Prophylactic oxytocin for the third stage of labour (Review)

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ABSTRACT

Background
Complications of the third stage of labour are a significant cause of maternal mortality worldwide.

Objectives
To examine the effect of oxytocin given prophylactically in the third stage of labour on maternal and neonatal outcomes.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group's Specialised Register of Controlled Trials (December 2004).

Selection criteria
Randomised or quasi-randomised controlled trials including pregnant women anticipating a vaginal delivery where oxytocin was given prophylactically for the third stage of labour.

Data collection and analysis
The review authors independently assessed trial quality and extracted data. Analysis was by intention to treat. Subgroup analyses were based on extent of selection bias, oxytocin in the context of active or expectant management of the third stage, and timing of administration. Results are presented as relative risks, and weighted mean difference, both with 95% confidence intervals using a fixed-effect model.

Main results
Fourteen trials are included.

In seven trials involving over 3000 women, prophylactic oxytocin showed benefits (reduced blood loss (relative risk (RR) for blood loss greater than 500 ml 0.50; 95% confidence interval (CI) 0.43 to 0.59) and need for therapeutic oxytocics (RR 0.50; 95% CI 0.39 to 0.64) compared to no uterotonics.

In six trials involving over 2800 women, there was little evidence of differential effects for oxytocin versus ergot alkaloids, except that oxytocin was associated with fewer manual removals of the placenta (RR 0.57; 95% CI 0.41 to 0.79), and with the suggestion of less raised blood pressure (RR 0.53; 95% CI 0.19 to 1.52) than with ergot alkaloids.

In five trials involving over 2800 women, there was little evidence of a synergistic effect of adding oxytocin to ergometrine versus ergometrine alone.

Authors' conclusions
Oxytocin appears to be beneficial for the prevention of postpartum haemorrhage. However, there is insufficient information about other outcomes and side-effects hence it is difficult to be confident about the trade-offs for these benefits. There seems little evidence in favour of ergot alkaloids alone compared to either oxytocin alone, or to ergometrine-oxytocin, but the data are sparse. More trials are needed in domiciliary deliveries in developing countries, which shoulder most of the burden of third stage complications.

PLAIN LANGUAGE SUMMARY

Oxytocin used routinely after birth can reduce blood loss, but more research is needed on possible adverse effects

The third stage of labour is that period from birth of the baby until delivery of the placenta. The degree of blood loss depends on how quickly the placenta separates from the uterine wall and the uterine muscle contracts. Severe blood loss - postpartum haemorrhage, is a major problem, particularly where there is poor nutrition and lack of access to treatment. The review of trials found routine use of oxytocin, a drug which helps the uterus contract, may reduce the amount of blood loss, but there is not enough evidence about adverse effects. More research is needed.

BACKGROUND

The most reliable estimates of global mortality for mothers in childbirth are reported as between 500,000 and 600,000 annually (UNICEF 1996; WHO 1990). Many of these deaths result from complications of the third stage of labour.

The third stage of labour is that period from delivery of the baby until delivery of the placenta. After delivery of the baby and cessation of umbilical cord pulsation the placenta separates from the uterine wall through the spongy lining of the womb (decidua spongiosa) and is delivered through the birth canal. The placenta separates as a result of capillary haemorrhage and the shearing effect of uterine muscle contraction. The degree of blood loss associated with placental separation and delivery depends on how quickly the placenta separates from the uterine wall and how effectively uterine muscle contracts around the placental bed (where the placenta is attached to the wall of the uterus), and the blood vessels, during and after separation, and expels the placenta through the birth canal.

Moderate loss of blood is physiological and unlikely to lead to later problems except for women who are already anaemic. The major complication associated with this stage is postpartum haemorrhage (PPH). This is not necessarily torrential bleeding, and is usually defined as bleeding from the genital tract of 500 ml or more in the first 24 hours following delivery of the baby. Alternative cut-off points of 600 ml (Beischer 1986) and 1000 ml (Burchell 1980) have also been suggested, and it has long been recognised that such clinical estimation is likely to underestimate the actual volume of blood lost by 34% to 50% (Newton 1961). This may in part explain the variation in estimated incidence of PPH between 5% and 18% (Hall 1985; Gilbert 1987; Prendiville 1988a), even within a single country like the UK, where PPH remains an important cause of maternal mortality (DoH 2004; Hall 1985; Gilbert 1987). Effects on maternal morbidity are less well documented, but are likely to include such inter-related outcomes as anaemia, fatigue and depression.

Nearly all maternal deaths (99%) occur in the developing world (Kwast 1991), where other factors, such as infection (especially HIV infection), poor nutritional status and lack of easy access to treatment, may contribute to death in the presence of severe postpartum haemorrhage. Many more women survive and suffer serious illness as a result, not only from the effects of acute anaemia but also from the interventions which a severe haemorrhage may necessitate (such as general anaesthesia, manual removal of the placenta, blood transfusion, hysterectomy). Other aspects of the management of labour such as induction and augmentation of labour, or the duration of the second stage in the context of epidural anaesthesia may also have relevance for the third stage. Reducing the likelihood of postpartum haemorrhage by avoiding the use of birth chairs in the second stage (Crowley 1991) could play a part in reducing maternal morbidity and mortality.

This review concentrates on components of such management in the third stage of labour. One component may be uterotonic drugs which increase the tone of the uterine muscles. These uterotonics were initially introduced for the treatment of PPH. Moir (Moir 1932) showed that ergometrine was the active principle on which the known uterotonic effect of ergot had depended. Reviewing its use in obstetric practice by the early 1950s, his opinion was that "Few drugs can have become so firmly established in so short a time and few drugs can be so completely indispensable as ergometrine is now" (Moir 1955). Ergometrine (ergonovine in the United States) became popular for routine management in the early 1950s. Oxytocin is a naturally occurring uterotonic, which Du Vigneaud et al synthesised and reported in 1953 (Du Vigneaud 1953). Embrey et al (Embrey 1963) reported advantages of combining this with ergometrine (as Syntometrine - oxytocin five international units plus ergometrine 0.5 mg). In order to prevent blood loss, these uterotonics and, more recently, prostaglandins are also being used for prophylactic third stage management.

While few would dispute the contribution of uterotonic drugs in the treatment of PPH, their role in routine prophylaxis is less clear. This review considers the prophylactic role of one of these uterotonics, oxytocin, in the third stage of labour. Other relevant published reviews are by Prendiville 2000, which compare active with expectant third stage management (where active management involves the package of interconnected interventions of prophylactic uterotonics, early cutting and clamping of the umbilical cord, and controlled cord traction); Gülmezoglu 2004 and McDonald 2004, which both consider the role of different prophylactic uterotonics (prostaglandins, and ergometrine-oxytocin compared to oxytocin, respectively) in third stage management; and Carroli 2001 look-

ing at the role of umbilical vein injection for the treatment of retained placenta. Subsequent third stage management reviews will consider the role of prophylactic uterotonics more generally, and of prophylactic ergot alkaloids particularly. As these interventions are very inter-related, some aspects of the role of oxytocin may be found in these other reviews (e.g. Prendiville 2000; Gülmezoglu 2004; McDonald 2004).

OBJECTIVES

The objective of this review is to examine the effect of oxytocin given prophylactically in the third stage of labour, defined as that period from birth of the baby until delivery of the placenta, on outcomes such as maternal blood loss and the length of the third stage of labour, other effects on the mother, and the outcome for the newborn baby. The objectives of this review will consider the following comparisons:

(1) oxytocin versus no uterotonics;
(2) oxytocin versus ergot alkaloids;
(3) oxytocin plus ergometrine versus ergot alkaloids.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All acceptably randomised or quasi-randomised controlled trials were considered for inclusion, with exclusions on quality grounds if there was potential for significant selection bias after trial entry.

Types of participants

All trials including pregnant women anticipating a vaginal delivery were considered, regardless of other aspects of third stage management.

Types of intervention

Oxytocin given prophylactically for the third stage of labour, at whatever dose. The current review concentrates on oxytocin given by injection, usually into a maternal vein or a muscle. The role of prophylactic prostaglandins or ergot alkaloids, and uterotonics given through the umbilical vein, or for the treatment of blood loss or retained placenta, will be the subject of other reviews and are not included here. Similarly, endogenous oxytocin (nipple stimulation) is not included in this review.

Types of outcome measures

- Postpartum haemorrhage (PPH) (reported estimates of blood loss greater than or equal to 500 ml)
- Severe PPH (clinically estimated blood loss greater than or equal to 1000 ml)
- Mean blood loss (ml)
- Maternal haemoglobin concentration (Hb) less than 9 gm/decilitre 24 to 48 hours postpartum
- Blood transfusion
- Iron tablets during the puerperium
- Therapeutic uterotonics
- Third stage greater than 20 minutes
- Third stage greater than 40 minutes
- Mean length of third stage (minutes)
- Manual removal of the placenta
- Subsequent surgical evacuation of retained products of conception
- Diastolic blood pressure greater than 100 mmHg between delivery of baby and discharge from the labour ward
- Vomiting between delivery of baby and discharge from the labour ward
- Nausea between delivery of baby and discharge from the labour ward
- Headache between delivery of baby and discharge from the labour ward
- Maternal pain during third stage of labour
- Maternal dissatisfaction with third stage management
- Secondary PPH (after 24 hours and before six weeks)
- Bleeding needing readmission or antibiotics
- Maternal fatigue at six weeks
- Apgar score less than seven at five minutes
- Admission to special care baby unit
- Jaundice (as defined by the authors)
- Not breastfeeding at discharge from hospital
- Not breastfeeding at six weeks

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group Trials Register by contacting the Trials Search Co-ordinator (December 2004).

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.

METHODS OF THE REVIEW

For the first publication, two review authors checked the titles and abstracts identified from the search. Two of the review authors obtained the full text of all studies of possible relevance for independent assessment. The methodological quality of the studies was assessed with particular concentration on allocation concealment, ranked using the Cochrane approach of adequate, uncertain or inadequate. Two review authors performed the data extraction. Trial authors were contacted for clarification where relevant. Analysis was by intention to treat.

For this update the following methods were used.

Selection of studies
We assessed for inclusion all potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion.

Assessment of methodological quality of included studies
We assessed the validity of each study using the criteria outlined in the Cochrane Reviewers' Handbook (Alderson 2004).

(1) Selection bias (randomisation and allocation concealment)
We planned to assign a quality score for each trial, using the following criteria:
(A) adequate concealment of allocation, such as telephone randomisation, consecutively numbered sealed opaque envelopes;
(B) unclear whether adequate concealment of allocation; such as list or table used, sealed envelopes, or study does not report any concealment approach;
(C) inadequate concealment of allocation, such as open list of random number tables, use of case record numbers, dates of birth or days of the week.

(2) Performance bias (blinding of participants, researchers and outcome assessment)
We planned to assess blinding using the following criteria:
(A) blinding of participants (yes/no/unclear);
(B) blinding of caregiver (yes/no/unclear);
(C) blinding of outcome assessment (yes/no/unclear).

(3) Attrition bias (loss of participants, e.g. withdrawals, dropouts, protocol deviations)
We planned to assess completeness to follow up using the following criteria:
(A) less than 5% loss of participants;
(B) 5% to 10% loss of participants;
(C) more than 10% and less than 20% loss of participants;
(D) more than 20% loss of participants.

Data extraction and management
We planned for all three review authors to extract the data and to resolve discrepancies through discussion. We planned to use the Review Manager software (RevMan 2003) to double-enter the data.

Measures of treatment effect
We planned to carry out statistical analysis using the Review Manager software (RevMan 2003) and would have used a fixed-effect meta-analysis for combining data if trials were sufficiently similar.

For dichotomous data: we planned to present results as summary relative risk with 95% confidence intervals.

For continuous data: we planned to use the weighted mean difference if outcomes were measured in the same way between trials. We planned to use the standardised mean difference to combine trials that measured the same outcome, but used different methods. If there was evidence of skewness this would have been reported.

We planned to analyse data on an intention-to-treat basis. Therefore, all participants with available data would have been included in the analysis in the group to which they were allocated, regardless of whether or not they received the allocated intervention. If in the original reports participants were not analysed in the group to which they were randomised, and there was sufficient information in the trial report, we would have attempted to restore them to the correct group.

Assessment of heterogeneity
Tests of heterogeneity between trials would have been applied if appropriate using the I^2 statistic. If we identified high levels of heterogeneity among the trials, (exceeding 50%), we would have explored it by prespecified subgroup analysis and have performed sensitivity analysis. A random-effects meta-analysis would have been used as an overall summary if considered appropriate.

Three comparisons would have been considered:
(a) oxytocin versus no uterotonics;
(b) oxytocin versus ergot alkaloids;
(c) oxytocin plus ergometrine versus ergot alkaloids.

Subgroup analyses were planned based on extent of control for selection bias, on whether the oxytocin is administered within the context of active or expectant management of the third stage of labour, and on the timing of administration. Further subgroup analyses may consider the effects of different doses or different routes of administration if appropriate data become available.

Results are presented as relative risks for dichotomous data, and weighted mean difference for continuous data, both

with 95% confidence intervals using a fixed-effect model. If sufficient heterogeneity existed, sensitivity analyses would have be performed.

