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Amnioinfusion for meconium-stained liquor in labour (Review)

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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	3
OBJECTIVES	3
METHODS	3
RESULTS	6
Figure 1.	7
Figure 2.	7
DISCUSSION	8
AUTHORS' CONCLUSIONS	9
ACKNOWLEDGEMENTS	10
REFERENCES	11
CHARACTERISTICS OF STUDIES	15
DATA AND ANALYSES	29
Analysis 1.1. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 1 Meconium aspiration syndrome.	33
Analysis 1.2. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 2 Perinatal death or serious morbidity (post hoc).	34
Analysis 1.3. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 3 Maternal death or serious morbidity (post hoc).	34
Analysis 1.4. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 4 Heavy meconium staining.	35
Analysis 1.5. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 5 Variable decelerations.	35
Analysis 1.6. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 6 Caesarean for fetal distress.	36
Analysis 1.7. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 7 Caesarean overall.	36
Analysis 1.8. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 8 1-minute Apgar < 4.	37
Analysis 1.9. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 9 1-minute Apgar < 7.	37
Analysis 1.10. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 10 5-minute Apgar < 7.	38
Analysis 1.11. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 11 Umbilical artery pH < 7.20.	39
Analysis 1.12. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 12 Meconium below vocal cords.	39
Analysis 1.13. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 13 Neonatal ventilation/neonatal intensive care unit admission.	40
Analysis 1.14. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 14 Neonatal encephalopathy.	40
Analysis 1.15. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 15 Perinatal death.	41
Analysis 1.16. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 16 Puerperal pyrexia.	42
Analysis 1.17. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 17 Puerperal endometritis.	42
Analysis 1.18. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 18 Oxytocin augmentation.	43
Analysis 1.19. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 19 Narcotic analgesic.	43
Analysis 1.20. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 20 Epidural analgesia.	44
Analysis 1.21. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 21 First stage labour (minutes). ..	44
Analysis 1.22. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 22 Instrumental vaginal delivery for fetal distress.	45
Analysis 1.23. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 23 Instrumental vaginal delivery.	45
Analysis 1.25. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 25 Respiratory Distress (post hoc).	46
Analysis 1.26. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 26 Mean maternal hospital stay (post hoc).	46
WHAT'S NEW	47
HISTORY	47
CONTRIBUTIONS OF AUTHORS	48
DECLARATIONS OF INTEREST	48
SOURCES OF SUPPORT	48
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	48

NOTES	48
INDEX TERMS	48

[Intervention Review]

Amnioinfusion for meconium-stained liquor in labour

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ABSTRACT

Background

Amnioinfusion is thought to dilute meconium present in the amniotic fluid and so reduce the risk of meconium aspiration.

Objectives

To assess the effects of amnioinfusion for meconium-stained liquor on perinatal outcome.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (1 December 2013).

Selection criteria

Randomised trials comparing amnioinfusion with no amnioinfusion for women in labour with moderate or thick meconium staining of the amniotic fluid.

Data collection and analysis

Three review authors independently assessed eligibility and trial quality, and extracted data.

Main results

Fourteen studies of variable quality (4435 women) are included.

Subgroup analysis was performed for studies from settings with limited facilities to monitor the baby's condition during labour and intervene effectively, and settings with standard peripartum surveillance.

Settings with standard peripartum surveillance: there was considerable heterogeneity for several outcomes. There was no significant reduction in the primary outcomes meconium aspiration syndrome, perinatal death or severe morbidity, and maternal death or severe morbidity. There was a reduction in caesarean sections (CSs) for fetal distress but not overall. Meconium below the vocal cords diagnosed by laryngoscopy was reduced, as was neonatal ventilation or neonatal intensive care unit admission, but there was no significant reduction in perinatal deaths or other morbidity. Planned sensitivity analysis excluding trials with greater risk of bias resulted in an absence of benefits for any of the outcomes studied.

Settings with limited peripartum surveillance: three studies were included. In the amnioinfusion group there was a reduction in CS for fetal distress and overall; meconium aspiration syndrome (three studies, 1144 women; risk ratio (RR) 0.17, 95% confidence interval (CI) 0.05 to 0.52); perinatal mortality (three studies, 1151 women; RR 0.24, 95% CI 0.11 to 0.53) and neonatal ventilation or neonatal intensive care unit admission. In one of the studies, meconium below the vocal cords was reduced and, in the other, neonatal encephalopathy was reduced.

Authors' conclusions

Amnioinfusion is associated with substantive improvements in perinatal outcome only in settings where facilities for perinatal surveillance are limited. It is not clear whether the benefits are due to dilution of meconium or relief of oligohydramnios.

In settings with standard peripartum surveillance, some non-substantive outcomes were improved in the initial analysis, but sensitivity analysis excluding trials with greater risk of bias eliminated these differences. Amnioinfusion is either ineffective in this setting, or its effects are masked by other strategies to optimise neonatal outcome.

The trials reviewed are too small to address the possibility of rare but serious maternal adverse effects of amnioinfusion.

PLAIN LANGUAGE SUMMARY

Amnioinfusion for meconium-stained liquor in labour

Amnioinfusion is not beneficial for babies releasing medium to heavy meconium during labour, except in settings with limited facilities to monitor the baby's condition during labour.

A bowel movement (meconium) from the unborn baby during labour can enter the baby's lungs, causing breathing difficulties after birth. Extra liquid can be injected through the woman's vagina or abdomen into the womb (amnioinfusion) to provide more liquid to dilute the meconium and surround the baby. The review of 14 trials (4435 women) found that amnioinfusion with a salt (saline) solution is beneficial for babies only in settings in which babies are at high risk due to limited monitoring facilities. Further research into the effects on women is needed.

BACKGROUND

Amnioinfusion has been used to improve neonatal outcomes in cases complicated by meconium aspiration ([Sadovsky 1989](#); [Wenstrom 1989](#)). Meconium aspiration may occur before birth, or during the birth process, and is associated with significant mortality. Airways suctioning of the neonate has been suggested to reduce, but does not eliminate, the occurrence of meconium aspiration ([Davis 1985](#)). Strategies have therefore, been sought to reduce fetal meconium aspiration before birth.

The presence of thick meconium staining of the amniotic fluid is an indication of oligohydramnios, as meconium passed into a normal volume of amniotic fluid will usually appear thin. Amnioinfusion may thus at the same time dilute the meconium and correct oligohydramnios, relieving umbilical cord compression. It is difficult to distinguish effects of amnioinfusion due to these two mechanisms.

Readers are referred to other reviews of the subject ([Gelfand 2004](#); [Gramellini 2003](#); [Hofmeyr 1996](#); [Hofmeyr 2000](#); [Lameier 1993](#); [Pierce 2000](#); [Velaphi 2006](#); [Xu 2007](#)), and to related Cochrane reviews ([Hofmeyr 2012](#); [Novikova 2012](#)).

Description of the condition

Meconium aspiration refers to fetal aspiration of meconium-stained amniotic fluid (MSAF) during the antepartum or intrapartum period. Meconium aspiration syndrome (MAS) refers to newborn respiratory distress secondary to the presence of meconium in the tracheobronchial airways. Passage of fetal meconium before birth occurs in 8% to 20% of pregnancies ([Nathan 1994](#); [Woods 1994](#)). It occurs mainly in term and post-term pregnancies. It may be associated with fetal compromise, but is also common in uncompromised labours. Possible causes that have been proposed include fetal hypoxia, a normal physiological function of the mature gastro-intestinal tract, vagally-mediated peristalsis in response to cord compression, and a direct effect on the fetal gastro-intestinal tract of maternal medication such as misoprostol ([Hofmeyr 2003](#)), castor oil and certain herbal remedies ([Mitri 1987](#)). Thick, but not thin meconium staining of the amniotic fluid is associated with poor perinatal outcome ([Mahomed 1994](#); [Ziadeh 2000](#)). The association between severe meconium aspiration syndrome and aspiration of meconium has been challenged ([Ghidini 2001](#)).

Amnioinfusion has been described as a method of preventing or relieving umbilical cord compression during labour ([Miyazaki 1983](#)), eliciting fetal heart rate accelerations during labour ([Wax 2004](#)), or of diluting meconium in the amniotic fluid to try to reduce the risk of meconium aspiration. Saline or Ringer's lactate is infused transcervically through a catheter into the uterine cavity, or transabdominally through a 'spinal' needle when membranes are intact. Amnioinfusion has also been used transabdominally for antepartum indications ([Gramellini 2003b](#)) and to facilitate external cephalic version at term ([Benifla 1995](#)).

