Prostaglandins for preventing postpartum haemorrhage (Review)

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ABSTRACT

Background
Prostaglandins have mainly been used for postpartum haemorrhage (PPH) when other measures fail. Misoprostol, a new and inexpensive prostaglandin E1 analogue, has been suggested as an alternative for routine management of the third stage of labour.

Objectives
To assess the effects of prophylactic prostaglandin use in the third stage of labour.

Search strategy
The Cochrane Pregnancy and Childbirth Group's Trials Register (February 2007) and PubMed (July 2006).

Selection criteria
Randomized trials comparing a prostaglandin agent with another uterotonic or no prophylactic uterotonic (nothing or placebo) as part of management of the third stage of labour. The primary outcomes were blood loss 1000 ml or more and the use of additional uterotonics.

Data collection and analysis
Two review authors independently assessed eligibility and trial quality and extracted data.

Main results
Thirty-seven misoprostol and nine intramuscular prostaglandin trials (42,621 women) were included. Oral (seven trials, 2849 women) or sublingual misoprostol (relative risk (RR) 0.66; 95% confidence interval (CI) 0.45 to 0.98; one trial, 661 women) compared to placebo may be effective in reducing severe PPH and blood transfusion (RR 0.31; 95% CI 0.10 to 0.94; five oral misoprostol trials, 3519 women). The severe PPH analysis of oral misoprostol trials was not totalled due to significant heterogeneity.

Compared to conventional injectable uterotonics, oral misoprostol was associated with higher risk of severe PPH (RR 1.32; 95% CI 1.16 to 1.51; 16 trials, 29,042 women) and use of additional uterotonics but with fewer blood transfusions (RR 0.81; 95% CI 0.64 to 1.02; 15 trials, 27,858 women). Additional uterotonic data were not totalled due to heterogeneity. Misoprostol use is associated with significant increases in shivering and a temperature of 38 ºCelsius.

There are scarce data comparing injectable prostaglandins with the conventional injectable uterotonics on severe PPH and the use of additional uterotonics, the primary outcomes of this review.

Authors' conclusions
Misoprostol orally or sublingually at a dose of 600 mcg shows promising results when compared to placebo in reducing blood loss after delivery. The margin of benefit may be affected by whether other components of management of the third stage of labour are used or not. As side-effects are dose-related, research should be directed towards establishing the lowest effective dose for routine use, and the optimal route of administration.

Neither intramuscular prostaglandins nor misoprostol are preferable to conventional injectable uterotonics as part of the management of the third stage of labour especially for low-risk women.

PLAIN LANGUAGE SUMMARY

Injectable uterotonic is the drug of choice for routine third stage management. Misoprostol may be used where no injectable uterotonic is available

After her baby is born, the woman's womb (uterus) muscles contract and bleeding decreases. If the womb does not contract, postpartum haemorrhage (heavy bleeding) can occur, which can be life threatening. Prostaglandin, oxytocin and ergometrine are drugs that cause contractions of the womb (uterotonics). The review of 46 trials, involving 42,621 women, found that oral or sublingual prostaglandin (misoprostol) may be useful in places where injectable uterotonics are not available, and is not as effective as oxytocin and has more side-effects. The main side-effects are shivering and high temperature occurring in a significant proportion of women. Injectable prostaglandin may be effective in reducing blood loss but has adverse effects and costs more.

BACKGROUND

Postpartum haemorrhage (PPH) is a major cause of morbidity and mortality during childbirth, especially in low- and middle-income countries. The contribution of PPH to maternal death in low- and middle-income countries is more marked in domiciliary or rural settings where trained staff are scarce, transport facilities are inadequate and the availability of uterotonic agents and blood are limited. In a community-based study in Zimbabwe, PPH was the leading cause of maternal death in rural (40 per 100,000) but not urban (eight per 100,000) women (Fawcus 1995).

The third stage of labour is defined as the period from delivery of the baby until the delivery of the placenta and its membranes. This stage usually takes less than 10 minutes when active management is used. Active management of the third stage of labour is a term to express the use of uterotonics, early cord clamping and active efforts to deliver the placenta following delivery. It is not always clearly defined and universally applied in a standard manner. PPH is usually defined as blood loss of 500 ml or more and severe PPH as 1000 ml or more in the third stage of labour. The 'normal' amount of blood loss is difficult to ascertain because different ways of managing the third stage and assessing the blood loss lead to markedly different amounts. It is well demonstrated that active management of the third stage of labour is associated with less blood loss. There seems to be general agreement that if the blood loss exceeds 500 ml close monitoring and additional measures such as administering uterotonics or checking for a cause of bleeding are prudent measures.

Traditionally, oxytocin and ergot preparations have been used as uterotonic agents for PPH prophylaxis mostly as part of active management of the third stage of labour. These agents, although effective in decreasing the blood loss, have the disadvantage of instability in tropical climates (Hogerzeil 1996) and also require syringes and trained personnel for administration. Another disadvantage, mainly related to ergot preparations, is the relatively high incidence of side-effects such as nausea, vomiting and increase in blood pressure.

Prostaglandins have strong uterotonic properties and are used widely in obstetric and gynaecological practice for cervical ripening, together with mifepristone for termination of pregnancy and for induction of labour. Prostaglandin preparations are available in injectable, tablet or gel forms according to their intended use. These agents do not cause hypertension, which enables them to be used in hypertensive patients. In the management of the third stage of labour, prostaglandins have been mainly used for intractable PPH as a last resort when other measures fail. To date, the main disadvantages of prostaglandins have been their cost and availability. Recently, misoprostol, a prostaglandin E1 analogue used orally for the prevention of peptic ulcer disease has also been reported for use in the management of the third stage of labour (El-Refaey 1997). Misoprostol is inexpensive, administered orally and stable at ambient temperatures. There is considerable experience with misoprostol use, both for peptic ulcer disease and as a uterotonic in obstetrics and gynaecology. The main side-effects of prostaglandins are nausea, vomiting and diarrhoea. Shivering and elevated body temperature have been reported with the use of misoprostol in the third stage of labour.

The use of prostaglandins in general, and of misoprostol in particular, could have implications for the efficacy and acceptability of active management of the third stage of labour. The rate and nature of side-effects (nausea, vomiting, diarrhoea, shivering) could influence the immediate relationship between the mother and her baby in the hours following birth.

Active management of the third stage of labour (by use of uterotonics, early cord clamping and active efforts to deliver the placenta) decreases blood loss during the third stage of labour (Prendiville 2000). This review is one in a series of reviews evaluating

strategies to prevent PPH (Cotter 2001; McDonald 2004; Prendiville 2000) and focuses on the role prostaglandins in the active management of the third stage of labour.

OBJECTIVES

To determine the effectiveness of prophylactic prostaglandin use compared to placebo or conventional uterotonics as part of the routine management of the third stage of labour.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomized controlled trials with a comparison between a prostaglandin and either another uterotonic agent or no uterotonic agent (placebo or nothing) were considered for inclusion in the review.

Types of participants

Women after delivery of the baby were the participants of this review. These women may be at high or low risk for postpartum haemorrhage. The definitions of high risk used by the trialists are accepted in general. These typically include having had a previous PPH, grand multiparity and multiple pregnancy among others. Data relating to high- and low-risk women are analysed separately as well as together (totals). Recent trials (mostly misoprostol) focused on a general population of women with vaginal or caesarean section delivery without specifying any risk status. Therefore, the high- and low-risk subgroupings were not used in the misoprostol comparisons. However, if future trials falling into these comparisons specifically study a risk group these subgroups will be added to the list of comparisons.

If a particular (risk) group is not specified, this implies that all women are included in that analysis regardless of their risk status. Studies that do not specify the risk status of women included are put in the low-risk category where such distinctions are made.

Studies including women with caesarean deliveries were eligible.

Types of intervention

In the earlier version of this review we included the use of prostaglandins when used 'as part of active management of the third stage of labour'. Recently, there has been increasing interest in evaluating the individual components of the 'active management' package and at least one trial that evaluated the use of a uterotonic without other components of active management of the third stage of labour. We included the use of only a prostaglandin within the scope of this review.

The experimental intervention evaluated in this review is the prophylactic use of prostaglandins in the management of the third stage of labour. Prostaglandin preparations are currently available in injectable and tablet forms, therefore different routes may be used and compared either with each other or with conventional injectable uterotonic agents. Different routes of administration are analysed in separate comparisons.

The choice of routine uterotonic drug used during the third stage of labour varies greatly around the world. In this review, oxytocin (Syntocinon®), ergometrine-oxytocin (Syntometrine®) and ergometrine are grouped together as 'conventional injectable uterotonics'. In cases where comparison is made with two different types of conventional uterotonics, oxytocin is selected as the conventional uterotonic as it is the drug used in most of the studies included in this review.

The main categories of prostaglandins evaluated in the review are misoprostol (prostaglandin E1 analogue), which is available in tablets and PGF2alpha and E2 preparations that are administered parenterally for use in the third stage of labour. Misoprostol tablets are administered either by mouth or rectally. Since the absorption of misoprostol from these two routes is currently unknown and likely to be different, these routes have been evaluated separately.

Injection of oxytocin or saline, or both, into the umbilical vein (reviewed elsewhere on retained placenta) and intramyometrial injection of prostaglandins other than at caesarean section (not used for routine active management) were not eligible for inclusion in this review.

The following comparisons have been used in the review:
(1) oral misoprostol versus no uterotonic/placebo;
(2) oral misoprostol versus injectable (conventional) uterotonics;
(3) rectal misoprostol versus no uterotonic/placebo;
(4) rectal misoprostol versus injectable uterotonics;
(5) rectal misoprostol versus intramuscular prostaglandins;
(6) sublingual misoprostol versus no uterotonics/placebo;
(7) sublingual misoprostol versus injectable uterotonics;
(8) intramuscular prostaglandins versus rectal misoprostol;
(9) intramuscular prostaglandin versus no uterotonic/placebo;
(10) intramuscular prostaglandin versus injectable uterotonics;
(11) comparisons of different prostaglandins or different dose/routes of the same prostaglandin;
(12) comparisons of different prostaglandins plus injectable uterotonics versus injectable uterotonics or other prostaglandins.

Types of outcome measures

The primary outcomes of this review are blood loss of 1000 ml or more and the use of additional uterotonics in the third stage of labour. Maternal death is included as an outcome but it is unlikely that the review will have power to evaluate this outcome.

A. Outcomes related to blood loss

Reported blood loss is influenced by the assessment technique. Measurement of blood and clots in jars and weighing of linen are likely to be more precise than clinical estimation used in some

studies. The latter is known to underestimate blood loss (Andolina 1999). Also, the duration of measurement and reporting the amount as 'greater than' or 'greater than or equal to' a certain cut-off level (e.g. 500 or 1000 ml) may affect the total reported amount of blood loss especially when this amount is estimated.

(1) Postpartum haemorrhage (at least 500 ml);
(2) severe postpartum haemorrhage (at least 1000 ml);
(3) mean blood loss (ml);
(4) use of additional uterotonics;
(5) blood transfusion;
(6) manual removal of placenta;
(7) duration of third stage (minutes);
(8) third stage longer than 30 minutes.

B. Side-effects
(1) Any side-effect reported;
(2) any side-effect requiring treatment;
(3) nausea;
(4) vomiting;
(5) diarrhoea;
(6) headache;
(7) abdominal pain;
(8) high blood pressure;
(9) shivering;
(10) severe shivering;
(11) pyrexia (at least 38 °C);
(12) severe pyrexia (at least 40 °C);
(13) other.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (February 2007)

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:
(1) quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
(2) monthly searches of MEDLINE;
(3) handsearches of 30 journals and the proceedings of major conferences;
(4) weekly current awareness search of a further 37 journals.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

In addition, we searched PubMed with the search term 'misoprostol' in July 2006.

We did not apply any language restrictions.

METHODS OF THE REVIEW

Two review authors independently evaluated trials under consideration for methodological quality and appropriateness for inclusion without consideration of their results. No language preferences were applied either during the search or selection of trials. Two authors independently extracted data regardless of whether they participated in a particular included trial or not.

We assessed methodological quality in terms of adequacy of allocation concealment as described in Higgins 2005.

In addition to the main outcomes, we systematically extracted the following data for each study:
(1) trial entry criteria (high versus low risk, other specific exclusion criteria);
(2) exclusions and missing data after randomization;
(3) management of the third stage of labour;
(4) the duration and technique of assessment of blood loss.

We evaluated statistical heterogeneity across trial results using the chi-square test as calculated in MetaView. Whenever statistical ($P < 0.1$) or visual heterogeneity was encountered, we explored the possible reasons. In meta-analyses with significant heterogeneity (statistical or visual), we discuss the trials individually (i.e. without totals).

It is not clear how components of third stage management, other than the uterotonic, affect the blood loss. While the comparison of the uterotonic might be valid, if other components of active management are effective, then the scope for any difference between a prostaglandin and a placebo or another uterotonic could be minimized if those components are used.

These factors are assessed as possible sources of heterogeneity where appropriate and if there are adequate numbers of studies to allow such assessments.

Because of the significant differences in pharmacokinetics and possibly other properties, we analysed oral, rectal, sublingual and buccal misoprostol and intramuscular prostaglandins (PGF2alpha and synthetic E2) separately.

We did not exclude trials on the basis of a predetermined cut-off value for loss to follow ups and postrandomization exclusions.

We systematically extracted this information and discussed as appropriate for each trial.

DESCRIPTION OF STUDIES

Seventy-five trials were identified and considered for inclusion in this review. Twenty-nine were excluded (*see* 'Characteristics of excluded studies' table). Altogether, 46 trials were included, involving 42,621 women - *see* 'Characteristics of includes studies' for details. Of these, 37 evaluated misoprostol and the remainder evaluated injectable prostaglandins (seven PGF2alpha and two PGE2). One trial compared misoprostol with intramuscular prostaglandin.

Settings
The review includes trials conducted in all continents from both low- to middle-income countries and industrialized countries. Twenty-seven trials included centres in low- and middle-income countries only. The WHO 2001 trial was conducted in nine countries in Africa, Asia, Europe and Latin America. In Africa, seven countries contributed 14 trials (five in South Africa). Eight trials were conducted in India.

The WHO 2001 trial is the largest trial in the review with 18,530 participants from nine countries. The WHO 1999 trial is a pilot dose-finding trial which preceded the WHO 2001 trial and used the same protocol. Side-effects of misoprostol during the first hour after delivery from the WHO 2001 trial are included in the meta-analyses, but further data describing side-effects in the first 24 hours after delivery were published in a separate article and are described in the results section.

Most trials (423/46) were conducted in hospitals where deliveries were performed by skilled caregivers. The Gambia trial (Gambia 2005) was conducted at the community level. Traditional birth attendants trained in trial procedures and blood loss measurement provided the interventions (oral misoprostol and oral ergometrine). In the Guinea-Bissau 2005 trial, trained midwives administered sublingual misoprostol or placebo to women delivering at primary care centres. In the India 2006c trial, auxiliary nurse-midwives administered oral misoprostol or placebo tablets to women delivering either at primary care centres (approximately 55%) or at home (approximately 45%).

Management of the third stage of labour
In 28 trials, the third stage was managed actively (at least two of the components of active management described, or specified as 'active'); two trials used 'passive management' (Holland 1991; India 2006c); nine trials did not mention and two were mixed with components of both active or passive management used. The remainder included women with caesarean section deliveries and did not report any particular form of management.

Risk status
Three studies specifically studied women who were at high risk for postpartum haemorrhage (PPH) (Egypt 1997; Holland 1995; India 2001b). The participants were classified as high risk if they had a history of PPH or conditions such as multiple pregnancy and grand multiparity.

Mode of delivery
Five trials included only caesarean section deliveries (India 2006a; United Kingdom 1994; United Kingdom 2001b; USA 1990; USA 2005).

Blood loss assessment
The majority of the trials (n = 24) used some form of measurement, some using detailed weighing and hematin-dye techniques. Clinical estimation was used in 16 trials, haemoglobin change or level, or both, was used in three and no method was mentioned in the remaining three trials (Colombia 2002; India 2001b; India 2005a).

Comparisons
Of the 46 trials included in the review, 37 evaluated misoprostol in doses ranging from 50 mcg to 800 mcg and using oral, sublingual, buccal and rectal routes. Misoprostol was compared to placebo in nine trials (France 2001; Gambia 2005; Guinea-Bissau 2005; India 2006c; South Africa 1998b; South Africa 1998c; South Africa 1998d; South Africa 2001; Switzerland 1999) and to conventional injectable uterotonics in 25 trials. The uterotonic agent was oxytocin 10 international units (IU) intramuscularly in most of these trials. In some trials the uterotonic group received oxytocin or ergometrine-oxytocin depending on the hospital routine (Australia 1999) or depending on whether the woman was hypertensive or not (United Kingdom 2000).

Some trials had several treatment arms. One of the intramuscular prostaglandin trials (Holland 1991) and two misoprostol trials (France 2001; South Africa 1998d) had three arms, one of which was a placebo control group. The WHO 1999 trial is also a three-arm trial comparing misoprostol 600 mcg, 400 mcg orally and oxytocin 10 IU. The United Kingdom 2003 trial had three arms comparing oral misoprostol 600 mcg, rectal misoprostol 600 mcg, and rectal misoprostol 400 mcg.

Concurrent routine uterotonic use
Two trials from Turkey had four arms, comparing misoprostol 400 mcg after cord clamp followed by misoprostol 100 mcg at four and eight hours postpartum; the same regimen of misoprostol combined with intravenous oxytocin; intravenous oxytocin only; and intramuscular methyl ergometrine only. For blood loss and other early outcomes assessed before the follow-up doses of misoprostol were given, the dosage is regarded as 400 mcg. The only differences between these two trials were that Turkey 2002 used rectal misoprostol and Turkey 2003 used oral misoprostol. The USA 2004 and USA 2005 trials compared 200 mcg buccal misoprostol to placebo in women delivering vaginally and by caesarean section respectively. All women received 20 IU oxytocin infusion at a rate

of 10 ml/minute for 30 minutes and then 125 ml/hour for eight hours.

The review includes unpublished data from Canada 2005, South Africa 1998d, WHO 1999, United Kingdom 2000 and WHO 2001 trials.

METHODOLOGICAL QUALITY

Allocation concealment was considered adequate in thirty-two studies that used sealed envelopes, opaque containers, or identical numbered boxes containing trial medications. Holland 1995 had 15% of the women excluded after randomization, mostly due to women being randomized despite being ineligible (for augmentation of labour), and Turkey 2003 had 12.6% of the women excluded after randomization secondary to them requiring caesarean sections. There were an unspecified but small number of postrandomization exclusions in South Africa 1998a. These were due to hypertension being discovered after randomization, which resulted in exclusion of some women allocated to ergometrine-oxytocin.

In trials evaluating different interventions in the third stage of labour, postpartum haemorrhage (PPH) is often the primary outcome. Assessment of PPH is prone to bias if the staff making the assessments are not blind to the intervention. In this review, outcome assessments were blinded in nineteen trials. Some outcome assessments were blinded in two trials.

In this review, trials comparing misoprostol with other uterotonics are, in essence, equivalence trials designed to evaluate whether misoprostol is as effective as others given its advantage of oral or rectal route of administration. The majority of such trials have set relatively large margins of equivalence and are therefore, in practical terms, underpowered to test an equivalence hypothesis. The WHO 2001 trial is the largest trial in the review which set an a priori clinical equivalence margin (within 35% efficacy of oxytocin). In this trial the primary outcomes were blood loss greater than or equal to 1000 ml and the use of additional uterotonics. Misoprostol versus placebo or no treatment trials are non-equivalence trials and do not have the problem mentioned above.

The South African trials and the United Kingdom 2001b trial evaluating oral misoprostol used non-identical placebos. The women participating in the South African trials took the medications out of an opaque container with care being taken to conceal the tablets from midwives. Although this method of blinding is not 100% safe, the authors provided the review authors with the information that unblinding was unlikely to occur in the settings in which the trials were conducted. In the United Kingdom 2001b trial, side-effect assessments were blinded.

One study (Holland 1995) was stopped prematurely before reaching a prespecified interim analysis to determine an appropriate sample size. This was due to the manufacturer of the drug issuing a warning about serious cardiovascular side-effects after intramuscular use of sulprostone, a synthetic PGE2 derivative.

RESULTS

The results are based on 37 misoprostol and nine intramuscular prostaglandin trials.

Misoprostol trials

Primary outcomes

Misoprostol versus placebo/no treatment (nine trials, comparisons 01, 02, 04, 07, 20)

Oral misoprostol was used in seven trials(comparison 01: 5153 women total, 4253 in five 600 mcg trials), rectal (comparison 03), sublingual (06) and buccal (18) in one trial each. There were three maternal deaths in misoprostol and one in placebo groups overall in nine trials.

There was significant qualitative and statistical heterogeneity for the outcome severe postpartum haemorrhage (PPH) in the oral misoprostol versus placebo comparison. Earlier trials (France 2001; South Africa 1998d; South Africa 2001) did not indicate any reduction in severe PPH while the more recent Gambia 2005 (relative risk (RR) 0.48; 95% confidence interval (CI) 0.09 to 2.59, 2/629 versus 4/599) and India 2006c (RR 0.20; 95% CI 0.04 to 0.91, 2/812 versus 10/808) trials suggest some protective effect of misoprostol on severe PPH. The use of additional uterotonics was less when misoprostol was used in four out of six trials but not in the South Africa 1998d trial that had both 600 and 400 mcg treatment arms. Compared to placebo, oral misoprostol reduced blood transfusion (RR 0.31; 95% CI 0.10 to 0.94, five trials, 3519 women).

One rectal misoprostol trial using 400 mcg did not show statistically significant difference in severe PPH (RR 0.69; 95% CI 0.35 to 1.37).

The Guinea-Bissau trial used 600 mcg sublingual misoprostol and showed a statistically significant difference in reducing severe PPH (RR 0.66; 95% CI 0.45 to 0.98, 37/330 versus 56/331).

The USA 2004 and USA 2005 trials used 200 mcg buccal misoprostol in women undergoing vaginal delivery and caesarean section respectively. All women received 20 IU oxytocin infusion in 1 litre of saline. In the USA 2005 trial there were 24/173 versus 22/179 cases of severe PPH in the misoprostol and placebo groups respectively whereas there were no cases of severe PPH in the USA 2004 trial. In both trials the protocol included oxytocin infusion after delivery of the placenta.

Misoprostol versus conventional injectable uterotonics (25 trials, comparisons 03, 05, 08)

Sixteen trials compared oral misoprostol (comparison 03), five compared rectal (comparison 05) and four compared sublingual

(comparison 08) to injectable uterotonics (oxytocin intramuscular or intravenous, ergometrine, ergometrine + oxytocin). Maternal deaths were reported only in the WHO 2001 trial (2/9264 versus 2/9266). There were no deaths in the Ghana 2006, Canada 2005, Turkey 2002 and WHO 1999 trials. Others did not mention whether there were any deaths or not.

Oral misoprostol was associated with a statistically significant higher risk of severe PPH (RR 1.32; 95% CI 1.16 to 1.51, 16 trials, 29,042 women). While the large WHO 2001 trial results dominate the meta-analysis the majority of trials show similar results with no statistically significant heterogeneity across different doses or trials. The use of additional uterotonics shows a similar trend but the results were not totalled because of significant statistical heterogeneity. There was a trend towards fewer blood transfusions with misoprostol (RR 0.81; 95% CI 0.64 to 1.02, 15 trials, 27,858 women).

Three rectal misoprostol versus injectables trials reported on severe PPH and there were similar numbers of women with this outcome in the two groups (RR 1.14; 95% CI 0.70 to 1.85, 1784 women). More women who received misoprostol required additional uterotonics (RR 1.64; 95% CI 1.16 to 2.31).

Four small trials compared sublingual misoprostol to injectables. The meta-analysis (graphs 08.02, 08.05) is too small to give any meaningful results.

Concurrent routine uterotonic use (Comparisons 16 and 18)
Oral and rectal misoprostol combined with oxytocin were compared to conventional uterotonics in the Turkey 2003 and Turkey 2002 trials respectively. Oral misoprostol when combined with oxytocin was more effective than placebo and oxytocin in decreasing severe PPH (RR 0.38; 95% CI 0.15 to 0.97), and PPH (RR 0.44; 95% CI 0.23 to 0.84). We were not able to use the additional uterotonic data from these trials.

Side-effects
Oral misoprostol 600 mcg was consistently associated with higher rates of prostaglandin-related side-effects such as nausea, vomiting, diarrhoea as well as for 'any' shivering, severe shivering and pyrexia (greater than 38 °C) when compared with placebo as well as with conventional uterotonics. We did not total most of these comparisons (graphs 01.17, 01.19, 02.18, 02.20) because of heterogeneity but the heterogeneity was quantitative, i.e. all studies showed an increase in these events. For 'any' shivering the individual trial RRs ranged between 1.43 to 69.10.

Further analysis of side-effects during the first 24 hours in the WHO 2001 trial showed that in comparison to oxytocin, women who received misoprostol had a higher incidence of 'any' shivering (RR 4.70; 95% CI 1.90 to 11.20), and of pyrexia (RR 6.3; 95% CI 3.70 to 10.80) in the period two to six hours after delivery. Diarrhoea was also more common in the misoprostol group in the period two to six hours (RR 21.00; 95% CI 5.10 to 86.50) and seven to 12 hours (RR 7.70; 95% CI 2.30 to 25.40).

The results of two trials (South Africa 1998d; WHO 1999) where 600 mcg and 400 mcg doses of oral misoprostol were compared indicate that side-effects are dose-related (any shivering RR 1.33; 95% CI 1.07 to 1.64) (Comparison 12.15). This might not apply, however, to rectal misoprostol, as there were no significant differences in the one trial (United Kingdom 2003) that evaluated 600 mcg and 400 mcg doses of rectal misoprostol. A comparison of 600 mcg rectal versus 600 mcg oral misoprostol in the same trial showed that rectal misoprostol had less pyrexia, 'any' shivering, and severe shivering (RR 0.27; 95% CI 0.16 to 0.46) (Comparison 14.08) than oral misoprostol.

Intramuscular prostaglandin trials (comparisons 09, 10, 11)
Ten trials compared injectable prostaglandins with conventional injectable uterotonics. One trial (Holland 1991) was a three-arm trial with a placebo arm in addition to sulprostone and oxytocin. The occurrence of primary outcomes such as blood loss 1000 ml or more and the use of additional uterotonics were too few to give reliable estimates.

Intramuscular prostaglandins had less mean blood loss when compared with no uterotonic use in one trial with 50 women (Holland 1991) that examined this outcome (-224 ml weighted mean difference; 95% CI -420.30 to -27.60 ml). Other outcomes evaluated in this study were not statistically significant.

When compared with conventional uterotonics, intramuscular prostaglandins had less blood loss and shorter duration of the third stage (-1.10 minutes weighted mean difference; 95% CI -1.40 to -0.89 minutes). Blood loss data were not totalled because of heterogeneity due to one small trial having result in the opposite direction. Three other trials showed less blood loss with injectable prostaglandin.

Vomiting, abdominal pain and diarrhoea were more common with intramuscular prostaglandins.

Intramuscular prostaglandin F2alpha was compared to rectal misoprostol 400 mcg in one small trial with 120 women (India 2006d). There were more women requiring additional uterotonics (2/60 versus 10/60) but the study was too small to give any guiding evidence. Another small trial compared intramyometrial injection of PGF2alpha with intramyometrial oxytocin to women having caesarean section deliveries (USA 1990).

DISCUSSION

This review includes comparisons of intramuscularly, orally, and rectally administered prostaglandins with placebo, and with conventional injectable uterotonics. We did not combine misoprostol with other prostaglandins in the meta-analyses. Misoprostol tablets are used via oral, rectal, sublingual or buccal routes while other prostaglandins are used intramuscularly (or intramyometrial during caesarean section). In terms of outcomes, we gave emphasis to blood loss of at least 1000 ml and the use of additional

uterotonics as the most clinically relevant outcomes. We recorded maternal death data systematically but did not anticipate having sufficient power to analyse this outcome.

While the results of earlier trials comparing misoprostol (used orally or rectally) to placebo or no treatment were somewhat equivocal, the results of the recent trials are more promising (Gambia 2005, Guinea-Bissau 2005; India 2006c). It is important to note that all three recent trials have design and setting differences that make the summing up of their results difficult. The Gambia 2005 trial had lower than expected number of events and although the direction of effect favours misoprostol the trial is not powered adequately. In addition, oral ergometrine was assumed to be equivalent to placebo and although the value of oral ergometrine is questionable (WHO 1994), it may not be zero. The third stage management was 'active'. This trial is the only trial that used traditional birth attendants to administer the trial interventions. The Guinea-Bissau 2005 trial used sublingual misoprostol within the context of active management and showed greater effect with higher blood loss (i.e. 1000 ml compared to 500 ml). Almost half of the women in this trial (150/330 and 170/331 in the misoprostol and placebo groups) experienced blood loss of 500 ml or more which is unusual in PPH trials with active management. The India 2006c trial used oral misoprostol in the context of 'passive' management of the third stage of labour. Therefore, its findings are more applicable to settings where this type of third stage management is the norm. It is not known whether with other components of active management being in place the same magnitude of effect would hold or not.

With the addition of three non-hospital based trials, it is possible to make some inferences for those settings although all three trials have important differences. All three trials were conducted either at home or at primary care centres and it is reassuring to see that there were no major adverse events related to misoprostol use. The Guinea-Bissau and India trials were conducted by caregivers skilled in third stage management although only the former had fully qualified midwives.

The addition of several smaller misoprostol versus injectable uterotonic trials confirm the findings of the earlier version of the review. Overall injectable uterotonics are more effective than misoprostol. Various injectables were used in the included trials. The data with regard to the comparative efficacy of oxytocin 10 international units (IU) versus ergometrine suggest that there are no major advantages of either of them (McDonald 2004). Ergot preparations seem to be somewhat more effective in reducing blood loss but are associated with a higher rate of side-effects and the choice should be made according to the trade-off between the benefit and harm (Carroli 2001).

The results of the large WHO 2001 trial, conducted in nine countries with the participation of 18,530 women, dominate the systematic review's comparison between misoprostol 600 mcg and injectable uterotonics, mostly 10 IU of oxytocin. This comparison demonstrates that oral misoprostol up to 600 mcg is associated with a higher risk of blood loss and the use of additional uterotonics (up to 16% of women will require additional uterotonic treatment) when compared with a policy of injectable uterotonics. There is a consistent increase in all prostaglandin-related side-effects. Considering that the observed rate of side-effects is already high, it is unlikely that higher doses of oral misoprostol (to increase efficacy) could be used for the routine prevention of postpartum haemorrhage among healthy women although the recent Ghana 2006 trial used 800 mcg misoprostol.

Although in almost all of the trials these side-effects were reported as not severe, they cause discomfort. For example, women in the WHO 2001 trial rated to have severe shivering needed extra blankets or other comfort measures. Amant reported that women who had shivering had their teeth chattering for 10 to 20 minutes and had no control over their body movements during this period (Amant 2001). On the other hand, in the case of pyrexia (greater than 38 °C), the staff may be concerned for the woman about the risk of postpartum infections and the need for initiating any unnecessary antibiotic treatment. Furthermore, fever may delay blood transfusion.

The largest trial (WHO 2001) used oxytocin both intramuscularly or intravenously. While it is obvious that intravenous injection provides faster availability of the drug, pharmacokinetic data show that with the intramuscular route oxytocin is circulating in the blood within two to three minutes (Gibbens 1972). Furthermore, the pharmacokinetics of oral misoprostol demonstrate that misoprostol acid reaches its peak in the plasma between 20 to 30 minutes after oral administration (Zieman 1997), well after the mean time from delivery until placental expulsion observed in the WHO 2001 (8.3 minutes, standard deviation (SD) 14.6) and Mozambique 2001 (9.0 minutes, SD 3.6) trials. Therefore, we do not think that the route of administration of oxytocin will affect its efficacy.

The three studies which enrolled women undergoing caesarean section deliveries have been included together with the others in the analysis. The amount of blood loss during and after caesarean section may be different, due to additional bleeding not directly related to the contractility of the uterus and, due to inevitable contamination with other fluids. However, a differential effect between different uterotonics is unlikely. Therefore, a sensitivity analysis according to the mode of delivery was not conducted. The problems associated with measurement of blood loss at caesarean section may, however, obscure any smaller differences in efficacy and push the results towards 'no difference'. In this review these studies were analysed within the group of studies which included women at low risk for postpartum haemorrhage.

With the data available so far there do not seem to be major differences between intramuscular prostaglandins and conventional injectable uterotonics (oxytocin or ergometrine) in reducing the blood loss in the third stage of labour. These trials had few women

who experienced the primary outcomes of this review, although the mean blood loss (a secondary outcome) was reduced by 70 ml on average for women who received intramuscular prostaglandins. Vomiting and diarrhoea were common side-effects. The studies reported, however, that side-effects did not need treatment. The concerns of safety, cost and side-effects are important limitations of intramuscular prostaglandins.

The recent WHO systematic review on cause of maternal deaths identified obstetric haemorrhage as the largest cause of maternal death in Africa and Asia where the majority of maternal deaths occur (Khan 2006). Prevention of PPH with appropriate, evidence-based interventions such as oxytocin (and misoprostol when oxytocin is not available) could prevent a substantial proportion of deaths in these two regions.

AUTHORS' CONCLUSIONS

Implications for practice

The uterotonic of choice in settings where active management is practiced is oxytocin 10 IU administered intravenously or intramuscularly. Getting oxytocin used as widely as possible should be the primary aim for deliveries occurring outside hospitals at peripheral levels of the healthcare system or at home. Oxytocin retains more than 85% active drug after storage for one year at under 30 °Celsius and is less expensive than misoprostol in most settings. If these conditions for oxytocin use cannot be met then misoprostol could be used based on the current evidence. The empirical dosage most used in trials to date is 600 mcg orally. Promising results against placebo have also been reported in individual trials of 400 mcg orally (over and above the routine use of oxytocin), and 600 mcg sublingually.

More efforts should be devoted to making injectable uterotonics available especially using strategies such as that of disposable prefilled syringes, e.g. Uniject (PATH 2001). Developing the skills to administer injections in areas where this is not currently available will have the additional benefit of enabling other effective treatments such as parenteral antibiotics or anticonvulsants to be used.

Intramuscular prostaglandins are not preferable to conventional uterotonics in the routine management of the third stage of labour especially for low-risk women.

Implications for research

The recent misoprostol versus placebo trials conducted outside hospitals that showed promising results should be replicated in order to strengthen the evidence base for justifying any use of misoprostol for routine third stage of labour management when conventional uterotonics are not available. As side-effects are dose-related and life-threatening hyperpyrexia has been reported with 800 mcg orally (Chong 1997), research should be directed towards establishing the lowest effective dose for routine use, and the optimal route of administration.

For the settings in which active management of the third stage is the norm, there is no need for further trials comparing misoprostol with injectable uterotonics. Future research in the third stage of labour could focus on investigating the effectiveness of the particular components of active management.

Intramuscular prostaglandins may be studied for the management of high-risk cases since they are unlikely to find widespread use in low-risk cases due to their costs and side-effects.

POTENTIAL CONFLICT OF INTEREST

Three review authors (AM Gülmezoglu, J Villar, GJ Hofmeyr) participated in the WHO 1999 and WHO 2001 trials and one review author (GJ Hofmeyr) participated in South African trials.

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** Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Australia 1999**
Methods	Random allocation from a table of random numbers with sequentially numbered, sealed, opaque envelopes. Block randomization was utilized. The study was not blinded.
Participants	930 women with vaginal delivery in 4 centres in Australia, China, and Papua New Guinea. Exclusion criteria: coagulation disorders, asthma, severe renal disease, epilepsy, elective caesarean section, severe hypertension.
Interventions	Misoprostol 400 mcg orally vs IM injection of either oxytocin (10 IU) (1 centre) or ergometrine-oxytocin (5 IU oxytocin + 0.5 mg ergometrine) (3 centres).
Outcomes	Blood loss, duration of third stage, use of additional uterotonics, blood transfusion, side-effects, haemoglobin level. Measurement of blood loss: by combining estimated (assessment by clinician) and measured (measuring volume with calibrated measuring jug, and weighing of linen). It is unclear if some centres used one or the other method.
Notes	Management of third stage: no mention of third stage management technique. 31/455 (7%) were excluded after randomization in the misoprostol group, and 36/475 (8%) were excluded after randomization in the oxytocin/ergometrine-oxytocin group. This trial was stopped after recruitment of 863/1862 women following the unsatisfactory results of an interim analysis.
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Belgium 1999**
Methods	Random allocation from a computer-generated list of study numbers. Randomization in blocks. Identical numbered study boxes were used. Outcome assessments were blinded.
Participants	213 women with vaginal delivery in Leuven, Belgium. Exclusion criteria: caesarean section, hypertensive disorders, gestational age < 32 weeks, intrauterine death, uterine malformations, allergy to prostaglandins or alkaloids, inflammatory bowel disease, coronary disease, vascular disease, sepsis.
Interventions	Misoprostol 600 mcg orally vs methylergometrine 200 mcg IV. Both oral and IV placebos were used.
Outcomes	Blood loss, need for additional uterotonics, side-effects. Blood loss was estimated.
Notes	Management of third stage: uterine massage, cord traction, manual removal of placenta after 30-60 minutes. 5/100 (5%) were excluded after randomization in the misoprostol group, and 8/108 (7.4%) were excluded in the methylergometrine group.
Allocation concealment	A – Adequate

Study	**Canada 2002**
Methods	Random allocation from a central centre statistician using block randomization for each participating centre. Consecutively-numbered opaque, sealed packets for allocation concealment. No blinding of treatment or outcome assessments.
Participants	223 women with vaginal delivery from 3 hospitals in Toronto, Canada. Exclusion criteria: parity > 6, gestational age < 32 wks, clotting disorder, anticoagulant therapy, history of postpartum haemorrhage, previous caesarean delivery.
Interventions	Misoprostol 400 mcg rectally after delivery vs oxytocin 5 IU IV or IM, or 10 IU IM given after delivery (sometimes given after placenta delivered).
Outcomes	Blood loss was captured by measuring change in measured haemoglobin. Other outcomes were duration of third stage, need for additional uterotonics, manual removal of placenta, blood transfusion, side-effects.
Notes	No description of third stage management. 13 women excluded after randomization secondary to having a caesarean section. 2 women lost to follow up.
Allocation concealment	A – Adequate

Study	**Canada 2005**
Methods	Randomized double blind, no further details. Unclear if outcome assessments were blinded.
Participants	622 women with vaginal delivery at a university hospital in Halifax, Nova Scotia, Canada. Women with multiple pregnancy, placenta previa, abruptio placentae, coagulation abnormalities, caesarean delivery and asthma were excluded.
Interventions	Misoprostol 400 mcg orally after delivery of anterior shoulder vs oxytocin 5 IU IV.
Outcomes	Blood loss measured by haematocrit drop greater than 10%, haemoglobin drop greater than 30%, additional uterotonics, blood loss greater than 1000 ml and 500 ml.
Notes	Third stage management was 'active'. No mention of postrandomization exclusion or loss to follow up. The authors attribute the high numbers of additional uterotonic use to most women having IV lines during labour and the threshold for bolus oxytocin administration being low.
Allocation concealment	B – Unclear

Study	**China 2004a**
Methods	Open, randomized trial. Randomization generated by a random-number table. Unclear if outcome assessments were blinded.