DESCRIPTION OF STUDIES

Forty-six trials were identified as being potentially eligible for this review. Twenty-nine of these trials were excluded because: oxytocin was being compared to ergometrine-oxytocin (Docherty 1982; Dumoulin 1981; Soriano 1995; Symes 1984; Yuen 1995); no clinical outcome data were available (Hacker 1979; Muller 1996; Vaughan Williams1974); very strong likelihood of selection bias (Friedman 1957; Nieminen 1963; Stearn 1963; Thornton 1988); comparison of oxytocin given by different routes or at different times (Francis (1) 1965b; Huh 2000; Khan 1997; Thornton 1988; Hoffman 2004; Jackson 2001; Porter 1991; Schaefer 2004) (*see* 'Characteristics of excluded studies). The remaining 14 trials conducted in hospital and/or developed country settings were included in this review (*see* 'Characteristics of included studies).

METHODOLOGICAL QUALITY

Comparison A: oxytocin versus no uterotonics
Eight trials are potentially included in this comparison (De Groot 1996; Howard 1964; Ilancheran 1990; McGinty 1956; Newton 1961; Nordstrom 1997; Pierre 1992; Poeschmann 1991), but McGinty 1956 provides no usable data for this part of the review. Four of the remaining seven had adequate allocation concealment (De Groot 1996; Howard 1964; Nordstrom 1997; Poeschmann 1991).

Comparison B: oxytocin versus ergot alkaloids
Six trials are included in this comparison (De Groot 1996; Fugo 1958; Howard 1964; Ilancheran 1990; McGinty 1956; Sorbe 1978). Three had adequate allocation concealment (De Groot 1996; Fugo 1958; Howard 1964).

Comparison C: oxytocin plus ergometrine versus ergot alkaloids
Five trials are included in this comparison (Barbaro 1961; Bonham 1963; Francis (2) 1965a; Ilancheran 1990; Soiva 1964). Two had adequate allocation concealment (Bonham 1963; Francis (2) 1965a).

RESULTS

Fourteen trials are included.

Comparison A: oxytocin versus no uterotonics
Over 3000 women were entered into the trials of this comparison. There was considerable variation even within these seven trials. For instance, the sample size ranged from 10 to 1000 women. The oxytocin was given intramuscularly in three trials (De Groot 1996; Newton 1961; Poeschmann 1991), and intravenously in four trials (Howard 1964; Ilancheran 1990; Nordstrom 1997; Pierre 1992). The dose also varied from three international units (IU) (Howard 1964) to 5 IU (De Groot 1996; Pierre 1992; Poeschmann 1991) to 10 IU (Nordstrom 1997). In the trial by Ilancheran 1990, the only information given is that it was the 'standard dose'. The non-oxytocin group was either 'nothing' (Ilancheran 1990; Newton 1961; Pierre 1992) or a saline placebo (Howard 1964; Nordstrom 1997; Poeschmann 1991). In one trial (De Groot 1996), an oral placebo was given to allow blinding with a third group given oral ergometrine. In two trials, the oxytocin was given after placental delivery (Howard 1964; Newton 1961). In two trials, the study was carried out within the context of expectant management of the third stage of labour (De Groot 1996; Nordstrom 1997), and in one within active management (Pierre 1992). For the remainder, the context was unclear.

The data from these studies reveal some clear benefits to women who received prophylactic oxytocin as part of the routine management of the third stage of labour when compared to women who did not receive a uterotonic. These benefits relate specifically to indicators of blood loss such as postpartum haemorrhage (whether greater than 500 ml (relative risk (RR) 0.50; 95% confidence interval (CI) 0.43 to 0.59) or greater than 1000 ml (RR 0.61; 95% CI 0.44 to 0.87)) and the need for therapeutic oxytocics (RR 0.50; 95% CI 0.39 to 0.64). This conclusion holds regardless of the pre-specified stratifying factors detailed in the Methods section above, although with wider confidence intervals as the numbers of trials and therefore women is reduced. It is not feasible to comment on a possible relationship with manual removal of the placenta or the need for a blood transfusion. For all other outcomes in the review, either there are no data or the number of adverse events is very small, and so definite conclusions cannot be drawn.

Comparison B: oxytocin versus ergot alkaloids
Over 2800 women were entered into the trials of this comparison. There was considerable variation even within these six trials. For instance, the sample size ranged from 10 to over 1000 women. The oxytocin was given intramuscularly in only one trial (De Groot 1996), intravenously in four trials (Fugo 1958; Howard 1964; Ilancheran 1990; Sorbe 1978) and both intramuscularly and intravenously in one trial (McGinty 1956). The dose also varied from 2 IU (Fugo 1958), to 3 IU (Howard 1964) to 5 IU (De Groot 1996) to 10 IU (McGinty 1956; Sorbe 1978). In the trial by Ilancheran 1990, the only information given is that it was the 'standard dose'. The ergot alkaloid arm was even more varied, ranging from slightly different preparations - ergometrine/ergonovine (De Groot 1996; Fugo 1958; Ilancheran 1990; McGinty 1956; Sorbe 1978), methylergonovine maleate (Howard 1964), and methergine (McGinty 1956); different doses - from 0.2 mg (Howard 1964; McGinty 1956; Sorbe 1978), to 0.4 mg (De Groot 1996), 4 mg (Fugo 1958), and the 'standard dose' in Ilancheran 1990; and different routes - all intravenous except oral in De Groot

1996. In one trial, the oxytocin was given after placental delivery (Howard 1964), and in one trial, the study was carried out within the context of expectant management of the third stage of labour (De Groot 1996). For the remainder, the context was unclear.

Overall there is little evidence of differential effects of these two oxytocics. There are only two exceptions to this picture: oxytocin is associated with fewer manual removals of the placenta (RR 0.57; 95% CI 0.41 to 0.79), and with the suggestion of less raised blood pressure (RR 0.53; 95% CI 0.19 to 1.52), than are ergot alkaloids. For all other outcomes in the review, either there are no data or the number of adverse events is very small, and so definite conclusions cannot be drawn.

Comparison C: oxytocin plus ergometrine versus ergot alkaloids

Over 2800 women were entered into the trials of this comparison. There was considerable variation even within these five trials. For instance, the sample size ranged from 10 to over 1000 women. The ergometrine-oxytocin was generally given intramuscularly, although in one trial it was given intravenously (Ilancheran 1990). The dose was standard-one ampoule containing oxytocin 5 IU and ergometrine 0.5 mg. The ergot alkaloid arm was more varied, ranging from slightly different preparations - ergometrine (Bonham 1963; Francis (2) 1965a; Ilancheran 1990), ergometrine maleate (Barbaro 1961), and methergine (Soiva 1964); different doses - from 0.12 mg (Soiva 1964), to 0.5 mg (Bonham 1963; Francis (2) 1965a), 0.10 mg (Barbaro 1961), and the 'standard dose' in Ilancheran 1990; and different routes - intravenous in Ilancheran 1990 and Soiva 1964, intramuscular in Bonham 1963 and Francis (2) 1965a, and both in Barbaro 1961. The oxytocics were given before placental delivery in all the trials. Whether the trial was carried out within the context of expectant or of active management was usually unclear (although one (Bonham 1963) was a factorial design in which the other factors were controlled cord traction or maternal effort).

Overall, there is little evidence of a synergistic effect of adding oxytocin to ergometrine alone, other than in terms of reducing the rate of blood loss greater than 500 ml in the subgroup of well-randomised trials (RR 0.44; 95% CI 0.20 to 0.94). For all other outcomes in the review, either there are no data or the number of adverse events is very small, and so definite conclusions cannot be drawn.

DISCUSSION

Overall, there are too few data available for many definite conclusions to be drawn about the role of prophylactic oxytocin in the third stage of labour. There are strong suggestions of benefit in terms of postpartum haemorrhage, and the need for therapeutic oxytocics, when compared to using no uterotonic, but without sufficient information about other outcomes and side-effects, it is difficult to be confident about the trade-offs for these benefits. Indeed, there is a suggestion that the risk of manual removal of the placenta may be increased, particularly within the context of oxytocin without the other components of active management (early cord clamping/cutting and controlled cord traction). There seems little evidence in favour of ergot alkaloids alone compared to either oxytocin alone, or to ergometrine-oxytocin, but the data are sparse.

There were insufficient data to examine the role of different doses or routes of administration.

Suggested implications of the findings for practice and research are shown below.

AUTHORS' CONCLUSIONS

Implications for practice

Before making major changes to practice based on the current review, further information from other reviews considering the role of active management (Prendiville 2000), of prostaglandins (Gülmezoglu 2004), and of ergot alkaloids (McDonald 2004) needs to be taken into account.

Nevertheless, given the benefit of oxytocin in terms of reducing postpartum haemorrhage and the need for therapeutic oxytocics, when compared to using no uterotonic, there appears to be a clear practice implication in favour of using oxytocin. This has to be tempered, however, by the knowledge that there is insufficient information about most other outcomes and side-effects, and that all the trials were conducted in hospitals and/or developed country settings.

Similarly, although the data are sparse, the balance of evidence does not support the prophylactic use of ergot alkaloids alone (in contrast to either oxytocin alone, or to ergometrine-oxytocin).

Implications for research

Domiciliary deliveries in developing countries shoulder the burden of most of the major adverse effects of complications arising from the management of the third stage of labour. In order to improve this situation, especially where the routine management is expectant, there is a need to conduct a trial to see whether active management would be preferable in these settings. Prior to this, there needs to be evidence about which form of active management might be most appropriate to consider. This implies the need for a trial of alternative uterotonics such as the current World Health Organization trial comparing oral misoprostol with oxytocin in the context of full active management, and a trial to see whether all the components of the full active management package are useful. The optimal dosing of oxytocin and route of administration need to be determined in addition to dispelling concerns of potential side-effects. Delivery systems for oxytocin need to be addressed especially in developing countries such as oxytocin delivery in the

prefilled Uniject injection device. These trials should address outcomes which are of immediate relevance to the majority of postpartum women such as fatigue, and the ability to care for their babies.

POTENTIAL CONFLICT OF INTEREST

None known.

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SOURCES OF SUPPORT

External sources of support

- No sources of support supplied

Internal sources of support

- No sources of support supplied

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TABLES

Characteristics of included studies

Study	**Barbaro 1961**
Methods	'No selection was made'. Timing of randomisation not stated. Not blinded.
Participants	Women admitted for delivery in one of 2 obstetric units in hospital in Melbourne, Australia. Over 28 weeks.
Interventions	(1) Intramuscular SE505 (synthetic preparation-mixture of 5 units of syntocin and 0.5 mg ergometrine maleate in 1 ml) given immediately after delivery of the baby (n = 300). (2) Intravenous 0.5 mg ergometrine maleate given immediately after delivery of the baby + intramuscular 0.5 mg ergometrine maleate after delivery of placenta (n = 300). Otherwise expectant 3rd stage management (?).
Outcomes	Postpartum haemorrhage (> 600 ml); average blood loss 266 vs 219 ml (SD not given); average duration of 3rd stage 16 vs 13 minutes (SD not given).
Notes	
Allocation concealment	C – Inadequate

Study	**Bonham 1963**
Methods	Selection of drug was made by random numbers. Timing of randomisation not stated.

Characteristics of included studies (*Continued*)

	Not blinded.
Participants	All vaginal deliveries April 1961 to October 1962 in hospital in London, except: multiple pregnancies, previous PPH or manual removal, forceps and breech deliveries must be postrandomisation exclusions but does not state how many were randomised), parity 4 or more, induction or augmentation with syntocinon.
Interventions	(1) Intramuscular 0.5 mg ergometrine + 5 units synthetic oxytocin, given at crowning of the head (n = 391). (2) Intramuscular 0.5 mg ergometrine, given at crowning of the head (n = 416). [Third group of ergometrine + hyaluronidase not considered for this review.] Women were also selected in random two-week groups to either controlled cord traction (n = 199 ergometrine + oxytocin vs 217 ergometrine alone) or maternal effort/fundal pressure (192 vs 199). No information about timing of cord clamping/cutting.
Outcomes	Primary postpartum haemorrhage (> 568 ml estimated by adding to measured quantity a figure for loss on linen and swabs used for perineal repair); mean blood loss (154 vs 178 ml, SD not given); mean length of third stage (6.3 vs 6.2 mins, SD not given); prolonged third stage (> 30 minutes); manual removal of placenta.
Notes	
Allocation concealment	A – Adequate

Study	**De Groot 1996**
Methods	Hospital pharmacy supplied numbered boxes of tablets and ampoules according to computer-generated randomisation list. Informed consent asked in early labour. Assigned before delivery of baby's head. Double-blind for oral ergometrine vs placebo and unblinded for ergometrine and/or placebo vs oxytocin. Randomisation 1:2:2, oxytocin to ergometrine to placebo. Multicentre.
Participants	Two university hospitals, a midwifery school and independent midwives in and around Nijmegen, Netherlands. Women expecting to deliver in one of these settings, and who did not develop following exclusion criteria: refusal, cardiovascular disease/hypertension, multiple pregnancy, non-cephalic presentation, polyhydramnios, tocolysis 2 hours prior to delivery, anticoagulant therapy, stillbirth, antepartum haemorrhage, chemical induction or augmentation (oxytocin, prostaglandins), instrumental/operative delivery (some of these must have been postrandomisation exclusions), anaemia Hb < 6.8 mmol/L (timing not stated), previous third stage complications. Four of 371 women were assigned to the study erroneously (3 forceps, 1 augmentation) and were excluded postrandomisation. Otherwise eligible women wishing a natural childbirth refused to enter the trial (numbers not stated).
Interventions	All three interventions given immediately after birth of baby: (1) intramuscular 5 IU oxytocin; (2) oral 0.4 mg ergometrine; (3) oral placebo. Other third stage management expectant (although no information given about timing of cord clamping/cutting). When mother feels contractions or there are signs of separation, maternal effort encouraged, adopting position to aid gravity. If necessary, flat hand on abdomen to act as brace to aid pushing. Re-attempt if placenta does not deliver spontaneously. If haemorrhage, administer extra oxytocics and/or controlled cord traction.
Outcomes	Mean blood loss (ml); PPH (>= 500 ml); severe PPH (>= 1000 ml) (blood loss measured gravimetrically (fresh perineal pad under perineum to absorb blood or fluid; gauzes and pads collected until one hour after delivery of placenta and weighed. 100 g increase in weight considered equivalent to 100 ml blood); length of third stage (11 (range 4-90), 15 (2-90), 14 (3-55) in oxytocin, ergometrine and placebo groups respectively. No information about whether mean or median, and SD not given); blood pressure 15, 30, 45 and 60 minutes after delivery of placenta, in institutional deliveries only (oral ergometrine showed no significant elevation); use of further oxytocics; manual removal of placenta; transfusion.
Notes	