Description of the intervention

The technique for amnioinfusion has been clearly described ([Weismiller 1998](#)). Saline or Ringer's lactate is usually infused through a purpose-designed intrauterine pressure catheter using an infusion pump. However, studies from low-income countries where such catheters are unaffordable have demonstrated that amnioinfusion can be successfully achieved using inexpensive

infant feeding tubes or suction catheters, and gravity infusion ([Abdel-Aleem 2005](#); [Ashfaq 2004](#); [Mahomed 1998](#); [Moodley 1998](#)). A study in which women with meconium-stained amniotic fluid were randomly allocated to receive amnioinfusion with saline or lactated Ringer's solution found no effect on neonatal plasma concentrations or pH, compared with a non-randomised normal control group ([Gonzalez 2002](#)). While randomised trials have not found increased risks associated with amnioinfusion, isolated case reports have documented complications following amnioinfusion ([Dorairajan 2005](#)). It is difficult to know whether there was a causal relationship in such reports. Amnioinfusion in women with previous caesarean section has not been found to carry risks of uterine rupture, though larger studies are needed ([Hicks 2005](#)).

How the intervention might work

Amnioinfusion has been used to improve neonatal outcomes in cases complicated by meconium aspiration ([Sadovsky 1989](#); [Wenstrom 1989](#)). Amnioinfusion has also proven effective for reducing overall complication rates in meconium aspiration syndrome. The success of amnioinfusion for prevention of meconium aspiration syndrome may be secondary to a dilutional effect. The amnioinfusion dilutes the meconium thereby reducing complications following meconium aspiration. Other investigators have shown a significant reduction in meconium concentration when amnioinfusion is used ([Ashfaq 2004](#); [Weismiller 1998](#)).

Why it is important to do this review

Amnioinfusion has been shown to be beneficial in reducing the complications following meconium-stained amniotic fluid in several randomised clinical trials. However, there has been no systematic review to address this topic, hence this review.

In several perinatal interventions, differences in effectiveness have been reported in studies conducted in low-income compared with high-income settings. Possible explanations include less stringent methodology in under-resourced settings; or the fact that in well-resourced settings outcomes are close to optimal, leaving little scope for further improvement with additional interventions. The latter concept has been discussed recently with respect to the potential benefits of early pregnancy ultrasound ([Hofmeyr 2009](#)). For this reason we have undertaken subgroup analyses for settings with limited and with standard peripartum surveillance.

OBJECTIVES

To assess the effects of amnioinfusion for meconium-stained liquor in labour on maternal and perinatal morbidity and mortality.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials comparing the effect of amnioinfusion for meconium-stained liquor on clinically meaningful outcomes, with a control group (no or sham amnioinfusion). Quasi-randomised (alternate allocation) were considered eligible, but cross-over and cluster-randomised trials were not considered.

Types of participants

Women in labour with moderate or thick meconium staining of the amniotic fluid.

Types of interventions

Amnioinfusion (the infusion of physiological saline or lactated Ringer's solution into the amniotic cavity) compared with no or sham amnioinfusion.

Types of outcome measures

Method of delivery, neonatal outcome and maternal complications. Two additional composite outcomes were added post hoc to accommodate data from [Fraser 2005](#): perinatal death or severe morbidity; and maternal death or severe morbidity.

Primary outcomes

1. Meconium aspiration syndrome
2. Perinatal death or serious morbidity (post hoc)
3. Maternal death or serious morbidity (post hoc)

Secondary outcomes

4. Heavy meconium staining of amniotic fluid
5. Variable fetal heart rate decelerations
6. Caesarean section for fetal distress
7. Caesarean section overall
8. One-minute Apgar score less than four
9. One-minute Apgar score less than seven
10. Five-minute Apgar score less than seven
11. Umbilical arterial blood pH less than 7.20
12. Meconium below the vocal cords
13. Neonatal ventilation/neonatal intensive care unit admission
14. Neonatal encephalopathy
15. Perinatal death
16. Puerperal pyrexia (as defined by trial authors)
17. Puerperal endometritis
18. Oxytocin augmentation of labour
19. Narcotic analgesia
20. Epidural analgesia
21. First stage of labour (minutes)
22. Instrumental vaginal delivery for fetal distress
23. Instrumental vaginal delivery overall
24. Second stage of labour (minutes)
25. Respiratory distress syndrome (post hoc)
26. Mean maternal hospital stay (post hoc)

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (1 December 2013).

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. weekly searches of MEDLINE;
3. weekly searches of Embase;

4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and Embase, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the [Cochrane Pregnancy and Childbirth Group](#).

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

For the methods used when assessing the trials identified in the previous version of this review, see [Hofmeyr 2010](#).

For this update we used the following methods when assessing the report identified by the updated search - [Choudhary 2010](#).

Selection of studies

Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion with the third review author. We created a study flow diagram to map out the number of records identified, included and excluded.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors extracted data using the agreed form. We resolved discrepancies through discussion or, when required, we consulted the third review author. We entered data into Review Manager software ([RevMan 2012](#)) and checked for accuracy.

When information regarding any of the above was unclear, we attempted to contact the authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). Any disagreements were resolved by involving the third author.

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

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

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

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

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

We assessed the methods as:

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

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

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

We assessed the methods as:

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

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

We described for each included study all the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We also provided information on whether the intended blinding was effective. Where blinding was not possible, we assessed whether the lack of blinding was likely to have introduced bias. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as:

- low, high or unclear risk of bias.

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

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

We assessed the methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done

with substantial departure of intervention received from that assigned at randomisation);

- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how the possibility of selective outcome reporting bias was examined by us and what we found.

We assessed methods as:

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

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

We described for each included study any important concerns we have about other possible sources of bias. We assessed whether each study was free of other problems that could put it at risk of bias:

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

(7) Overall risk of bias

We made explicit judgements about whether studies were at a high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses - see [Sensitivity analysis](#).

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we planned to use the mean difference for outcomes measured in the same way between trials and the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Only randomised clinical trials were included in this review. We did not include cluster-randomised trials or cross-over trials.

Dealing with missing data

For included studies, levels of attrition were noted. The impact of including studies with high levels of missing data in the overall assessment of treatment effect was explored by using sensitivity analysis. For all outcomes analyses were carried out, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau, I^2 and χ^2 statistics. We regarded heterogeneity as substantial if an I^2 was greater than 30% and either a τ^2 was greater than zero, or there was a low P value (< 0.10) in the χ^2 test for heterogeneity.

Assessment of reporting biases

Where we suspected reporting bias (see 'Selective reporting bias' above), we attempted to contact study authors to ask them to provide missing outcome data. Where this was not possible, and the missing data were thought to introduce serious bias, the impact of including such studies in the overall assessment of results was explored by a sensitivity analysis.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2012). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials.

If we used random-effects analyses, the results were presented as the average treatment effect with 95% confidence intervals, and the estimates of τ^2 and I^2 .

Subgroup analysis and investigation of heterogeneity

We carried out the following subgroup analyses.

1. Standard peripartum surveillance.
2. Limited peripartum surveillance.

All the outcomes were used in the subgroup analysis.

We assessed subgroup differences by interaction tests available within RevMan (RevMan 2012). We reported the results of subgroup analyses quoting the χ^2 statistic and P value, and the interaction test I^2 value.

For significant heterogeneity within subgroups, we used a random-effects model and explored the heterogeneity by planned sensitivity analysis excluding trials with greater risk of bias, as well as a post hoc sensitivity analysis based on sample size. In view of considerable heterogeneity and differences in adverse events rates between the two subgroups, overall meta-analyses were not reported for outcomes with significant heterogeneity.

Sensitivity analysis

We conducted a sensitivity analysis by excluding trials with greater risk of bias and examining the effect on the outcomes. A post-hoc sensitivity analysis was also performed to assess the effect of trial size on heterogeneity

RESULTS

Description of studies

Of 30 studies identified, 14 studies with data on 4435 women met the predefined criteria for inclusion for this update - see [Characteristics of included studies](#).

