notes	Definition of abortion: expulsion of the fetus. If the placenta remained undelivered after 2h, an attempt was made at manual extraction under gener- al anaesthesia.		
	No major complications reported.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal	

age, gestational age and parity.

#### Behrashi 2008

Methods	Random assignment, not specified.			
Participants	60 pregnant women (group I: 30, group II: 30)			
	Inclusion criteria: 14-28	3 weeks gestation.		
	Exclusion criteria: cont controlled convulsion,	raindications to prostaglandin therapy, placenta previa, cervical changes, un- glaucoma, inflammatory bowel disease.		
Interventions	Group I: 400 μg misoprostol, vaginally			
	Group II: 400 µg misop	rostol, orally		
	These regimens was fo	These regimens was followed by 400 $\mu g$ of misoprostol up to 3 doses, if needed.		
	After delivery: 30 unit oxytocin (in 1000 ml Ringer's solution).			
Outcomes	Complete expulsion, in	duction to abortion interval, side-effects, surgical evacuation.		
Notes	Definition of abortion: expulsion of fetus and placenta.			
	No major complications occurred.			
	No time interval was given by the authors.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Allocation concealment?	Low risk	B - unclear		
Blinding? All outcomes	High risk			

#### Behrashi 2008 (Continued)

Free of other bias?

Low risk

No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Bhattacharjee 2008				
Methods	The patients were rand protocol. A computer-generated groups. The allocation was com prepared by the statistician of ea	domly allocated into two groups using a computer-generated randomisation randomisation sequence was used to assign participants into two treatment acealed in sealed, sequentially numbered, brown envelopes, which had been ach centre and handed over to the respective pharmacy department.		
Participants	277 pregnant women (	group l: 139, group ll: 138)		
	Inclusion criteria: 13 - 2	20 weeks singleton pregnancy, young healthy women.		
	Exclusion criteria: gest	Exclusion criteria: gestation < 13 or > 20 weeks, contraindication for misoprostol use.		
Interventions	Group I: vaginal administration 400 $\mu g$ misoprostol at the interval of three hours, up to a ma five doses over 24h.			
	Group II: sublingual ad	ministration 400 $\mu g$ misoprostol, at the interval of three hours, up to a maxi-		
	mum five doses over 24h. The patients were instructed to keep the tablets under the tongue until these were dissolved and not to spit out or swallow the content for at least one hour post-administration.			
	Those women, who fai of misoprostol, with th abort after 48 h, the re ic 0.1% ethacridine lac in the cervical canal six	led to abort within 24 h of initiation of the treatment,received a second course le same allocated regimen, over a period of another 24 h. If a woman failed to gimen was declared unsuccessful and she was offered a regimen of extra amniot- tate infusion (single instillation) or repeated doses of dinoprostone gel (0.5 mg) (-hourly up to a maximum of three doses.		
Outcomes	Primary outcomes: ind	luction to abortion interval, abortion within 24 and 48 hours.		
	Secondary outcomes:	blood loss, surgical evacuations, side-effects.		
Notes	Definition of abortion: expulsion of fetus and placenta without operative intervention.			
	Exploration of the uter centa was found to be	us was performed under deep sedation or short general anaesthesia if the pla- incompletely expelled.		
	No major complications reported.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Allocation concealment?	Low risk	A - adequate		
Blinding? All outcomes	High risk			
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.		

#### Borgida 1995 Methods Sequentially numbered, sealed, opaque envelopes containing indicator cards and were opened at enrolment. The randomisation sequence was determined by a random-number table and a block size of 6. Participants 50 pregnant women (group I: 27, group II: 23) Inclusion criteria: abnormal 14-24 weeks pregnancy, age 18-45 years. Exclusion criteria: allergies to medications, cardiac/pulmonary/renal disease. Interventions All: pre-med (25 mg diphenhydramine hydrochloride, 10 mg metoclopramide hydrochloride, 5 mg diphenoxylate hydrochloride, 650 mg acetaminophen) every 4-6 hours + 30 minutes after first dose: Group I: 250 $\mu$ g IM 15M PGF<sub>2 $\alpha$ </sub> injections every 3 hours; Group II: 20 mg intravaginal PGE<sub>2</sub> every 3 hours. After delivery, all patients received oxytocin 40 U/L, and if the placenta was not delivered within approximally 2 hours or excessive bleeding occurred, a curettage was performed. Outcomes Primary outcomes: induction to abortion interval, abortion within 24 hours. Secondary outcomes: surgical evacuation, side-effects. Notes Definition of abortion: expulsion of fetus. No major complications reported.

Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Chai 2009

Methods	The randomisation was done by computer-generated random numbers and the group assignments were put into sealed, opaque envelopes. The randomisation envelope was opened by the research nurse after recruitment. The investigating team members and the research nurse responsible for recruitment were not aware of the randomisation.
Participants	141 pregnant women (group I: 70, group II: 71) were recruited from the Hong Kong centre and Shanghai centre.
	Inclusion criteria: healthy women aged 18 or older who requested termination of second trimester pregnancy at 12–20 weeks of gestation and were willing to comply with the schedule of follow-up visits.
	Exclusion criteria: any contraindications to mifepristone, including adrenal disease or steroid-depen- dent cancer; any contraindications to misoprostol, including mitral stenosis, glaucoma, sickle cell anaemia, diastolic pressure over 100 mmHg, severe asthma or known allergy to prostaglandin; history or evidence of thrombo-embolism, severe or recurrent liver disease or pruritus of pregnancy; a known



Chai 2009 (Continued)	
	history of or active medical disease; a history of regular use of prescription drugs; an intrauterine con- traceptive device in utero; a haemoglobin level ,100 g/l or abnormal liver or renal function tests; breast- feeding or heavy smoker of more than 20 cigarettes per day.
Interventions	Group I: 200 mg mifepristone and 36–38 h later: 600 μg misoprostol vaginally every 3 h for a maximum of four doses.
	Group II: 200 mg mifepristone was given orally and 600 μg misoprostol was given vaginally simultane- ously, followed by 400 μg vaginal misoprostol every 3 h for a maximum of four doses.
	The patient was reassessed if abortion had not occurred after 24 h. If there were no signs and symp- toms suggestive of imminent abortion, a second course of vaginal misoprostol was given for a maxi- mum of five doses (600 µg for the first dose followed by 400 µg every 3 h for a maximum of four doses). If abortion still did not occur, gemeprost was given to terminate the pregnancy.
Outcomes	Primary outcomes: success rate at 24 h.
	Secondary outcomes: difference in the induction-to-abortion interval and the frequency of side effects between two groups.
Notes	Definition of abortion: expulsion of fetus.
	No major complications reported.
	Six patients from Hong Kong centre (five from the immediate dosing group and one from the conven- tional dosing group) required suction evacuation of the uterus for retained placenta before discharge from the hospital. All patients from Shanghai centre had dilatation and curettage the day following abortion, as it was the routine practice in that hospital.
Risk of bias	
Bias	Authors' judgement Support for judgement

Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

el-Refaey 1993			
Methods	Randomisation by sealed envelope selection.		
Participants	60 pregnant women (group I: 30, group II: 30)		
	Inclusion criteria: 13-20 weeks gestation.		
	Exclusion criteria: none reported.		
Interventions	600mg mifepristone (36-48 hours later followed by):		
	Group I: misoprostol 400 μg orally, every 3 hrs, max 3 doses. If abortion did not occur: two further doses of vaginal gemeprost 1 mg, every 3 hrs;		
	Group II: gemeprost 1 mg pessaries vaginally, every 3 hrs, max 5 doses.		

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#### el-Refaey 1993 (Continued)

Outcomes	Primary outcome: abortion within 24 hours.		
	Secondary outcomes: surgical evacuation, side-effects.		
Notes	Definition of abortion: expulsion of fetus and placenta.		
	No information was provided regarding the policy of evacuation of the uterus.		
	No major complications reported.		

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

#### El-refaey 1995

Methods	Randomisation using computer-generated random number tables. A series of numbered, sealed, opaque envelopes was prepared containing allocation.		
Participants	69 pregnant women (group I: 34, group II: 35)		
	Inclusion criteria: 13-20	) weeks gestation.	
	Exclusion criteria: none	e reported.	
Interventions	All: mifepristone 600 μg orally + vaginal misoprostol 600 μg (first dose)		
	Group I: oral misoprost	col 400 μg every 3 hours, max 5d;	
	Group II: vaginal misop	prostol 400 μg every 3 hours, max 5d.	
	If after the fifth dose, a	bortion had not occurred, 1 mg gemeprost was administered the next morning.	
Outcomes	Primary outcomes: ind	uction to abortion interval, abortion within 24 hours.	
	Secondary outcomes:	side-effects.	
Notes	Definition of abortion:	abortion occurring after the fifth dose.	
	One patient suffered fr istration of 600 μg miso	om rigours, vomiting and eruption of a maculopapular rash following the admin- oprostol.	
	If the placenta was reta	ained, the uterus was surgically evacuated.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	

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 El-refaey 1995 (Continued)

 Blinding?
 High risk

 All outcomes
 Free of other bias?

 Low risk
 No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Faktor 1988			
Methods	Randomisation. Authors report that there was 'no selection bias in the choice of the patients'.		
Participants	77 pregnant women (group la: 35, group lb: 17, group ll: 16, group lll: 9)		
	Inclusion criteria: mid-	trimester abortion (15-26 weeks gestation).	
	Exclusion criteria: non	e given.	
Interventions	Group Ia: 1.0g oxytetracycline hydrochloride, dissolved in 16-20 ml of normal physiological saline, in- tra-amniotic. Patients received oxytocin i.v. in increasing dosage after the appearance of uterine con- tractions un till time of abortion.		
	Group lb: 1.0g oxytetra tra-amniotic. No oxyto	cycline hydrochloride, dissolved in 16-20 ml of normal physiological saline, in- cin was given.	
	Group II: 200 cm3 amn	iotic fluid was exchanged for 200 cm3 of 20% of hypertonic saline.	
	Group III: 40 mg of PGF	$z_{2\alpha}$ , intra-amniotic.	
	Group I is considered a	s the intervention group and group II and III are considered control groups.	
Outcomes	Abortion interval, side-	-effects.	
Notes	Definition of abortion: expulsion of the fetus.		
	After expulsion of the f thesia.	etus, all patients underwent revision of the uterine cavity under general anaes-	
	No major complicatior	is described.	
	For our analysis, we die	d not include oxytetracycline hydrochloride.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	B - unclear	

Free of other bias?

No baseline characteristics of the separate groups were provided.

#### Hamoda 2005

Blinding?

All outcomes

Methods	Randomisatin by opening consecutive sealed opaque envelopes generated using random number ta-
	bles.

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High risk

Unclear risk

Hamoda 2005 (Continued)			
Participants	69 pregnant women (group I: 32, group II: 37)		
	Inclusion criteria: single	eton intrauterine pregnancy, 13-20 weeks gestation.	
	Exclusion criteria: < 16 known allergy to prosta abnormalities, breast fo	years, severe asthma, haemorrhagic disorders, treatment with anticoagulants, aglandins, history of cardiac disease, smoking over the age of 35 years with ECG eeding.	
Interventions	All: mifepristone 200mg followed 36-48 hours later by:		
	Group I: misoprostol 60	00 μg sublingually and misoprostol 400 μg sublingually every 3h;	
	Group II: misoprostol 8	00 $\mu g$ vaginally and misoprostol 400mg $\mu g$ vaginally every 3h.	
Outcomes	Primary outcome: induction to abortion interval.		
	Secondary outcomes: a side-effects.	acceptability of the route of misoprostol administration to the women and staff,	
Notes	Definition of abortion:	not specified.	
	Surgical evacuation wa fetus.	is offered to women if the placenta was not delivered within 1h of delivery of the	
	Two women suffered fr	om heavy bleeding during the abortion and needed a surgical evacuation.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding?	High risk		

All outcomes		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

#### Herabutya 2005

Methods	Random allocation by computer generated numbers. The assignments were put into sealed envelopes, which were opened when the women were recruited.	
Participants	279 pregnant women (group I: 140, group II: 139)	
	Inclusion criteria: 14-26 weeks gestation (abortion was not offered > 22 weeks apart from lethal fetal conditions).	
	Exclusion criteria: unstable cardiac disease, recent severe asthmatic attack, severe hepatic or renal im- pairment, ruptured membranes.	
Interventions	All: 600 μg misoprostol vaginally	
	Group I: every 6 hrs, max 9 d;	
	Group II: every 12 hrs, max 5 d.	
Outcomes	Primary outcome: induction to abortion interval, abortion within 24 hours.	

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#### Herabutya 2005 (Continued)

Bias	Authors' judgement Support for judgement
Risk of bias	
	No major complications reported.
	If the placenta was incomplete or failed to be expelled after 1h, an evacuation of the uterus was carried out under general anaesthesia.
Notes	Definition of abortion: expulsion of fetus.
	Secondary outcomes: side-effects.

Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Ho 1996			
Methods	Randomisation schedule was prepared as described by Meinert. Sealed envelopes with serial numbe on the front and containing the group to which the woman was randomised were opened at recruit- ment.		
Participants	50 pregnant women (g	roup I: 25, group II: 25)	
	Inclusion criteria: 14-20	) weeks gestation.	
	Exclusion criteria: regu cies, heavy smokers.	lar use of prescription drugs, IUD in utero, nursing mothers, multiple pregnan-	
Interventions	All: 200mg mifepristone orally (36-48 hours later):		
	Group I: 400 μg misopr	ostol orally, every 3 h, max 5 doses;	
	Group II: 1mg gemepro	st vaginally, every 6 hours, max 4 doses.	
	The patient was reasse tion, the pregnancy wa	essed after 24h. If there were no signs or symptoms suggestive of imminent abor- is terminated with 1 mg gemeprost every 3 hours.	
Outcomes	Primary outcome: indu	iction of abortion interval, abortion within 24 hours.	
	Secondary outcomes:	side-effects, uterine contractions, blood pressure, pulse rate.	
Notes	Definition of abortion:	not specified.	
	If the placenta was inc	omplete, an evacuation of the uterus was carried out.	
	No major complicatior	is reported.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	

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Ho 1996 (Continued)		
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and gravidity.

Ho 1997		
Methods	Randomisation schedu cans.	le as described by Meinert. Schedules were unknown to both patient and clini-
Participants	98 pregnant women (g	roup I: 49, group II: 49)
	Inclusion criteria: good	l general health, age 16-35 years, singleton pregnancy, 14-20 weeks gestation.
	Exclusion criteria: past	or present ill health, nursing mothers, IUD, smoking >10 cigarettes/day.
Interventions	All: mifepristone 200 m	ng 36-48 hours later:
	Group I: misoprostol 2	00 μg orally, and a placebo vaginally every 3 hours, max 5 doses;
	Group II: misoprostol 2	200 μg vaginally, and a placebo orally, every 3 hours, max 5 doses.
Outcomes	Primary outcome: induction of abortion, abortion within 24 hours.	
	Secondary outcomes:	side-effects, uterine contractions, blood pressure, pulse rate.
Notes	Definition of abortion: expulsion of fetus.	
	If the placenta was inc ried out.	omplete or failed to be expelled after 1/2h, an evacuation of the uterus was car-
	No major complicatior	ns reported.
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	Low risk	Blinding of participants and clinicians.
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Inan 1997

Methods	Randomly assigned.	
Participants	78 pregnant women (group I: 48, group II: 30)	
	Inclusion criteria: 13-24 weeks gestation, Bishop score <4.	
	Exclusion criteria: none described.	



Inan 1997 (Continued)		
Interventions	Group I: extra-amniotic ethacridine lactate (Rivanol). A No 16 Foley catheter was placed into the uterus. Following inflammation of the balloon of the catheter to 20-30 ml, an average of 10 ml of 0.1 % sterile ethacridine lactate solution per gestational week was instilled extra-amniotically. The catheter was left in place for 24 hours, if not expelled earlier.	
	Group II: 2.5 ml gel containing 0.5 mg PGE2, intracervical (Cerviprost 0.5 mg gel Organon).	
	Group III: extra-amniotic ethacridine lactate combined with oxytocin infusion. 10-20 units/5% DW IV oxytocin induction was started within 2-4 hours following the ethacridine lactate instillation.	
	For analyses, we did not include group III.	
Outcomes	Successful abortion rates, side-effects.	
Notes	Definition of abortion: Complete evacuation of fetus and placental tissues from the uterus within 24 hours.	
	No major complications described.	

#### Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Карр 2007	
Methods	Sequentially distributed study number in an allocation ratio of 1:1. The randomisation scheme used permuted blocks of eight, selected by a random number generator created using SAS V.9.3. The pharmacy dispensed the study medication.
Participants	64 pregnant women (group I: 32, group II: 32)
	Inclusion criteria: 18-23 weeks of gestation.
	Exclusion criteria: known allergy to mifepristone/misoprostol/prostaglandins, preexisting intrauterine fetal demise, premature preterm rupture of membranes, IUD in place, history of chronic adrenal failure, porphyrias, concurrent long term corticosteroid treatment.
Interventions	All: intra-amniotic injection of 1.5 mg digoxin, then:
	Group I: 200 mg mifepristone, 20–24 hours after study capsule: misoprostol induction using 400 μg misoprostol, followed by 200 μg every 6h (buccally);
	Group II: 2 placebo tablets (vitamin C). 20–24 hours after study capsule: misoprostol induction using 400 μg misoprostol, followed by 200 μg every 6h (buccally).
Outcomes	Primary outcome: median interval from first misoprostol dose to fetal expulsion.
	Secondary outcomes: women delivering within 24 hours, proportion of women with a complete deliv- ery requiring additional


Kapp 2007 (Continued)	treatment for retained placenta, the amount of required pain medication, length of hospital stay, side- effects.			
Notes	Definition of abortion: expulsion of fetus.			
	If the placenta was incomplete or failed to be expelled after 4h, an evacuation of the uterus was carried out under general anaesthesia.			
	Heavy bleeding occurr	ed in two women.		
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Allocation concealment?	Low risk	A - adequate		

Blinding? All outcomes	Low risk	Blinding for participants, clinicians, and researchers.
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

## Kelekci 2006

Methods	Patients were randomised to one of four treatment groups by a series of computer-generated random numbers.	
Participants	178 pregnant women (group I: 93, group II: 85)	
	Inclusion criteria: genetic indications, 13-24 weeks gestation.	
	Exclusion criteria: previous uterine scar, pulmonary, hepatic, renal or cardiovascular disease, intrauter- ine death, vaginal bleeding, uterine contractions, any signs of cervical dilatation, a Bishop score of 4, vaginal infection, a discrepancy of 2 weeks between the gestational age determined by last menstrual period and ultrasonographic gestational age	
Interventions	Group I: 200 $\mu g$ misoprostol, vaginally, followed by 100 $\mu g$ of oral misoprostol every 4 hour for 24 hrs.	
	Group II: extra-amniotic ethacridine lactate, 10 ml instilled per gestational week, to a maximum of 200 ml.	
	Group III: combination of misoprostol and oxytocin. 200 μg misoprostol, vaginally, followed by 100 μg of oral misoprostol every 4 hour for 24 hrs. An initial dose of 6 mU/min oxytocin was given, followed by additional 6 mU/min doses every 20 min.	
	Group IV: combination of ethacridine lactate and oxytocin. Ethacridine lactate was given extra-amniot- ic, 10 ml instilled per gestational week, to a maximum of 200 ml. Oxytocin was administered in a similar way as in group III.	
	For analyses, we did not include group III and IV.	
Outcomes	Time to induce abortion, success/failure rates, side-effects and complications.	
Notes	Definition of abortion: complete evacuation of fetal and placental tissues within 24 h of the initiation of medical abortion.	
	14 cases of endometritis and 20 cases of incomplete abortions were described.	

## Kelekci 2006 (Continued)

# Risk of bias

RISK OF DIUS					
Bias	Authors' judgement	Support for judgement			
Allocation concealment?	Low risk	B -unclear			
Blinding? All outcomes	High risk				
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.			
Makhlouf 2003					
Methods First 90 patient were randomly assigned into three groups (see notes). Randomisation of the remain 40 patients involved the group using misoprostol and glyceryl trinitrate only, because of shortage of nance to buy more prostaglandin tablets. Randomisation involved computer-generated random ta		andomly assigned into three groups (see notes). Randomisation of the remainig ne group using misoprostol and glyceryl trinitrate only, because of shortage of fi- istaglandin tablets. Randomisation involved computer-generated random tables.			
Participants	80 pregnant women (group I: 50, group II: 30)				
	Inclusion criteria: 13-2	8 weeks gestation, Bishop score ≤ 4.			
	Exclusion criteria: cont preterm rupture of me vious scarred uterus or	tra-indication to induction of abortion by medical methods, e.g. placenta previa, mbranes (PROM) and transverse lie, grand-multiparous women (parity ≥ 5), pre- r contra-indications to the drugs.			
Interventions Group I: 100 μg misopros		rostol, vaginally every 4 hours, with a maximum dose of 500 $\mu$ g (five doses).			
	Group II: 6 mg prostagl	andin E2 , vaginally every 6 hours, with a maximum of 24 mg (four doses).			
	Women with a method by using a Foley's cath not occur after 24 hou sion was used. We excl 24 hour.	I failure and a Bishop score ≤ 4 or absence of uterine activity continued abortion eter. If uterine contractions started or the Bishop score was > 4, but expulsion did rs of after expulsion of the Foley catheter, intravenous 5mIU/min of oxytocin infu- uded the outcome 'induction to abortion interval' because of this method after			
Outcomes	Induction to abortion i	nterval, abortion within 24 hours, side-effects.			
Notes	Definition of method failure: absence of fetal expulsion of absence of signs of impending expulsion (regular uterine contractions and cervical dilatation) at the end of 24 hours.				
	No clear information w	vas provided regarding the policy of evacuation of the uterus.			
	No major complicatior	ns described.			
	Study included 130 pre the use of nitric oxide o evert 6h, with a maxim	egnant women into three groups. The third group (n = 50) were randomised for donor (glyceryl trinitrate) tablets. Women received 500 μg of glyceryl trimitrate num of 5 doses. For this review, this group was excluded.			

**Risk of bias** 

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	

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## Makhlouf 2003 (Continued)

Free of other bias?

Low risk

No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Mehta 1975 a	
Methods	Prepared envelopes indicating one of the methods were picked up serially; the investigators being blind to what the envelopes contained till they opened them.
Participants	67 pregnant women (group I: 33, group II: 34)
	Inclusion criteria: 15-20 weeks gestation.
	Exclusion criteria: none given.
Interventions	Group I: 20% hypertonic saline, 200 ml.
	Group II: single dose, 50mg PGF $_{2\alpha}$ .
Outcomes	Abortion rates, side-effects.
Notes	Definition of abortion: when complete (spontaneous evacuation of all products of conception) or in- complete abortion (total or partial retainment of placenta or membranes) occurred within 72 hours.
	No information was provided regarding the policy of evacuation of the uterus.
	One women in the single dose $PGF_{2\alpha}$ group received a blood transfusion.

### **Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Mehta 1975 b	
Methods	Prepared envelopes indicating one of the methods were picked up serially; the investigators being blind to what the envelopes contained till they opened them.
Participants	66 pregnant women (group I: 33, group II: 33)
	Inclusion criteria: 15-20 weeks gestation.
	Exclusion criteria: none given.
Interventions	Group I: 20% hypertonic saline, 200 ml.
	Group II: multiple doses of 25mg PGF $_{2\alpha}$ , given at 0 hours and 6 hours. Similar doses were instilled at 24 hours and 30 hours when necessary.

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## Mehta 1975 b (Continued)

Outcomes	Abortion rates, side-effects.
Notes	Definition of abortion: when complete (spontaneous evacuation of all products of conception) or in- complete abortion (total or partial retainment of placenta or membranes) occurred within 72 hours.
	No information was provided regarding the policy of evacuation of the uterus.

One women in the single dose  $\mathsf{PGF}_{2\alpha}$  group received a blood transfusion.

## **Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

### Muzsnai 1979 a

Methods	Random assignment.		
Participants	100 pregnant women (group I: 50, group II: 50)		
	Inclusion criteria: 16-24 weeks of gestation.		
	Exclusion criteria: history of uterine surgery.		
Interventions	Group I: PGF $_{2\alpha}$ (20mg) + 100 mL 5% NaCl (5g), intra-amniotic. No amniotic fluid removed.		
	Group II: PGF $_{2\alpha}$ (20mg) + 100 mL 10% NaCl (10g), intra-amniotic. No amniotic fluid removed.		
	All patients received i.v. oxytocin stimulation 40 mU/min.		
Outcomes	Instillation to abortion time, abortion interval, complications, side-effects.		
Notes	Definition of abortion: none given.		
	Incomplete abortion: if placenta was not expelled within 2h after delivery of the fetus, of if haemor- rhage occurred.		
	Failure of abortion: if fetus was not expelled within 48h. The procedure was then repeated.		
	Instillation abortion interval: time from amniocentesis to expulsion of fetus.		
	No major complications described.		
Risk of bias			
Bias	Authors' judgement Support for judgement		
Allocation concoalmont?	Low risk Punclear		

	Low Hold	0	difeted
Blinding?	High risk		



Muzsnai 1979 a (Continued) All outcomes

Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal
		age, gestational age and parity.

Muzsnai 1979 b	
Methods	Random assignment. After completion of 50 patients in group I and II, the remaining patients were as- signed to group II, because of favourable outcome.
Participants	130 pregnant women (group I: 50, group II:80)
	Inclusion criteria: 16-24 weeks of gestation.
	Exclusion criteria: history of uterine surgery.
Interventions	Group I: PGF $_{2\alpha}$ (20mg) + 100 mL 5% NaCl (5g), intra-amniotic. No amniotic fluid removed.
	Group II: PGF $_{2\alpha}$ (20mg) + 100 mL 10% NaCl (10g), intra-amniotic. 100mL amniotic fluid removed.
	All patients received i.v. oxytocin stimulation 40 mU/min.
Outcomes	Instillation to abortion time, abortion interval, complications, side-effects.
Notes	Definition of abortion: none given.
	Incomplete abortion: if placenta was not expelled within 2h after delivery of the fetus, of if haemor- rhage occurred.
	Failure of abortion: if fetus was not expelled within 48h. The procedure was then repeated.
	Instillation abortion interval: time from amniocentesis to expulsion of fetus.
	No major complications described.
Risk of bias	
Bias	Authors' judgement Support for judgement

Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

# Muzsnai 1979 c

Methods	Random assignment. After completion of 50 patients in group I and II, the remaining patients were as- signed to group I, because of favourable outcome.	
Participants	255 pregnant women (group I: 205, group II: 50)	
	Inclusion criteria: 16-24 weeks of gestation.	

Muzsnai 1979 c (Continued)	Exclusion criteria: history of uterine surgery.		
Interventions	Group I: PGF <sub>2<math>\alpha</math></sub> (20mg) + 25 mL 20% NaCl (5g), intra-amniotic. All amniotic fluid removed.		
	Group II: PGF $_{2\alpha}$ (20mg) + 100 mL 10% NaCl (10g), intra-amniotic. No amniotic fluid removed.		
	All patients received i.v. oxytocin stimulation 40 mU/min.		
Outcomes	Instillation to abortion time, abortion interval, complications, side-effects.		
Notes	Definition of abortion: none given.		
	Incomplete abortion: if placenta was not expelled within 2h after delivery of the fetus, of if haemor- rhage occurred.		
	Failure of abortion: if fetus was not expelled within 48h. The procedure was then repeated.		
	Instillation abortion interval: time from amniocentesis to expulsion of fetus.		
	No major complications described.		
Risk of bias			

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Muzsnai 1979 d	
Methods	Random assignment. After completion of 50 patients in group I and II, the remaining patients were as- signed to both groups, because of favourable outcome.
Participants	285 pregnant women (group I: 205, group II: 80)
	Inclusion criteria: 16-24 weeks of gestation.
	Exclusion criteria: history of uterine surgery.
Interventions	Group I: PGF $_{2\alpha}$ (20mg) + 25 mL 20% NaCl (5g), intra-amniotic. All amniotic fluid removed.
	Group II: PGF $_{2\alpha}$ (20mg) + 100 mL 10% NaCl (10g), intra-amniotic. 100mL amniotic fluid removed.
	All patients received i.v. oxytocin stimulation 40 mU/min.
Outcomes	Instillation to abortion time, abortion interval, complications, side-effects.
Notes	Definition of abortion: none given.
	Incomplete abortion: if placenta was not expelled within 2h after delivery of the fetus, of if haemor- rhage occurred.
	Failure of abortion: if fetus was not expelled within 48h. The procedure was then repeated.