Characteristics of included studies (*Continued*)

Allocation concealment	A – Adequate

Study	**Francis (2) 1965a**
Methods	'Ampoules used in rotation and participants were unselected'. Blinded.
Participants	Two maternity hospitals in Liverpool, UK. All women expected to deliver except those in whom an abnormal third stage was anticipated (previous PPH, instrumental or breech deliveries, twin pregnancies, antepartum haemorrhage, severe anaemia, intravenous oxytocin for induction or augmentation).
Interventions	(1) 1 ml intramuscular ergometrine-oxytocin (5 IU oxytocin + 0.5 mg per 1 ml ergometrine) after delivery of baby and cord divided , AND 1 ml water after placental delivery (n = 171). (2) 0.5 mg intramuscular ergometrine after delivery of baby and cord divided, AND 1 ml water after placental delivery (n = 183). (3) 1 ml intramuscular water after delivery of baby and cord divided, AND 0.5 mg intramuscular ergometrine after placental delivery (n = 167). No information about controlled cord traction or timing of cord clamping, so not clear whether in context of active or expectant management. Comparison in review is between groups 1 and 2.
Outcomes	Blood loss (average 4.9, 6.4, 7.0 in groups 1, 2 and 3 respectively - not clear whether mean or median and no SD given); for the review, loss of > 20 oz has been taken as PPH; retained placenta (> 20 minutes).
Notes	
Allocation concealment	A – Adequate

Study	**Fugo 1958**
Methods	Numbered identical drug packages administered in rotation. Number meaningless to obstetrician. Blinded.
Participants	Women delivering in a hospital in Chicago, USA. No details given of inclusion/exclusion criteria, but description of study participants showed that half had labour over 8 hours, and 98% received some anaesthetic agent.
Interventions	All administered intravenously in 2 ml with anterior shoulder. (1) 2 IU pitocin (natural oxytocin) n = 168. (2) 2 IU syntocinon (synthetic oxytocin) n = 156. (3) 4 mg ergonovine 149. (4) 80 mg U3772 (alpha, alpha diphenyl gamma dimethylamino N-methyl valeramide-HCl) n = 151. No other information about management of third stage. Comparison for review is groups 1 and 2 combined vs group 3. No information about other aspects of third stage management.
Outcomes	Method of placental delivery (high % of manual removals for teaching purposes if haemorrhage or undelivered within 10 minutes); length of third stage (not significantly different between groups but data only given for those delivered spontaneously ie within 10 minutes); blood loss with placenta; (one hour postpartum (?)average blood loss 50.2 vs 40.8 ml; no SDs given).
Notes	
Allocation concealment	A – Adequate

Study	**Howard 1964**
Methods	Participants randomly selected for one of the 3 study drugs. A double-blind technique was used. Vials identical in appearance. Contents not known until completion of the study.

Characteristics of included studies (*Continued*)

Participants	Women delivering vaginally in hospital in Iowa, USA between August 1962 and July 1963.
Interventions	Following placental delivery, slow intravenous 1 cc injection of A. 0.9% sodium chloride (n = 475). B. 0.2 mg methylergonovine maleate (n = 505). C. 3.0 IU oxytocin (n = 479). Comparisons in this review between C and A, and C and B. No information about other aspects of third stage management.
Outcomes	Blood pressure 1, 2, 5, 10 and 40 minutes after placental delivery and then hourly for 4 hours; blood loss as estimated by attending physician; further treatment for uterine atony.
Notes	
Allocation concealment	A – Adequate

Study	**Ilancheran 1990**
Methods	'Consecutive participants divided equally into 4 subgroups, distribution being done on a random basis'.
Participants	Women in spontaneous labour between 38 and 42 weeks' gestation with normal vertex deliveries in hospital in Singapore. 17/20 were multigravid.
Interventions	A. No oxytocic in 3rd stage and three groups given intravenous uterotonic in 'standard' doses with the delivery of the anterior shoulder. B. Oxytocin. C. Ergometrine-oxytocin. D. Ergometrine. Comparisons for this review are: B vs A; B vs D; C vs D.
Outcomes	Prostaglandin levels 5, 15b and 30 minutes after delivery (significant rise in all four groups but no differences between the groups); postpartum haemorrhage.
Notes	
Allocation concealment	B – Unclear

Study	**McGinty 1956**
Methods	'Cases picked at random'. Unblinded.
Participants	All vaginally delivered under pudendal block and demorol/scopolamine, in hospital in United States of America.
Interventions	Drug given at birth of anterior shoulder: A. 1 cc normal saline intravenously (n = 50). B. 0.2 mg methergine intravenously (n = 50). C. 0.2 mg ergonovine intravenously (n = 50). D. pitocin 5 IU each intravenously and intramuscularly (n = 50). Comparisons for this review: D vs A; D vs B and C. No information about other aspects of third stage management.
Outcomes	Diastolic and systolic blood pressure 5, 15 and 60 minutes after administration - although data not provided for control group; estimated severe blood loss over 1000 ml mentioned for one women in methergine series and one in control group (not included in data tables as unlikely to have been systematically recorded).
Notes	
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Newton 1961**
Methods	Alternate allocation not blinded.
Participants	Hospital in USA. No antenatal complications, term, no likely complication of labour and delivery.
Interventions	A. 1 ml synthetic oxytocin intramuscularly after placental delivery (n = 50). B. Control (n = 50). No information about other aspects of third stage management.
Outcomes	Blood loss, blood pressure, need for therapeutic oxytocics.
Notes	
Allocation concealment	D – Not used

Study	**Nordstrom 1997**
Methods	Double-blind randomised. 2 sets of ampoules prepared and numbered according to computer generated schedule. Contents unknown to women or caregivers.
Participants	Hospital in Sweden. Singleton cephalic vaginal deliveries.
Interventions	1 ml intravenous after delivery of baby. Passive (expectant) management of the placenta. 10 IU oxytocin. Saline.
Outcomes	Blood loss; additional oxytocin (data tables give methylergometrine; clarification about other oxytocics sought from authors), Hb, blood transfusion; manual removal.
Notes	Additional oxytocin (data tables give methylergometrine; clarification about other oxytocics sought from authors).
Allocation concealment	A – Adequate

Study	**Pierre 1992**
Methods	Leaflets marked from 1-1000 alternate allocation 'this made possible a control of selection bias at entry by the authors as the order in the trial had the same chronology as the date and time of entry in the labour ward'.
Participants	Women expecting to deliver vaginally in hospital in France. Only exclusions - breech, twins, APH, refusal.
Interventions	Active management of third stage with (n = 488) and without 5 IU IV oxytocin (n = 488) with the anterior shoulder.
Outcomes	Blood loss; length of third stage, MRP, maternal side-effects.
Notes	
Allocation concealment	C – Inadequate

Study	**Poeschmann 1991**
Methods	Hospital pharmacy supplied numbered boxes. Allocation of boxes was by order of entry to the labour ward. A nurse not working in the labour room prepared the injection.
Participants	April 1986 -88, 2 hospitals in Netherlands. Uncomplicated singleton term pregnancies in spontaneous labour with spontaneous vaginal deliveries and Hobel score of less than 10.
Interventions	After birth of baby: A. IM 5 IU oxytocin. B. 500 micrograms sulprostone. C. saline.

	Comparison in this review is A vs C. Not sure whether active or expectant as says 3rd stage managed conservatively (expectantly) but cord clamped within 1 minute of birth.
Outcomes	Blood loss; need for additional oxytocics; length of third stage.
Notes	
Allocation concealment	A – Adequate

Study	**Soiva 1964**
Methods	Every third normal parturient.
Participants	Hospital, Finland. Spontaneous, singleton, cephalic.
Interventions	Immediately after birth of baby. No efforts to expel placenta during first contraction of third stage. IV methergine 0.12-0.2 mg IM ergometrine-oxytocin (IU oxytocin + 0.5 ergometrine). Not clear whether rest of third stage managed actively or expectantly.
Outcomes	Blood loss; duration of third stage, retained placenta, complications, MRP.
Notes	
Allocation concealment	C – Inadequate

Study	**Sorbe 1978**
Methods	Alternate - odd and even numbers of mothers' hospital records. Not blinded.
Participants	Hospital in Sweden.
Interventions	IV after delivery of anterior shoulder. 0.2 mg ergometrine. 10 IU oxytocin. Not clear whether rest of third stage managed actively or expectantly. (historical (?) control group given no uterotonic not included in the comparison).
Outcomes	Blood loss; MRP, placental separation time.
Notes	
Allocation concealment	C – Inadequate

APH: antepartum haemorrhage
Hb: haemoglobin
IM: intramuscular
IU: international units
IV: intravenous
MRP: manual removal of placenta
PPH: postpartum haemorrhage
SD: standard deviation
vs: versus

Characteristics of excluded studies

Study	**Reason for exclusion**
Bader 2000	Comparison of oxytocin to acupuncture not the subject of this review.

Boucher 2004	Comparison of intramuscular carbetocin to a 2 hour intravenous oxytocin infusion administered after delivery of the fetus and placenta.
Docherty 1982	Comparison of oxytocin to acupuncture not the subject of this review.
Dumoulin 1981	Oxytocin (different doses) versus ergometrine-oxytocin (subject of separate review).
Francis (1) 1965b	Excluded because ergometrine-oxytocin given after end of 2nd stage and ergometrine given after end of third stage, so the comparison of the two drugs is inextricably confounded with the timing of administration.
Friedman 1957	Likely to be considerable bias after entry to study as 27% of the 1221 were 'deleted from the study' as inadequate observations were obtained. No other reasons given, and no indication of whether these women were missing in similar proportions from the five intervention groups.
Gerstenfeld 2001	Comparison of oxytocin to misoprostol (subject of separate review).
Hacker 1979	Excluded because no clinical outcome date available except for information on blood pressure which is only given as mean changes from baseline.
Hoffman 2004	Comparison of oxytocin within the context of active versus expectant management (subject of seperate review).
Huh 2000	Excluded as only different timing of administration.
Irons 1994	Comparison of nipple stimulation to ergometrine-oxytocin which is not a subject of this review.
Jackson 2001	Comparison of oxytocin administered before and after placental delivery so the only difference is timing of administration.
Khan 1997	Comparison of prophylactic oxytocin within context of active management vs oxytocin after placental delivery within context of expectant management (subject of separate review by Prendiville et al: Active versus expectant management of third stage of labour - see Prendiville 2000).
Kundodyiwa 2001	Comparison of oxytocin to misoprostol (subject of separate review).
Lokugamage 2001	Comparison of oxytocin to misoprostol (subject of separate review) and at caesarean section.
Muller 1996	5 IU IV oxytocin with crowning of head and Brandt-Andrews vs expectant. Abstract only, in French and German. No clinical data available from authors.
Nieminen 1963	No details of how allocated 'women divided into three groups' - methergine, OCM505, oxytocin.
Parsons 2004	Comparison of oxytocin to misoprostol (subject of separate review).
Porter 1991	Only difference is different route of administration.
Ramirez 2001	Inadequate information available about randomization and available only as abstract.
Schaefer 2004	Excluded as only difference is timing of administration.
Schemmer 2001	Comparison of oxytocin administered before and after placental delivery so the only difference is timing of administration.
Soriano 1995	Compares oxytocin to oxytocin plus ergometrine (subject of separate review).
Stearn 1963	Allocation was to two different consultants one of whom gave all patients ergometrine-oxytocin, and the other to give 'normal' cases ergometrine with hyalase and abnormal given IV ergometrine.
Symes 1984	Compares oxytocin to oxytocin plus ergometrine. No clinical outcomes (serum prolactin levels only).
Tessier 2000	Excluded as only different routes of administration.
Thornton 1988	Strong likelihood of post-entry bias as alternate allocation used for 65, but 40 were withdrawn 40 as did not meet inclusion criteria, leaving 10 and 15 in trial comparing oxytocin vs no oxytocin within active management. Primary outcome plasma oxytocin concentration.
Vaughan Williams1974	Excluded because no clinical outcome data available.
Yuen 1995	Oxytocin versus ergometrine-oxytocin (subject of separate review).