Characteristics of included studies (*Continued*)

Participants	60 low-risk women delivering vaginally in Hong Kong, China.
Interventions	Misoprostol 600 mcg sublingually vs syntometrine IV.
Outcomes	Blood loss, side-effects. Blood loss was both estimated visually and measured using alkaline hematin technique.
Notes	Third stage management was 'active' using early cord clamping and cord traction.
Allocation concealment	C – Inadequate

Study	**Colombia 2002**
Methods	Method of random allocation not stated. No placebo use or blinding of outcome assessments
Participants	75 women with vaginal delivery in Colombia. Exclusion criteria: asthma, coagulopathy, twins, stillbirth, lacerations, and "amniotic fluid in the blood collection".
Interventions	Misoprostol 50 mcg sublingually after cord clamp vs oxytocin 16 m IU per minute intravenously after cord clamp vs methylergometrine 0.2 mg after placenta delivery.
Outcomes	Blood loss, side-effects, cost. Method of collection or estimation of blood loss not stated.
Notes	Management of third stage: no mention of third stage management technique. No reported postrandomization exclusions or loss to follow up. Analysis was based on the total population of 75 women.
Allocation concealment	B – Unclear

Study	**Egypt 1993**
Methods	Random allocation from a table of random numbers. No mention of blinding or placebo use.
Participants	150 low-risk women after vaginal delivery in Assiut, Egypt. Excluded: labour < 2 hours, prolonged labour (> 24 hours), magnesium sulphate therapy during labour, history of postpartum haemorrhage, chorioamnionitis, multiple pregnancy, antepartum haemorrhage and episiotomy.
Interventions	Carboprost trometamol* 0.250 mg IM vs methylergometrine maleate 0.2 mg IV.
Outcomes	Blood loss, duration of third stage, side-effects. Measurement of blood loss: immediate blood loss was collected in trays and measured. Also, pads were used to collect blood for 4 hours and weighed.
Notes	Management of third stage: reported as active but only uterotonic use is mentioned. No mention of exclusions or missing data.
Allocation concealment	C – Inadequate

Study	**Egypt 1997**
Methods	Randomization using table of random numbers. No mention of blinding or placebo use.
Participants	132 high-risk women after vaginal delivery in Assiut, Egypt. 'High risk' risk factors included: previous history of postpartum haemorrhage, high parity, uterine overdistention due to multiple pregnancy, polyhydramnios or fetal macrosomia, prolonged labour, placental abnormalities or chorioamnionitis. Exclusion criteria: organic heart disease, bronchial asthma, epilepsy, renal disease, caesarean section, episiotomy.
Interventions	Carboprost trometamol* 250 mcg IM vs methylergonovine maleate 0.4 mg IV, vs oxytocin 10 IU IV.
Outcomes	Blood loss, duration of third stage. Measurement of blood loss - blood collected in trays and measured. Sterile pads were weighed.
Notes	Management of third stage: reported only as active.

	No report of exclusion after randomization.
Allocation concealment	B – Unclear

Study	**France 2001**
Methods	Randomly drawn envelopes containing the treatment codes. Placebos were not used. No placebo use.
Participants	602 women after vaginal delivery in France. Exclusion criteria: preterm birth (< 32 weeks), antepartum haemorrhage, intrauterine fetal death, uterine scar, caesarean section, multiple pregnancy, pre-eclampsia.
Interventions	Misoprostol 600 mcg orally vs oxytocin 2.5 IU IV given after cord clamp, vs no uterotonic.
Outcomes	Blood loss, duration of third stage, side-effects. Blood loss was measured.
Notes	Management of the third stage: active with immediate cord clamping.
Allocation concealment	A – Adequate

Study	**Gambia 2005**
Methods	Randomization generated by computer, allocation concealment by sealed, opaque envelopes. Power calculation made. Outcome assessments were blinded.
Participants	1229 women delivering vaginally at home by trained birth attendants in rural Gambia.
Interventions	Misoprostol 600 mcg orally vs oral ergometrine 2 mg.
Outcomes	Blood loss, postpartum haemoglobin. Blood loss was measured by collection of blood, pads and linen and weighing until 1 hour after delivery.
Notes	Management of the third stage: controlled cord traction, delayed cord clamping (after cessation of pulsation), early suckling of the breast. No loss to follow up.
Allocation concealment	A – Adequate

Study	**Ghana 2000**
Methods	Randomized, double-blind, controlled trial. Randomization sequence generated by computer. Allocation by sequentially numbered, opaque packets containing active and placebo medications. The packets and misoprostol solution were prepared by a pharmacist not involved in the trial. Power calculation was based on a difference of drop in haemoglobin concentration (> 0.1 g/dl).
Participants	401 women delivering vaginally at the Korle Bu teaching hospital and its clinics in Accra, Ghana. Women were excluded if they were at risk of postpartum haemorrhage (grand multiparae, multiple gestation, gestation < 32 weeks, gestational hypertension with haemolysis-elevated liver enzymes-low platelets syndrome, hydramnios, previous postpartum haemorrhage, coagulation abnormalities, precipitous labour, chorioamnionitis and oxytocin induction or augmentation of labour.
Interventions	Misoprostol 400 mcg in powdered form orally (in 50 ml of water) and 1 ml IM injection of normal saline (placebo) vs powdered lactose placebo orally (in 50 ml of water) and 1 ml IM injection of 10 IU oxytocin.
Outcomes	Primary outcome: drop in haemoglobin concentration; side-effects. Blood loss measurement: clinical estimation.
Notes	Management of third stage: active with cord traction. The authors mention that they report the data as intention to treat although outcome data are missing for 9/401 women.
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Ghana 2006**
Methods	Random-number scheme generated by computer. Allocation concealment by opening the next sequentially-numbered, sealed, opaque envelope. The study was not blinded. Power calculation is reported.
Participants	450 women delivering vaginally at Holy Family hospital, Techiman, Ghana. Women at both high and low risk for PPH were included.
Interventions	Misoprostol 800 mcg orally vs oxytocin 10 IU IM.
Outcomes	Primary outcome: change in haemoglobin concentration, other measures of blood loss, side-effects. Blood loss was estimated.
Notes	Management of the third stage: 'active', no further details. No loss to follow up.
Allocation concealment	A – Adequate

Study	**Guinea-Bissau 2005**
Methods	Random-number list used for randomization scheme. Allocation concealment by sealed, opaque, consecutively-numbered envelopes. Outcome assessments were blinded.
Participants	661 women delivering at a primary care centre in Guinea-Bissau.
Interventions	Misoprostol 600 mcg sublingual vs identical placebo.
Outcomes	Blood loss, side-effects. Blood loss was measured by collecting blood in swabs and absorbent drape and then weighing them.
Notes	Management of the third stage: active with early cord clamping and controlled cord traction. The midwives were trained in these procedures before the start of the trial.
Allocation concealment	A – Adequate

Study	**Holland 1991**
Methods	Random allocation was by allocating identical numbered boxes containing trial medications. Method of generation of numbers was not stated. Outcome assessments were not blinded. Saline injections were used as placebo.
Participants	74 low-risk women with spontaneous labour and vaginal delivery in Nijmegen and Bergen op Zoom, Holland.
Interventions	Sulprostone** 0.5 mg IM vs oxytocin 5 IU IM vs saline.
Outcomes	Blood loss, duration of third stage, side-effects. Measurement of blood loss: blood and clots collected in trays, swabs and linen weighed for the first hour after delivery.
Notes	Management of third stage: 'conservatively', cord clamped within 1 minute, women asked to push after signs of separation, no cord traction or fundal pressure. 3/77 excluded (2 because of induction of labour, 1 vacuum delivery). There were more multiparous women with fewer episiotomies in the sulprostone group despite randomization.
Allocation concealment	A – Adequate

Study	**Holland 1995**
Methods	Random allocation to pharmacy coded identical boxes containing trial medications. Outcome assessments were blinded. Placebo use.
Participants	69 women with a history of previous postpartum blood loss of more than 1000 ml were eligible for this trial conducted in Leiden, Holland. Exclusion criteria: coagulation disorders, anticoagulant treatment, fibroids, multiple pregnancy, hypertension and induction of labour were excluded.
Interventions	Sulprostone** 0.5 mg IM at delivery of anterior shoulder + placebo after delivery of placenta vs oxytocin 5 IU IM at delivery of anterior shoulder + methylergometrine 0.2 mg IM after delivery of placenta.

Characteristics of included studies (*Continued*)

Outcomes	Blood loss, duration of third stage, side-effects. Measurement of blood loss: blood and clots were collected in trays and linen weighed.
Notes	Management of third stage: fundal pressure while holding lower segment of the uterus after signs of placental detachment. 12/81 (15%) excluded after randomization and before the intervention. No further exclusions after participation in the trial.
Allocation concealment	A – Adequate

Study	**Hong Kong 2001**
Methods	Random allocation was by sealed, consecutively-numbered, opaque envelopes. Random allocation scheme was generated by computer. Outcome assessments were not blinded. Power calculation was done.
Participants	2058 women with singleton pregnancies and vaginal delivery in 3 hospitals in Hong Kong participated in the trial. Women with pre-eclampsia, cardiac disease and asthma, conditions requiring prophylactic oxytocin infusion after delivery (uterine fibroids, grand multiparity) were excluded.
Interventions	Misoprostol 600 mcg oral after delivery of the baby, vs oxytocin 5 IU + ergometrine 0.5 mg IM at delivery of anterior shoulder.
Outcomes	Blood loss, duration of third stage, delayed haemorrhage, maternal haemoglobin after delivery, side-effects. Shivering was assessed using a visual analogue scale. Blood loss was estimated.
Notes	Management of third stage: controlled cord traction after signs of placental separation. No loss to follow up or postrandomization exclusions were reported.
Allocation concealment	A – Adequate

Study	**India 1988c**
Methods	Random allocation by serially numbered, sealed envelopes. There was no placebo use or blinding of outcome assessments.
Participants	300 women in 3 centres in India. No mention of risk status. No note of exclusion criteria.
Interventions	PGF2alpha 0.125 mg IM vs methylergometrine 0.2 mg IV.
Outcomes	Blood loss, duration of third stage, side-effects. Measurement of blood loss: blood was collected in trays for 4 hours postpartum and measured.
Notes	Management of third stage: no mention of the third stage management technique.
Allocation concealment	A – Adequate

Study	**India 2001b**
Methods	Randomized trial. No further details. Unclear if outcome assessments were blinded.
Participants	120 women with at least 1 risk factor for atonic haemorrhage at Jawaharial Institute of Medical Education and Research Hospital in Pondicherry, India.
Interventions	Group A: methylergometrine 0.2 mg IV. Group B: oxytocin 10 IU in 10 ml saline into the umbilical cord. Group C: carboprost 0.250 mg IM.
Outcomes	Blood loss, side-effects. Blood loss measurement not mentioned.
Notes	Management of third stage: 'active' with controlled cord traction following signs of separation. No loss to follow up.
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**India 2004b**
Methods	Random allocation by sealed, consecutively-numbered envelopes. Unclear if outcome assessments were blinded.
Participants	120 low-risk women at a rural health centre in New Delhi, India.
Interventions	Misoprostol 400 mcg sublingually vs 0.2 mg methylergometrine IV.
Outcomes	Blood loss, side effects. Blood loss was measured collecting all blood and weighing the linen and swabs.
Notes	Management of the third stage: active with cord traction.
Allocation concealment	A – Adequate

Study	**India 2005a**
Methods	Random allocation, no further details. Unclear if outcome assessments were blinded.
Participants	200 primiparous women with singleton deliveries at Lok Nayak Hospital, New Delhi, India.
Interventions	Misoprostol 600 mcg orally immediately after delivery vs 0.2 mg methylergometrine IV at delivery of anterior shoulder.
Outcomes	Blood loss, side-effects. Blood loss measurement method not mentioned.
Notes	Management of the third stage: early cord clamping but no mention of placental delivery. No mention of missing data or loss to follow up.
Allocation concealment	B – Unclear

Study	**India 2006a**
Methods	Randomization by computer-generated random-number list, allocation concealment by opening sealed opaque envelopes. Unclear if outcome assessments were blinded.
Participants	100 women undergoing caesarean section at the All India Institute of Medical Sciences, New Delhi, India. Women with risk factors for PPH were not eligible.
Interventions	Misoprostol 400 mcg sublingually vs 20 IU oxytocin in 1 litre lactated Ringer's solution at 125 ml/h. All women had spinal anaesthesia.
Outcomes	Blood loss, side-effects. Blood loss measurement: Volume of blood in the suction bottle + weighing of blood soaked linen.
Notes	Management of the third stage: not applicable.
Allocation concealment	B – Unclear

Study	**India 2006b**
Methods	Randomization achieved by computer-generated numbers. No details regarding allocation concealment available.
Participants	2023 women delivering at the Christian Medical College Hospital, Vellore, India. Women with cardiac disease, bronchial asthma, rhesus factor incompatibility, pregnancy-induced or pregnancy-aggravated hypertension and caesarean delivery were excluded.
Interventions	Misoprostol 400 mcg orally vs oxytocin 10 IU IM versus ergometrine 0.2 mg IV.
Outcomes	Blood loss, haemoglobin levels, side-effects. Blood loss measurement: large plastic bag placed under the buttocks following drainage of amniotic fluid. The blood was then transferred to a measuring jar.
Notes	Management of the third stage: active management.
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**India 2006c**
Methods	Computer-generated, random-number schedule with a random block list. Random allocation by giving the next of a series of non-distinguishable envelopes containing active or placebo tablets. Identical placebos were used. Outcome assessments were blinded.
Participants	1620 women delivering at home or primary care centre in 4 primary health centre areas of Belgaum District, Karnataka State, India. Women were delivered by ANMs who were trained in the trial procedures and the intervention. 2 sets of midwives were involved in the study. 18 at the beginning and 12 leaving and replaced by 7 new ANMs.
Interventions	Misoprostol 600 mcg orally vs identical placebos.
Outcomes	Blood loss, side-effects. Blood loss measurement: A calibrated blood collection drape placed under the buttocks following delivery. Blood loss was measured after 1 hour and 2 hours.
Notes	Management of the third stage: the ANMs practised expectant management of the third stage of labour apart from the uterotonic in the intervention arm.
Allocation concealment	A – Adequate

Study	**India 2006d**
Methods	Randomized study, no further details presented. Unclear if outcome assessments were blinded.
Participants	120 low-risk women delivering at the Comprehensive Rural Health Services Project, a rural health centre affiliated with the All India Institute of Medical Sciences, New Delhi, India. Women who received oxytocin during labour, caesarean section delivery, multiple pregnancy and Hb < 8 g/dl were excluded.
Interventions	Misoprostol 400 mcg rectally vs PG-F2alpha 125 mcg IM.
Outcomes	Blood loss. Blood loss measurement: by clinical estimation.
Notes	Management of the third stage: not mentioned.
Allocation concealment	B – Unclear

Study	**Mozambique 2001**
Methods	Randomized double-blind trial. Generation of allocation sequence unclear. Double placebos prepared by a pharmacist independent of the trial on a daily basis and provided to the investigators upon request. Outcome assessments were blinded.
Participants	663 women with uncomplicated vaginal delivery between 30 and 42 weeks of gestation at Central Hospital of Maputo, Mozambique. Women undergoing induction or augmentation of labour were excluded.
Interventions	Misoprostol 400 mcg dissolved in 5 ml saline and administered rectally as a micro-enema + 1 ml saline placebo IM vs oxytocin 10 IU administered IM + 5 ml saline micro-enema (placebo).
Outcomes	Blood loss, side-effects. Blood loss measured by a metal collector placed under the buttocks after delivery until the woman was moved from the delivery room.
Notes	Management of third stage not described. 26/350 (7.4%) in the misoprostol group and 11/350 (3.1%) in the oxytocin group were excluded after randomization because of emergency caesarean section or incomplete data collection.
Allocation concealment	B – Unclear

Study	**Nigeria 2003**
Methods	Randomized double-blind trial with identical looking double placebos. Randomization schedule generated using random-number tables. Allocation concealment achieved by using sealed opaque packets containing both active and the corresponding placebo medication.

Characteristics of included studies (*Continued*)

Participants	496 low-risk women having vaginal deliveries in 2 hospitals in Delta State, Nigeria. Women undergoing caesarean section and who had other risk factors for haemorrhage were excluded.
Interventions	Misoprostol 600 mcg in powder form dissolved in 50 ml water per os vs oxytocin 10 IU IM at delivery of anterior shoulder.
Outcomes	Blood loss, postdelivery haemoglobin, side-effects. Blood loss estimated by the clinicians.
Notes	Management of third stage: controlled cord traction, no other details. No loss to follow up or postrandomization exclusions reported.
Allocation concealment	A – Adequate

Study	**Singapore 1995**
Methods	Random allocation by a random-number table. Blinding of some outcome assessments.
Participants	115 women with spontaneous labour and delivery in Singapore. Exclusion criteria: multiple pregnancy, any antenatal complications.
Interventions	Carboprost trometamol* 125 mcg IM vs ergometrine-oxytocin 0.5 mg IM.
Outcomes	Blood loss, need for additional uterotonics, transfusion, haemoglobin levels, side-effects. Measurement of blood loss: blood and clots in the first 2 hours after delivery mopped with absorbent paper, sanitary pads collected for the next 22 hours, and then measured.
Notes	Management of third stage: controlled cord traction after placenta separation. 3/115 (2.6%) women were excluded after randomization.
Allocation concealment	A – Adequate

Study	**South Africa 1998a**
Methods	Random allocation by computer-generated, random sequence for sealed opaque envelopes. No placebo use. Outcome assessments were not blinded.
Participants	491 women at low risk for PPH at Natalspruit Hospital, Johannesburg, South Africa. Exclusion criteria: not noted.
Interventions	Misoprostol 400 mcg rectally vs ergometrine-oxytocin 1 ampoule IM.
Outcomes	Blood loss, duration of third stage, side-effects. Measurement of blood loss: by estimation.
Notes	Loss to follow up was minimal for primary outcomes (2-3%) with the exception of postpartum haemoglobin which was measured in 67% and 65% of women in the misoprostol and ergometrine-oxytocin groups respectively. A small number of women (unspecified) allocated to ergometrine-oxytocin were excluded because of high blood pressure discovered after randomization. However, results were similar to the whole group when all hypertensives were excluded in a subgroup analysis. Third stage management was active.
Allocation concealment	A – Adequate

Study	**South Africa 1998b**
Methods	Random allocation by computer-generated random sequence. Double-blinded, placebo-controlled trial. Tablets kept in numbered, sealed, opaque containers. Non-identical placebo tablets.
Participants	500 women after delivery at Coronation Hospital, Johannesburg, South Africa. No mention of risk status. Exclusion criteria: oxytocin infusion in progress at the time of delivery, hypertension, diabetes, previous caesarean section delivery.

Characteristics of included studies (*Continued*)

Interventions	Misoprostol 400 mcg orally vs placebo.
Outcomes	Blood loss greater than or equal to 1000 ml within first hour of birth, use of additional uterotonics, side-effects, third stage 30 minutes or longer, manual removal of the placenta, blood transfusion. Measurement of blood loss: blood and clots collected in bedpans and volume assessed. Linen weighed.
Notes	Management of third stage: placenta removed by cord traction once firm uterine contraction diagnosed by palpation. No withdrawals after randomization.
Allocation concealment	A – Adequate

Study	**South Africa 1998c**
Methods	Random allocation by computer-generated random numbers. Tablets kept in numbered, sealed, opaque containers. Non-identical placebo tablets. Outcome assessments were blinded.
Participants	550 low-risk women after delivery at Coronation Hospital Johannesburg, South Africa. Exclusion criteria: not noted.
Interventions	Misoprostol 400 mcg rectally vs placebo.
Outcomes	Blood loss greater than or equal to 1000 ml, use of additional uterotonics, spontaneous delivery of the placenta, third stage longer than or equal to thirty minutes, side-effects. Measurement of blood loss: blood collected in bedpan until 1 hour after delivery. Linens weighed.
Notes	Management of third stage: placenta delivered either by cord traction or spontaneous expulsion. Exclusions after randomization: records for 4 allocations (all in placebo group), could not be traced.
Allocation concealment	A – Adequate

Study	**South Africa 1998d**
Methods	Random allocation according to a computer-generated random sequence. Serially numbered, opaque test tubes. Outcome assessments were blinded.
Participants	600 women after delivery at Coronation Hospital, Johannesburg, South Africa. No mention of whether they are high or low risk. No mention of exclusion criteria.
Interventions	Misoprostol 600 mcg orally vs misoprostol 400 mcg orally vs placebo.
Outcomes	Shivering, pyrexia. Blood loss was measured using a flat bed pan.
Notes	Management of third stage: placenta removed by cord traction after firm contraction of uterus. No exclusions after randomization.
Allocation concealment	A – Adequate

Study	**South Africa 2001**
Methods	Random allocation according to a computer-generated random sequence. Serially numbered, opaque test tubes. Outcome assessments were blinded.
Participants	600 women after delivery at Coronation Hospital, Johannesburg, South Africa. Exclusion criteria: no mention of exclusion criteria.
Interventions	Misoprostol 600 mcg oral vs placebo.
Outcomes	Shivering, pyrexia. Measurement of blood loss: blood in bed pan measured, linen and sanitary towels weighed.
Notes	Management of third stage: placenta removed by cord traction after firm contraction of uterus. No exclusions after randomization.
Allocation concealment	A – Adequate

Characteristics of included studies (*Continued*)

Study	**Switzerland 1999**
Methods	Random allocation using random-number tables. Trial was double blinded.
Participants	65 low-risk women with vaginal deliveries at Basel University Hospital, Basel, Switzerland. Exclusion criteria: multiple pregnancy, pre-eclampsia, previous PPH or antepartum haemorrhage, caesarean delivery.
Interventions	Misoprostol 600 mcg orally vs placebo.
Outcomes	Blood loss, length of third stage, use of additional uterotonics, side-effects, haematocrit values. Measurement of blood loss: estimation by delivery physicians.
Notes	Management of third stage: early cord clamping and cord traction. No exclusions after randomization.
Allocation concealment	A – Adequate

Study	**Turkey 2002**
Methods	Randomization based on computer-generated random numbers. Sealed, consecutively-numbered, opaque envelopes were used. Identical placebos were used except for the misoprostol tablets which were similar in size and colour but not in shape. There was blinding of outcome assessments. Midwives administered the misoprostol tablets, but residents that were blinded to the intervention, did the outcome assessments.
Participants	1633 women with vaginal deliveries in Ankara, Turkey. Exclusion criteria: Gestational age < 32 wks, caesarean delivery, hypersensitivity to prostaglandins.
Interventions	Women randomized into 4 groups, all received corresponding placebos. Group 1: oxytocin 10 IU IV plus misoprostol 400 mcg rectally after cord clamp, followed by 2 doses 4 and 8 hours after delivery of 100 mcg misoprostol. Group 2: misoprostol 400 mcg rectally after cord clamp followed by 2 doses 4 hours apart of 100 mcg misoprostol. Group 3: oxytocin 10 IU IV. Group 4: oxytocin 10 IU IV plus 1 ml methylergometrine IM.
Outcomes	Blood loss, transfusion, change in Hgb, need for additional uterotonics, length of the third stage, subsequent evacuation of uterus, frequency of delayed haemorrhage, side-effects. Clinical estimation of blood loss was done.
Notes	Active management of third stage with early cord clamping, traction, and uterine massage. 27 exclusions after randomization secondary to lack of Hgb measurements. These were spread out among the 4 groups. Concurrent study at this institution with similar design but evaluating oral misoprostol also published and is included in this meta-analysis.
Allocation concealment	A – Adequate

Study	**Turkey 2003**
Methods	Randomization based on computer generated random numbers. Sealed, consecutively numbered, opaque envelopes were used. Identical placebos were used except for the misoprostol tablets which were similar in size and color but not in shape. There was blinding of outcome assessments. Midwives administered the misoprostol tablets, but residents that were blinded to the intervention, did the outcome assessments.
Participants	1800 women with vaginal deliveries in Ankara, Turkey. Exclusion criteria: Gestational age < 32 wks, caesarean delivery, hypersensitivity to prostaglandins.
Interventions	Women randomized into 4 groups, all received corresponding placebos. Group 1: oxytocin 10 IU IV plus misoprostol 400 mcg orally after cord clamp, followed by 2 doses 4 and 8 hours after delivery of 100 mcg misoprostol. Group 2: misoprostol 400 mcg orally after cord clamp followed by 2 doses 4 hours apart of 100 mcg misoprostol. Group 3: oxytocin 10 IU IV. Group 4: oxytocin 10 IU IV plus 1 ml methylergometrine IM.

Characteristics of included studies (*Continued*)

Outcomes	Blood loss, transfusion, change in Hgb, need for additional uterotonics, length of the third stage, subsequent evacuation of uterus, frequency of delayed haemorrhage, side effects. Clinical estimation of blood loss was done.
Notes	Active management of third stage with early cord clamping, traction, and uterine massage. 226 (12.6%) exclusions after randomization secondary to lack of haemoglobin measurements. Concurrent study at this institution with similar design but evaluating oral misoprostol also published and is included in this meta-analysis.
Allocation concealment	A – Adequate

Study	**USA 1990**
Methods	Method of random allocation not stated. Double-blinded trial.
Participants	46 women at low risk for postpartum haemorrhage undergoing delivery by caesarean section in Arkansas, USA. Exclusion criteria: hypertension, asthma, pre-eclampsia, chorioamnionitis, multiple gestation or were receiving tocolytic agents.
Interventions	Carboprost tromethamine* 0.125 mg intramyometrial vs oxytocin 20 IU intramyometrial. Both groups received 20 IU of oxytocin in 1 litre saline after delivery.
Outcomes	Haematocrit change after delivery, blood loss not measured.
Notes	Management of third stage: not applicable. No losses to follow up.
Allocation concealment	A – Adequate

Study	**USA 2001**
Methods	Random allocation sequence concealed until enrolment. Packs containing both active and placebo were made available after random allocation. It is not clear if the placebos are identical. No mention of blind outcome assessments.
Participants	400 women in active labour or undergoing induction of labour in Los Angeles, USA were enrolled. Women with multiple gestation, known coagulation disorders, contraindication to prostaglandin or oxytocin use, known initial haemoglobin below 7.0 mg/dl and an indication for caesarean section were excluded.
Interventions	Misoprostol 400 mcg rectally + placebo (2 ml saline) vs oxytocin 20 IU + placebo (lactose tablets). Oxytocin (and its placebo) was administered as IV infusion in 1 L of Ringer's lactate solution.
Outcomes	Blood loss (estimated and measured by weighing linen etc.), haematocrit, side-effects.
Notes	Management of the third stage not mentioned. Exclusions after randomization: 75/400 (18.75%), 73 had caesarean section during labour, one had Hb < 7.0 mg/dl and one was discharged home before delivery.
Allocation concealment	B – Unclear

Study	**USA 2004**
Methods	Random allocation sequence generated by using a table of random numbers. Active and placebo (similar but not identical) were placed in opaque, numbered vials. Power calculation was made. Outcome assessments were not blinded.
Participants	756 women with anticipated vaginal delivery at a maternity hospital in Florida, USA.
Interventions	Misoprostol 200 mcg buccal vs placebo. All women received intravenous infusion of 20 IU oxytocin in 1 litre of saline at 10 ml/min for 30 minutes (i.e. received approximately 6 IU oxytocin IV).
Outcomes	Blood loss, haemoglobin measurements, side-effects. Blood loss was estimated by the attending physician.

Characteristics of included studies (*Continued*)

Notes	Management of the third stage: active management with early cord clamping. controlled cord traction and oxytocin after delivery of the placenta. 756/848 eligible women were randomized. Analysis by intention to treat.
Allocation concealment	B – Unclear

Study	**USA 2005**
Methods	Randomized, placebo-controlled. No mention of random-number generation scheme. Allocation concealment by pharmacy-assigned numbers to opaque vials containing either misoprostol tablets or oxytocin ampoules. Outcome assessments were blinded.
Participants	352 women undergoing caesarean section in Orlando, Florida, USA.
Interventions	Misoprostol 200 mcg buccal vs placebo at cord clamping. All women received 20 IU IV oxytocin in 1000 ml saline.
Outcomes	Blood loss, additional uterotonics. Blood loss was estimated following 'standard' procedures.
Notes	No loss to follow up.
Allocation concealment	A – Adequate

Study	**United Kingdom 1994**
Methods	Method of random allocation not stated. Sealed opaque envelopes used for allocation concealment. Interventions prepared by someone not involved in the study, outside the intervention area (operating theatre). Outcome assessments were blinded.
Participants	60 low-risk women undergoing elective caesarean section in an academic hospital in Oxford, UK. Exclusion criteria: hypertensive disease, asthma, heart disease.
Interventions	Prostaglandin group: 15-methyl prostaglandin F2alpha, 125 mcg intramyometrial + placebo. Oxytocin group: 5 IU oxytocin IV bolus injection followed by 15 IU in 500 ml of Ringer's lactate solution + placebo. Both interventions were started after delivery of the baby but before delivery of the placenta.
Outcomes	Blood loss, use of additional uterotonics, blood transfusion, side-effects, change in haemoglobin (subset of patients). Measurement of blood loss: clinical estimation.
Notes	Management of third stage: not applicable. No losses to follow up or postrandomization exclusions reported.
Allocation concealment	A – Adequate

Study	**United Kingdom 2000**
Methods	Random allocation by sealed, opaque, consecutively-numbered envelopes. No blinding of outcome assessments.
Participants	1000 women delivering vaginally, in London, UK. Women with a history of asthma, planned caesarean section and water birth were excluded.
Interventions	Misoprostol group: 500 mcg misoprostol orally after baby delivered and cord clamped. Uterotonic group: this group was given uterotonics at delivery of anterior shoulder. The choice of uterotonics varied according to the hospital policy for different groups of women. Women at high risk of haemorrhage received ergometrine (2%), those with hypertension received oxytocin (18%). All others received ergometrine-oxytocin (80%).
Outcomes	Blood loss, side-effects. Measurement of blood loss: clinical estimation by the midwives.

Characteristics of included studies (*Continued*)

Notes	Management of third stage: 'active': cord traction with signs of separation, oxytocics at anterior shoulder delivery. No mention of postrandomization exclusions or protocol violations.
Allocation concealment	A – Adequate

Study	**United Kingdom 2001b**
Methods	Random allocation schedule generated by computer. Allocation made by opening sealed opaque envelopes which contained the names of the groups. No mention of consecutive numbering and opening. The obstetrician, surgical assistant, scrub nurse and recovery midwives were blinded to the group while anaesthetist was not. Double, nonidentical placebos were used.
Participants	40 women undergoing elective or emergency caesarean section in a university hospital in London, United Kingdom. Women with 2 or more caesarean sections or a history of previous ruptured uterus were excluded. Other eligibility criteria are not mentioned.
Interventions	Misoprostol 500 mcg orally + 2 ml IV normal saline bolus vs 10 IU oxytocin bolus + 2 placebo tablets.
Outcomes	Blood loss (clinical estimation), change in Hgb levels, shivering (assessed in the recovery room), temperature within 1 hour.
Notes	Management of third stage: 'active' during caesarean section. No withdrawals after caesarean section.
Allocation concealment	B – Unclear

Study	**United Kingdom 2003**
Methods	Random allocation prepared by independent statistician using computer-generated random numbers with blocked randomization. Sequentially numbered, sealed, opaque, envelopes used. No placebos used. No blinding of outcome assessments.
Participants	275 women with vaginal delivery in London, UK. Exclusion criteria: < 37 wks gestation, < 18 yrs old, multiple gestation, induced labour, asthma, cardiac, renal or hepatic disorder. Study was reported in conjunction with a misoprostol pharmacokinetics trial.
Interventions	Misoprostol 600 mcg orally vs 600 mcg rectally vs 400 mcg rectally.
Outcomes	Side-effects, clinical estimation of blood loss, duration of third stage, manual removal of placenta.
Notes	"Usual" management of third stage with cord traction. No losses to follow up or postrandomization exclusions. Blood loss estimated.
Allocation concealment	A – Adequate

Study	**WHO 1999**
Methods	Random allocation sequence, generated centrally. Sealed and numbered identical treatment packs taken consecutively from a dispenser. Double-blinded, placebo controlled pilot trial.
Participants	597 women after delivery in Khon Kaen, Thailand and Johannesburg, South Africa. Risk status not stated. Exclusion criteria: asthma, other severe chronic allergic condition, if delivery considered an abortion, planned caesarean section, not willing or able to give informed consent.
Interventions	Misoprostol 600 mcg orally vs misoprostol 400 mcg orally vs oxytocin 10 IU IV.
Outcomes	Shivering, pyrexia, side-effects, blood loss from delivery to transferral of mother to postnatal care. Measurement of blood loss: collected blood poured in standard measuring jar. Linen not weighed. Small gauze swabs soaked with blood put into measuring jar and included in measurement.
Notes	Management of third stage: uterotonics, clamping and cutting of cord immediately after delivery, fundal or suprapubic pressure with cord traction after signs of placental separation.

	Exclusion after randomization: 8 women in the oxytocin group did not comply with treatment (6 had an emergency caesarean section, 1 was HIV positive and mistakenly excluded, 1 whose ampoule was not located). One woman in the 600 mcg group was excluded because her tablets could not be located, and one woman in the 400 mcg group was excluded because of an emergency caesarean section.
Allocation concealment	A – Adequate

Study	**WHO 2001**
Methods	Random allocation sequence, generated centrally. Sequentially-numbered, identical treatment packs drawn from a treatment pack dispenser. Double blinding achieved by use of double placebos.
Participants	18,530 women expecting vaginal delivery in 9 countries. Countries were Argentina, China, Egypt, Ireland, Nigeria, South Africa, Switzerland, Thailand, and Vietnam. Exclusion criteria: pyrexia (> 38 degrees C) on admission to labour ward, severe asthma, bleeding disorders, elective caesarean section, no consent.
Interventions	Misoprostol 600 mcg orally + placebo IV/IM, vs oxytocin 10 IU IV/IM + placebo tablets.
Outcomes	Blood loss, shivering, pyrexia, nausea, vomiting, diarrhoea, need for transfusion, manual removal of placenta, exploration under general anaesthesia, hysterectomy, admission to ICU, maternal deaths. Measurement of blood loss: collected blood poured in standard measuring jar. Small gauze swabs soaked with blood put into measuring jar and included in measurement. Linen weighed in some centres.
Notes	Management of third stage: uterotonics, clamping and cutting of cord immediately after delivery, fundal or suprapubic pressure with cord traction after signs of placental separation. 50/9264 (0.54%) excluded after randomization in the misoprostol group, 37 because of an emergency caesarean section, and 13 for loss to follow up. 38/9226 (0.41%) excluded after randomization in the oxytocin group, 34 for emergency caesarean section and 4 lost to follow up.
Allocation concealment	A – Adequate

Study	**Zimbabwe 2001**
Methods	Random allocation sequence generated by computer, allocation by numbered, sealed, opaque envelopes. Placebos used but were not identical. It is not mentioned whether outcome assessments were blinded or not.
Participants	500 low-risk women delivering at Harare Maternity Hospital, Zimbabwe were included. Women with a history of PPH, disseminated intravascular coagulation, antepartum haemorrhage, coagulation disorders, operative delivery, multiple pregnancy, history of asthma and known allergies to misoprostol or oxytocin were excluded.
Interventions	Misoprostol 400 mcg orally + 1 ml saline (placebo) vs oxytocin 10 IU IM + 2 placebo tablets.
Outcomes	Blood loss, side-effects. Measurement of blood loss: Blood volume in jug + weighing of soiled linen.
Notes	Management of the third stage not described. Exclusions after randomization: one women excluded because of undiagnosed twin delivery.
Allocation concealment	A – Adequate

* (15(S) 15 methyl PGF2alpha)
** Synthetic PGE2 derivative (16-phenoxy-17,18,19,20-tetranor-PGE2-methylsulphonamide)
ANM: auxiliary nurse midwives
Hgb: haemoglobin
ICU: intensive care unit
IM: intramuscular(ly)
IU: international unit(s)
IV: intravenous(ly)
PPH: postpartum haemorrhage
vs: versus

Characteristics of excluded studies

Study	Reason for exclusion
Austria 1983	No clinically relevant outcomes reported. Healthy women delivering at term who had a normal duration of labour (< 12 hours) and without the use of oxytocics before delivery were recruited. Immediately following the separation of the placenta, a twin catheter was introduced into the cavity for intrauterine pressure measurement which was recorded on the cardiotocograph. The women were randomized to receive methergin (methylergometrine) 0.2 mg, or oxytocin 2 IU, or sulprostone 0.5 mg or saline, all administered intramuscularly. Sulprostone had the quickest onset of action and strongest increase in uterine contractility whereas methergin had the longest duration of action on uterine contractility.
Canada 2004	Not a randomized controlled trial. A nested study within a randomised controlled trial to look at peripheral blood flow and temperature changes in women receiving misoprostol or oxytocin.
China 1997	This trial was reported as randomized but no details of the method of randomization were given. The two study groups were not balanced (260 versus 100), and they were further randomized into subgroups.
China 1998	Randomized controlled trial of misoprostol versus oxytocin in caesarean section deliveries only. Data are not presented in a form that can be extracted for the meta-analysis.
China 1998b	This trial randomized 80 women to 1 mg carboprost methylate intravaginally versus sublingually vs ergometrine IV. The data were not in a form suitable for extraction for this meta-analysis.
China 2001	This trial randomized 348 women into 4 groups of misoprostol 200, 400, and 600 micrograms orally, and oxytocin 20 units intramuscularly. Data were presented only in means, and were not presented in a form suitable for extraction and inclusion in this meta-analysis.
China 2004b	Randomized, double blind trial of 298 low-risk women delivering vaginally in Hong Kong, China. Oral misoprostol vs IV oxytocin. The trial is excluded because the number of women in each group are not described and the report is available as an abstract. The authors have not responded to the request for additional information and clarification. There was no statistically significant difference in blood loss > 500 and 1000 ml. Additional oxytocics were used in 25.2 vs 7.5% in the misoprostol and oxytocin groups respectively.
China 2004c	Data are not in a usable format. RCT comparing misoprostol 400 mcg + syntometrine vs syntometrine. The author contacted but no response.
Egypt 1999	140 women were allocated to receive either 2 different doses of rectal misoprostol or 5 units of oxytocin and 0.2 mg ergometrine intramuscularly. There is no indication of any randomized comparison between the groups.
Hungary 1979	The reason for exclusion is that the data are not presented in a usable form. The study is a randomized comparison of 1 mg intramyometrial prostaglandin F2alpha (47 women), 0.2 mg intravenous ergometrine (50) and no treatment (43). Prostaglandin F2alpha reduced the blood loss in the third stage of labour significantly when compared with ergometrine and no treatment.
India 1988a	60 women were allocated to 125 microgram PGF2alpha intramuscularly or no uterotonic. There is no indication of any randomized comparison between the 2 groups.
India 1988b	Multicentre study carried out in 4 centres. Of these, 2 employed a random allocation scheme and 2 used a sequential scheme. The reason for exclusion is that the results are presented together and it is not possible to extract data for those utilising random allocation.
India 2000a	There are no data that can be extracted to evaluate the validity of the methods used and the outcome data in this study from the conference abstract. When the study is published in full it will be evaluated again.
India 2000b	There are no data that can be extracted to evaluate the validity of the methods used and the outcome data in this study from the conference abstract. When the study is published in full it will be evaluated again.