Muzsnai 1979 d (Continued)

Instillation abortion interval: time from amniocentesis to expulsion of fetus.

No major complications described.

Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Ngai 2000	
Methods	Randomisation schedule as described by Meinert. Sealed envelopes with serial numbers were pre- pared. At enrolment, a serial number was given according to the sequence of entry.
Participants	139 pregnant women (group I: 70, group II: 69)
	Inclusion criteria: healthy women between 16-35 years, 14-20 weeks gestation.
	Exclusion criteria: regular use of prescription drugs, IUD in utero, nursing mothers, multiple pregnan- cies, heavy smokers.
Interventions	All: 200mg mifepristone + (36 - 48 h later):
	Group Ι: 400 μg misoprostol oral and a vaginal placebo (vitamin B6) every 3 hours;
	Group II: 200 $\mu g$ misoprostol vaginally and an oral placebo (vitamin B6) every 3 hours.
Outcomes	Primary outcome: abortion within 24 hours.
	Secondary outcomes: induction to abortion interval, side-effects.
Notes	Definition of abortion: not specified.
	If the placenta was incomplete, an evacuation of the uterus was carried out under general anaesthesia.
	No major complications occurred.

**Risk of bias** 

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	Low risk	Blinding for participants.
Free of other bias?	Unclear risk	No statistically significant differences between the groups in terms of maternal age and gestational age.



## Nielsen 1975

Methods	Randomisation.	
Participants	32 pregnant women (group I: 16, group II: 16)	
	Inclusion criteria: gesta	ation more than 14 weeks.
	Exclusion criteria: none	e reported.
Interventions	Group I: suprapublical/transvaginal injection of 20% saline, preceded by removal of 50 mL of amniot- ic fluid. Amount of saline depending on gestation; 14 <sup>th</sup> week 75 mL, 15 <sup>th</sup> week 100 mL, >16 <sup>th</sup> week 150 mL.	
	Group II: suprapublical niotic fluid.	/transvaginal injection of 40 mg of $PGF_{2\alpha}$ , preceded by removal of 50 mL of am-
	Both groups received a abortion did not occur restarted. PG/saline inj	an 10 IU/h oxytocin drip (100IU in one litre of 5% glucose) within half an hour. If before 200IU oxytocin was given, the infusion was stopped for 6-8h and then jection was not repeated.
Outcomes	Abortion interval, complications, side-effects.	
Notes	Definition of abortion: none given.	
	Curettage was perform	ned in cases which were considered incomplete.
	No major complication	ns described.
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No apparant differences between the groups in terms of maternal age, gesta- tional age and parity.
Nuutila 1997 a		
Methods	Randomisation was do sealed envelopes were	ne using random numbers tables into three groups. A series of numbered, prepared containing the allocation.
Participants	55 pregnant women (g	roup I: 27, group II: 28)

	Inclusion criteria: 12-24 weeks gestation, singleton pregnancies.
	Exclusion criteria: none reported.
Interventions	Group I: 100 μg misoprostol vaginally, every 6 hours, max max 6 doses.
	Group II: 1 mg gemeprost vaginally, every 3 hours, max 8 doses.
Outcomes	Primary outcome: induction to abortion interval.



## Nuutila 1997 a (Continued)

	Secondary outcomes: side-effects.	
Notes	Definition of abortion: expulsion of fetus and placenta.	
	Within 1h after the passage of the fetus, whether or not the placenta was passed, an evacuation of the uterus was carried out under general anaesthesia.	
	No major complications occurred.	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Nuutila 1997 b

Methods	Randomisation was done using random numbers tables into three groups. A series of numbered, sealed envelopes were prepared containing the allocation.		
Participants	54 pregnant women (group I: 26, group II: 28)		
	Inclusion criteria: 12-24	4 weeks gestation, singleton pregnancies.	
	Exclusion criteria: none	e reported.	
Interventions	Group Ι: 200 μg misoprostol vaginally, every 12 hours, max 3 doses.		
	Group II: 1 mg gemepro	ost vaginally, every 3 hours, max 8 doses.	
Outcomes	Primary outcome: induction to abortion interval.		
	Secondary outcomes: s	side-effects.	
Notes	Definition of abortion: expulsion of fetus and placenta.		
	Within 1h after the pass uterus was carried out	sage of the fetus, whether or not the placenta was passed, an evacuation of the under general anaesthesia.	
	No major complications occurred.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		



## Nuutila 1997 b (Continued)

Free of other bias?

Low risk

No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Nuutila 1997 c			
Methods	Randomisation was done using random numbers tables into three groups. A series of numbered, sealed envelopes were prepared containing the allocation.		
Participants	53 pregnant women (group I: 27, group II: 26)		
	Inclusion criteria: 12-24	4 weeks gestation, singletone pregnancies.	
	Exclusion criteria: non	e reported.	
Interventions	Group I: 100 μg misoprostol vaginally, every 6 hours, max 6 doses.		
	Group II: 200 μg misop	rostol vaginally, every 12 hours, max 3 doses.	
Outcomes	Primary outcome: induction to abortion interval.		
	Secondary outcomes:	side-effects.	
Notes	Definition of abortion: expulsion of fetus and placenta.		
	Within 1h after the pas uterus was carried out	sage of the fetus, whether or not the placenta was passed, an evacuation of the under general anaesthesia.	
	No major complications occurred.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.	

### **Olund 1978**

Methods	Randomly assigned.	
Participants	92 pregnant women (group I: 23, group II: 23, group III: 23, group IV: 23)	
	Inclusion criteria: 13-25 weeks gestation.	
	Exclusion criteria: none described.	
Interventions	Group I: extra-amniotic instillation of 0.1% solution of rivanol, 10 ml per gestational week. Maximum of 150 ml.	



Olund 1978 (Continued)			
	Group II: extra-amnioti hours for up to 24 hour	c instillation of 1 ml of saline containing 0.25 mg PGF <sub>2α</sub> per ml, 3 ml every 2 s. At a gestational age >16 weeks, the dose was doubled.	
	Group III: Rivanol + PGF <sub>2<math>\alpha</math></sub> , as in group I and II.		
	Group IV: Rivanol + a half dose of PGF_{2\alpha}, as in group III, except for a half dose of PGF_{2\alpha}.		
	NB: For our analysis, we	e included group I and II.	
Outcomes	Abortion time, abortion interval, side-effects.		
Notes	No definition of abortion was given.		
	No major complications described.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	B - unclear	
Blinding? All outcomes	High risk		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.	

### Ozerkan 2009

Methods	Randomisation by computer-generated number lists to two groups of 30.	
Participants	60 pregnant women (group I: 30, group II: 30)	
	Inclusion criteria: 13-24 weeks gestation.	
	Exclusion criteria: none reported.	
Interventions	Group I: 400 μg of misoprostol, vaginally, with an additional 200 μg at two-hour intervals up to five dos- es.	
	Group ΙΙ: 600 μg of misoprostol, vaginally, with an additional 400μg at four-hour intervals up to two doses.	
	Patients in either group received a maximum total dose of 1400g of misoprostol. The next dose was skipped whenever there were effective uterine contractions. If the procedure failed on the first day, it was undertaken the next day using the same protocol. Another method of termination was called in case the procedure failed on two consecutive days.	
Outcomes	Primary outcome: success rates, time to termination, blood loss, complications, side-effects and cervi- cal features defined ultrasonographically.	
Notes	Definition of abortion: expulsion of fetus.	
	Post-abortion curettage of the uterine cavity.	
	No major complications reported.	

### **Risk of bias**

Ξ



## Ozerkan 2009 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age and gestational age.

# Pongsatha 2008

Methods	Randomisation through block randomisation by the authors.	
Participants	148 pregnant women (group I: 72, group II: 76)	
	Inclusion criteria: second trimester abortion, live fetuses, closed/uneffaced cervix without labor.	
	Exclusion criteria: previous uterine scar, hypersensitivity to prostaglandins.	
Interventions	Group I: 400 mg misoprostol tablet insertion, every 3h.	
	Group II: 400 mg misoprostol gel insertion, every 3h.	
Outcomes	Primary outcome: abortion within 24 hours.	
	Secondary outcomes: side-effects.	
Notes	Misoprostol in gel form: mixing misoprostol with 3 mL 1% carboxy methyl cellulose.	
	Definition of abortion: expulsion of fetus.	
	No information was provided regarding the policy of evacuation of the uterus.	
	No major complications reported.	

## **Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

### Sorensen 1984

Methods	Use of random numbers.	
Participants	39 pregnant women (group I: 20, group II: 19)	
	Inclusion criteria:13-24 weeks of gestation.	



Sorensen 1984 (Continued)		
	Exclusion criteria: intra-uterine fetal death, cardiopulmonary disease, nephropathy, liver diseases, pre- vious operation on the uterus	
Interventions	Group I: 2x PGE2 0.75 mg within 5 hours intracervical/extra amniotic, 5 hours, later followed by oxy- tocin infusion 0.15 IU/min if no contractions.	
	Group II: PGF $_{2\alpha}$ 40 mg intra-amniotically 5 hours later followed by oxytocin drip 0.15 IU/min if no contractions.	
Outcomes	Primary outcomes: abortion success rate, induction-abortion interval.	
	Secondary outcomes: side-effects.	
Notes	Definition of abortion: expulsion of fetus.	
	If the placenta was not expelled within 2 hours, an evacuation of the uterus was performed.	
	No major complications reported.	
Risk of bias		

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Steyn 1993	
Methods	Randomisation using the balanced block method. Instructions were placed in sealed envelopes.
Participants	20 pregnant women (group I: 10, group II: 10)
	Inclusion criteria: 14-26 weeks of gestation.
	Exclusion criteria: fetal death on admission, previous uterine scars, history of asthma, active vaginal or intra-uterine infection, anhydramnios.
Interventions	Group I: 1.5 mg prostaglandin E2 (PGE2) gel extra-amniotically.
	Group II: 25 mg prostaglandin $F_{2\alpha}$ (PGF_{2\alpha}) intra-amniotically.
	Patients in both groups received oxytocin to a maximum dosage of 120 mU per minute if they had not aborted 18 hours after the original administration of either prostaglandin regimen. If the patient had not aborted within 36h, the method was regarded unsuccessful and the managing physician was free to change the management of choice.
Outcomes	Primary outcome: induction to abortion interval.
	Secondary outcomes: complications, side effects.
	Proportion of successful inductions and complications.
Notes	Definition of abortion: none given.

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Steyn 1993 (Continued)

No information was provided regarding the policy of evacuation of the uterus.

No major complications reported.

Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Su 2005	
Methods	Random allocation; computer-generated schedule randomisation; numbered, sealed, opaque enve- lope; envelopes were drawn in consecutive order.
Participants	125 pregnant women (group I: 61, group II: 64)
	Inclusion criteria: 12-24 weeks gestation.
	Exclusion criteria: multiple pregnancies, ≥ 2 previous cesarean sections, missed abortion, oligohydram- nios, severe asthma, allergy to prostaglandins.
Interventions	Group I: vaginal misoprostol 400 μg /3h, max 5d in 24 hrs.
	Group II: intra amniotic PGF2 $\alpha$ 1,5mg, max 5d in 24 hrs.
Outcomes	Primary outcome: induction to abortion interval.
	Secondary outcomes: abortion within 24 and 48 hours, the need for repeat course of medications, evacuation of uterus, adverse effects.
Notes	Definition of abortion: expulsion of the fetus.
	Evacuation of the uterus was not performed routinely.
	No major complications reported.
Risk of bias	
Bias	Authors' judgement Support for judgement

Dias	Authors Judgement	Support for Judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.



Tang 2004		
Methods	Computer-generated r	andom numbers; sealed envelopes, opened at recruitment.
Participants	220 pregnant women (group I: 112, group II: 108)	
	Inclusion criteria: 12-2	0 weeks gestation.
	Exclusion criteria: regucies, heavy smokers.	llar use of prescription drugs, IUD in utero, nursing mothers, multiple pregnan-
Interventions	Group I: Vaginal admin	istration 400 $\mu g$ misoprostol every 3h, max 5 doses in 24 hours.
	Group II: Sublingual ac	Iministration 400 $\mu g$ misoprostol every 3h, max 5 doses in 24 hours.
Outcomes	Primary outcome: succ	cess rate at 48 hours.
	Secondary outcomes:	success rate at 24 hours, side-effects.
Notes	Definition of abortion: expulsion of the fetus and placenta.	
	If the placenta was inc	omplete, evacuation of the uterus was performed.
	No major complications occurred.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.
Tang 2005		
Methods	Computer-generated r were filled and labelled	andomisation sequence; sealed, sequentially numbered treatment packs, which d in accordance with the list of randomisation.
Participants	118 women (group l: 58	8, group II: 60)

Inclusion criteria: >18 years, 12-20 weeks gestation.

Exclusion criteria: regular use of prescription drugs, IUD in utero, nursing mothers, multiple pregnancies, heavy smokers.

Interventions	all: mifepristone 200mg orally, 36-48h later:		
	Group 1: misoprostol 400 $\mu g$ sublingual and 2 placebo tablets orally every 3 hrs, max 5 d; Group 2: misoprostol 400 $\mu g$ orally and 2 placebo tablets sublingually every 3 hrs, max 5 d.		
Outcomes	Primary outcome: success rate at 24 h.		
	Secondary outcomes: induction-to-abortion interval, side-effects.		

Notes Definition of abortion: not specified.



Tang 2005 (Continued)

If the placenta was incomplete, evacuation of the uterus was performed.

No major complications occurred.

Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	Low risk	Blinding for participants and clinicians.
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

Thong 1996			
Methods	Sealed, opaque envelopes containing either of the two treatment groups. These envelopes were shuf- fled and numbered consecutively.		
Participants	100 pregnant women (group I: 50, group II: 50)		
	Inclusion criteria: 12-1	9 weeks gestation.	
	Exclusion criteria: <16	years.	
Interventions	All: 200mg mifepriston	e, 36 hours later:	
	Group I: 1mg pessary g without abortion 1 mg	gemeprost vaginally in 6 hour intervals, max 4 doses in 24 hour. After 24 hours gemeprost in 3 hour intervals, max 24 hours;	
	Group II: 0.5mg pessar mg gemeprost in 3 hou	y gemeprost vaginally in 6 hour intervals, max 4 doses in 24 h. After 24 hours 1 ur intervals.	
Outcomes	Primary outcome: abortion within 24h.		
	Secondary outcomes:	side-effects.	
Notes	Definition of abortion:	expulsion of fetus and placenta.	
	Evacuation of the uter judged to be incomple	us was carried out if the placenta was not expelled spontaneously or if it was te.	
	One woman in group II required a blood transfusion of two units because of heavy ble tion with a retained placenta after expulsion of the fetus.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		

## Thong 1996 (Continued)

Free of other bias?

Low risk

No apparent differences between the groups in terms of maternal age, gestational age and parity.

von Hertzen 2009		
Methods	A computer-generated r ipants within each centr a fixed block size of six. velopes, which were fille Magistra, Geneva, Switz	randomisation sequence was produced by WHO staff in Geneva to assign partic- re to sublingual or vaginal treatment group by randomly permuted blocks with Allocation was concealed by using sealed, opaque, sequentially numbered en- ed and labelled in accordance with the list of randomization for each centre by erland.
Participants	681 pregnant women (g	roup I: 340, group II: 341)
	Inclusion criteria: health 13–20 weeks (91–140 da	ny, older than the age of legal consent, had a single intrauterine pregnancy of ays) duration as verified by ultrasound and had haemoglobin 100 g/l or higher.
	Exclusion criteria: any ir of heavy smoking (.20 ci tected with ultrasound; mmHg; uncontrolled bro thromboembolism or liv	ndication of serious past or present illness; an allergy to misoprostol; a habit garettes/day); a scar in the uterus or cervix or any gynaecological anomaly de- mitral stenosis, glaucoma or sickle cell anaemia; diastolic blood pressure .90 onchial asthma; systolic blood pressure ,90 mmHg; history or evidence of ver disease; presence of an intrauterine device; or haemolytic disorders.
Interventions	Group I: 400 μg misopro til abortion took place.	stol vaginally, 2 placebo tablets sublingually, every 3 hours up to five doses un-
	Group II: 400 μg misopro til abortion took place.	ostol sublingually, 2 placebo tablets vaginally, every 3 hours up to five doses un-
	Placebo tablets were ma prostol tablets. The blisters wer tablets vaginally. Additio for those women who di tablets was administere	anufactured by Labatec, Geneva, Switzerland; similar shape and colour as miso- re labelled indicating which tablets were to be taken sublingually and which onal misoprostol tablets were provided to the centres to be used sublingually id not abort within 24 h. After expulsion of the fetus, one additional dose of the d.
Outcomes	Primary outcome: succe	essful abortion (including complete and incomplete abortion) within 24 h.
	Secondary outcome: su ment to expulsion of fet	ccessful abortion within 48 h induction-to-abortion interval (the start of treat- us, side effects and women's perceptions of the method.
Notes	Definition of abortion: c abortion, continuing pre	omplete or incomplete abortion, while treatment failures included missed egnancy and undetermined outcomes.
	Ten women received a b two of them for surgical	blood transfusion and three women required hospitalization after discharge, evacuation of the uterus and one for reasons unrelated to the study.
	After abortion, the prod necessary, or if it was a l was performed.	ucts of gestation were examined to see whether the abortion was complete. If local routine practice (three centres), exploration and evacuation of the uterus
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	Low risk	

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von Hertzen 2009 (Continued)

Free of other bias?

Low risk

A stratified analysis was conducted by parity because there was a highly significant interaction of treatment by parity. No apparent differences between the groups in terms of maternal age and gestational age.

Waldron 1990				
Methods	Randomisation.			
Participants	58 pregnant women (group I: 29, group II: 29)			
	Inclusion criteria: 14-20	) weeks of gestation.		
	Exclusion criteria: sign prostaglandins, cardio epilepsy, renal disease	s or symptoms of spontaneous abortion, known or suspected hypersensitivity to -pulmonary disease, hypertension, urticaria, eczema, ulcerative colitis, diabetes, , liver disease.		
Interventions	Group I: 1 mg gemepro	Group I: 1 mg gemeprost in vaginal pessaries, 3h interval, maximum of 5 doses.		
	Group II: 20 mg of PGF <sub>2</sub> hours, an alternative tr	$_{2lpha}$ in 40 ml of 20% NaCl, intra-amniotic. If abortion had not occurred within 24 reatment was commenced at the discretion of the clinician.		
	Following delivery of th discretion, and surgica in two hours.	ne fetus, oxytocin or ergometrine in routine dosages were used at the clinician's l evacuation of the uterus was performed if the placenta was not delivered with-		
Outcomes	Abortion interval, side-	effects, complications.		
Notes	Definition of abortion: abortion within 24 hours.			
	If the placenta was not	expelled within 2 hours, an evacuation of the uterus was performed.		
	No major complications described.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Allocation concealment?	Low risk	B - unclear		
Blinding? All outcomes	High risk			
Free of other bias?	Low risk	No apparent differences between the groups in terms of maternal age, gesta- tional age and parity.		

Webster 1996	
Methods	Women were randomly allocated using a series op opaque envelopes that had been prepared by using random number tables.
Participants	70 pregnant women (group I: 35, group II: 35)
	Inclusion criteria: 13-20 weeks of gestation.
	Exclusion criteria: none given.

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Webster 1996 (Continued)	
Interventions	Group I: 200 mg mifepristone prior to admission for prostaglandin. A first dose of 800 μg of misopros- tol (8.00 am) was given vaginally, followed by 400 μg doses administered orally on a 3h basis, to a maxi- mum of 4 doses.
	Group II: 600 mg mifepristone prior to admission for prostaglandin. A first dose of 800 μg of misopros- tol (8.00 am) was given vaginally, followed by 400 μg doses administered orally on a 3h basis, to a maxi- mum of 4 doses.
	If abortion had not occured following the final dose of misoprostol, the treatment was considered to be a failure and mifepristone 600 mg was given at midnight, followed by a course of 1 mg gemeprost pes- saries at 3h intervals commenced the following morning.
Outcomes	Induction to abortion interval, side effects.
Notes	Complete abortion: on clinical grounds, and then no further interventions were undertaken.
	Surgical evacuation of the uterus was performed if women did not pass the complete placenta.
	One woman from each group required a blood transfusion as a result of blood loss at this time.
Risk of bias	

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	Women in the 600 mg group were significantly older than their counterparts in the 200 mg group. No apparent differences between the groups in terms of gestational age and parity.

WHO 1976	
Methods	Computer-generated randomisation table. Identity of the compound was kept in a sealed envelope un- til the patient was accepted for the study.
Participants	1513 pregnant women (group I: 717, group II: 796)
	Inclusion criteria: 13-22 weeks of gestation.
	Exclusion criteria: previous heart disease, hypertension, respiratory disease, ulcerative colitis, diabetes mellitus, disorders of blood coagulation, kidney disease, liver disease, sickle-cell anaemia, severe hypersensitivity, serious systemic disease, contraindication to transperitoneal uterine puncture (previous abdominal surgery on the body of the uterus, large uterine myomata/pelvic tumors, major congenital abnormalities of the uterus, rupture of membranes, earlier failed saline induction).
Interventions	Both groups were punctured with a fine-bore needle and a small amount of amniotic fluid withdrawn to confirm the intra-amniotic position.
	Group I: 200 mL 20% saline was slowly injected, intra-amniotic;
	Group II: 5 mL tromethamine salt of PGF <sub>2</sub> $\alpha$ (= 25mg PGF <sub>2<math>\alpha</math></sub> ) was injected, intra-amniotic. A catheter was left in position and 6h later a second injection op 25mg PGF <sub>2<math>\alpha</math></sub> was given.
Outcomes	Abortion interval, complications, side-effects.

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### WHO 1976 (Continued)

Notes

Definition of abortion: spontaneous expulsion of placenta through the cervix into the vagina.

If the placenta was incomplete, evacuation of the uterus was performed.

Re-admission to hospital was necessary for 17 patients given  $PGF_{2\alpha}$  and 13 patients given saline (excessive blood loss, retained products of conception, signs of genital tract infection).

## Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No apparant differences between the groups in terms of maternal age, gesta- tional age and parity.

|--|

Methods	Randomisation schedu as described by Meiner	Ile, (sealed) envelopes bearing the subject number and allocation were prepared t. The envelopes were opened only when recruited.	
Participants	140 pregnant women (group I: 70, group II: 70)		
	Inclusion criteria: heal	thy women, age 16-40 years, 14-20 weeks gestation.	
	Exclusion criteria: regu multiple pregnancy, nu	lar use of prescription drugs, cardiac disorders, IUD in situ, missed abortion, ursing mothers.	
Interventions	Group I: misoprostol 4	Group I: misoprostol 400 μg vaginally every 3 hours, max 5d.	
	Group II: gemeprost 1 i	ng vaginally every 3 hours, max 5d.	
Outcomes	Primary outcomes: induction-abortion interval, rates of successful abortion (within 24 h), complete abortion.		
	Secondary outcomes:	side-effects.	
Notes	Definition of abortion: expulsion of fetus.		
	If the placenta was inc	omplete, evacuation of the uterus was performed under general anaesthesia.	
	No major complicatior	is reported.	
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Allocation concealment?	Low risk	A - adequate	
Blinding? All outcomes	High risk		
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.	

Medical methods for mid-trimester termination of pregnancy (Review)



# Wong 2000

Methods	Randomisation schedu scribed by Meinert. The	ile, envelopes bearing the subject number and allocation were prepared as de- e envelopes were opened only when recruited.
Participants	148 pregnant women (group I: 74, group II: 74)	
	Inclusion criteria: healt	hy women, 14-20 weeks' gestation.
	Exclusion criteria: regu nursing mothers.	lar use of prescription drugs, IUD in situ, missed abortion, multiple pregnancy,
Interventions	All: vaginal misoprosto	l 400 μg
	Group I: every 3 hours;	
	Group II: every 6 hours	
Outcomes	Primary outcomes: ind	uction to abortion interval, abortion within 24 hours, complete abortion.
	Secondary outcomes:	side-effects.
Notes	Definition of abortion:	expulsion of fetus and placenta.
	If the placenta was inco	omplete, evacuation of the uterus was performed under general anaesthesia.
	No major complication	is reported.
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - adequate
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

### Zauva 1989

Methods	Random allocation.
Participants	37 pregnant women (group I: 19, group II: 18)
	Inclusion criteria: normal physical investigations, 12-20 weeks gestation, regular menstrual cycles, cer- tain last menstrual period.
	Exclusion criteria: previous Caesarian section, hysterotomy, myomectomy, any other surgery on the uterus.
Interventions	Group I: 150 ml (0.1%) emcredil by extra-amniotic instillation.
	Group II: 150 ml normal saline.
Outcomes	Induction-abortion interval, side-effects.

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## Zauva 1989 (Continued)

Notes

Definition of abortion: expulsion of the fetus.

No major complications described.

## Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	B - unclear
Blinding? All outcomes	High risk	
Free of other bias?	Low risk	No statistically significant differences between the groups in terms of maternal age, gestational age and parity.

# Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Allahbadia 1992	No randomisation
Ballard 1981	No randomisation
Ben-Meir 2009	Fetal demise > 20%
Caliskan 2005	Fetal demise > 20%
Caliskan 2009	Fetal demise > 20%
Carbonell 2008	Different primary outcomes
Dickinson 1998	Multiple pregnancies, previous uterine scar included
Dickinson 2002	Multiple pregnancies, previous uterine scar, fetal death included
Dickinson 2003	Multiple pregnancies included, previous uterine scar included
Feldman 2003	27% of the women did not meet the inclusion criteria
Frydman 1988	Pre-treatment trial
Ghorab 1998	Fetal demise > 20%, cervix dilatation before treatment
Ghosh 1980	Authors excluded women with incomplete abortion
Gilbert 2001	Simple randomisation
Goswami 1982	No randomisation
Guix 2005	Concealment score: C
Herabutya 2001	Odd and even number randomisation, biased and concealment score C



Study	Reason for exclusion
Hidar 2001	Inclusion of fetal death, premature rupture of membranes
Hill 1991	No randomisation
Но 1993	Mifepristone pre-treatment trial
Jain 1994	Fetal demise > 20%, live fetuses received a lethal cardiac injection
Jain 1999	Fetal demise included
Jansen 2008	Cervical dilatation
Jarnbert 1999	Cervical ripening
Kamali 1998	No randomisation
Карр 2007 (2)	Fetal demise > 20%
Klinte 1983	No randomisation
le Roux 2002	Trilostane and danazol as pre-treatments to misoprostol
Manabe 1981	Inclusion of quinine
Munthali 2001	Fetal demise > 20%
Nigam 2006	Simple randomisation
Niromanesh 2005	Concealment allocation: C
Nor Azlin 2006	Cervical dilatation
Nuthalapaty 2005	Use of catheter which was left in place during treatment to promote cervical ripening
Olund 1979	No randomisation
Owen 1996	First dilatation with hygroscopic dilatators and oxytocin infusion
Owen 1999	Women received laminaria for cervical ripening
Perry 1999	Complex and unconventional regime, use of laminaria and cardiac injection
Pulkkinen 1980	No randomisation
Ragab 1976	No primary outcomes could be read off the tables
Ramsey 2004	Cervical dilatation
Shukla 1984	No randomisation
Sørensen 1986	Open list of random numbers
Thong 1993	No randomisation
Thong KJ, Baird 1992	Dilapan laminaria tents, cervical dilatation



Study	Reason for exclusion
Wong 1996	Pre-treatment trial
Yapar 1996	Fetal demise > 20%
Yilmaz 2007	Fetal demise > 20%

## DATA AND ANALYSES

## Comparison 1. Comparison: mifepristone+misoprostol versus mifepristone+gemeprost

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-4.89, 4.09]
2 Abortion within 24 hours	3	210	Odds Ratio (M-H, Fixed, 95% CI)	0.72 [0.23, 2.24]
3 Surgical evacuation	3	209	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.27, 1.35]
4 Pain	3	199	Odds Ratio (M-H, Fixed, 95% CI)	0.47 [0.19, 1.21]
5 Nausea	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.19, 1.90]
6 Vomiting	2	110	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.47, 2.13]
7 Diarrhoea	2	110	Odds Ratio (M-H, Fixed, 95% CI)	2.09 [0.83, 5.23]

# Analysis 1.1. Comparison 1 Comparison: mifepristone+misoprostol versus mifepristone+gemeprost, Outcome 1 Induction to abortion interval.