IU: international unit
IV: intravenous

Characteristics of excluded studies (*Continued*)

vs: versus

ANALYSES

Comparison 01. Oxytocin versus no uterotonics (all trials)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	6	3193	Relative Risk (Fixed) 95% CI	0.50 [0.43, 0.59]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	4	2243	Relative Risk (Fixed) 95% CI	0.61 [0.44, 0.87]
03 Mean blood loss (ml)	4	1373	Weighted Mean Difference (Fixed) 95% CI	-101.93 [-134.89, -68.97]
04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum	1	943	Relative Risk (Fixed) 95% CI	0.63 [0.36, 1.09]
05 Blood transfusion	2	1221	Relative Risk (Fixed) 95% CI	1.30 [0.50, 3.39]
07 Therapeutic uterontonics	5	2327	Relative Risk (Fixed) 95% CI	0.50 [0.39, 0.64]
10 Mean length of third stage (minutes)	1	52	Weighted Mean Difference (Fixed) 95% CI	-1.80 [-5.55, 1.95]
11 Manual removal of the placenta	4	2243	Relative Risk (Fixed) 95% CI	1.17 [0.79, 1.73]
15 Nausea between delivery of the baby and discharge from the labour ward	1	52	Relative Risk (Fixed) 95% CI	0.29 [0.01, 6.74]

Comparison 02. Oxytocin versus no uterotonics (randomised trials only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	4	2213	Relative Risk (Fixed) 95% CI	0.61 [0.51, 0.72]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	3	1273	Relative Risk (Fixed) 95% CI	0.72 [0.49, 1.05]
03 Mean blood loss (ml)	3	1273	Weighted Mean Difference (Fixed) 95% CI	-109.12 [-151.93, -66.32]
04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum	1	943	Relative Risk (Fixed) 95% CI	0.63 [0.36, 1.09]
05 Blood transfusion	2	1221	Relative Risk (Fixed) 95% CI	1.30 [0.50, 3.39]
07 Therapeutic uterontonics	4	2227	Relative Risk (Fixed) 95% CI	0.53 [0.41, 0.69]
10 Mean length of third stage (minutes)	1	52	Weighted Mean Difference (Fixed) 95% CI	-1.80 [-5.55, 1.95]
11 Manual removal of the placenta	3	1273	Relative Risk (Fixed) 95% CI	1.67 [0.82, 3.41]
15 Nausea between delivery of the baby and discharge from the labour ward	1	52	Relative Risk (Fixed) 95% CI	0.29 [0.01, 6.74]

Comparison 03. Oxytocin versus no uterotonics (active management only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	1	970	Relative Risk (Fixed) 95% CI	0.29 [0.21, 0.41]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	1	970	Relative Risk (Fixed) 95% CI	0.33 [0.14, 0.77]
11 Manual removal of the placenta	1	970	Relative Risk (Fixed) 95% CI	0.99 [0.62, 1.59]

Comparison 04. Oxytocin versus no uterotonics (expectant management only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	2	1221	Relative Risk (Fixed) 95% CI	0.61 [0.51, 0.73]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	2	1221	Relative Risk (Fixed) 95% CI	0.73 [0.49, 1.07]
03 Mean blood loss (ml)	2	1221	Weighted Mean Difference (Fixed) 95% CI	-83.58 [-118.01, -49.14]
04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum	1	943	Relative Risk (Fixed) 95% CI	0.63 [0.36, 1.09]
05 Blood transfusion	2	1221	Relative Risk (Fixed) 95% CI	1.30 [0.50, 3.39]
07 Therapeutic uterontonics	2	1221	Relative Risk (Fixed) 95% CI	0.66 [0.48, 0.90]
11 Manual removal of the placenta	2	1221	Relative Risk (Fixed) 95% CI	1.67 [0.82, 3.41]

Comparison 05. Oxytocin versus no uterotonics (given before placental delivery)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	5	2253	Relative Risk (Fixed) 95% CI	0.50 [0.42, 0.58]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	4	2243	Relative Risk (Fixed) 95% CI	0.61 [0.44, 0.87]
03 Mean blood loss (ml)	3	1273	Weighted Mean Difference (Fixed) 95% CI	-109.12 [-151.93, -66.32]
04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum	1	943	Relative Risk (Fixed) 95% CI	0.63 [0.36, 1.09]
05 Blood transfusion	2	1221	Relative Risk (Fixed) 95% CI	1.30 [0.50, 3.39]
07 Therapeutic uterontonics	3	1273	Relative Risk (Fixed) 95% CI	0.64 [0.47, 0.87]
10 Mean length of third stage (minutes)	1	52	Weighted Mean Difference (Fixed) 95% CI	-1.80 [-5.55, 1.95]
11 Manual removal of the placenta	4	2243	Relative Risk (Fixed) 95% CI	1.17 [0.79, 1.73]

15 Nausea between delivery of the baby and discharge from the labour ward	1	52	Relative Risk (Fixed) 95% CI	0.29 [0.01, 6.74]

Comparison 06. Oxytocin versus no uterotonics (given after placental delivery)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	1	940	Relative Risk (Fixed) 95% CI	0.60 [0.32, 1.12]
03 Mean blood loss (ml)	1	100	Weighted Mean Difference (Fixed) 95% CI	12.00 [-102.29, 126.29]
07 Therapeutic uterontonics	2	1054	Relative Risk (Fixed) 95% CI	0.32 [0.20, 0.50]

Comparison 07. Oxytocin versus ergot alkaloids (all trials)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	5	2719	Relative Risk (Fixed) 95% CI	0.90 [0.70, 1.16]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	3	1746	Relative Risk (Fixed) 95% CI	0.99 [0.56, 1.74]
03 Mean blood loss (ml)	2	1273	Weighted Mean Difference (Fixed) 95% CI	-29.12 [-59.36, 1.12]
05 Blood transfusion	1	224	Relative Risk (Fixed) 95% CI	3.74 [0.34, 40.64]
07 Therapeutic uterontonics	2	1208	Relative Risk (Fixed) 95% CI	1.02 [0.67, 1.55]
08 Third stage > 20 minutes	1	473	Relative Risk (Fixed) 95% CI	Not estimable
09 Third stage > 40 minutes	1	383	Relative Risk (Fixed) 95% CI	Not estimable
10 Mean length of third stage (minutes)	1	1049	Weighted Mean Difference (Fixed) 95% CI	-0.80 [-1.65, 0.05]
11 Manual removal of the placenta	3	1746	Relative Risk (Fixed) 95% CI	0.57 [0.41, 0.79]
13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward	1	150	Relative Risk (Fixed) 95% CI	0.53 [0.19, 1.52]

Comparison 08. Oxytocin versus ergot alkaloids (randomised trials only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	3	1660	Relative Risk (Fixed) 95% CI	1.03 [0.73, 1.47]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	2	697	Relative Risk (Fixed) 95% CI	1.09 [0.45, 2.66]
03 Mean blood loss (ml)	1	224	Weighted Mean Difference (Fixed) 95% CI	23.00 [-91.86, 137.86]
05 Blood transfusion	1	224	Relative Risk (Fixed) 95% CI	3.74 [0.34, 40.64]
07 Therapeutic uterontonics	2	1208	Relative Risk (Fixed) 95% CI	1.02 [0.67, 1.55]
08 Third stage > 20 minutes	1	473	Relative Risk (Fixed) 95% CI	Not estimable
09 Third stage > 40 minutes	1	473	Relative Risk (Fixed) 95% CI	Not estimable

11 Manual removal of the placenta	2	697	Relative Risk (Fixed) 95% CI	0.71 [0.49, 1.03]

Comparison 10. Oxytocin versus ergot alkaloids (expectant management only)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	1	224	Relative Risk (Fixed) 95% CI	0.87 [0.59, 1.28]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	1	224	Relative Risk (Fixed) 95% CI	1.09 [0.45, 2.66]
03 Mean blood loss (ml)	1	224	Weighted Mean Difference (Fixed) 95% CI	23.00 [-91.86, 137.86]
05 Blood transfusion	1	224	Relative Risk (Fixed) 95% CI	3.74 [0.34, 40.64]
07 Therapeutic uterontonics	1	224	Relative Risk (Fixed) 95% CI	1.25 [0.67, 2.31]
11 Manual removal of the placenta	1	224	Relative Risk (Fixed) 95% CI	0.94 [0.09, 10.16]

Comparison 11. Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	4	1756	Relative Risk (Fixed) 95% CI	0.83 [0.64, 1.08]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	3	1746	Relative Risk (Fixed) 95% CI	0.99 [0.56, 1.74]
03 Mean blood loss (ml)	2	1273	Weighted Mean Difference (Fixed) 95% CI	-29.12 [-59.36, 1.12]
05 Blood transfusion	1	224	Relative Risk (Fixed) 95% CI	3.74 [0.34, 40.64]
07 Therapeutic uterontonics	1	224	Relative Risk (Fixed) 95% CI	1.25 [0.67, 2.31]
08 Third stage > 20 minutes	1	473	Relative Risk (Fixed) 95% CI	Not estimable
09 Third stage > 40 minutes	1	473	Relative Risk (Fixed) 95% CI	Not estimable
10 Mean length of third stage (minutes)	1	1049	Weighted Mean Difference (Fixed) 95% CI	-0.80 [-1.65, 0.05]
11 Manual removal of the placenta	3	1746	Relative Risk (Fixed) 95% CI	0.57 [0.41, 0.79]
13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward	1	150	Relative Risk (Fixed) 95% CI	0.53 [0.19, 1.52]

Comparison 12. Oxytocin versus ergot alkaloids (given after placental delivery)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	1	963	Relative Risk (Fixed) 95% CI	1.75 [0.77, 3.96]
07 Therapeutic uterontonics	1	984	Relative Risk (Fixed) 95% CI	0.89 [0.50, 1.56]

Comparison 13. Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	5	2891	Relative Risk (Fixed) 95% CI	1.29 [0.90, 1.84]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	1	1120	Relative Risk (Fixed) 95% CI	1.67 [0.40, 6.94]
05 Blood transfusion	1	1120	Relative Risk (Fixed) 95% CI	0.71 [0.23, 2.24]
08 Third stage > 20 minutes	3	2281	Relative Risk (Fixed) 95% CI	0.89 [0.67, 1.19]
11 Manual removal of the placenta	2	1927	Relative Risk (Fixed) 95% CI	1.02 [0.48, 2.20]

Comparison 14. Oxytocin + ergometrine versus ergot alkaloids alone (randomised trials)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	2	1161	Relative Risk (Fixed) 95% CI	0.44 [0.20, 0.94]
08 Third stage > 20 minutes	1	354	Relative Risk (Fixed) 95% CI	3.21 [0.34, 30.57]

Comparison 15. Oxytocin + ergometrine versus ergot alkaloids alone (active management)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	1	416	Relative Risk (Fixed) 95% CI	0.22 [0.03, 1.85]
08 Third stage > 20 minutes	1	416	Relative Risk (Fixed) 95% CI	6.54 [0.79, 53.87]
11 Manual removal of the placenta	1	416	Relative Risk (Fixed) 95% CI	4.36 [0.49, 38.70]

Comparison 17. Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 PPH (clinically estimated blood loss > or = 500 ml)	5	2891	Relative Risk (Fixed) 95% CI	1.29 [0.90, 1.84]
02 Severe PPH (clinically estimated blood loss > or = 1000 ml)	1	1120	Relative Risk (Fixed) 95% CI	1.67 [0.40, 6.94]
05 Blood transfusion	1	1120	Relative Risk (Fixed) 95% CI	0.71 [0.23, 2.24]
08 Third stage > 20 minutes	3	2281	Relative Risk (Fixed) 95% CI	0.89 [0.67, 1.19]
11 Manual removal of the placenta	2	1927	Relative Risk (Fixed) 95% CI	1.02 [0.48, 2.20]

INDEX TERMS

Medical Subject Headings (MeSH)

Ergot Alkaloids; Labor Stage, Third [*drug effects]; Maternal Mortality; *Oxytocics; *Oxytocin; Postpartum Hemorrhage [mortality; *prevention & control]

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Prophylactic oxytocin for the third stage of labour
Authors	Cotter A, Ness A, Tolosa J
Contribution of author(s)	The protocol was developed by Diana Elbourne, with Walter Prendiville and Sue McDonald. For the review, Diana Elbourne identified the potentially relevant papers. Diana Elbourne and Walter Prendiville independently extracted data from the papers, and compared and agreed the results. Diana Elbourne wrote the first draft of the text and revised it following comments from Guillermo Carroli, Juliet Wood, Walter Prendiville and Sue McDonald. The December 2004 update was prepared by Amanda Cotter, Amen Ness and Jorge Tolosa, who independently assessed the new papers, compiled and agreed the results. Amanda Cotter and Jorge Tolosa reread the review and its objectives which they elected to keep.
Issue protocol first published	1999/4
Review first published	2001/4
Date of most recent amendment	24 August 2005
Date of most recent SUBSTANTIVE amendment	17 July 2001
What's New	December 2004 Search updated. We identified 16 new studies; however, none fulfilled the inclusion criteria.
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
Date new studies found and included/excluded	01 December 2004
Date authors' conclusions section amended	01 December 2004
Contact address	Dr Amanda Cotter Assistant Professor of Clinical Obstetrics and Gynecology Department of Obstetrics and Gynecology University of Miami PO Box 016960 (D-53) Miami Florida 33101 USA E-mail: acotter@med.miami.edu Tel: +1 305 2434020
DOI	10.1002/14651858.CD001808
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Analysis 01.01. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