The rate of saline infusion varied between studies. [Sadovsky 1989](#) infused 600 mL in one hour, then 180 mL per hour continuously. [Adam 1989](#) used a single infusion of 1000 mL. [Wenstrom 1989](#) infused 1000 mL over 20 to 40 minutes, repeated six-hourly. [Macri 1992](#) infused 500 mL initially, then 250 to 500 mL as required to maintain a four-quadrant amniotic fluid index above 10 cm. [Ilagan 1992](#) infused 500 mL saline. [Cialone 1994](#) infused 600 mL over one hour followed by 150 mL per hour. [Eriksen 1994](#) infused 800 mL over one hour, then 180 mL per hour. [Spong 1994](#) infused 600 mL as a bolus, followed by 3 mL per minute. [Moodley 1998](#) used amnioinfusion with normal saline 10 to 15 mL per minute by gravity via a central venous manometer set and a size eight nasogastric infant feeding tube (1 litre over four hours). [Hofmeyr 1998a](#) infused saline 800 mL at 15 mL per minute, then 3 mL per minute maintenance infusion. [Mahomed 1998](#) infused saline 500 mL over 30 minutes then 500 mL at 30 drops per minute. [Puertas 2001](#) used saline via an infusion pump at 600 mL per hour for one hour, then 180 mL per hour until full cervical dilation, or basal uterine pressure increase to 20 mmHg. [Rathore 2002](#) used saline via an FG 8 nasogastric tube, 500 mL over 30 minutes, then 3 mL per minute, to a maximum dose of 1000 mL. [Sood 2004](#) infused saline through a plastic suction catheter (50 cases) or an amnioinfusion catheter (46 cases) until the returning fluid was clear. In most women 1000 mL was infused over 30 to 45 minutes. [Fraser 2005](#) used 800 mL saline over 40 minutes, then at 3 mL per minute to a maximum of 1500 mL. [Choudhary 2010](#) passed transcervical nasogastric tubes cephalad to the baby's head with infusion of 500 cc's of normal saline over a period of 30 minutes, followed by 2 mL/min under gravity till time of delivery.

Results of the search

Thirty studies were identified after the search. Of the 30 studies, 14 studies with data on 4435 women met the predefined criteria for inclusion.

Included studies

Fourteen studies were included ([Choudhary 2010](#); [Cialone 1994](#); [Eriksen 1994](#); [Fraser 2005](#); [Hofmeyr 1998a](#); [Macri 1992](#); [Mahomed 1998](#); [Moodley 1998](#); [Puertas 2001](#); [Rathore 2002](#); [Sadovsky 1989](#); [Sood 2004](#); [Spong 1994](#); [Wenstrom 1989](#)).

Excluded studies

Sixteen studies were excluded (Adam 1989; Ashfaq 2004; Das 2007; Edwards 1999; Engel 2008; Gonzalez 1998; Gonzalez 2002; Gupta 2011; Ilagan 1992; Khosla 1997; Kirubamani 2000; Lembet 1999; Lo 1993; Mukhopadhyay 2006; Nageotte 1991; Regi 2009).

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Allocation

Choudhary 2010, Moodley 1998, Puertas 2001 and Sadovsky 1989 randomly assigned women to two groups according to a list of randomly generated numbers in a sealed envelope assigned to each woman. However, they did not specify how participants were 'randomly' assigned to these groups (e.g. computer-generated, shuffling envelopes). Cialone 1994 and Spong 1994 used computer-generated random numbers methods for sequence generation, but they did not describe methods of allocation concealment. Eriksen 1994, Hofmeyr 1998a, Macri 1992, Mahomed 1998, Rathore 2002 and Wenstrom 1989 used computer randomisation and prevented selection bias due to allocation concealment by using sealed envelopes. Fraser 2005 used a centralised computer randomisation service, while Sood 2004 assigned women to each group by a coin toss.

Blinding

Blinding of the intervention was not possible, though some of the outcome measures could be assessed in a blinded fashion. In none of the studies were obstetricians blinded to the treatment, and only Choudhary 2010; Cialone 1994; Fraser 2005; Hofmeyr 1998a; Macri 1992; Mahomed 1998; Puertas 2001; Sadovsky 1989 and Wenstrom 1989 specified that the neonatologists evaluating the babies were blind to the assigned group of each baby.

Incomplete outcome data

Comparability of the groups was compromised by the following exclusions after randomisation: Wenstrom 1989 excluded 5/41 (12%) of women allocated to receive amnioinfusion but who did not (four gave birth spontaneously after 30, 45, 60 and 180 minutes, and one required emergency caesarean section for fetal distress - this information has been included in the analysis for this review in respect of delivery outcomes); Cialone 1994 excluded 7/54 (13%) of the study group who had diabetes (three) or requested withdrawal (four) and 1/59 (1.7%) allocated to the control group who requested withdrawal; Eriksen 1994 excluded 9/139 (6%) women whose records were unavailable or incomplete, and 6/71 (8%) randomised to the amnioinfusion group who delivered before they could receive amnioinfusion. In the study by Hofmeyr et al (Hofmeyr 1998a), one woman in the control group received amnioinfusion (analysis was by intention-to-treat), and data were missing on about 7% of outcome measures. In Mahomed 1998, four amnioinfusion allocations were missed and could not be traced. Sood 2004 excluded 3/99 women from the amnioinfusion group in whom amnioinfusion was abandoned because of vaginal bleeding.

Risk of bias in included studies

See [Characteristics of included studies](#), particularly the 'Methods' and 'Notes' sections and [Figure 1](#) and [Figure 2](#) for summaries of 'Risk of bias' assessments.

Fetal heart rate abnormalities before enrolment were present in 48/96 women in the amnioinfusion versus 60/100 in the control group. The perinatal mortality data are difficult to interpret because the reported rate (2.8%) in the amnioinfusion group does not reflect a whole number of the group of 96. In Fraser 2005, 1.2% of women were excluded from the analysis because of loss to follow-up (amnioinfusion 7/995; control 12/1003), because they did not meet inclusion criteria (breech presentation or multiple pregnancy: two in each group).

Selective reporting

All expected outcomes were reported in one study Choudhary 2010 and a published protocol was available for another study (Fraser 2005). All predefined outcomes were reported (Fraser 2005).

Other potential sources of bias

Spong 1994 do not account for a small discrepancy in group size (43 versus 50) despite using computer-generated allocation to create equal sized groups. The Cialone 1994 report does not account for a discrepancy in birth weights between the groups. There are thus several methodological shortcomings in all the studies except Fraser 2005. A potential source of bias in this review was the degree of heterogeneity in the individual trials.

Effects of interventions

Settings with standard peripartum surveillance

Primary outcomes

There was no significant reduction in meconium aspiration syndrome (11 studies, 3374 women; average risk ratio (RR) 0.52, 95% confidence interval (CI) 0.26 to 1.06; Heterogeneity: $\tau^2 = 0.56$; $\chi^2 = 20.08$, $df = 9$ ($P = 0.02$); $I^2 = 55\%$), [Analysis 1.1](#), nor in perinatal deaths (seven studies, 2762 women; RR 1.00, 95% CI 0.29 to 3.45), [Analysis 1.15](#), nor the combined outcome perinatal death or severe morbidity (one study, 1975 women; RR 1.13, 95% CI 0.88 to 1.47), [Analysis 1.2](#). Analgesia use recorded in one trial and first stage of labour duration in two, were not significantly different between groups. The incidence of puerperal infection was not statistically different between the groups in these studies.

Secondary outcomes

There was considerable heterogeneity for several outcomes, in which case a random-effects model has been used. In two small studies (138 women) with relevant data, heavy meconium staining

was virtually eliminated (RR 0.03, 95% CI 0.01 to 0.15), [Analysis 1.4](#). There was a reduction in caesarean sections for fetal distress (eight studies, 2765 women; average RR 0.40, 95% CI 0.19 to 0.86; Heterogeneity: $\tau^2 = 0.70$; $\chi^2 = 24.49$, $df = 7$ ($P = 0.0009$); $I^2 = 71\%$), [Analysis 1.6](#), and a trend overall (11 studies, 3380 women; average RR 0.78, 95% CI 0.60 to 1.02; Heterogeneity: $\tau^2 = 0.11$; $\chi^2 = 32.97$, $df = 10$ ($P = 0.0003$); $I^2 = 70\%$), [Analysis 1.7](#). There was a reduction in variable fetal heart rate decelerations (five studies, 2101 women; average RR 0.67, 95% CI 0.47 to 0.96; Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 20.46$, $df = 4$ ($P = 0.0004$); $I^2 = 80\%$), [Analysis 1.5](#). There was no statistically significant reduction in five-minute Apgar score less than seven (seven studies, 2868 women; RR 0.80, 95% CI 0.52 to 1.22), [Analysis 1.10](#). Cord arterial pH less than 7.20 was reduced (seven studies, 1788 women; average RR 0.62, 95% CI 0.40 to 0.96; Heterogeneity: $\tau^2 = 0.23$; $\chi^2 = 21.95$, $df = 6$ ($P = 0.001$); $I^2 = 73\%$), [Analysis 1.11](#). Meconium below the vocal cords diagnosed by laryngoscopy was reduced (10 studies, 3298 women; RR 0.31, 95% CI 0.18 to 0.53; Heterogeneity: $\tau^2 = 0.46$; $\chi^2 = 33.13$, $df = 9$ ($P = 0.0001$); $I^2 = 73\%$), [Analysis 1.12](#), as was neonatal ventilation or neonatal intensive care unit admission (three studies, 472 women; RR 0.45, 95% CI 0.23 to 0.90), [Analysis 1.13](#).