Study or subgroup	Mi tone/n	ifepris- I nisoprostol tone		ifepris- gemeprost	Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Ho 1996	25	11.8 (9)	25	12.2 (7.1)		100%	-0.4[-4.89,4.09]
Total ***	25		25			100%	-0.4[-4.89,4.09]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(	P<0.0001	); I <sup>2</sup> =100%					
Test for overall effect: Z=0.17(P=0.86)	)						
			Favour	s misoprostol	-10 -5 0 5 10	Favours gen	neprost

# Analysis 1.2. Comparison 1 Comparison: mifepristone+misoprostol versus mifepristone+gemeprost, Outcome 2 Abortion within 24 hours.

Study or subgroup	Mifepris- tone/miso- prostol	Mifepris- tone/geme- prost		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-Н,	Fixed, 95	5% CI			M-H, Fixed, 95% CI
Bartley 2002	47/50	48/50			-	-		40.57%	0.65[0.1,4.09]
el-Refaey 1993	28/30	30/30		-		-		34.64%	0.19[0.01,4.06]
Ho 1996	23/25	22/25		-				24.79%	1.57[0.24,10.3]
	105	105						100%	0 70[0 00 0 0 14]
10tal (95% CI)	105	105						100%	0.72[0.23,2.24]
Total events: 98 (Mifepristone/miso	prostol), 100 (Mifepris	stone/gemeprost)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.41, df	f=2(P=0.5); I <sup>2</sup> =0%								
Test for overall effect: Z=0.57(P=0.57	7)					1	1		
	F	avours gemeprost	0.005	0.1	1	10	200	Favours misoprostol	

# Analysis 1.3. Comparison 1 Comparison: mifepristone+misoprostol versus mifepristone+gemeprost, Outcome 3 Surgical evacuation.

Study or subgroup	Mifepris- tone/miso- prostol	Mifepris- tone/geme- prost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		М	H, Fixed, 959	% CI			M-H, Fixed, 95% Cl
Bartley 2002	5/50	6/49						35.6%	0.8[0.23,2.8]
el-Refaey 1993	2/30	2/30		_				12.18%	1[0.13,7.6]
Ho 1996	5/25	10/25						52.22%	0.38[0.11,1.33]
Total (95% CI)	105	104						100%	0.6[0.27,1.35]
Total events: 12 (Mifepristone/misop	orostol), 18 (Mifeprist	one/gemeprost)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.97, df	=2(P=0.62); I <sup>2</sup> =0%								
Test for overall effect: Z=1.24(P=0.22	)						1		
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

## Analysis 1.4. Comparison 1 Comparison: mifepristone +misoprostol versus mifepristone+gemeprost, Outcome 4 Pain.

Study or subgroup	Mifepris- tone/miso- prostol	Mifepris- tone/geme- prost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-	H, Fixed, 95%	CI			M-H, Fixed, 95% Cl
Bartley 2002	44/50	47/49						43.23%	0.31[0.06,1.63]
el-Refaey 1993	14/25	17/25		-				56.77%	0.6[0.19,1.9]
Ho 1996	25/25	25/25							Not estimable
Total (95% CI)	100	99		-				100%	0.47[0.19,1.21]
Total events: 83 (Mifepristone/miso	prostol), 89 (Mifeprist	one/gemeprost)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.4, df=	=1(P=0.53); I <sup>2</sup> =0%								
Test for overall effect: Z=1.56(P=0.12	2)					1	1		
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

#### Study or subgroup Mifepris-Mifepris-Odds Ratio Weight Odds Ratio tone/misotone/gemeprostol prost n/N n/N M-H, Fixed, 95% CI M-H, Fixed, 95% CI Ho 1996 11/25 8/25 100% 0.6[0.19,1.9] Total (95% CI) 25 25 100% 0.6[0.19,1.9] Total events: 8 (Mifepristone/misoprostol), 11 (Mifepristone/gemeprost) Heterogeneity: Not applicable Test for overall effect: Z=0.87(P=0.38)

## Analysis 1.5. Comparison 1 Comparison: mifepristone +misoprostol versus mifepristone+gemeprost, Outcome 5 Nausea.

Favours misoprostol 0.01 0.1 1 10 100 Favours gemeprost

# Analysis 1.6. Comparison 1 Comparison: mifepristone +misoprostol versus mifepristone+gemeprost, Outcome 6 Vomiting.

Study or subgroup	Mifepris- tone/miso- prostol	Mifepris- tone/geme- prost		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		М-Н, F	ixed, 95% CI			M-H, Fixed, 95% CI
el-Refaey 1993	11/30	13/30			-		60.93%	0.76[0.27,2.13]
Ho 1996	13/25	11/25		-			39.07%	1.38[0.45,4.2]
Total (95% CI)	55	55			◆		100%	1[0.47,2.13]
Total events: 24 (Mifepristone/mis	soprostol), 24 (Mifeprist	one/gemeprost)						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.6, c	df=1(P=0.44); I <sup>2</sup> =0%							
Test for overall effect: Z=0(P=1)								
	For	ours mison rostol	0.01	0.1	1 10	100	Favours gamaprast	

Favours misoprostol 0.01 0.1 1 10 <sup>100</sup> Favours gemeprost

# Analysis 1.7. Comparison 1 Comparison: mifepristone +misoprostol versus mifepristone+gemeprost, Outcome 7 Diarrhoea.

Study or subgroup	Mifepris- tone/miso- prostol	Mifepris- tone/geme- prost		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	, Fixed, 95%	CI			M-H, Fixed, 95% CI
el-Refaey 1993	6/30	2/30						24.84%	3.5[0.65,18.98]
Ho 1996	14/25	11/25				-		75.16%	1.62[0.53,4.95]
Total (95% CI)	55	55				•		100%	2.09[0.83,5.23]
Total events: 20 (Mifepristone/misop	orostol), 13 (Mifepristo	one/gemeprost)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.56, df	=1(P=0.46); I <sup>2</sup> =0%								
Test for overall effect: Z=1.57(P=0.12)	)								
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

Outcome or sub- group title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24 hours	1	64	Odds Ratio (M-H, Fixed, 95% CI)	12.13 [1.43, 102.61]
2 Surgical evacuation	1	64	Odds Ratio (M-H, Fixed, 95% CI)	0.23 [0.02, 2.14]
3 Pain	1	64	Odds Ratio (M-H, Fixed, 95% CI)	1.94 [0.70, 5.38]
4 Nausea	1	64	Odds Ratio (M-H, Fixed, 95% CI)	1.29 [0.48, 3.44]
5 Vomiting	1	64	Odds Ratio (M-H, Fixed, 95% CI)	1.14 [0.42, 3.07]

## Comparison 2. Comparison: mifepristone+misoprostol versus placebo+misoprostol

# Analysis 2.1. Comparison 2 Comparison: mifepristone+misoprostol versus placebo+misoprostol, Outcome 1 Abortion within 24 hours.

Study or subgroup	Mifepristone	Placebo	Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fixe	ed, 95% CI			M-H, Fixed, 95% CI
Kapp 2007	31/32	23/32					100%	12.13[1.43,102.61]
Total (95% CI)	32	32					100%	12.13[1.43,102.61]
Total events: 31 (Mifepristone), 23 (F	Placebo)							
Heterogeneity: Not applicable								
Test for overall effect: Z=2.29(P=0.02	:)							
		Favours placebo	0.002	0.1	1 10	500	Favours mifepristone	

# Analysis 2.2. Comparison 2 Comparison: mifepristone+misoprostol versus placebo+misoprostol, Outcome 2 Surgical evacuation.

Study or subgroup	Mifepristone	Placebo		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-Н, F	ixed, 95	% CI			M-H, Fixed, 95% CI
Карр 2007	1/32	4/32	_					100%	0.23[0.02,2.14]
Total (95% CI)	32	32						100%	0.23[0.02,2.14]
Total events: 1 (Mifepristone), 4 (Place	bo)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.3(P=0.19)									
	Favo	ours mifepristone	0.01	0.1	1	10	100	Favours placebo	

## Analysis 2.3. Comparison 2 Comparison: mifepristone+misoprostol versus placebo+misoprostol, Outcome 3 Pain.

Study or subgroup	Mifepristone n/N	Placebo n/N	Odds Ratio M-H, Fixed, 95% Cl				Weight	Odds Ratio M-H, Fixed, 95% Cl	
Карр 2007	15/32	10/32				_		100%	1.94[0.7,5.38]
	Favoi	urs mifepristone	0.01	0.1	1	10	100	Favours placebo	



Study or subgroup	Mifepristone n/N	Placebo n/N		( М-Н,	Odds Ratio Fixed, 95%	% CI		Weight	Odds Ratio M-H, Fixed, 95% Cl
Total (95% CI)	32	32				►		100%	1.94[0.7,5.38]
Total events: 15 (Mifepristone), 10 (Pl	acebo)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.27(P=0.2)									
	Favo	urs mifepristone	0.01	0.1	1	10	100	Favours placebo	

## Analysis 2.4. Comparison 2 Comparison: mifepristone +misoprostol versus placebo+misoprostol, Outcome 4 Nausea.

Study or subgroup	Mifepristone	Placebo		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, S	95% CI			M-H, Fixed, 95% CI
Kapp 2007	18/32	16/32			<u> </u>		100%	1.29[0.48,3.44]
Total (95% CI)	32	32		-			100%	1.29[0.48,3.44]
Total events: 18 (Mifepristone), 16 (Pl	acebo)							
Heterogeneity: Not applicable								
Test for overall effect: Z=0.5(P=0.62)								
	Favo	urs mifepristone	0.01 0	0.1 1	10	100	Favours placebo	

# Analysis 2.5. Comparison 2 Comparison: mifepristone +misoprostol versus placebo+misoprostol, Outcome 5 Vomiting.

Study or subgroup	Mifepristone	Placebo		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	l, Fixed, 95%	6 CI			M-H, Fixed, 95% Cl
Карр 2007	14/32	13/32						100%	1.14[0.42,3.07]
Total (95% CI)	32	32			-			100%	1.14[0.42,3.07]
Total events: 14 (Mifepristone), 13 (Pl	acebo)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.25(P=0.8)									
	Favo	ours mifepristone	0.01	0.1	1	10	100	Favours placebo	

## Comparison 3. Comparison: mifepristone+misoprostol, vaginal versus oral

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	2	237	Mean Difference (IV, Fixed, 95% CI)	7.03 [-0.13, 14.20]
1.1 Misoprostol, 200 mcg oral versus 200 mcg vaginal	1	98	Mean Difference (IV, Fixed, 95% CI)	13.0 [2.77, 23.23]
1.2 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Mean Difference (IV, Fixed, 95% CI)	1.30 [-8.73, 11.33]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2 Abortion within 24 hours	3	306	Odds Ratio (M-H, Fixed, 95% Cl)	0.53 [0.28, 1.02]
2.1 Misoprostol, 200 mcg oral versus 200 mcg vaginal	1	98	Odds Ratio (M-H, Fixed, 95% Cl)	0.26 [0.09, 0.78]
2.2 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% CI)	0.83 [0.34, 2.01]
2.3 Misoprostol, 400 mcg oral versus 400 mcg vaginal	1	69	Odds Ratio (M-H, Fixed, 95% Cl)	0.97 [0.06, 16.17]
3 Surgical evacuation	2	208	Odds Ratio (M-H, Fixed, 95% Cl)	0.99 [0.48, 2.04]
3.1 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% Cl)	0.70 [0.31, 1.57]
3.2 Misoprostol, 400 mcg oral versus 400 mcg vaginal	1	69	Odds Ratio (M-H, Fixed, 95% CI)	5.86 [0.65, 53.09]
4 Pain	2	208	Odds Ratio (M-H, Fixed, 95% CI)	1.32 [0.66, 2.62]
4.1 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% CI)	1.1 [0.43, 2.79]
4.2 Misoprostol, 400 mcg oral versus 400 mcg vaginal	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.64 [0.59, 4.57]
5 Nausea	2	237	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.61, 1.70]
5.1 Misoprostol, 200 mcg oral versus 200 mcg vaginal	1	98	Odds Ratio (M-H, Fixed, 95% Cl)	0.64 [0.28, 1.47]
5.2 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% Cl)	1.37 [0.70, 2.68]
6 Vomiting	3	306	Odds Ratio (M-H, Fixed, 95% Cl)	0.98 [0.61, 1.56]
6.1 Misoprostol, 200 mcg oral versus 200 mcg vaginal	1	98	Odds Ratio (M-H, Fixed, 95% Cl)	0.64 [0.25, 1.63]
6.2 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% Cl)	1.10 [0.56, 2.15]
6.3 Misoprostol, 400 mcg oral versus 400 mcg vaginal	1	69	Odds Ratio (M-H, Fixed, 95% Cl)	1.21 [0.46, 3.17]
7 Diarrhoea	3	306	Odds Ratio (M-H, Fixed, 95% CI)	1.95 [1.18, 3.22]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
7.1 Misoprostol, 200 mcg oral versus 200 mcg vaginal	1	98	Odds Ratio (M-H, Fixed, 95% CI)	2.15 [0.84, 5.50]
7.2 Misoprostol, 400 mcg oral versus 200 mcg vaginal	1	139	Odds Ratio (M-H, Fixed, 95% CI)	2.21 [1.06, 4.61]
7.3 Misoprostol, 400 mcg oral versus 400 mcg vaginal	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.36 [0.49, 3.77]

# Analysis 3.1. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 1 Induction to abortion interval.

Study or subgroup	Oral m	isoprostol	Vagina	l misoprostol		Меа	n Differen	ce		Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		Fix	ed, 95% C	l			Fixed, 95% CI
3.1.1 Misoprostol, 200 mcg oral vers	us 200 i	mcg vaginal									
Ho 1997	49	27.8 (31.7)	49	14.8 (18.2)				-		49%	13[2.77,23.23]
Subtotal ***	49		49							<b>49</b> %	13[2.77,23.23]
Heterogeneity: Not applicable											
Test for overall effect: Z=2.49(P=0.01)											
3.1.2 Misoprostol, 400 mcg oral vers	us 200 i	mcg vaginal									
Ngai 2000	70	20.8 (25.3)	69	19.5 (34.3)						51%	1.3[-8.73,11.33]
Subtotal ***	70		69							51%	1.3[-8.73,11.33]
Heterogeneity: Not applicable											
Test for overall effect: Z=0.25(P=0.8)											
Total ***	119		118				•			100%	7.03[-0.13,14.2]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =2.56, df=	1(P=0.11	.); I <sup>2</sup> =60.94%									
Test for overall effect: Z=1.92(P=0.05)											
Test for subgroup differences: Chi <sup>2</sup> =2.	56, df=1	(P=0.11), l <sup>2</sup> =60.9	94%		1						
				Favours oral	-40	-20	0	20	40	Favours vaginal	

## Analysis 3.2. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 2 Abortion within 24 hours.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H, Fixe	ed, 95% CI			M-H, Fixed, 95% CI
3.2.1 Misoprostol, 200 mcg oral ver	sus 200 mcg vagina	ι						
Ho 1997	34/49	44/49					53.23%	0.26[0.09,0.78]
Subtotal (95% CI)	49	49					53.23%	0.26[0.09,0.78]
Total events: 34 (Oral misoprostol), 4	4 (Vaginal misoprost	col)						
Heterogeneity: Not applicable								
Test for overall effect: Z=2.4(P=0.02)								
3.2.2 Misoprostol, 400 mcg oral ver	sus 200 mcg vagina	ι						
Ngai 2000	57/70	58/69		. –	<u> </u>		42.87%	0.83[0.34,2.01]
		Favours vaginal	0.01	0.1	1 10	100	Favours oral	

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Study or subgroup	Oral miso- prostol	Vaginal misoprostol	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl
Subtotal (95% CI)	70	69	•	42.87%	0.83[0.34,2.01]
Total events: 57 (Oral misoprostol), 58	(Vaginal misopros	tol)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(P<	<0.0001); l <sup>2</sup> =100%				
Test for overall effect: Z=0.41(P=0.68)					
3.2.3 Misoprostol, 400 mcg oral verse	us 400 mcg vagina	ıl			
El-refaey 1995	33/34	34/35		- 3.89%	0.97[0.06,16.17]
Subtotal (95% CI)	34	35		3.89%	0.97[0.06,16.17]
Total events: 33 (Oral misoprostol), 34	(Vaginal misopros	tol)			
Heterogeneity: Not applicable					
Test for overall effect: Z=0.02(P=0.98)					
Total (95% CI)	153	153	•	100%	0.53[0.28,1.02]
Total events: 124 (Oral misoprostol), 13	36 (Vaginal misopr	ostol)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =2.81, df=2	(P=0.25); I <sup>2</sup> =28.859	6			
Test for overall effect: Z=1.9(P=0.06)					
Test for subgroup differences: Not app	licable				
		Favours vaginal	0.01 0.1 1 10	<sup>100</sup> Favours oral	

# Analysis 3.3. Comparison 3 Comparison: mifepristone +misoprostol, vaginal versus oral, Outcome 3 Surgical evacuation.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	l, Fixed, 959	% CI			M-H, Fixed, 95% CI
3.3.1 Misoprostol, 400 mcg oral vers	us 200 mcg vaginal								
Ngai 2000	13/70	17/69			_ <b>_</b>			94.31%	0.7[0.31,1.57]
Subtotal (95% CI)	70	69						94.31%	0.7[0.31,1.57]
Total events: 13 (Oral misoprostol), 17	(Vaginal misoprosto	l)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.87(P=0.39)									
3.3.2 Misoprostol, 400 mcg oral vers	us 400 mcg vaginal								
El-refaey 1995	5/34	1/35				+		5.69%	5.86[0.65,53.09]
Subtotal (95% CI)	34	35						5.69%	5.86[0.65,53.09]
Total events: 5 (Oral misoprostol), 1 (V	aginal misoprostol)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.57(P=0.12)									
Total (95% CI)	104	104			•			100%	0.99[0.48,2.04]
Total events: 18 (Oral misoprostol), 18	(Vaginal misoprosto	l)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =3.21, df=1	1(P=0.07); I <sup>2</sup> =68.89%								
Test for overall effect: Z=0.02(P=0.98)									
Test for subgroup differences: Not app	olicable								
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 3.4. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 4 Pain.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		м-н,	Fixed, 95%	CI			M-H, Fixed, 95% CI
3.4.1 Misoprostol, 400 mcg oral vers	us 200 mcg vagina	ι							
Ngai 2000	11/70	10/69			_ <b>_</b>			59.66%	1.1[0.43,2.79]
Subtotal (95% CI)	70	69			-			59.66%	1.1[0.43,2.79]
Total events: 11 (Oral misoprostol), 10	(Vaginal misoprost	ol)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.2(P=0.84)									
3.4.2 Misoprostol, 400 mcg oral vers	us 400 mcg vagina	ι							
El-refaey 1995	25/34	22/35						40.34%	1.64[0.59,4.57]
Subtotal (95% CI)	34	35						40.34%	1.64[0.59,4.57]
Total events: 25 (Oral misoprostol), 22	(Vaginal misoprost	ol)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.95(P=0.34)									
Total (95% CI)	104	104			•			100%	1.32[0.66,2.62]
Total events: 36 (Oral misoprostol), 32	(Vaginal misoprost	ol)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.32, df=	L(P=0.57); I <sup>2</sup> =0%								
Test for overall effect: Z=0.79(P=0.43)									
Test for subgroup differences: Not app	licable								
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 3.5. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 5 Nausea.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	сі			M-H, Fixed, 95% CI
3.5.1 Misoprostol, 200 mcg oral vers	sus 200 mcg vaginal								
Ho 1997	15/49	20/49		-				48.53%	0.64[0.28,1.47]
Subtotal (95% CI)	49	49		-				48.53%	0.64[0.28,1.47]
Total events: 15 (Oral misoprostol), 20	) (Vaginal misoprosto	l)							
Heterogeneity: Not applicable									
Test for overall effect: Z=1.05(P=0.29)									
3.5.2 Misoprostol, 400 mcg oral ver	sus 200 mcg vaginal								
Ngai 2000	39/70	33/69			-			51.47%	1.37[0.7,2.68]
Subtotal (95% CI)	70	69			-			51.47%	1.37[0.7,2.68]
Total events: 39 (Oral misoprostol), 3	3 (Vaginal misoprosto	l)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.93(P=0.35)									
Total (95% CI)	119	118			•			100%	1.02[0.61,1.7]
Total events: 54 (Oral misoprostol), 53	3 (Vaginal misoprosto	l)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.96, df=	1(P=0.16); I <sup>2</sup> =49.11%								
Test for overall effect: Z=0.06(P=0.95)									
Test for subgroup differences: Not ap	olicable								
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 3.6. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 6 Vomiting.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio	Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
3.6.1 Misoprostol, 200 mcg oral versu	ıs 200 mcg vaginal					
Ho 1997	10/49	14/49			31.88%	0.64[0.25,1.63]
Subtotal (95% CI)	49	49		-	31.88%	0.64[0.25,1.63]
Total events: 10 (Oral misoprostol), 14	(Vaginal misoprosto	l)				
Heterogeneity: Not applicable						
Test for overall effect: Z=0.94(P=0.35)						
3.6.2 Misoprostol, 400 mcg oral versu	ıs 200 mcg vaginal					
Ngai 2000	31/70	29/69			46.56%	1.1[0.56,2.15]
Subtotal (95% CI)	70	69		+	46.56%	1.1[0.56,2.15]
Total events: 31 (Oral misoprostol), 29	(Vaginal misoprosto	l)				
Heterogeneity: Not applicable						
Test for overall effect: Z=0.27(P=0.79)						
3.6.3 Misoprostol, 400 mcg oral versu	ıs 400 mcg vaginal					
El-refaey 1995	21/34	20/35			21.56%	1.21[0.46,3.17]
Subtotal (95% CI)	34	35		-	21.56%	1.21[0.46,3.17]
Total events: 21 (Oral misoprostol), 20	(Vaginal misoprosto	l)				
Heterogeneity: Not applicable						
Test for overall effect: Z=0.39(P=0.7)						
Total (95% CI)	153	153		•	100%	0.98[0.61,1.56]
Total events: 62 (Oral misoprostol), 63	(Vaginal misoprosto	l)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.09, df=2	(P=0.58); I <sup>2</sup> =0%					
Test for overall effect: Z=0.1(P=0.92)						
Test for subgroup differences: Not appl	icable					
		Favours oral	0.01	0.1 1 10	<sup>100</sup> Favours vaginal	

# Analysis 3.7. Comparison 3 Comparison: mifepristone+misoprostol, vaginal versus oral, Outcome 7 Diarrhoea.

Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		м-н, і	ixed, 95% (	CI			M-H, Fixed, 95% CI
3.7.1 Misoprostol, 200 mcg oral vers	us 200 mcg vaginal								
Ho 1997	16/49	9/49			+			27.42%	2.15[0.84,5.5]
Subtotal (95% CI)	49	49						27.42%	2.15[0.84,5.5]
Total events: 16 (Oral misoprostol), 9 (	Vaginal misoprostol)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.6(P=0.11)									
3.7.2 Misoprostol, 400 mcg oral vers	us 200 mcg vaginal								
Ngai 2000	28/70	16/69						43.74%	2.21[1.06,4.61]
Subtotal (95% CI)	70	69			-			43.74%	2.21[1.06,4.61]
Total events: 28 (Oral misoprostol), 16	(Vaginal misoprostol	)							
Heterogeneity: Not applicable									
Test for overall effect: Z=2.11(P=0.03)									
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

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Study or subgroup	Oral miso- prostol	Vaginal misoprostol		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-Н	, Fixed, 95%	6 CI			M-H, Fixed, 95% CI
3.7.3 Misoprostol, 400 mcg oral vers	sus 400 mcg vaginal								
El-refaey 1995	12/34	10/35						28.85%	1.36[0.49,3.77]
Subtotal (95% CI)	34	35			-			28.85%	1.36[0.49,3.77]
Total events: 12 (Oral misoprostol), 10	) (Vaginal misoproste	ol)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.6(P=0.55)									
Total (95% CI)	153	153			•			100%	1.95[1.18,3.22]
Total events: 56 (Oral misoprostol), 35	5 (Vaginal misoproste	ol)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.63, df=	2(P=0.73); I <sup>2</sup> =0%								
Test for overall effect: Z=2.61(P=0.01)									
Test for subgroup differences: Not app	olicable		L						
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

# Comparison 4. Comparison: mifepristone+misoprostol, vaginal versus sublingual

Outcome or sub- group title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Surgical evacua- tion	1	69	Odds Ratio (M-H, Fixed, 95% CI)	3.72 [0.37, 37.72]
2 Pain	1	69	Odds Ratio (M-H, Fixed, 95% CI)	0.56 [0.16, 1.97]
3 Nausea	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.83 [0.59, 5.70]
4 Vomiting	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.71 [0.58, 5.07]
5 Diarrhoea	1	69	Odds Ratio (M-H, Fixed, 95% CI)	1.11 [0.43, 2.91]

# Analysis 4.1. Comparison 4 Comparison: mifepristone+misoprostol, vaginal versus sublingual, Outcome 1 Surgical evacuation.

Study or subgroup	Sublingual	Vaginal		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fi	ixed, 95	% CI			M-H, Fixed, 95% Cl
Hamoda 2005	3/32	1/37		_	_	+	-	100%	3.72[0.37,37.72]
Total (95% CI)	32	37		-			-	100%	3.72[0.37,37.72]
Total events: 3 (Sublingual), 1 (Vaginal)	1								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.11(P=0.27)									
		Favours sublingual	0.01	0.1	1	10	100	Favours vaginal	

## Analysis 4.2. Comparison 4 Comparison: mifepristone+misoprostol, vaginal versus sublingual, Outcome 2 Pain.

Study or subgroup	Sublingual	Vaginal		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	I, Fixed, 95%	CI			M-H, Fixed, 95% CI
Hamoda 2005	25/32	32/37		_				100%	0.56[0.16,1.97]
Total (95% CI)	32	37						100%	0.56[0.16,1.97]
Total events: 25 (Sublingual), 32 (Vagina	al)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.91(P=0.36)									
		Favours sublingual	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 4.3. Comparison 4 Comparison: mifepristone+misoprostol, vaginal versus sublingual, Outcome 3 Nausea.

Study or subgroup	Sublingual	Vaginal	Odds Ratio				Weight	Odds Ratio	
	II/N	11/11		141-1	n, Fixeu, 95%				M-H, Fixeu, 55% Ci
Hamoda 2005	26/32	26/37				-		100%	1.83[0.59,5.7]
Total (95% CI)	32	37				-		100%	1.83[0.59,5.7]
Total events: 26 (Sublingual), 26 (Vagin	al)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.05(P=0.29)									
				1			L		
	F	avours sublingual	0.01	0.1	1	10	100	Favours vaginal	

## Analysis 4.4. Comparison 4 Comparison: mifepristone+misoprostol, vaginal versus sublingual, Outcome 4 Vomiting.

Study or subgroup	Sublingual	Vaginal	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		M-H	, Fixed, 95	% CI			M-H, Fixed, 95% Cl
Hamoda 2005	25/32	25/37						100%	1.71[0.58,5.07]
Total (95% CI)	32	37			-			100%	1.71[0.58,5.07]
Total events: 25 (Sublingual), 25 (Vagina	al)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.97(P=0.33)									
	F	Favours sublingual	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 4.5. Comparison 4 Comparison: mifepristone +misoprostol, vaginal versus sublingual, Outcome 5 Diarrhoea.

Study or subgroup	Sublingual	Vaginal		Odds Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 9	5% CI		M-H, Fixed, 95% Cl
Hamoda 2005	19/32	21/37			_	100%	1.11[0.43,2.91]
Total (95% CI)	32	37		-	•	100%	1.11[0.43,2.91]
Total events: 19 (Sublingual), 21 (Vagi	nal)						
Heterogeneity: Not applicable							
Test for overall effect: Z=0.22(P=0.83)							
	F	avours sublingual	0.01	0.1 1	10 1	<sup>00</sup> Favours vaginal	

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24h	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.53 [0.17, 1.70]
2 Pain (need of analgesic)	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.88 [0.40, 1.94]
3 Nausea	1	118	Odds Ratio (M-H, Fixed, 95% CI)	1.25 [0.60, 2.61]
4 Diarrhoea	1	118	Odds Ratio (M-H, Fixed, 95% CI)	1.73 [0.66, 4.54]

## Comparison 5. Comparison: mifepristone+misoprostol, oral versus sublingual

# Analysis 5.1. Comparison 5 Comparison: mifepristone +misoprostol, oral versus sublingual, Outcome 1 Abortion within 24h.