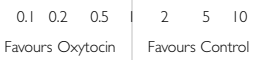
Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	55/143		10.2	0.83 [0.57, 1.22]
Howard 1964	15/470	25/470		6.6	0.60 [0.32, 1.12]
× Ilancheran 1990	0/5	0/5		0.0	Not estimable
Nordstrom 1997	104/513	175/487		47.1	0.56 [0.46, 0.70]
Pierre 1992	37/488	126/482		33.3	0.29 [0.21, 0.41]
Poeschmann 1991	7/28	10/24		2.8	0.60 [0.27, 1.33]
Total (95% CI)	1582	1611		100.0	0.50 [0.43, 0.59]

Total events: 188 (Oxytocin), 391 (Control)

Test for heterogeneity chi-square=18.10 df=4 p=0.001 I^2 =77.9%

Test for overall effect z=8.76 p<0.00001



Analysis 01.02. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	16/143		14.2	0.80 [0.34, 1.87]
Nordstrom 1997	32/513	43/487		55.3	0.71 [0.45, 1.10]
Pierre 1992	7/488	21/482		26.5	0.33 [0.14, 0.77]
Poeschmann 1991	2/28	3/24		4.0	0.57 [0.10, 3.14]
Total (95% CI)	1107	1136		100.0	0.61 [0.44, 0.87]

Total events: 48 (Oxytocin), 83 (Control)

Test for heterogeneity chi-square=2.86 df=3 p=0.41 I^2 =0.0%

Test for overall effect z=2.78 p=0.006

Analysis 01.03. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Groot 1996	78	499.00 (454.00)	143	520.00 (419.00)		7.3	-21.00 [-142.93, 100.93]
Newton 1961	50	345.00 (285.00)	50	333.00 (298.00)		8.3	12.00 [-102.29, 126.29]
Nordstrom 1997	513	409.00 (3.45)	487	527.00 (412.00)		81.1	-118.00 [-154.59, -81.41]
Poeschmann 1991	28	374.00 (279.00)	24	548.00 (376.00)		3.3	-174.00 [-356.51, 8.51]
Total (95% CI)	669		704			100.0	-101.93 [-134.89, -68.97]

Test for heterogeneity chi-square=6.85 df=3 p=0.08 I^2 =56.2%

Test for overall effect z=6.06 p<0.00001

Analysis 01.04. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nordstrom 1997	20/485	30/458		100.0	0.63 [0.36, 1.09]
Total (95% CI)	485	458		100.0	0.63 [0.36, 1.09]

Total events: 20 (Oxytocin), 30 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=1.65 p=0.1

Analysis 01.05. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 05 Blood transfusion

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	2/78	3/143		29.2	1.22 [0.21, 7.16]
Nordstrom 1997	7/513	5/487		70.8	1.33 [0.42, 4.16]
Total (95% CI)	591	630		100.0	1.30 [0.50, 3.39]

Total events: 9 (Oxytocin), 8 (Control)

Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%

Test for overall effect z=0.53 p=0.6

Analysis 01.07. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

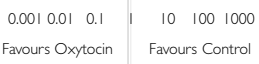
Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	26/143		11.5	0.99 [0.55, 1.78]
Howard 1964	21/479	58/475		36.6	0.36 [0.22, 0.58]
Newton 1961	1/50	11/50		6.9	0.09 [0.01, 0.68]
Nordstrom 1997	40/513	67/487		43.2	0.57 [0.39, 0.82]
Poeschmann 1991	0/28	2/24		1.7	0.17 [0.01, 3.42]
Total (95% CI)	1148	1179		100.0	0.50 [0.39, 0.64]

Total events: 76 (Oxytocin), 164 (Control)

Test for heterogeneity chi-square=10.64 df=4 p=0.03 I^2 =62.4%

Test for overall effect z=5.33 p<0.00001

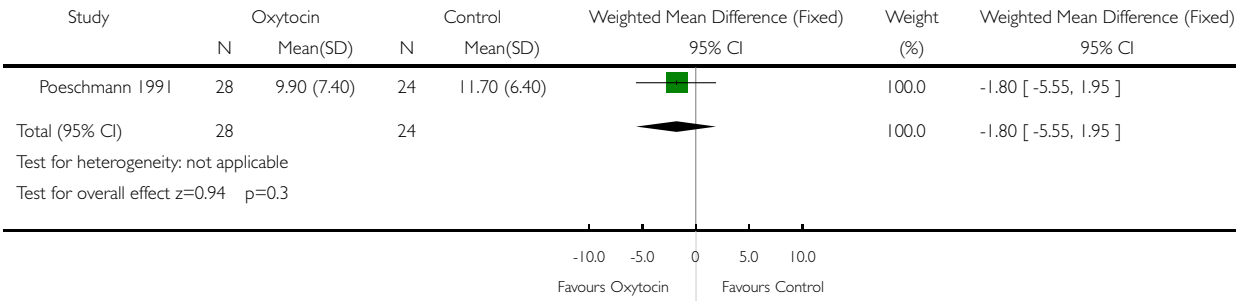


Analysis 01.10. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 10 Mean length of third stage (minutes)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 10 Mean length of third stage (minutes)

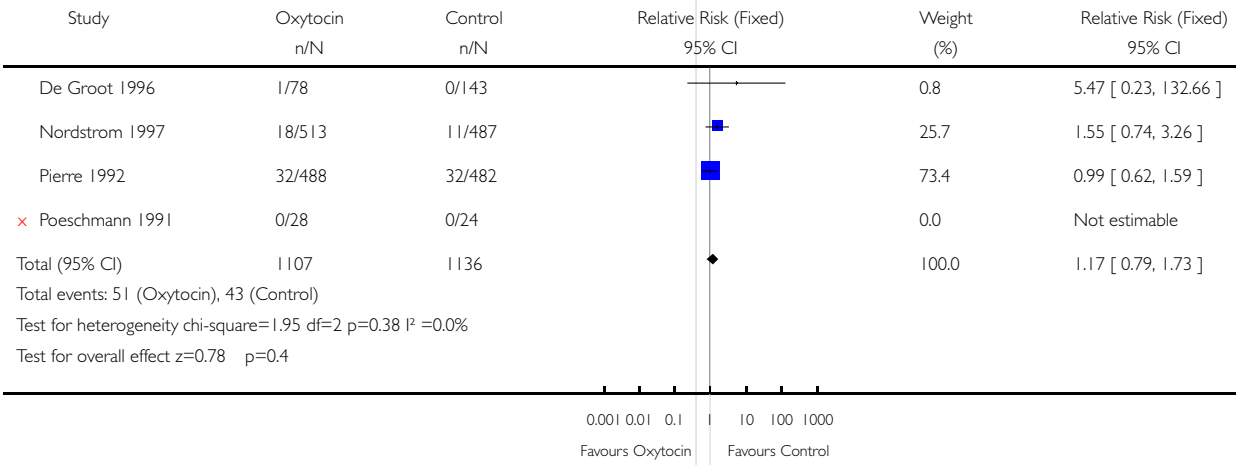


Analysis 01.11. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 11 Manual removal of the placenta



Analysis 01.15. Comparison 01 Oxytocin versus no uterotonics (all trials), Outcome 15 Nausea between delivery of the baby and discharge from the labour ward

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 01 Oxytocin versus no uterotonics (all trials)

Outcome: 15 Nausea between delivery of the baby and discharge from the labour ward

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Poeschmann 1991	0/28	1/24		100.0	0.29 [0.01, 6.74]
Total (95% CI)	28	24		100.0	0.29 [0.01, 6.74]
Total events: 0 (Oxytocin), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.77 p=0.4					

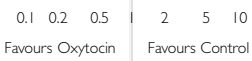
Analysis 02.01. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	55/143		15.3	0.83 [0.57, 1.22]
Howard 1964	15/470	25/470		9.8	0.60 [0.32, 1.12]
Nordstrom 1997	104/513	175/487		70.6	0.56 [0.46, 0.70]
Poeschmann 1991	7/28	10/24		4.2	0.60 [0.27, 1.33]
Total (95% CI)	1089	1124		100.0	0.61 [0.51, 0.72]
Total events: 151 (Oxytocin), 265 (Control)					
Test for heterogeneity chi-square=3.08 df=3 p=0.38 I^2 =2.6%					
Test for overall effect z=5.62 p<0.00001					



Analysis 02.02. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	16/143		19.3	0.80 [0.34, 1.87]
Nordstrom 1997	32/513	43/487		75.2	0.71 [0.45, 1.10]
Poeschmann 1991	2/28	3/24		5.5	0.57 [0.10, 3.14]
Total (95% CI)	619	654		100.0	0.72 [0.49, 1.05]

Total events: 41 (Oxytocin), 62 (Control)

Test for heterogeneity chi-square=0.14 df=2 p=0.93 I^2 =0.0%

Test for overall effect z=1.71 p=0.09

Analysis 02.03. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Groot 1996	78	499.00 (454.00)	143	520.00 (419.00)		12.3	-21.00 [-142.93, 100.93]
Nordstrom 1997	513	409.00 (345.00)	487	527.00 (412.00)		82.2	-118.00 [-165.23, -70.77]
Poeschmann 1991	28	374.00 (279.00)	24	548.00 (376.00)		5.5	-174.00 [-356.51, 8.51]
Total (95% CI)	619		654			100.0	-109.12 [-151.93, -66.32]

Test for heterogeneity chi-square=2.63 df=2 p=0.27 I^2 =23.9%

Test for overall effect z=5.00 p<0.00001

Analysis 02.04. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nordstrom 1997	20/485	30/458		100.0	0.63 [0.36, 1.09]
Total (95% CI)	485	458		100.0	0.63 [0.36, 1.09]
Total events: 20 (Oxytocin), 30 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.65 p=0.1					

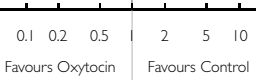
Analysis 02.05. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 05 Blood transfusion

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	2/78	3/143		29.2	1.22 [0.21, 7.16]
Nordstrom 1997	7/513	5/487		70.8	1.33 [0.42, 4.16]
Total (95% CI)	591	630		100.0	1.30 [0.50, 3.39]
Total events: 9 (Oxytocin), 8 (Control)					
Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%					
Test for overall effect z=0.53 p=0.6					



Analysis 02.07. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	26/143		12.4	0.99 [0.55, 1.78]
Howard 1964	21/479	58/475		39.3	0.36 [0.22, 0.58]
Nordstrom 1997	40/513	67/487		46.4	0.57 [0.39, 0.82]
Poeschmann 1991	0/28	2/24		1.8	0.17 [0.01, 3.42]
Total (95% CI)	1098	1129		100.0	0.53 [0.41, 0.69]
Total events: 75 (Oxytocin), 153 (Control)					
Test for heterogeneity chi-square=7.46 df=3 p=0.06 I^2 =59.8%					
Test for overall effect z=4.80 p<0.00001					

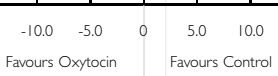
Analysis 02.10. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 10 Mean length of third stage (minutes)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 10 Mean length of third stage (minutes)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Poeschmann 1991	28	9.90 (7.40)	24	11.70 (6.40)		100.0	-1.80 [-5.55, 1.95]
Total (95% CI)	28		24			100.0	-1.80 [-5.55, 1.95]
Test for heterogeneity: not applicable							
Test for overall effect z=0.94 p=0.3							



Analysis 02.11. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	0/143		3.0	5.47 [0.23, 132.66]
Nordstrom 1997	18/513	11/487		97.0	1.55 [0.74, 3.26]
× Poeschmann 1991	0/28	0/24		0.0	Not estimable
Total (95% CI)	619	654		100.0	1.67 [0.82, 3.41]

Total events: 19 (Oxytocin), 11 (Control)

Test for heterogeneity chi-square=0.57 df=1 p=0.45 I^2 =0.0%

Test for overall effect z=1.41 p=0.2

Analysis 02.15. Comparison 02 Oxytocin versus no uterotonics (randomised trials only), Outcome 15 Nausea between delivery of the baby and discharge from the labour ward

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 02 Oxytocin versus no uterotonics (randomised trials only)

Outcome: 15 Nausea between delivery of the baby and discharge from the labour ward

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Poeschmann 1991	0/28	1/24		100.0	0.29 [0.01, 6.74]
Total (95% CI)	28	24		100.0	0.29 [0.01, 6.74]

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

Test for heterogeneity: not applicable

Test for overall effect z=0.77 p=0.4

Analysis 03.01. Comparison 03 Oxytocin versus no uterotonics (active management only), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 03 Oxytocin versus no uterotonics (active management only)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Pierre 1992	37/488	126/482		100.0	0.29 [0.21, 0.41]
Total (95% CI)	488	482		100.0	0.29 [0.21, 0.41]
Total events: 37 (Oxytocin), 126 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=7.05 p<0.00001					

Analysis 03.02. Comparison 03 Oxytocin versus no uterotonics (active management only), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 03 Oxytocin versus no uterotonics (active management only)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Pierre 1992	7/488	21/482		100.0	0.33 [0.14, 0.77]
Total (95% CI)	488	482		100.0	0.33 [0.14, 0.77]
Total events: 7 (Oxytocin), 21 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.57 p=0.01					

Analysis 03.11. Comparison 03 Oxytocin versus no uterotonics (active management only), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 03 Oxytocin versus no uterotonics (active management only)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Pierre 1992	32/488	32/482		100.0	0.99 [0.62, 1.59]
Total (95% CI)	488	482		100.0	0.99 [0.62, 1.59]
Total events: 32 (Oxytocin), 32 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.05 p=1					