Because in the outcomes with significant heterogeneity, the magnitude of effects tended to be greater in the smaller studies, a post-hoc sensitivity analysis was performed to assess the effect of trial size on heterogeneity. Successive elimination of trials with fewer than 100, 200 and 300 participants did not eliminate the heterogeneity for the outcomes variable decelerations; caesarean section (for fetal distress and overall); umbilical artery pH less than 7.2; and meconium below vocal cords. For the primary outcome, meconium aspiration syndrome, exclusion of trials with fewer than 200 participants reduced the heterogeneity ($I^2 = 0\%$: three trials, 2506 women; RR 1.22, 95% CI 0.82 to 1.84 fixed-effect model). Planned sensitivity analysis excluding trials with greater risk of bias (all trials except [Fraser 2005](#)) rendered results showing no benefits from amnioinfusion for any of the outcomes measured. As this trial included considerably more women than the other trials combined, the interpretation of results below has taken account of the negative results of this trial.

Studies with limited peripartum surveillance

Three studies were included ([Choudhary 2010](#); [Mahomed 1998](#); [Rathore 2002](#)).

Primary outcomes

In the amnioinfusion group there was a reduction in meconium aspiration syndrome (three studies, 1144 women; average RR 0.17, 95% CI 0.05 to 0.52; Heterogeneity: $\tau^2 = 0.39$; $\chi^2 = 2.94$, $df = 2$ ($P = 0.23$); $I^2 = 32\%$), [Analysis 1.1](#), and perinatal mortality (three studies, 1151 women; RR 0.24, 95% CI 0.11 to 0.53), [Analysis 1.15](#).

Secondary outcomes

In the amnioinfusion group there was a reduction in caesarean section for fetal distress (three studies, 1147 women; RR 0.38, 95% CI 0.27 to 0.54), [Analysis 1.6](#), and overall (three studies, 1137 women; average RR 0.59, 95% CI 0.41 to 0.84; Heterogeneity: $\tau^2 = 0.06$; $\chi^2 = 4.94$, $df = 2$ ($P = 0.08$); $I^2 = 60\%$), [Analysis 1.7](#); one minute Apgar scores (two studies, 492 women; RR 0.32, 95% CI 0.19 to 0.54), [Analysis 1.9](#); five-minute Apgar score less than seven (three studies, 1152 women; RR 0.28, 95% CI 0.14 to 0.53), [Analysis 1.10](#); neonatal ventilation or neonatal intensive care unit admission

(two studies, 853 women; RR 0.52, 95% CI 0.37 to 0.73), [Analysis 1.13](#); and no measurable effect on instrumental delivery or puerperal pyrexia. In one of the studies ([Rathore 2002](#)) meconium below the vocal cords was reduced (200 women; RR 0.42, 95% CI 0.21 to 0.83), [Analysis 1.12](#); and in the other ([Mahomed 1998](#)) neonatal encephalopathy was reduced (649 women; RR 0.07, 95% CI 0.01 to 0.56), [Analysis 1.14](#). In another study ([Choudhary 2010](#)) respiratory distress was reduced.

DISCUSSION

Summary of main results

Fourteen studies of variable quality (4435 women) are included. Subgroup analysis was performed for studies from settings with limited facilities to monitor the baby's condition during labour and intervene effectively, and settings with standard peripartum surveillance.

Settings with standard peripartum surveillance: there was considerable heterogeneity for several outcomes. There was no significant reduction in the primary outcomes meconium aspiration syndrome, perinatal death or severe morbidity, and maternal death or severe morbidity. There was a reduction in caesarean sections (CSs) for fetal distress but not overall. Meconium below the vocal cords diagnosed by laryngoscopy was reduced, as was neonatal ventilation or neonatal intensive care unit admission, but there was no significant reduction in perinatal deaths or other morbidity. Planned sensitivity analysis excluding trials with greater risk of bias resulted in an absence of benefits for any of the outcomes studied.

Several of the smaller studies reviewed were compromised by exclusion of significant numbers of women from the analyses. In addition, outcomes such as the decision to perform caesarean section might have been influenced by the fact that caregivers were not blind to the group allocation, and may have been more motivated to avoid caesarean section in those women subjected to amnioinfusion. The reported reduction in caesarean sections for fetal distress must be interpreted in the light of large variations among institutions with respect to thresholds for intervention for 'fetal distress'. The rates of caesarean section in the control groups ranged from under 10% to 47.5%. Overall, caesarean sections were not significantly reduced.

As thick meconium staining of the amniotic fluid is usually associated with oligohydramnios, beneficial perinatal outcomes seen in some smaller studies may have been related to correction of oligohydramnios rather than dilution of amniotic fluid. In [Spong 1994](#), the results were generally less favourable than in the other smaller studies. The use of amnioinfusion in 8/50 of the control group who developed fetal heart rate decelerations may have obscured beneficial effects of amnioinfusion related to correction of oligohydramnios. This is in keeping with the finding that prophylactic amnioinfusion for oligohydramnios does not have demonstrable benefits over amnioinfusion used only when fetal heart rate decelerations occur ([Novikova 2012](#)).

Settings with limited peripartum surveillance: three studies were included. In the amnioinfusion group there was a reduction in CS for fetal distress and overall; meconium aspiration syndrome (three studies, 1141 women; average RR 0.17, 95% CI 0.05 to 0.52); perinatal mortality (three studies, 1151 women; RR 0.24, 95% CI

0.11 to 0.53) and neonatal ventilation or neonatal intensive care unit admission. In one of the studies, meconium below the vocal cords was reduced and, in the other, neonatal encephalopathy was reduced.

Perinatal outcomes in these under-resourced settings were worse than in the settings with standard peripartum surveillance (perinatal deaths 22/1000 versus 3.6/1000; meconium aspiration syndrome 6.2% versus 2.2%). Under these conditions, with limited facilities to diagnose fetal distress during labour and intervene effectively, amnioinfusion appears to significantly improve perinatal outcome. It is not possible to be sure whether this improvement is due to dilution of amniotic fluid, or correction of oligohydramnios. Interpretation of the data must take into account methodological shortcomings noted above.

Overall completeness and applicability of evidence

This systematic review is relevant to current day practice of obstetrics and gynaecology, showing the impact of amnioinfusion on meconium aspiration syndrome.

Risks

The trials reviewed are too small to address the possibility of rare but serious maternal side-effects of amnioinfusion. Several case reports have been published of cardiac failure or amniotic fluid embolism following amnioinfusion, though a causal relationship has not been established. The benefits shown in the trials reviewed need to be weighed against the theoretical small risk of serious maternal complications (see [Dibble 1992](#); [Dragich 1991](#); [Hofmeyr 1996](#); [Maher 1994](#); [Wegnelius 1996](#); [Wenstrom 1994](#)).

HIV

The diagnosis of meconium-stained liquor may be limited by a policy of maintaining intact membranes during labour in areas with a high prevalence of HIV infection. Once meconium-stained liquor is diagnosed, whether amnioinfusion would increase the risk of vertical HIV transmission to the fetus because of placement of the intrauterine catheter, or reduce the risk by irrigation of the genital tract and dilution of maternal fluids, is not known.

A simplified method of amnioinfusion was shown to be feasible in an under-resourced labour ward environment.

Quality of the evidence

The quality of evidence reflects the extent to which the confidence in an estimate of effect is adequate to support recommendations ([Guyatt 2008](#)). For systematic reviews, the quality of evidence reflects the extent to which the confidence of an estimate of effect is correct ([Guyatt 2008](#)). The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for assessing quality of evidence in systematic reviews involves making separate ratings for quality of evidence outcomes, and identifies five factors that can lower the quality of the evidence ([Guyatt 2008](#)). Considering these five factors in this systematic review; first, the majority of the trials had limitations with allocation concealment and blinding and in accounting for losses to follow-up (low quality); second, the estimates of treatment effect (heterogeneity) and outcomes across trials were not too different (moderate quality). This suggests similarities in the underlying treatment effects across trials (moderate quality). Third, all trials were randomised trials, comparing amnioinfusion to no intervention (high quality). Fourth,

majority of the trials recruited relatively few patients and never reported confidence intervals in their analysis (low quality); and finally, there were no instances of publication bias noted in this systematic review. Therefore, overall, the quality of evidence of this systematic review using the GRADE approach, is of low quality.