Study or subgroup	Oral	Sublingual		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, F	ixed, 95%	CI			M-H, Fixed, 95% CI
Tang 2005	51/60	53/58			-			100%	0.53[0.17,1.7]
Total (95% CI)	60	58						100%	0.53[0.17,1.7]
Total events: 51 (Oral), 53 (Sublingual)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.06(P=0.29)									
	F	avours sublingual	0.01	0.1	1	10	100	Favours oral	

# Analysis 5.2. Comparison 5 Comparison: mifepristone+misoprostol, oral versus sublingual, Outcome 2 Pain (need of analgesic).

Study or subgroup	Oral	Sublingual		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		<b>M</b> -	H, Fixed, 95% C	1			M-H, Fixed, 95% Cl
Tang 2005	17/60	18/58			— <mark>—</mark> —			100%	0.88[0.4,1.94]
Total (95% CI)	60	58			-			100%	0.88[0.4,1.94]
Total events: 17 (Oral), 18 (Sublingual)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.32(P=0.75)									
		Favours oral	0.01	0.1	1	10	100	Favours sublingual	

# Analysis 5.3. Comparison 5 Comparison: mifepristone+misoprostol, oral versus sublingual, Outcome 3 Nausea.

Study or subgroup	Oral	Sublingual	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		M-H	l, Fixed, 95%	6 CI			M-H, Fixed, 95% CI
Tang 2005	26/60	22/58	_1	1		1	L	100%	1.25[0.6,2.61]
		Favours oral	0.01	0.1	1	10	100	Favours sublingual	


Study or subgroup	Oral		Sublingual		Odds Ratio			Weight	Odds Ratio	
	n/N		n/N		M-I	H, Fixed, 9	5% CI			M-H, Fixed, 95% CI
Total (95% CI)		60	58			-			100%	1.25[0.6,2.61]
Total events: 26 (Oral), 22 (Sublingual)										
Heterogeneity: Not applicable										
Test for overall effect: Z=0.6(P=0.55)							T			
			Favours oral	0.01	0.1	1	10	100	Favours sublingual	

#### Analysis 5.4. Comparison 5 Comparison: mifepristone+misoprostol, oral versus sublingual, Outcome 4 Diarrhoea.

Study or subgroup	Oral	Sublingual		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-P	i, Fixea, 95% (				M-H, Fixed, 95% Cl
Tang 2005	13/60	8/58						100%	1.73[0.66,4.54]
Total (95% CI)	60	58			-			100%	1.73[0.66,4.54]
Total events: 13 (Oral), 8 (Sublingual)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.11(P=0.27)									
		Favours oral	0.01	0.1	1	10	100	Favours sublingual	

#### Comparison 6. Comparison: dosing interval of misoprostol following mifepristone

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24 hours	1	141	Odds Ratio (M-H, Fixed, 95% CI)	13.99 [0.77, 253.29]
2 Surgical evacuation	1	40	Odds Ratio (M-H, Fixed, 95% CI)	0.16 [0.02, 1.50]
3 Pain (need for analge- sia)	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.20, 1.67]
4 Nausea	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.97 [0.50, 1.89]
5 Diarrhoea	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.21, 1.16]

# Analysis 6.1. Comparison 6 Comparison: dosing interval of misoprostol following mifepristone, Outcome 1 Abortion within 24 hours.

Study or subgroup	Conven- tional dose	Immidiate dose			Odds Ratio		Weight	Odds Ratio	
	n/N	n/N		M-H	, Fixed, 95%	% CI			M-H, Fixed, 95% CI
Chai 2009	70/70	65/71				-		100%	13.99[0.77,253.29]
Total (95% CI)	70	71						100%	13.99[0.77,253.29]
Total events: 70 (Conventional dose	), 65 (Immidiate dose	e)		i.		i.	ı		
	F	avours immediate	0.01	0.1	1	10	100	Favours conventional	



Study or subgroup	Conven- tional dose	Immidiate dose	midiate dose Odds		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95	5% CI			M-H, Fixed, 95% CI
Heterogeneity: Not applicable									
Test for overall effect: Z=1.79(P=0.07)						1	1		
		Favours immediate	0.01	0.1	1	10	100	Favours conventional	

# Analysis 6.2. Comparison 6 Comparison: dosing interval of misoprostol following mifepristone, Outcome 2 Surgical evacuation.

Study or subgroup	Conven- tional dose	Immidiate dose		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		м-н,	Fixed, 95% (	CI			M-H, Fixed, 95% CI
Chai 2009	1/20	5/20						100%	0.16[0.02,1.5]
Total (95% CI)	20	20						100%	0.16[0.02,1.5]
Total events: 1 (Conventional dose), 5	5 (Immidiate dose)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.61(P=0.11)						1			
	Fav	vours conventional	0.01	0.1	1	10	100	Favours immidiate	

# Analysis 6.3. Comparison 6 Comparison: dosing interval of misoprostol following mifepristone, Outcome 3 Pain (need for analgesia).

Study or subgroup	Conven- tional dose	Immidiate dose	ate dose		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		М-Н, F	ixed, 95%	CI			M-H, Fixed, 95% CI
Chai 2009	6/70	10/71						100%	0.57[0.2,1.67]
Total (95% CI)	70	71						100%	0.57[0.2,1.67]
Total events: 6 (Conventional dose), 1	0 (Immidiate dose)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.02(P=0.31)									
	Fav	ours conventional	0.01	0.1	1	10	100	Favours immidiate	

### Analysis 6.4. Comparison 6 Comparison: dosing interval of misoprostol following mifepristone, Outcome 4 Nausea.

Study or subgroup	Conven- tional dose	Immidiate dose		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	<b>H, Fixed, 95</b> %	% CI			M-H, Fixed, 95% CI
Chai 2009	37/70	38/71						100%	0.97[0.5,1.89]
Total (95% CI)	70	71			•			100%	0.97[0.5,1.89]
Total events: 37 (Conventional dose),	38 (Immidiate dose	e)							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.08(P=0.94)						1			
	Fav	ours conventional	0.01	0.1	1	10	100	Favours immidiate	

# Analysis 6.5. Comparison 6 Comparison: dosing interval of misoprostol following mifepristone, Outcome 5 Diarrhoea.

Study or subgroup	Conven- tional dose	Immidiate dose	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		м-н,	Fixed, 95%	6 CI			M-H, Fixed, 95% CI
Chai 2009	10/70	18/71		-	+			100%	0.49[0.21,1.16]
Total (95% CI)	70	71		-				100%	0.49[0.21,1.16]
Total events: 10 (Conventional dose),	18 (Immidiate dose	2)							
Heterogeneity: Not applicable									
Test for overall effect: Z=1.63(P=0.1)									
	Fav	ours conventional	0.01	0.1	1	10	100	Favours immidiate	

# Comparison 7. Comparison: dosage of mifepristone

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	70	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.88, 0.72]
2 Abortion within 24h	1	70	Odds Ratio (M-H, Fixed, 95% CI)	2.06 [0.18, 23.83]
3 Surgical evacuation	1	70	Odds Ratio (M-H, Fixed, 95% CI)	0.56 [0.12, 2.56]
4 Pain	1	70	Odds Ratio (M-H, Fixed, 95% CI)	2.03 [0.78, 5.31]
5 Vomiting	1	70	Odds Ratio (M-H, Fixed, 95% CI)	2.25 [0.86, 5.85]
6 Diarrhoea	1	70	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.34, 2.92]

### Analysis 7.1. Comparison 7 Comparison: dosage of mifepristone, Outcome 1 Induction to abortion interval.

Study or subgroup	2	200 mg		600 mg		Mean Difference				Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		F	ixed, 95% CI				Fixed, 95% CI
Webster 1996	35	6.9 (1.7)	35	6.9 (1.8)			÷.			100%	-0.08[-0.88,0.72]
Total ***	35		35							100%	-0.08[-0.88,0.72]
Heterogeneity: Not applicable											
Test for overall effect: Z=0.2(P=0.85)											
			Fa	vours 200 mg	-100	-50	0	50	100	Favours 600 mg	

# Analysis 7.2. Comparison 7 Comparison: dosage of mifepristone, Outcome 2 Abortion within 24h.

Study or subgroup	200 mg	600 mg		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	l, Fixed, 95%	% CI			M-H, Fixed, 95% CI
Webster 1996	34/35	33/35						100%	2.06[0.18,23.83]
Total (95% CI)	35	35		_				100%	2.06[0.18,23.83]
Total events: 34 (200 mg), 33 (600 mg)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.58(P=0.56)									
		Favours 600 mg	0.01	0.1	1	10	100	Favours 200 mg	

#### Analysis 7.3. Comparison 7 Comparison: dosage of mifepristone, Outcome 3 Surgical evacuation.

Study or subgroup	200 mg	600 mg		Od	ds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H, Fi	xed, 95%	СІ			M-H, Fixed, 95% CI
Webster 1996	3/35	5/35						100%	0.56[0.12,2.56]
Total (95% CI)	35	35						100%	0.56[0.12,2.56]
Total events: 3 (200 mg), 5 (600 mg)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.74(P=0.46)									
		Favours 200 mg	0.01	0.1	1	10	100	Favours 600 mg	

#### Analysis 7.4. Comparison 7 Comparison: dosage of mifepristone, Outcome 4 Pain.

Study or subgroup	200 mg	600 mg			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	CI			M-H, Fixed, 95% CI
Webster 1996	23/35	17/35				_		100%	2.03[0.78,5.31]
Total (95% CI)	35	35				•		100%	2.03[0.78,5.31]
Total events: 23 (200 mg), 17 (600 mg)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.44(P=0.15)				1					
		Favours 200 mg	0.01	0.1	1	10	100	Favours 600 mg	

#### Analysis 7.5. Comparison 7 Comparison: dosage of mifepristone, Outcome 5 Vomiting.

Study or subgroup	200 mg	600 mg		c	dds Ratio			Weight	Odds Ratio
	n/N	n/N		м-н,	Fixed, 95%	CI			M-H, Fixed, 95% CI
Webster 1996	21/35	14/35				_		100%	2.25[0.86,5.85]
Total (95% CI)	35	35				•		100%	2.25[0.86,5.85]
Total events: 21 (200 mg), 14 (600 mg)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.66(P=0.1)									
		Favours 200 mg	0.01	0.1	1	10	100	Favours 600 mg	

### Analysis 7.6. Comparison 7 Comparison: dosage of mifepristone, Outcome 6 Diarrhoea.

Study or subgroup	200 mg	600 mg			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	CI			M-H, Fixed, 95% CI
Webster 1996	9/35	9/35						100%	1[0.34,2.92]
Total (95% CI)	35	35			-			100%	1[0.34,2.92]
Total events: 9 (200 mg), 9 (600 mg)									
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
		Favours 200 mg	0.01	0.1	1	10	100	Favours 600 mg	

### Comparison 8. Comparison: combined regimen of mifepristone and gemeprost

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24 hours	1	100	Odds Ratio (M-H, Fixed, 95% CI)	2.04 [0.18, 23.27]
2 Blood loss	1	100	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 8.21]
3 Surgical evacuation	1	100	Odds Ratio (M-H, Fixed, 95% CI)	1.44 [0.55, 3.80]
4 Vomiting	1	90	Odds Ratio (M-H, Fixed, 95% CI)	2.83 [1.04, 7.66]
5 Diarrhoea	1	100	Odds Ratio (M-H, Fixed, 95% CI)	3.27 [0.63, 17.07]

# Analysis 8.1. Comparison 8 Comparison: combined regimen of mifepristone and gemeprost, Outcome 1 Abortion within 24 hours.

Study or subgroup	1 mg geme- prost	0.5 mg gemeprost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	СІ			M-H, Fixed, 95% CI
Thong 1996	49/50	48/50						100%	2.04[0.18,23.27]
Total (95% CI)	50	50		-				100%	2.04[0.18,23.27]
Total events: 49 (1 mg gemeprost), 48	(0.5 mg gemeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.57(P=0.57)									
	Favours	1 mg gemeprost	0.01	0.1	1	10	100	Favours 0.5 mg gemepre	ost

#### Analysis 8.2. Comparison 8 Comparison: combined regimen of mifepristone and gemeprost, Outcome 2 Blood loss.

Study or subgroup	Experimental	Control		Od	ds Rati	o		Weight	Odds Ratio
	n/N	n/N		M-H, Fi	xed, 9	5% CI		I	M-H, Fixed, 95% CI
Thong 1996	0/50	1/50		-				100%	0.33[0.01,8.21]
Total (95% CI)	50	50						100%	0.33[0.01,8.21]
Total events: 0 (Experimental), 1 (Con	trol)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.68(P=0.5)									
	Favours	1 mg gemeprost	0.01	0.1	1	10	100	Favours 0.5 mg gemepro	ost

# Analysis 8.3. Comparison 8 Comparison: combined regimen of mifepristone and gemeprost, Outcome 3 Surgical evacuation.

Study or subgroup	1 mg geme- prost	0.5 mg gemeprost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95% C	:1			M-H, Fixed, 95% CI
Thong 1996	12/50	9/50						100%	1.44[0.55,3.8]
Total (95% CI)	50	50			-			100%	1.44[0.55,3.8]
Total events: 12 (1 mg gemeprost), 9 (	(0.5 mg gemeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.73(P=0.46)									
	Favours	1 mg gemeprost	0.01	0.1	1	10	100	Favours 0.5 mg gemepro	ost

### Analysis 8.4. Comparison 8 Comparison: combined regimen of mifepristone and gemeprost, Outcome 4 Vomiting.

Study or subgroup	1 mg geme- prost	0.5 mg gemeprost		00	lds Ratio			Weight	Odds Ratio
	n/N	n/N		М-Н, Р	ixed, 959	% CI		Ν	1-H, Fixed, 95% Cl
Thong 1996	14/40	8/50						100%	2.83[1.04,7.66]
Total (95% CI)	40	50						100%	2.83[1.04,7.66]
Total events: 14 (1 mg gemeprost), 8	(0.5 mg gemeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.04(P=0.04)	)					l.	i.		
	Favours	1 mg gemeprost	0.01	0.1	1	10	100	Favours 0.5 mg gemepro	st

#### Analysis 8.5. Comparison 8 Comparison: combined regimen of mifepristone and gemeprost, Outcome 5 Diarrhoea.

Study or subgroup	1 mg geme- prost	0.5 mg gemeprost		Odds Ratio		Weight	Odds Ratio	
	n/N	n/N		M-H, Fixed, 95%	% CI			M-H, Fixed, 95% Cl
Thong 1996	6/50	2/50					100%	3.27[0.63,17.07]
Total (95% CI)	50	50					100%	3.27[0.63,17.07]
	Favours	1 mg gemeprost	0.01 0.1	. 1	10	100	Favours 0.5 mg gemepr	ost



Study or subgroup	1 mg geme- prost	0.5 mg gemeprost		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	, Fixed, 95	% CI			M-H, Fixed, 95% CI
Total events: 6 (1 mg gemeprost), 2 (0	.5 mg gemeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.41(P=0.16)									
	Favou	rs 1 mg gemeprost	0.01	0.1	1	10	100	Favours 0.5 mg geme	prost

### Comparison 9. Comparison: misoprostol versus PGF

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion inter- val	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Vaginal misoprostol ver- sus PGF	1	118	Mean Difference (IV, Fixed, 95% CI)	-4.60 [-7.74, -1.46]
2 Abortion within 24 hours	1	122	Odds Ratio (M-H, Fixed, 95% CI)	1.18 [0.53, 2.60]
2.1 Vaginal misoprostol ver- sus PGF	1	122	Odds Ratio (M-H, Fixed, 95% CI)	1.18 [0.53, 2.60]
3 Surgical evacuation	1	122	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.32, 2.02]
3.1 Vaginal misoprostol ver- sus PGF	1	122	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.32, 2.02]
4 Nausea	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.62 [0.26, 1.47]
4.1 Vaginal misoprostol ver- sus PGF	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.62 [0.26, 1.47]
5 Vomiting	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.63 [0.25, 1.59]
5.1 Vaginal misoprostol ver- sus PGF	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.63 [0.25, 1.59]
6 Diarrhoea	1		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Vaginal misoprostol ver- sus PGF	1	118	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.21, 1.14]

### Analysis 9.1. Comparison 9 Comparison: misoprostol versus PGF, Outcome 1 Induction to abortion interval.

Study or subgroup	Mis	oprostol	PGF2a		Mean Difference				Weight	Mean Difference	
	Ν	Mean(SD)	Ν	Mean(SD)		Fix	(ed, 95% C	I			Fixed, 95% CI
9.1.1 Vaginal misoprostol versus F	GF										
Su 2005	57	16.2 (8.3)	61	20.8 (9.1)			-			100%	-4.6[-7.74,-1.46]
Subtotal ***	57		61			◄				100%	-4.6[-7.74,-1.46]
			Favour	s misoprostol	-20	-10	0	10	20	Favours PGF2a	

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Study or subgroup	Misoprostol		PGF2a			Меа	an Differe	nce	Weight	Mean Difference	
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% Cl			Fixed, 95% CI			
Heterogeneity: Not applicable											
Test for overall effect: Z=2.87(P=0)											
			Favou	rs misoprostol	-20	-10	0	10	20	Favours PGF2a	

### Analysis 9.2. Comparison 9 Comparison: misoprostol versus PGF, Outcome 2 Abortion within 24 hours.

Study or subgroup	Misoprostol	PGF2a			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	l, Fixed, 959	% CI			M-H, Fixed, 95% Cl
9.2.1 Vaginal misoprostol versus PG	=								
Su 2005	45/61	43/61						100%	1.18[0.53,2.6]
Subtotal (95% CI)	61	61			-			100%	1.18[0.53,2.6]
Total events: 45 (Misoprostol), 43 (PGF	2a)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.4(P=0.69)									
Total (95% CI)	61	61			•			100%	1.18[0.53,2.6]
Total events: 45 (Misoprostol), 43 (PGF	2a)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.4(P=0.69)									
		Favours PGF2a	0.01	0.1	1	10	100	Favours misoprostol	

### Analysis 9.3. Comparison 9 Comparison: misoprostol versus PGF, Outcome 3 Surgical evacuation.

Study or subgroup	Misoprostol	PGF2a	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
9.3.1 Vaginal misoprostol versus PGF	-				
Su 2005	10/61	12/61		100%	0.8[0.32,2.02]
Subtotal (95% CI)	61	61	-	100%	0.8[0.32,2.02]
Total events: 10 (Misoprostol), 12 (PGF	2a)				
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)					
	61	(1		100%	0 9 0 22 2 021
Totat (95% CI)	01	61		100%	0.8[0.32,2.02]
Total events: 10 (Misoprostol), 12 (PGF:	2a)				
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)		-			
		urs misoprostal	01 01 1 10		

Favours misoprostol 0.01 0.1 1 10 100 Favours PGF2a

#### Analysis 9.4. Comparison 9 Comparison: misoprostol versus PGF, Outcome 4 Nausea.

Study or subgroup	Misoprostol	PGF2a		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-F	I, Fixed, 95	5% CI			M-H, Fixed, 95% CI
9.4.1 Vaginal misoprostol versus P	GF								
Su 2005	11/57	17/61		-				100%	0.62[0.26,1.47]
	Favo	urs misoprostol	0.01	0.1	1	10	100	Favours PGF2a	



Study or subgroup	Misoprostol	PGF2a		Odds	Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed	l, 95% CI			M-H, Fixed, 95% CI
Subtotal (95% CI)	57	61			•		100%	0.62[0.26,1.47]
Total events: 11 (Misoprostol), 17 (PGF	2a)							
Heterogeneity: Not applicable								
Test for overall effect: Z=1.09(P=0.28)								
Total (95% CI)	57	61			•		100%	0.62[0.26,1.47]
Total events: 11 (Misoprostol), 17 (PGF	2a)							
Heterogeneity: Not applicable								
Test for overall effect: Z=1.09(P=0.28)					i.			
	Favo	urs misoprostol	0.01	0.1 1	10	100	Favours PGF2a	

### Analysis 9.5. Comparison 9 Comparison: misoprostol versus PGF, Outcome 5 Vomiting.

Study or subgroup	Misoprostol	PGF2a			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	6 CI			M-H, Fixed, 95% CI
9.5.1 Vaginal misoprostol versus PGF	-								
Su 2005	9/57	14/61		-				100%	0.63[0.25,1.59]
Subtotal (95% CI)	57	61		-				100%	0.63[0.25,1.59]
Total events: 9 (Misoprostol), 14 (PGF2	a)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.98(P=0.33)									
Total (95% CI)	57	61		-	•			100%	0.63[0.25,1.59]
Total events: 9 (Misoprostol), 14 (PGF2	a)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.98(P=0.33)									
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours PGF2a	

# Analysis 9.6. Comparison 9 Comparison: misoprostol versus PGF, Outcome 6 Diarrhoea.

Study or subgroup	Misoprostol	PGF2a		Odd	ls Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fiz	(ed, 95% (	CI		M-H, Fixed, 95% CI
9.6.1 Vaginal misoprostol versus PGF	-							
Su 2005	11/57	20/61			+		100%	0.49[0.21,1.14]
Subtotal (95% CI)	57	61					100%	0.49[0.21,1.14]
Total events: 11 (Misoprostol), 20 (PGF	2a)							
Heterogeneity: Not applicable								
Test for overall effect: Z=1.65(P=0.1)								
	Favo	ours misoprostol	0.002	0.1	1 10	500	Favours PGF2a	



# Comparison 10. Comparison: misoprostol versus gemeprost

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	3	249	Mean Difference (IV, Fixed, 95% CI)	8.73 [5.11, 12.35]
1.1 Misoprostol, 100 mcg, versus gemeprost	1	55	Mean Difference (IV, Fixed, 95% CI)	8.60 [3.11, 14.09]
1.2 Misoprostol, 200 mcg versus gemeprost	1	54	Mean Difference (IV, Fixed, 95% CI)	13.3 [7.90, 18.70]
1.3 Misoprostol, 400 mcg, versus gemeprost	1	140	Mean Difference (IV, Fixed, 95% CI)	-8.90 [-19.65, 1.85]
2 Abortion within 24 hours	1	140	Odds Ratio (M-H, Fixed, 95% CI)	2.83 [1.33, 6.02]
2.1 Misoprostol, 400 mcg, versus gemeprost	1	140	Odds Ratio (M-H, Fixed, 95% CI)	2.83 [1.33, 6.02]
3 Blood loss (mL)	3	249	Mean Difference (IV, Fixed, 95% CI)	-23.75 [-47.80, 0.30]
3.1 Misoprostol, 100 mcg, versus gemeprost	1	55	Mean Difference (IV, Fixed, 95% CI)	-61.0 [-145.71, 23.71]
3.2 Misoprostol, 200 mcg, versus gemeprost	1	54	Mean Difference (IV, Fixed, 95% CI)	-146.0 [-219.02, -72.98]
3.3 Misoprostol, 400 mcg, versus gemeprost	1	140	Mean Difference (IV, Fixed, 95% CI)	-3.70 [-30.40, 23.00]
4 Surgical evacuation	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.48, 1.85]
4.1 Misoprostol, 400 mcg, versus gemeprost	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.48, 1.85]
5 Pain	2	109	Odds Ratio (M-H, Fixed, 95% CI)	0.23 [0.10, 0.52]
5.1 Misoprostol, 100 mcg, versus gemeprost	1	55	Odds Ratio (M-H, Fixed, 95% CI)	0.22 [0.07, 0.71]
5.2 Misoprostol, 200 mcg, versus gemeprost	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.23 [0.07, 0.77]
6 Nausea	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.38, 1.70]
6.1 Misoprostol, 400 mcg, versus gemeprost	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.38, 1.70]
7 Vomiting	3	249	Odds Ratio (M-H, Fixed, 95% CI)	0.38 [0.21, 0.67]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
7.1 Misoprostol, 100 mcg, versus gemeprost	1	55	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.10, 1.06]
7.2 Misoprostol, 200 mcg, versus gemeprost	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.15 [0.04, 0.62]
7.3 Misoprostol, 400 mcg, versus gemeprost	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.55 [0.25, 1.18]
8 Diarrhoea	3	249	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.17, 0.58]
8.1 Misoprostol, 100 mcg, versus gemeprost	1	55	Odds Ratio (M-H, Fixed, 95% CI)	0.04 [0.00, 0.68]
8.2 Misoprostol, 200 mcg, versus gemeprost	1	54	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.03, 0.91]
8.3 Misoprostol, 400 mcg, versus gemeprost	1	140	Odds Ratio (M-H, Fixed, 95% CI)	0.48 [0.23, 0.99]

# Analysis 10.1. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 1 Induction to abortion interval.

Study or subgroup	Misoprostol		Ger	neprost	Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
10.1.1 Misoprostol, 100 mcg, versus	gemep	rost					
Nuutila 1997 a	27	23.1 (12.3)	28	14.5 (7.9)	— <b>∎</b> —	43.61%	8.6[3.11,14.09]
Subtotal ***	27		28			43.61%	8.6[3.11,14.09]
Heterogeneity: Not applicable							
Test for overall effect: Z=3.07(P=0)							
10.1.2 Misoprostol, 200 mcg versus	gemepr	ost					
Nuutila 1997 b	26	27.8 (11.8)	28	14.5 (7.9)	— <del>—</del> —	45.04%	13.3[7.9,18.7]
Subtotal ***	26		28		•	45.04%	13.3[7.9,18.7]
Heterogeneity: Not applicable							
Test for overall effect: Z=4.83(P<0.000	1)						
10.1.3 Misoprostol, 400 mcg, versus	gemep	rost					
Wong 1998	70	23.6 (33.1)	70	32.5 (31.8)	+	11.35%	-8.9[-19.65,1.85]
Subtotal ***	70		70			11.35%	-8.9[-19.65,1.85]
Heterogeneity: Not applicable							
Test for overall effect: Z=1.62(P=0.1)							
Total ***	123		126		•	100%	8.73[5.11,12.35]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =13.08, df	=2(P=0);	l <sup>2</sup> =84.71%					
Test for overall effect: Z=4.72(P<0.000	1)						
Test for subgroup differences: Chi <sup>2</sup> =13	3.08, df=:	1 (P=0), I <sup>2</sup> =84.710	6				
			Favours	s misoprostol	-20 -10 0 10 20	Favours ger	neprost

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### Analysis 10.2. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 2 Abortion within 24 hours.