Analysis 04.01. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	55/143		17.8	0.83 [0.57, 1.22]
Nordstrom 1997	104/513	175/487		82.2	0.56 [0.46, 0.70]
Total (95% CI)	591	630		100.0	0.61 [0.51, 0.73]
Total events: 129 (Oxytocin), 230 (Control)					
Test for heterogeneity chi-square=3.07 df=1 p=0.08 I^2 =67.4%					
Test for overall effect z=5.26 p<0.00001					

Analysis 04.02. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

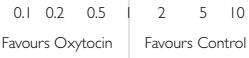
Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	16/143		20.4	0.80 [0.34, 1.87]
Nordstrom 1997	32/513	43/487		79.6	0.71 [0.45, 1.10]
Total (95% CI)	591	630		100.0	0.73 [0.49, 1.07]

Total events: 39 (Oxytocin), 59 (Control)

Test for heterogeneity chi-square=0.07 df=1 p=0.79 I^2 =0.0%

Test for overall effect z=1.61 p=0.1



Analysis 04.03. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Groot 1996	78	499.00 (454.00)	143	520.00 (419.00)		8.0	-21.00 [-142.93, 100.93]
Nordstrom 1997	513	270.00 (260.00)	487	359.00 (315.00)		92.0	-89.00 [-124.90, -53.10]
Total (95% CI)	591		630			100.0	-83.58 [-118.01, -49.14]

Test for heterogeneity chi-square=1.10 df=1 p=0.29 I^2 =9.0%

Test for overall effect z=4.76 p<0.00001

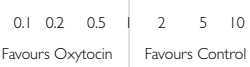
Analysis 04.04. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

Outcome: 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nordstrom 1997	20/485	30/458		100.0	0.63 [0.36, 1.09]
Total (95% CI)	485	458		100.0	0.63 [0.36, 1.09]
Total events: 20 (Oxytocin), 30 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.65 p=0.1					



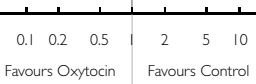
Analysis 04.05. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

Outcome: 05 Blood transfusion

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	2/78	3/143		29.2	1.22 [0.21, 7.16]
Nordstrom 1997	7/513	5/487		70.8	1.33 [0.42, 4.16]
Total (95% CI)	591	630		100.0	1.30 [0.50, 3.39]
Total events: 9 (Oxytocin), 8 (Control)					
Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%					
Test for overall effect z=0.53 p=0.6					



Analysis 04.07. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

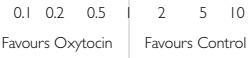
Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	26/143		21.1	0.99 [0.55, 1.78]
Nordstrom 1997	40/513	67/487		78.9	0.57 [0.39, 0.82]
Total (95% CI)	591	630		100.0	0.66 [0.48, 0.90]

Total events: 54 (Oxytocin), 93 (Control)

Test for heterogeneity chi-square=2.45 df=1 p=0.12 I^2 =59.2%

Test for overall effect z=2.65 p=0.008



Analysis 04.11. Comparison 04 Oxytocin versus no uterotonics (expectant management only), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 04 Oxytocin versus no uterotonics (expectant management only)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	0/143		3.0	5.47 [0.23, 132.66]
Nordstrom 1997	18/513	11/487		97.0	1.55 [0.74, 3.26]
Total (95% CI)	591	630		100.0	1.67 [0.82, 3.41]

Total events: 19 (Oxytocin), 11 (Control)

Test for heterogeneity chi-square=0.57 df=1 p=0.45 I^2 =0.0%

Test for overall effect z=1.41 p=0.2

Analysis 05.01. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

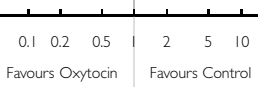
Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	55/143		10.9	0.83 [0.57, 1.22]
× Ilancheran 1990	0/5	0/5		0.0	Not estimable
Nordstrom 1997	104/513	175/487		50.4	0.56 [0.46, 0.70]
Pierre 1992	37/488	126/482		35.6	0.29 [0.21, 0.41]
Poeschmann 1991	7/28	10/24		3.0	0.60 [0.27, 1.33]
Total (95% CI)	1112	1141		100.0	0.50 [0.42, 0.58]

Total events: 173 (Oxytocin), 366 (Control)

Test for heterogeneity chi-square=18.00 df=3 p=0.0004 I^2 =83.3%

Test for overall effect z=8.67 p<0.00001



Analysis 05.02. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

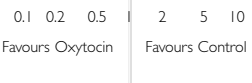
Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	16/143		14.2	0.80 [0.34, 1.87]
Nordstrom 1997	32/513	43/487		55.3	0.71 [0.45, 1.10]
Pierre 1992	7/488	21/482		26.5	0.33 [0.14, 0.77]
Poeschmann 1991	2/28	3/24		4.0	0.57 [0.10, 3.14]
Total (95% CI)	1107	1136		100.0	0.61 [0.44, 0.87]

Total events: 48 (Oxytocin), 83 (Control)

Test for heterogeneity chi-square=2.86 df=3 p=0.41 I^2 =0.0%

Test for overall effect z=2.78 p=0.006



Analysis 05.03. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Groot 1996	78	499.00 (454.00)	143	520.00 (419.00)		12.3	-21.00 [-142.93, 100.93]
Nordstrom 1997	513	409.00 (345.00)	487	527.00 (412.00)		82.2	-118.00 [-165.23, -70.77]
Poeschmann 1991	28	374.00 (279.00)	24	548.00 (376.00)		5.5	-174.00 [-356.51, 8.51]
Total (95% CI)	619		654			100.0	-109.12 [-151.93, -66.32]

Test for heterogeneity chi-square=2.63 df=2 p=0.27 I^2 =23.9%

Test for overall effect z=5.00 p<0.00001

Analysis 05.04. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 04 Maternal haemoglobin concentration (Hb) < 9 gm/deciltre 24 to 48 hours postpartum

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nordstrom 1997	20/485	30/458		100.0	0.63 [0.36, 1.09]
Total (95% CI)	485	458		100.0	0.63 [0.36, 1.09]

Total events: 20 (Oxytocin), 30 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=1.65 p=0.1

Analysis 05.05. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 05 Blood transfusion

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	2/78	3/143		29.2	1.22 [0.21, 7.16]
Nordstrom 1997	7/513	5/487		70.8	1.33 [0.42, 4.16]
Total (95% CI)	591	630		100.0	1.30 [0.50, 3.39]

Total events: 9 (Oxytocin), 8 (Control)

Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%

Test for overall effect z=0.53 p=0.6

Analysis 05.07. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

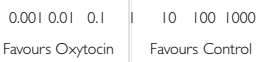
Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	26/143		20.4	0.99 [0.55, 1.78]
Nordstrom 1997	40/513	67/487		76.6	0.57 [0.39, 0.82]
Poeschmann 1991	0/28	2/24		3.0	0.17 [0.01, 3.42]
Total (95% CI)	619	654		100.0	0.64 [0.47, 0.87]

Total events: 54 (Oxytocin), 95 (Control)

Test for heterogeneity chi-square=3.23 df=2 p=0.20 I^2 =38.2%

Test for overall effect z=2.81 p=0.005

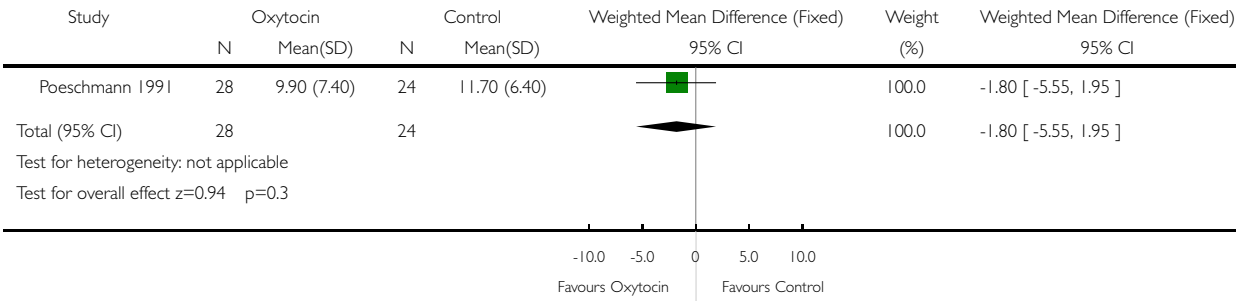


Analysis 05.10. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 10 Mean length of third stage (minutes)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 10 Mean length of third stage (minutes)

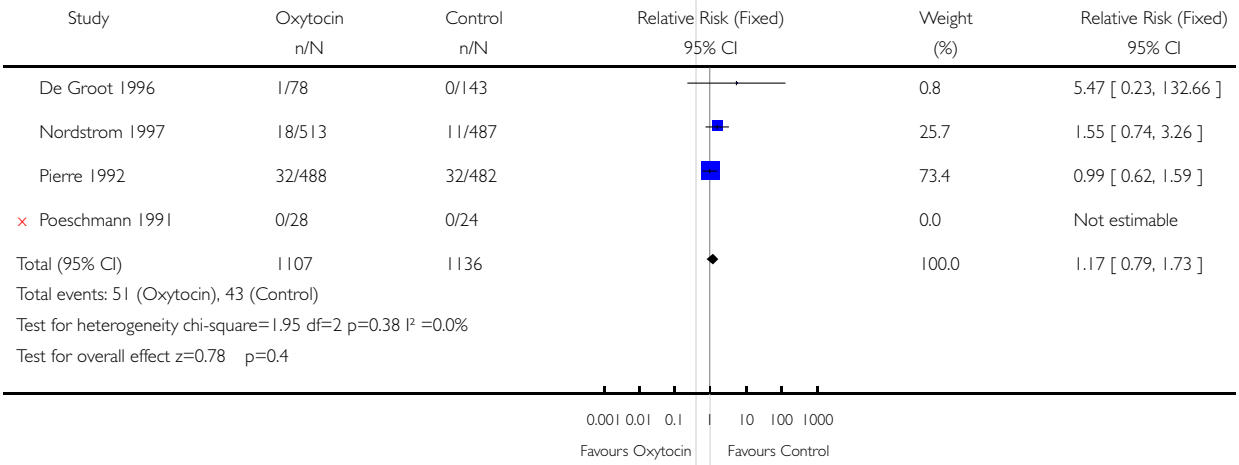


Analysis 05.11. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 11 Manual removal of the placenta



Analysis 05.15. Comparison 05 Oxytocin versus no uterotonics (given before placental delivery), Outcome 15 Nausea between delivery of the baby and discharge from the labour ward

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 05 Oxytocin versus no uterotonics (given before placental delivery)

Outcome: 15 Nausea between delivery of the baby and discharge from the labour ward

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Poeschmann 1991	0/28	1/24		100.0	0.29 [0.01, 6.74]
Total (95% CI)	28	24		100.0	0.29 [0.01, 6.74]
Total events: 0 (Oxytocin), 1 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.77 p=0.4					

Analysis 06.01. Comparison 06 Oxytocin versus no uterotonics (given after placental delivery), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 06 Oxytocin versus no uterotonics (given after placental delivery)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Howard 1964	15/470	25/470		100.0	0.60 [0.32, 1.12]
Total (95% CI)	470	470		100.0	0.60 [0.32, 1.12]
Total events: 15 (Oxytocin), 25 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.60 p=0.1					

Analysis 06.03. Comparison 06 Oxytocin versus no uterotonics (given after placental delivery), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 06 Oxytocin versus no uterotonics (given after placental delivery)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Control N	Control Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Newton 1961	50	345.00 (285.00)	50	333.00 (298.00)		100.0	12.00 [-102.29, 126.29]
Total (95% CI)	50		50			100.0	12.00 [-102.29, 126.29]

Test for heterogeneity: not applicable

Test for overall effect z=0.21 p=0.8

Analysis 06.07. Comparison 06 Oxytocin versus no uterotonics (given after placental delivery), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 06 Oxytocin versus no uterotonics (given after placental delivery)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Howard 1964	21/479	58/475		84.1	0.36 [0.22, 0.58]
Newton 1961	1/50	11/50		15.9	0.09 [0.01, 0.68]
Total (95% CI)	529	525		100.0	0.32 [0.20, 0.50]

Total events: 22 (Oxytocin), 69 (Control)

Test for heterogeneity chi-square=1.74 df=1 p=0.19 I^2 =42.6%

Test for overall effect z=4.85 p<0.00001

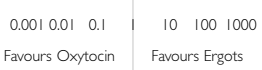
Analysis 07.01. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	54/146		34.6	0.87 [0.59, 1.28]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Howard 1964	15/470	9/493		8.1	1.75 [0.77, 3.96]
Ilancheran 1990	0/5	1/5		1.4	0.33 [0.02, 6.65]
Sorbe 1978	48/506	63/543		55.9	0.82 [0.57, 1.17]
Total (95% CI)	1383	1336		100.0	0.90 [0.70, 1.16]
Total events: 88 (Oxytocin), 127 (Ergot Alkaloids)					
Test for heterogeneity chi-square=3.28 df=3 p=0.35 I² =8.6%					
Test for overall effect z=0.80 p=0.4					



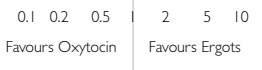
Analysis 07.02. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	12/146		36.6	1.09 [0.45, 2.66]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Sorbe 1978	13/506	15/543		63.4	0.93 [0.45, 1.94]
Total (95% CI)	908	838		100.0	0.99 [0.56, 1.74]
Total events: 20 (Oxytocin), 27 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.07 df=1 p=0.78 I² =0.0%					
Test for overall effect z=0.04 p=1					