India 2000c	There are no data that can be extracted to evaluate the validity of the methods used and the outcome data in this study from the conference abstract. When the study is published in full it will be evaluated again.
India 2001a	This study is reported as randomized double blind but there is no mention of placebos. There is also a discrepancy in the results between the text and the tables. 200 women were assigned either misoprostol orally 400 mcg or methylergometrine.
India 2005b	The study is reported as a RCT comparing carboprost with methylergometrine but the results are analysed by risk subgroups only and they are imbalanced between the two random allocation groups.
India 2006e	This is a randomized trial (cluster) of an educational intervention to implement active management of the third stage of labour using misoprostol. The control group received standard practice which was 'no special training' and no use of misoprostol.
Indonesia 2002	Data to evaluate the validity of the methods used are not available in this published abstract. When the study is published in full it will be evaluated again. This study involves 196 women undergoing full term vaginal delivery. 98 women were randomly allocated to 600 micrograms of oral misoprostol or 10 IU of oxytocin intramuscularly immediately after the baby was born. The length of the third stage of labour was 8.122 minutes for the misoprostol group and 8.388 minutes for the oxytocin group. Third stage blood loss for the misoprostol and oxytocin group was respectively 144.286 ml and 131.020 ml. Shivering occurred in 13.3% in the misoprostol group and 2.0% in the oxytocin group.
Israel 1992	This is a randomized controlled trial comparing intraumbilical PGF2alpha with saline injection. Although a prostaglandin was used for the management of the third stage of labour the mechanism of action may not be comparable to other routes of administration. This paper will be considered for inclusion in another review on the management of the third stage (intraumbilical uterotonics).
Italy 1988	Data from this trial were published in an abstract. It is excluded because no full publication of the trial data could be located.
Japan 1976	There does not seem to be a randomized comparison between study groups. 4 prostaglandin groups were studied: a. systemic: a.1. intramuscular (gluteal), a.2. continuous intravenous drip infusion, b. local: b.1. transabdominal intramyometrial injection, b.2. transvaginal intramyometrial injection. These groups were compared to ergot alkaloids. Number of participants are also not balanced (46 in prostaglandin vs 13 in ergot group).
Singapore 1990	The outcome examined in this trial was serum prostaglandin levels.
Singapore 2001	This trial has 57 women randomly assigned to receive oral misoprostol 200, 400, 500, 600, or 800 micrograms or ergometrine-oxytocin. Uterine activity was the main outcome, but side-effects were also reported. The data are incomplete and not in a suitable form for extraction.
South Africa 1999	Data from this trial were published in an abstract. It is excluded because no further publication of complete trial data was located. This trial evaluates treatment of primary postpartum haemorrhage.
Turkey 2005	Randomized, placebo-controlled trial comparing 400 mcg rectal vs 400 mcg vaginal misoprostol vs placebo after delivery of the placenta. Women with haemorrhage were excluded from the analysis after randomization. Authors contacted for clarification.
USA 1983	75 women were randomized to 3e groups of different doses of prostaglandin F2alpha (62.5, 125, 250 microgram intramuscularly). Then another 15 women were sequentially allocated to the same treatment groups, in groups of 5. The randomized and non-randomized groups have been reported together in the paper to increase the sample size. It is not possible to extract data on the randomized women alone.
USA 1999	Data from this trial were published in an abstract. It is excluded because no further publication of the completed trial data was located and the data presented in the abstract is incomplete.
United Kingdom 2001a	Randomized controlled trial of 400 mcg oral misoprostol versus 10 IU IV oxytocin. Primary outcome was 'intraoperative blood loss', which is not one of the outcomes for this review.

IU: international unit
IV: intravenous
vs: versus

Characteristics of excluded studies (*Continued*)

ANALYSES

Comparison 01. Any misoprostol versus no uterotonic/placebo (primary outcomes only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
02 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Totals not selected

Comparison 02. Oral misoprostol versus no uterotonic/placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	2	2849	Relative Risk (Fixed) 95% CI	1.46 [0.24, 8.81]
02 Maternal death or severe morbidity	2	2848	Relative Risk (Fixed) 95% CI	1.16 [0.36, 3.80]
03 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
04 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
05 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
06 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Totals not selected
07 Blood transfusion	5	3519	Relative Risk (Fixed) 95% CI	0.31 [0.10, 0.94]
08 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only
09 Duration of third stage (minutes)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
10 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
11 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
12 Nausea			Relative Risk (Fixed) 95% CI	Totals not selected
13 Vomiting			Relative Risk (Fixed) 95% CI	Totals not selected
14 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
15 Abdominal pain			Relative Risk (Fixed) 95% CI	Totals not selected
16 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
17 Any shivering			Relative Risk (Fixed) 95% CI	Totals not selected
18 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
19 Pyrexia (>= 38 degrees C)	5	3424	Relative Risk (Fixed) 95% CI	6.40 [4.47, 9.18]

Comparison 03. Oral misoprostol versus injectable uterotonics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	5	20199	Relative Risk (Fixed) 95% CI	1.00 [0.14, 7.10]
02 Severe postpartum haemorrhage (>= 1000 ml)	16	29042	Relative Risk (Fixed) 95% CI	1.32 [1.16, 1.51]
03 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
04 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
05 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Totals not selected
06 Blood transfusion	15	27858	Relative Risk (Fixed) 95% CI	0.81 [0.64, 1.02]
07 Postpartum haemoglobin	1	450	Weighted Mean Difference (Fixed) 95% CI	0.10 [-0.23, 0.43]
08 Haematocrit drop 10% or more	1	585	Relative Risk (Fixed) 95% CI	1.09 [0.47, 2.52]

09 Haemoglobin drop 30 mg/L or more	1	585	Relative Risk (Fixed) 95% CI	1.14 [0.69, 1.88]
10 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only
11 Duration of third stage (minutes)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
12 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
13 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
14 Nausea			Relative Risk (Fixed) 95% CI	Totals not selected
15 Vomiting			Relative Risk (Fixed) 95% CI	Totals not selected
16 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
17 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
18 Any shivering			Relative Risk (Fixed) 95% CI	Totals not selected
19 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
20 Pyrexia (>= 38 degrees C)			Relative Risk (Fixed) 95% CI	Totals not selected

Comparison 04. Rectal misoprostol versus no uterotonic/placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	0	0	Relative Risk (Fixed) 95% CI	Not estimable
02 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
03 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
05 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Subtotals only
06 Blood transfusion			Relative Risk (Fixed) 95% CI	Subtotals only
07 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only
08 Duration of third stage (minutes)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
09 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
10 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
11 Nausea			Relative Risk (Fixed) 95% CI	Subtotals only
12 Vomiting			Relative Risk (Fixed) 95% CI	Subtotals only
13 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
14 Abdominal pain			Relative Risk (Fixed) 95% CI	Subtotals only
15 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
16 Any shivering			Relative Risk (Fixed) 95% CI	Subtotals only
17 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
18 Pyrexia (>= 38 degrees C)			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 05. Rectal misoprostol versus injectable uterotonics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	1	803	Relative Risk (Fixed) 95% CI	Not estimable
02 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
03 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
05 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Subtotals only
06 Blood transfusion			Relative Risk (Fixed) 95% CI	Subtotals only

07 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only
08 Duration of third stage (minutes)	3	1941	Weighted Mean Difference (Fixed) 95% CI	0.25 [-0.08, 0.58]
09 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
10 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
11 Nausea			Relative Risk (Fixed) 95% CI	Subtotals only
12 Vomiting			Relative Risk (Fixed) 95% CI	Subtotals only
13 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
14 Abdominal pain			Relative Risk (Fixed) 95% CI	Subtotals only
15 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
16 Any shivering			Relative Risk (Fixed) 95% CI	Subtotals only
17 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
18 Pyrexia (>= 38 degrees C)			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 06. Rectal misoprostol versus intramuscular prostaglandin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	0	0	Relative Risk (Fixed) 95% CI	Not estimable
02 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
03 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
05 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Subtotals only
06 Blood transfusion			Relative Risk (Fixed) 95% CI	Subtotals only
07 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only
08 Duration of third stage (minutes)	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable
09 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
10 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
11 Nausea			Relative Risk (Fixed) 95% CI	Subtotals only
12 Vomiting			Relative Risk (Fixed) 95% CI	Subtotals only
13 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
14 Abdominal pain			Relative Risk (Fixed) 95% CI	Subtotals only
15 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
16 Any shivering			Relative Risk (Fixed) 95% CI	Subtotals only
17 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
18 Pyrexia (>= 38 degrees C)			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 07. Sublingual misoprostol versus no uterotonic/placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	1	661	Relative Risk (Fixed) 95% CI	3.01 [0.12, 73.60]
02 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
03 Postpartum haemorrhage (>= 500 ml)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Blood loss (ml)	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable
05 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Subtotals only
06 Blood transfusion			Relative Risk (Fixed) 95% CI	Subtotals only
07 Manual removal of placenta			Relative Risk (Fixed) 95% CI	Subtotals only

08 Duration of third stage (minutes)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
09 Third stage >= 30 minutes			Relative Risk (Fixed) 95% CI	Subtotals only
10 Any side-effect			Relative Risk (Fixed) 95% CI	Subtotals only
11 Nausea			Relative Risk (Fixed) 95% CI	Subtotals only
12 Vomiting			Relative Risk (Fixed) 95% CI	Subtotals only
13 Headache			Relative Risk (Fixed) 95% CI	Subtotals only
14 Abdominal pain	0	0	Relative Risk (Fixed) 95% CI	Not estimable
15 Diarrhoea			Relative Risk (Fixed) 95% CI	Subtotals only
16 Any shivering			Relative Risk (Fixed) 95% CI	Subtotals only
17 Severe shivering			Relative Risk (Fixed) 95% CI	Subtotals only
18 Pyrexia (>= 38 degrees C)	1	661	Relative Risk (Fixed) 95% CI	7.11 [3.85, 13.12]

Comparison 08. Sublingual misoprostol versus injectable uterotonic

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	0	0	Relative Risk (Fixed) 95% CI	Not estimable
02 Severe postpartum haemorrhage (>= 1000 ml)	3	270	Relative Risk (Fixed) 95% CI	0.54 [0.23, 1.27]
03 Postpartum haemorrhage (>= 500 ml)	4	330	Relative Risk (Fixed) 95% CI	1.07 [0.90, 1.27]
04 Blood loss (ml)			Weighted Mean Difference (Fixed) 95% CI	Totals not selected
05 Use of additional uterotonics	3	280	Relative Risk (Fixed) 95% CI	1.14 [0.69, 1.87]
06 Blood transfusion	1	120	Relative Risk (Fixed) 95% CI	Not estimable
07 Postpartum haemoglobin	1	100	Weighted Mean Difference (Fixed) 95% CI	-0.10 [-0.63, 0.43]
08 Manual removal of placenta	1	120	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.02]
09 Duration of third stage (minutes)	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable
10 Third stage >= 30 minutes	0	0	Relative Risk (Fixed) 95% CI	Not estimable
11 Any side-effect	0	0	Relative Risk (Fixed) 95% CI	Not estimable
12 Nausea	0	0	Relative Risk (Fixed) 95% CI	Not estimable
13 Vomiting	2	150	Relative Risk (Fixed) 95% CI	1.13 [0.45, 2.84]
14 Headache	1	100	Relative Risk (Fixed) 95% CI	0.75 [0.28, 2.00]
15 Abdominal pain	0	0	Relative Risk (Fixed) 95% CI	Not estimable
16 Diarrhoea	0	0	Relative Risk (Fixed) 95% CI	Not estimable
17 Any shivering	2	150	Relative Risk (Fixed) 95% CI	5.80 [1.58, 21.24]
18 Severe shivering	0	0	Relative Risk (Fixed) 95% CI	Not estimable
19 Pyrexia >= 38 degrees C	2	220	Relative Risk (Fixed) 95% CI	5.00 [1.33, 18.81]

Comparison 09. Intramuscular prostaglandin versus rectal misoprostol

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)	0	0	Relative Risk (Fixed) 95% CI	Not estimable
02 Postpartum haemorrhage (>= 500 ml)	1	120	Relative Risk (Fixed) 95% CI	0.75 [0.18, 3.21]
03 Blood loss (ml)	1	120	Weighted Mean Difference (Fixed) 95% CI	-40.00 [-99.66, 19.66]
04 Use of additional uterotonics	1	120	Relative Risk (Fixed) 95% CI	0.20 [0.05, 0.87]
05 Blood transfusion	1	120	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.02]
06 Any shivering	1	120	Relative Risk (Fixed) 95% CI	0.09 [0.01, 1.61]

07 Pyrexia >= 38 degrees C	0	0	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 10. Intramuscular prostaglandin versus no uterotonic/placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Postpartum haemorrhage (>= 500 ml)	1	46	Relative Risk (Fixed) 95% CI	0.55 [0.22, 1.35]
02 Severe postpartum haemorrhage (>= 1000 ml)	1	46	Relative Risk (Fixed) 95% CI	0.36 [0.04, 3.24]
03 Blood loss (ml)	1	46	Weighted Mean Difference (Fixed) 95% CI	-224.00 [-420.35, -27.65]
04 Use of additional uterotonics	1	46	Relative Risk (Fixed) 95% CI	0.22 [0.01, 4.29]
05 Blood transfusion	0	0	Relative Risk (Fixed) 95% CI	Not estimable
06 Manual removal of placenta	1	46	Relative Risk (Fixed) 95% CI	Not estimable
07 Duration of third stage (minutes)	1	46	Weighted Mean Difference (Fixed) 95% CI	-3.60 [-7.65, 0.45]
08 Third stage >= 30 minutes	0	0	Relative Risk (Fixed) 95% CI	Not estimable
09 Any side-effect	1	46	Relative Risk (Fixed) 95% CI	0.36 [0.02, 8.46]
10 Nausea	1	46	Relative Risk (Fixed) 95% CI	0.36 [0.02, 8.46]
11 Vomiting	0	0	Relative Risk (Fixed) 95% CI	Not estimable
12 Headache	0	0	Relative Risk (Fixed) 95% CI	Not estimable
13 Abdominal pain	0	0	Relative Risk (Fixed) 95% CI	Not estimable
14 Diarrhoea	0	0	Relative Risk (Fixed) 95% CI	Not estimable
15 Shivering	0	0	Relative Risk (Fixed) 95% CI	Not estimable
16 Pyrexia (>= 38 degrees C)	0	0	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 11. Intramuscular prostaglandin versus injectable uterotonics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Postpartum haemorrhage (>= 500 ml)	4	349	Relative Risk (Fixed) 95% CI	0.99 [0.64, 1.55]
02 Severe postpartum haemorrhage (>= 1000 ml)	2	119	Relative Risk (Fixed) 95% CI	0.41 [0.14, 1.20]
03 Blood loss (ml)	5	417	Weighted Mean Difference (Fixed) 95% CI	-45.14 [-54.18, -36.11]
04 Use of additional uterotonics	3	222	Relative Risk (Fixed) 95% CI	2.05 [0.39, 10.92]
05 Blood transfusion	2	129	Relative Risk (Fixed) 95% CI	1.05 [0.39, 2.86]
06 Manual removal of placenta	3	231	Relative Risk (Fixed) 95% CI	1.09 [0.31, 3.81]
07 Duration of third stage (minutes)	4	357	Weighted Mean Difference (Fixed) 95% CI	-1.16 [-1.43, -0.89]
08 Third stage >= 30 minutes	0	0	Relative Risk (Fixed) 95% CI	Not estimable
09 Any side-effect	1	50	Relative Risk (Fixed) 95% CI	Not estimable
10 Nausea	3	280	Relative Risk (Fixed) 95% CI	2.39 [0.36, 16.09]
11 Vomiting	2	210	Relative Risk (Fixed) 95% CI	10.74 [2.06, 56.02]
12 Headache	1	80	Relative Risk (Fixed) 95% CI	2.00 [0.39, 10.31]
13 Abdominal pain	3	331	Relative Risk (Fixed) 95% CI	4.99 [1.46, 17.05]
14 Diarrhoea	4	402	Relative Risk (Fixed) 95% CI	7.86 [2.64, 23.46]
15 Shivering	0	0	Relative Risk (Fixed) 95% CI	Not estimable
16 Pyrexia (>= 38 degrees C)	1	112	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 12. Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Postpartum haemorrhage (>= 500 ml)	1	397	Relative Risk (Fixed) 95% CI	0.88 [0.62, 1.24]
02 Severe postpartum haemorrhage (>= 1000 ml)	2	797	Relative Risk (Fixed) 95% CI	0.83 [0.50, 1.39]
03 Blood loss (ml)	1	397	Weighted Mean Difference (Fixed) 95% CI	-30.00 [-91.27, 31.27]
04 Use of additional uterotonics	2	797	Relative Risk (Fixed) 95% CI	0.98 [0.68, 1.41]
05 Blood transfusion	2	797	Relative Risk (Fixed) 95% CI	Not estimable
06 Manual removal of placenta	2	797	Relative Risk (Fixed) 95% CI	1.22 [0.35, 4.20]
07 Duration of third stage (minutes)	1	397	Weighted Mean Difference (Fixed) 95% CI	-2.20 [-4.42, 0.02]
08 Third stage >= 30 minutes	1	400	Relative Risk (Fixed) 95% CI	3.00 [0.31, 28.60]
09 Any side-effect	0	0	Relative Risk (Fixed) 95% CI	Not estimable
10 Nausea	2	792	Relative Risk (Fixed) 95% CI	1.65 [0.22, 12.48]
11 Vomiting	2	792	Relative Risk (Fixed) 95% CI	1.00 [0.06, 15.88]
12 Headache	1	398	Relative Risk (Fixed) 95% CI	1.50 [0.25, 8.88]
13 Abdominal pain	1	398	Relative Risk (Fixed) 95% CI	1.50 [0.63, 3.59]
14 Diarrhoea	1	397	Relative Risk (Fixed) 95% CI	8.96 [0.49, 165.23]
15 Shivering	2	795	Relative Risk (Fixed) 95% CI	1.33 [1.07, 1.64]
16 Pyrexia (>= 38 degrees C)	2	794	Relative Risk (Fixed) 95% CI	2.12 [1.44, 3.12]

Comparison 13. Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Manual removal of placenta	1	183	Relative Risk (Fixed) 95% CI	0.20 [0.01, 4.06]
02 Nausea	1	183	Relative Risk (Fixed) 95% CI	0.52 [0.27, 1.01]
03 Vomiting	1	183	Relative Risk (Fixed) 95% CI	0.79 [0.33, 1.91]
04 Headache	1	183	Relative Risk (Fixed) 95% CI	0.64 [0.29, 1.39]
05 Abdominal pain	1	183	Relative Risk (Fixed) 95% CI	0.86 [0.66, 1.12]
06 Diarrhoea	1	183	Relative Risk (Fixed) 95% CI	2.97 [0.12, 71.91]
07 Any shivering	1	183	Relative Risk (Fixed) 95% CI	1.02 [0.67, 1.56]
08 Severe shivering	1	183	Relative Risk (Fixed) 95% CI	0.77 [0.41, 1.45]
09 Pyrexia	1	183	Relative Risk (Fixed) 95% CI	0.33 [0.01, 7.99]

Comparison 14. Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Manual removal of placenta	1	184	Relative Risk (Fixed) 95% CI	0.33 [0.01, 8.08]
02 Nausea	1	184	Relative Risk (Fixed) 95% CI	0.55 [0.28, 1.08]
03 Vomiting	1	184	Relative Risk (Fixed) 95% CI	2.67 [0.73, 9.74]
04 Headache	1	184	Relative Risk (Fixed) 95% CI	1.50 [0.56, 4.04]
05 Abdominal pain	1	184	Relative Risk (Fixed) 95% CI	0.98 [0.74, 1.30]
06 Diarrhoea	1	184	Relative Risk (Fixed) 95% CI	3.00 [0.12, 72.70]
07 Any shivering	1	184	Relative Risk (Fixed) 95% CI	0.46 [0.33, 0.64]
08 Severe shivering	1	184	Relative Risk (Fixed) 95% CI	0.27 [0.16, 0.46]

09 Pyrexia	1	184	Relative Risk (Fixed) 95% CI	0.06 [0.00, 1.00]

Comparison 15. Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Manual removal of placenta	1	183	Relative Risk (Fixed) 95% CI	1.01 [0.06, 15.92]
02 Nausea	1	183	Relative Risk (Fixed) 95% CI	1.06 [0.62, 1.82]
03 Vomiting	1	183	Relative Risk (Fixed) 95% CI	3.37 [0.96, 11.85]
04 Headache	1	183	Relative Risk (Fixed) 95% CI	2.36 [0.95, 5.87]
05 Abdominal pain	1	183	Relative Risk (Fixed) 95% CI	1.14 [0.87, 1.49]
06 Diarrhoea	1	183	Relative Risk (Fixed) 95% CI	Not estimable
07 Any shivering	1	183	Relative Risk (Fixed) 95% CI	0.45 [0.32, 0.63]
08 Severe shivering	1	183	Relative Risk (Fixed) 95% CI	0.36 [0.23, 0.56]
09 Pyrexia	1	183	Relative Risk (Fixed) 95% CI	1.01 [0.06, 15.92]

Comparison 16. Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)	1	808	Relative Risk (Fixed) 95% CI	0.80 [0.37, 1.74]
02 Postpartum haemorrhage (>= 500 ml)	1	808	Relative Risk (Fixed) 95% CI	0.86 [0.53, 1.40]
03 Duration of third stage (minutes)	1	808	Weighted Mean Difference (Fixed) 95% CI	-0.10 [-0.46, 0.26]
04 Third stage >= 30 minutes	1	808	Relative Risk (Fixed) 95% CI	1.01 [0.14, 7.17]
05 Blood transfusion	1	808	Relative Risk (Fixed) 95% CI	0.31 [0.10, 0.95]
06 Vomiting	1	808	Relative Risk (Fixed) 95% CI	1.52 [0.26, 9.06]
07 Diarrhoea	1	808	Relative Risk (Fixed) 95% CI	1.01 [0.41, 2.53]
08 Any shivering	1	808	Relative Risk (Fixed) 95% CI	3.30 [1.92, 5.68]
09 Pyrexia (>= 38 degrees C)	1	808	Relative Risk (Fixed) 95% CI	3.21 [1.30, 7.96]

Comparison 17. Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)	1	797	Relative Risk (Fixed) 95% CI	0.64 [0.30, 1.35]
02 Postpartum haemorrhage (>= 500 ml)	1	797	Relative Risk (Fixed) 95% CI	0.71 [0.45, 1.13]
03 Duration of third stage (minutes)	1	797	Weighted Mean Difference (Fixed) 95% CI	-0.70 [-1.21, -0.19]
04 Third stage >= 30 minutes	1	797	Relative Risk (Fixed) 95% CI	0.16 [0.04, 0.73]
05 Blood transfusion	1	797	Relative Risk (Fixed) 95% CI	0.33 [0.11, 1.01]
06 Vomiting	1	797	Relative Risk (Fixed) 95% CI	1.48 [0.25, 8.82]
07 Diarrhoea	1	797	Relative Risk (Fixed) 95% CI	0.81 [0.34, 1.93]
08 Any shivering	1	797	Relative Risk (Fixed) 95% CI	1.09 [0.76, 1.58]
09 Pyrexia (>= 38 degrees C)	1	797	Relative Risk (Fixed) 95% CI	1.17 [0.61, 2.25]
10 Maternal death	1	797	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 18. Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)	1	788	Relative Risk (Fixed) 95% CI	0.38 [0.15, 0.97]
02 Postpartum haemorrhage (>= 500 ml)	1	788	Relative Risk (Fixed) 95% CI	0.44 [0.23, 0.84]
03 Blood loss (ml)	1	788	Weighted Mean Difference (Fixed) 95% CI	-32.00 [-55.00, -7.00]
04 Duration of third stage (mins)	1	788	Weighted Mean Difference (Fixed) 95% CI	0.10 [-0.31, 0.51]
05 Third stage >= 30 minutes	1	788	Relative Risk (Fixed) 95% CI	1.43 [0.24, 8.49]
06 Blood transfusion	1	788	Relative Risk (Fixed) 95% CI	0.37 [0.13, 1.02]
07 Vomiting	1	788	Relative Risk (Fixed) 95% CI	0.95 [0.19, 4.68]
08 Diarrhoea	1	788	Relative Risk (Fixed) 95% CI	1.03 [0.48, 2.23]
09 Any shivering	1	788	Relative Risk (Fixed) 95% CI	2.45 [1.47, 4.09]
10 Pyrexia (>= 38 degrees C)	1	788	Relative Risk (Fixed) 95% CI	3.04 [1.13, 8.22]

Comparison 19. Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)	1	792	Relative Risk (Fixed) 95% CI	0.41 [0.16, 1.06]
02 Postpartum haemorrhage (>= 1000 ml)	1	792	Relative Risk (Fixed) 95% CI	0.36 [0.19, 0.66]
03 Blood loss (ml)	1	792	Weighted Mean Difference (Fixed) 95% CI	-48.00 [-71.32, -24.68]
04 Duration of third stage (mins)	1	413	Weighted Mean Difference (Fixed) 95% CI	6.80 [4.81, 8.79]
05 Third stage >= 30 minutes	1	792	Relative Risk (Fixed) 95% CI	0.96 [0.20, 4.73]
06 Blood transfusion	1	792	Relative Risk (Fixed) 95% CI	0.34 [0.12, 0.94]
07 Vomiting	1	792	Relative Risk (Fixed) 95% CI	0.72 [0.16, 3.20]
08 Diarrhoea	1	792	Relative Risk (Fixed) 95% CI	0.83 [0.40, 1.73]
09 Any shivering	1	792	Relative Risk (Fixed) 95% CI	1.07 [0.73, 1.57]
10 Pyrexia (>= 38 degrees C)	1	792	Relative Risk (Fixed) 95% CI	0.90 [0.46, 1.76]

Comparison 20. Buccal misoprostol versus no uterotonic/placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Severe postpartum haemorrhage (>= 1000 ml)			Relative Risk (Fixed) 95% CI	Totals not selected
02 Use of additional uterotonics			Relative Risk (Fixed) 95% CI	Totals not selected
03 Blood transfusion			Relative Risk (Fixed) 95% CI	Totals not selected
04 Blood loss (ml)	1	352	Weighted Mean Difference (Fixed) 95% CI	24.00 [-16.36, 64.36]

INDEX TERMS

Medical Subject Headings (MeSH)

Labor Stage, Third; Misoprostol [adverse effects; *therapeutic use]; Oxytocics [adverse effects; *therapeutic use]; Postpartum Hemorrhage [*prevention & control]; Prostaglandins [therapeutic use]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Prostaglandins for preventing postpartum haemorrhage
Authors	Gülmezoglu AM, Forna F, Villar J, Hofmeyr GJ
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What's New	May 2007 Search updated on 28 February 2007. The current update includes 14 new trials bringing the total to 46 trials. The review now includes more evidence on misoprostol compared to placebo at non-hospital, peripheral settings. The conclusions related to misoprostol comparison to conventional injectable uterotonics and that of intramuscular prostaglandins remain unchanged. Three papers from China (Fu 2003; Xu 2003; Yuan 2003) are included in the awaiting assessment section pending their translation. The statistics editor noticed some discrepancies in standard deviation figures of continuous data in some trials. In Switzerland 1999 the data were actually reported as standard error and this has been corrected. Continuous data from India 1988c, Nigeria 2003 and Ghana 2000 have ben excluded because they could not be reconciled by looking at the paper again.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Any misoprostol versus no uterotonic/placebo (primary outcomes only), Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 01 Any misoprostol versus no uterotonic/placebo (primary outcomes only)

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

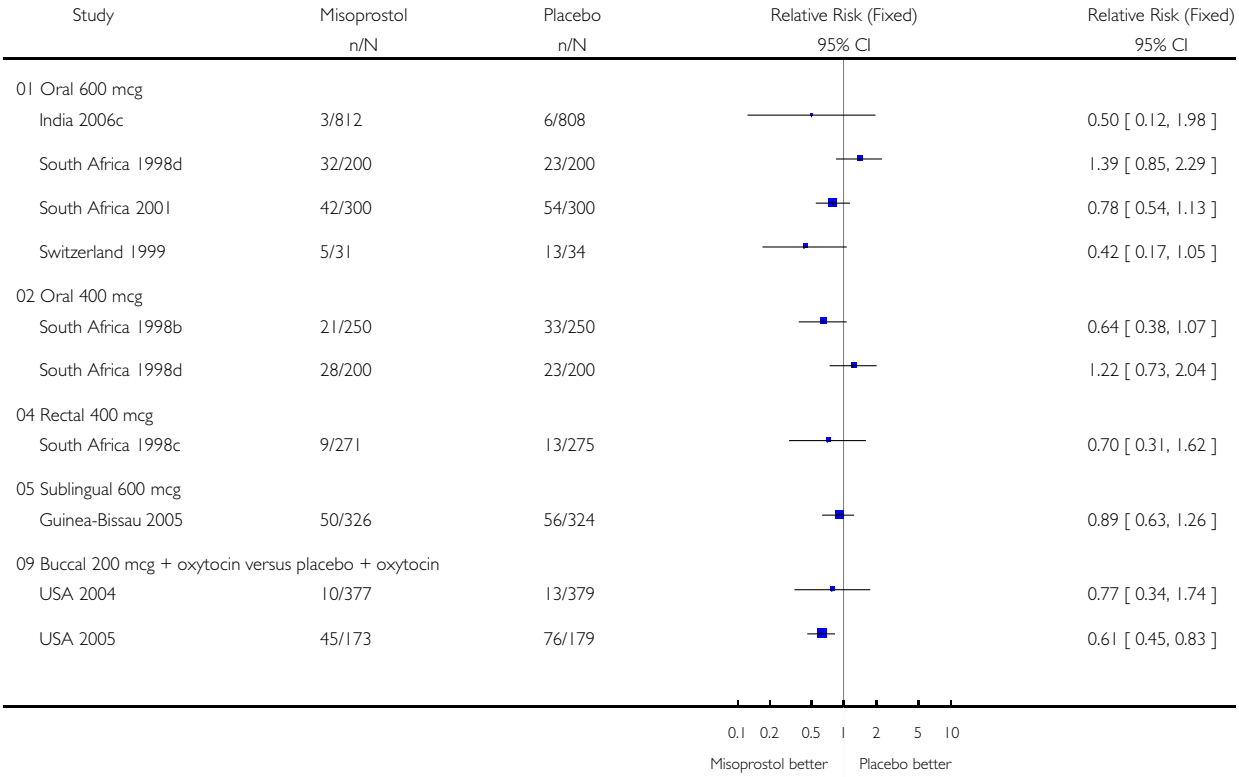
Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 Oral 600 mcg				
France 2001	16/186	13/220		1.46 [0.72, 2.95]
Gambia 2005	2/629	4/599		0.48 [0.09, 2.59]
India 2006c	2/812	10/808		0.20 [0.04, 0.91]
South Africa 1998d	17/200	6/200		2.83 [1.14, 7.04]
South Africa 2001	27/300	29/299		0.93 [0.56, 1.53]
02 Oral 400 mcg				
South Africa 1998b	15/250	23/250		0.65 [0.35, 1.22]
South Africa 1998d	16/200	6/200		2.67 [1.07, 6.68]
04 Rectal 400 mcg				
South Africa 1998c	13/270	19/272		0.69 [0.35, 1.37]
05 Sublingual 600 mcg				
Guinea-Bissau 2005	37/330	56/331		0.66 [0.45, 0.98]
07 Oral misoprostol 400 mcg + oxytocin versus oxytocin				
Turkey 2003	6/404	15/384		0.38 [0.15, 0.97]
08 Rectal misoprostol 400 mcg + oxytocin versus oxytocin				
Turkey 2002	11/401	14/407		0.80 [0.37, 1.74]

Analysis 01.02. Comparison 01 Any misoprostol versus no uterotonic/placebo (primary outcomes only), Outcome 02 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 01 Any misoprostol versus no uterotonic/placebo (primary outcomes only)

Outcome: 02 Use of additional uterotonics

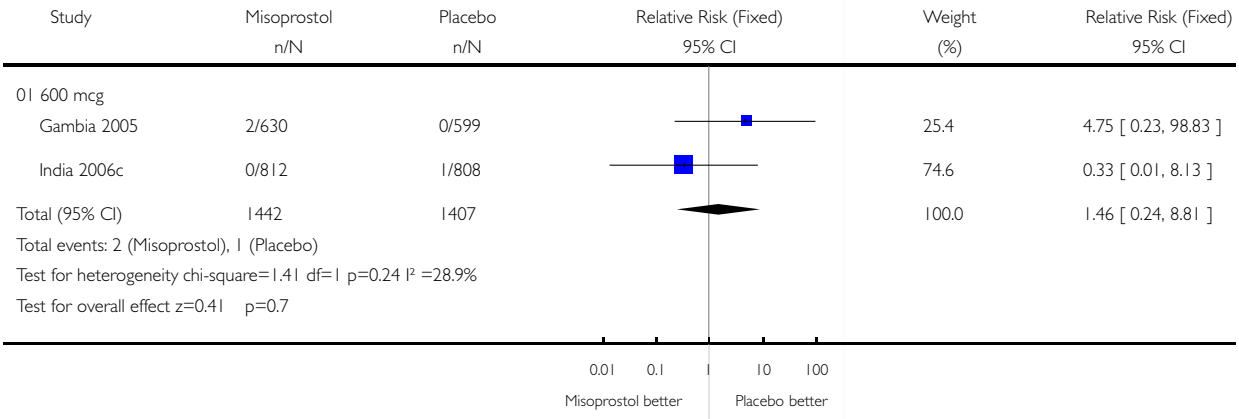


Analysis 02.01. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 01 Maternal death

Review: Prostaglandins for preventing postpartum haemorrhage

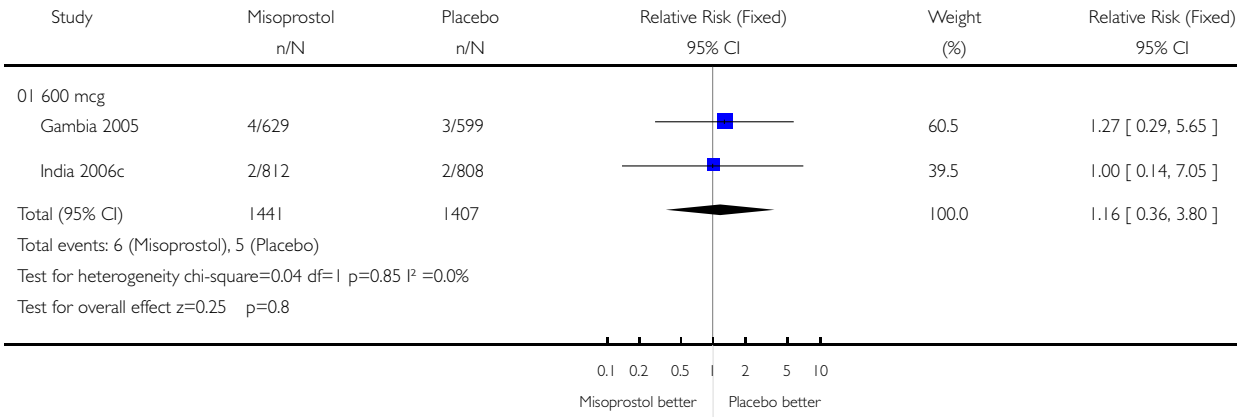
Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 01 Maternal death