Study or subgroup	Misoprostol	Gemeprost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	Fixed, 95%	6 CI			M-H, Fixed, 95% Cl
10.2.1 Misoprostol, 400 mcg, versu	s gemeprost								
Wong 1998	56/70	41/70				-		100%	2.83[1.33,6.02]
Subtotal (95% CI)	70	70				•		100%	2.83[1.33,6.02]
Total events: 56 (Misoprostol), 41 (Ge	emeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.7(P=0.01)									
Total (95% CI)	70	70						100%	2.83[1.33,6.02]
Total events: 56 (Misoprostol), 41 (Ge	emeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.7(P=0.01)									
	E	avours gemenrost	0.01	0.1	1	10	100	Favours misoprostol	

s gemeprost

### Analysis 10.3. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 3 Blood loss (mL).

Study or subgroup	Misa	prostol	Gemeprost		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
10.3.1 Misoprostol, 100 mcg, versus	gemepi	rost					
Nuutila 1997 a	27	287 (136)	28	348 (182)		8.06%	-61[-145.71,23.71]
Subtotal ***	27		28			8.06%	-61[-145.71,23.71]
Heterogeneity: Not applicable							
Test for overall effect: Z=1.41(P=0.16)							
10.3.2 Misoprostol, 200 mcg, versus	gemepi	ost					
Nuutila 1997 b	26	202 (73)	28	348 (182)	<b>+</b>	10.85%	-146[-219.02,-72.98]
Subtotal ***	26		28		•	10.85%	-146[-219.02,-72.98]
Heterogeneity: Not applicable							
Test for overall effect: Z=3.92(P<0.000	1)						
10.3.3 Misoprostol, 400 mcg, versus	gemepi	rost					
Wong 1998	70	87.9 (80.7)	70	91.6 (80.5)		81.1%	-3.7[-30.4,23]
Subtotal ***	70		70		<b></b>	81.1%	-3.7[-30.4,23]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(P	<0.0001)	; I <sup>2</sup> =100%					
Test for overall effect: Z=0.27(P=0.79)							
Total ***	123		126		•	100%	-23.75[-47.8,0.3]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =13.68, df	=2(P=0);	l <sup>2</sup> =85.38%					
Test for overall effect: Z=1.94(P=0.05)							
Test for subgroup differences: Chi <sup>2</sup> =13	8.68, df=1	L (P=0), I <sup>2</sup> =85.38	%				
			Favours	s misoprostol	-200 -100 0 100 200	Favours ger	neprost

### Analysis 10.4. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 4 Surgical evacuation.

Study or subgroup	Misoprostol	Gemeprost		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	СІ			M-H, Fixed, 95% Cl
10.4.1 Misoprostol, 400 mcg, versu	is gemeprost								
Wong 1998	28/70	29/70						100%	0.94[0.48,1.85]
Subtotal (95% CI)	70	70			•			100%	0.94[0.48,1.85]
Total events: 28 (Misoprostol), 29 (Ge	emeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.17(P=0.86	)								
Total (95% CI)	70	70			•			100%	0.94[0.48,1.85]
Total events: 28 (Misoprostol), 29 (Ge	emeprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.17(P=0.86	)					1			
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

#### Analysis 10.5. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 5 Pain.

Study or subgroup	Misoprostol	Gemeprost	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% Cl		M-H, Fixed, 95% CI
10.5.1 Misoprostol, 100 mcg, versus	gemeprost				
Nuutila 1997 a	12/27	22/28	— <b>—</b>	51.27%	0.22[0.07,0.71]
Subtotal (95% CI)	27	28		51.27%	0.22[0.07,0.71]
Total events: 12 (Misoprostol), 22 (Ger	neprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=2.53(P=0.01)					
10.5.2 Misoprostol, 200 mcg, versus	gemeprost				
Nuutila 1997 b	12/26	22/28	<b></b>	48.73%	0.23[0.07,0.77]
Subtotal (95% CI)	26	28		48.73%	0.23[0.07,0.77]
Total events: 12 (Misoprostol), 22 (Ger	neprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=2.4(P=0.02)					
Total (95% CI)	53	56		100%	0.23[0.1,0.52]
Total events: 24 (Misoprostol), 44 (Ger	neprost)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.01, df=1	L(P=0.94); I <sup>2</sup> =0%				
Test for overall effect: Z=3.49(P=0)					
Test for subgroup differences: Not app	licable				
	Fav	ours misoprostol	0.01 0.1 1 10	<sup>100</sup> Favours gemeprost	

#### Analysis 10.6. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 6 Nausea.

Study or subgroup	Misoprostol	Gemeprost			Odds Ratio	)		Weight	Odds Ratio
	n/N	n/N		M-H	l, Fixed, 95	% CI			M-H, Fixed, 95% Cl
10.6.1 Misoprostol, 400 mcg, ve	rsus gemeprost								
Wong 1998	17/70	20/70						100%	0.8[0.38,1.7]
Subtotal (95% CI)	70	70			•	I		100%	0.8[0.38,1.7]
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	



Study or subgroup	Misoprostol	Gemeprost			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-I	H, Fixed, 959	% CI			M-H, Fixed, 95% Cl
Total events: 17 (Misoprostol), 20 (Ger	meprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.57(P=0.57)									
Total (95% CI)	70	70			•			100%	0.8[0.38,1.7]
Total events: 17 (Misoprostol), 20 (Ger	meprost)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.57(P=0.57)									
	Fa	vours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

### Analysis 10.7. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 7 Vomiting.

Study or subgroup	Misoprostol	Gemeprost	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% Cl		M-H, Fixed, 95% CI
10.7.1 Misoprostol, 100 mcg, versus	s gemeprost				
Nuutila 1997 a	6/27	13/28		25.72%	0.33[0.1,1.06]
Subtotal (95% CI)	27	28		25.72%	0.33[0.1,1.06]
Total events: 6 (Misoprostol), 13 (Gen	neprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=1.85(P=0.06)					
10.7.2 Misoprostol, 200 mcg, versus	sgemeprost				
Nuutila 1997 b	3/26	13/28	<b>_</b>	28.69%	0.15[0.04,0.62]
Subtotal (95% CI)	26	28		28.69%	0.15[0.04,0.62]
Total events: 3 (Misoprostol), 13 (Gen	neprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=2.63(P=0.01)					
10.7.3 Misoprostol, 400 mcg, versus	sgemeprost				
Wong 1998	14/70	22/70	— <b>—</b> —	45.59%	0.55[0.25,1.18]
Subtotal (95% CI)	70	70		45.59%	0.55[0.25,1.18]
Total events: 14 (Misoprostol), 22 (Ge	meprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=1.54(P=0.12)					
Total (95% CI)	123	126	•	100%	0.38[0.21,0.67]
Total events: 23 (Misoprostol), 48 (Ge	meprost)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =2.55, df=	2(P=0.28); I <sup>2</sup> =21.51%				
Test for overall effect: Z=3.32(P=0)					
Test for subgroup differences: Not ap	plicable				
	Favo	ours misoprostol	0.01 0.1 1 10	<sup>100</sup> Favours gemeprost	

### Analysis 10.8. Comparison 10 Comparison: misoprostol versus gemeprost, Outcome 8 Diarrhoea.

Study or subgroup	Misoprostol n/N	Gemeprost n/N	Odds Ratio M-H, Fixed, 95% Cl				Weight	Odds Ratio M-H, Fixed, 95% Cl	
10.8.1 Misoprostol, 100 mcg, versu	ıs gemeprost								
		Favours misoprostol	0.01	0.1	1	10	100	Favours gemeprost	

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Study or subgroup	Misoprostol	Gemeprost	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Nuutila 1997 a	0/27	9/28	•	23.89%	0.04[0,0.68]
Subtotal (95% CI)	27	28		23.89%	0.04[0,0.68]
Total events: 0 (Misoprostol), 9 (Ge	meprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=2.22(P=0.0	)3)				
10.8.2 Misoprostol, 200 mcg, ver	sus gemeprost				
Nuutila 1997 b	2/26	9/28		20.85%	0.18[0.03,0.91]
Subtotal (95% CI)	26	28		20.85%	0.18[0.03,0.91]
Total events: 2 (Misoprostol), 9 (Ge	meprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=2.07(P=0.0	04)				
10.8.3 Misoprostol, 400 mcg, ver	sus gemeprost				
Wong 1998	17/70	28/70		55.26%	0.48[0.23,0.99]
Subtotal (95% CI)	70	70	-	55.26%	0.48[0.23,0.99]
Total events: 17 (Misoprostol), 28 (	Gemeprost)				
Heterogeneity: Not applicable					
Test for overall effect: Z=1.98(P=0.0	05)				
Total (95% CI)	123	126	•	100%	0.31[0.17,0.58]
Total events: 19 (Misoprostol), 46 (	Gemeprost)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =3.89, (	df=2(P=0.14); I <sup>2</sup> =48.63%				
Test for overall effect: Z=3.71(P=0)					
Test for subgroup differences: Not	applicable				
	Fav	ours misoprostol	0.01 0.1 1 10	<sup>100</sup> Favours gemeprost	

### Comparison 11. Comparison: misoprostol versus dinoprost

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24 hours	1	80	Odds Ratio (M-H, Fixed, 95% CI)	51.73 [2.89, 924.42]
2 Blood loss	1	80	Odds Ratio (M-H, Fixed, 95% CI)	10.52 [0.58, 191.12]
3 Surgical evacuation	1	80	Odds Ratio (M-H, Fixed, 95% CI)	5.90 [0.31, 113.60]
4 Pain (need analgesia)	1	80	Odds Ratio (M-H, Fixed, 95% CI)	1.56 [0.59, 4.08]
5 Vomiting	1	80	Odds Ratio (M-H, Fixed, 95% CI)	1.42 [0.52, 3.85]
6 Diarrhoea	1	80	Odds Ratio (M-H, Fixed, 95% CI)	1.85 [0.07, 46.83]

#### Analysis 11.1. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 1 Abortion within 24 hours.

Study or subgroup	Misoprostol	PGE2		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fix	ed, 9	5% CI			M-H, Fixed, 95% CI
Makhlouf 2003	50/50	20/30				-		100%	51.73[2.89,924.42]
Total (95% CI)	50	30						100%	51.73[2.89,924.42]
Total events: 50 (Misoprostol), 20 (PGE	2)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.68(P=0.01)									
		Favours PGE2	0.001	0.1	1	10	1000	Favours misoprostol	

#### Analysis 11.2. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 2 Blood loss.

Study or subgroup	Misoprostol	PGE2		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-Н, І	ixed, 95%	5 CI			M-H, Fixed, 95% CI
Makhlouf 2003	7/50	0/30				-		100%	10.52[0.58,191.12]
Total (95% CI)	50	30						100%	10.52[0.58,191.12]
Total events: 7 (Misoprostol), 0 (PGE2)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.59(P=0.11)				i		- i			
	Favo	ours misoprostol	0.01	0.1	1	10	100	Favours PGE2	

#### Analysis 11.3. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 3 Surgical evacuation.

Study or subgroup	Misoprostol	PGE2		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		М-Н, Р	ixed, 9	5% CI			M-H, Fixed, 95% CI
Makhlouf 2003	4/50	0/30		-				100%	5.9[0.31,113.6]
Total (95% CI)	50	30		-			-	100%	5.9[0.31,113.6]
Total events: 4 (Misoprostol), 0 (PGE2)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.18(P=0.24)									
	Favo	ours misoprostol	0.002	0.1	1	10	500	Favours PGE2	

#### Analysis 11.4. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 4 Pain (need analgesia).

Study or subgroup	Misoprostol	PGE2		Odds Ra	tio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, S	95% CI			M-H, Fixed, 95% Cl
Makhlouf 2003	20/50	9/30			-		100%	1.56[0.59,4.08]
					_			
Total (95% CI)	50	30					100%	1.56[0.59,4.08]
Total events: 20 (Misoprostol), 9 (PGE2	2)							
Heterogeneity: Not applicable								
Test for overall effect: Z=0.9(P=0.37)					1			
	Favo	ours misoprostol	0.01 0.	.1 1	10	100	Favours PGE2	

### Analysis 11.5. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 5 Vomiting.

Study or subgroup	Misoprostol	PGE2			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	6 CI			M-H, Fixed, 95% Cl
Makhlouf 2003	17/50	8/30						100%	1.42[0.52,3.85]
Total (95% CI)	50	30			-			100%	1.42[0.52,3.85]
Total events: 17 (Misoprostol), 8 (PGE2	:)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.68(P=0.49)									
	Fav	ours misoprostol	0.01	0.1	1	10	100	Favours PGE2	

# Analysis 11.6. Comparison 11 Comparison: misoprostol versus dinoprost, Outcome 6 Diarrhoea.

Study or subgroup	Misoprostol	PGE2		00	lds Ratio	<b>b</b>		Weight	Odds Ratio
	n/N	n/N		М-Н, F	ixed, 95	% CI			M-H, Fixed, 95% Cl
Makhlouf 2003	1/50	0/30					_	100%	1.85[0.07,46.83]
Total (95% CI)	50	30					_	100%	1.85[0.07,46.83]
Total events: 1 (Misoprostol), 0 (PGE2)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.37(P=0.71)									
	Favo	ours misoprostol	0.01	0.1	1	10	100	Favours PGE2	

### Comparison 12. Comparison: misoprostol, vaginal versus oral

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	2	196	Mean Difference (IV, Fixed, 95% CI)	-6.04 [-8.51, -3.58]
1.2 Misoprostol, 400 mcg vaginal versus 200 mcg oral	1	114	Mean Difference (IV, Fixed, 95% CI)	-14.9 [-23.33, -6.47]
2 Abortion within 24 hours	1	114	Odds Ratio (M-H, Fixed, 95% CI)	9.6 [3.74, 24.66]
2.1 Misoprostol 400 mcg vaginal versus 200 mcg oral	1	114	Odds Ratio (M-H, Fixed, 95% CI)	9.6 [3.74, 24.66]
3 Blood loss (mL)	1	114	Mean Difference (IV, Fixed, 95% CI)	24.00 [-70.90, 118.90]
3.1 Misoprostol 400 mcg vaginal versus 200 mcg oral	1	114	Mean Difference (IV, Fixed, 95% CI)	24.00 [-70.90, 118.90]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
4 Pain	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.08, 1.07]
4.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.08, 1.07]
5 Surgical evacuation	3	310	Odds Ratio (M-H, Fixed, 95% CI)	0.63 [0.34, 1.17]
5.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	2	196	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.30, 1.21]
5.2 Misoprostol 400 mcg vaginal versus 200 mcg oral	1	114	Odds Ratio (M-H, Fixed, 95% CI)	0.74 [0.20, 2.67]
6 Nausea	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.18, 0.93]
6.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.41 [0.18, 0.93]
7 Vomiting	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.43 [0.19, 0.98]
7.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	1	108	Odds Ratio (M-H, Fixed, 95% CI)	0.43 [0.19, 0.98]
8 Diarrhoea	1	108	Odds Ratio (M-H, Fixed, 95% CI)	1.23 [0.39, 3.85]
8.1 Misoprostol 400 mcg vaginal versus 400 mcg oral	1	108	Odds Ratio (M-H, Fixed, 95% CI)	1.23 [0.39, 3.85]

# Analysis 12.1. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 1 Induction to abortion interval.

Study or subgroup	Va	nginal	Oral		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% Cl
12.1.1 Misoprostol 400 mcg vaginal	versus 4	00 mcg oral					
Akoury 2004	84	18.3 (8.2)	52	30.5 (14.4)		33.06%	-12.2[-16.49,-7.91]
Behrashi 2008	30	9.7 (4.2)	30	12.7 (7.3)		66.94%	-3[-6.01,0.01]
Subtotal ***	114		82		•	100%	-6.04[-8.51,-3.58]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =11.83, df	=1(P=0);	l <sup>2</sup> =91.55%					
Test for overall effect: Z=4.8(P<0.0001)	)						
12.1.2 Misoprostol, 400 mcg vaginal	versus	200 mcg oral					
Bebbington 2002	49	19.6 (17.5)	65	34.5 (28.2)	— <u>—</u>	100%	-14.9[-23.33,-6.47]
Subtotal ***	49		65			100%	-14.9[-23.33,-6.47]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(P	<0.0001)	; I <sup>2</sup> =100%					
Test for overall effect: Z=3.47(P=0)							
			Fav	vours vaginal	-20 -10 0 10 20	Favours oral	

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Study or subgroup	Vaginal			Oral	Mean Difference					Weight Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI					Fixed, 95% CI
Test for subgroup differences: Chi <sup>2</sup> =	3.91, df	=1 (P=0.05), I <sup>2</sup> =74.439	6						I	
				Favours vaginal	-20	-10	0	10	20	Favours oral

#### Analysis 12.2. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 2 Abortion within 24 hours.

Study or subgroup	Vaginal	Oral			Odds Rati	0		Weight	Odds Ratio
	n/N	n/N		M-	H, Fixed, 95	5% CI			M-H, Fixed, 95% Cl
12.2.1 Misoprostol 400 mcg vaginal ve	ersus 200 mcg oral								
Bebbington 2002	42/49	25/65						100%	9.6[3.74,24.66]
Subtotal (95% CI)	49	65				$\blacklozenge$		100%	9.6[3.74,24.66]
Total events: 42 (Vaginal), 25 (Oral)									
Heterogeneity: Not applicable									
Test for overall effect: Z=4.7(P<0.0001)									
Total (95% CI)	49	65						100%	9.6[3.74,24.66]
Total events: 42 (Vaginal), 25 (Oral)									
Heterogeneity: Not applicable									
Test for overall effect: Z=4.7(P<0.0001)						1			
		Favours oral	0.01	0.1	1	10	100	Favours vaginal	

### Analysis 12.3. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 3 Blood loss (mL).

Study or subgroup	Va	aginal	Oral			Mean D	ifference	Weight	Mean Difference
	N	Mean(SD)	Ν	Mean(SD)		Fixed	, 95% CI		Fixed, 95% CI
12.3.1 Misoprostol 400 mcg vaginal	versus	200 mcg oral							
Bebbington 2002	49	264 (270)	65	240 (236)				100%	24[-70.9,118.9]
Subtotal ***	49		65					100%	24[-70.9,118.9]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(F	< 0.0001	; I <sup>2</sup> =100%							
Test for overall effect: Z=0.5(P=0.62)									
Total ***	49		65					100%	24[-70.9,118.9]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(F	<0.0001	; I <sup>2</sup> =100%							
Test for overall effect: Z=0.5(P=0.62)									
			Fa	ours vaginal	-200	-100	0 100 2	00 Favours oral	

### Analysis 12.4. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 4 Pain.

Study or subgroup	Vaginal	Oral	Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fix	ed, 95% CI			M-H, Fixed, 95% Cl
12.4.1 Misoprostol 400 mcg vaginal v	versus 400 mcg ora	ıl						
Akoury 2004	54/70	35/38			+		100%	0.29[0.08,1.07]
Subtotal (95% CI)	70	38			-		100%	0.29[0.08,1.07]
Total events: 54 (Vaginal), 35 (Oral)								
Heterogeneity: Not applicable				1				
		Favours vaginal	0.01	0.1	1 10	100	Favours oral	

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Study or subgroup	Vaginal n/N	Oral n/N		Ode M-H, Fi	ds Rat xed, 9	tio 95% Cl		Weight	Odds Ratio M-H, Fixed, 95% Cl
Test for overall effect: Z=1.86(P=0.06)									
Total (95% CI)	70	38						100%	0.29[0.08,1.07]
Total events: 54 (Vaginal), 35 (Oral) Heterogeneity: Not applicable									
Test for overall effect: Z=1.86(P=0.06)									
		Favours vaginal	0.01	0.1	1	10	100	Favours oral	

### Analysis 12.5. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 5 Surgical evacuation.

Study or subgroup	Vaginal	Oral		Odds Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% (	1		M-H, Fixed, 95% CI
12.5.1 Misoprostol 400 mcg vaginal v	versus 400 mcg oral						
Akoury 2004	20/84	18/52		<b></b> +		67.05%	0.59[0.28,1.26]
Behrashi 2008	2/30	3/30		+		11.08%	0.64[0.1,4.15]
Subtotal (95% CI)	114	82				78.13%	0.6[0.3,1.21]
Total events: 22 (Vaginal), 21 (Oral)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.01, df=1	(P=0.93); I <sup>2</sup> =0%						
Test for overall effect: Z=1.43(P=0.15)							
12.5.2 Misoprostol 400 mcg vaginal v	versus 200 mcg oral						
Bebbington 2002	4/49	7/65				21.87%	0.74[0.2,2.67]
Subtotal (95% CI)	49	65				21.87%	0.74[0.2,2.67]
Total events: 4 (Vaginal), 7 (Oral)							
Heterogeneity: Not applicable							
Test for overall effect: Z=0.47(P=0.64)							
Total (95% CI)	163	147		•		100%	0.63[0.34,1.17]
Total events: 26 (Vaginal), 28 (Oral)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.08, df=2	(P=0.96); I <sup>2</sup> =0%						
Test for overall effect: Z=1.47(P=0.14)							
Test for subgroup differences: Not appl	licable						
		Favours vaginal	0.01	0.1 1	10 100	Favours oral	

# Analysis 12.6. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 6 Nausea.

Study or subgroup	Vaginal	Oral		Odds Ratio		Weight	Odds Ratio
	n/N	n/N	M	H, Fixed, 95% CI			M-H, Fixed, 95% CI
12.6.1 Misoprostol 400 mcg vaginal v	ersus 400 mcg ora	l					
Akoury 2004	22/70	20/38	-	- <mark></mark>		100%	0.41[0.18,0.93]
Subtotal (95% CI)	70	38		•		100%	0.41[0.18,0.93]
Total events: 22 (Vaginal), 20 (Oral)							
Heterogeneity: Not applicable							
Test for overall effect: Z=2.14(P=0.03)							
Total (95% CI)	70	38	-	•		100%	0.41[0.18,0.93]
Total events: 22 (Vaginal), 20 (Oral)							
		Favours vaginal	0.01 0.1	1 10	100	Favours oral	

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Study or subgroup	Vaginal n/N	Oral n/N	Odds Ratio M-H, Fixed, 95% Cl					Weight	Odds Ratio M-H, Fixed, 95% Cl
Heterogeneity: Not applicable									
Test for overall effect: Z=2.14(P=0.03)						1			
		Favours vaginal	0.01	0.1	1	10	100	Favours oral	

### Analysis 12.7. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 7 Vomiting.

Study or subgroup	Vaginal	Oral		Odds Ratio	<b>)</b>	Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95	% CI		M-H, Fixed, 95% Cl
12.7.1 Misoprostol 400 mcg vaginal	versus 400 mcg ora	al					
Akoury 2004	18/70	17/38		<b></b> +		100%	0.43[0.19,0.98]
Subtotal (95% CI)	70	38				100%	0.43[0.19,0.98]
Total events: 18 (Vaginal), 17 (Oral)							
Heterogeneity: Not applicable							
Test for overall effect: Z=2(P=0.05)							
Total (95% CI)	70	38		•		100%	0.43[0.19,0.98]
Total events: 18 (Vaginal), 17 (Oral)							
Heterogeneity: Not applicable							
Test for overall effect: Z=2(P=0.05)							
		Favours vaginal	0.01	0.1 1	10 10	<sup>D</sup> Favours oral	

### Analysis 12.8. Comparison 12 Comparison: misoprostol, vaginal versus oral, Outcome 8 Diarrhoea.

Study or subgroup	Vaginal	Oral		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H	, Fixed, 95%	CI			M-H, Fixed, 95% Cl
12.8.1 Misoprostol 400 mcg vaginal v	versus 400 mcg ora	al							
Akoury 2004	11/70	5/38						100%	1.23[0.39,3.85]
Subtotal (95% CI)	70	38			-			100%	1.23[0.39,3.85]
Total events: 11 (Vaginal), 5 (Oral)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.36(P=0.72)									
Total (95% CI)	70	38			-			100%	1.23[0.39,3.85]
Total events: 11 (Vaginal), 5 (Oral)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.36(P=0.72)									
		Eavours vaginal	0.01	0.1	1	10	100	Favours oral	

#### Comparison 13. Comparison: misoprostol, vaginal versus sublingual

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	277	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.00, 0.80]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2 Abortion within 24 hours	3	1178	Odds Ratio (M-H, Fixed, 95% CI)	1.39 [1.05, 1.83]
3 Blood loss	1	277	Odds Ratio (M-H, Fixed, 95% CI)	1.80 [0.52, 6.31]
4 Pain	2	497	Odds Ratio (M-H, Fixed, 95% CI)	1.09 [0.73, 1.63]
5 Surgical evacuation	2	497	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.52, 1.58]
6 Nausea	3	1178	Odds Ratio (M-H, Fixed, 95% CI)	1.09 [0.81, 1.48]
7 Vomiting	2	958	Odds Ratio (M-H, Fixed, 95% CI)	0.85 [0.55, 1.30]
8 Diarrhoea	3	1178	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.71, 1.25]

# Analysis 13.1. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 1 Induction to abortion interval.

Study or subgroup	v	ginal Sublingual		olingual	Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Bhattacharjee 2008	138	14.5 (1.6)	139	14.1 (1.8)		100%	0.4[-0,0.8]
Total ***	138		139			100%	0.4[-0,0.8]
Heterogeneity: Not applicable							
Test for overall effect: Z=1.96(P=0.05)							
			Fa	vours vaginal	-1 -0.5 0 0.5 1	Favours subling	gual

# Analysis 13.2. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 2 Abortion within 24 hours.

Study or subgroup	Vaginal	Sublingual		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fixe	d, 95% C	I			M-H, Fixed, 95% Cl
Bhattacharjee 2008	85/138	89/139			-			40.67%	0.9[0.55,1.47]
Tang 2004	96/112	78/108						13.55%	2.31[1.17,4.54]
von Hertzen 2009	292/340	272/341						45.79%	1.54[1.03,2.31]
Total (95% CI)	590	588			•			100%	1.39[1.05,1.83]
Total events: 473 (Vaginal), 439 (Subli	ngual)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =5.45, df=2	2(P=0.07); I <sup>2</sup> =63.32%	)							
Test for overall effect: Z=2.28(P=0.02)									
	Fa	avours sublingual	0.01	0.1	1	10	100	Favours vaginal	

# Analysis 13.3. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 3 Blood loss.

Study or subgroup	Vaginal	Sublingual	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		M-H	i, Fixed, 95%	% CI			M-H, Fixed, 95% CI
Bhattacharjee 2008	7/138	4/139						100%	1.8[0.52,6.31]
Total (95% CI)	138	139			-			100%	1.8[0.52,6.31]
Total events: 7 (Vaginal), 4 (Sublingual)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.92(P=0.36)									
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

### Analysis 13.4. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 4 Pain.

Study or subgroup	Vaginal	Sublingual		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-	H, Fixed, 95% C	:I			M-H, Fixed, 95% CI
Bhattacharjee 2008	36/138	40/139						64.52%	0.87[0.51,1.48]
Tang 2004	31/112	22/108						35.48%	1.5[0.8,2.8]
Total (95% CI)	250	247			•			100%	1.09[0.73,1.63]
Total events: 67 (Vaginal), 62 (Sublingu	al)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.66, df=1	(P=0.2); I <sup>2</sup> =39.77%								
Test for overall effect: Z=0.44(P=0.66)									
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

#### Analysis 13.5. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 5 Surgical evacuation.

Study or subgroup	Vaginal	Sublingual		(	Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	Fixed, 95%	CI			M-H, Fixed, 95% CI
Bhattacharjee 2008	11/138	12/139						42.58%	0.92[0.39,2.15]
Tang 2004	16/112	17/108						57.42%	0.89[0.43,1.87]
Total (95% CI)	250	247			•			100%	0.9[0.52,1.58]
Total events: 27 (Vaginal), 29 (Sublingu	ial)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=1(P=	0.96); l <sup>2</sup> =0%								
Test for overall effect: Z=0.36(P=0.72)									
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

#### Analysis 13.6. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 6 Nausea.

Study or subgroup	Vaginal	Sublingual	Odds Ratio					Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% CI					M-H, Fixed, 95% CI
Bhattacharjee 2008	10/138	14/139		-	•			16.25%	0.7[0.3,1.63]
Tang 2004	53/112	45/108			- <b>+=</b>			30.32%	1.26[0.74,2.14]
von Hertzen 2009	56/340	51/341			-#-			53.43%	1.12[0.74,1.69]
Total (95% CI)	590	588			•			100%	1.09[0.81,1.48]
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

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Study or subgroup	Vaginal n/N	Sublingual n/N		Odds Ratio M-H, Fixed, 95% Cl				Weight	Odds Ratio M-H, Fixed, 95% Cl
Total events: 119 (Vaginal), 110 (Sub	lingual)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.36, df									
Test for overall effect: Z=0.58(P=0.56	)								
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

### Analysis 13.7. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 7 Vomiting.

Study or subgroup	Vaginal	Sublingual		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	I, Fixed, 95%	СІ			M-H, Fixed, 95% CI
Bhattacharjee 2008	4/138	8/139			•			16.96%	0.49[0.14,1.66]
von Hertzen 2009	40/340	43/341			<b>-</b>			83.04%	0.92[0.58,1.46]
Total (95% CI)	478	480			•			100%	0.85[0.55,1.3]
Total events: 44 (Vaginal), 51 (Sublingu	ial)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.91, df=1	(P=0.34); I <sup>2</sup> =0%								
Test for overall effect: Z=0.74(P=0.46)									
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