Analysis 07.03. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin		Ergot Alkaloids		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
De Groot 1996	78	499.00 (454.00)	146	476.00 (340.00)		6.9	23.00 [-91.86, 137.86]
Sorbe 1978	506	273.00 (247.00)	543	306.00 (271.00)		93.1	-33.00 [-64.35, -1.65]
Total (95% CI)	584		689			100.0	-29.12 [-59.36, 1.12]

Test for heterogeneity chi-square=0.85 df=1 p=0.36 I^2 =0.0%

Test for overall effect z=1.89 p=0.06

Analysis 07.05. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 05 Blood transfusion

Study	Oxytocin	Ergot Alkaloids	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
De Groot 1996	2/78	1/146		100.0	3.74 [0.34, 40.64]
Total (95% CI)	78	146		100.0	3.74 [0.34, 40.64]

Total events: 2 (Oxytocin), 1 (Ergot Alkaloids)

Test for heterogeneity: not applicable

Test for overall effect z=1.08 p=0.3

Analysis 07.07. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	21/146		37.5	1.25 [0.67, 2.31]
Howard 1964	21/479	25/505		62.5	0.89 [0.50, 1.56]
Total (95% CI)	557	651		100.0	1.02 [0.67, 1.55]
Total events: 35 (Oxytocin), 46 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.65 df=1 p=0.42 I^2 =0.0%					
Test for overall effect z=0.10 p=0.9					

Analysis 07.08. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 08 Third stage > 20 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	324	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

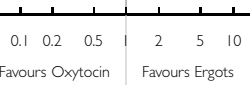
Analysis 07.09. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 09 Third stage > 40 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 09 Third stage > 40 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/234	0/149		0.0	Not estimable
Total (95% CI)	234	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 07.10. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 10 Mean length of third stage (minutes)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 10 Mean length of third stage (minutes)

Study	Oxytocin N	Oxytocin Mean(SD)	Ergot Alkaloids N	Ergot Alkaloids Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Sorbe 1978	506	9.50 (7.10)	543	10.30 (6.90)		100.0	-0.80 [-1.65, 0.05]
Total (95% CI)	506		543			100.0	-0.80 [-1.65, 0.05]
Test for heterogeneity: not applicable							
Test for overall effect z=1.85 p=0.06							

Analysis 07.11. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	2/146		1.7	0.94 [0.09, 10.16]
Fugo 1958	55/324	36/149		60.5	0.70 [0.48, 1.02]
Sorbe 1978	10/506	32/543		37.8	0.34 [0.17, 0.68]
Total (95% CI)	908	838		100.0	0.57 [0.41, 0.79]
Total events: 66 (Oxytocin), 70 (Ergot Alkaloids)					
Test for heterogeneity chi-square=3.60 df=2 p=0.17 I^2 =44.5%					
Test for overall effect z=3.39 p=0.0007					

Analysis 07.13. Comparison 07 Oxytocin versus ergot alkaloids (all trials), Outcome 13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 07 Oxytocin versus ergot alkaloids (all trials)

Outcome: 13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
McGinty 1956	4/50	15/100		100.0	0.53 [0.19, 1.52]
Total (95% CI)	50	100		100.0	0.53 [0.19, 1.52]
Total events: 4 (Oxytocin), 15 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.17 p=0.2					

Analysis 08.01. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	54/146		81.1	0.87 [0.59, 1.28]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Howard 1964	15/470	9/493		18.9	1.75 [0.77, 3.96]
Total (95% CI)	872	788		100.0	1.03 [0.73, 1.47]
Total events: 40 (Oxytocin), 63 (Ergot Alkaloids)					
Test for heterogeneity chi-square=2.39 df=1 p=0.12 I^2 =58.2%					
Test for overall effect z=0.18 p=0.9					

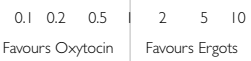
Analysis 08.02. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	12/146		100.0	1.09 [0.45, 2.66]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	402	295		100.0	1.09 [0.45, 2.66]
Total events: 7 (Oxytocin), 12 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.19 p=0.8					

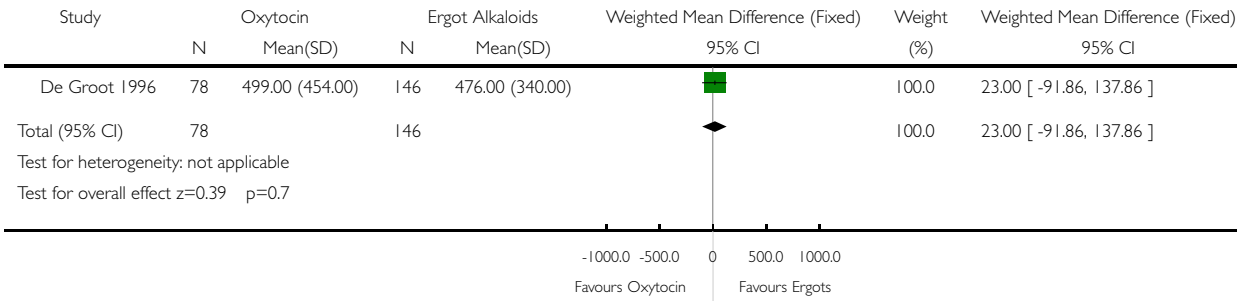


Analysis 08.03. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 03 Mean blood loss (ml)

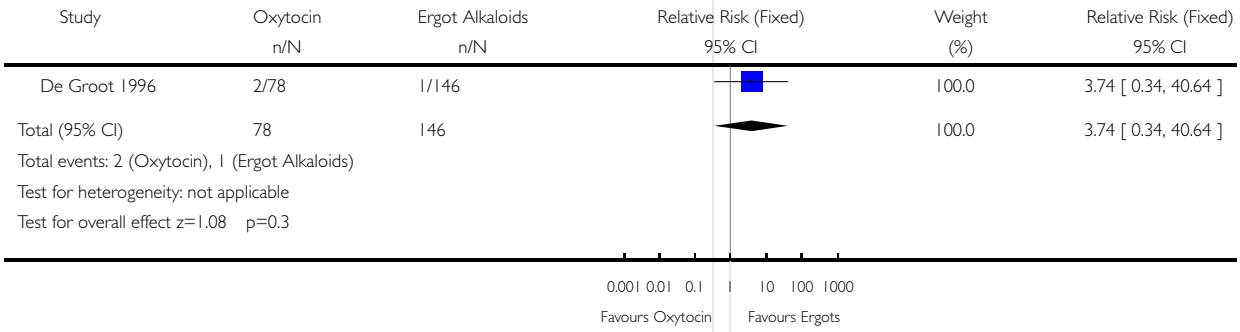


Analysis 08.05. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 05 Blood transfusion



Analysis 08.07. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	21/146		37.5	1.25 [0.67, 2.31]
Howard 1964	21/479	25/505		62.5	0.89 [0.50, 1.56]
Total (95% CI)	557	651		100.0	1.02 [0.67, 1.55]
Total events: 35 (Oxytocin), 46 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.65 df=1 p=0.42 I^2 =0.0%					
Test for overall effect z=0.10 p=0.9					

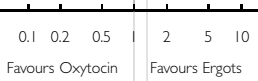
Analysis 08.08. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 08 Third stage > 20 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	324	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



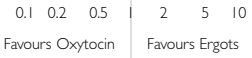
Analysis 08.09. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 09 Third stage > 40 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 09 Third stage > 40 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	324	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



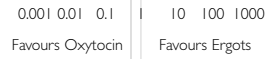
Analysis 08.11. Comparison 08 Oxytocin versus ergot alkaloids (randomised trials only), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 08 Oxytocin versus ergot alkaloids (randomised trials only)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	2/146		2.7	0.94 [0.09, 10.16]
Fugo 1958	55/324	36/149		97.3	0.70 [0.48, 1.02]
Total (95% CI)	402	295		100.0	0.71 [0.49, 1.02]
Total events: 56 (Oxytocin), 38 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.05 df=1 p=0.82 I^2 =0.0%					
Test for overall effect z=1.83 p=0.07					



Analysis 10.01. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	54/146		100.0	0.87 [0.59, 1.28]
Total (95% CI)	78	146		100.0	0.87 [0.59, 1.28]
Total events: 25 (Oxytocin), 54 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.73 p=0.5					

Analysis 10.02. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	12/146		100.0	1.09 [0.45, 2.66]
Total (95% CI)	78	146		100.0	1.09 [0.45, 2.66]
Total events: 7 (Oxytocin), 12 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.19 p=0.8					

Analysis 10.03. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 03 Mean blood loss (ml)

Study	Oxytocin N	Oxytocin Mean(SD)	Ergot Alkaloids N	Ergot Alkaloids Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Groot 1996	78	499.00 (454.00)	146	476.00 (340.00)		100.0	23.00 [-91.86, 137.86]
Total (95% CI)	78		146			100.0	23.00 [-91.86, 137.86]
Test for heterogeneity: not applicable							
Test for overall effect z=0.39 p=0.7							

Analysis 10.05. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 05 Blood transfusion

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	2/78	1/146		100.0	3.74 [0.34, 40.64]
Total (95% CI)	78	146		100.0	3.74 [0.34, 40.64]
Total events: 2 (Oxytocin), 1 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.08 p=0.3					

Analysis 10.07. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	21/146		100.0	1.25 [0.67, 2.31]
Total (95% CI)	78	146		100.0	1.25 [0.67, 2.31]
Total events: 14 (Oxytocin), 21 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					

Analysis 10.11. Comparison 10 Oxytocin versus ergot alkaloids (expectant management only), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 10 Oxytocin versus ergot alkaloids (expectant management only)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	2/146		100.0	0.94 [0.09, 10.16]
Total (95% CI)	78	146		100.0	0.94 [0.09, 10.16]
Total events: 1 (Oxytocin), 2 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.05 p=1					

Analysis 11.01. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	25/78	54/146		37.7	0.87 [0.59, 1.28]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Ilancheran 1990	0/5	1/5		1.5	0.33 [0.02, 6.65]
Sorbe 1978	48/506	63/543		60.8	0.82 [0.57, 1.17]
Total (95% CI)	913	843		100.0	0.83 [0.64, 1.08]
Total events: 73 (Oxytocin), 118 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.41 df=2 p=0.81 I^2 =0.0%					
Test for overall effect z=1.40 p=0.2					

Analysis 11.02. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

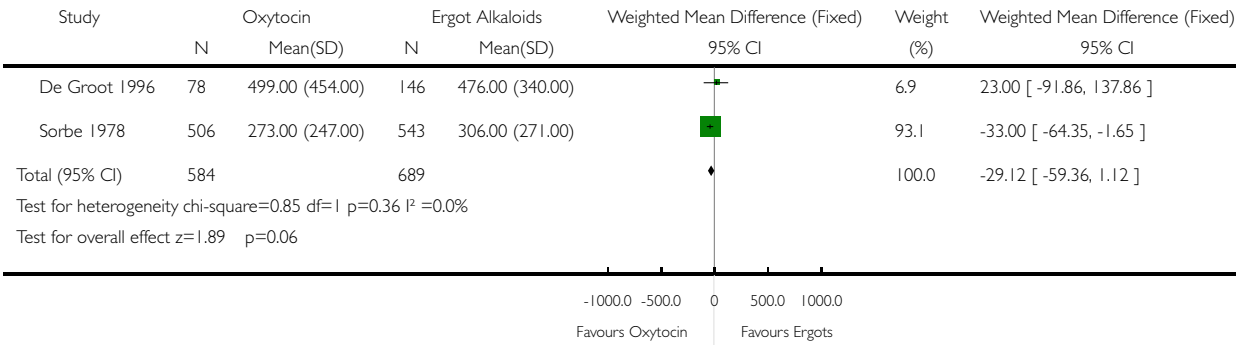
Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	7/78	12/146		36.6	1.09 [0.45, 2.66]
× Fugo 1958	0/324	0/149		0.0	Not estimable
Sorbe 1978	13/506	15/543		63.4	0.93 [0.45, 1.94]
Total (95% CI)	908	838		100.0	0.99 [0.56, 1.74]
Total events: 20 (Oxytocin), 27 (Ergot Alkaloids)					
Test for heterogeneity chi-square=0.07 df=1 p=0.78 I^2 =0.0%					
Test for overall effect z=0.04 p=1					

Analysis 11.03. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 03 Mean blood loss (ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 03 Mean blood loss (ml)

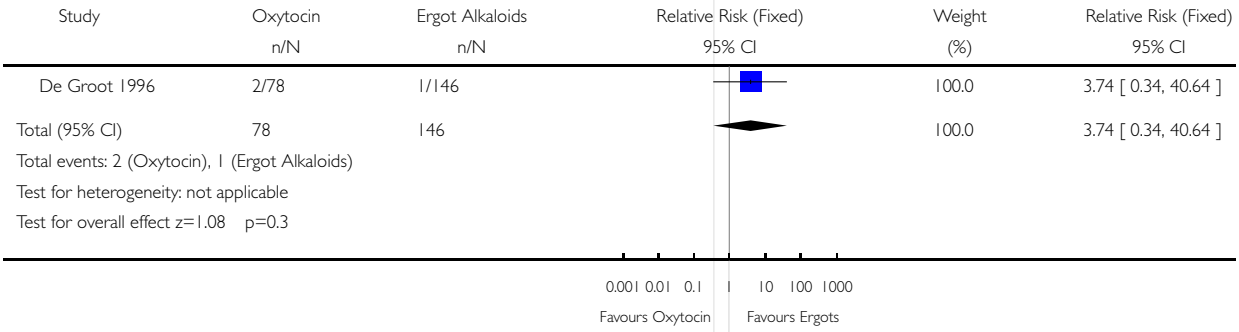


Analysis 11.05. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 05 Blood transfusion