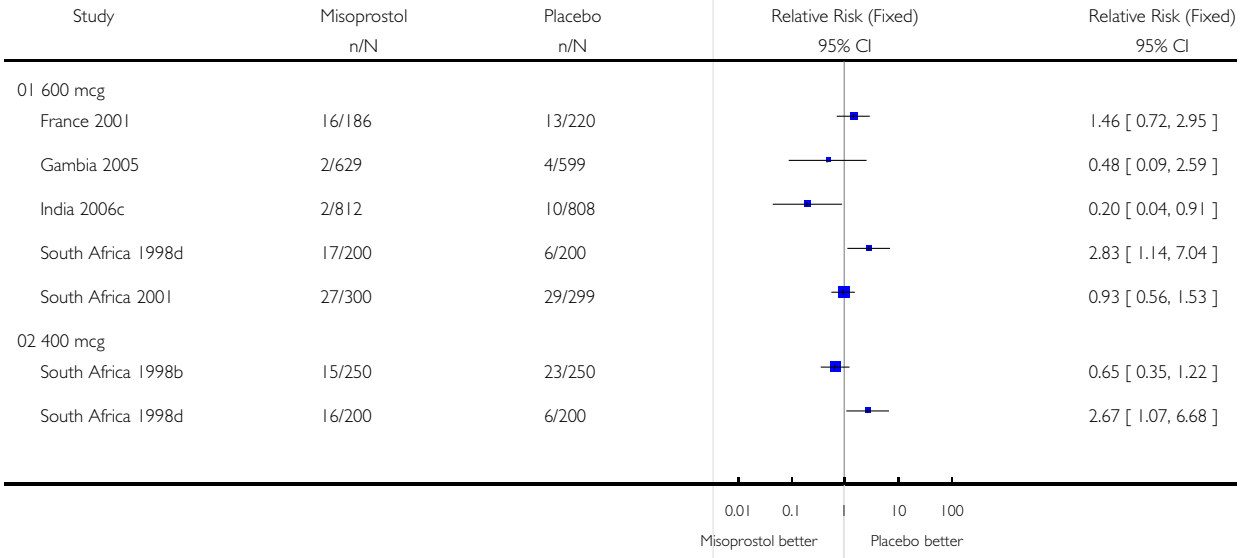
Analysis 02.02. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 02 Maternal death or severe morbidity

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 02 Oral misoprostol versus no uterotonic/placebo
Outcome: 02 Maternal death or severe morbidity



Analysis 02.03. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 03 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 02 Oral misoprostol versus no uterotonic/placebo
Outcome: 03 Severe postpartum haemorrhage (>= 1000 ml)

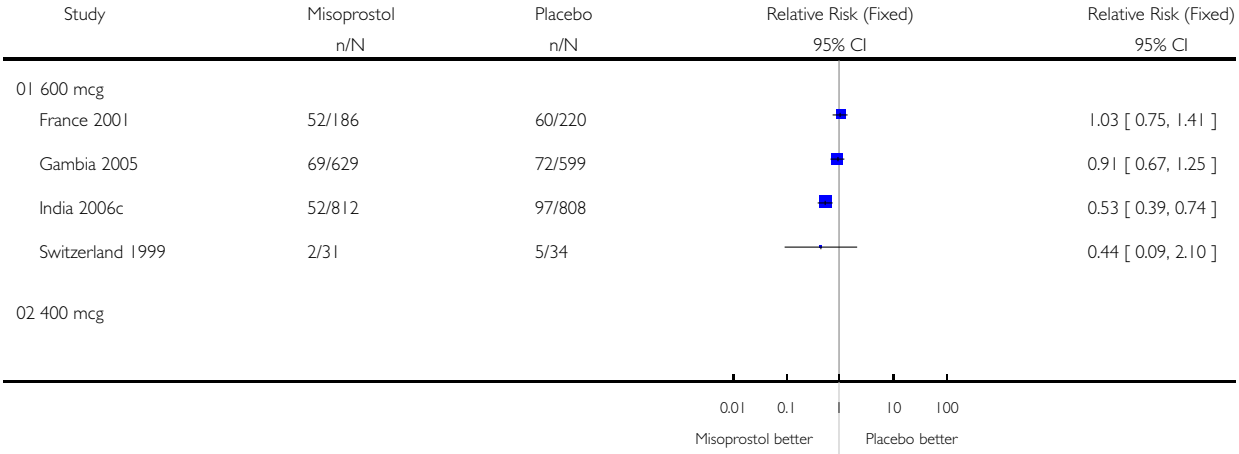


Analysis 02.04. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 04 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 04 Postpartum haemorrhage (>= 500 ml)

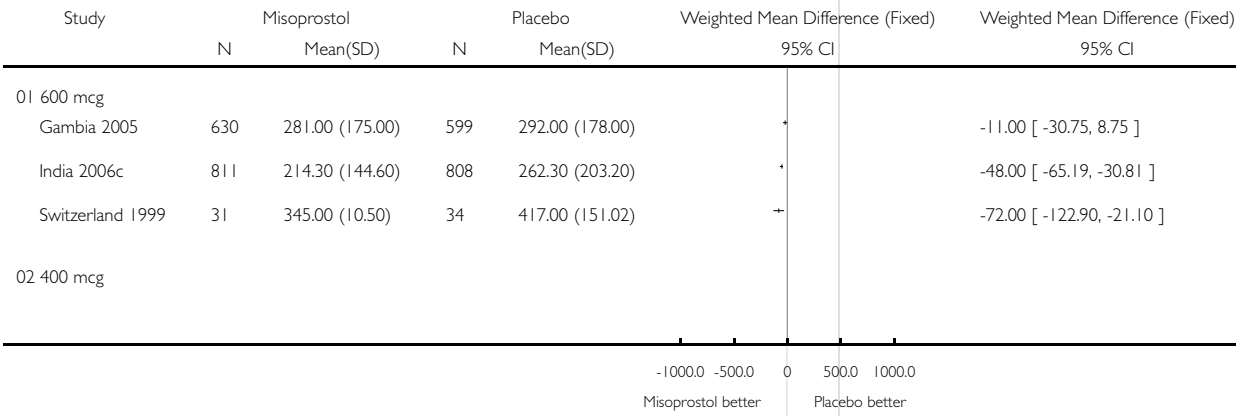


Analysis 02.05. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 05 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 05 Blood loss (ml)

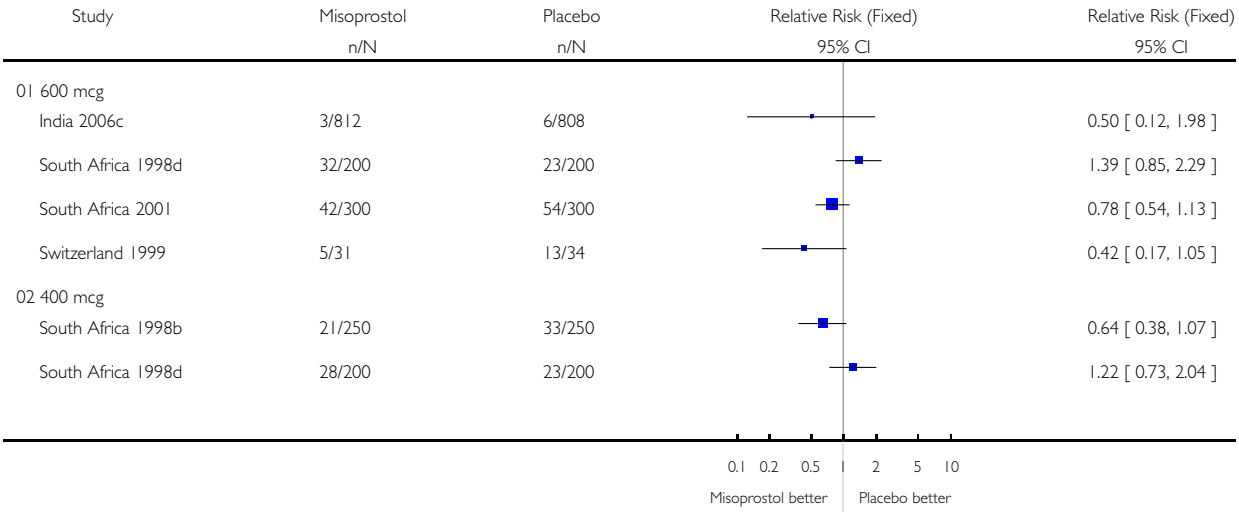


Analysis 02.06. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 06 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 06 Use of additional uterotonics

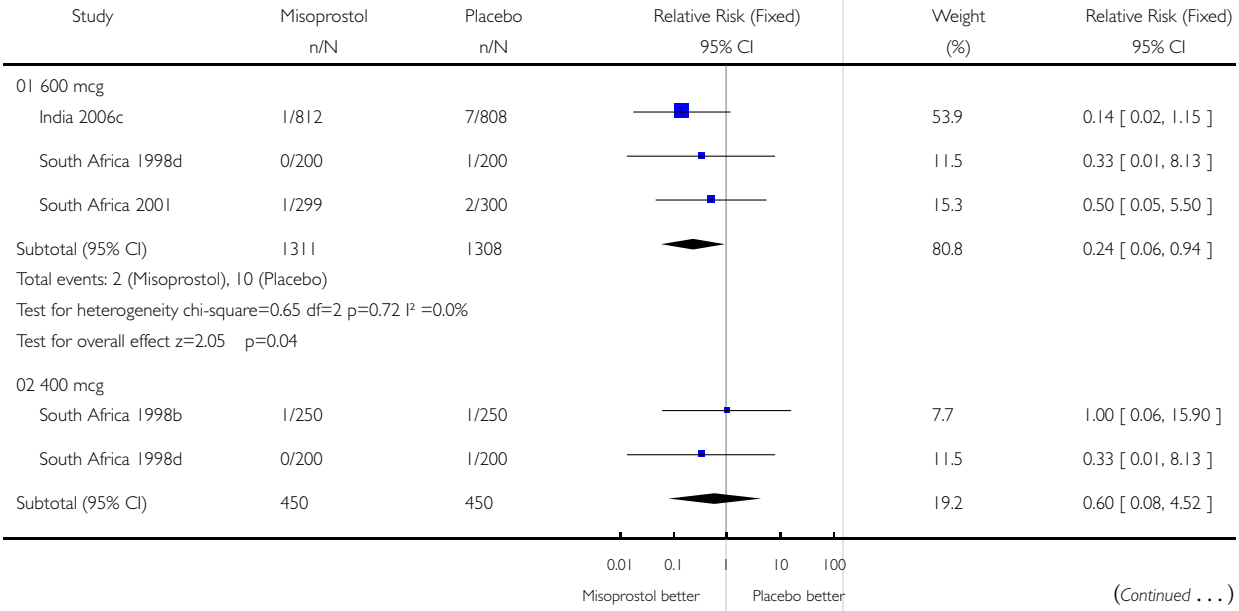


Analysis 02.07. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 07 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 07 Blood transfusion



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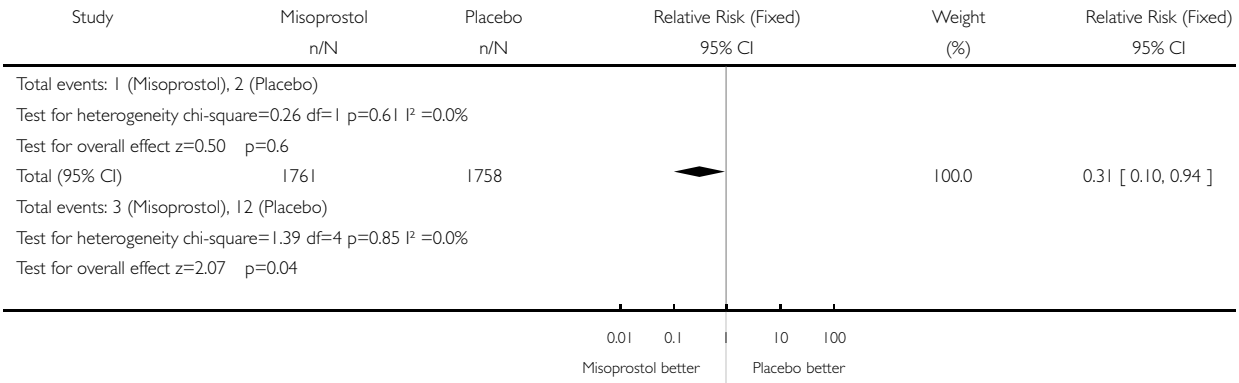
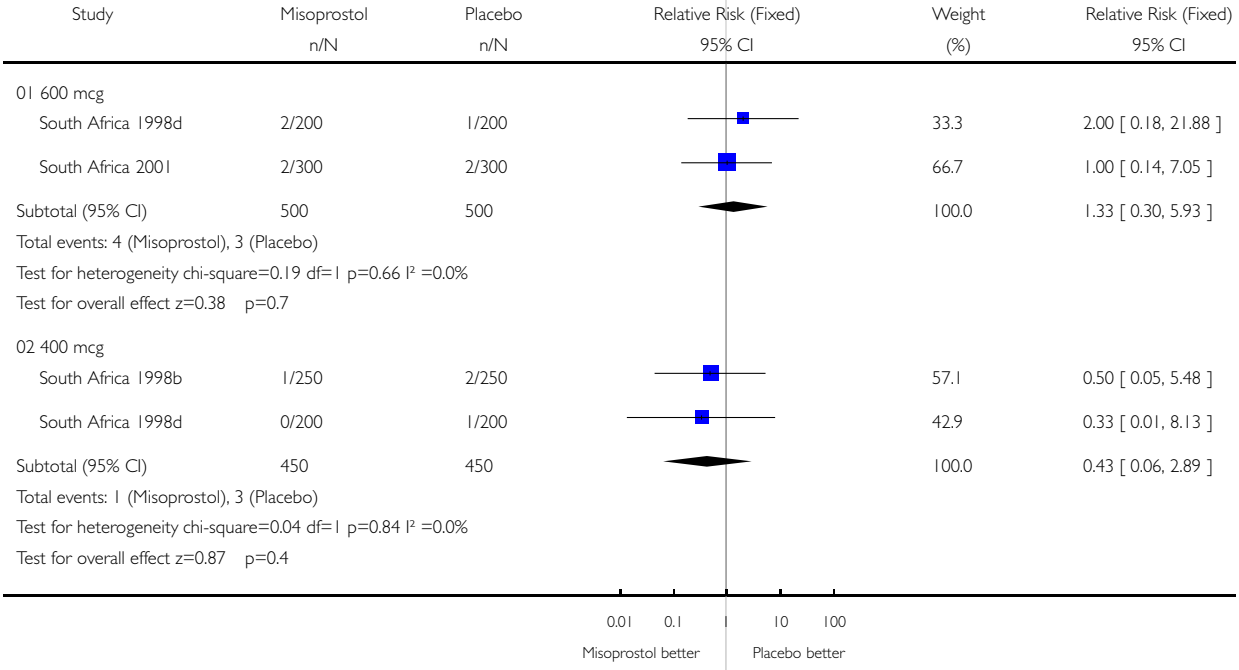


Analysis 02.08. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 08 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 08 Manual removal of placenta



Analysis 02.09. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 09 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 02 Oral misoprostol versus no uterotonic/placebo
Outcome: 09 Duration of third stage (minutes)

Study	Misoprostol N	Misoprostol Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg							
Switzerland 1999	31	8.00 (5.01)	34	9.00 (5.83)		100.0	-1.00 [-3.64, 1.64]
Subtotal (95% CI)	31		34			100.0	-1.00 [-3.64, 1.64]
Test for heterogeneity: not applicable							
Test for overall effect z=0.74 p=0.5							
02 400 mcg							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							

Analysis 02.10. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 10 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 02 Oral misoprostol versus no uterotonic/placebo
Outcome: 10 Third stage >= 30 minutes

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
South Africa 1998d	3/200	2/200		40.0	1.50 [0.25, 8.88]
South Africa 2001	6/299	3/300		60.0	2.01 [0.51, 7.95]
Subtotal (95% CI)	499	500		100.0	1.80 [0.61, 5.34]
Total events: 9 (Misoprostol), 5 (Placebo)					
Test for heterogeneity chi-square=0.06 df=1 p=0.80 I^2 =0.0%					
Test for overall effect z=1.06 p=0.3					
02 400 mcg					
South Africa 1998b	8/250	2/250		50.0	4.00 [0.86, 18.65]
South Africa 1998d	1/200	2/200		50.0	0.50 [0.05, 5.47]
Subtotal (95% CI)	450	450		100.0	2.25 [0.70, 7.26]
Total events: 9 (Misoprostol), 4 (Placebo)					
Test for heterogeneity chi-square=2.05 df=1 p=0.15 I^2 =51.3%					
Test for overall effect z=1.36 p=0.2					

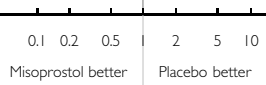
Analysis 02.11. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 11 Any side-effect

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 11 Any side-effect

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998b	54/250	26/250		100.0	2.08 [1.35, 3.20]
Subtotal (95% CI)	250	250		100.0	2.08 [1.35, 3.20]
Total events: 54 (Misoprostol), 26 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.30 p=0.001					



Analysis 02.12. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 12 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 12 Nausea

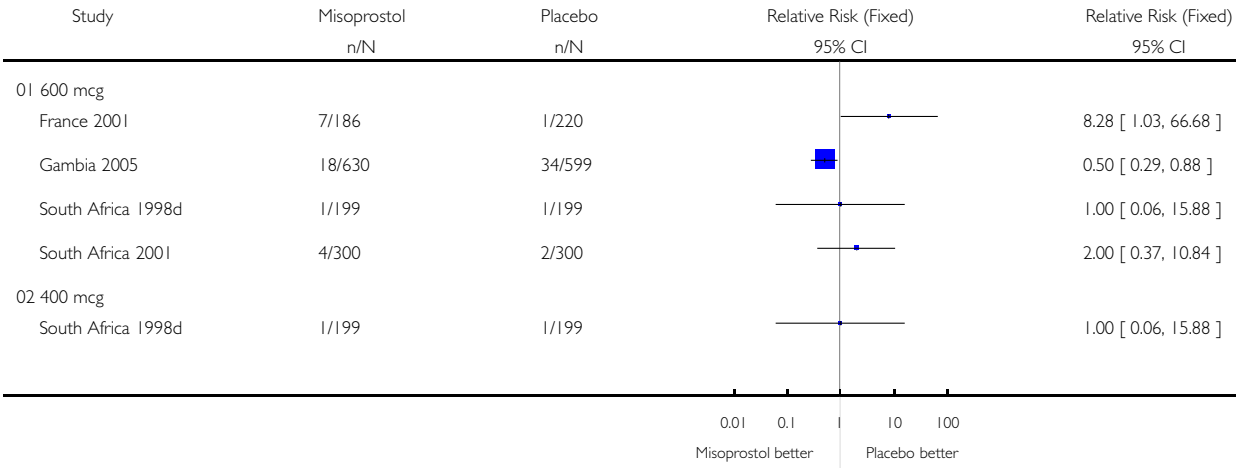
Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 600 mcg				
Gambia 2005	6/630	14/599		0.41 [0.16, 1.05]
South Africa 1998d	1/199	0/199		3.00 [0.12, 73.20]
South Africa 2001	5/300	1/300		5.00 [0.59, 42.54]
02 400 mcg				
South Africa 1998d	1/199	0/199		3.00 [0.12, 73.20]

Analysis 02.13. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 13 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 13 Vomiting

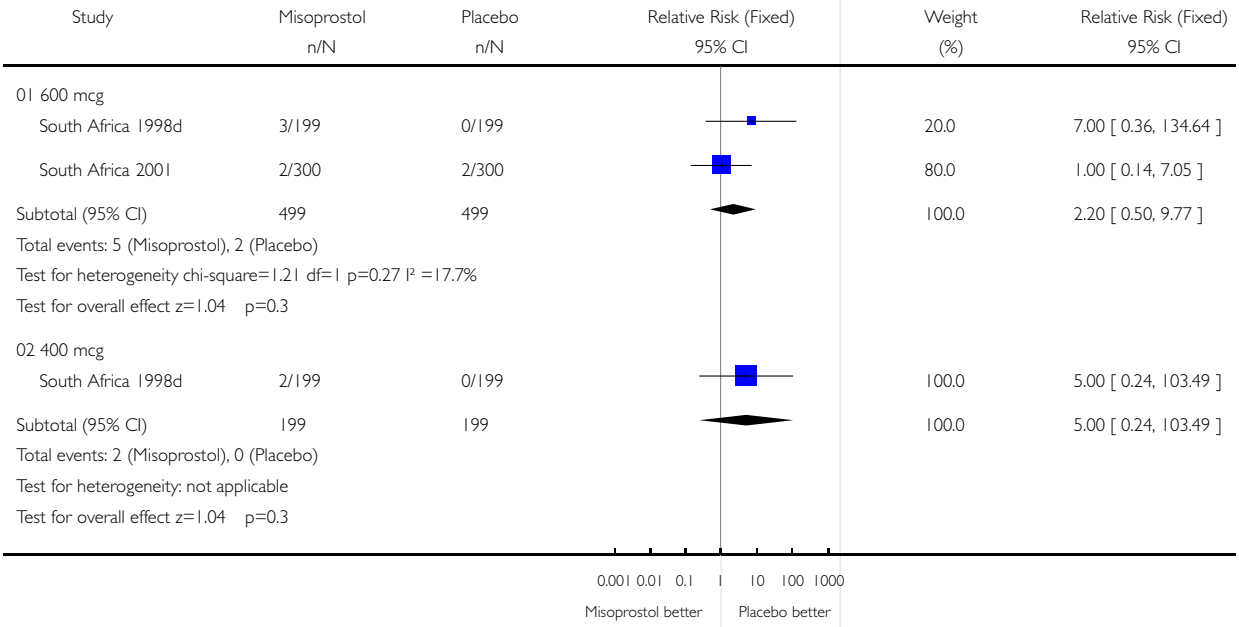


Analysis 02.14. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 14 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 14 Headache

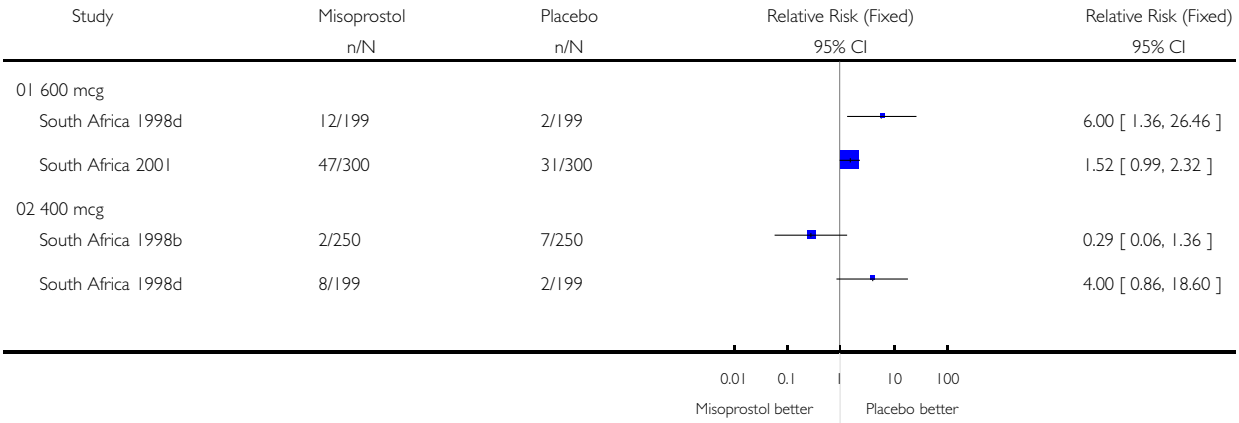


Analysis 02.15. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 15 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 15 Abdominal pain

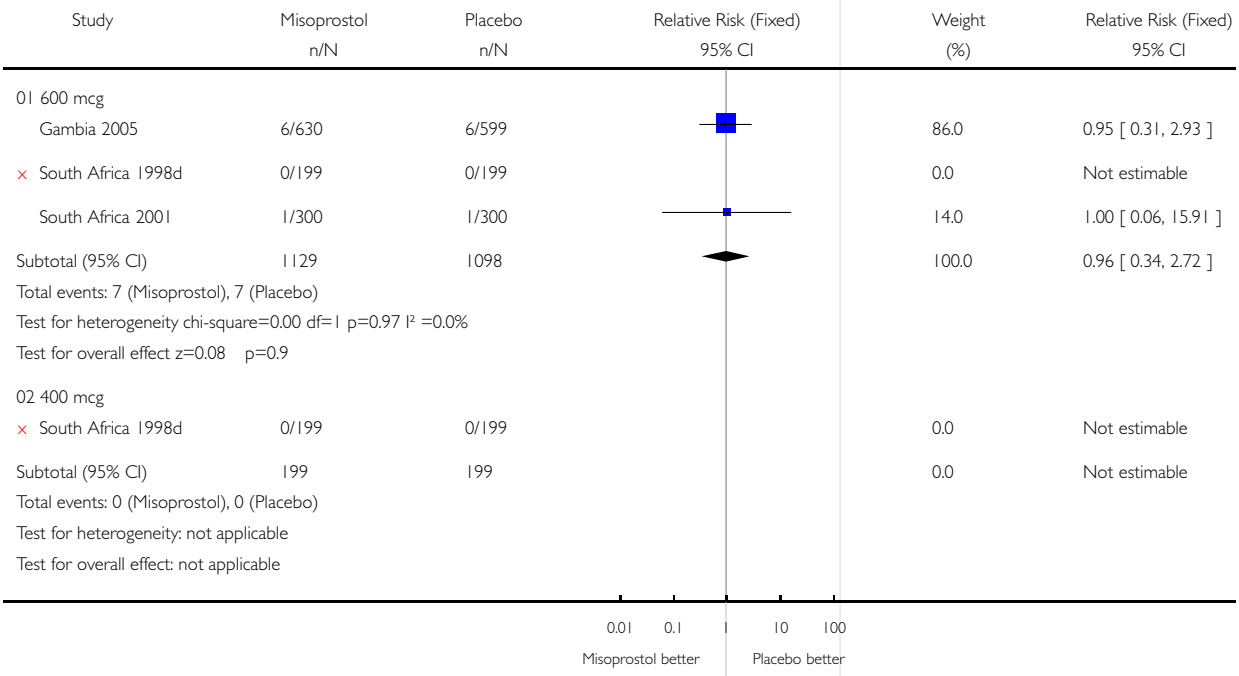


Analysis 02.16. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 16 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 16 Diarrhoea



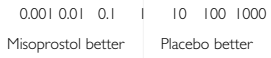
Analysis 02.17. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 17 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 17 Any shivering

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 600 mcg				
France 2001	5/186	0/220		13.00 [0.72, 233.56]
Gambia 2005	202/630	70/599		2.74 [2.14, 3.52]
India 2006c	424/812	140/808		3.01 [2.56, 3.55]
South Africa 1998d	81/199	30/199		2.70 [1.87, 3.91]
South Africa 2001	133/300	33/300		4.03 [2.85, 5.70]
Switzerland 1999	7/31	1/34		7.68 [1.00, 58.92]
02 400 mcg				
South Africa 1998b	48/250	13/250		3.69 [2.05, 6.64]
South Africa 1998d	65/199	30/199		2.17 [1.47, 3.19]



Analysis 02.19. Comparison 02 Oral misoprostol versus no uterotonic/placebo, Outcome 19 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 02 Oral misoprostol versus no uterotonic/placebo

Outcome: 19 Pyrexia (>= 38 degrees C)

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
France 2001	6/186	0/220		1.4	15.36 [0.87, 270.93]
India 2006c	34/812	9/808		27.8	3.76 [1.81, 7.79]
South Africa 1998d	53/200	5/200		15.4	10.60 [4.33, 25.96]
South Africa 2001	86/299	13/299		40.0	6.62 [3.78, 11.59]
Subtotal (95% CI)	1497	1527		84.6	6.55 [4.43, 9.67]
Total events: 179 (Misoprostol), 27 (Placebo)					
Test for heterogeneity chi-square=3.68 df=3 p=0.30 I^2 =18.5%					
Test for overall effect z=9.44 p<0.00001					

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Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
02 400 mcg					
South Africa 1998d	28/200	5/200		15.4	5.60 [2.21, 14.21]
Subtotal (95% CI)	200	200		15.4	5.60 [2.21, 14.21]
Total events: 28 (Misoprostol), 5 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.63 p=0.0003					
Total (95% CI)	1697	1727		100.0	6.40 [4.47, 9.18]
Total events: 207 (Misoprostol), 32 (Placebo)					
Test for heterogeneity chi-square=3.72 df=4 p=0.45 I^2 =0.0%					
Test for overall effect z=10.11 p<0.00001					

Analysis 03.01. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 01 Maternal death

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 01 Maternal death

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 800 mcg					
× Ghana 2006	0/225	0/225		0.0	Not estimable
Subtotal (95% CI)	225	225		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 600 mcg					
× WHO 1999	0/199	0/100		0.0	Not estimable
WHO 2001	2/9264	2/9266		100.0	1.00 [0.14, 7.10]
Subtotal (95% CI)	9463	9366		100.0	1.00 [0.14, 7.10]
Total events: 2 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					
03 400 mcg					
× Canada 2005	0/311	0/311		0.0	Not estimable
× WHO 1999	0/198	0/100		0.0	Not estimable

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Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Subtotal (95% CI)	509	411		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	10197	10002		100.0	1.00 [0.14, 7.10]
Total events: 2 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					

Analysis 03.02. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 800 mcg					
× Ghana 2006	0/225	0/225		0.0	Not estimable
Subtotal (95% CI)	225	225		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 600 mcg					
Belgium 1999	1/100	0/100		0.1	3.00 [0.12, 72.77]
France 2001	16/186	12/196		3.3	1.41 [0.68, 2.89]
Hong Kong 2001	5/1026	4/1032		1.1	1.26 [0.34, 4.67]
× Nigeria 2003	0/247	0/249		0.0	Not estimable
WHO 1999	8/199	13/200		3.6	0.62 [0.26, 1.46]
WHO 2001	366/9214	263/9228		73.2	1.39 [1.19, 1.63]
Subtotal (95% CI)	10972	11005		81.3	1.36 [1.17, 1.58]
Total events: 396 (Misoprostol), 292 (Inject. uterotonics)					
Test for heterogeneity chi-square=3.59 df=4 p=0.46 I^2 =0.0%					
Test for overall effect z=4.07 p=0.00005					

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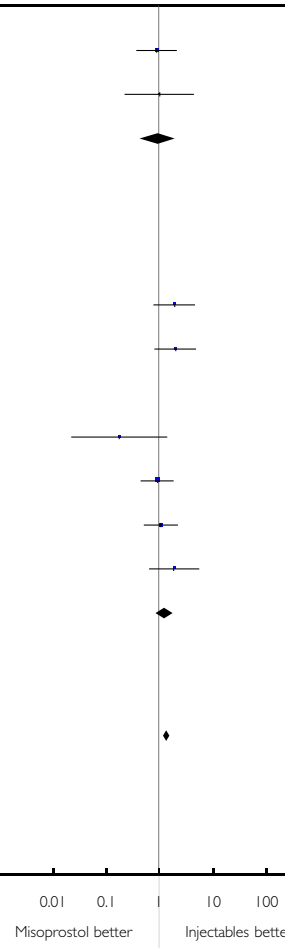
Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
03 500 mcg					
United Kingdom 2000	9/501	10/499		2.8	0.90 [0.37, 2.19]
United Kingdom 2001b	3/20	3/20		0.8	1.00 [0.23, 4.37]
Subtotal (95% CI)	521	519		3.6	0.92 [0.43, 1.98]
Total events: 12 (Misoprostol), 13 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.02 df=1 p=0.90 I^2 =0.0%					
Test for overall effect z=0.21 p=0.8					
04 400 mcg					
Australia 1999	13/424	7/439		1.9	1.92 [0.77, 4.77]
Canada 2005	14/311	7/311		2.0	2.00 [0.82, 4.89]
× Ghana 2000	0/202	0/196		0.0	Not estimable
India 2006b	1/730	10/1293		2.0	0.18 [0.02, 1.38]
Turkey 2003	14/388	15/384		4.2	0.92 [0.45, 1.89]
WHO 1999	14/198	13/200		3.6	1.09 [0.52, 2.25]
Zimbabwe 2001	9/243	5/256		1.4	1.90 [0.64, 5.58]
Subtotal (95% CI)	2496	3079		15.0	1.22 [0.85, 1.74]
Total events: 65 (Misoprostol), 57 (Inject. uterotonics)					
Test for heterogeneity chi-square=6.85 df=5 p=0.23 I^2 =27.0%					
Test for overall effect z=1.09 p=0.3					
Total (95% CI)	14214	14828		100.0	1.32 [1.16, 1.51]
Total events: 473 (Misoprostol), 362 (Inject. uterotonics)					
Test for heterogeneity chi-square=11.43 df=12 p=0.49 I^2 =0.0%					
Test for overall effect z=4.07 p=0.00005					



Analysis 03.03. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 03 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 03 Postpartum haemorrhage (>= 500 ml)

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 800 mcg				
Ghana 2006	0/225	5/225		0.09 [0.01, 1.63]
02 600 mcg				
Belgium 1999	8/96	4/93		1.94 [0.60, 6.22]
France 2001	52/186	29/196		1.89 [1.26, 2.84]
Hong Kong 2001	60/1026	44/1032		1.37 [0.94, 2.00]
India 2005a	8/100	6/100		1.33 [0.48, 3.70]
Nigeria 2003	3/247	1/249		3.02 [0.32, 28.88]
WHO 1999	45/199	52/200		0.87 [0.61, 1.23]
WHO 2001	1793/9213	1248/9227		1.44 [1.35, 1.54]
03 500 mcg				
United Kingdom 2000	62/501	56/499		1.10 [0.79, 1.55]
United Kingdom 2001b	17/20	17/20		1.00 [0.77, 1.30]
04 400 mcg				
Australia 1999	63/424	24/439		2.72 [1.73, 4.27]
Ghana 2000	0/202	2/196		0.19 [0.01, 4.02]
India 2006b	19/730	13/617		1.24 [0.62, 2.48]
Turkey 2003	35/388	28/384		1.24 [0.77, 1.99]
WHO 1999	51/198	52/200		0.99 [0.71, 1.38]
Zimbabwe 2001	37/243	34/256		1.15 [0.74, 1.76]

Analysis 03.04. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 04 Blood loss (ml)

Study	Misoprostol		Inject. uterotonics		Weighted Mean Difference (Fixed)	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	95% CI
01 600 mcg						
Hong Kong 2001	1026	296.00 (160.00)	1032	254.00 (157.00)		42.00 [28.30, 55.70]
WHO 1999	199	340.90 (295.08)	200	352.60 (309.59)		-11.70 [-71.04, 47.64]
WHO 2001	9213	332.80 (274.60)	9227	289.70 (262.10)		43.10 [35.35, 50.85]
02 400 mcg						
Australia 1999	424	279.00 (300.60)	439	209.00 (188.55)		70.00 [36.39, 103.61]
India 2006b	730	192.50 (131.00)	617	183.00 (130.00)		9.50 [-4.48, 23.48]
Turkey 2003	388	328.00 (152.00)	384	312.00 (176.00)		16.00 [-7.21, 39.21]
WHO 1999	100	370.90 (326.55)	99	352.60 (309.59)		18.30 [-70.10, 106.70]

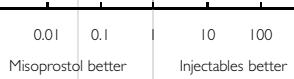
Analysis 03.05. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 05 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 05 Use of additional uterotonics

Study	Misoprostol	Inject. uterotonics	Relative Risk (Fixed)	Relative Risk (Fixed)
	n/N	n/N	95% CI	95% CI
01 800 mcg				
Ghana 2006	16/225	21/225		0.76 [0.41, 1.42]
02 600 mcg				
Belgium 1999	12/94	4/91		2.90 [0.97, 8.67]
Hong Kong 2001	232/1026	144/1032		1.62 [1.34, 1.96]
India 2005a	10/100	7/100		1.43 [0.57, 3.60]
Nigeria 2003	31/247	27/249		1.16 [0.71, 1.88]
WHO 1999	18/199	28/200		0.65 [0.37, 1.13]
WHO 2001	1398/9225	1002/9228		1.40 [1.29, 1.51]
03 500 mcg				



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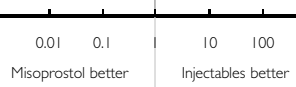
Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
United Kingdom 2000	68/501	50/499		1.35 [0.96, 1.91]
United Kingdom 2001b	6/20	1/20		6.00 [0.79, 45.42]
04 400 mcg				
Australia 1999	95/424	34/439		2.89 [2.00, 4.18]
Canada 2005	159/311	126/311		1.26 [1.06, 1.50]
Ghana 2000	6/168	8/172		0.77 [0.27, 2.17]
India 2006b	63/730	38/617		1.40 [0.95, 2.07]
WHO 1999	23/198	28/200		0.83 [0.50, 1.39]
Zimbabwe 2001	13/243	7/256		1.96 [0.79, 4.82]



Analysis 03.06. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 06 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 06 Blood transfusion

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 800 mcg					
Ghana 2006	1/222	2/221		1.3	0.50 [0.05, 5.45]
Subtotal (95% CI)	222	221		1.3	0.50 [0.05, 5.45]
Total events: 1 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					
02 600 mcg					
Belgium 1999	1/100	1/100		0.7	1.00 [0.06, 15.77]
Hong Kong 2001	15/1026	16/1032		10.7	0.94 [0.47, 1.90]
× Nigeria 2003	0/247	0/249		0.0	Not estimable
× WHO 1999	0/199	0/200		0.0	Not estimable
WHO 2001	72/9221	97/9226		64.8	0.74 [0.55, 1.01]
Subtotal (95% CI)	10793	10807		76.2	0.77 [0.59, 1.02]
Total events: 88 (Misoprostol), 114 (Inject. uterotonics)					