### Analysis 13.8. Comparison 13 Comparison: misoprostol, vaginal versus sublingual, Outcome 8 Diarrhoea.

Study or subgroup	Vaginal	Sublingual		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-ł	H, Fixed, 95%	5 CI			M-H, Fixed, 95% CI
Bhattacharjee 2008	12/138	9/139			+			8.42%	1.38[0.56,3.38]
Tang 2004	29/112	34/108						26.39%	0.76[0.42,1.37]
von Hertzen 2009	80/340	83/341			-			65.19%	0.96[0.67,1.36]
Total (95% CI)	590	588			•			100%	0.94[0.71,1.25]
Total events: 121 (Vaginal), 126 (Subli	ngual)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.2, df=2	(P=0.55); I <sup>2</sup> =0%								
Test for overall effect: Z=0.42(P=0.67)									
		Favours vaginal	0.01	0.1	1	10	100	Favours sublingual	

#### Comparison 14. Comparison: misoprostol, tablet versus gel

No. of studies	No. of partici- pants	Statistical method	Effect size
1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.72 [0.37, 1.43]
1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.34 [0.03, 3.37]
1	148	Odds Ratio (M-H, Fixed, 95% CI)	1.46 [0.67, 3.15]
1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.46, 1.93]
	No. of studies   1   1   1   1   1   1   1	No. of studiesNo. of participants11481148114811481148	No. of studiesNo. of participantsStatistical method1148Odds Ratio (M-H, Fixed, 95% Cl)1148Odds Ratio (M-H, Fixed, 95% Cl)

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Outcome or sub- group title	No. of studies	No. of partici- pants	Statistical method	Effect size
5 Nausea	1	148	Odds Ratio (M-H, Fixed, 95% CI)	1.61 [0.26, 9.92]
6 Vomiting	1	148	Odds Ratio (M-H, Fixed, 95% CI)	3.26 [0.33, 32.09]
7 Diarrhoea	1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.15 [0.03, 0.71]

### Analysis 14.1. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 1 Abortion within 24 hours.

Study or subgroup	Dry tablet	<b>Gel insertion</b>		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fix	ed, 95% C	I			M-H, Fixed, 95% Cl
Pongsatha 2008	45/72	53/76			-			100%	0.72[0.37,1.43]
Total (95% CI)	72	76						100%	0.72[0.37,1.43]
Total events: 45 (Dry tablet), 53 (Gel in	sertion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.93(P=0.35)									
	Fav	ours gel insertion	0.01	0.1	1	10	100	Favours dry tablet	

### Analysis 14.2. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 2 Blood loss > 500 mL.

Study or subgroup	Dry tablet	<b>Gel insertion</b>		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixe	d, 95% CI				M-H, Fixed, 95% CI
Pongsatha 2008	1/72	3/76		-				100%	0.34[0.03,3.37]
Total (95% CI)	72	76						100%	0.34[0.03,3.37]
Total events: 1 (Dry tablet), 3 (Gel inse	rtion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.92(P=0.36)									
		Favours dry tablet	0.01 0	.1 1		10	100	Favours gel insertion	

### Analysis 14.3. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 3 Surgical evacuation.

Study or subgroup	Dry tablet	Gel insertion		Odds Ratio M-H. Fixed, 95% Cl				Weight	Odds Ratio
	ių i	11/13		M-11	, 1 IACU, 33 /0 (	<b>61</b>			M-11, 1 Acu, 55 /6 Cl
Pongsatha 2008	19/72	15/76						100%	1.46[0.67,3.15]
Total (95% CI)	72	76			-			100%	1.46[0.67,3.15]
Total events: 19 (Dry tablet), 15 (Gel i	nsertion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.96(P=0.34)									
		Favours dry tablet	0.01	0.1	1	10	100	Favours gel insertion	

#### Analysis 14.4. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 4 Pain.

Study or subgroup	Dry tablet	<b>Gel insertion</b>		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	H, Fixed, 95% C	1			M-H, Fixed, 95% CI
Pongsatha 2008	20/72	22/76						100%	0.94[0.46,1.93]
Total (95% CI)	72	76			•			100%	0.94[0.46,1.93]
Total events: 20 (Dry tablet), 22 (Gel in	sertion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.16(P=0.87)						1			
		Favours dry tablet	0.01	0.1	1	10	100	Favours gel insertion	

### Analysis 14.5. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 5 Nausea.

Study or subgroup	Dry tablet	<b>Gel insertion</b>		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	I, Fixed, 959	% CI			M-H, Fixed, 95% CI
Pongsatha 2008	3/72	2/76						100%	1.61[0.26,9.92]
Total (95% CI)	72	76						100%	1.61[0.26,9.92]
Total events: 3 (Dry tablet), 2 (Gel inse	rtion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.51(P=0.61)									
		Favours dry tablet	0.01	0.1	1	10	100	Favours gel insertion	

#### Analysis 14.6. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 6 Vomiting.

Study or subgroup	Dry tablet	<b>Gel insertion</b>		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	% CI			M-H, Fixed, 95% CI
Pongsatha 2008	3/72	1/76			——— <mark>—</mark> —		-	100%	3.26[0.33,32.09]
						_			
Total (95% CI)	72	76					-	100%	3.26[0.33,32.09]
Total events: 3 (Dry tablet), 1 (Gel inse	rtion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.01(P=0.31)				1		1	1		
		Favours dry tablet	0.01	0.1	1	10	100	Favours gel insertion	

#### Analysis 14.7. Comparison 14 Comparison: misoprostol, tablet versus gel, Outcome 7 Diarrhoea.

Study or subgroup	Dry tablet	Gel insertion		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fix	ed, 95%	CI			M-H, Fixed, 95% Cl
Pongsatha 2008	2/72	12/76		-				100%	0.15[0.03,0.71]
Total (95% CI)	72	76						100%	0.15[0.03,0.71]
Total events: 2 (Dry tablet), 12 (Gel ins	ertion)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.4(P=0.02)						i.			
		Favours dry tablet	0.01	0.1	1	10	100	Favours gel insertion	



# Comparison 15. Comparison: time interval misoprostol

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	148	Mean Difference (IV, Fixed, 95% CI)	-19.2 [-36.02, -2.38]
2 Abortion within 24 hours	2	427	Odds Ratio (M-H, Fixed, 95% CI)	1.50 [0.99, 2.26]
2.1 Misoprostol 400 mcg, every 3h versus every 6h	1	148	Odds Ratio (M-H, Fixed, 95% Cl)	1.74 [0.87, 3.48]
2.2 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% Cl)	1.38 [0.82, 2.31]
3 Blood loss (mL)	1	148	Mean Difference (IV, Fixed, 95% CI)	-39.7 [-83.12, 3.72]
4 Blood loss (>500 mL)	1	279	Odds Ratio (M-H, Fixed, 95% CI)	1.33 [0.29, 6.07]
4.1 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% CI)	1.33 [0.29, 6.07]
5 Surgical evacuation	1	155	Odds Ratio (M-H, Fixed, 95% CI)	6.14 [0.31, 120.92]
5.1 Misoprostol 600 mcg, every 6h versus every 12h	1	155	Odds Ratio (M-H, Fixed, 95% CI)	6.14 [0.31, 120.92]
6 Pain	2	427	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.75, 1.70]
6.1 Misoprostol 400 mcg, every 3h versus every 6h	1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.45, 1.74]
6.2 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% CI)	1.30 [0.78, 2.16]
7 Nausea	2	427	Odds Ratio (M-H, Fixed, 95% CI)	1.26 [0.64, 2.45]
7.1 Misoprostol 400 mcg, every 3h versus every 6h	1	148	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.27, 2.15]
7.2 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% CI)	1.82 [0.74, 4.49]
8 Vomiting	2	427	Odds Ratio (M-H, Fixed, 95% Cl)	1.47 [0.72, 3.00]
8.1 Misoprostol 400 mcg, every 3h versus every 6h	1	148	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.35, 2.82]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
8.2 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% CI)	2.08 [0.76, 5.70]
9 Diarrhoea	2	427	Odds Ratio (M-H, Fixed, 95% CI)	1.28 [0.80, 2.04]
9.1 Misoprostol 400 mcg, every 3h versus every 6h	1	148	Odds Ratio (M-H, Fixed, 95% CI)	2.06 [0.37, 11.59]
9.2 Misoprostol 600 mcg, every 6h versus every 12h	1	279	Odds Ratio (M-H, Fixed, 95% CI)	1.23 [0.75, 2.00]

### Analysis 15.1. Comparison 15 Comparison: time interval misoprostol, Outcome 1 Induction to abortion interval.

Study or subgroup	Sma inte	ller time erval (1)	Larger time interval (2)			Mean Difference			Weight	Mean Difference	
	Ν	Mean(SD)	Ν	Mean(SD)		I	Fixed, 95% CI				Fixed, 95% CI
Wong 2000	74	24.2 (35.4)	74	43.4 (64.8)		_				100%	-19.2[-36.02,-2.38]
Total ***	74		74			•	$\bullet$			100%	-19.2[-36.02,-2.38]
Heterogeneity: Not applicable											
Test for overall effect: Z=2.24(P=0.03)											
			Favo	urs interval 1	-100	-50	0	50	100	Favours interv	al 2

#### Analysis 15.2. Comparison 15 Comparison: time interval misoprostol, Outcome 2 Abortion within 24 hours.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		м-н,	Fixed, 95% C	I		M-H, Fixed, 95% CI
15.2.1 Misoprostol 400 mcg, every 3	3h versus every 6h							
Wong 2000	54/74	45/74					33.02%	1.74[0.87,3.48]
Subtotal (95% CI)	74	74			-		33.02%	1.74[0.87,3.48]
Total events: 54 (Smaller time interva	al (1)), 45 (Larger tim	e interval (2))						
Heterogeneity: Not applicable								
Test for overall effect: Z=1.57(P=0.12)								
15.2.2 Misoprostol 600 mcg, every (	6h versus every 12h	I						
Herabutya 2005	103/140	93/139					66.98%	1.38[0.82,2.31]
Subtotal (95% CI)	140	139			•		66.98%	1.38[0.82,2.31]
Total events: 103 (Smaller time interv	/al (1)), 93 (Larger tir	ne interval (2))						
Heterogeneity: Not applicable								
Test for overall effect: Z=1.22(P=0.22)								
Total (95% CI)	214	213			•		100%	1.5[0.99,2.26]
Total events: 157 (Smaller time interv	/al (1)), 138 (Larger ti	ime interval (2))						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.28, df=	=1(P=0.6); l <sup>2</sup> =0%							
Test for overall effect: Z=1.91(P=0.06)								
		Favours interval 2	0.01	0.1	1	10 100	<sup>)</sup> Favours interval 1	



Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixed, 95% CI					M-H, Fixed, 95% CI
Test for subgroup differences: Not applicable			_			1			
		Favours interval 2	0.01	0.1	1	10	100	Favours interval 1	

### Analysis 15.3. Comparison 15 Comparison: time interval misoprostol, Outcome 3 Blood loss (mL).

Study or subgroup	Sma inte	naller time Larger ti nterval (1) interval		ger time erval (2)	e Mean Differe		Weight I	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed	, 95% CI		Fixed, 95% CI
Wong 2000	74	100.7 (98.2)	74	140.4 (163.3)		H	100%	-39.7[-83.12,3.72]
Total ***	74		74		-	•	100%	-39.7[-83.12,3.72]
Heterogeneity: Not applicable								
Test for overall effect: Z=1.79(P=0.07)								
			Favo	urs interval 1	-200 -100	0 100 200	Favours interval	2

#### Analysis 15.4. Comparison 15 Comparison: time interval misoprostol, Outcome 4 Blood loss (>500 mL).

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-I	I, Fixed, 95%	CI			M-H, Fixed, 95% CI
15.4.1 Misoprostol 600 mcg, every	6h versus every 12	h							
Herabutya 2005	4/140	3/139				-		100%	1.33[0.29,6.07]
Subtotal (95% CI)	140	139			-	-		100%	1.33[0.29,6.07]
Total events: 4 (Smaller time interva	al (1)), 3 (Larger time	interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.37(P=0.71	L)								
Total (95% CI)	140	139				-		100%	1.33[0.29,6.07]
Total events: 4 (Smaller time interva	al (1)), 3 (Larger time	interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.37(P=0.7)	L)								
		Favours interval 1	0.01	0.1	1	10	100	Favours interval 2	

### Analysis 15.5. Comparison 15 Comparison: time interval misoprostol, Outcome 5 Surgical evacuation.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio		Weight	Odds Ratio		
	n/N	n/N		м-н,	Fixed, 9	5% CI			M-H, Fixed, 95% CI
15.5.1 Misoprostol 600 mcg, every	6h versus every 12h	1							
Herabutya 2005	3/84	0/71		-		-		100%	6.14[0.31,120.92]
Subtotal (95% CI)	84	71		-				100%	6.14[0.31,120.92]
Total events: 3 (Smaller time interval	(1)), 0 (Larger time i	nterval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=1.19(P=0.23)			1						
		Favours interval 1	0.005	0.1	1	10	200	Favours interval 2	

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Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		м-н,	Fixed, 9	5% CI			M-H, Fixed, 95% CI
Total (95% CI)	84	71						100%	6.14[0.31,120.92]
Total events: 3 (Smaller time inter	val (1)), 0 (Larger time i	interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=1.19(P=0.2	23)								
		Favours interval 1	0.005	0.1	1	10	200	Favours interval 2	

# Analysis 15.6. Comparison 15 Comparison: time interval misoprostol, Outcome 6 Pain.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		м-н,	Fixed, 95%	CI			M-H, Fixed, 95% CI
15.6.1 Misoprostol 400 mcg, every	3h versus every 6h								
Wong 2000	25/74	27/74						40.75%	0.89[0.45,1.74]
Subtotal (95% CI)	74	74			•			40.75%	0.89[0.45,1.74]
Total events: 25 (Smaller time interva	al (1)), 27 (Larger tim	e interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.34(P=0.73)	1								
15.6.2 Misoprostol 600 mcg, every	6h versus every 12h	ı							
Herabutya 2005	47/140	39/139			- <mark></mark>			59.25%	1.3[0.78,2.16]
Subtotal (95% CI)	140	139			•			59.25%	1.3[0.78,2.16]
Total events: 47 (Smaller time interva	al (1)), 39 (Larger tim	e interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=1(P=0.32)									
Total (95% CI)	214	213			•			100%	1.13[0.75,1.7]
Total events: 72 (Smaller time interva	al (1)), 66 (Larger tim	e interval (2))							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.77, df	=1(P=0.38); I <sup>2</sup> =0%								
Test for overall effect: Z=0.59(P=0.56)	)								
Test for subgroup differences: Not ap	plicable								
		Favours interval 1	0.01	0.1	1	10	100	Favours interval 2	

### Analysis 15.7. Comparison 15 Comparison: time interval misoprostol, Outcome 7 Nausea.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ra				Weight	Odds Ratio
	n/N	n/N		м-н,	Fixed, 95%	CI			M-H, Fixed, 95% Cl
15.7.1 Misoprostol 400 mcg, every	3h versus every 6h								
Wong 2000	7/74	9/74		_				53%	0.75[0.27,2.15]
Subtotal (95% CI)	74	74		-				53%	0.75[0.27,2.15]
Total events: 7 (Smaller time interval	(1)), 9 (Larger time i	nterval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.53(P=0.6)									
15.7.2 Misoprostol 600 mcg, every	6h versus every 12h								
		Favours interval 1	0.01	0.1	1	10	100	Favours interval 2	



Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	Fixed, 95% CI			M-H, Fixed, 95% Cl
Herabutya 2005	14/140	8/139			+		47%	1.82[0.74,4.49]
Subtotal (95% CI)	140	139					47%	1.82[0.74,4.49]
Total events: 14 (Smaller time interv	al (1)), 8 (Larger time	interval (2))						
Heterogeneity: Not applicable								
Test for overall effect: Z=1.3(P=0.19)								
Total (95% CI)	214	213			+		100%	1.26[0.64,2.45]
Total events: 21 (Smaller time interv	al (1)), 17 (Larger tim	e interval (2))						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.56, df	=1(P=0.21); I <sup>2</sup> =35.94%	6						
Test for overall effect: Z=0.66(P=0.51)	)							
Test for subgroup differences: Not ap	plicable							
		Favours interval 1	0.01	0.1	1	10 100	Favours interval 2	

### Analysis 15.8. Comparison 15 Comparison: time interval misoprostol, Outcome 8 Vomiting.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds Ratio	Weight	Odds Ratio
	n/N	n/N	М-	H, Fixed, 95% Cl		M-H, Fixed, 95% CI
15.8.1 Misoprostol 400 mcg, every	3h versus every 6h					
Wong 2000	8/74	8/74			56.45%	1[0.35,2.82]
Subtotal (95% CI)	74	74		-	56.45%	1[0.35,2.82]
Total events: 8 (Smaller time interval	(1)), 8 (Larger time i	nterval (2))				
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						
15.8.2 Misoprostol 600 mcg, every	6h versus every 12h	1				
Herabutya 2005	12/140	6/139		+	43.55%	2.08[0.76,5.7]
Subtotal (95% CI)	140	139			43.55%	2.08[0.76,5.7]
Total events: 12 (Smaller time interva	al (1)), 6 (Larger time	interval (2))				
Heterogeneity: Not applicable						
Test for overall effect: Z=1.42(P=0.16)						
Total (95% CI)	214	213		-	100%	1.47[0.72,3]
Total events: 20 (Smaller time interva	al (1)), 14 (Larger tim	e interval (2))				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.98, df=	=1(P=0.32); I <sup>2</sup> =0%					
Test for overall effect: Z=1.06(P=0.29)						
Test for subgroup differences: Not ap	plicable					
		Favours interval 1	0.01 0.1	1 10	<sup>100</sup> Favours interval 2	

### Analysis 15.9. Comparison 15 Comparison: time interval misoprostol, Outcome 9 Diarrhoea.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds R	atio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% CI				M-H, Fixed, 95% CI
15.9.1 Misoprostol 400 mcg, every	3h versus every 6h							
Wong 2000	4/74	2/74			+		6.08%	2.06[0.37,11.59]
		Favours interval 1	0.001	0.1 1	10	1000	Favours interval 2	

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Study or subgroup	Smaller time interval (1)	Larger time interval (2)	0	dds Ratio	Weight	Odds Ratio
	n/N	n/N	М-Н,	Fixed, 95% CI		M-H, Fixed, 95% Cl
Subtotal (95% CI)	74	74			6.08%	2.06[0.37,11.59]
Total events: 4 (Smaller time interva	l (1)), 2 (Larger time i	interval (2))				
Heterogeneity: Not applicable						
Test for overall effect: Z=0.82(P=0.41)	)					
15.9.2 Misoprostol 600 mcg, every	6h versus every 12h	ı				
Herabutya 2005	55/140	48/139		<b>_+</b> _	93.92%	1.23[0.75,2]
Subtotal (95% CI)	140	139		•	93.92%	1.23[0.75,2]
Total events: 55 (Smaller time interv	al (1)), 48 (Larger tim	ie interval (2))				
Heterogeneity: Not applicable						
Test for overall effect: Z=0.82(P=0.41)	)					
Total (95% CI)	214	213		•	100%	1.28[0.8,2.04]
Total events: 59 (Smaller time interv	al (1)), 50 (Larger tim	e interval (2))				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.32, df	=1(P=0.57); I <sup>2</sup> =0%					
Test for overall effect: Z=1.03(P=0.31)	)					
Test for subgroup differences: Not ap	oplicable					
		Favours interval 1	0.001 0.1	1 10	1000 Favours interval 2	2

# Comparison 16. Comparison: time interval gemeprost

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Abortion within 24 hours	1	99	Odds Ratio (M-H, Fixed, 95% CI)	1.03 [0.42, 2.52]
2 Surgical evacuations	1	99	Odds Ratio (M-H, Fixed, 95% CI)	0.51 [0.21, 1.25]
3 Pain	1	99	Odds Ratio (M-H, Fixed, 95% CI)	1.90 [0.71, 5.09]

# Analysis 16.1. Comparison 16 Comparison: time interval gemeprost, Outcome 1 Abortion within 24 hours.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)	Odds Ratio					Weight	Odds Ratio
	n/N	n/N		M-H	l, Fixed, 95%	CI			M-H, Fixed, 95% Cl
Armatage 1996	37/50	36/49						100%	1.03[0.42,2.52]
Total (95% CI)	50	49			•			100%	1.03[0.42,2.52]
Total events: 37 (Smaller time interva	al (1)), 36 (Larger time	e interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=0.06(P=0.95)							I		
	I	Favours interval 1	0.01	0.1	1	10	100	Favours interval 2	

### Analysis 16.2. Comparison 16 Comparison: time interval gemeprost, Outcome 2 Surgical evacuations.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95% C	I			M-H, Fixed, 95% CI
Armatage 1996	32/50	38/49		_				100%	0.51[0.21,1.25]
Total (95% CI)	50	49		-				100%	0.51[0.21,1.25]
Total events: 32 (Smaller time interv	al (1)), 38 (Larger time	e interval (2))							
Heterogeneity: Not applicable									
Test for overall effect: Z=1.47(P=0.14)	)								
		Favours interval 1	0.01	0.1	1	10	100	Favours interval 2	

# Analysis 16.3. Comparison 16 Comparison: time interval gemeprost, Outcome 3 Pain.

Study or subgroup	Smaller time interval (1)	Larger time interval (2)		Odds	Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixe	d, 95% CI			M-H, Fixed, 95% Cl
Armatage 1996	42/50	36/49		_			100%	1.9[0.71,5.09]
Total (95% CI)	50	49		-			100%	1.9[0.71,5.09]
Total events: 42 (Smaller time inter	val (1)), 36 (Larger time	e interval (2))						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0	0(P<0.0001); I <sup>2</sup> =100%							
Test for overall effect: Z=1.27(P=0.2	)							
		avours interval 1	0.01	0.1	L 10	100	Favours interval 2	

#### Comparison 17. Comparison: low dose versus high dose of misoprostol

Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion in- terval	2	113	Mean Difference (IV, Fixed, 95% CI)	1.29 [-3.12, 5.69]
1.1 100 mcg versus 200 mcg	1	53	Mean Difference (IV, Fixed, 95% CI)	-4.70 [-11.19, 1.79]
1.2 400 mcg versus 600 mcg	1	60	Mean Difference (IV, Fixed, 95% CI)	6.4 [0.40, 12.40]
2 Pain	2	113	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.29, 1.95]
2.1 100 mcg versus 200 mcg	1	53	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.32, 2.75]
2.2 400 mcg versus 600 mcg	1	60	Odds Ratio (M-H, Fixed, 95% CI)	0.31 [0.03, 3.17]
3 Nausea	1	60	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.10, 4.15]
3.1 400 mcg versus 600 mcg	1	60	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.10, 4.15]

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Outcome or subgroup ti- tle	No. of studies	No. of partici- pants	Statistical method	Effect size
4 Vomiting	2	113	Odds Ratio (M-H, Fixed, 95% CI)	1.42 [0.42, 4.85]
4.1 100 mcg versus 200 mcg	1	53	Odds Ratio (M-H, Fixed, 95% CI)	2.19 [0.49, 9.88]
4.2 400 mcg versus 600 mcg	1	60	Odds Ratio (M-H, Fixed, 95% CI)	0.48 [0.04, 5.63]
5 Diarrhoea	2	113	Odds Ratio (M-H, Fixed, 95% CI)	0.53 [0.11, 2.58]
5.1 100 mcg versus 200 mcg	1	53	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 3.90]
5.2 400 mcg versus 600 mcg	1	60	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.13, 7.60]

# Analysis 17.1. Comparison 17 Comparison: low dose versus high dose of misoprostol, Outcome 1 Induction to abortion interval.

Study or subgroup	Lo	w dose	Hig	h dose	I	/lean Differ	ence		Weight	Mean Difference
	Ν	Mean(SD)	N	Mean(SD)		Fixed, 95%	6 CI			Fixed, 95% CI
17.1.1 100 mcg versus 200 mcg										
Nuutila 1997 c	27	23.1 (12.3)	26	27.8 (11.8)	-				46.06%	-4.7[-11.19,1.79]
Subtotal ***	27		26		-				46.06%	-4.7[-11.19,1.79]
Heterogeneity: Not applicable										
Test for overall effect: Z=1.42(P=0.16)										
17.1.2 400 mcg versus 600 mcg										
Ozerkan 2009	30	21.8 (13.8)	30	15.4 (9.5)			-		53.94%	6.4[0.4,12.4]
Subtotal ***	30		30						53.94%	6.4[0.4,12.4]
Heterogeneity: Not applicable										
Test for overall effect: Z=2.09(P=0.04)										
Total ***	57		56			-	•		100%	1.29[-3.12,5.69]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =6.06, df=1	L(P=0.01	.); I²=83.51%								
Test for overall effect: Z=0.57(P=0.57)										
Test for subgroup differences: Chi <sup>2</sup> =6.0	06, df=1	(P=0.01), I <sup>2</sup> =83.51%	Ď							
			Favo	urs low dose	-20 -1	0 0	10	20	Favours hi	gh dose

### Analysis 17.2. Comparison 17 Comparison: low dose versus high dose of misoprostol, Outcome 2 Pain.

Study or subgroup	Low dose	High dose		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 9		ixed, 95% CI			M-H, Fixed, 95% Cl
17.2.1 100 mcg versus 200 mcg									
Nuutila 1997 c	12/27	12/26			— <mark>—</mark> —			70.08%	0.93[0.32,2.75]
Subtotal (95% CI)	27	26			$\bullet$			70.08%	0.93[0.32,2.75]
Total events: 12 (Low dose), 12 (High o	lose)								
		Favours low dose	0.01	0.1	1	10	100	Favours high dose	

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					<b>_</b>			
Study or subgroup	Low dose	High dose		Odds	Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixe	d, 95% CI			M-H, Fixed, 95% Cl
Heterogeneity: Not applicable								
Test for overall effect: Z=0.12(P=0.9)								
17.2.2.400								
17.2.2 400 mcg versus 600 mcg								
Ozerkan 2009	1/30	3/30					29.92%	0.31[0.03,3.17]
Subtotal (95% CI)	30	30					29.92%	0.31[0.03,3.17]
Total events: 1 (Low dose), 3 (High dos	e)							
Heterogeneity: Not applicable								
Test for overall effect: Z=0.99(P=0.32)								
Total (95% CI)	57	56					100%	0.75[0.29,1.95]
Total events: 13 (Low dose), 15 (High d	ose)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.71, df=1	(P=0.4); I <sup>2</sup> =0%							
Test for overall effect: Z=0.6(P=0.55)								
Test for subgroup differences: Not appl	licable							
		Favours low dose	0.01	0.1	L 10	100	Favours high dose	

### Analysis 17.3. Comparison 17 Comparison: low dose versus high dose of misoprostol, Outcome 3 Nausea.

Study or subgroup	Low dose	High dose		C	Odds Ratio			Weight	Odds Ratio
	n/N	n/N		М-Н,	Fixed, 95%	6 CI			M-H, Fixed, 95% CI
17.3.1 400 mcg versus 600 mcg									
Ozerkan 2009	2/30	3/30			-	-		100%	0.64[0.1,4.15]
Subtotal (95% CI)	30	30						100%	0.64[0.1,4.15]
Total events: 2 (Low dose), 3 (High dose	)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.46(P=0.64)									
Total (95% CI)	30	30				-		100%	0.64[0.1,4.15]
Total events: 2 (Low dose), 3 (High dose	)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.46(P=0.64)									
		Favours low dose	0.01	0.1	1	10	100	Favours high dose	

# Analysis 17.4. Comparison 17 Comparison: low dose versus high dose of misoprostol, Outcome 4 Vomiting.

Study or subgroup	Low dose	High dose			Odds Rat	io		Weight	Odds Ratio
	n/N	n/N		М-	H, Fixed, 9	5% CI			M-H, Fixed, 95% Cl
17.4.1 100 mcg versus 200 mcg									
Nuutila 1997 c	6/27	3/26				<b>—</b>		55.15%	2.19[0.49,9.88]
Subtotal (95% CI)	27	26						55.15%	2.19[0.49,9.88]
Total events: 6 (Low dose), 3 (High dose	·)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.02(P=0.31)									
17.4.2 400 mcg versus 600 mcg									
Ozerkan 2009	1/30	2/30			-			44.85%	0.48[0.04,5.63]
		Favours low dose	0.01	0.1	1	10	100	Favours high dose	