Potential biases in the review process

There are some potential biases in the review process. Several of the randomised clinical trials that were included did not blind the investigators, especially obstetricians. This is also another potential for bias in this review. Again, while assessing trials for inclusion, we might have omitted some trials that used amnioinfusion for the reduction of meconium aspiration syndrome, as authors may not have included any of the search terms in their title or abstract. Also, the majority of the trials in this review have methodological limitations capable of increasing the risk of bias, hence compromising the strength of evidence.

Agreements and disagreements with other studies or reviews

Evidence concerning the efficacy of amnioinfusion for reducing the impact of meconium aspiration syndrome is in tandem with the findings from another systematic review ([Xu 2007](#)) that was published in the British Journal of Obstetrics and Gynaecology in 2007. In another multicentre, randomised controlled trial with 1998 pregnant women comparing amnioinfusion with standard care, there were no significant differences in composite primary outcome, perinatal death, caesarean delivery, meconium aspiration syndrome ([Fraser 2005](#)). The American College of Obstetricians and Gynecologists (ACOG) Committee Opinion 346 concluded that amnioinfusion does not prevent meconium aspiration syndrome ([ACOG 2006](#)).

AUTHORS' CONCLUSIONS

Implications for practice

Units with standard peripartum surveillance

The evidence reviewed does not support the use of amnioinfusion for meconium-stained amniotic fluid (as opposed to oligohydramnios-related fetal heart rate decelerations) in clinical practice, given that it is an invasive procedure and has not been shown to have clear benefits in terms of substantive clinical outcomes, and no benefits were found following sensitivity analysis excluding trials with greater risk of bias.

Units with limited peripartum surveillance

The three studies reviewed showed significant improvements in perinatal outcome with a simplified technique of amnioinfusion. The use of amnioinfusion should be considered for women with meconium-stained liquor in units with limited facilities for peripartum surveillance and high rates of meconium aspiration syndrome. The reduction in the diagnosis of meconium aspiration syndrome after amnioinfusion in these studies may possibly be due to a reduction in fetal distress related to oligohydramnios (see Cochrane review 'Amnioinfusion for potential or suspected umbilical cord compression in labour' ([Hofmeyr 2012](#))).

Implications for research

Units with standard peripartum surveillance

Future research should be directed towards the use of amnioinfusion for the correction of oligohydramnios rather than meconium-stained amniotic fluid.

Units with limited peripartum surveillance

Further research is needed to confirm the results of the three included studies, to determine whether the benefits of amnioinfusion for meconium-stained liquor may be limited to women with oligohydramnios, to determine the effect of

amnioinfusion in women infected with HIV, and to investigate the possible risks of amnioinfusion to the mother.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Choudhary 2010

Methods	Randomly generated number using sealed envelopes.
Participants	<p>Inclusion criteria: term pregnancy (> 37 weeks); singleton pregnancy; cephalic presentation; moderate or thick meconium; adequate pelvis.</p> <p>Exclusion criteria: cord prolapse; persistent fetal bradycardia; presence of chorioamnionitis; antepartum haemorrhage; fetal malpresentation; fetal congenital anomaly; polyhydramnios; maternal cardiac or pulmonary disease; multiple gestations.</p>
Interventions	Amnioinfusion – Transcervical nasogastric tube was passed cephalad to the baby's head with infusion of 500 cc's of normal saline over a period of 30 minutes, followed by 2 mL/min under gravity until time of delivery (n = 146) compared with standard labour management without amnioinfusion (n = 146). All newborns were managed by standard protocol of immediate oropharyngeal suctioning post delivery; tracheal suctioning if not breathing vigorously.
Outcomes	Outcomes: Incidence of caesarean section; maternal hospital stay; maternal febrile morbidity (temperature of > 38°C, 24 hours after delivery); low Apgar score (at 1 and 5 minutes); MAS; perinatal morbidity.
Notes	Trial was carried out in a single teaching hospital in Northern India.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The authors did not describe how the random sequences were generated (e.g. computer-generated, shuffling envelopes).
Allocation concealment (selection bias)	Low risk	Allocation by sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	High risk	No.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to outcome assessor (paediatrician).
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Unclear risk	Not described by the authors

Cialone 1994

Methods	Computerised randomisation.
Participants	Inclusion criteria: labouring term and post-term women; uncomplicated antepartum course; singleton vertex presenting fetus; gestation > 36 weeks; moderate to thick meconium assessed clinically. Exclusion criteria: any obstetric risk factor other than meconium.
Interventions	Amnioinfusion of room temperature normal saline 600 mL over 1 hour followed by 150 mL per hour (n = 54), compared with control group (n = 59). Pad weight measured hourly. If vaginal effluent < 100 mL per hour, ultrasound examination performed to exclude overdistension of the uterus.
Outcomes	'Meconiumcrit', delivery mode, duration of first and second stage, oxytocin, analgesia, 1-minute Apgar < 7, nuchal cord, maternal infection, meconium below cords, MAS, neonatal ICU admission.
Notes	Discrepancy in birthweights not accounted for. Neonatologists but not obstetricians blinded to group allocation. FHR tracings analysed in a blind fashion. 7 withdrawals from the study group because of diabetes (3) and request (4). 1 withdrawal from the control group on request. Meconium below vocal cords in 33/58 controls according to table vs 34/58 according to text, whereas in previous report of same trial (Cialone 1993), reported in 36/58 controls.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers.
Allocation concealment (selection bias)	Unclear risk	Unclear. The method of allocation concealment was not described.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described by the authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to outcome assessor (neonatologists).
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Eriksen 1994

Methods	Computer randomisation using sealed packets.
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Amnioinfusion for meconium-stained liquor in labour (Review)

Eriksen 1994 (Continued)

Participants	Inclusion criteria: > 36 weeks' gestation; active labour; thick meconium fluid. Exclusion criteria: multiple gestation; malpresentation; fetal distress on admission; cervical dilation =/ > 7 cm; intra-amniotic infection.
Interventions	Amnioinfusion with 800 mL normal saline at room temperature over 1 hour followed by 180 mL per hour (n = 71), compared with control group (n = 24).
Outcomes	Labour characteristics, fetal distress, operative delivery for fetal distress, meconium below the cords, MAS, fetal acid-base status, infectious morbidity.
Notes	Of 139 women who consented to the study, 9 were excluded because of incomplete records and 6 because they were randomised to amnioinfusion but delivered before amnioinfusion could be administered. The latter exclusions could have biased results against the study group by excluding those with more rapid labours. There were also somewhat more primiparous women in the study group (35/65 vs 27/59). This could possibly have been due to exclusion of more multiples who had rapid labours. The n value for umbilical artery pH is given as the whole group, yet in the text at least 1 infant with MAS had no cord blood result.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer randomisation.
Allocation concealment (selection bias)	Low risk	Sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described by the authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described by the authors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Fraser 2005

Methods	1998 women allocation by single, centralised computer-randomisation service, stratified by site and presence or absence of 3 or more variable FHR decelerations in 30 minutes prior to randomisation.
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Fraser 2005 (Continued)

Participants	Women in labour with: thick meconium-stained amniotic fluid; single fetus; cephalic presentation; gestational age 36 weeks or more; ruptured membranes; cervical dilation 2-7 cm; no indication for urgent delivery. Exclusion criteria: suspected major fetal anomaly; chorioamnionitis; placenta praevia; vaginal bleeding; seropositivity for HIV or hepatitis B or C; active genital herpes; polyhydramnios; previous uterine incision other than low transverse; inability to comprehend the consent form.
Interventions	Amnioinfusion: a sterile catheter was introduced transcervically, and 800 mL saline infused over 40 minutes, followed by 2 mL per minute to a maximum of 1500 mL. The infusion was discontinued if the baseline uterine pressure increased by 15 mmHg, the uterus failed to relax between contractions as assessed by palpation, or ultrasound examination revealed polyhydramnios. Control group: no amnioinfusion. Both groups had continuous electronic FHR monitoring and suctioning of the baby's nasopharynx and oropharynx during and after delivery.
Outcomes	Primary outcome: perinatal death and/or moderate or severe MAS, determined by 3 neonatologists blinded to the group allocation. Secondary outcomes included perinatal death or serious morbidity and maternal death or serious morbidity.
Notes	56 centres in 13 countries, April 1999 to August 2003.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated using a centralised computer-randomisation service.
Allocation concealment (selection bias)	Low risk	Centralised computer randomisation service.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not feasible.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	3 neonatologists were blinded to outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Adequately described
Selective reporting (reporting bias)	Low risk	Protocol published. All predefined outcomes reported.
Other bias	Low risk	Adequately described