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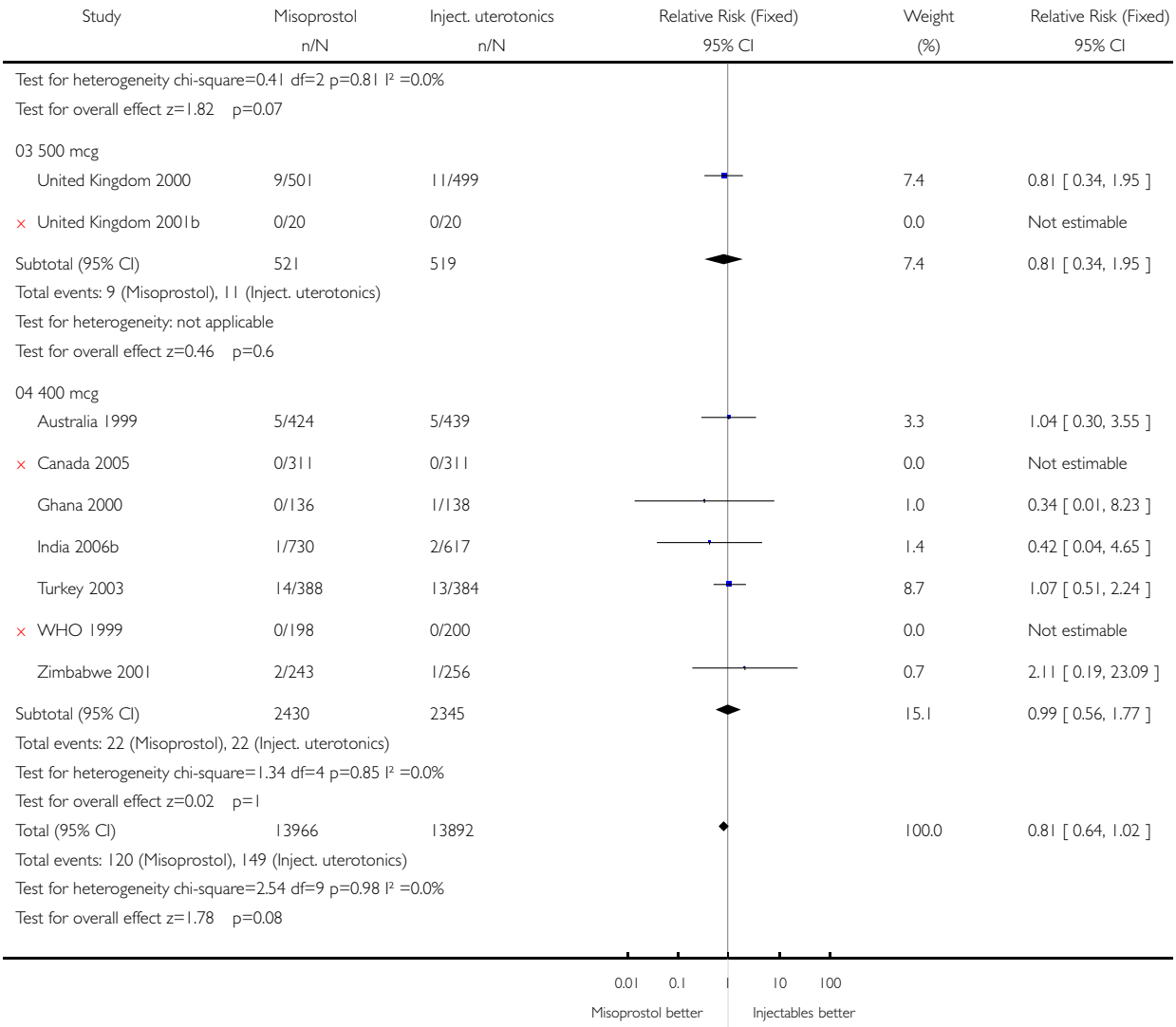
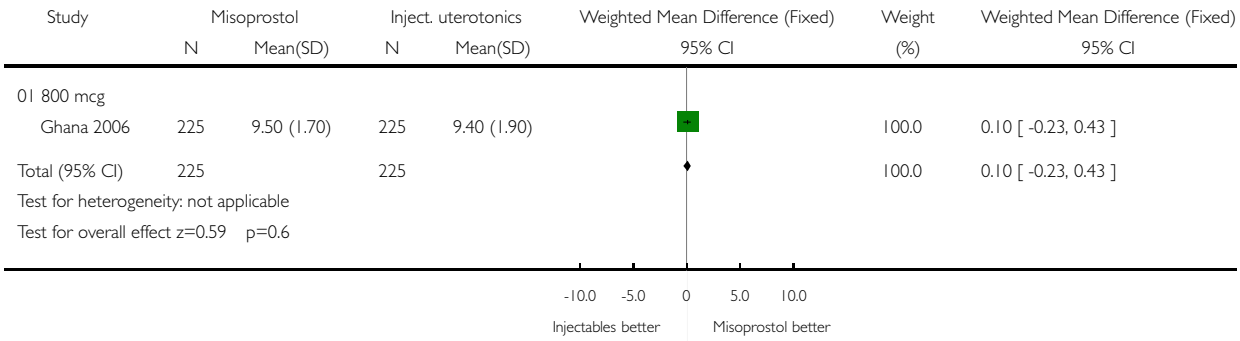


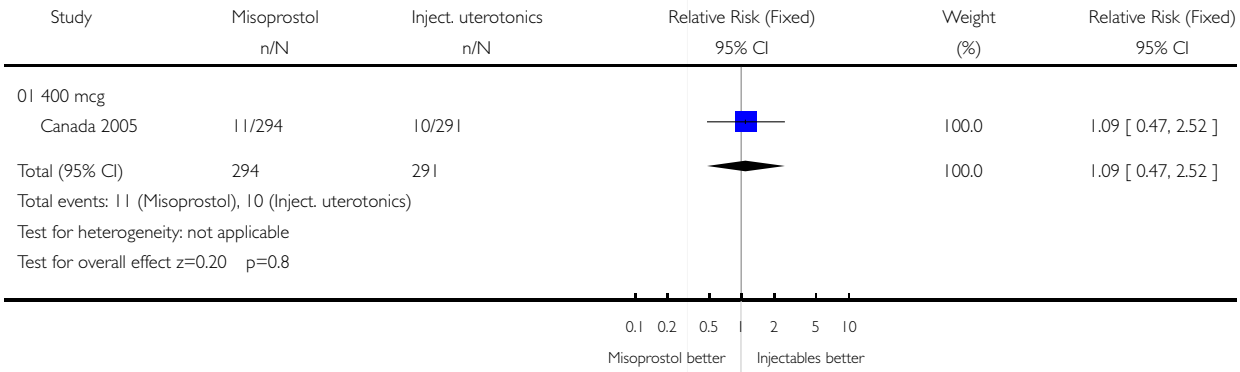
Analysis 03.07. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 07 Postpartum haemoglobin

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 03 Oral misoprostol versus injectable uterotonics
Outcome: 07 Postpartum haemoglobin



Analysis 03.08. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 08 Haematocrit drop 10% or more

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 03 Oral misoprostol versus injectable uterotonics
Outcome: 08 Haematocrit drop 10% or more

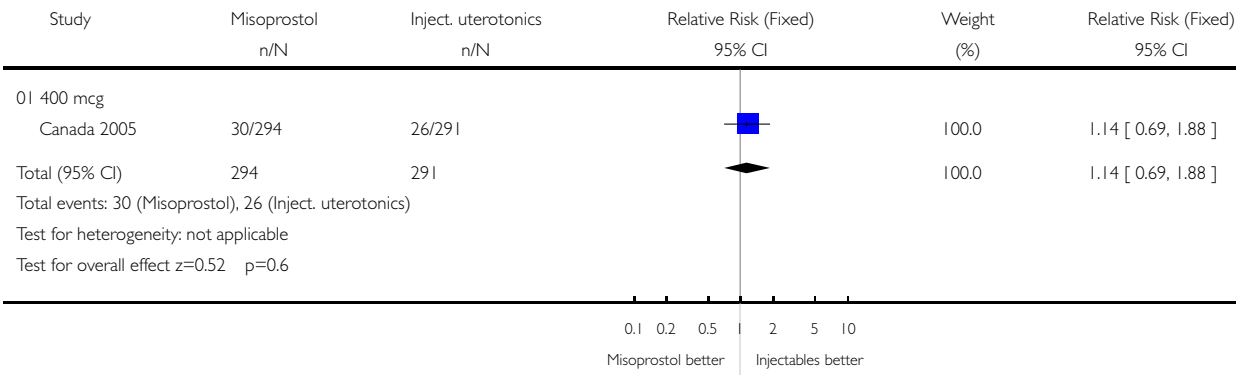


Analysis 03.09. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 09 Haemoglobin drop 30 mg/L or more

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 09 Haemoglobin drop 30 mg/L or more

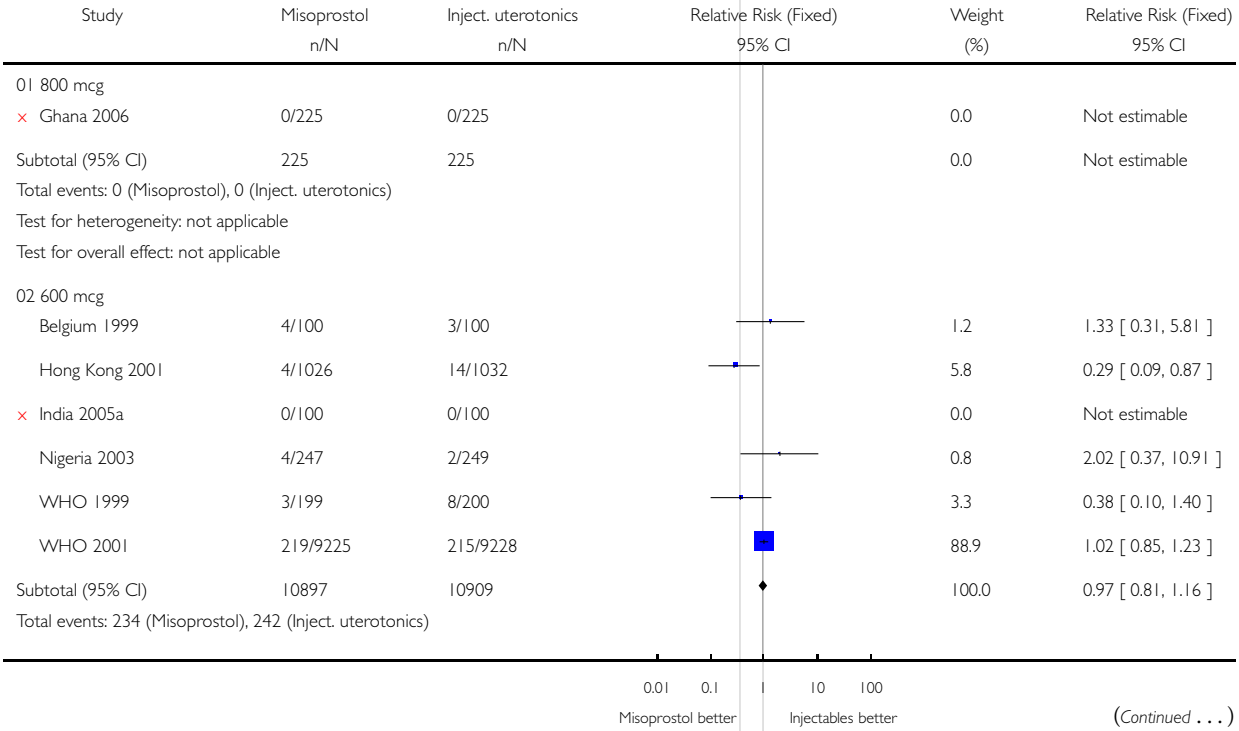


Analysis 03.10. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 10 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 10 Manual removal of placenta



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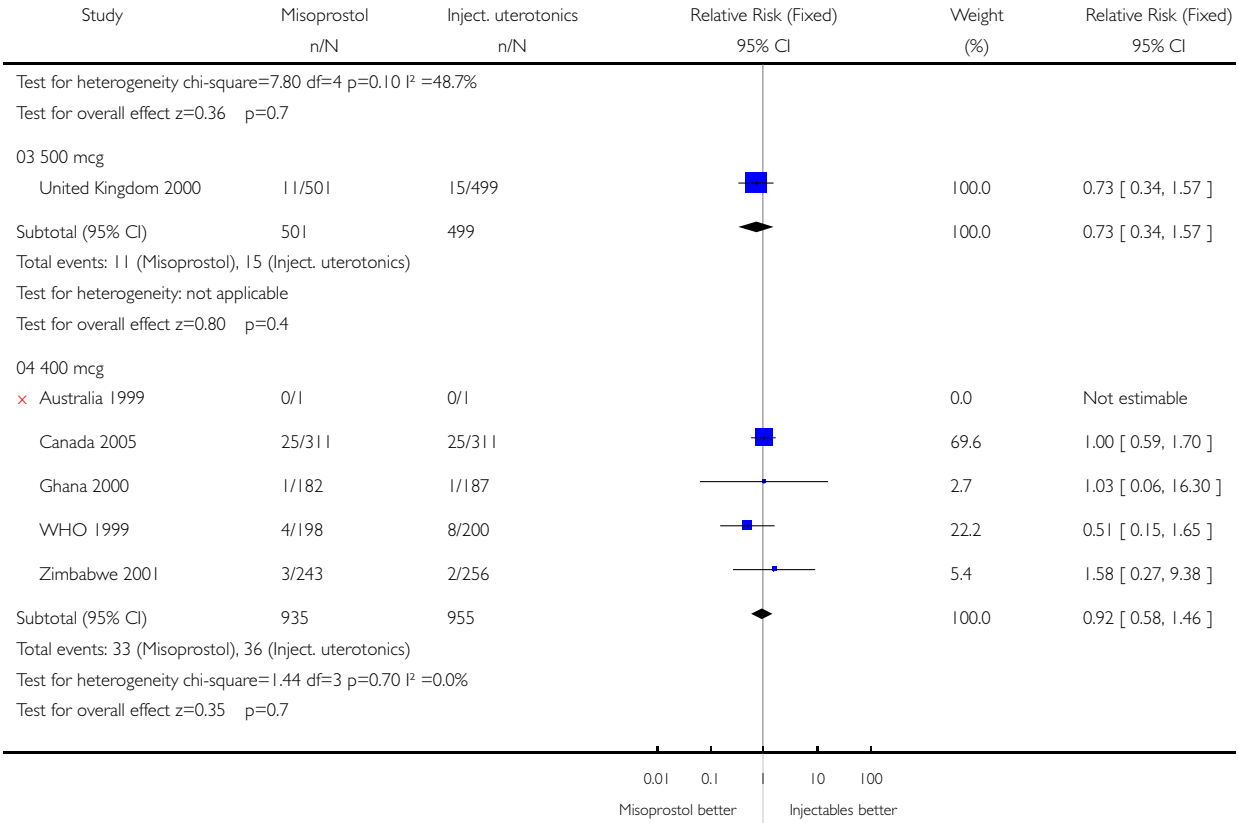

Analysis 03.11. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 11 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 11 Duration of third stage (minutes)

Study	Misoprostol N	Misoprostol Mean(SD)	Inject. uterotonics N	Inject. uterotonics Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg						
WHO 1999	199	6.40 (6.62)	200	6.30 (4.01)		0.10 [-0.97, 1.17]
WHO 2001	9208	8.40 (16.00)	9204	8.20 (13.10)		0.20 [-0.22, 0.62]
02 400 mcg						
Australia 1999	424	8.40 (8.23)	439	9.00 (16.76)		-0.60 [-2.35, 1.15]
India 2006b	730	4.87 (5.28)	617	4.37 (4.66)		0.50 [-0.03, 1.03]
Turkey 2003	388	9.20 (3.00)	384	8.70 (1.70)		0.50 [0.16, 0.84]
WHO 1999	198	8.60 (14.53)	200	6.30 (4.01)		2.30 [0.20, 4.40]
Zimbabwe 2001	243	6.90 (4.70)	256	6.00 (3.50)		0.90 [0.17, 1.63]

Analysis 03.12. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 12 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 12 Third stage >= 30 minutes

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Belgium 1999	2/100	1/100		5.3	2.00 [0.18, 21.71]
Hong Kong 2001	14/1026	16/1032		84.2	0.88 [0.43, 1.79]
× India 2005a	0/100	0/100		0.0	Not estimable
Nigeria 2003	3/247	2/249		10.5	1.51 [0.25, 8.97]
Subtotal (95% CI)	1473	1481		100.0	1.01 [0.53, 1.89]
Total events: 19 (Misoprostol), 19 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.66 df=2 p=0.72 I² =0.0%					
Test for overall effect z=0.02 p=1					
02 500 mcg					

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Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2000	13/501	14/499		100.0	0.92 [0.44, 1.95]
Subtotal (95% CI)	501	499		100.0	0.92 [0.44, 1.95]
Total events: 13 (Misoprostol), 14 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.21 p=0.8					
03 400 mcg					
Turkey 2003	3/388	2/384		67.4	1.48 [0.25, 8.84]
Zimbabwe 2001	1/243	1/256		32.6	1.05 [0.07, 16.75]
Subtotal (95% CI)	631	640		100.0	1.34 [0.30, 5.99]
Total events: 4 (Misoprostol), 3 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.04 df=1 p=0.84 I^2 =0.0%					
Test for overall effect z=0.39 p=0.7					

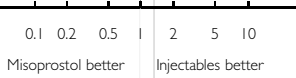
Analysis 03.13. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 13 Any side-effect

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 13 Any side-effect

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 500 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 400 mcg					
Zimbabwe 2001	121/243	89/256		100.0	1.43 [1.16, 1.77]
Subtotal (95% CI)	243	256		100.0	1.43 [1.16, 1.77]
Total events: 121 (Misoprostol), 89 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.35 p=0.0008					



Analysis 03.14. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 14 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 14 Nausea

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 800 mcg				
Ghana 2006	2/223	4/222		0.50 [0.09, 2.69]
02 600 mcg				
Belgium 1999	20/87	30/94		0.72 [0.44, 1.17]
Hong Kong 2001	20/1026	27/1032		0.75 [0.42, 1.32]
India 2005a	20/100	30/100		0.67 [0.41, 1.09]
Nigeria 2003	8/247	10/249		0.81 [0.32, 2.01]
WHO 1999	1/199	1/200		1.01 [0.06, 15.96]
WHO 2001	77/9227	34/9232		2.27 [1.52, 3.39]
03 500 mcg				
United Kingdom 2000	138/445	175/401		0.71 [0.59, 0.85]
04 400 mcg				
Ghana 2000	5/152	6/159		0.87 [0.27, 2.80]
India 2006b	5/730	11/617		0.38 [0.13, 1.10]
WHO 1999	0/198	1/200		0.34 [0.01, 8.22]
Zimbabwe 2001	7/243	5/256		1.47 [0.47, 4.58]

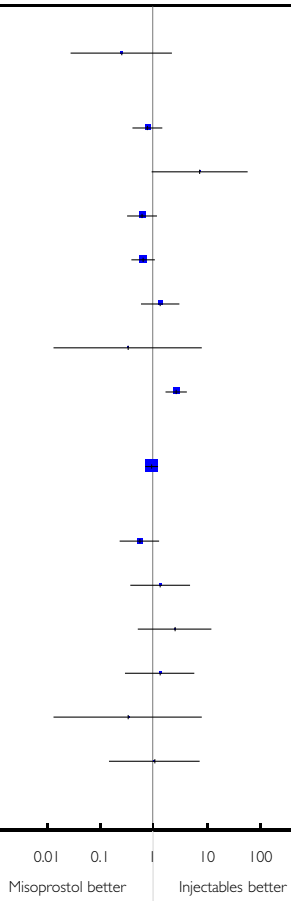
Analysis 03.15. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 15 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 15 Vomiting

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 800 mcg				
Ghana 2006	1/221	4/224		0.25 [0.03, 2.25]
02 600 mcg				
Belgium 1999	13/87	18/94		0.78 [0.41, 1.50]
France 2001	7/186	1/196		7.38 [0.92, 59.38]
Hong Kong 2001	14/1026	23/1032		0.61 [0.32, 1.18]
India 2005a	19/100	30/100		0.63 [0.38, 1.05]
Nigeria 2003	12/247	9/249		1.34 [0.58, 3.13]
WHO 1999	0/199	1/200		0.34 [0.01, 8.17]
WHO 2001	66/9227	25/9232		2.64 [1.67, 4.18]
03 500 mcg				
United Kingdom 2000	79/445	77/401		0.92 [0.70, 1.23]
04 400 mcg				
Australia 1999	8/424	15/439		0.55 [0.24, 1.29]
Ghana 2000	5/164	4/177		1.35 [0.37, 4.94]
India 2006b	6/730	2/617		2.54 [0.51, 12.52]
Turkey 2003	4/388	3/384		1.32 [0.30, 5.86]
WHO 1999	0/198	1/200		0.34 [0.01, 8.22]
Zimbabwe 2001	2/243	2/256		1.05 [0.15, 7.42]

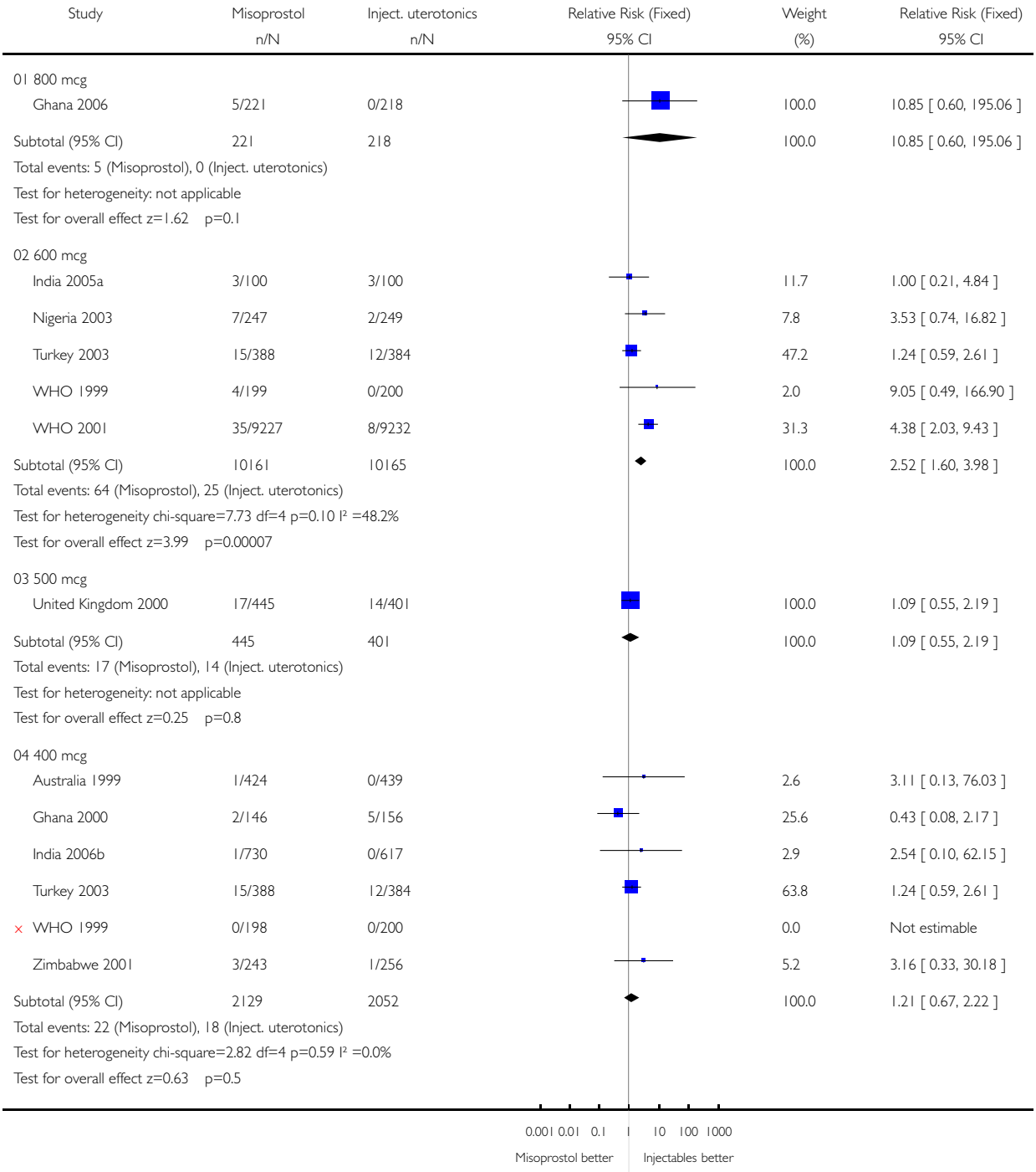


Analysis 03.16. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 16 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 16 Diarrhoea



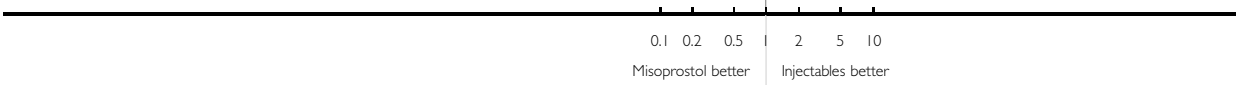
Analysis 03.17. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 17 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 17 Headache

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Belgium 1999	10/87	12/94		12.2	0.90 [0.41, 1.98]
Hong Kong 2001	81/1026	83/1032		87.8	0.98 [0.73, 1.32]
Subtotal (95% CI)	1113	1126		100.0	0.97 [0.74, 1.28]
Total events: 91 (Misoprostol), 95 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.04 df=1 p=0.84 I^2 =0.0%					
Test for overall effect z=0.20 p=0.8					
02 500 mcg					
United Kingdom 2000	46/445	78/401		100.0	0.53 [0.38, 0.75]
Subtotal (95% CI)	445	401		100.0	0.53 [0.38, 0.75]
Total events: 46 (Misoprostol), 78 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.66 p=0.0003					
04 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



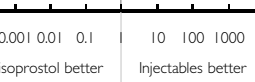
Analysis 03.18. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 18 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 18 Any shivering

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 800 mcg				
Ghana 2006	180/223	8/223		22.50 [11.36, 44.56]
02 600 mcg				
Belgium 1999	66/86	38/94		1.90 [1.45, 2.49]
France 2001	5/186	0/196		11.59 [0.65, 208.12]
Hong Kong 2001	310/1026	102/1032		3.06 [2.49, 3.76]
India 2005a	31/100	10/100		3.10 [1.61, 5.98]
Nigeria 2003	141/247	35/249		4.06 [2.93, 5.62]
WHO 1999	56/199	25/200		2.25 [1.47, 3.46]
WHO 2001	1620/9227	466/9232		3.48 [3.15, 3.84]
03 500 mcg				
United Kingdom 2000	319/445	147/401		1.96 [1.70, 2.25]
United Kingdom 2001b	13/20	8/20		1.63 [0.87, 3.04]
04 400 mcg				
Australia 1999	79/424	31/439		2.64 [1.78, 3.91]
Canada 2005	21/311	0/311		43.00 [2.62, 706.74]
Ghana 2000	39/176	10/176		3.90 [2.01, 7.57]
India 2006b	68/730	14/617		4.11 [2.33, 7.22]
Turkey 2003	44/388	19/384		2.29 [1.36, 3.85]
WHO 1999	38/198	25/200		1.54 [0.96, 2.44]
Zimbabwe 2001	106/243	78/256		1.43 [1.13, 1.81]

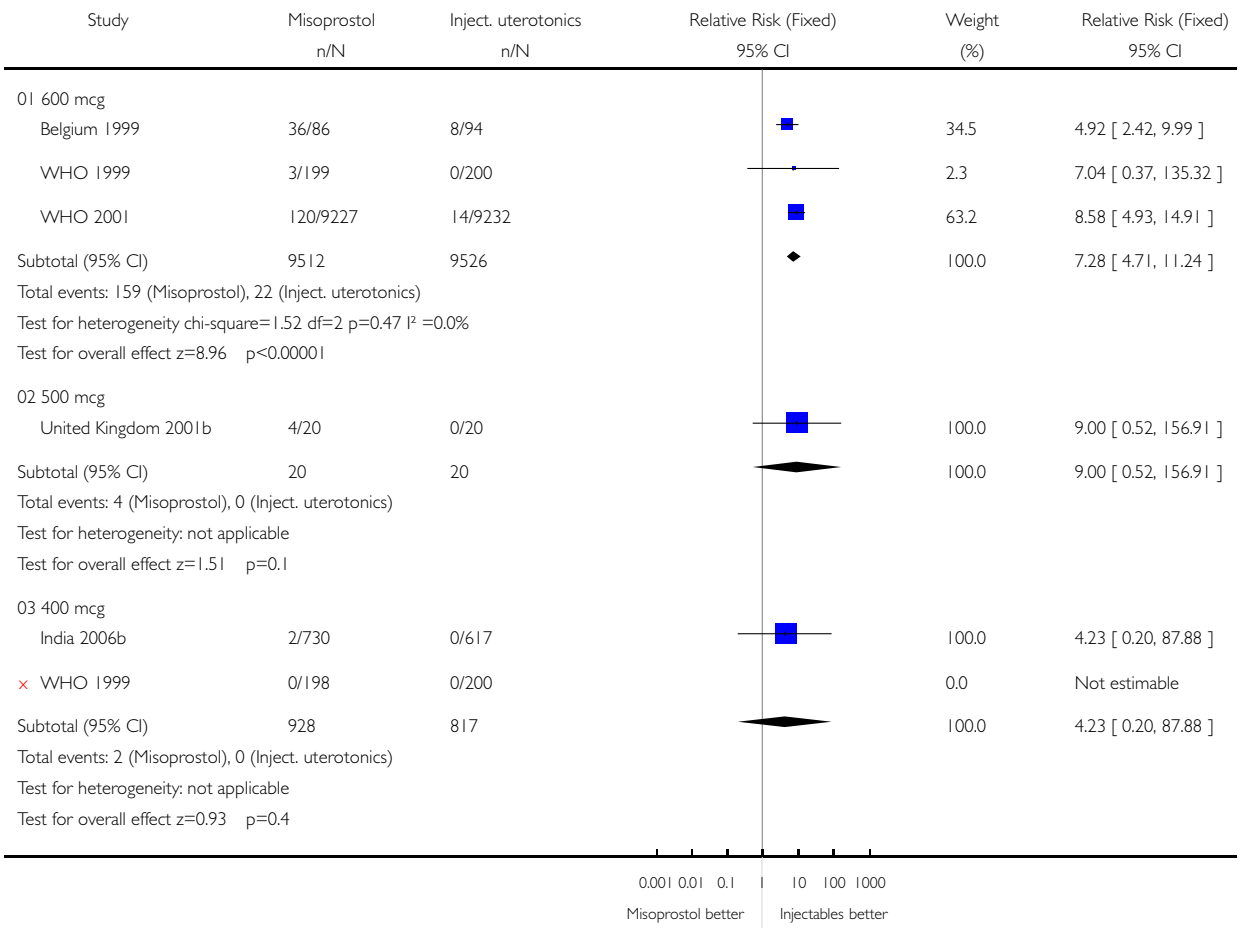


Analysis 03.19. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 19 Severe shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 19 Severe shivering

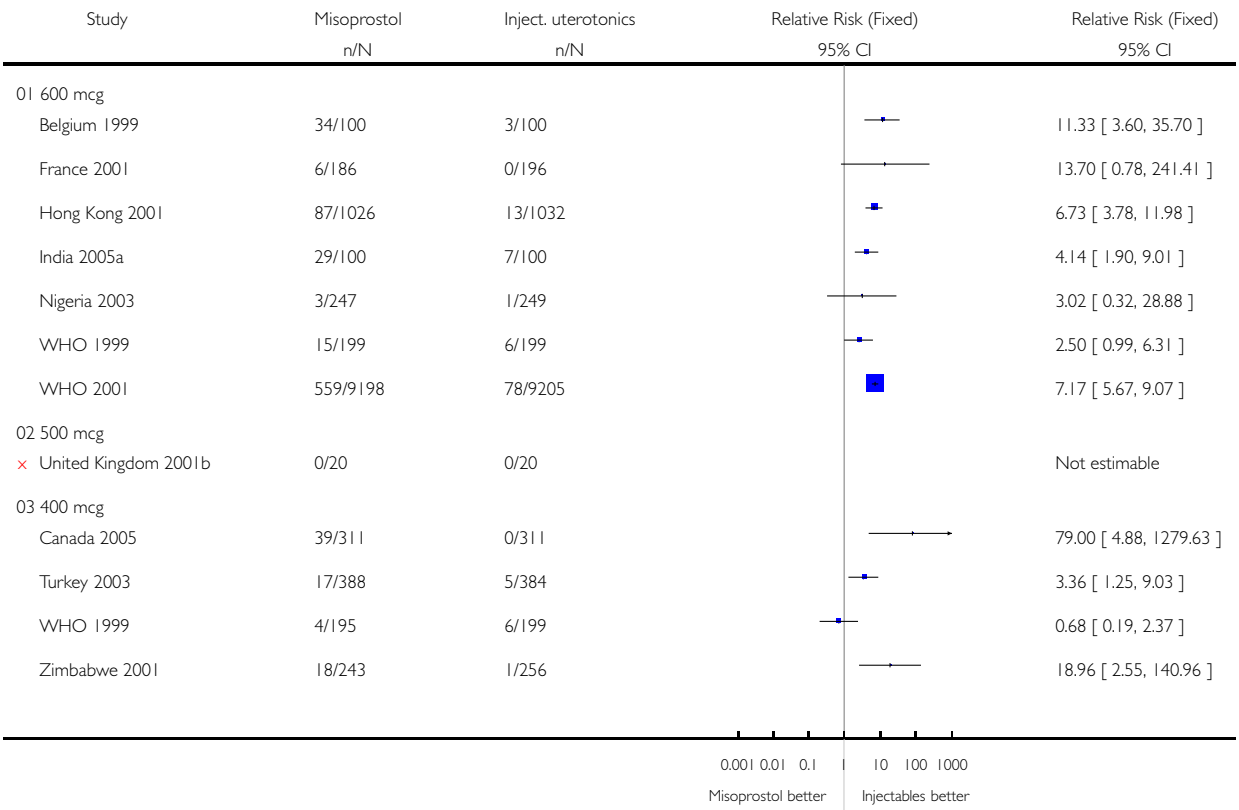


Analysis 03.20. Comparison 03 Oral misoprostol versus injectable uterotonics, Outcome 20 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 03 Oral misoprostol versus injectable uterotonics

Outcome: 20 Pyrexia (>= 38 degrees C)



Analysis 04.03. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 03 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 03 Severe postpartum haemorrhage (>= 1000 ml)

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	13/270	19/272		100.0	0.69 [0.35, 1.37]
Subtotal (95% CI)	270	272		100.0	0.69 [0.35, 1.37]
Total events: 13 (Misoprostol), 19 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.06 p=0.3					

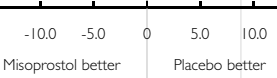
Analysis 04.04. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 04 Blood loss (ml)

Study	Misoprostol N Mean(SD)	Placebo N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 04.05. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 05 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 05 Use of additional uterotonics

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	9/271	13/275		100.0	0.70 [0.31, 1.62]
Subtotal (95% CI)	271	275		100.0	0.70 [0.31, 1.62]
Total events: 9 (Misoprostol), 13 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.83 p=0.4					

Analysis 04.07. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 07 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

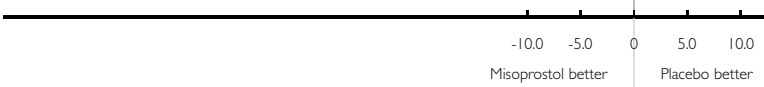
Outcome: 07 Manual removal of placenta

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	1/271	0/275		100.0	3.04 [0.12, 74.40]
Subtotal (95% CI)	271	275		100.0	3.04 [0.12, 74.40]
Total events: 1 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

Analysis 04.08. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 08 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 04 Rectal misoprostol versus no uterotonic/placebo
Outcome: 08 Duration of third stage (minutes)

Study	Misoprostol N Mean(SD)	Placebo N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 04.09. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 09 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage
Comparison: 04 Rectal misoprostol versus no uterotonic/placebo
Outcome: 09 Third stage >= 30 minutes

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	1/268	2/272		100.0	0.51 [0.05, 5.56]
Subtotal (95% CI)	268	272		100.0	0.51 [0.05, 5.56]
Total events: 1 (Misoprostol), 2 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.56 p=0.6					

Analysis 04.12. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 12 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 12 Vomiting

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	1/271	1/275		100.0	1.01 [0.06, 16.14]
Subtotal (95% CI)	271	275		100.0	1.01 [0.06, 16.14]
Total events: 1 (Misoprostol), 1 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.01 p=1					

Analysis 04.14. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 14 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 14 Abdominal pain

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	1/271	0/275		100.0	3.04 [0.12, 74.40]
Subtotal (95% CI)	271	275		100.0	3.04 [0.12, 74.40]
Total events: 1 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

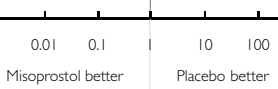
Analysis 04.16. Comparison 04 Rectal misoprostol versus no uterotonic/placebo, Outcome 16 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 04 Rectal misoprostol versus no uterotonic/placebo

Outcome: 16 Any shivering

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
South Africa 1998c	1/34	4/36		100.0	0.26 [0.03, 2.25]
Subtotal (95% CI)	34	36		100.0	0.26 [0.03, 2.25]
Total events: 1 (Misoprostol), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.22 p=0.2					



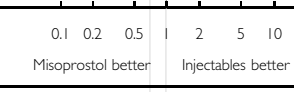
Analysis 05.01. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 01 Maternal death

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 01 Maternal death

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
× Turkey 2002	0/396	0/407		0.0	Not estimable
Subtotal (95% CI)	396	407		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	396	407		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 05.02. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