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Study or subgroup	Low dose	High dose			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		М-Н	, Fixed, 95%	o CI			M-H, Fixed, 95% CI
Subtotal (95% CI)	30	30				-		44.85%	0.48[0.04,5.63]
Total events: 1 (Low dose), 2 (High dose	e)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.58(P=0.56)									
Total (95% CI)	57	56			-	-		100%	1.42[0.42,4.85]
Total events: 7 (Low dose), 5 (High dose	e)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.06, df=1	(P=0.3); I <sup>2</sup> =5.56%								
Test for overall effect: Z=0.57(P=0.57)									
Test for subgroup differences: Not appl	icable						1		
		Favours low dose	0.01	0.1	1	10	100	Favours high dose	

# Analysis 17.5. Comparison 17 Comparison: low dose versus high dose of misoprostol, Outcome 5 Diarrhoea.

Study or subgroup	Low dose	High dose			Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 95%	5 CI			M-H, Fixed, 95% Cl
17.5.1 100 mcg versus 200 mcg									
Nuutila 1997 c	0/27	2/26	←	-				57.25%	0.18[0.01,3.9]
Subtotal (95% CI)	27	26						57.25%	0.18[0.01,3.9]
Total events: 0 (Low dose), 2 (High dose	)								
Heterogeneity: Not applicable									
Test for overall effect: Z=1.1(P=0.27)									
17.5.2 400 mcg versus 600 mcg									
Ozerkan 2009	2/30	2/30			•			42.75%	1[0.13,7.6]
Subtotal (95% CI)	30	30						42.75%	1[0.13,7.6]
Total events: 2 (Low dose), 2 (High dose	)								
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
Total (95% CI)	57	56						100%	0.53[0.11,2.58]
Total events: 2 (Low dose), 4 (High dose	)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.86, df=1(I	P=0.35); I <sup>2</sup> =0%								
Test for overall effect: Z=0.79(P=0.43)									
Test for subgroup differences: Not appli	cable								
		Favours low dose	0.01	0.1	1	10	100	Favours high dose	

### Comparison 18. Comparison: PGE2 versus PGF2

Outcome or sub- group title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abor- tion interval	1	50	Mean Difference (IV, Fixed, 95% CI)	-9.10 [-13.68, -4.52]
2 Abortion within 24 hours	1	50	Odds Ratio (M-H, Fixed, 95% CI)	11.29 [1.29, 98.89]


Outcome or sub- group title	No. of studies	No. of partici- pants	Statistical method	Effect size
3 Pain	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.09 [0.00, 1.84]
4 Nausea	1	50	Odds Ratio (M-H, Fixed, 95% CI)	0.29 [0.07, 1.26]
5 Vomiting	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.32, 0.92]
6 Diarrhoea	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-2.28, 0.68]

#### Analysis 18.1. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 1 Induction to abortion interval.

Study or subgroup	PGE2		PGF2a			Mean Difference				Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		I	Fixed, 95% CI				Fixed, 95% CI
Borgida 1995	25	13.5 (4.7)	25	22.6 (10.7)			+			100%	-9.1[-13.68,-4.52]
Total ***	25		25				•			100%	-9.1[-13.68,-4.52]
Heterogeneity: Not applicable											
Test for overall effect: Z=3.89(P<0.000	1)										
				Favours PGE2	-100	-50	0	50	100	Favours PGF2a	

#### Analysis 18.2. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 2 Abortion within 24 hours.

Study or subgroup	PGE2	PGF2a		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% CI					M-H, Fixed, 95% CI
Borgida 1995	24/25	17/25			—			100%	11.29[1.29,98.89]
Total (95% CI)	25	25			-			100%	11.29[1.29,98.89]
Total events: 24 (PGE2), 17 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=2.19(P=0.03)									
		Favours PGF2a	0.01	0.1	1	10	100	Favours PGE2	

#### Analysis 18.3. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 3 Pain.

Study or subgroup	PGE2	PGF2a	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		М-Н,	Fixed, 95	% CI			M-H, Fixed, 95% Cl
Borgida 1995	21/25	25/25	•					100%	0.09[0,1.84]
Total (95% CI)	25	25						100%	0.09[0,1.84]
Total events: 21 (PGE2), 25 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.56(P=0.12)				1					
		Favours PGE2	0.01	0.1	1	10	100	Favours PGF2a	

#### Analysis 18.4. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 4 Nausea.

Study or subgroup	PGE2	PGF2a		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixed, 95% Cl					M-H, Fixed, 95% CI
Borgida 1995	17/25	22/25			-			100%	0.29[0.07,1.26]
Total (95% CI)	25	25						100%	0.29[0.07,1.26]
Total events: 17 (PGE2), 22 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.65(P=0.1)									
		Favours PGE2	0.01	0.1	1	10	100	Favours PGF2a	

#### Analysis 18.5. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 5 Vomiting.

Study or subgroup		PGE2		PGF2a		Mean Difference				Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		Fi	xed, 95% (	3			Fixed, 95% CI
Borgida 1995	25	2.2 (2.5)	25	2.9 (3.3)						100%	-0.7[-2.32,0.92]
Total ***	25		25				•			100%	-0.7[-2.32,0.92]
Heterogeneity: Not applicable											
Test for overall effect: Z=0.85(P=0.4)											
				Favours PGE2	-10	-5	0	5	10	Favours PGF2a	

#### Analysis 18.6. Comparison 18 Comparison: PGE2 versus PGF2, Outcome 6 Diarrhoea.

Study or subgroup		PGE2		PGF2a		Mean Difference				Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		Fixe	ed, 95% C	1			Fixed, 95% CI
Borgida 1995	25	2.2 (2.4)	25	3 (2.9)						100%	-0.8[-2.28,0.68]
Total ***	25		25							100%	-0.8[-2.28,0.68]
Heterogeneity: Not applicable											
Test for overall effect: Z=1.06(P=0.29)									i.		
				Favours PGE2	-5	-2.5	0	2.5	5	Favours PGF2a	

#### Comparison 19. Comparison: PGE2 versus PGF2+oxytocin

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion in- terval	1	39	Mean Difference (IV, Fixed, 95% CI)	2.00 [0.90, 3.10]
1.1 PGE + oxytocin versus PGF + oxytocin	1	39	Mean Difference (IV, Fixed, 95% CI)	2.00 [0.90, 3.10]
2 Surgical evacuation	2	59	Odds Ratio (M-H, Fixed, 95% CI)	0.25 [0.07, 0.90]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2.1 PGE + oxytocin versus PGF + oxytocin	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.28 [0.07, 1.15]
2.2 PGE versus PGF	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.16 [0.01, 3.85]
3 Pain	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.03 [0.00, 0.72]
3.1 PGE versus PGF	1	20	Odds Ratio (M-H, Fixed, 95% CI)	0.03 [0.00, 0.72]
4 Vomiting	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.17, 2.17]
4.1 PGE + oxytocin versus PGF + oxytocin	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.17, 2.17]
5 Diarrhoea	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.11 [0.01, 1.06]
5.1 PGE + oxytocin versus PGF + oxytocin	1	39	Odds Ratio (M-H, Fixed, 95% CI)	0.11 [0.01, 1.06]

#### Analysis 19.1. Comparison 19 Comparison: PGE2 versus PGF2+oxytocin, Outcome 1 Induction to abortion interval.

Study or subgroup	PGE2			PGF2a		Меа	n Difference	Weight	Mean Difference
	N	Mean(SD)	Ν	Mean(SD)		Fix	ed, 95% CI		Fixed, 95% CI
19.1.1 PGE + oxytocin versus PGF +	oxytocir	1							
Sorensen 1984	20	17.6 (2.2)	19	15.6 (1.2)				100%	2[0.9,3.1]
Subtotal ***	20		19					100%	2[0.9,3.1]
Heterogeneity: Not applicable									
Test for overall effect: Z=3.55(P=0)									
Total ***	20		19					100%	2[0.9,3.1]
Heterogeneity: Not applicable									
Test for overall effect: Z=3.55(P=0)									
				Favours PGE2	-4	-2	0 2	4 Favours P	GF2a

#### Analysis 19.2. Comparison 19 Comparison: PGE2 versus PGF2+oxytocin, Outcome 2 Surgical evacuation.

Study or subgroup	PGE2	PGF2a		Odds	Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% Cl			M-H, Fixed, 95% CI	
19.2.1 PGE + oxytocin versus PGF + o	oxytocin							
Sorensen 1984	4/20	9/19			ŀ		75.58%	0.28[0.07,1.15]
Subtotal (95% CI)	20	19			1		75.58%	0.28[0.07,1.15]
Total events: 4 (PGE2), 9 (PGF2a)								
Heterogeneity: Not applicable								
Test for overall effect: Z=1.77(P=0.08)								
19.2.2 PGE versus PGF								
Steyn 1993	0/10	2/10					24.42%	0.16[0.01,3.85]
		Favours PGE2	0.005	0.1	1 10	200	Favours PGF2a	



Study or subgroup	PGE2	PGF2a	Odds Ratio			Weight	Odds Ratio		
	n/N	n/N		M-H, F	ixed, 95	5% CI			M-H, Fixed, 95% CI
Subtotal (95% CI)	10	10				-		24.42%	0.16[0.01,3.85]
Total events: 0 (PGE2), 2 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.13(P=0.26)									
Total (95% CI)	30	29						100%	0.25[0.07,0.9]
Total events: 4 (PGE2), 11 (PGF2a)									
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.09, df=1	(P=0.76); I <sup>2</sup> =0%								
Test for overall effect: Z=2.11(P=0.03)									
Test for subgroup differences: Not appl	licable			1					
		Favours PGE2	0.005	0.1	1	10	200	Favours PGF2a	

#### Analysis 19.3. Comparison 19 Comparison: PGE2 versus PGF2+oxytocin, Outcome 3 Pain.

Study or subgroup	PGE2	PGF2a	Odds	Odds Ratio		Weight	Odds Ratio
	n/N	n/N	M-H, Fixe	M-H, Fixed, 95% CI			M-H, Fixed, 95% Cl
19.3.1 PGE versus PGF							
Steyn 1993	4/10	10/10				100%	0.03[0,0.72]
Subtotal (95% CI)	10	10				100%	0.03[0,0.72]
Total events: 4 (PGE2), 10 (PGF2a)							
Heterogeneity: Not applicable							
Test for overall effect: Z=2.17(P=0.03)							
Total (95% CI)	10	10				100%	0.03[0,0.72]
Total events: 4 (PGE2), 10 (PGF2a)							
Heterogeneity: Not applicable							
Test for overall effect: Z=2.17(P=0.03)							
		Favours PGE2	0.001 0.1 1	10	1000	Favours PGF2a	

### Analysis 19.4. Comparison 19 Comparison: PGE2 versus PGF2+oxytocin, Outcome 4 Vomiting.

Study or subgroup	PGE2	PGF2a		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-I	H, Fixed, 95%	6 CI			M-H, Fixed, 95% Cl
19.4.1 PGE + oxytocin versus PGF + o	xytocin								
Sorensen 1984	7/20	9/19						100%	0.6[0.17,2.17]
Subtotal (95% CI)	20	19						100%	0.6[0.17,2.17]
Total events: 7 (PGE2), 9 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.78(P=0.43)									
Total (95% CI)	20	19		-				100%	0.6[0.17,2.17]
Total events: 7 (PGE2), 9 (PGF2a)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.78(P=0.43)									
		Favours PGE2	0.01	0.1	1	10	100	Favours PGF2a	

#### Analysis 19.5. Comparison 19 Comparison: PGE2 versus PGF2+oxytocin, Outcome 5 Diarrhoea.

Study or subgroup	PGE2	PGF2a		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H, Fix	ed, 95% CI			M-H, Fixed, 95% CI
19.5.1 PGE + oxytocin versus PGF + ox	ytocin							
Sorensen 1984	1/20	6/19		-	+		100%	0.11[0.01,1.06]
Subtotal (95% CI)	20	19			-		100%	0.11[0.01,1.06]
Total events: 1 (PGE2), 6 (PGF2a)								
Heterogeneity: Not applicable								
Test for overall effect: Z=1.91(P=0.06)								
Total (95% CI)	20	19			-		100%	0.11[0.01,1.06]
Total events: 1 (PGE2), 6 (PGF2a)								
Heterogeneity: Not applicable								
Test for overall effect: Z=1.91(P=0.06)								
		Favours PGE2	0.01	0.1	1 10	100	Favours PGF2a	

### Comparison 20. Comparison: PGF2 versus hypertonic saline

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	25	Mean Difference (IV, Fixed, 95% CI)	-5.30 [-6.67, -3.93]
1.1 20% NaCL versus single dose of 40 mg PGF	1	25	Mean Difference (IV, Fixed, 95% CI)	-5.30 [-6.67, -3.93]
2 Abortion within 24 hours	4		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 20% NaCL versus single dose of 50 mg PGF	1	67	Odds Ratio (M-H, Fixed, 95% CI)	1.52 [0.58, 3.98]
2.2 20% NaCl versus multiple dos- es of 25mg PGF	2	1579	Odds Ratio (M-H, Fixed, 95% CI)	6.14 [4.91, 7.68]
2.3 20% NaCL versus single dose of 40 mg PGF	1	32	Odds Ratio (M-H, Fixed, 95% CI)	15.78 [0.79, 314.27]
3 Blood loss >100 ml	3	165	Odds Ratio (M-H, Fixed, 95% CI)	2.50 [0.79, 7.91]
3.1 20% NaCL versus single dose of 50 mg PGF	1	67	Odds Ratio (M-H, Fixed, 95% CI)	8.30 [0.96, 71.72]
3.2 20% NaCL versus multuple dos- es of 25 mg PGF	1	66	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 8.23]
3.3 20% NaCL versus single dose of 40 mg PGF	1	32	Odds Ratio (M-H, Fixed, 95% CI)	1.62 [0.23, 11.26]
4 Blood loss >500 ml	1	1513	Odds Ratio (M-H, Fixed, 95% CI)	3.05 [1.56, 5.97]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
4.1 20% NaCL versus multiple dos- es of 25 mg PGF	1	1513	Odds Ratio (M-H, Fixed, 95% CI)	3.05 [1.56, 5.97]
5 Nausea	1	1513	Odds Ratio (M-H, Fixed, 95% CI)	3.01 [1.17, 7.72]
5.1 20% NaCL versus multiple dos- es of 25 mg PGF	1	1513	Odds Ratio (M-H, Fixed, 95% CI)	3.01 [1.17, 7.72]
6 Vomiting	3	1646	Odds Ratio (M-H, Fixed, 95% CI)	5.16 [4.12, 6.46]
6.1 20% NaCL versus single dose of 50 mg PGF	1	67	Odds Ratio (M-H, Fixed, 95% CI)	22.4 [2.73, 183.71]
6.2 20% NaCL versus multiple dos- es of 25 mg PGF	2	1579	Odds Ratio (M-H, Fixed, 95% CI)	5.01 [3.99, 6.28]
7 Diarrhoea	3	1646	Odds Ratio (M-H, Fixed, 95% CI)	10.83 [6.17, 19.02]
7.1 20% NaCL versus single dose of 50 mg PGF	1	67	Odds Ratio (M-H, Fixed, 95% CI)	2.07 [0.35, 12.13]
7.2 20% NaCL versus multiple dos- es of 25 mg PGF	2	1579	Odds Ratio (M-H, Fixed, 95% CI)	12.47 [6.81, 22.82]
8 Surgical evacuation	3	1646	Odds Ratio (M-H, Fixed, 95% CI)	1.60 [1.30, 1.96]
8.1 20% NaCL versus single dose of 50 mg PGF	1	67	Odds Ratio (M-H, Fixed, 95% CI)	7.89 [2.01, 30.95]
8.2 20% NaCL versus multiple dos- es of 25 mg PGF	2	1579	Odds Ratio (M-H, Fixed, 95% CI)	1.52 [1.24, 1.87]

# Analysis 20.1. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 1 Induction to abortion interval.

Study or subgroup	PGF2a		Hypertonic saline			Mean D	oifference	We	ight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		Fixed	, 95% CI			Fixed, 95% CI
20.1.1 20% NaCL versus single dose	of 40 m	g PGF								
Faktor 1988	9	13.1 (1.3)	16	18.4 (2.2)		+-		1	00%	-5.3[-6.67,-3.93]
Subtotal ***	9		16			•		10	00%	-5.3[-6.67,-3.93]
Heterogeneity: Not applicable										
Test for overall effect: Z=7.57(P<0.000)	L)									
Total ***	9		16			•		1	00%	-5.3[-6.67,-3.93]
Heterogeneity: Not applicable										
Test for overall effect: Z=7.57(P<0.000)	L)							1		
			Fa	vours PGF2a	-20	-10	0 10	20 Fav	ours hype	tonic saline

### Analysis 20.2. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 2 Abortion within 24 hours.

Study or subgroup	PGF2a	Hyperton- ic saline	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
20.2.1 20% NaCL versus single do	se of 50 mg PGF				
Mehta 1975 a	19/34	15/33		100%	1.52[0.58,3.98]
Subtotal (95% CI)	34	33	<b>•</b>	100%	1.52[0.58,3.98]
Total events: 19 (PGF2a), 15 (Hyper	tonic saline)				
Heterogeneity: Not applicable					
Test for overall effect: Z=0.85(P=0.3	9)				
20.2.2 20% NaCl versus multiple	doses of 25mg PGF				
Mehta 1975 b	26/33	15/33	— <b>+</b> —	5.1%	4.46[1.51,13.12]
WHO 1976	439/717	161/796	+	94.9%	6.23[4.95,7.83]
Subtotal (95% CI)	750	829	•	100%	6.14[4.91,7.68]
Total events: 465 (PGF2a), 176 (Hyp	pertonic saline)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.35, c	f=1(P=0.55); I <sup>2</sup> =0%				
Test for overall effect: Z=15.87(P<0.	.0001)				
20.2.3 20% NaCL versus single do	se of 40 mg PGF				
Nielsen 1975	16/16	11/16		100%	15.78[0.79,314.27]
Subtotal (95% CI)	16	16		100%	15.78[0.79,314.27]
Total events: 16 (PGF2a), 11 (Hyper	tonic saline)				
Heterogeneity: Not applicable					
Test for overall effect: Z=1.81(P=0.0	7)				
	Favours	hypertonic saline	0.001 0.1 1 10	1000 Favours PGF2a	

## Analysis 20.3. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 3 Blood loss >100 ml.

Study or subgroup	PGF2a	Hyperton- ic saline	Odds	Odds Ratio		Odds Ratio
	n/N	n/N	M-H, Fixed	d, 95% CI		M-H, Fixed, 95% CI
20.3.1 20% NaCL versus single dos	e of 50 mg PGF					
Mehta 1975 a	7/34	1/33	ł		20.62%	8.3[0.96,71.72]
Subtotal (95% CI)	34	33	-		20.62%	8.3[0.96,71.72]
Total events: 7 (PGF2a), 1 (Hyperton	ic saline)					
Heterogeneity: Not applicable						
Test for overall effect: Z=1.92(P=0.05	)					
20.3.2 20% NaCL versus multuple of	loses of 25 mg PGF					
Mehta 1975 b	0/33	1/33			37.81%	0.32[0.01,8.23]
Subtotal (95% CI)	33	33			37.81%	0.32[0.01,8.23]
Total events: 0 (PGF2a), 1 (Hyperton	ic saline)					
Heterogeneity: Not applicable						
Test for overall effect: Z=0.68(P=0.49	)					
20.3.3 20% NaCL versus single dos	e of 40 mg PGF					
Nielsen 1975	3/16	2/16			41.57%	1.62[0.23,11.26]
Subtotal (95% CI)	16	16			41.57%	1.62[0.23,11.26]
		Favours PGF2a	0.01 0.1 1	10 10	<sup>00</sup> Favours hypertonic s	aline



Study or subgroup	PGF2a	Hyperton- ic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-Н,	Fixed, 95	% CI			M-H, Fixed, 95% CI
Total events: 3 (PGF2a), 2 (Hypertoni	c saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.48(P=0.63)	I								
Total (95% CI)	83	82						100%	2.5[0.79,7.91]
Total events: 10 (PGF2a), 4 (Hypertor	iic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =2.92, df	=2(P=0.23); I <sup>2</sup> =31.43	3%							
Test for overall effect: Z=1.56(P=0.12)	1								
Test for subgroup differences: Not ap	plicable								
		Favours PGF2a	0.01	0.1	1	10	100	Favours hypertonic sali	ne

#### Analysis 20.4. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 4 Blood loss >500 ml.

Study or subgroup	PGF2a	Hyperton- ic saline		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-I	H, Fixed	, 95% CI			M-H, Fixed, 95% CI
20.4.1 20% NaCL versus multiple do	oses of 25 mg PGF								
WHO 1976	32/717	12/796						100%	3.05[1.56,5.97]
Subtotal (95% CI)	717	796				•		100%	3.05[1.56,5.97]
Total events: 32 (PGF2a), 12 (Hyperto	nic saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=3.26(P=0)									
Total (95% CI)	717	796				<b>•</b>		100%	3.05[1.56,5.97]
Total events: 32 (PGF2a), 12 (Hyperto	nic saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=3.26(P=0)									
		Favours PGF2a	0.01	0.1	1	10	100	Favours hypertonic sa	ine

### Analysis 20.5. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 5 Nausea.

Study or subgroup	PGF2a	Hyperton- ic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-	H, Fixed, 9	5% CI			M-H, Fixed, 95% CI
20.5.1 20% NaCL versus multiple do	oses of 25 mg PGF								
WHO 1976	16/717	6/796				+		100%	3.01[1.17,7.72]
Subtotal (95% CI)	717	796						100%	3.01[1.17,7.72]
Total events: 16 (PGF2a), 6 (Hyperton	ic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(F	P<0.0001); I <sup>2</sup> =100%								
Test for overall effect: Z=2.29(P=0.02)									
Total (95% CI)	717	796						100%	3.01[1.17,7.72]
Total events: 16 (PGF2a), 6 (Hyperton	ic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(F	P<0.0001); I <sup>2</sup> =100%								
Test for overall effect: Z=2.29(P=0.02)									
		Favours PGF2a	0.01	0.1	1	10	100	Favours hypertonic sali	ne



### Analysis 20.6. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 6 Vomiting.

Study or subgroup	PGF2a	Hyperton- ic saline		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H, Fi	ixed, 95	% CI			M-H, Fixed, 95% CI
20.6.1 20% NaCL versus single dose	of 50 mg PGF								
Mehta 1975 a	14/34	1/33			-	-		0.87%	22.4[2.73,183.71]
Subtotal (95% CI)	34	33			-			0.87%	22.4[2.73,183.71]
Total events: 14 (PGF2a), 1 (Hypertoni	c saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=2.9(P=0)									
20.6.2 20% NaCL versus multiple do	ses of 25 mg PGF								
Mehta 1975 b	14/33	1/33				•		0.84%	23.58[2.87,193.84]
WHO 1976	384/717	153/796			-	-		98.29%	4.85[3.85,6.1]
Subtotal (95% CI)	750	829				•		99.13%	5.01[3.99,6.28]
Total events: 398 (PGF2a), 154 (Hyper	tonic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =2.16, df=	1(P=0.14); I <sup>2</sup> =53.6%								
Test for overall effect: Z=13.89(P<0.00	01)								
Total (95% CI)	784	862				•		100%	5.16[4.12,6.46]
Total events: 412 (PGF2a), 155 (Hyper	tonic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =4.15, df=2	2(P=0.13); I <sup>2</sup> =51.84%								
Test for overall effect: Z=14.27(P<0.00	01)								
Test for subgroup differences: Not app	olicable								
		Favours PGF2a	0.002	0.1	1	10	500	Favours hypertonic sali	ne

#### Analysis 20.7. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 7 Diarrhoea.

Study or subgroup	PGF2a	Hyperton- ic saline	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% Cl
20.7.1 20% NaCL versus single dose o	f 50 mg PGF				
Mehta 1975 a	4/34	2/33		- 15.71%	2.07[0.35,12.13]
Subtotal (95% CI)	34	33		- 15.71%	2.07[0.35,12.13]
Total events: 4 (PGF2a), 2 (Hypertonic s	aline)				
Heterogeneity: Not applicable					
Test for overall effect: Z=0.8(P=0.42)					
20.7.2 20% NaCL versus multiple dos	es of 25 mg PGF				
Mehta 1975 b	7/33	2/33	+-+	13.82%	4.17[0.8,21.85]
WHO 1976	109/717	10/796	-	<b>-</b> 70.48%	14.09[7.31,27.16]
Subtotal (95% CI)	750	829	•	♦ 84.29%	12.47[6.81,22.82]
Total events: 116 (PGF2a), 12 (Hypertor	nic saline)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.81, df=1	(P=0.18); I <sup>2</sup> =44.82%	5			
Test for overall effect: Z=8.18(P<0.0001)	)				
Total (95% CI)	784	862		100%	10.83[6.17,19.02]
Total events: 120 (PGF2a), 14 (Hypertor	nic saline)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =5.26, df=2	(P=0.07); I <sup>2</sup> =61.96%	ò			
		Favours PGF2a	0.01 0.1 1 1	0 <sup>100</sup> Favours hypertonic	saline



Study or subgroup	PGF2a	Hyperton- ic saline	Odds Ratio			Weight	Odds Ratio		
	n/N	n/N		м-н,	Fixed, 95	% CI			M-H, Fixed, 95% Cl
Test for overall effect: Z=8.3(P<0.00	01)								
Test for subgroup differences: Not a	applicable						1		
		Favours PGF2a	0.01	0.1	1	10	100	Favours hypertonic	saline

#### Analysis 20.8. Comparison 20 Comparison: PGF2 versus hypertonic saline, Outcome 8 Surgical evacuation.

Study or subgroup	PGF2a	Hyperton- ic saline		Odds Ratio		Weight	Odds Ratio
	n/N	n/N		M-H, Fixed, 95% CI			M-H, Fixed, 95% Cl
20.8.1 20% NaCL versus single dos	e of 50 mg PGF						
Mehta 1975 a	15/34	3/33			$\longrightarrow$	1.17%	7.89[2.01,30.95]
Subtotal (95% CI)	34	33				1.17%	7.89[2.01,30.95]
Total events: 15 (PGF2a), 3 (Hyperto	nic saline)						
Heterogeneity: Not applicable							
Test for overall effect: Z=2.96(P=0)							
20.8.2 20% NaCL versus multiple of	loses of 25 mg PGF						
Mehta 1975 b	6/33	3/33				1.69%	2.22[0.51,9.76]
WHO 1976	296/717	253/796				97.13%	1.51[1.22,1.86]
Subtotal (95% CI)	750	829		•		98.83%	1.52[1.24,1.87]
Total events: 302 (PGF2a), 256 (Hype	ertonic saline)						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.26, d	f=1(P=0.61); I <sup>2</sup> =0%						
Test for overall effect: Z=3.94(P<0.00	001)						
Total (95% CI)	784	862		•		100%	1.6[1.3,1.96]
Total events: 317 (PGF2a), 259 (Hype	ertonic saline)						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =5.72, d	f=2(P=0.06); I <sup>2</sup> =65.06%						
Test for overall effect: Z=4.47(P<0.00	001)						
Test for subgroup differences: Not a	pplicable						
		Favours PGF2a	0.1 0.2	0.5 1 2	5 10 Fa	avours hypertonic sali	ne

#### Comparison 21. Comparison: combined regimen PGF2+hypertonic saline

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	4	770	Mean Difference (IV, Fixed, 95% CI)	-1.55 [-3.53, 0.44]
1.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Mean Difference (IV, Fixed, 95% CI)	2.21 [-1.59, 6.00]
1.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Mean Difference (IV, Fixed, 95% CI)	-2.96 [-5.29, -0.64]
2 Abortion within 24 hours	4	770	Odds Ratio (M-H, Fixed, 95% CI)	1.33 [0.90, 1.97]

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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	0.69 [0.38, 1.26]
2.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	2.30 [1.38, 3.86]
3 Blood loss (>500 ml)	4	770	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.66, 1.95]
3.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.23, 1.78]
3.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	1.44 [0.74, 2.80]
4 Surgical evacuation	4	770	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.66, 1.95]
4.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.23, 1.78]
4.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	1.44 [0.74, 2.80]
5 Nausea	4	770	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.35, 0.94]
5.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.52, 2.19]
5.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	0.33 [0.17, 0.62]
6 Vomiting	4	770	Odds Ratio (M-H, Fixed, 95% CI)	0.87 [0.44, 1.72]
6.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.33, 3.06]
6.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.34, 1.87]
7 Diarrhoea	4	770	Odds Ratio (M-H, Fixed, 95% CI)	1.09 [0.24, 4.83]
7.1 100 ml 5% NaCl versus 100 ml 10% NaCl combined with PGF	2	230	Odds Ratio (M-H, Fixed, 95% CI)	0.52 [0.02, 13.13]
7.2 25 ml 20% NaCl versus 100 ml 10% NaCl combined with PGF	2	540	Odds Ratio (M-H, Fixed, 95% CI)	1.38 [0.23, 8.33]

# Analysis 21.1. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 1 Induction to abortion interval.

Study or subgroup	5g hyper- tonic saline		10g hyper- tonic saline		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
21.1.1 100 ml 5% NaCl versus 100 m	l 10% Na	aCl combined w	ith PGF				
Muzsnai 1979 a	50	20.7 (15.7)	50	19.6 (13.3)		12.15%	1.07[-4.62,6.76]
Muzsnai 1979 b	50	20.7 (15.7)	80	17.6 (12)		15.25%	3.11[-1.97,8.19]
Subtotal ***	100		130			27.4%	2.21[-1.59,6]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.27, df=	1(P=0.6);	I <sup>2</sup> =0%					
Test for overall effect: Z=1.14(P=0.25)							
21.1.2 25 ml 20% NaCl versus 100 m	l 10% Na	aCl combined w	ith PGF				
Muzsnai 1979 c	205	15.3 (9.1)	50	19.6 (13.3)		26.14%	-4.27[-8.15,-0.39]
Muzsnai 1979 d	205	15.3 (9.1)	80	17.6 (12)		46.46%	-2.23[-5.14,0.68]
Subtotal ***	410		130		•	72.6%	-2.96[-5.29,-0.64]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.68, df=	1(P=0.41	); I²=0%					
Test for overall effect: Z=2.49(P=0.01)							
Total ***	510		260		•	100%	-1.55[-3.53,0.44]
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =6.14, df=	3(P=0.11	); I <sup>2</sup> =51.13%					
Test for overall effect: Z=1.53(P=0.13)							
Test for subgroup differences: Chi <sup>2</sup> =5.	19, df=1	(P=0.02), I <sup>2</sup> =80.7	2%				
				Favours 5g	-10 -5 0 5 10	– Favours 10g	

# Analysis 21.2. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 2 Abortion within 24 hours.

Study or subgroup	Experimental	Control	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% Cl		M-H, Fixed, 95% Cl
21.2.1 100 ml 5% NaCl versus 1	00 ml 10% NaCl combine	ed with PGF			
Muzsnai 1979 a	35/50	36/50		25.24%	0.91[0.38,2.15]
Muzsnai 1979 b	35/50	65/80	<b>—•·</b>	35.06%	0.54[0.24,1.23]
Subtotal (95% CI)	100	130		60.3%	0.69[0.38,1.26]
Total events: 70 (Experimental),	101 (Control)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.73	3, df=1(P=0.39); I <sup>2</sup> =0%				
Test for overall effect: Z=1.21(P=	0.23)				
21.2.2 25 ml 20% NaCl versus 1	.00 ml 10% NaCl combine	ed with PGF			
Muzsnai 1979 c	182/205	36/50		15.18%	3.08[1.45,6.54]
Muzsnai 1979 d	182/205	65/80	<b>+•</b>	24.52%	1.83[0.9,3.71]
Subtotal (95% CI)	410	130	•	39.7%	2.3[1.38,3.86]
Total events: 364 (Experimental)	, 101 (Control)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.98	8, df=1(P=0.32); I <sup>2</sup> =0%				
Test for overall effect: Z=3.17(P=	0)				
Total (95% CI)	510	260	•	100%	1.33[0.9,1.97]
Total events: 434 (Experimental)	, 202 (Control)				
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =10.8	88, df=3(P=0.01); l <sup>2</sup> =72.429	6			
Test for overall effect: Z=1.44(P=	0.15)				
Test for subgroup differences: No	ot applicable				
		Favours 10g	0.05 0.2 1 5 20	Favours 5g	

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### Analysis 21.3. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 3 Blood loss (>500 ml).

Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline		Odds Ratio			We	eight	Odds Ratio	
	n/N	n/N		М-Н,	Fixed, 95% C	l			M-H, Fixed, 95% Cl	
21.3.1 100 ml 5% NaCl versus 100 m	l 10% NaCl combii	ned with PGF								
Muzsnai 1979 a	3/50	4/50			-+			14.92%	0.73[0.16,3.46]	]
Muzsnai 1979 b	3/50	8/80			•			22.95%	0.57[0.14,2.28]	]
Subtotal (95% CI)	100	130						37.86%	0.64[0.23,1.78]	]
Total events: 6 (5g hypertonic saline),	12 (10g hypertonic	saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.05, df=	1(P=0.82); I <sup>2</sup> =0%									
Test for overall effect: Z=0.86(P=0.39)										
21.3.2 25 ml 20% NaCl versus 100 m	l 10% NaCl combii	ned with PGF								
Muzsnai 1979 c	26/205	4/50						22.28%	1.67[0.56,5.03]	]
Muzsnai 1979 d	26/205	8/80						39.86%	1.31[0.57,3.02]	]
Subtotal (95% CI)	410	130			•			62.14%	1.44[0.74,2.8]	]
Total events: 52 (5g hypertonic saline)	), 12 (10g hypertoni	c saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.12, df=	1(P=0.73); I <sup>2</sup> =0%									
Test for overall effect: Z=1.07(P=0.29)										
Total (95% CI)	510	260			•			100%	1.13[0.66,1.95]	]
Total events: 58 (5g hypertonic saline	), 24 (10g hypertoni	c saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.82, df=	3(P=0.61); I <sup>2</sup> =0%									
Test for overall effect: Z=0.46(P=0.65)										
Test for subgroup differences: Not app	olicable									
		Favours 5g	0.01	0.1	1	10	100 Favours	s 10g		

### Analysis 21.4. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 4 Surgical evacuation.

Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% Cl
21.4.1 100 ml 5% NaCl versus 100 m	l 10% NaCl combin	ed with PGF			
Muzsnai 1979 a	3/50	4/50	+	14.92%	0.73[0.16,3.46]
Muzsnai 1979 b	3/50	8/80		22.95%	0.57[0.14,2.28]
Subtotal (95% CI)	100	130		37.86%	0.64[0.23,1.78]
Total events: 6 (5g hypertonic saline),	12 (10g hypertonic	saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.05, df=	1(P=0.82); I <sup>2</sup> =0%				
Test for overall effect: Z=0.86(P=0.39)					
21.4.2 25 ml 20% NaCl versus 100 m	l 10% NaCl combin	ed with PGF			
Muzsnai 1979 c	26/205	4/50		22.28%	1.67[0.56,5.03]
Muzsnai 1979 d	26/205	8/80	<b>_</b>	39.86%	1.31[0.57,3.02]
Subtotal (95% CI)	410	130	-	62.14%	1.44[0.74,2.8]
Total events: 52 (5g hypertonic saline	), 12 (10g hypertonio	c saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.12, df=	1(P=0.73); I <sup>2</sup> =0%				
Test for overall effect: Z=1.07(P=0.29)					
		Favours 5g	0.01 0.1 1 10	<sup>100</sup> Favours 10g	



Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		М-	H, Fixed, 95%	CI			M-H, Fixed, 95% Cl
Total (95% CI)	510	260			•			100%	1.13[0.66,1.95]
Total events: 58 (5g hypertonic salin	e), 24 (10g hypertoni	c saline)							
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.82, df	=3(P=0.61); I <sup>2</sup> =0%								
Test for overall effect: Z=0.46(P=0.65	)								
Test for subgroup differences: Not ap	oplicable								
		Favours 5g	0.01	0.1	1	10	100	Favours 10g	

### Analysis 21.5. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 5 Nausea.

Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
21.5.1 100 ml 5% NaCl versus 100 m	l 10% NaCl combir	ned with PGF			
Muzsnai 1979 a	8/50	10/50		20.15%	0.76[0.27,2.12]
Muzsnai 1979 b	8/50	9/80		13.95%	1.5[0.54,4.19]
Subtotal (95% CI)	100	130	<b>•</b>	34.1%	1.06[0.52,2.19]
Total events: 16 (5g hypertonic saline)	, 19 (10g hypertoni	c saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.84, df=	1(P=0.36); I <sup>2</sup> =0%				
Test for overall effect: Z=0.17(P=0.86)					
21.5.2 25 ml 20% NaCl versus 100 m	l 10% NaCl combir	ned with PGF			
Muzsnai 1979 c	11/205	10/50		36.5%	0.23[0.09,0.57]
Muzsnai 1979 d	11/205	9/80		29.39%	0.45[0.18,1.12]
Subtotal (95% CI)	410	130	•	65.9%	0.33[0.17,0.62]
Total events: 22 (5g hypertonic saline	, 19 (10g hypertoni	c saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =1.05, df=	1(P=0.31); I <sup>2</sup> =4.46%	1			
Test for overall effect: Z=3.39(P=0)					
Total (95% CI)	510	260	•	100%	0.58[0.35,0.94]
Total events: 38 (5g hypertonic saline	, 38 (10g hypertoni	c saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =7.86, df=	3(P=0.05); I <sup>2</sup> =61.850	%			
Test for overall effect: Z=2.21(P=0.03)					
Test for subgroup differences: Not app	olicable				
		Favours 5g	0.01 0.1 1 10	<sup>100</sup> Favours 10g	

## Analysis 21.6. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 6 Vomiting.

Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline	Odd	Odds Ratio			Odds Ratio
	n/N	n/N	M-H, Fix	ed, 95% CI			M-H, Fixed, 95% CI
21.6.1 100 ml 5% NaCl versus 100 n	nl 10% NaCl combir	ed with PGF					
Muzsnai 1979 a	3/50	2/50		+		10.75%	1.53[0.24,9.59]
Muzsnai 1979 b	3/50	6/80		<b></b>		24.81%	0.79[0.19,3.3]
Subtotal (95% CI)	100	130				35.56%	1.01[0.33,3.06]
Total events: 6 (5g hypertonic saline	), 8 (10g hypertonic s	aline)					
		Favours 5g	0.01 0.1	1 10	100	Favours 10g	



Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline	Odds Ratio	Weight	Odds Ratio
	n/N	n/N	M-H, Fixed, 95% Cl		M-H, Fixed, 95% CI
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.31, df=	1(P=0.58); I <sup>2</sup> =0%				
Test for overall effect: Z=0.02(P=0.98)					
21.6.2 25 ml 20% NaCl versus 100 m	l 10% NaCl combi	ned with PGF			
Muzsnai 1979 c	10/205	2/50	+	17.49%	1.23[0.26,5.8]
Muzsnai 1979 d	10/205	6/80	<b></b>	46.95%	0.63[0.22,1.8]
Subtotal (95% CI)	410	130	-	64.44%	0.79[0.34,1.87]
Total events: 20 (5g hypertonic saline	), 8 (10g hypertonic	saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.49, df=	1(P=0.48); I <sup>2</sup> =0%				
Test for overall effect: Z=0.53(P=0.6)					
Total (95% CI)	510	260	-	100%	0.87[0.44,1.72]
Total events: 26 (5g hypertonic saline	), 16 (10g hypertoni	c saline)			
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.93, df=	3(P=0.82); I <sup>2</sup> =0%				
Test for overall effect: Z=0.39(P=0.69)					
Test for subgroup differences: Not app	olicable				
		Favours 5g	0.01 0.1 1 10	<sup>100</sup> Favours 10g	

#### Analysis 21.7. Comparison 21 Comparison: combined regimen PGF2+hypertonic saline, Outcome 7 Diarrhoea.

Study or subgroup	5g hyper- tonic saline	10g hyper- tonic saline		Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H, Fix	ed, 95% CI			M-H, Fixed, 95% CI
21.7.1 100 ml 5% NaCl versus 100	) ml 10% NaCl combii	ned with PGF						
Muzsnai 1979 a	0/50	0/50						Not estimable
Muzsnai 1979 b	0/50	1/80					34.23%	0.52[0.02,13.13]
Subtotal (95% CI)	100	130					34.23%	0.52[0.02,13.13]
Total events: 0 (5g hypertonic salin	ne), 1 (10g hypertonic s	aline)						
Heterogeneity: Not applicable								
Test for overall effect: Z=0.39(P=0.6	59)							
21.7.2 25 ml 20% NaCl versus 100	) ml 10% NaCl combii	ned with PGF						
Muzsnai 1979 c	3/205	0/50			+		23.5%	1.75[0.09,34.34]
Muzsnai 1979 d	3/205	1/80					42.27%	1.17[0.12,11.45]
Subtotal (95% CI)	410	130					65.77%	1.38[0.23,8.33]
Total events: 6 (5g hypertonic salin	ne), 1 (10g hypertonic s	aline)						
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.04, o	df=1(P=0.84); I <sup>2</sup> =0%							
Test for overall effect: Z=0.35(P=0.7	73)							
Total (95% CI)	510	260					100%	1.09[0.24.4.83]
Total events: 6 (5g hypertonic salin	ne), 2 (10g hypertonic s	aline)						, , , , , , , , , , , , , , , , , , , ,
Heterogeneity: Tau <sup>2</sup> =0: Chi <sup>2</sup> =0.3 d	f=2(P=0.86): l <sup>2</sup> =0%	,						
Test for overall effect: 7=0 11(P=0.9	a1)							
Test for subgroup differences: Not	applicable							
			0.01	0.1	1 12	100		
		Favours 5g	0.01	0.1	1 10	100	Favours 10g	

Comparison 22.	<b>Comparison: PGE1</b>	versus PGF2+hypertonic saline
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Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	58	Mean Difference (IV, Fixed, 95% CI)	0.90 [0.10, 1.70]
2 Abortion within 24h	1	58	Odds Ratio (M-H, Fixed, 95% CI)	0.16 [0.04, 0.67]
3 Blood loss (>300ml)	1	58	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.06, 16.79]
4 Surgical evacuation	1	58	Odds Ratio (M-H, Fixed, 95% CI)	1.53 [0.54, 4.34]
5 Pain (pethidine)	1	58	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.10, 4.16]
6 Vomiting	1	58	Odds Ratio (M-H, Fixed, 95% CI)	3.11 [1.06, 9.08]
7 Diarrhoea	1	58	Odds Ratio (M-H, Fixed, 95% CI)	19.13 [3.80, 96.18]

# Analysis 22.1. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 1 Induction to abortion interval.

Study or subgroup	PGE1 PGF to		PGF2 ton	a + hyper- ic saline	Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Waldron 1990	29	12.6 (1.9)	29	11.7 (1.1)	-	100%	0.9[0.1,1.7]
Total ***	29		29		•	100%	0.9[0.1,1.7]
Heterogeneity: Not applicable							
Test for overall effect: Z=2.21(P=0.03)							
				Favours PGE1	-5 -2.5 0 2.5 5	Favours PGF	2a+saline

#### Analysis 22.2. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 2 Abortion within 24h.

Study or subgroup	PGE1	PGF2a + hyper- tonic saline	C	Odds Ratio		Weight	Odds Ratio
	n/N	n/N	м-н,	Fixed, 95% CI			M-H, Fixed, 95% CI
Waldron 1990	17/29	26/29		—		100%	0.16[0.04,0.67]
Total (95% CI)	29	29				100%	0.16[0.04,0.67]
Total events: 17 (PGE1), 26 (PGF2a + hyp	ertonic saline)						
Heterogeneity: Not applicable							
Test for overall effect: Z=2.53(P=0.01)			_11				
	Fav	ours PGF2a+saline	0.01 0.1	1 10	100	Favours PGE1	

#### Analysis 22.3. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 3 Blood loss (>300ml).

Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		М-Н,	Fixed, 95	% CI			M-H, Fixed, 95% CI
Waldron 1990	1/29	1/29						100%	1[0.06,16.79]
Total (95% CI)	29	29						100%	1[0.06,16.79]
Total events: 1 (PGE1), 1 (PGF2a + hyper	tonic saline)								
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	

#### Analysis 22.4. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 4 Surgical evacuation.

Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	l, Fixed, 95%	CI			M-H, Fixed, 95% CI
Waldron 1990	18/29	15/29						100%	1.53[0.54,4.34]
Total (95% CI)	29	29			-			100%	1.53[0.54,4.34]
Total events: 18 (PGE1), 15 (PGF2a + hy	pertonic saline)								
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(P<	0.0001); I <sup>2</sup> =100%								
Test for overall effect: Z=0.79(P=0.43)							1		
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	

#### Analysis 22.5. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 5 Pain (pethidine).

Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds F		s Ratio		Weight	Odds Ratio
	n/N	n/N		м-н,	Fixed, 95%	6 CI			M-H, Fixed, 95% Cl
Waldron 1990	26/29	27/29			+	-		100%	0.64[0.1,4.16]
Total (95% CI)	29	29				-		100%	0.64[0.1,4.16]
Total events: 26 (PGE1), 27 (PGF2a + hyp	pertonic saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=0.46(P=0.64)									
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	

#### Analysis 22.6. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 6 Vomiting.

Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N	_	M-H	, Fixed, 95	% CI			M-H, Fixed, 95% CI
Waldron 1990	18/29	10/29				<b>1</b>		100%	3.11[1.06,9.08]
Total (95% CI)	29	29						100%	3.11[1.06,9.08]
Total events: 18 (PGE1), 10 (PGF2a + I	nypertonic saline)								
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	



Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-I	H, Fixed, 95	5% CI			M-H, Fixed, 95% Cl
Heterogeneity: Not applicable									
Test for overall effect: Z=2.07(P=0.04)									
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	

#### Analysis 22.7. Comparison 22 Comparison: PGE1 versus PGF2+hypertonic saline, Outcome 7 Diarrhoea.

Study or subgroup	PGE1	PGF2a + hyper- tonic saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, F	ixed, 95	% CI			M-H, Fixed, 95% CI
Waldron 1990	17/29	2/29						100%	19.13[3.8,96.18]
Total (95% CI)	29	29						100%	19.13[3.8,96.18]
Total events: 17 (PGE1), 2 (PGF2a + hyp	ertonic saline)								
Heterogeneity: Not applicable									
Test for overall effect: Z=3.58(P=0)									
		Favours PGE1	0.01	0.1	1	10	100	Favours PGF2a+saline	

## Comparison 23. Comparison: prostaglandin versus ethacridine lactate

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	178	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-2.03, 0.03]
2 Abortion within 24h	2	256	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.33, 0.98]
2.1 PGE2 versus EL	1	78	Odds Ratio (M-H, Fixed, 95% CI)	0.18 [0.06, 0.48]
2.2 Misoprostol versus EL	1	178	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.50, 1.99]
3 Blood loss	1	46	Odds Ratio (M-H, Fixed, 95% CI)	2.10 [0.18, 24.87]
4 Nausea	2	124	Odds Ratio (M-H, Fixed, 95% CI)	2.26 [0.79, 6.46]
5 Vomiting	1	46	Odds Ratio (M-H, Fixed, 95% CI)	1.19 [0.37, 3.81]
6 Diarrhoea	1	46	Odds Ratio (M-H, Fixed, 95% CI)	5.47 [0.25, 120.37]

# Analysis 23.1. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 1 Induction to abortion interval.

Study or subgroup		PG		EL		Mea	n Difference		Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)		Fix	ed, 95% CI			Fixed, 95% Cl
Kelekci 2006	93	13.2 (3.4)	85	14.2 (3.6)					100%	-1[-2.03,0.03]
Total ***	93		85						100%	-1[-2.03,0.03]
Heterogeneity: Not applicable										
Test for overall effect: Z=1.9(P=0.06)										
				Favours PG	-5	-2.5	0 2.5	5	Favours EL	

# Analysis 23.2. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 2 Abortion within 24h.

Study or subgroup	PG	EL		(	Odds Ratio			Weight	Odds Ratio
	n/N	n/N		M-H	Fixed, 95%	CI			M-H, Fixed, 95% Cl
23.2.1 PGE2 versus EL									
Inan 1997	12/30	38/48			-			52.19%	0.18[0.06,0.48]
Subtotal (95% CI)	30	48			-			52.19%	0.18[0.06,0.48]
Total events: 12 (PG), 38 (EL)									
Heterogeneity: Not applicable									
Test for overall effect: Z=3.38(P=0)									
23.2.2 Misoprostol versus EL									
Kelekci 2006	71/93	65/85						47.81%	0.99[0.5,1.99]
Subtotal (95% CI)	93	85			•			47.81%	0.99[0.5,1.99]
Total events: 71 (PG), 65 (EL)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.02(P=0.98)									
Total (95% CI)	123	133			◆			100%	0.57[0.33,0.98]
Total events: 83 (PG), 103 (EL)									
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =7.7, df=1(P=	0.01); I <sup>2</sup> =87.02%								
Test for overall effect: Z=2.02(P=0.04)									
Test for subgroup differences: Not applic	able								
		Favours EL	0.01	0.1	1	10	100	Favours PG	

#### Analysis 23.3. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 3 Blood loss.

Study or subgroup	PG	EL	Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixe	d, 95% CI			M-H, Fixed, 95% CI
Olund 1978	2/23	1/23					100%	2.1[0.18,24.87]
					_			
Total (95% CI)	23	23					100%	2.1[0.18,24.87]
Total events: 2 (PG), 1 (EL)								
Heterogeneity: Not applicable								
Test for overall effect: Z=0.59(P=0.56)								
		Favours PG	0.01 0	).1 1		10 10	<sup>0</sup> Favours EL	

### Analysis 23.4. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 4 Nausea.

Study or subgroup	PG	EL		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 959	% CI			M-H, Fixed, 95% Cl
Inan 1997	1/30	2/48			-			32.82%	0.79[0.07,9.15]
Olund 1978	13/23	7/23				<b>—</b>		67.18%	2.97[0.88,9.98]
Total (95% CI)	53	71						100%	2.26[0.79,6.46]
Total events: 14 (PG), 9 (EL)									
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0.9, df=2	1(P=0.34); I <sup>2</sup> =0%								
Test for overall effect: Z=1.52(P=0.13)	)								
		Favours PG	0.01	0.1	1	10	100	Favours EL	

#### Analysis 23.5. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 5 Vomiting.

Study or subgroup	PG	EL	Odds Ratio				Weight	Odds Ratio	
	n/N	n/N		M-	H, Fixed, 95%	CI			M-H, Fixed, 95% Cl
Olund 1978	11/23	10/23			<mark>_</mark>			100%	1.19[0.37,3.81]
Total (95% CI)	23	23			-			100%	1.19[0.37,3.81]
Total events: 11 (PG), 10 (EL)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.3(P=0.77)									
		Favours PG	0.01	0.1	1	10	100	Favours EL	

#### Analysis 23.6. Comparison 23 Comparison: prostaglandin versus ethacridine lactate, Outcome 6 Diarrhoea.

Study or subgroup	PG	EL		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fi	xed, 95% (	CI			M-H, Fixed, 95% Cl
Olund 1978	2/23	0/23				-	$\rightarrow$	100%	5.47[0.25,120.37]
						_			
Total (95% CI)	23	23						100%	5.47[0.25,120.37]
Total events: 2 (PG), 0 (EL)									
Heterogeneity: Tau <sup>2</sup> =0; Chi <sup>2</sup> =0, df=0(P<	0.0001); l <sup>2</sup> =100%								
Test for overall effect: Z=1.08(P=0.28)									
		Favours PG	0.01	0.1	1	10	100	Favours EL	

#### Comparison 24. Comparison: ethacridine lactate versus normal saline

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction to abortion interval	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-4.02, 3.42]



Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
2 Blood loss (need for blood transfusion)	1	40	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 8.26]
3 Pain (use of analgestics)	1	40	Odds Ratio (M-H, Fixed, 95% CI)	1.0 [0.13, 7.89]
4 Vomiting (use of antimetics)	1	40	Odds Ratio (M-H, Fixed, 95% CI)	6.33 [0.67, 60.16]
5 Uterine rupture	1	40	Odds Ratio (M-H, Fixed, 95% CI)	0.32 [0.01, 8.26]

# Analysis 24.1. Comparison 24 Comparison: ethacridine lactate versus normal saline, Outcome 1 Induction to abortion interval.

Study or subgroup		EL	Normal saline		Mean Difference	Weight	Mean Difference
	Ν	Mean(SD)	Ν	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
Zauva 1989	19	17.2 (4.6)	18	17.5 (6.7)		100%	-0.3[-4.02,3.42]
Total ***	19		18		-	100%	-0.3[-4.02,3.42]
Heterogeneity: Not applicable							
Test for overall effect: Z=0.16(P=0.87)							
				Favours EL	-10 -5 0 5 10	Favours nor	mal saline

# Analysis 24.2. Comparison 24 Comparison: ethacridine lactate versus normal saline, Outcome 2 Blood loss (need for blood transfusion).

Study or subgroup	EL	Normal saline		Odds Ratio				Weight	Odds Ratio
	n/N	n/N		M-H	, Fixed, 9	95% CI			M-H, Fixed, 95% CI
Zauva 1989	0/20	1/20						100%	0.32[0.01,8.26]
Total (95% CI)	20	20						100%	0.32[0.01,8.26]
Total events: 0 (EL), 1 (Normal saline)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.69(P=0.49)									
		Favours FI	0.01	0.1	1	10	100	Favours normal saline	

# Analysis 24.3. Comparison 24 Comparison: ethacridine lactate versus normal saline, Outcome 3 Pain (use of analgestics).

Study or subgroup	EL	Normal saline	Normal saline			Odds Ratio			Odds Ratio
	n/N	n/N		M-H	H, Fixed, 959	% CI			M-H, Fixed, 95% CI
Zauva 1989	2/20	2/20						100%	1[0.13,7.89]
Total (95% CI)	20	20						100%	1[0.13,7.89]
Total events: 2 (EL), 2 (Normal saline)									
Heterogeneity: Not applicable									
		Favours EL	0.01	0.1	1	10	100	Favours normal saline	

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Study or subgroup	EL n/N	Normal saline n/N		M-H	Odds Ratio	9 % CI		Weight M-H	Odds Ratio I, Fixed, 95% Cl
Test for overall effect: Not applicable				1		1			
		Favours EL	0.01	0.1	1	10	100	Favours normal saline	

# Analysis 24.4. Comparison 24 Comparison: ethacridine lactate versus normal saline, Outcome 4 Vomiting (use of antimetics).

Study or subgroup	EL	Normal saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixed, 95% Cl				M-H, Fixed, 95% Cl	
Zauva 1989	5/20	1/20				1		100%	6.33[0.67,60.16]
Total (95% CI)	20	20						100%	6.33[0.67,60.16]
Total events: 5 (EL), 1 (Normal saline)									
Heterogeneity: Not applicable									
Test for overall effect: Z=1.61(P=0.11)						1			
		Favours EL	0.01	0.1	1	10	100	Favours normal saline	

# Analysis 24.5. Comparison 24 Comparison: ethacridine lactate versus normal saline, Outcome 5 Uterine rupture.

Study or subgroup	EL	Normal saline		Odds Ratio			Weight	Odds Ratio	
	n/N	n/N		M-H, Fixed, 95% CI				M-H, Fixed, 95% CI	
Zauva 1989	0/20	1/20						100%	0.32[0.01,8.26]
Total (95% CI)	20	20						100%	0.32[0.01,8.26]
Total events: 0 (EL), 1 (Normal saline)									
Heterogeneity: Not applicable									
Test for overall effect: Z=0.69(P=0.49)						1			
		Favours EL	0.01	0.1	1	10	100	Favours normal saline	

# CONTRIBUTIONS OF AUTHORS

HIJ Wildschut: study design, writing, editing and overall supervision

MI Both: literature search, data analyses and writing

S Medema: literature search and data management

E Thomee: data management

MF Wildhagen: statistics

N Kapp: review design, writing, editing and critical evaluation

# DECLARATIONS OF INTEREST

None declared

# DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None



### ΝΟΤΕS

None

### INDEX TERMS

### **Medical Subject Headings (MeSH)**

Abortifacient Agents [\*administration & dosage] [adverse effects]; Abortion, Induced [\*methods]; Administration, Intravaginal; Drug Administration Schedule; Drug Therapy, Combination; Mifepristone [\*administration & dosage]; Misoprostol [\*administration & dosage] [adverse effects]; Pregnancy Trimester, Second; Prostaglandins A [administration & dosage]; Randomized Controlled Trials as Topic

### **MeSH check words**

Female; Humans; Pregnancy