Analysis 11.07. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	14/78	21/146		100.0	1.25 [0.67, 2.31]
Total (95% CI)	78	146		100.0	1.25 [0.67, 2.31]
Total events: 14 (Oxytocin), 21 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					

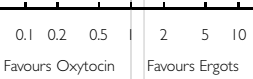
Analysis 11.08. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 08 Third stage > 20 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	324	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



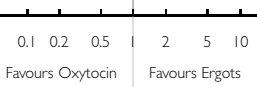
Analysis 11.09. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 09 Third stage > 40 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 09 Third stage > 40 minutes

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Fugo 1958	0/324	0/149		0.0	Not estimable
Total (95% CI)	324	149		0.0	Not estimable
Total events: 0 (Oxytocin), 0 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 11.10. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 10 Mean length of third stage (minutes)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 10 Mean length of third stage (minutes)

Study	Oxytocin N	Oxytocin Mean(SD)	Ergot Alkaloids N	Ergot Alkaloids Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Sorbe 1978	506	9.50 (7.10)	543	10.30 (6.90)		100.0	-0.80 [-1.65, 0.05]
Total (95% CI)	506		543			100.0	-0.80 [-1.65, 0.05]
Test for heterogeneity: not applicable							
Test for overall effect z=1.85 p=0.06							

Analysis 11.11. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 11 Manual removal of the placenta

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Groot 1996	1/78	2/146		1.7	0.94 [0.09, 10.16]
Fugo 1958	55/324	36/149		60.5	0.70 [0.48, 1.02]
Sorbe 1978	10/506	32/543		37.8	0.34 [0.17, 0.68]
Total (95% CI)	908	838		100.0	0.57 [0.41, 0.79]
Total events: 66 (Oxytocin), 70 (Ergot Alkaloids)					
Test for heterogeneity chi-square=3.60 df=2 p=0.17 I^2 =44.5%					
Test for overall effect z=3.39 p=0.0007					

Analysis 11.13. Comparison 11 Oxytocin versus ergot alkaloids (given before placental delivery), Outcome 13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 11 Oxytocin versus ergot alkaloids (given before placental delivery)

Outcome: 13 Diastolic blood pressure > 100 mm Hg between delivery of the baby and discharge from the labour ward

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
McGinty 1956	4/50	15/100		100.0	0.53 [0.19, 1.52]
Total (95% CI)	50	100		100.0	0.53 [0.19, 1.52]
Total events: 4 (Oxytocin), 15 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.17 p=0.2					

Analysis 12.01. Comparison 12 Oxytocin versus ergot alkaloids (given after placental delivery), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 12 Oxytocin versus ergot alkaloids (given after placental delivery)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Howard 1964	15/470	9/493		100.0	1.75 [0.77, 3.96]
Total (95% CI)	470	493		100.0	1.75 [0.77, 3.96]
Total events: 15 (Oxytocin), 9 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.34 p=0.2					

Analysis 12.07. Comparison 12 Oxytocin versus ergot alkaloids (given after placental delivery), Outcome 07 Therapeutic uterontonics

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 12 Oxytocin versus ergot alkaloids (given after placental delivery)

Outcome: 07 Therapeutic uterontonics

Study	Oxytocin n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Howard 1964	21/479	25/505		100.0	0.89 [0.50, 1.56]
Total (95% CI)	479	505		100.0	0.89 [0.50, 1.56]
Total events: 21 (Oxytocin), 25 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.42 p=0.7					

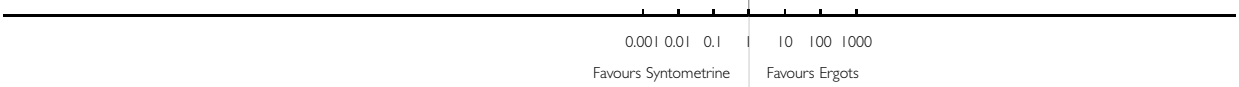
Analysis 13.01. Comparison 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Barbaro 1961	39/300	10/300		19.3	3.90 [1.98, 7.67]
Bonham 1963	5/391	13/416		24.3	0.41 [0.15, 1.14]
Francis (2) 1965a	4/171	9/183		16.8	0.48 [0.15, 1.52]
Ilancheran 1990	0/5	1/5		2.9	0.33 [0.02, 6.65]
Soiva 1964	18/560	19/560		36.7	0.95 [0.50, 1.79]
Total (95% CI)	1427	1464		100.0	1.29 [0.90, 1.84]
Total events: 66 (Syntometrine), 52 (Ergot Alkaloids)					
Test for heterogeneity chi-square=19.68 df=4 p=0.0006 I^2 =79.7%					
Test for overall effect z=1.40 p=0.2					



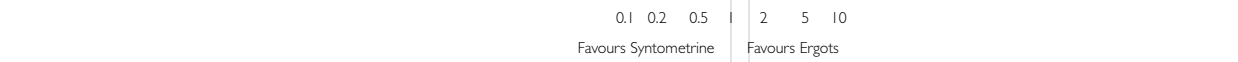
Analysis 13.02. Comparison 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials), Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Soiva 1964	5/560	3/560		100.0	1.67 [0.40, 6.94]
Total (95% CI)	560	560		100.0	1.67 [0.40, 6.94]
Total events: 5 (Syntometrine), 3 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					



Analysis 13.05. Comparison 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials), Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

Outcome: 05 Blood transfusion

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Soiva 1964	5/560	7/560		100.0	0.71 [0.23, 2.24]
Total (95% CI)	560	560		100.0	0.71 [0.23, 2.24]
Total events: 5 (Syntometrine), 7 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.58 p=0.6					

Analysis 13.08. Comparison 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

Outcome: 08 Third stage > 20 minutes

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	10/391	7/416		7.6	1.52 [0.58, 3.95]
Francis (2) 1965a	3/171	1/183		1.1	3.21 [0.34, 30.57]
Soiva 1964	66/560	81/560		91.3	0.81 [0.60, 1.10]
Total (95% CI)	1122	1159		100.0	0.89 [0.67, 1.19]
Total events: 79 (Syntometrine), 89 (Ergot Alkaloids)					
Test for heterogeneity chi-square=2.78 df=2 p=0.25 I^2 =28.1%					
Test for overall effect z=0.77 p=0.4					

Analysis 13.11. Comparison 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 13 Oxytocin + ergometrine versus ergot alkaloids alone (all trials)

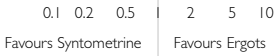
Outcome: 11 Manual removal of the placenta

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	5/391	5/416		37.7	1.06 [0.31, 3.65]
Soiva 1964	8/560	8/560		62.3	1.00 [0.38, 2.65]
Total (95% CI)	951	976		100.0	1.02 [0.48, 2.20]

Total events: 13 (Syntometrine), 13 (Ergot Alkaloids)

Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%

Test for overall effect z=0.06 p=1



Analysis 14.01. Comparison 14 Oxytocin + ergometrine versus ergot alkaloids alone (randomised trials), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 14 Oxytocin + ergometrine versus ergot alkaloids alone (randomised trials)

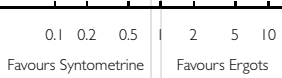
Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	5/391	13/416		59.2	0.41 [0.15, 1.14]
Francis (2) 1965a	4/171	9/183		40.8	0.48 [0.15, 1.52]
Total (95% CI)	562	599		100.0	0.44 [0.20, 0.94]

Total events: 9 (Syntometrine), 22 (Ergot Alkaloids)

Test for heterogeneity chi-square=0.04 df=1 p=0.85 I^2 =0.0%

Test for overall effect z=2.12 p=0.03



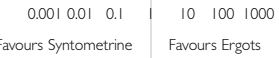
Analysis 14.08. Comparison 14 Oxytocin + ergometrine versus ergot alkaloids alone (randomised trials), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 14 Oxytocin + ergometrine versus ergot alkaloids alone (randomised trials)

Outcome: 08 Third stage > 20 minutes

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Francis (2) 1965a	3/171	1/183		100.0	3.21 [0.34, 30.57]
Total (95% CI)	171	183		100.0	3.21 [0.34, 30.57]
Total events: 3 (Syntometrine), 1 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.01 p=0.3					



Analysis 15.01. Comparison 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management), Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management)

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	1/199	5/217		100.0	0.22 [0.03, 1.85]
Total (95% CI)	199	217		100.0	0.22 [0.03, 1.85]
Total events: 1 (Syntometrine), 5 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.40 p=0.2					

Analysis 15.08. Comparison 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management), Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management)

Outcome: 08 Third stage > 20 minutes

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	6/199	1/217		100.0	6.54 [0.79, 53.87]
Total (95% CI)	199	217		100.0	6.54 [0.79, 53.87]
Total events: 6 (Syntometrine), 1 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.75 p=0.08					

Analysis 15.11. Comparison 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management), Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 15 Oxytocin + ergometrine versus ergot alkaloids alone (active management)

Outcome: 11 Manual removal of the placenta

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	4/199	1/217		100.0	4.36 [0.49, 38.70]
Total (95% CI)	199	217		100.0	4.36 [0.49, 38.70]
Total events: 4 (Syntometrine), 1 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					

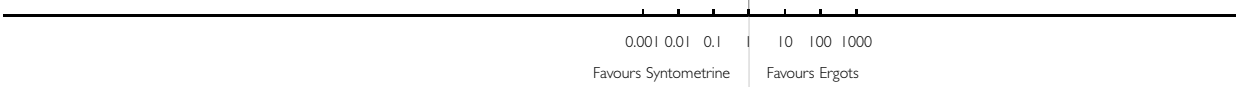
Analysis 17.01. Comparison 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery, Outcome 01 PPH (clinically estimated blood loss > or = 500 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome: 01 PPH (clinically estimated blood loss > or = 500 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Barbaro 1961	39/300	10/300		19.3	3.90 [1.98, 7.67]
Bonham 1963	5/391	13/416		24.3	0.41 [0.15, 1.14]
Francis (2) 1965a	4/171	9/183		16.8	0.48 [0.15, 1.52]
Ilancheran 1990	0/5	1/5		2.9	0.33 [0.02, 6.65]
Soiva 1964	18/560	19/560		36.7	0.95 [0.50, 1.79]
Total (95% CI)	1427	1464		100.0	1.29 [0.90, 1.84]
Total events: 66 (Syntometrine), 52 (Ergot Alkaloids)					
Test for heterogeneity chi-square=19.68 df=4 p=0.0006 I^2 =79.7%					
Test for overall effect z=1.40 p=0.2					



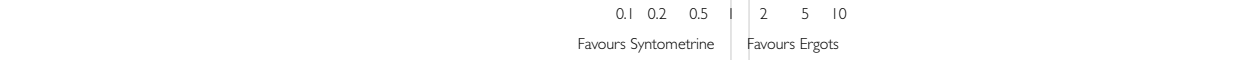
Analysis 17.02. Comparison 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery, Outcome 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome: 02 Severe PPH (clinically estimated blood loss > or = 1000 ml)

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Soiva 1964	5/560	3/560		100.0	1.67 [0.40, 6.94]
Total (95% CI)	560	560		100.0	1.67 [0.40, 6.94]
Total events: 5 (Syntometrine), 3 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.70 p=0.5					



Analysis 17.05. Comparison 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery, Outcome 05 Blood transfusion

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome: 05 Blood transfusion

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Soiva 1964	5/560	7/560		100.0	0.71 [0.23, 2.24]
Total (95% CI)	560	560		100.0	0.71 [0.23, 2.24]
Total events: 5 (Syntometrine), 7 (Ergot Alkaloids)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.58 p=0.6					

Analysis 17.08. Comparison 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery, Outcome 08 Third stage > 20 minutes

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome: 08 Third stage > 20 minutes

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	10/391	7/416		7.6	1.52 [0.58, 3.95]
Francis (2) 1965a	3/171	1/183		1.1	3.21 [0.34, 30.57]
Soiva 1964	66/560	81/560		91.3	0.81 [0.60, 1.10]
Total (95% CI)	1122	1159		100.0	0.89 [0.67, 1.19]
Total events: 79 (Syntometrine), 89 (Ergot Alkaloids)					
Test for heterogeneity chi-square=2.78 df=2 p=0.25 I^2 =28.1%					
Test for overall effect z=0.77 p=0.4					

Analysis 17.11. Comparison 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery, Outcome 11 Manual removal of the placenta

Review: Prophylactic oxytocin for the third stage of labour

Comparison: 17 Oxytocin + ergometrine versus ergot alkaloids alone (given before placental delivery

Outcome: 11 Manual removal of the placenta

Study	Syntometrine n/N	Ergot Alkaloids n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bonham 1963	5/391	5/416		37.7	1.06 [0.31, 3.65]
Soiva 1964	8/560	8/560		62.3	1.00 [0.38, 2.65]
Total (95% CI)	951	976		100.0	1.02 [0.48, 2.20]

Total events: 13 (Syntometrine), 13 (Ergot Alkaloids)

Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%

Test for overall effect z=0.06 p=1