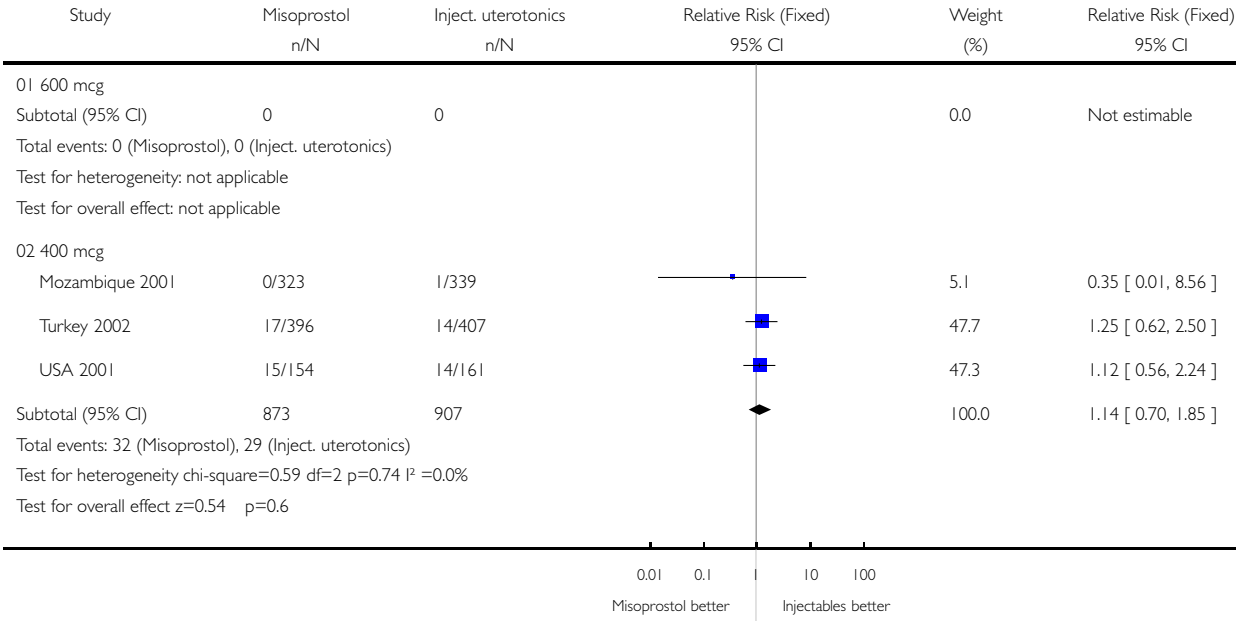
Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Mozambique 2001	10/323	15/339		13.6	0.70 [0.32, 1.53]
South Africa 1998a	2/231	1/233		0.9	2.02 [0.18, 22.09]
Turkey 2002	39/396	33/407		30.2	1.21 [0.78, 1.89]
USA 2001	70/154	61/161		55.3	1.20 [0.92, 1.56]
Subtotal (95% CI)	1104	1140		100.0	1.14 [0.92, 1.43]
Total events: 121 (Misoprostol), 110 (Inject. uterotonics)					
Test for heterogeneity chi-square=1.92 df=3 p=0.59 I^2 =0.0%					
Test for overall effect z=1.19 p=0.2					

Analysis 05.03. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 03 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 03 Severe postpartum haemorrhage (>= 1000 ml)

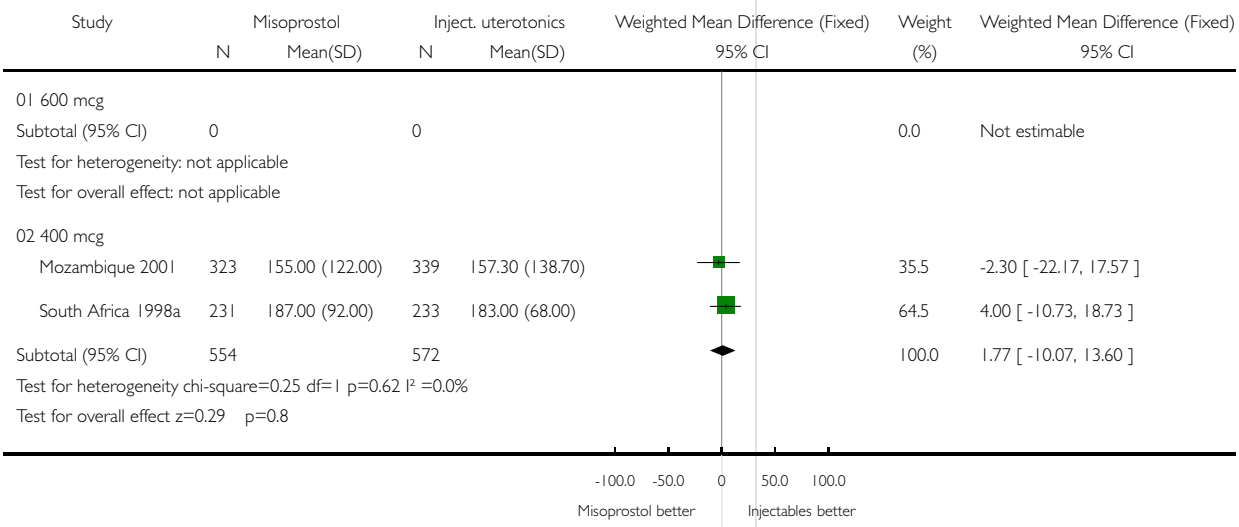


Analysis 05.04. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 04 Blood loss (ml)

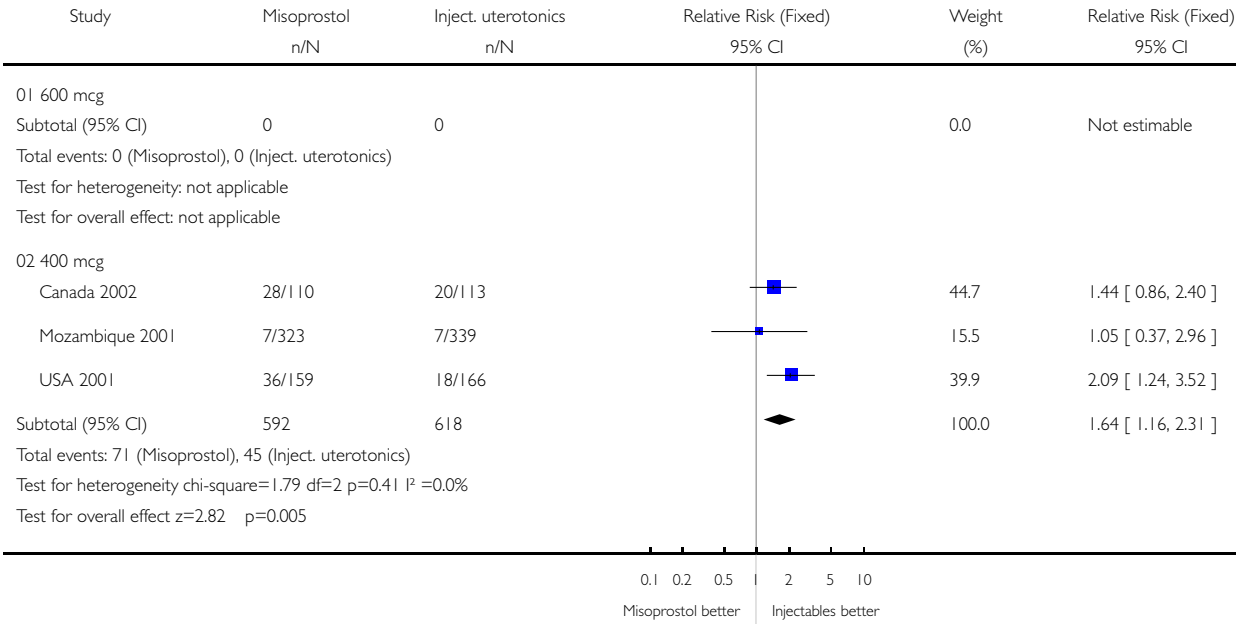


Analysis 05.05. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 05 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 05 Use of additional uterotonics



Analysis 05.06. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 06 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 06 Blood transfusion

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
× Canada 2002	0/110	0/113		0.0	Not estimable
Mozambique 2001	2/323	1/339		6.2	2.10 [0.19, 23.04]
Turkey 2002	12/396	13/407		81.4	0.95 [0.44, 2.05]
USA 2001	2/159	2/166		12.4	1.04 [0.15, 7.32]
Subtotal (95% CI)	988	1025		100.0	1.03 [0.52, 2.04]
Total events: 16 (Misoprostol), 16 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.38 df=2 p=0.83 I^2 =0.0%					
Test for overall effect z=0.09 p=0.9					

Analysis 05.07. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 07 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 07 Manual removal of placenta

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	1/110	6/113		100.0	0.17 [0.02, 1.40]
Subtotal (95% CI)	110	113		100.0	0.17 [0.02, 1.40]
Total events: 1 (Misoprostol), 6 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.65 p=0.1					

Analysis 05.08. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 08 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 08 Duration of third stage (minutes)

Study	Misoprostol N	Misoprostol Mean(SD)	Inject. uterotonics N	Inject. uterotonics Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							
02 400 mcg							
Mozambique 2001	323	9.00 (3.60)	339	9.30 (4.10)		32.0	-0.30 [-0.89, 0.29]
South Africa 1998a	232	7.70 (6.70)	244	7.90 (6.80)		7.5	-0.20 [-1.41, 1.01]
Turkey 2002	396	9.30 (4.00)	407	8.70 (1.70)		60.5	0.60 [0.17, 1.03]
Subtotal (95% CI)	951		990			100.0	0.25 [-0.08, 0.58]
Test for heterogeneity chi-square=6.48 df=2 p=0.04 I^2 =69.1%							
Test for overall effect z=1.49 p=0.1							
Total (95% CI)	951		990			100.0	0.25 [-0.08, 0.58]
Test for heterogeneity chi-square=6.48 df=2 p=0.04 I^2 =69.1%							
Test for overall effect z=1.49 p=0.1							

Analysis 05.09. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 09 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 09 Third stage >= 30 minutes

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Turkey 2002	12/396	2/407		100.0	6.17 [1.39, 27.38]
Subtotal (95% CI)	396	407		100.0	6.17 [1.39, 27.38]
Total events: 12 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.39 p=0.02					

Analysis 05.11. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 11 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 11 Nausea

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	8/105	5/110		100.0	1.68 [0.57, 4.96]
Subtotal (95% CI)	105	110		100.0	1.68 [0.57, 4.96]
Total events: 8 (Misoprostol), 5 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.93 p=0.4					

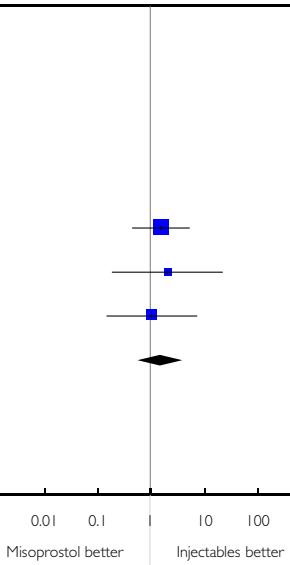
Analysis 05.12. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 12 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 12 Vomiting

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	6/105	4/110		57.0	1.57 [0.46, 5.41]
Mozambique 2001	2/323	1/337		14.3	2.09 [0.19, 22.90]
Turkey 2002	2/396	2/407		28.8	1.03 [0.15, 7.26]
Subtotal (95% CI)	824	854		100.0	1.49 [0.57, 3.86]
Total events: 10 (Misoprostol), 7 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.22 df=2 p=0.90 I^2 =0.0%					
Test for overall effect z=0.82 p=0.4					



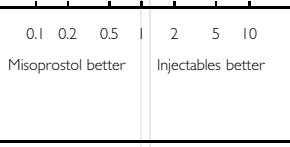
Analysis 05.13. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 13 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 13 Headache

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	9/105	4/110		100.0	2.36 [0.75, 7.42]
Subtotal (95% CI)	105	110		100.0	2.36 [0.75, 7.42]
Total events: 9 (Misoprostol), 4 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.47 p=0.1					



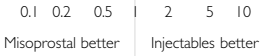
Analysis 05.14. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 14 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 14 Abdominal pain

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	12/105	13/110		100.0	0.97 [0.46, 2.02]
Subtotal (95% CI)	105	110		100.0	0.97 [0.46, 2.02]
Total events: 12 (Misoprostol), 13 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.09 p=0.9					



Analysis 05.15. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 15 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 15 Diarrhoea

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Mozambique 2001	0/323	2/338		21.6	0.21 [0.01, 4.34]
Turkey 2002	11/396	9/407		78.4	1.26 [0.53, 3.00]
Subtotal (95% CI)	719	745		100.0	1.03 [0.46, 2.31]
Total events: 11 (Misoprostol), 11 (Inject. uterotonics)					
Test for heterogeneity chi-square=1.26 df=1 p=0.26 I^2 =20.7%					
Test for overall effect z=0.07 p=0.9					

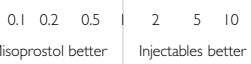
Analysis 05.16. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 16 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 16 Any shivering

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	26/105	15/110		16.8	1.82 [1.02, 3.23]
Mozambique 2001	123/323	51/337		57.2	2.52 [1.89, 3.36]
Turkey 2002	47/396	16/407		18.1	3.02 [1.74, 5.23]
USA 2001	7/159	7/166		7.9	1.04 [0.37, 2.91]
Subtotal (95% CI)	983	1020		100.0	2.37 [1.89, 2.98]
Total events: 203 (Misoprostol), 89 (Inject. uterotonics)					
Test for heterogeneity chi-square=4.19 df=3 p=0.24 I^2 =28.4%					
Test for overall effect z=7.46 p<0.00001					



Analysis 05.18. Comparison 05 Rectal misoprostol versus injectable uterotonics, Outcome 18 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 05 Rectal misoprostol versus injectable uterotonics

Outcome: 18 Pyrexia (>= 38 degrees C)

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Canada 2002	20/107	12/112		66.5	1.74 [0.90, 3.39]
Turkey 2002	16/396	6/407		33.5	2.74 [1.08, 6.93]
Subtotal (95% CI)	503	519		100.0	2.08 [1.21, 3.57]
Total events: 36 (Misoprostol), 18 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.61 df=1 p=0.44 I^2 =0.0%					
Test for overall effect z=2.66 p=0.008					

Analysis 06.02. Comparison 06 Rectal misoprostol versus intramuscular prostaglandin, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 06 Rectal misoprostol versus intramuscular prostaglandin

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

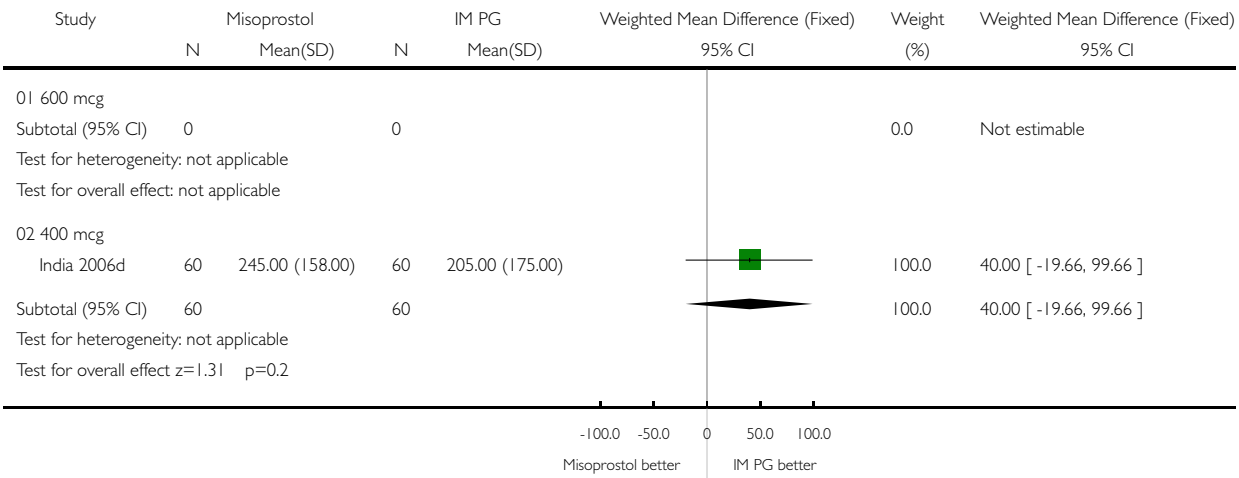
Study	Misoprostol n/N	IM PG n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (IM PG)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
India 2006d	4/60	3/60		100.0	1.33 [0.31, 5.70]
Subtotal (95% CI)	60	60		100.0	1.33 [0.31, 5.70]
Total events: 4 (Misoprostol), 3 (IM PG)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.39 p=0.7					

Analysis 06.04. Comparison 06 Rectal misoprostol versus intramuscular prostaglandin, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 06 Rectal misoprostol versus intramuscular prostaglandin

Outcome: 04 Blood loss (ml)

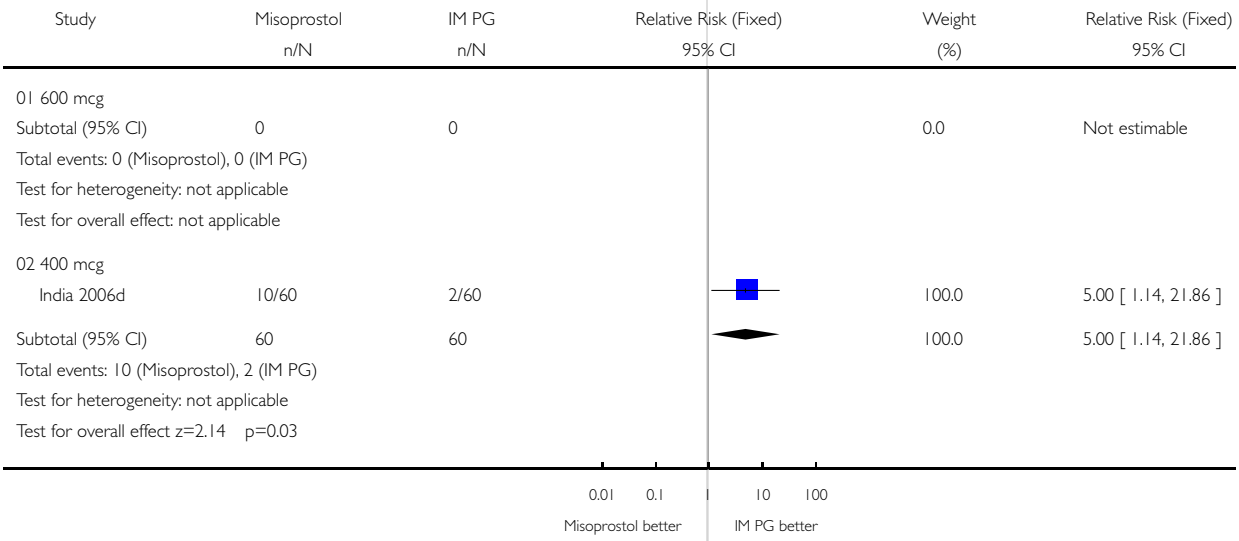


Analysis 06.05. Comparison 06 Rectal misoprostol versus intramuscular prostaglandin, Outcome 05 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 06 Rectal misoprostol versus intramuscular prostaglandin

Outcome: 05 Use of additional uterotonics



Analysis 06.08. Comparison 06 Rectal misoprostol versus intramuscular prostaglandin, Outcome 08 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 06 Rectal misoprostol versus intramuscular prostaglandin

Outcome: 08 Duration of third stage (minutes)

Study	Misoprostol N Mean(SD)	IM PG N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 07.01. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 01 Maternal death

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 01 Maternal death

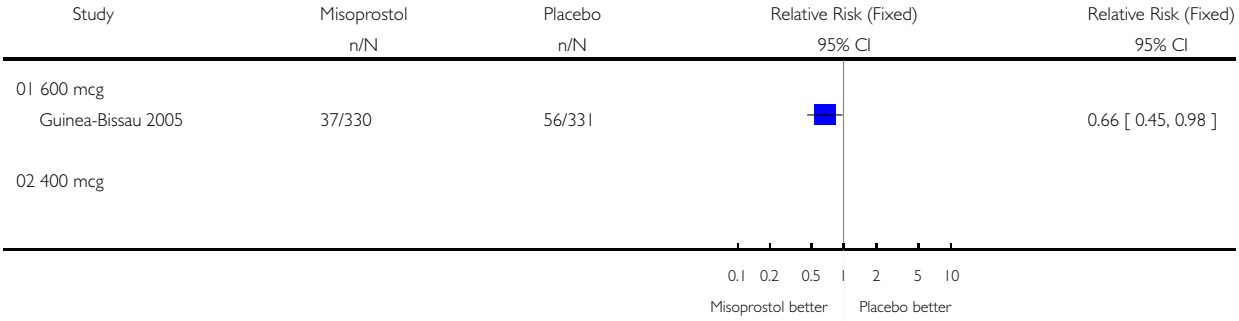
Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guinea-Bissau 2005	1/330	0/331		100.0	3.01 [0.12, 73.60]
Total (95% CI)	330	331		100.0	3.01 [0.12, 73.60]
Total events: 1 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

Analysis 07.02. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

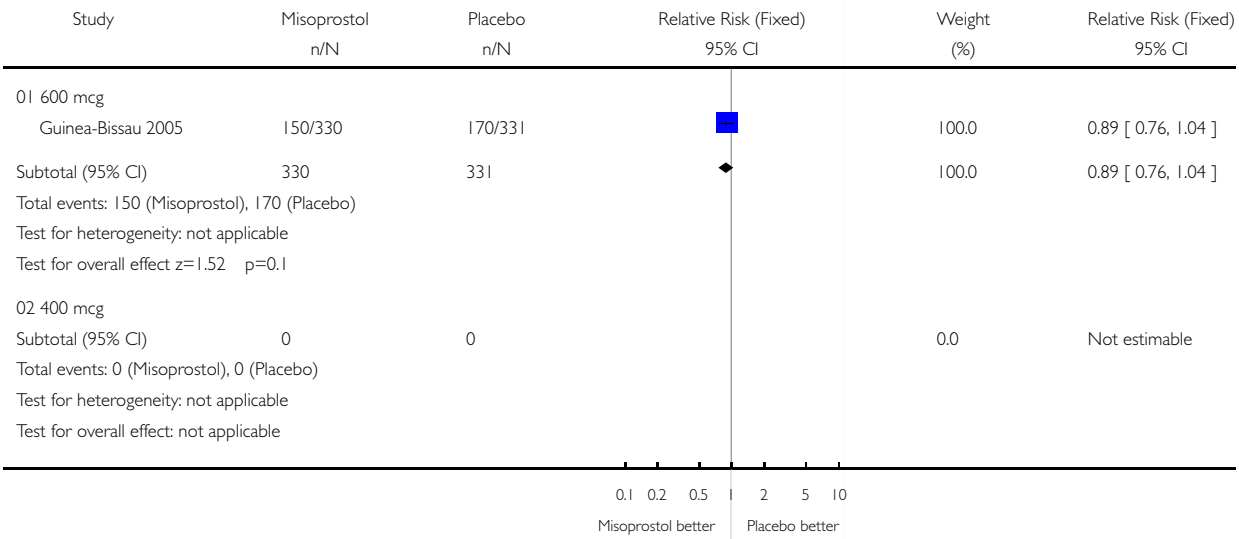


Analysis 07.03. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 03 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 03 Postpartum haemorrhage (>= 500 ml)



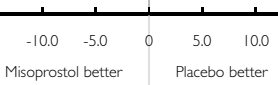
Analysis 07.04. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 04 Blood loss (ml)

Study	Misoprostol N Mean(SD)	Placebo N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 07.08. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 08 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 08 Duration of third stage (minutes)

Study	Misoprostol N Mean(SD)	Placebo N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

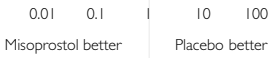
Analysis 07.11. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 11 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 11 Nausea

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Guinea-Bissau 2005	2/330	4/331		100.0	0.50 [0.09, 2.72]
Subtotal (95% CI)	330	331		100.0	0.50 [0.09, 2.72]
Total events: 2 (Misoprostol), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.80 p=0.4					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



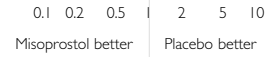
Analysis 07.12. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 12 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 12 Vomiting

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Guinea-Bissau 2005	10/330	4/331		100.0	2.51 [0.79, 7.92]
Subtotal (95% CI)	330	331		100.0	2.51 [0.79, 7.92]
Total events: 10 (Misoprostol), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.57 p=0.1					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 07.15. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 15 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 15 Diarrhoea

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Guinea-Bissau 2005	10/330	4/331		100.0	2.51 [0.79, 7.92]
Subtotal (95% CI)	330	331		100.0	2.51 [0.79, 7.92]
Total events: 10 (Misoprostol), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.57 p=0.1					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 07.16. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 16 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 16 Any shivering

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Guinea-Bissau 2005	189/330	78/331		100.0	2.43 [1.96, 3.01]
Subtotal (95% CI)	330	331		100.0	2.43 [1.96, 3.01]
Total events: 189 (Misoprostol), 78 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=8.09 p<0.00001					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

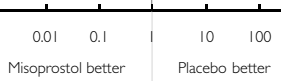
Analysis 07.18. Comparison 07 Sublingual misoprostol versus no uterotonic/placebo, Outcome 18 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 07 Sublingual misoprostol versus no uterotonic/placebo

Outcome: 18 Pyrexia (>= 38 degrees C)

Study	Misoprostol n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Guinea-Bissau 2005	78/330	11/331		100.0	7.11 [3.85, 13.12]
Subtotal (95% CI)	330	331		100.0	7.11 [3.85, 13.12]
Total events: 78 (Misoprostol), 11 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=6.28 p<0.00001					
02 400 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	330	331		100.0	7.11 [3.85, 13.12]
Total events: 78 (Misoprostol), 11 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=6.28 p<0.00001					

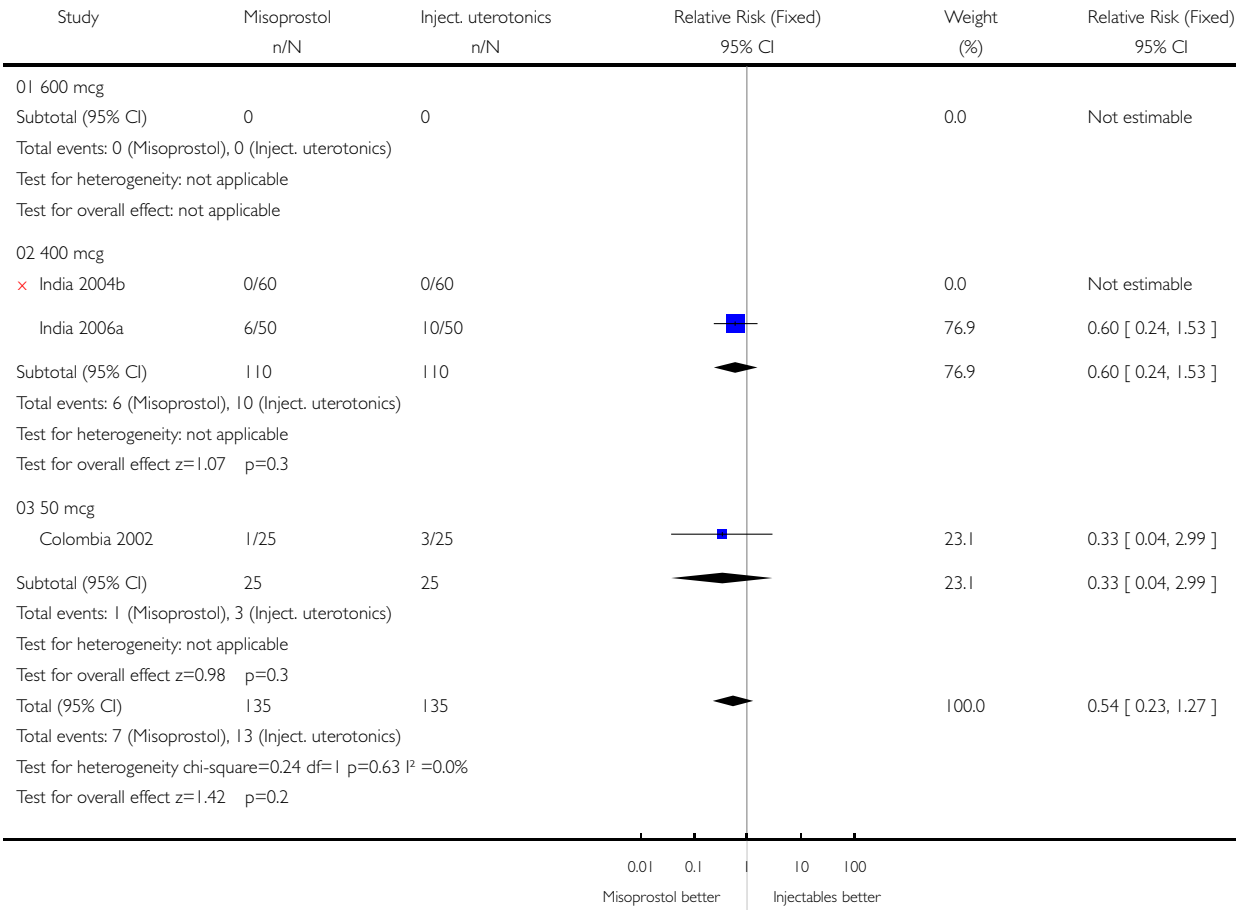


Analysis 08.02. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

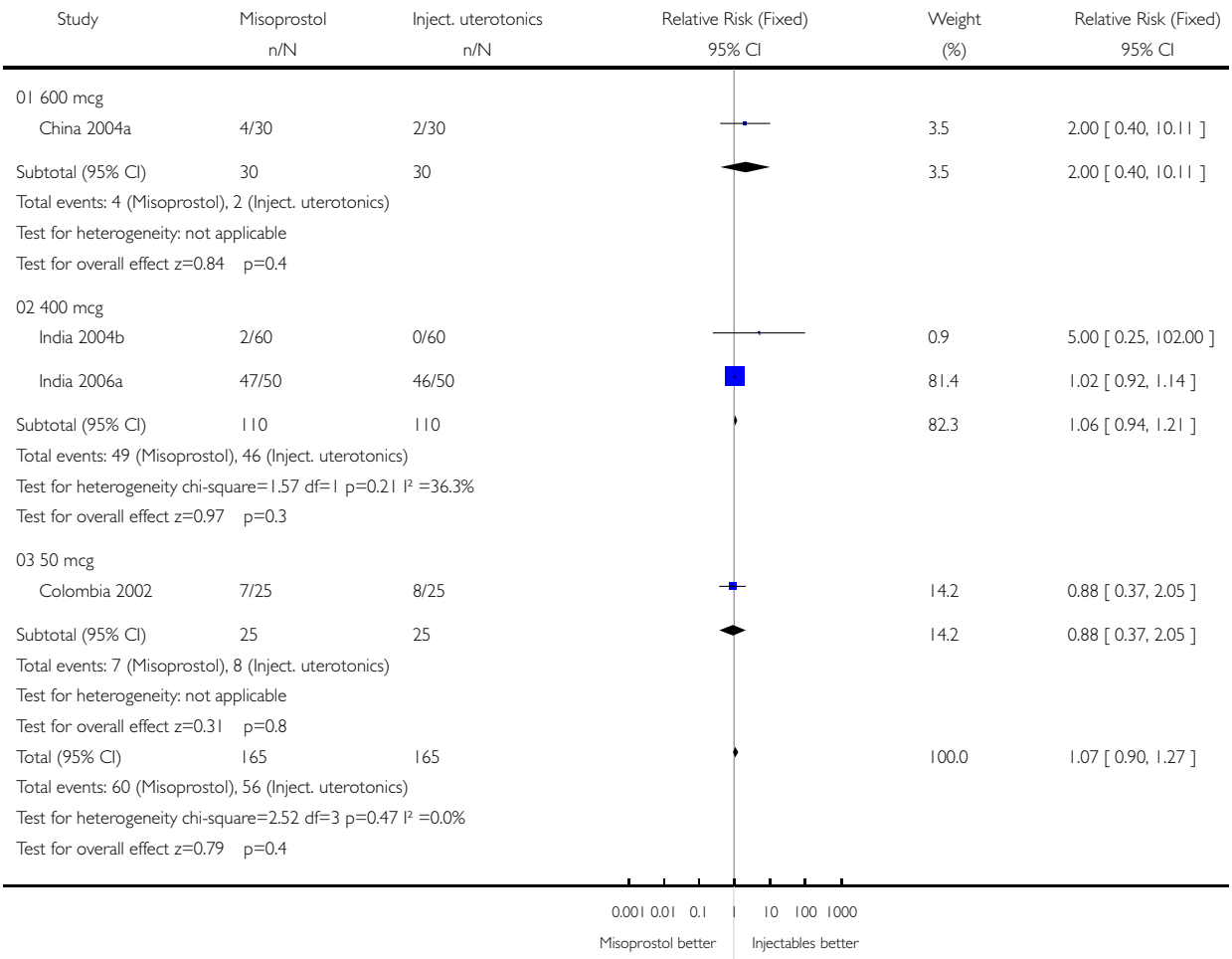


Analysis 08.03. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 03 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 03 Postpartum haemorrhage (>= 500 ml)

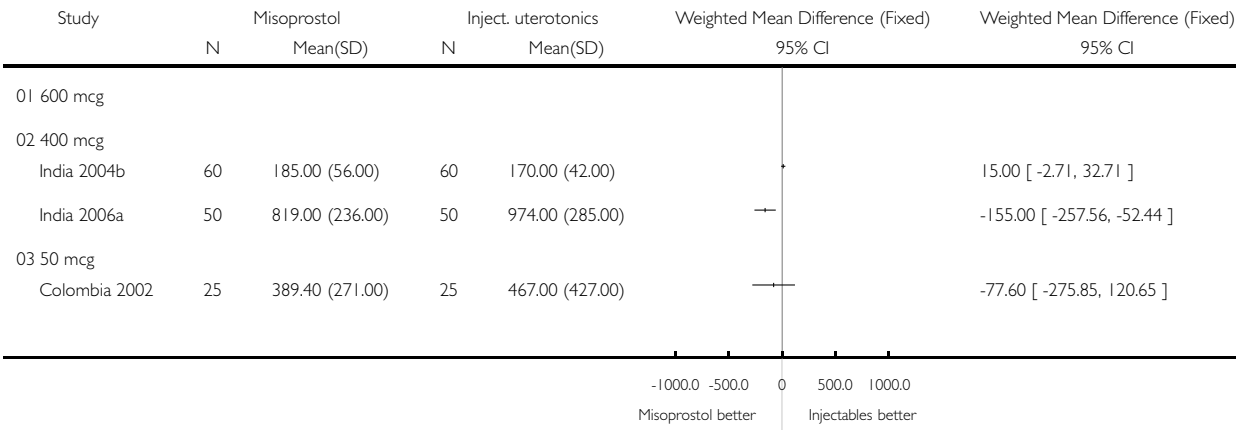


Analysis 08.04. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 04 Blood loss (ml)

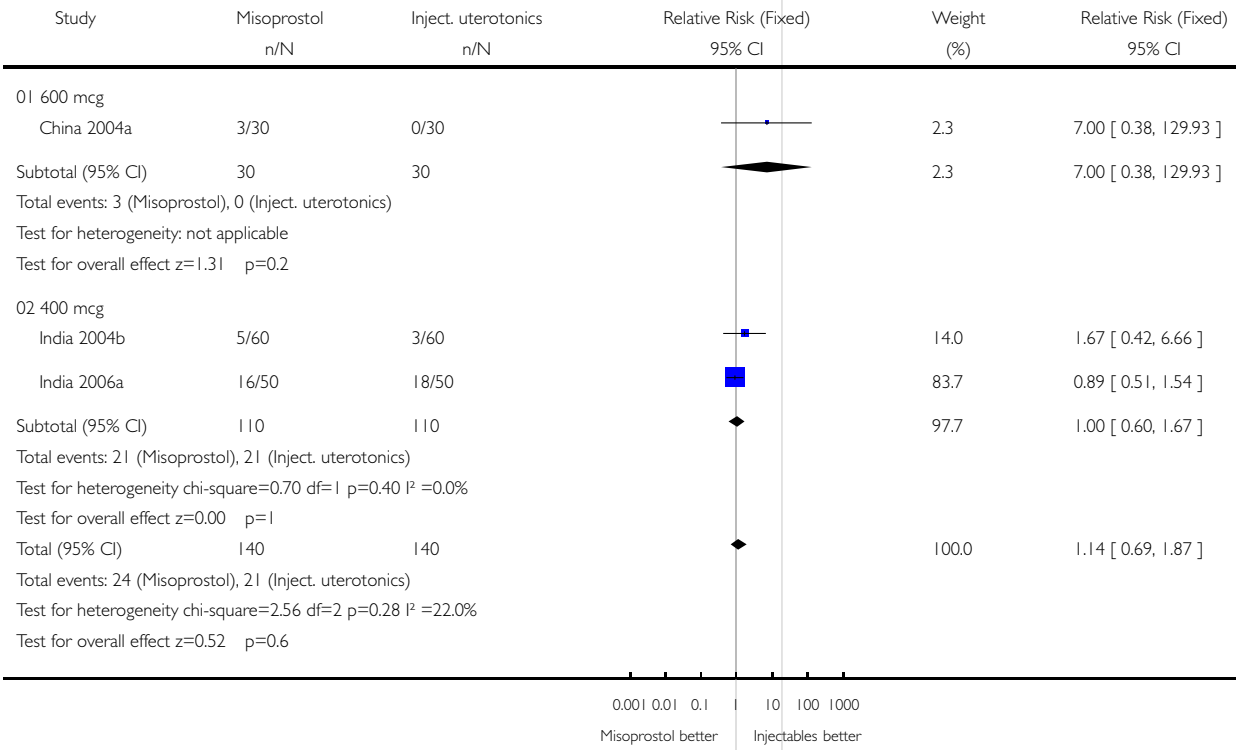


Analysis 08.05. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 05 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 05 Use of additional uterotonics



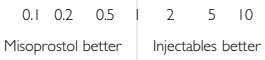
Analysis 08.06. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 06 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 06 Blood transfusion

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
× India 2004b	0/60	0/60		0.0	Not estimable
Subtotal (95% CI)	60	60		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	60	60		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 08.07. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 07 Postpartum haemoglobin

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 07 Postpartum haemoglobin

Study	Misoprostol N	Misoprostol Mean(SD)	Inject. uterotonics N	Inject. uterotonics Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 600 mcg							
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity: not applicable							
Test for overall effect: not applicable							
02 400 mcg							
India 2006a	50	10.50 (1.30)	50	10.60 (1.40)		100.0	-0.10 [-0.63, 0.43]
Subtotal (95% CI)	50		50			100.0	-0.10 [-0.63, 0.43]
Test for heterogeneity: not applicable							
Test for overall effect z=0.37 p=0.7							
Total (95% CI)	50		50			100.0	-0.10 [-0.63, 0.43]
Test for heterogeneity: not applicable							
Test for overall effect z=0.37 p=0.7							

Analysis 08.08. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 08 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 08 Manual removal of placenta