Hofmeyr 1998a

Methods	Allocation by opaque sealed envelopes in computer-generated random sequence. Blinding not possible.
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Amnioinfusion for meconium-stained liquor in labour (Review)

Hofmeyr 1998a (Continued)

Participants	Inclusion criteria: women in labour; moderate or heavy meconium staining of the liquor; gestation 37 weeks or more; singleton cephalic presentation.
Interventions	Amnioinfusion via an Intran or Nelaton intrauterine catheter: 800 mL normal saline at 15 mL per minute, then maintenance of 3 mL per minute (n = 176), compared with no amnioinfusion (n = 176). Electronic FHR monitoring in most cases. 1 woman in the control group received amnioinfusion. Analysis was by intention-to-treat.
Outcomes	Primary: caesarean section, MAS diagnosed clinically by paediatrician blind to group allocation, perinatal mortality. Secondary outcomes: assisted delivery; 5-minute Apgar score < 7; cord pH < 7.2; meconium below cords; X-ray diagnosis of MAS (amnioinfusion 2/163 vs control 3/161); neonatal ICU admission; neonatal ventilation (0/164 vs 2/163); postpartum temperature $\geq$ 38 degrees centigrade.
Notes	4 academic hospitals in South Africa.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence.
Allocation concealment (selection bias)	Low risk	Allocation by opaque sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Blinding not done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not done.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Macri 1992

Methods	Sealed envelopes randomised by computer.
Participants	Inclusion criteria: gestation $\geq$ 37 weeks; thick meconium; 4-quadrant amniotic fluid index < 5 cm; normal FHR pattern; vertex presentation; estimated fetal weight $\geq$ 2500 g; cervical dilation $\geq$ 5 cm; ruptured membranes.

Macri 1992 (Continued)

Exclusion criteria: vaginal bleeding, chorioamnionitis, fetal anomalies, uterine anomalies, contraindication to labour.

Interventions	Amnioinfusion with 500 mL warmed saline over 20-30 minutes followed by 250-500 mL as required to maintain a 4-quadrant amniotic fluid index above 10 cm (n = 85), compared with control group (n = 85).
Outcomes	Fetal distress, mode of delivery, Apgar scores, umbilical artery pH, meconium in oropharynx, meconium below cords, MAS, chorioamnionitis.
Notes	Neonatologists but not obstetricians stated to have been blinded to group allocation. The women in this report are also included in the report of Schrimmer 1991 on amnioinfusion for oligohydramnios (Paul RH, personal communication) (see review 'Amnioinfusion for potential or suspected umbilical cord compression in labour' (Hofmeyr 2012)).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers.
Allocation concealment (selection bias)	Low risk	Allocation by opaque sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described by the authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described by the authors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Adequately described
Selective reporting (reporting bias)	Low risk	Adequately described
Other bias	Unclear risk	Not described by the authors

Mahomed 1998

Methods	Allocation by opaque sealed envelopes in computer-generated random sequence.
Participants	Inclusion criteria: moderate or heavy meconium- stained amniotic fluid; singleton cephalic presentation; in labour; gestation 37 weeks or more. Exclusion criteria: indication for immediate delivery; chorioamnionitis; vaginal bleeding; fetal anomaly; maternal cardiac or pulmonary disease.
Interventions	Transcervical amnioinfusion using size 8 nasogastric tube. Normal saline 500 mL infused over 30 minutes, then 500 mL at 2 mL per minute (n = 325). Control group received no amnioinfusion (n = 336). Al-

Amnioinfusion for meconium-stained liquor in labour (Review)

Mahomed 1998 (Continued)

location not blinded. Level of intrapartum surveillance limited by number of midwives in a busy labour ward. FHR auscultated every 30 minutes using Pinard stethoscope or hand-held doptone FHR detector. Suctioning of the airways at delivery by attending midwives.

Outcomes	Primary outcomes: caesarean section; MAS diagnosed by a paediatrician blind to the group allocation; perinatal mortality. Secondary outcomes: FHR abnormality (amnioinfusion 30/320 vs control 34/334); contractions $\geq$ 40 seconds at 1 hour (206/323 vs 211/324); caesarean section for fetal distress; assisted delivery; 1-minute Apgar score < 4 (8/324 vs 18/336); 5-minute Apgar score < 7 ; X-ray diagnosis of MAS (2/319 vs 9/330); neonatal ICU admission; neonatal ventilation (10/320 vs 34/332); pneumothorax (0/320 vs 3/329); hypoxic ischaemic encephalopathy; > 4 days in neonatal ICU (5/320 vs 10/329); intra-partum and postpartum pyrexia.
Notes	4 amnioinfusion allocations early in the study unaccounted for. No electronic FHR monitoring. Neonatologist not usually present at the time of delivery.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random sequence.
Allocation concealment (selection bias)	Low risk	Allocation by opaque sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Blinding not done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not done.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Moodley 1998

Methods	Randomisation using sealed envelopes.
Participants	Inclusion criteria: singleton, term, cephalic pregnancies in active labour; meconium-stained amniotic fluid grade 1-3; normal cardiotocograph. Exclusion criteria: medical or surgical conditions; chorioamnionitis; previous caesarean section.

Moodley 1998 (Continued)

Interventions	Amnioinfusion with normal saline 10-15 mL per minute by gravity via a central venous manometer set and a size 8 nasogastric infant feeding tube (1 litre over 4 hours); versus standard care; continuous FHR monitoring.
Outcomes	Mean umbilical artery pH; mean Apgar scores; caesarean section; instrumental delivery; hypoxic ischaemic encephalopathy.
Notes	Durban, South Africa, January to April 1993.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear how the randomisation was carried out.
Allocation concealment (selection bias)	Low risk	Allocation using sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Blinding not done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not done.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Puertas 2001

Methods	Randomised sequence in sealed envelopes.
Participants	206 pregnant women admitted for labour and delivery with moderately or thickly stained amniotic fluid; term pregnancy; no uterine scarring; spontaneous labour or induction of labour for meconium staining of the amniotic fluid; single fetus; vertex presentation; no FHR changes suggesting fetal distress; no vaginal bleeding; and no indication of vertically transmitted infectious disease.
Interventions	Amnioinfusion with 0.9% saline via an infusion pump at 600 mL per hour for 1 hour, then 180 mL per hour until full cervical dilation, or basal uterine pressure increase to 20 mmHg; compared with no amnioinfusion. Continuous FHR monitoring and intrauterine pressure monitoring

Puertas 2001 (Continued)

Outcomes	Amniotic fluid index change after 1 hour; umbilical cord acid base status; meconium below cords > trace by paediatricians blind to the group allocation; umbilical cord complication; mean umbilical artery pH.
Notes	Granada, Southern Spain. Subdivided into thick (meconium concentration > 15%) and moderate meconium staining. Amnioinfusion stopped in 17 women for uterine hypertonia. Confirmed by correspondence with first author that the data from Alvarez 1999 are included in the final Puertas 2001 report.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	'Randomly generated numbers in sealed envelopes.' However, method of randomisation not described (e.g. computer-generated, shuffling envelopes).
Allocation concealment (selection bias)	Low risk	Sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not feasible.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not feasible.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to paediatricians.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Rathore 2002

Methods	Computer-generated random allocation by sequentially numbered sealed opaque envelopes.
Participants	Women in labour; 37 or more weeks' gestation; singleton cephalic presentation; moderate or thick meconium-stained fluid, or meconium crit > 10%. exclusions criteria: chorioamnionitis; indication for immediate delivery; fetal congenital anomaly, antepartum haemorrhage; polyhydramnios; and maternal cardiac or respiratory disease.
Interventions	Saline amnioinfusion via FG 8 nasogastric tube, 500 mL over 30 minutes, then 3 mL per minute. Maximum dose 1 L. Control group received no amnioinfusion or uterine catheter. No cardiotocography was available.
Outcomes	Caesarean section; meconium at vocal cords; Apgar scores < 7; neonatal ICU admission; respiratory distress, MAS; maternal pyrexia.