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
India 2004b	0/60	1/60		100.0	0.33 [0.01, 8.02]
Subtotal (95% CI)	60	60		100.0	0.33 [0.01, 8.02]
Total events: 0 (Misoprostol), 1 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

(*Continued . . .*)

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Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Total (95% CI)	60	60		100.0	0.33 [0.01, 8.02]
Total events: 0 (Misoprostol), 1 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

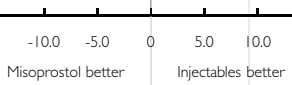
Analysis 08.09. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 09 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 09 Duration of third stage (minutes)

Study	Misoprostol N Mean(SD)	Inject. uterotonics N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



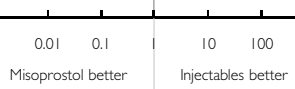
Analysis 08.13. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 13 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 13 Vomiting

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
India 2006a	8/50	6/50		80.0	1.33 [0.50, 3.56]
Subtotal (95% CI)	50	50		80.0	1.33 [0.50, 3.56]
Total events: 8 (Misoprostol), 6 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					
03 50 mcg					
Colombia 2002	0/25	1/25		20.0	0.33 [0.01, 7.81]
Subtotal (95% CI)	25	25		20.0	0.33 [0.01, 7.81]
Total events: 0 (Misoprostol), 1 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					
Total (95% CI)	75	75		100.0	1.13 [0.45, 2.84]
Total events: 8 (Misoprostol), 7 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.68 df=1 p=0.41 I^2 =0.0%					
Test for overall effect z=0.27 p=0.8					



Analysis 08.14. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 14 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 14 Headache

Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
India 2006a	6/50	8/50		100.0	0.75 [0.28, 2.00]
Subtotal (95% CI)	50	50		100.0	0.75 [0.28, 2.00]
Total events: 6 (Misoprostol), 8 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					
Total (95% CI)	50	50		100.0	0.75 [0.28, 2.00]
Total events: 6 (Misoprostol), 8 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					

Analysis 08.17. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 17 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 17 Any shivering

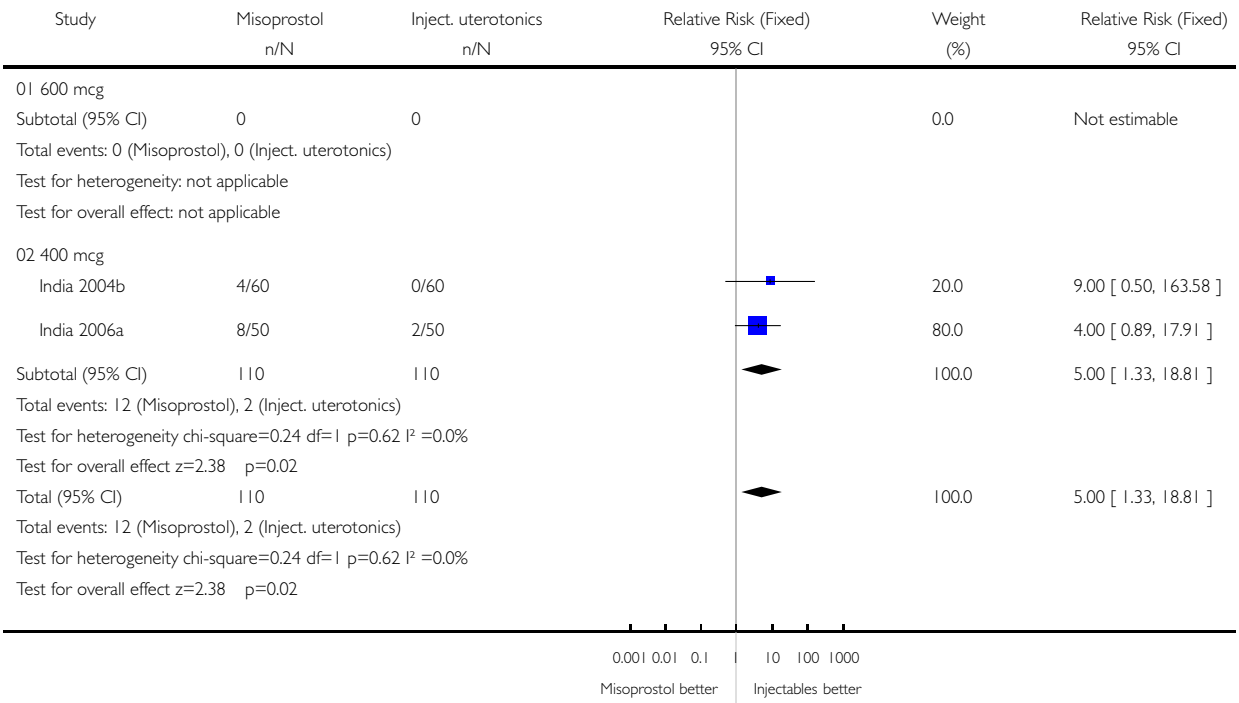
Study	Misoprostol n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 600 mcg					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 400 mcg					
India 2006a	13/50	2/50		80.0	6.50 [1.55, 27.33]
Subtotal (95% CI)	50	50		80.0	6.50 [1.55, 27.33]
Total events: 13 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.55 p=0.01					
03 50 mcg					
Colombia 2002	1/25	0/25		20.0	3.00 [0.13, 70.30]
Subtotal (95% CI)	25	25		20.0	3.00 [0.13, 70.30]
Total events: 1 (Misoprostol), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					
Total (95% CI)	75	75		100.0	5.80 [1.58, 21.24]
Total events: 14 (Misoprostol), 2 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.19 df=1 p=0.66 I^2 =0.0%					
Test for overall effect z=2.65 p=0.008					

Analysis 08.19. Comparison 08 Sublingual misoprostol versus injectable uterotonic, Outcome 19 Pyrexia >= 38 degrees C

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 08 Sublingual misoprostol versus injectable uterotonic

Outcome: 19 Pyrexia >= 38 degrees C

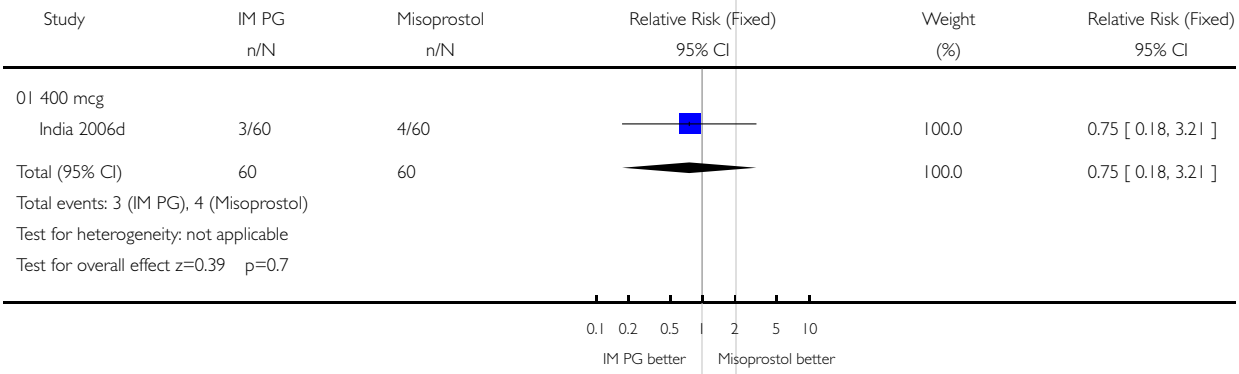


Analysis 09.02. Comparison 09 Intramuscular prostaglandin versus rectal misoprostol, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 09 Intramuscular prostaglandin versus rectal misoprostol

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

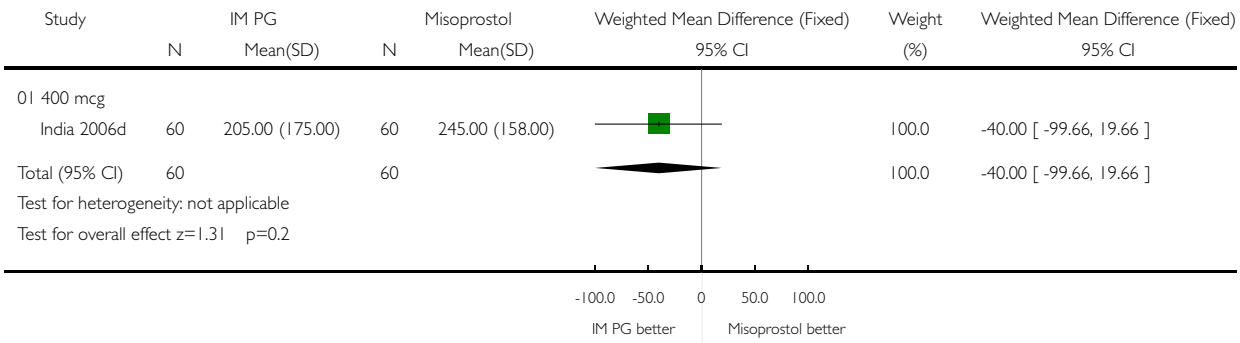


Analysis 09.03. Comparison 09 Intramuscular prostaglandin versus rectal misoprostol, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 09 Intramuscular prostaglandin versus rectal misoprostol

Outcome: 03 Blood loss (ml)

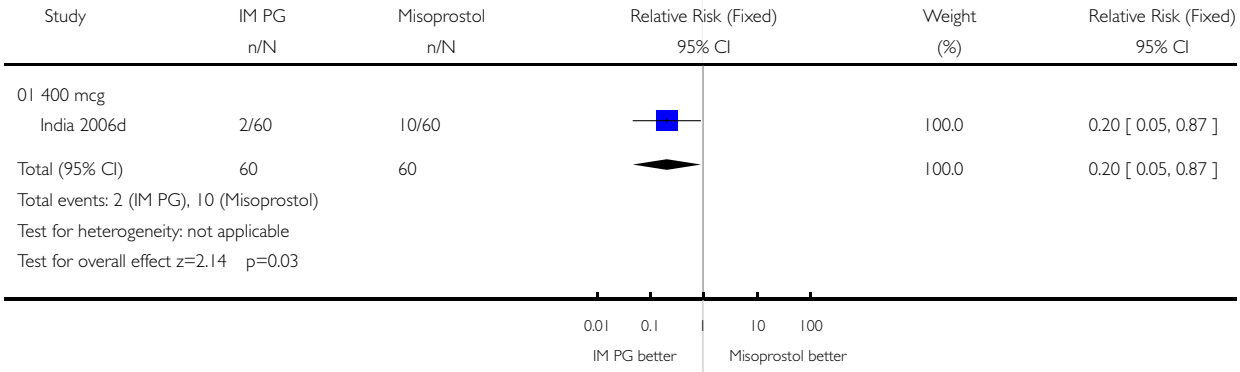


Analysis 09.04. Comparison 09 Intramuscular prostaglandin versus rectal misoprostol, Outcome 04 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 09 Intramuscular prostaglandin versus rectal misoprostol

Outcome: 04 Use of additional uterotonics

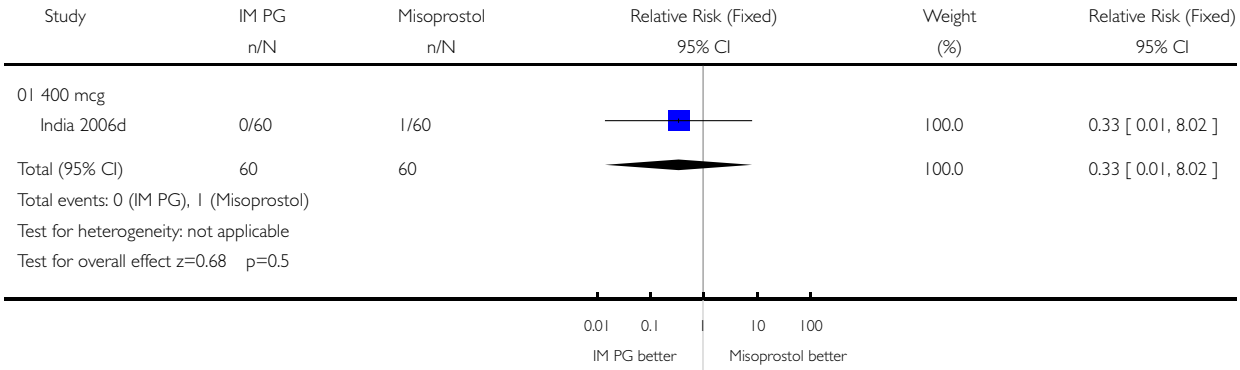


Analysis 09.05. Comparison 09 Intramuscular prostaglandin versus rectal misoprostol, Outcome 05 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 09 Intramuscular prostaglandin versus rectal misoprostol

Outcome: 05 Blood transfusion

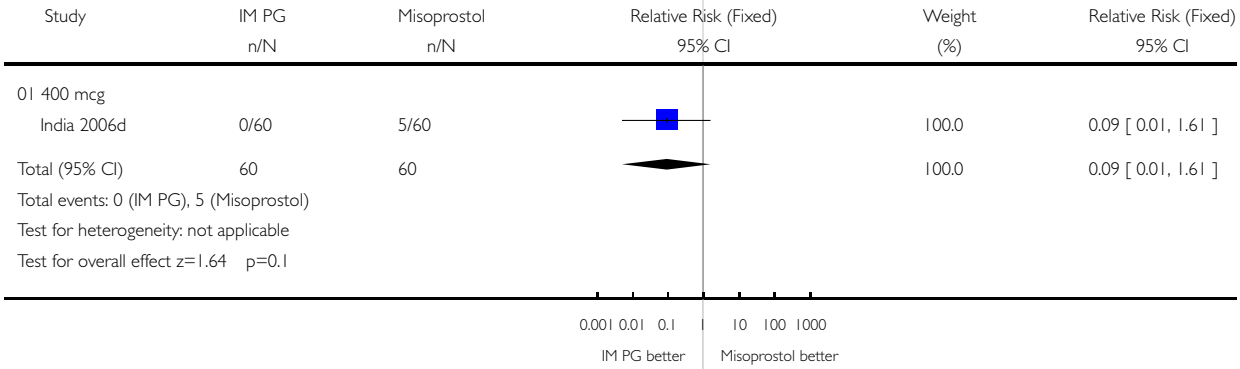


Analysis 09.06. Comparison 09 Intramuscular prostaglandin versus rectal misoprostol, Outcome 06 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 09 Intramuscular prostaglandin versus rectal misoprostol

Outcome: 06 Any shivering



Analysis 10.01. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 01 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 01 Postpartum haemorrhage (>= 500 ml)

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Holland 1991	5/22	10/24		100.0	0.55 [0.22, 1.35]
Total (95% CI)	22	24		100.0	0.55 [0.22, 1.35]
Total events: 5 (IM PG), 10 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.31 p=0.2					

Analysis 10.02. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Holland 1991	1/22	3/24		100.0	0.36 [0.04, 3.24]
Total (95% CI)	22	24		100.0	0.36 [0.04, 3.24]
Total events: 1 (IM PG), 3 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.91 p=0.4					

Analysis 10.03. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 03 Blood loss (ml)

Study	IM PG N	IM PG Mean(SD)	Nothing/placebo N	Nothing/placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Holland 1991	22	324.00 (302.00)	24	548.00 (376.00)		100.0	-224.00 [-420.35, -27.65]
Total (95% CI)	22		24			100.0	-224.00 [-420.35, -27.65]
Test for heterogeneity: not applicable							
Test for overall effect z=2.24 p=0.03							

Analysis 10.04. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 04 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 04 Use of additional uterotonics

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Holland 1991	0/22	2/24		100.0	0.22 [0.01, 4.29]
Total (95% CI)	22	24		100.0	0.22 [0.01, 4.29]
Total events: 0 (IM PG), 2 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.00 p=0.3					

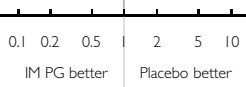
Analysis 10.06. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 06 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 06 Manual removal of placenta

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Holland 1991	0/22	0/24		0.0	Not estimable
Total (95% CI)	22	24		0.0	Not estimable
Total events: 0 (IM PG), 0 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



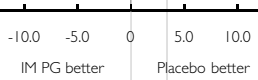
Analysis 10.07. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 07 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 07 Duration of third stage (minutes)

Study	IM PG N	IM PG Mean(SD)	Nothing/placebo N	Nothing/placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Holland 1991	22	8.10 (7.50)	24	11.70 (6.40)		100.0	-3.60 [-7.65, 0.45]
Total (95% CI)	22		24			100.0	-3.60 [-7.65, 0.45]
Test for heterogeneity: not applicable							
Test for overall effect z=1.74 p=0.08							



Analysis 10.09. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 09 Any side-effect

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 09 Any side-effect

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Holland 1991	0/22	1/24		100.0	0.36 [0.02, 8.46]
Total (95% CI)	22	24		100.0	0.36 [0.02, 8.46]
Total events: 0 (IM PG), 1 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					

Analysis 10.10. Comparison 10 Intramuscular prostaglandin versus no uterotonic/placebo, Outcome 10 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 10 Intramuscular prostaglandin versus no uterotonic/placebo

Outcome: 10 Nausea

Study	IM PG n/N	Nothing/placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Holland 1991	0/22	1/24		100.0	0.36 [0.02, 8.46]
Total (95% CI)	22	24		100.0	0.36 [0.02, 8.46]
Total events: 0 (IM PG), 1 (Nothing/placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					

Analysis 11.01. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 01 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 01 Postpartum haemorrhage (>= 500 ml)

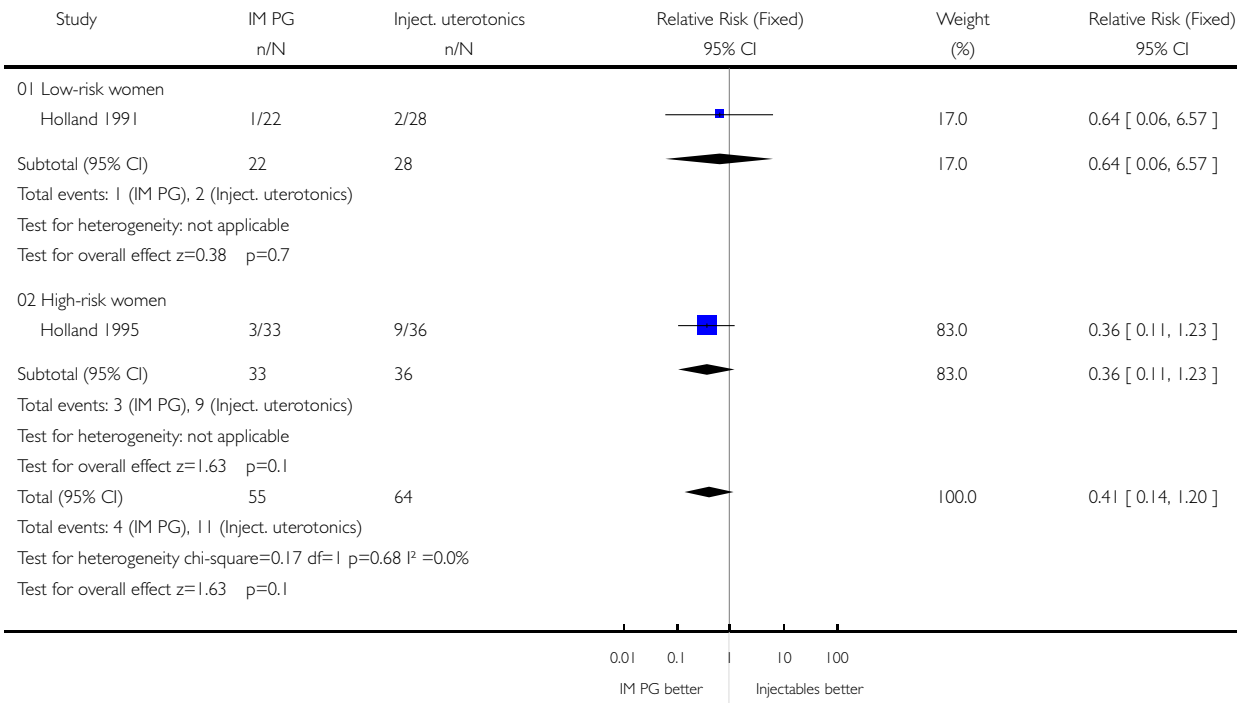
Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
× Egypt 1993	0/73	0/77		0.0	Not estimable
Holland 1991	5/22	7/28		25.2	0.91 [0.33, 2.48]
Subtotal (95% CI)	95	105		25.2	0.91 [0.33, 2.48]
Total events: 5 (IM PG), 7 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.19 p=0.9					
02 High-risk women					
Holland 1995	16/33	16/36		62.6	1.09 [0.66, 1.81]
India 2001b	2/40	3/40		12.3	0.67 [0.12, 3.78]
Subtotal (95% CI)	73	76		74.8	1.02 [0.62, 1.68]
Total events: 18 (IM PG), 19 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.30 df=1 p=0.59 I^2 =0.0%					
Test for overall effect z=0.08 p=0.9					
Total (95% CI)	168	181		100.0	0.99 [0.64, 1.55]
Total events: 23 (IM PG), 26 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.36 df=2 p=0.83 I^2 =0.0%					
Test for overall effect z=0.03 p=1					

Analysis 11.02. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)



Analysis 11.03. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 03 Blood loss (ml)

Study	IM PG		Inject. uterotonics		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
01 Low-risk women							
Egypt 1993	73	85.20 (39.80)	77	145.30 (44.40)		45.0	-60.10 [-73.58, -46.62]
Holland 1991	22	324.00 (302.00)	28	374.00 (279.00)		0.3	-50.00 [-213.11, 113.11]
United Kingdom 1994	30	645.00 (278.00)	30	605.00 (303.00)		0.4	40.00 [-107.15, 187.15]
Subtotal (95% CI)	125		135			45.7	-59.20 [-72.58, -45.83]
Test for heterogeneity chi-square=1.78 df=2 p=0.41 I² =0.0%							
Test for overall effect z=8.67 p<0.00001							
02 High-risk women							
Egypt 1997	45	93.10 (26.16)	43	126.20 (32.13)		54.2	-33.10 [-45.37, -20.83]
Holland 1995	33	568.00 (457.00)	36	717.00 (685.00)		0.1	-149.00 [-421.73, 123.73]
Subtotal (95% CI)	78		79			54.3	-33.33 [-45.60, -21.07]
Test for heterogeneity chi-square=0.69 df=1 p=0.41 I² =0.0%							
Test for overall effect z=5.33 p<0.00001							
Total (95% CI)	203		214			100.0	-45.14 [-54.18, -36.11]
Test for heterogeneity chi-square=10.27 df=4 p=0.04 I² =61.1%							
Test for overall effect z=9.79 p<0.00001							

Analysis 11.04. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 04 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 04 Use of additional uterotonics

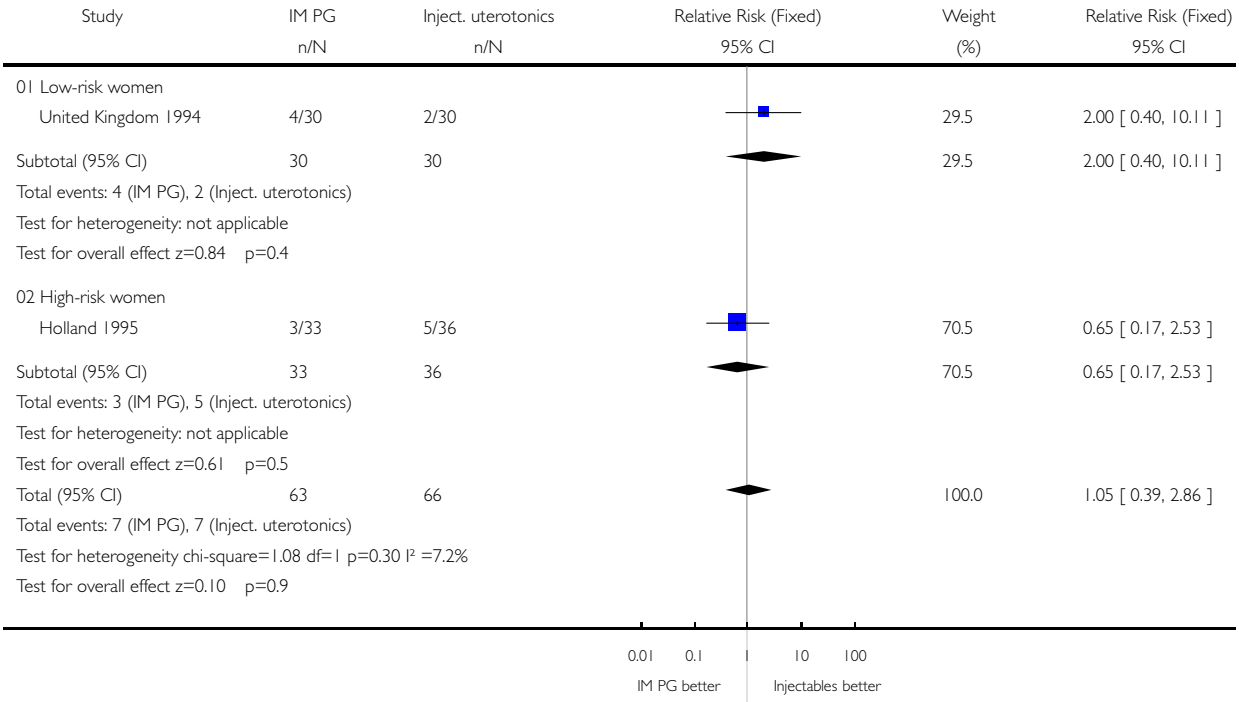
Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
× Holland 1991	0/22	0/28		0.0	Not estimable
Singapore 1995	1/54	1/58		49.1	1.07 [0.07, 16.75]
United Kingdom 1994	3/30	1/30		50.9	3.00 [0.33, 27.23]
Subtotal (95% CI)	106	116		100.0	2.05 [0.39, 10.92]
Total events: 4 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.33 df=1 p=0.57 I^2 =0.0%					
Test for overall effect z=0.84 p=0.4					
02 High-risk women					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	106	116		100.0	2.05 [0.39, 10.92]
Total events: 4 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.33 df=1 p=0.57 I^2 =0.0%					
Test for overall effect z=0.84 p=0.4					

Analysis 11.05. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 05 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 05 Blood transfusion

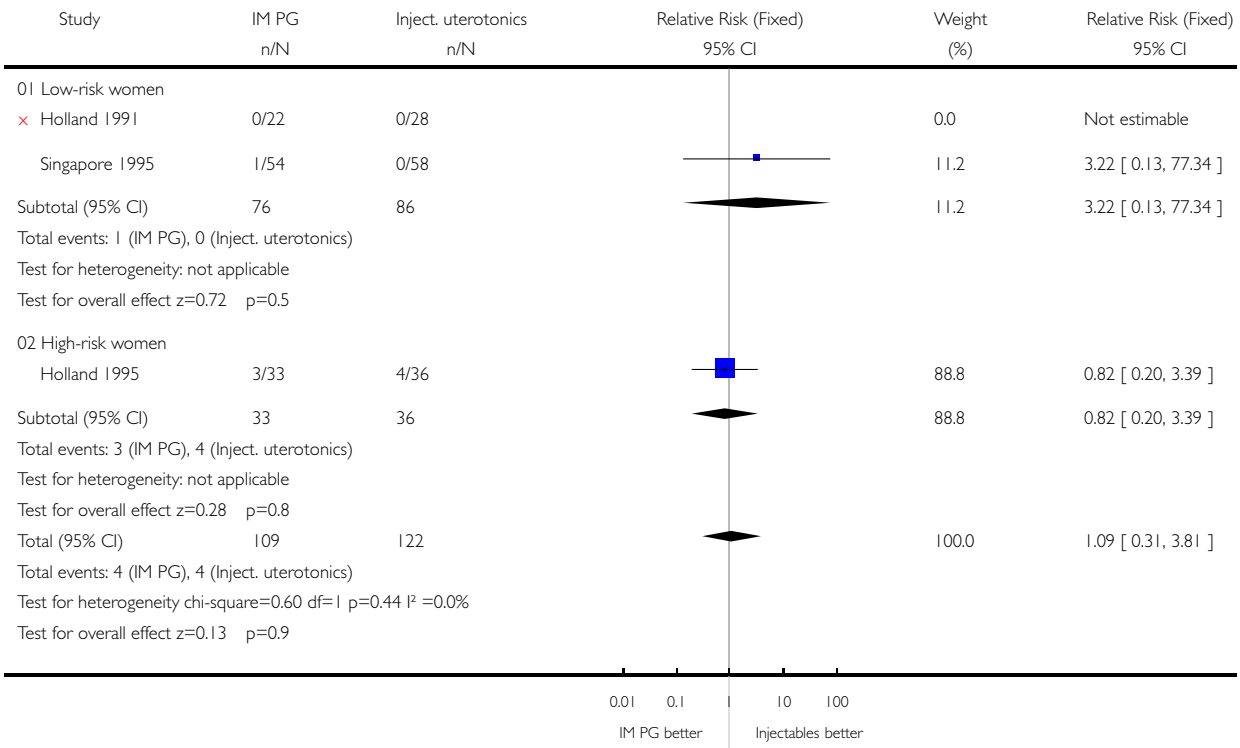


Analysis 11.06. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 06 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 06 Manual removal of placenta



Analysis 11.07. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 07 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 07 Duration of third stage (minutes)

Study	IM PG		Inject. uterotonics		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
01 Low-risk women							
Egypt 1993	73	2.30 (0.80)	77	3.40 (1.20)		70.0	-1.10 [-1.42, -0.78]
Holland 1991	22	8.10 (7.50)	28	9.90 (7.40)		0.4	-1.80 [-5.96, 2.36]
Subtotal (95% CI)	95		105			70.5	-1.10 [-1.43, -0.78]
Test for heterogeneity chi-square=0.11 df=1 p=0.74 I^2 =0.0%							
Test for overall effect z=6.68 p<0.00001							
02 High-risk women							
Egypt 1997	45	2.20 (0.74)	43	3.50 (1.51)		29.5	-1.30 [-1.80, -0.80]
Holland 1995	33	18.20 (32.90)	36	14.00 (18.90)		0.0	4.20 [-8.61, 17.01]
Subtotal (95% CI)	78		79			29.5	-1.29 [-1.79, -0.79]
Test for heterogeneity chi-square=0.71 df=1 p=0.40 I^2 =0.0%							
Test for overall effect z=5.06 p<0.00001							
Total (95% CI)	173		184			100.0	-1.16 [-1.43, -0.89]
Test for heterogeneity chi-square=1.19 df=3 p=0.75 I^2 =0.0%							
Test for overall effect z=8.36 p<0.00001							

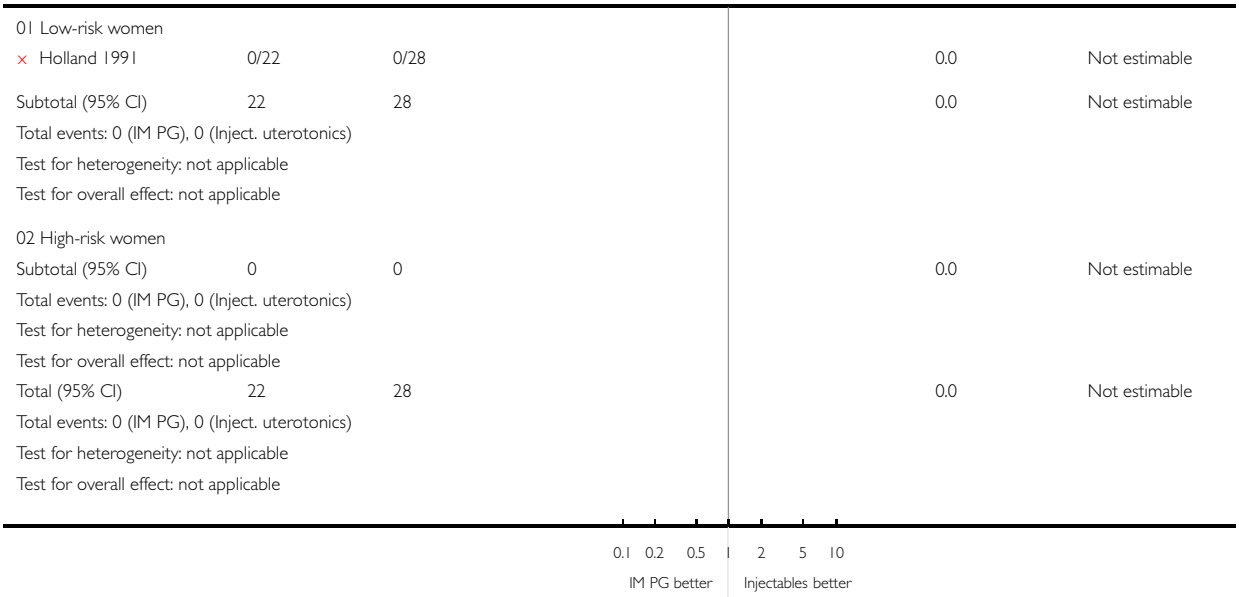
Analysis 11.09. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 09 Any side-effect

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 09 Any side-effect

Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
× Holland 1991	0/22	0/28		0.0	Not estimable
Subtotal (95% CI)	22	28		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 High-risk women					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	22	28		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

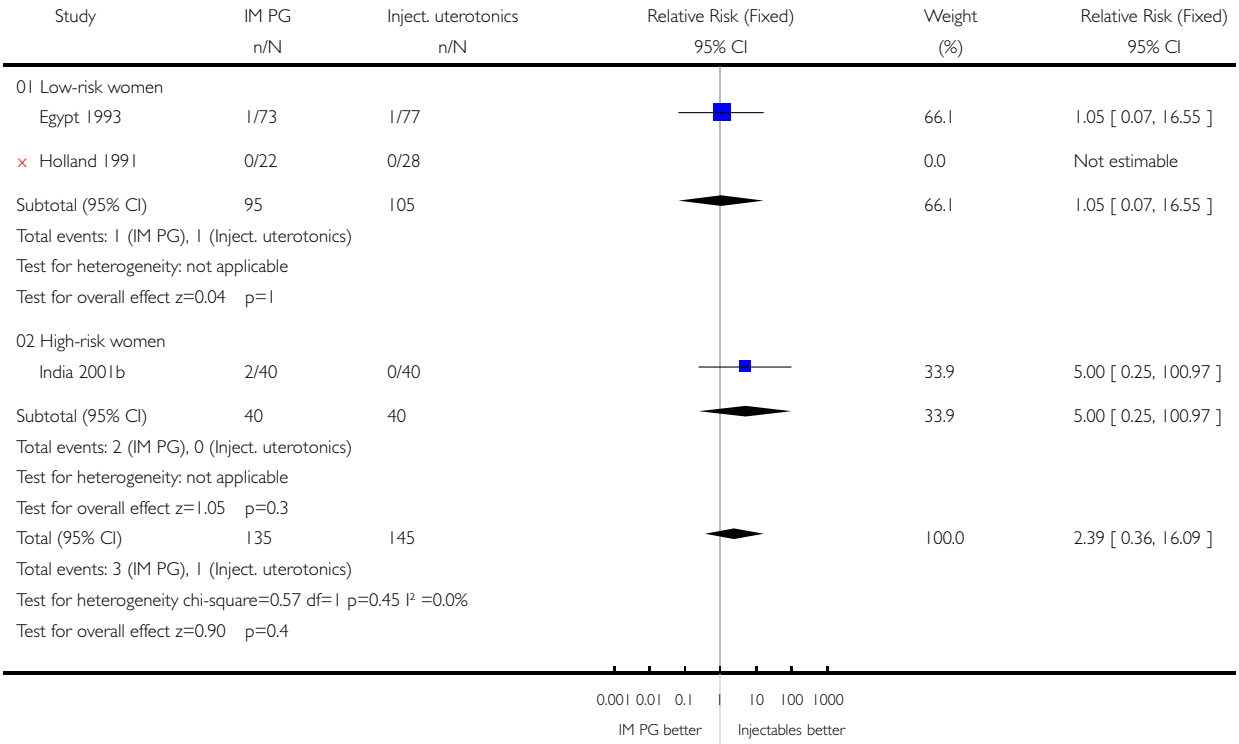


Analysis 11.10. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 10 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 10 Nausea



Analysis 11.11. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 11 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 11 Vomiting

Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
Egypt 1993	12/73	1/77		66.1	12.66 [1.69, 94.91]
United Kingdom 1994	3/30	0/30		33.9	7.00 [0.38, 129.93]
Subtotal (95% CI)	103	107		100.0	10.74 [2.06, 56.02]
Total events: 15 (IM PG), 1 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.11 df=1 p=0.74 I^2 =0.0%					
Test for overall effect z=2.82 p=0.005					
02 High-risk women					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	103	107		100.0	10.74 [2.06, 56.02]
Total events: 15 (IM PG), 1 (Inject. uterotonics)					
Test for heterogeneity chi-square=0.11 df=1 p=0.74 I^2 =0.0%					
Test for overall effect z=2.82 p=0.005					

Analysis 11.12. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 12 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 12 Headache

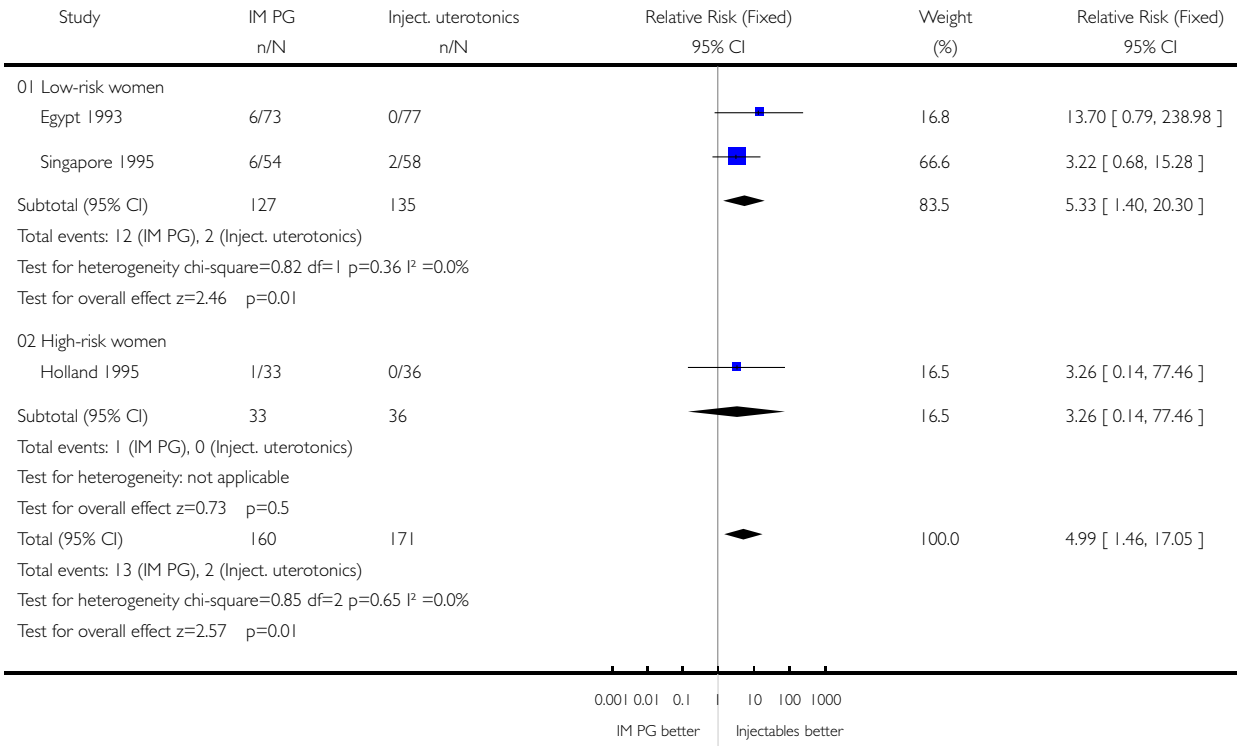
Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 High-risk women					
India 2001b	4/40	2/40		100.0	2.00 [0.39, 10.31]
Subtotal (95% CI)	40	40		100.0	2.00 [0.39, 10.31]
Total events: 4 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.83 p=0.4					
Total (95% CI)	40	40		100.0	2.00 [0.39, 10.31]
Total events: 4 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.83 p=0.4					

Analysis 11.13. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 13 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 13 Abdominal pain



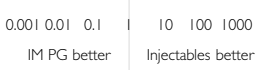
Analysis 11.14. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 14 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 14 Diarrhoea

Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
Egypt 1993	2/73	0/77		14.1	5.27 [0.26, 107.96]
Singapore 1995	16/54	1/58		27.9	17.19 [2.36, 125.22]
United Kingdom 1994	0/30	1/30		43.5	0.33 [0.01, 7.87]
Subtotal (95% CI)	157	165		85.5	6.65 [2.03, 21.85]
Total events: 18 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity chi-square=4.34 df=2 p=0.11 I^2 =54.0%					
Test for overall effect z=3.12 p=0.002					
02 High-risk women					
India 2001b	7/40	0/40		14.5	15.00 [0.89, 254.13]
Subtotal (95% CI)	40	40		14.5	15.00 [0.89, 254.13]
Total events: 7 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.88 p=0.06					
Total (95% CI)	197	205		100.0	7.86 [2.64, 23.46]
Total events: 25 (IM PG), 2 (Inject. uterotonics)					
Test for heterogeneity chi-square=4.70 df=3 p=0.19 I^2 =36.2%					
Test for overall effect z=3.70 p=0.0002					



Analysis 11.16. Comparison 11 Intramuscular prostaglandin versus injectable uterotonics, Outcome 16 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 11 Intramuscular prostaglandin versus injectable uterotonics

Outcome: 16 Pyrexia (>= 38 degrees C)

Study	IM PG n/N	Inject. uterotonics n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Low-risk women					
× Singapore 1995	0/54	0/58		0.0	Not estimable
Subtotal (95% CI)	54	58		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 High-risk women					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	54	58		0.0	Not estimable
Total events: 0 (IM PG), 0 (Inject. uterotonics)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 12.01. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 01 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 01 Postpartum haemorrhage (>= 500 ml)

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
WHO 1999	45/199	51/198		100.0	0.88 [0.62, 1.24]
Total (95% CI)	199	198		100.0	0.88 [0.62, 1.24]
Total events: 45 (Misoprostol 600 mcg), 51 (Misoprostol 400 mcg)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.73 p=0.5					

Analysis 12.02. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 02 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 02 Severe postpartum haemorrhage (>= 1000 ml)

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	17/200	16/200		53.3	1.06 [0.55, 2.04]
WHO 1999	8/199	14/198		46.7	0.57 [0.24, 1.33]
Total (95% CI)	399	398		100.0	0.83 [0.50, 1.39]

Total events: 25 (Misoprostol 600 mcg), 30 (Misoprostol 400 mcg)

Test for heterogeneity chi-square=1.32 df=1 p=0.25 I^2 =24.0%

Test for overall effect z=0.71 p=0.5

Analysis 12.03. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 03 Blood loss (ml)

Study	Misoprostol 600 mcg N	Mean(SD)	Misoprostol 400 mcg N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
WHO 1999	199	341.00 (295.00)	198	371.00 (327.00)		100.0	-30.00 [-91.27, 31.27]
Total (95% CI)	199		198			100.0	-30.00 [-91.27, 31.27]

Test for heterogeneity: not applicable

Test for overall effect z=0.96 p=0.3

Analysis 12.04. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 04 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 04 Use of additional uterotonics

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	32/200	28/200		54.8	1.14 [0.72, 1.82]
WHO 1999	18/199	23/198		45.2	0.78 [0.43, 1.40]
Total (95% CI)	399	398		100.0	0.98 [0.68, 1.41]

Total events: 50 (Misoprostol 600 mcg), 51 (Misoprostol 400 mcg)

Test for heterogeneity chi-square=1.01 df=1 p=0.31 I^2 =1.0%

Test for overall effect z=0.12 p=0.9

Analysis 12.05. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 05 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 05 Blood transfusion

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× South Africa 1998d	0/200	0/200		0.0	Not estimable
× WHO 1999	0/199	0/198		0.0	Not estimable
Total (95% CI)	399	398		0.0	Not estimable

Total events: 0 (Misoprostol 600 mcg), 0 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect: not applicable

Analysis 12.06. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 06 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 06 Manual removal of placenta

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	2/200	0/200		11.1	5.00 [0.24, 103.49]
WHO 1999	3/199	4/198		88.9	0.75 [0.17, 3.29]
Total (95% CI)	399	398		100.0	1.22 [0.35, 4.20]

Total events: 5 (Misoprostol 600 mcg), 4 (Misoprostol 400 mcg)

Test for heterogeneity chi-square=1.25 df=1 p=0.26 I^2 =20.2%

Test for overall effect z=0.31 p=0.8

Analysis 12.07. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 07 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 07 Duration of third stage (minutes)

Study	Misoprostol 600 mcg N	Mean(SD)	Misoprostol 400 mcg N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
WHO 1999	199	6.40 (6.62)	198	8.60 (14.53)		100.0	-2.20 [-4.42, 0.02]
Total (95% CI)	199		198			100.0	-2.20 [-4.42, 0.02]

Test for heterogeneity: not applicable

Test for overall effect z=1.94 p=0.05

Analysis 12.08. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 08 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 08 Third stage >= 30 minutes

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	3/200	1/200		100.0	3.00 [0.31, 28.60]
Total (95% CI)	200	200		100.0	3.00 [0.31, 28.60]
Total events: 3 (Misoprostol 600 mcg), 1 (Misoprostol 400 mcg)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.96 p=0.3					

Analysis 12.10. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 10 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 10 Nausea

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	1/199	1/199		66.4	1.00 [0.06, 15.88]
WHO 1999	1/199	0/195		33.6	2.94 [0.12, 71.73]
Total (95% CI)	398	394		100.0	1.65 [0.22, 12.48]
Total events: 2 (Misoprostol 600 mcg), 1 (Misoprostol 400 mcg)					
Test for heterogeneity chi-square=0.25 df=1 p=0.62 I^2 =0.0%					
Test for overall effect z=0.49 p=0.6					

Analysis 12.11. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 11 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 11 Vomiting

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	1/199	1/199		100.0	1.00 [0.06, 15.88]
× WHO 1999	0/199	0/195		0.0	Not estimable
Total (95% CI)	398	394		100.0	1.00 [0.06, 15.88]

Total events: 1 (Misoprostol 600 mcg), 1 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.00 p=1

Analysis 12.12. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 12 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

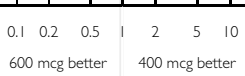
Outcome: 12 Headache

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	3/199	2/199		100.0	1.50 [0.25, 8.88]
Total (95% CI)	199	199		100.0	1.50 [0.25, 8.88]

Total events: 3 (Misoprostol 600 mcg), 2 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.45 p=0.7



Analysis 12.13. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 13 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 13 Abdominal pain

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	12/199	8/199		100.0	1.50 [0.63, 3.59]
Total (95% CI)	199	199		100.0	1.50 [0.63, 3.59]

Total events: 12 (Misoprostol 600 mcg), 8 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.91 p=0.4

Analysis 12.14. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 14 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 14 Diarrhoea

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
WHO 1999	4/199	0/198		100.0	8.96 [0.49, 165.23]
Total (95% CI)	199	198		100.0	8.96 [0.49, 165.23]

Total events: 4 (Misoprostol 600 mcg), 0 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=1.47 p=0.1

Analysis 12.15. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 15 Shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 15 Shivering

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	81/199	65/199		63.0	1.25 [0.96, 1.62]
WHO 1999	56/199	38/198		37.0	1.47 [1.02, 2.11]
Total (95% CI)	398	397		100.0	1.33 [1.07, 1.64]

Total events: 137 (Misoprostol 600 mcg), 103 (Misoprostol 400 mcg)

Test for heterogeneity chi-square=0.52 df=1 p=0.47 I^2 =0.0%

Test for overall effect z=2.61 p=0.009

Analysis 12.16. Comparison 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral, Outcome 16 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 12 Drug/dose: misoprostol 600 mcg oral versus 400 mcg oral

Outcome: 16 Pyrexia (>= 38 degrees C)

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
South Africa 1998d	53/200	28/200		87.4	1.89 [1.25, 2.86]
WHO 1999	15/199	4/195		12.6	3.67 [1.24, 10.88]
Total (95% CI)	399	395		100.0	2.12 [1.44, 3.12]

Total events: 68 (Misoprostol 600 mcg), 32 (Misoprostol 400 mcg)

Test for heterogeneity chi-square=1.27 df=1 p=0.26 I^2 =21.5%

Test for overall effect z=3.80 p=0.0001

Analysis 13.01. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 01 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 01 Manual removal of placenta

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	0/92	2/91		100.0	0.20 [0.01, 4.06]
Total (95% CI)	92	91		100.0	0.20 [0.01, 4.06]

Total events: 0 (Misoprostol 600 mcg), 2 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=1.05 p=0.3

Analysis 13.02. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 02 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

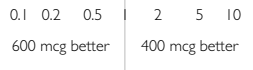
Outcome: 02 Nausea

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	11/92	21/91		100.0	0.52 [0.27, 1.01]
Total (95% CI)	92	91		100.0	0.52 [0.27, 1.01]

Total events: 11 (Misoprostol 600 mcg), 21 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=1.93 p=0.05



Analysis 13.03. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 03 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 03 Vomiting

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	8/92	10/91		100.0	0.79 [0.33, 1.91]
Total (95% CI)	92	91		100.0	0.79 [0.33, 1.91]

Total events: 8 (Misoprostol 600 mcg), 10 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.52 p=0.6

Analysis 13.04. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 04 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 04 Headache

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	9/92	14/91		100.0	0.64 [0.29, 1.39]
Total (95% CI)	92	91		100.0	0.64 [0.29, 1.39]

Total events: 9 (Misoprostol 600 mcg), 14 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=1.13 p=0.3

Analysis 13.05. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 05 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 05 Abdominal pain

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	46/92	53/91		100.0	0.86 [0.66, 1.12]
Total (95% CI)	92	91		100.0	0.86 [0.66, 1.12]

Total events: 46 (Misoprostol 600 mcg), 53 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=1.11 p=0.3

Analysis 13.06. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 06 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

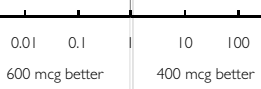
Outcome: 06 Diarrhoea

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	1/92	0/91		100.0	2.97 [0.12, 71.91]
Total (95% CI)	92	91		100.0	2.97 [0.12, 71.91]

Total events: 1 (Misoprostol 600 mcg), 0 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.67 p=0.5



Analysis 13.07. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 07 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 07 Any shivering

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	30/92	29/91		100.0	1.02 [0.67, 1.56]
Total (95% CI)	92	91		100.0	1.02 [0.67, 1.56]

Total events: 30 (Misoprostol 600 mcg), 29 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.11 p=0.9

Analysis 13.08. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 08 Severe shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 08 Severe shivering

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	14/92	18/91		100.0	0.77 [0.41, 1.45]
Total (95% CI)	92	91		100.0	0.77 [0.41, 1.45]

Total events: 14 (Misoprostol 600 mcg), 18 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.81 p=0.4

Analysis 13.09. Comparison 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal, Outcome 09 Pyrexia

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 13 Drug/dose: misoprostol 600 mcg rectal versus 400 mcg rectal

Outcome: 09 Pyrexia

Study	Misoprostol 600 mcg n/N	Misoprostol 400 mcg n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	0/92	1/91		100.0	0.33 [0.01, 7.99]
Total (95% CI)	92	91		100.0	0.33 [0.01, 7.99]

Total events: 0 (Misoprostol 600 mcg), 1 (Misoprostol 400 mcg)

Test for heterogeneity: not applicable

Test for overall effect z=0.68 p=0.5

Analysis 14.01. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 01 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 01 Manual removal of placenta

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	0/92	1/92		100.0	0.33 [0.01, 8.08]
Total (95% CI)	92	92		100.0	0.33 [0.01, 8.08]

Total events: 0 (Treatment), 1 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=0.68 p=0.5

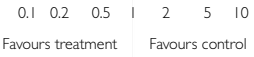
Analysis 14.02. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 02 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 02 Nausea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	11/92	20/92		100.0	0.55 [0.28, 1.08]
Total (95% CI)	92	92		100.0	0.55 [0.28, 1.08]
Total events: 11 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.73 p=0.08					



Analysis 14.03. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 03 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 03 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	8/92	3/92		100.0	2.67 [0.73, 9.74]
Total (95% CI)	92	92		100.0	2.67 [0.73, 9.74]
Total events: 8 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.48 p=0.1					

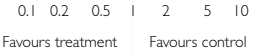
Analysis 14.04. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 04 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 04 Headache

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	9/92	6/92		100.0	1.50 [0.56, 4.04]
Total (95% CI)	92	92		100.0	1.50 [0.56, 4.04]
Total events: 9 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.80 p=0.4					



Analysis 14.05. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 05 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 05 Abdominal pain

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	46/92	47/92		100.0	0.98 [0.74, 1.30]
Total (95% CI)	92	92		100.0	0.98 [0.74, 1.30]
Total events: 46 (Treatment), 47 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.15 p=0.9					

Analysis 14.06. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 06 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 06 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	1/92	0/92		100.0	3.00 [0.12, 72.70]
Total (95% CI)	92	92		100.0	3.00 [0.12, 72.70]
Total events: 1 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

Analysis 14.07. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 07 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 07 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	30/92	65/92		100.0	0.46 [0.33, 0.64]
Total (95% CI)	92	92		100.0	0.46 [0.33, 0.64]
Total events: 30 (Treatment), 65 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.71 p<0.00001					

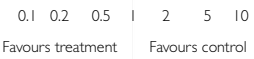
Analysis 14.08. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 08 Severe shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 08 Severe shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	14/92	51/92		100.0	0.27 [0.16, 0.46]
Total (95% CI)	92	92		100.0	0.27 [0.16, 0.46]
Total events: 14 (Treatment), 51 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.91 p<0.00001					



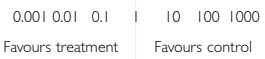
Analysis 14.09. Comparison 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral, Outcome 09 Pyrexia

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 14 Drug/route: misoprostol 600 mcg rectal versus 600 mcg oral

Outcome: 09 Pyrexia

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	0/92	8/92		100.0	0.06 [0.00, 1.00]
Total (95% CI)	92	92		100.0	0.06 [0.00, 1.00]
Total events: 0 (Treatment), 8 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.96 p=0.05					



Analysis 15.01. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 01 Manual removal of placenta

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 01 Manual removal of placenta

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	1/91	1/92		100.0	1.01 [0.06, 15.92]
Total (95% CI)	91	92		100.0	1.01 [0.06, 15.92]
Total events: 1 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.01 p=1					

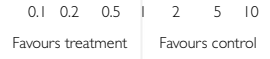
Analysis 15.02. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 02 Nausea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 02 Nausea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	21/91	20/92		100.0	1.06 [0.62, 1.82]
Total (95% CI)	91	92		100.0	1.06 [0.62, 1.82]
Total events: 21 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.22 p=0.8					



Analysis 15.03. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 03 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 03 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	10/91	3/92		100.0	3.37 [0.96, 11.85]
Total (95% CI)	91	92		100.0	3.37 [0.96, 11.85]
Total events: 10 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.89 p=0.06					

Analysis 15.04. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 04 Headache

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 04 Headache

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	14/91	6/92		100.0	2.36 [0.95, 5.87]
Total (95% CI)	91	92		100.0	2.36 [0.95, 5.87]
Total events: 14 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.85 p=0.06					

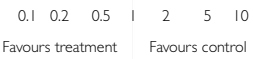
Analysis 15.05. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 05 Abdominal pain

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 05 Abdominal pain

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	53/91	47/92		100.0	1.14 [0.87, 1.49]
Total (95% CI)	91	92		100.0	1.14 [0.87, 1.49]
Total events: 53 (Treatment), 47 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.97 p=0.3					



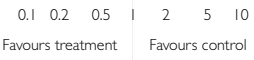
Analysis 15.06. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 06 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 06 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× United Kingdom 2003	0/91	0/92		0.0	Not estimable
Total (95% CI)	91	92		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



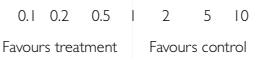
Analysis 15.07. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 07 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 07 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	29/91	65/92		100.0	0.45 [0.32, 0.63]
Total (95% CI)	91	92		100.0	0.45 [0.32, 0.63]
Total events: 29 (Treatment), 65 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.76 p<0.00001					



Analysis 15.08. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 08 Severe shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 08 Severe shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	18/91	51/92		100.0	0.36 [0.23, 0.56]
Total (95% CI)	91	92		100.0	0.36 [0.23, 0.56]
Total events: 18 (Treatment), 51 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.46 p<0.00001					

Analysis 15.09. Comparison 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral, Outcome 09 Pyrexia

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 15 Drug/dose/route: misoprostol 400 mcg rectal versus 600 mcg oral

Outcome: 09 Pyrexia

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
United Kingdom 2003	1/91	1/92		100.0	1.01 [0.06, 15.92]
Total (95% CI)	91	92		100.0	1.01 [0.06, 15.92]
Total events: 1 (Treatment), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.01 p=1					

Analysis 16.01. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	11/401	14/407		100.0	0.80 [0.37, 1.74]
Total (95% CI)	401	407		100.0	0.80 [0.37, 1.74]
Total events: 11 (Treatment), 14 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					

Analysis 16.02. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	28/401	33/407		100.0	0.86 [0.53, 1.40]
Total (95% CI)	401	407		100.0	0.86 [0.53, 1.40]
Total events: 28 (Treatment), 33 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.60 p=0.5					

Analysis 16.03. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 03 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 03 Duration of third stage (minutes)

Study	Treatment N	Mean(SD)	Control N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Turkey 2002	401	8.60 (3.30)	407	8.70 (1.70)		100.0	-0.10 [-0.46, 0.26]
Total (95% CI)	401		407			100.0	-0.10 [-0.46, 0.26]
Test for heterogeneity: not applicable							
Test for overall effect z=0.54 p=0.6							

Analysis 16.04. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 04 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 04 Third stage >= 30 minutes

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	2/401	2/407		100.0	1.01 [0.14, 7.17]
Total (95% CI)	401	407		100.0	1.01 [0.14, 7.17]
Total events: 2 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.01 p=1					

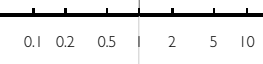
Analysis 16.05. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 05 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 05 Blood transfusion

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	4/401	13/407		100.0	0.31 [0.10, 0.95]
Total (95% CI)	401	407		100.0	0.31 [0.10, 0.95]
Total events: 4 (Treatment), 13 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.05 p=0.04					



Analysis 16.06. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 06 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 06 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	3/401	2/407		100.0	1.52 [0.26, 9.06]
Total (95% CI)	401	407		100.0	1.52 [0.26, 9.06]
Total events: 3 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.46 p=0.6					

Analysis 16.07. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 07 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 07 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	9/401	9/407		100.0	1.01 [0.41, 2.53]
Total (95% CI)	401	407		100.0	1.01 [0.41, 2.53]
Total events: 9 (Treatment), 9 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.03 p=1					

Analysis 16.08. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 08 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 08 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	52/401	16/407		100.0	3.30 [1.92, 5.68]
Total (95% CI)	401	407		100.0	3.30 [1.92, 5.68]
Total events: 52 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.31 p=0.00002					

Analysis 16.09. Comparison 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 09 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 16 Rectal misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 09 Pyrexia (>= 38 degrees C)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	19/401	6/407		100.0	3.21 [1.30, 7.96]
Total (95% CI)	401	407		100.0	3.21 [1.30, 7.96]
Total events: 19 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.52 p=0.01					

Analysis 17.01. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	11/401	17/396		100.0	0.64 [0.30, 1.35]
Total (95% CI)	401	396		100.0	0.64 [0.30, 1.35]
Total events: 11 (Treatment), 17 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.18 p=0.2					

Analysis 17.02. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	28/401	39/396		100.0	0.71 [0.45, 1.13]
Total (95% CI)	401	396		100.0	0.71 [0.45, 1.13]
Total events: 28 (Treatment), 39 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.45 p=0.1					

Analysis 17.03. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 03 Duration of third stage (minutes)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 03 Duration of third stage (minutes)

Study	Treatment		Control		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Turkey 2002	401	8.60 (3.30)	396	9.30 (4.00)		100.0	-0.70 [-1.21, -0.19]
Total (95% CI)	401		396			100.0	-0.70 [-1.21, -0.19]
Test for heterogeneity: not applicable							
Test for overall effect z=2.69 p=0.007							

Analysis 17.04. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 04 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 04 Third stage >= 30 minutes

Study	Treatment	Control	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Turkey 2002	2/401	12/396		100.0	0.16 [0.04, 0.73]
Total (95% CI)	401	396		100.0	0.16 [0.04, 0.73]
Total events: 2 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.37 p=0.02					

Analysis 17.05. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 05 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 05 Blood transfusion

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	4/401	12/396		100.0	0.33 [0.11, 1.01]
Total (95% CI)	401	396		100.0	0.33 [0.11, 1.01]
Total events: 4 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.94 p=0.05					

Analysis 17.06. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 06 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 06 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	3/401	2/396		100.0	1.48 [0.25, 8.82]
Total (95% CI)	401	396		100.0	1.48 [0.25, 8.82]
Total events: 3 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.43 p=0.7					

Analysis 17.07. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 07 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 07 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	9/401	11/396		100.0	0.81 [0.34, 1.93]
Total (95% CI)	401	396		100.0	0.81 [0.34, 1.93]
Total events: 9 (Treatment), 11 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.48 p=0.6					

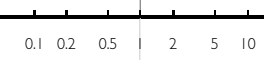
Analysis 17.08. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 08 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 08 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	52/401	47/396		100.0	1.09 [0.76, 1.58]
Total (95% CI)	401	396		100.0	1.09 [0.76, 1.58]
Total events: 52 (Treatment), 47 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.47 p=0.6					



Analysis 17.09. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 09 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 09 Pyrexia (>= 38 degrees C)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2002	19/401	16/396		100.0	1.17 [0.61, 2.25]
Total (95% CI)	401	396		100.0	1.17 [0.61, 2.25]
Total events: 19 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.48 p=0.6					

Analysis 17.10. Comparison 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol, Outcome 10 Maternal death

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 17 Rectal misoprostol plus injectable uterotonics versus rectal misoprostol

Outcome: 10 Maternal death

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Turkey 2002	0/401	0/396		0.0	Not estimable
Total (95% CI)	401	396		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 18.01. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	6/404	15/384		100.0	0.38 [0.15, 0.97]
Total (95% CI)	404	384		100.0	0.38 [0.15, 0.97]
Total events: 6 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.02 p=0.04					

Analysis 18.02. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 02 Postpartum haemorrhage (>= 500 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 02 Postpartum haemorrhage (>= 500 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	13/404	28/384		100.0	0.44 [0.23, 0.84]
Total (95% CI)	404	384		100.0	0.44 [0.23, 0.84]
Total events: 13 (Treatment), 28 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.49 p=0.01					

Analysis 18.03. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 03 Blood loss (ml)

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Turkey 2003	404	280.00 (182.00)	384	312.00 (176.00)		100.0	-32.00 [-57.00, -7.00]
Total (95% CI)	404		384			100.0	-32.00 [-57.00, -7.00]
Test for heterogeneity: not applicable							
Test for overall effect z=2.51 p=0.01							

Analysis 18.04. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 04 Duration of third stage (mins)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 04 Duration of third stage (mins)

Study	Treatment N	Treatment Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Turkey 2003	404	8.80 (3.80)	384	8.70 (1.70)		100.0	0.10 [-0.31, 0.51]
Total (95% CI)	404		384			100.0	0.10 [-0.31, 0.51]
Test for heterogeneity: not applicable							
Test for overall effect z=0.48 p=0.6							

Analysis 18.05. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 05 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 05 Third stage >= 30 minutes

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	3/404	2/384		100.0	1.43 [0.24, 8.49]
Total (95% CI)	404	384		100.0	1.43 [0.24, 8.49]
Total events: 3 (Treatment), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.39 p=0.7					

Analysis 18.06. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 06 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 06 Blood transfusion

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	5/404	13/384		100.0	0.37 [0.13, 1.02]
Total (95% CI)	404	384		100.0	0.37 [0.13, 1.02]
Total events: 5 (Treatment), 13 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.93 p=0.05					

Analysis 18.07. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 07 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 07 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	3/404	3/384		100.0	0.95 [0.19, 4.68]
Total (95% CI)	404	384		100.0	0.95 [0.19, 4.68]
Total events: 3 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.06 p=1					

Analysis 18.08. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 08 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 08 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	13/404	12/384		100.0	1.03 [0.48, 2.23]
Total (95% CI)	404	384		100.0	1.03 [0.48, 2.23]
Total events: 13 (Treatment), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.07 p=0.9					

Analysis 18.09. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 09 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 09 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	49/404	19/384		100.0	2.45 [1.47, 4.09]
Total (95% CI)	404	384		100.0	2.45 [1.47, 4.09]
Total events: 49 (Treatment), 19 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.44 p=0.0006					

Analysis 18.10. Comparison 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics, Outcome 10 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 18 Oral misoprostol plus injectable uterotonics versus injectable uterotonics

Outcome: 10 Pyrexia (>= 38 degrees C)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	16/404	5/384		100.0	3.04 [1.13, 8.22]
Total (95% CI)	404	384		100.0	3.04 [1.13, 8.22]
Total events: 16 (Treatment), 5 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.19 p=0.03					

Analysis 19.01. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	6/404	14/388		100.0	0.41 [0.16, 1.06]
Total (95% CI)	404	388		100.0	0.41 [0.16, 1.06]
Total events: 6 (Treatment), 14 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.84 p=0.07					

Analysis 19.02. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 02 Postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 02 Postpartum haemorrhage (>= 1000 ml)

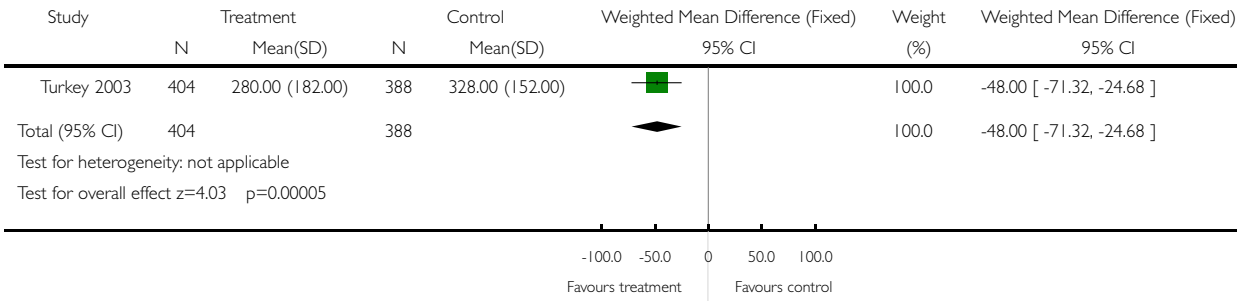
Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	13/404	35/388		100.0	0.36 [0.19, 0.66]
Total (95% CI)	404	388		100.0	0.36 [0.19, 0.66]
Total events: 13 (Treatment), 35 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.25 p=0.001					

Analysis 19.03. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 03 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 03 Blood loss (ml)

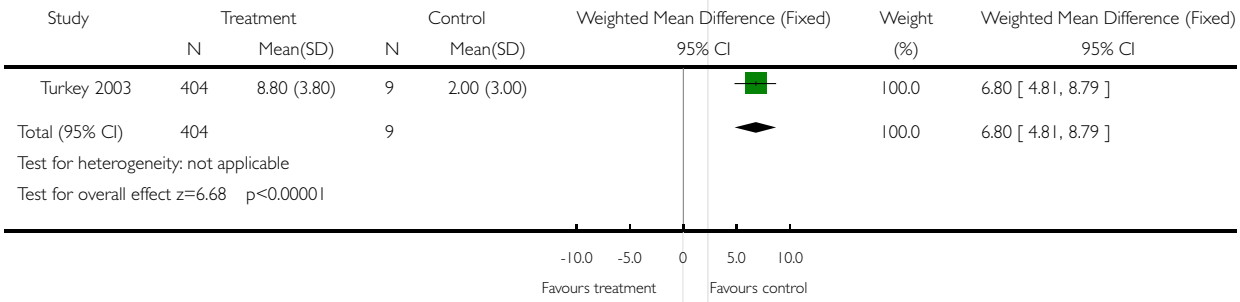


Analysis 19.04. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 04 Duration of third stage (mins)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 04 Duration of third stage (mins)



Analysis 19.05. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 05 Third stage >= 30 minutes

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 05 Third stage >= 30 minutes

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	3/404	3/388		100.0	0.96 [0.20, 4.73]
Total (95% CI)	404	388		100.0	0.96 [0.20, 4.73]
Total events: 3 (Treatment), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.05 p=1					

Analysis 19.06. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 06 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 06 Blood transfusion

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	5/404	14/388		100.0	0.34 [0.12, 0.94]
Total (95% CI)	404	388		100.0	0.34 [0.12, 0.94]
Total events: 5 (Treatment), 14 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.07 p=0.04					

Analysis 19.07. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 07 Vomiting

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 07 Vomiting

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	3/404	4/388		100.0	0.72 [0.16, 3.20]
Total (95% CI)	404	388		100.0	0.72 [0.16, 3.20]
Total events: 3 (Treatment), 4 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.43 p=0.7					

Analysis 19.08. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 08 Diarrhoea

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 08 Diarrhoea

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	13/404	15/388		100.0	0.83 [0.40, 1.73]
Total (95% CI)	404	388		100.0	0.83 [0.40, 1.73]
Total events: 13 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.49 p=0.6					

Analysis 19.09. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 09 Any shivering

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 09 Any shivering

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	49/404	44/388		100.0	1.07 [0.73, 1.57]
Total (95% CI)	404	388		100.0	1.07 [0.73, 1.57]
Total events: 49 (Treatment), 44 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.34 p=0.7					

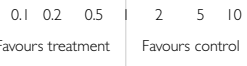
Analysis 19.10. Comparison 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol, Outcome 10 Pyrexia (>= 38 degrees C)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 19 Oral misoprostol plus injectable uterotonics versus oral misoprostol

Outcome: 10 Pyrexia (>= 38 degrees C)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Turkey 2003	16/404	17/388		100.0	0.90 [0.46, 1.76]
Total (95% CI)	404	388		100.0	0.90 [0.46, 1.76]
Total events: 16 (Treatment), 17 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.30 p=0.8					

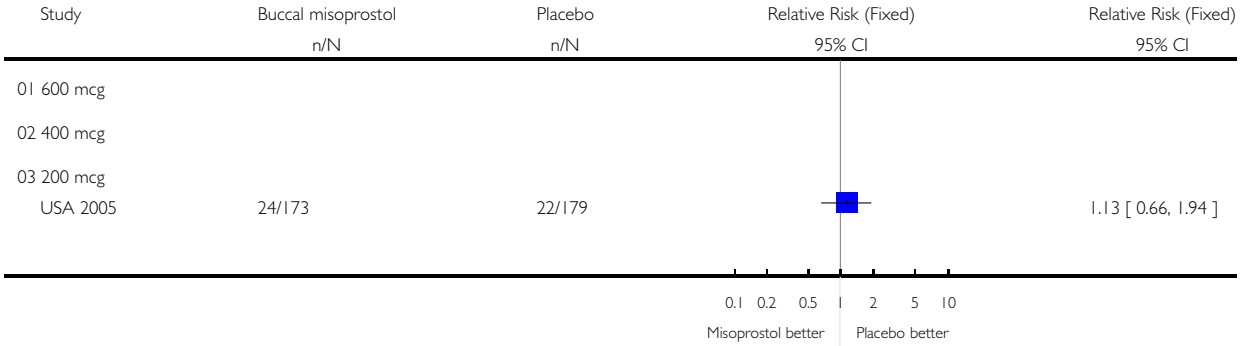


Analysis 20.01. Comparison 20 Buccal misoprostol versus no uterotonic/placebo, Outcome 01 Severe postpartum haemorrhage (>= 1000 ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 20 Buccal misoprostol versus no uterotonic/placebo

Outcome: 01 Severe postpartum haemorrhage (>= 1000 ml)

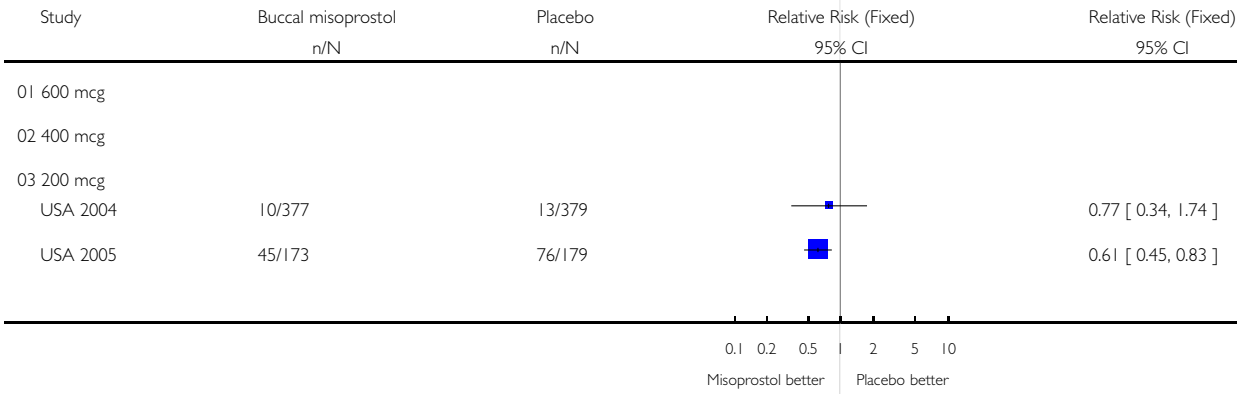


Analysis 20.02. Comparison 20 Buccal misoprostol versus no uterotonic/placebo, Outcome 02 Use of additional uterotonics

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 20 Buccal misoprostol versus no uterotonic/placebo

Outcome: 02 Use of additional uterotonics

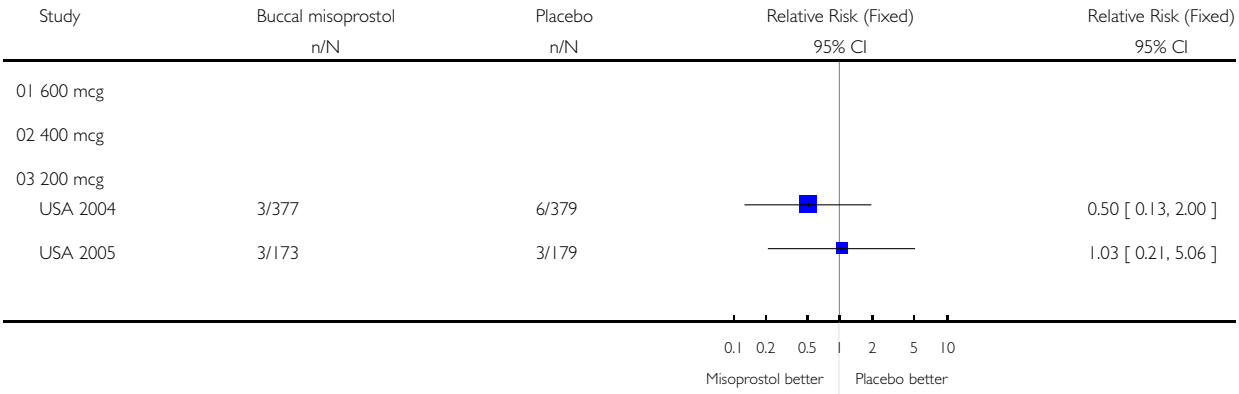


Analysis 20.03. Comparison 20 Buccal misoprostol versus no uterotonic/placebo, Outcome 03 Blood transfusion

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 20 Buccal misoprostol versus no uterotonic/placebo

Outcome: 03 Blood transfusion



Analysis 20.04. Comparison 20 Buccal misoprostol versus no uterotonic/placebo, Outcome 04 Blood loss (ml)

Review: Prostaglandins for preventing postpartum haemorrhage

Comparison: 20 Buccal misoprostol versus no uterotonic/placebo

Outcome: 04 Blood loss (ml)