Amnioinfusion for meconium-stained liquor in labour (Review)

Rathore 2002 (Continued)

Notes Tertiary level teaching hospital.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence.
Allocation concealment (selection bias)	Low risk	Adequate. Sealed opaque envelopes.
Blinding (performance bias and detection bias) All outcomes	High risk	Blinding not feasible.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described by the authors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Sadovsky 1989

Methods	'Random allocation' with sealed envelopes.
Participants	Inclusion criteria: singleton; more than a trace of meconium-stained liquor; vertex presentation; > 34 weeks; anticipate delivery > 1 hour. Exclusion criteria: malformations; chorioamnionitis; malpresentation; polyhydramnios; cord prolapse; urgent delivery needed; maternal cardiac disease.
Interventions	Amnioinfusion with saline 600 mL over 1 hour then 180 mL per hour (n = 19), compared with control group (n = 21).
Outcomes	Thick meconium on spectrophotometry, labour duration, labour augmentation, analgesia, mode of delivery, umbilical artery pH, meconium below cords, positive pressure ventilation.
Notes	Neither obstetricians nor neonatologists stated to have been blinded.

Risk of bias

Bias	Authors' judgement	Support for judgement
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Sadovsky 1989 (Continued)

Random sequence generation (selection bias)	Unclear risk	'Randomly generated numbers in sealed envelopes.' However, method of randomisation not described (e.g. computer-generated, shuffling envelopes).
Allocation concealment (selection bias)	Low risk	Allocation adequate with sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Blinding not done.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not done.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding not done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Sood 2004

Methods	199 women allocated by flip of a coin.
Participants	Women in labour with thick staining of the amniotic fluid. singleton, vertex presentation; adequate pelvis, cervical dilation > 5 cm, gestational age > 37 weeks.
Interventions	Amnioinfusion via a plastic suction catheter or amnioinfusion catheter with normal saline till the returning fluid was clear. Usually 1000 mL was infused over 30 to 45 minutes.
Outcomes	Persistent FHR decelerations; caesarean section; meconium below neonate's vocal cords; MAS diagnosed by X-ray, perinatal mortality, hospital stay; uterine atony (6/96 versus 1/100).
Notes	FHR abnormalities before enrolment were present in 48/96 women in the amnioinfusion versus 60/100 in the control group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Flip of a coin.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias)	High risk	Blinding not feasible.

Amnioinfusion for meconium-stained liquor in labour (Review)

Sood 2004 (Continued)

All outcomes

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described by the authors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Spong 1994

Methods	'Randomised' by computer-generated random number sequence.
Participants	Inclusion criteria: singleton; vertex presentation; 37 or more weeks; moderate to heavy meconium; no variable FHR decelerations. Exclusion criteria: prenatally diagnosed fetal malformations; maternal temperature > 100.4 degrees Fahrenheit; evidence of fetal distress.
Interventions	Amnioinfusion with 600 mL saline bolus followed by 3 mL per minute (n = 43), compared with standard care which included similar amnioinfusion in 8/50 for variable decelerations (n = 50).
Outcomes	Meconium below cords, MAS, Apgar scores, cord pH, neonatal complications, route of delivery, maternal infection.
Notes	Discrepancy in group numbers (43 vs 50), despite use of computer-generated random number sequence to create equal number groups, not accounted for.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised' by computer-generated random number sequence.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described by the authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors

Amnioinfusion for meconium-stained liquor in labour (Review)

Spong 1994 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described by the authors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described by the authors
Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

Wenstrom 1989

Methods	Sealed envelopes randomised by computer.
Participants	Inclusion criteria: thick meconium-stained amniotic fluid. Exclusion criteria: fetal distress, maternal pyrexia.
Interventions	Amnioinfusion of 1000 mL over 20-40 minutes, repeated 6-hourly (n = 41), compared with control group (n = 44).
Outcomes	Mode of delivery, Apgar scores, cord arterial pH, meconium below cords, meconium aspiration syndrome, postpartum endometritis.
Notes	5 study women who did not receive amnioinfusion excluded, of which 4 delivered spontaneously after 30, 45, 60 and 180 minutes and 1 required emergency caesarean section for fetal distress. These exclusions have been included in this review with respect to delivery outcomes. Obstetricians not blinded, but neonatologists blinded.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers.
Allocation concealment (selection bias)	Low risk	Allocation using sealed envelopes.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described by the authors
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described by the authors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Neonatologists blinded to outcome assessment.
Incomplete outcome data (attrition bias)	Unclear risk	Not described by the authors

Amnioinfusion for meconium-stained liquor in labour (Review)

Wenstrom 1989 (Continued)

All outcomes

Selective reporting (reporting bias)	Unclear risk	Not described by the authors
Other bias	Unclear risk	Not described by the authors

FHR: fetal heart rate

ICU: intensive care unit

MAS: meconium aspiration syndrome

vs: versus

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Adam 1989	Excluded because inadequate information to confirm acceptable allocation concealment.
Ashfaq 2004	Excluded because the report does not indicate that allocation was by randomisation. 400 patients were 'equally divided in study and control groups'. Amnioinfusion was associated with very large reductions in caesarean section, low Apgar scores, meconium aspiration syndrome and perinatal death (12/200 vs 36/200).
Das 2007	Comparative study in a low-resource setting, not randomised.
Edwards 1999	Excluded because comparison was between amnioinfusion with and without antibiotics.
Engel 2008	Excluded because not a randomised trial. Amnioinfusion had no statistically significant effects on the measures outcomes.
Gonzalez 1998	Excluded because no clinically meaningful data. 43 women undergoing amnioinfusion for meconium-stained liquor were randomly allocated to receive normal saline or lactate Ringer's solution. There were no significant differences in the umbilical artery electrolytes or pH.
Gonzalez 2002	Excluded because no clinically meaningful data. 40 women undergoing amnioinfusion for meconium-stained liquor were randomly allocated to receive amnioinfusion with normal saline or lactate Ringer's solution. There were no significant differences in the umbilical artery electrolytes or pH, nor were they different from non-randomised normal controls.
Gupta 2011	Excluded because only abstract available.
Ilagan 1992	Excluded because inadequate information to confirm acceptable allocation concealment.
Khosla 1997	Not a randomised trial. The study group was 25 consecutive patients who gave consent for amnioinfusion and controls were 25 similar patients of the alternative unit where amnioinfusion was not being carried out.
Kirubamani 2000	Excluded because only abstract available, with no figures; discrepancy in group numbers (30 vs 20) not accounted for.
Lembet 1999	Excluded because no data given. Women with thick meconium during labour randomised to trans-abdominal amnioinfusion (19) vs standard care (20).
Lo 1993	Excluded because allocation was not at random. Of 112 women with moderate or thick meconium-stained liquor, 63 chose to undergo amnioinfusion. In the amnioinfusion group, there were fewer operative deliveries for fetal distress but not overall, and neonatal outcomes were improved.

Study	Reason for exclusion
Mukhopadhyay 2006	Excluded because allocation was by alternation, not randomised. This study in a low-resource setting found that with amnioinfusion the rate of caesarean section was one-half and of meconium below the cords was one-fifth of that in the control group.
Nageotte 1991	Nageotte 1991 studied 86 women with oligohydramnios and/or thick meconium-stained liquor. As the reported results relate primarily to problems associated with oligohydramnios, these are considered in the review ' <i>Amnioinfusion for potential or suspected umbilical cord compression in labour</i> ' (Hofmeyr 2012). The authors state that there was no significant difference in meconium below the cords, but no figures are given.
Regi 2009	The primary indication for amnioinfusion was fetal heart rate decelerations, not meconium-stained liquor. See review: ' <i>Amnioinfusion for potential or suspected umbilical cord compression in labour</i> '.

vs: versus

DATA AND ANALYSES

Comparison 1. Amnioinfusion for meconium-stained liquor in labour

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Meconium aspiration syndrome	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Standard peripartum surveillance	11	3374	Risk Ratio (M-H, Random, 95% CI)	0.52 [0.26, 1.06]
1.2 Limited peripartum surveillance	3	1144	Risk Ratio (M-H, Random, 95% CI)	0.17 [0.05, 0.52]
2 Perinatal death or serious morbidity (post hoc)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Standard peripartum surveillance	1	1975	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.88, 1.47]
2.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Maternal death or serious morbidity (post hoc)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Standard peripartum surveillance	1	1975	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.49, 2.04]
3.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Heavy meconium staining	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Standard peripartum surveillance	2	138	Risk Ratio (M-H, Fixed, 95% CI)	0.03 [0.01, 0.15]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Variable decelerations	5		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 Standard peripartum surveillance	5	2101	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.47, 0.96]
5.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6 Caesarean for fetal distress	11		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Standard peripartum surveillance	8	2765	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.19, 0.86]
6.2 Limited peripartum surveillance	3	1147	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.27, 0.54]
7 Caesarean overall	14		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 Standard peripartum surveillance	11	3380	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.60, 1.02]
7.2 Limited peripartum surveillance	3	1137	Risk Ratio (M-H, Random, 95% CI)	0.59 [0.41, 0.84]
8 1-minute Apgar < 4	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Standard peripartum surveillance	2	1969	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.67, 1.45]
8.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 1-minute Apgar < 7	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 Standard peripartum surveillance	5	654	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.41, 1.60]
9.2 Limited peripartum surveillance	2	492	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.19, 0.54]
10 5-minute Apgar < 7	10	4020	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.39, 0.79]
10.1 Standard peripartum surveillance	7	2868	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.52, 1.22]
10.2 Limited peripartum surveillance	3	1152	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.14, 0.53]
11 Umbilical artery pH < 7.20	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Standard peripartum surveillance	7	1788	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.40, 0.96]
11.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
12 Meconium below vocal cords	11		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 Standard peripartum surveillance	10	3298	Risk Ratio (M-H, Random, 95% CI)	0.31 [0.18, 0.53]
12.2 Limited peripartum surveillance	1	200	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.21, 0.83]
13 Neonatal ventilation/neonatal intensive care unit admission	5	1325	Risk Ratio (M-H, Fixed, 95% CI)	0.51 [0.38, 0.68]
13.1 Standard peripartum surveillance	3	472	Risk Ratio (M-H, Fixed, 95% CI)	0.45 [0.23, 0.90]
13.2 Limited peripartum surveillance	2	853	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.37, 0.73]
14 Neonatal encephalopathy	2	709	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.02, 0.49]
14.1 Standard peripartum surveillance	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.2 [0.01, 4.00]
14.2 Limited peripartum surveillance	1	649	Risk Ratio (M-H, Fixed, 95% CI)	0.07 [0.01, 0.56]
15 Perinatal death	10	3913	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.18, 0.66]
15.1 Standard peripartum surveillance	7	2762	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.29, 3.45]
15.2 Limited peripartum surveillance	3	1151	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.11, 0.53]
16 Puerperal pyrexia	8	3859	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.65, 1.34]
16.1 Standard peripartum surveillance	5	2711	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.74, 1.78]
16.2 Limited peripartum surveillance	3	1148	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.29, 1.14]
17 Puerperal endometritis	5	532	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.53, 1.60]
17.1 Standard peripartum surveillance	5	532	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.53, 1.60]
17.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
18 Oxytocin augmentation	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 Standard peripartum surveillance	2	229	Risk Ratio (M-H, Random, 95% CI)	1.85 [0.67, 5.12]
18.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
19 Narcotic analgesic	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 Standard peripartum surveillance	1	105	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.66, 1.72]
19.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
20 Epidural analgesia	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
20.1 Standard peripartum surveillance	1	105	Risk Ratio (M-H, Fixed, 95% CI)	1.34 [0.90, 1.99]
20.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
21 First stage labour (minutes)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
21.1 Standard peripartum surveillance	2	229	Mean Difference (IV, Fixed, 95% CI)	32.46 [-68.78, 133.70]
21.2 Limited peripartum surveillance	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
22 Instrumental vaginal delivery for fetal distress	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
22.1 Standard peripartum surveillance	3	2286	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.76, 1.55]
22.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
23 Instrumental vaginal delivery	9	2059	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.50, 0.91]
23.1 Standard peripartum surveillance	6	914	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.51, 1.04]
23.2 Limited peripartum surveillance	3	1145	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.33, 1.01]
24 Second stage labour (minutes)	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
24.1 Standard peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
24.2 Limited peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
25 Respiratory Distress (post hoc)	1	292	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.04, 0.32]
25.1 Standard peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
25.2 Limited peripartum surveillance	1	292	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.04, 0.32]
26 Mean maternal hospital stay (post hoc)	1	292	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.17, 1.91]
26.1 Standard peripartum surveillance	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
26.2 Limited peripartum surveillance	1	292	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.17, 1.91]

Analysis 1.1. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 1 Meconium aspiration syndrome.

Analysis 1.2. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 2 Perinatal death or serious morbidity (post hoc).

Analysis 1.3. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 3 Maternal death or serious morbidity (post hoc).

Analysis 1.4. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 4 Heavy meconium staining.

Analysis 1.5. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 5 Variable decelerations.

Analysis 1.6. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 6 Caesarean for fetal distress.

Analysis 1.7. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 7 Caesarean overall.

Analysis 1.8. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 8 1-minute Apgar < 4.

Analysis 1.9. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 9 1-minute Apgar < 7.

Analysis 1.10. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 10 5-minute Apgar < 7.

Analysis 1.11. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 11 Umbilical artery pH < 7.20.

Analysis 1.12. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 12 Meconium below vocal cords.

Analysis 1.13. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 13 Neonatal ventilation/neonatal intensive care unit admission.

Analysis 1.14. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 14 Neonatal encephalopathy.

Analysis 1.15. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 15 Perinatal death.

Analysis 1.16. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 16 Puerperal pyrexia.

Analysis 1.17. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 17 Puerperal endometritis.

Analysis 1.18. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 18 Oxytocin augmentation.

Analysis 1.19. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 19 Narcotic analgesic.

Analysis 1.20. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 20 Epidural analgesia.

Analysis 1.21. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 21 First stage labour (minutes).

Analysis 1.22. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 22 Instrumental vaginal delivery for fetal distress.

Analysis 1.23. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 23 Instrumental vaginal delivery.

Analysis 1.25. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 25 Respiratory Distress (post hoc).

Analysis 1.26. Comparison 1 Amnioinfusion for meconium-stained liquor in labour, Outcome 26 Mean maternal hospital stay (post hoc).

WHAT'S NEW

Date	Event	Description
1 December 2013	New citation required but conclusions have not changed	Conclusions not changed.
1 December 2013	New search has been performed	Search updated. One new trial included (Choudhary 2010) and two new trials excluded (Gupta 2011 ; Regi 2009). In addition, two studies previously in Studies awaiting classification (Engel 2008 ; Mukhopadhyay 2006) have now been excluded. Methods updated.

HISTORY

Protocol first published: Issue 2, 1995

Review first published: Issue 2, 1995

Date	Event	Description
2 July 2010	Amended	Contact details edited.
25 May 2009	New search has been performed	Search updated. Four new trials included (Fraser 2005 ; Puertas 2001 ; Rathore 2002 ; Sood 2004); two new trials added to Studies awaiting classification (Engel 2008a ; Mukhopadhyay 2006a); two previously included trials have now been excluded (Adam 1989 ; Ilagan 1992) and the previously excluded Alvarez 1999 is now included as another report of Puertas 2001 (confirmed by correspondence with Dr Puertas). Four new trials have been excluded (Ashfaq 2004 ; Das 2007 ; Gonzalez 2002 ; Khosla 1997). Adam 1989 , previously included, is now excluded. We have added two additional outcomes post hoc and updated Background references.
14 March 2009	New citation required and conclusions have changed	Amnioinfusion is not beneficial for babies releasing medium to heavy meconium during labour, except in settings with limited facilities to monitor the baby's condition during labour. A new author helped to update this review.

Date	Event	Description
7 November 2008	Amended	Review withdrawn from publication.
31 October 2008	Amended	Converted to new review format.
5 October 2001	New search has been performed	Five studies have been assessed of which two have been included (Alvarez 1999 ; Moodley 1998) in this version of the review. Inclusion of these studies has not changed the substantive findings of the review.

CONTRIBUTIONS OF AUTHORS

GJ Hofmeyr prepared the original protocol and review. H Xu updated the review following the release of the results of the [Fraser 2005](#) trial, and AC Eke updated the review following the release of the results of the [Choudhary 2010](#) trial. All three review authors checked the data entry and contributed to the writing of the review.

DECLARATIONS OF INTEREST

G J Hofmeyr is an author of studies considered for inclusion in the review and has not participated in decisions regarding these studies.

SOURCES OF SUPPORT

Internal sources

- University of the Witwatersrand, South Africa.

External sources

- South African Medical Research Council, South Africa.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have added four additional outcomes (perinatal death or severe morbidity; maternal death or severe morbidity; respiratory distress; length of maternal hospital stay) and one sensitivity analysis post hoc and updated [Background](#) references.

NOTES

None.

INDEX TERMS

Medical Subject Headings (MeSH)

*Amnion; *Meconium; Cesarean Section [statistics & numerical data]; Injections; Meconium Aspiration Syndrome [*prevention & control]; Obstetric Labor Complications [*prevention & control]; Perinatal Mortality; Randomized Controlled Trials as Topic; Sodium Chloride [*administration & dosage]

MeSH check words

Female; Humans; Infant, Newborn; Pregnancy