Acupuncture for induction of labour (Review)

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[Intervention Review]

Acupuncture for induction of labour

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ABSTRACT

Background

This is one of a series of reviews of methods of cervical ripening and labour induction using standardised methodology. The use of complementary therapies is increasing and some women look to complementary therapies during pregnancy and childbirth to be used alongside conventional medical practice. Acupuncture involves the insertion of very fine needles into specific points of the body. The limited observational studies to date suggest acupuncture for induction of labour appears safe, has no known adverse effects to the fetus, and may be effective. However, the evidence regarding the clinical effectiveness of this technique is limited.

Objectives

To determine the effectiveness and safety of acupuncture for third trimester cervical ripening or induction of labour.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (23 November 2012), PubMed (1966 to 23 November 2012), Embase (1980 to 23 November 2012), Dissertation Abstracts (1861 to 23 November 2012), CINAHL (1982 to 23 November 2012), the WHO International Clinical Trials Registry Portal (ICTRP) (23 November 2012) and bibliographies of relevant papers.

Selection criteria

Clinical trials comparing acupuncture used for third trimester cervical ripening or labour induction with placebo/no treatment or other methods listed above it on a predefined list of labour induction methods.

Data collection and analysis

Two review authors independently assessed trials for inclusion, evaluated methodological quality and extracted data.

Main results

The original review included three trials and seven trials were excluded. This updated review includes 14 trials, and excludes eight trials. Three trials previously excluded due to no clinically relevant outcomes are now included. Eight new trials were included, and four new trials were excluded. We included 14 trials with data reporting on 2220 women.

Trials reported on three primary outcomes only caesarean section, serious neonatal morbidity and maternal mortality. No trial reported on vaginal delivery not achieved within 24 hours; and uterine hyperstimulation with fetal heart rate (FHR) changes. There was no

difference in caesarean deliveries between acupuncture and the sham control (average risk ratio (RR) 0.95, 95% confidence interval (CI) 0.69 to 1.30, six trials, 654 women), and acupuncture versus usual care (average RR 0.69, 95% CI 0.40, 1.20, six trials, 361 women). There was no difference in neonatal seizures between acupuncture and the sham group (RR 1.01, 95% CI 0.06 to 16.04, one trial, 364 women).

There was some evidence of a change in cervical maturation for women receiving acupuncture compared with the sham control, (mean difference (MD) 0.40. 95%CI 0.11 to 0.69, one trial, 125 women), and when compared with usual care (MD 1.30, 95% CI 0.11 to 2.49, one trial, 67 women). The length of labour was shorter in the usual care group compared with acupuncture (average standardised mean difference (SMD) 0.67, 95% CI 0.18 to 1.17, one trial 68 women). There were no other statistically significant differences between groups. Few studies reported on many clinically relevant outcomes. One trial was at a low risk of bias on all domains.

Authors' conclusions

Overall, there have been few studies assessing the role of acupuncture for induction of labour. Before implications for clinical practice can be made there is a need for well-designed randomised controlled trials to evaluate the role of acupuncture to induce labour and for trials to assess clinically meaningful outcomes.

PLAIN LANGUAGE SUMMARY

Acupuncture for induction of labour

There is insufficient evidence describing the efficacy of acupuncture to induce labour.

Sometimes it is necessary to bring on labour artificially because of safety concerns for the mother or baby. Induction of labour (getting labour started artificially) is common when the pregnancy is posing a risk. Various methods of preparing the cervix of the uterus and inducing labour are available to the pregnant woman or her unborn child. Some women look to complementary therapies during pregnancy and childbirth to be used alongside conventional medical practice.

Acupuncture is the insertion of fine needles into specific points of the body and has been used to help ripen the cervix, induce labour and reduce labour pains. The review included 14 trials with data reporting on 2220 women randomised to receive acupuncture compared with sham acupuncture or usual care. Most trials were from Western countries, with only two from Asia. The evidence regarding the clinical effectiveness of this technique was limited. No trial reported on vaginal delivery not achieved within 24 hours, uterine hyperstimulation with fetal heart rate changes, and serious maternal illness or death. Caesarean deliveries and neonatal seizures were no different. The trials used different acupuncture points, number of treatments and methods of acupuncture, (manual or electro-acupuncture). More research is needed.

BACKGROUND

Description of the condition

Sometimes it is necessary to bring on labour artificially because of safety concerns for the mother or baby. This review is one of a series of reviews of methods of labour induction using a standardised protocol. For more detailed information on the rationale for this methodological approach, please refer to the currently published 'generic' protocol (Hofmeyr 2000). The generic protocol describes how a number of standardised reviews will be combined to compare various methods of preparing the cervix of the uterus and inducing labour.

Description of the intervention

The use of complementary and alternative medicine (CM) has become popular with consumers worldwide. Studies suggest that between 36% and 62% of adults in industrialised nations use some form of CM to prevent or treat health-related problems (Barnes 2004). A recent review of 14 studies with large sample sizes (N > 200) on the use of CM in pregnancy identified a prevalence

rate ranging from1% to 87% (with nine falling between 20% and 60%) (Adams 2009). The review identified use of various complementary therapies including acupuncture and acupressure, aromatherapy, massage, yoga, homeopathy and chiropractic care. The review also showed many pregnant women had used more than one complementary product or service (Adams 2009). In Europe, between 12% and 19% of the population report using acupuncture, according to consumer surveys (Fisher 1994). Some women look to alternative therapies during pregnancy and childbirth to be used alongside conventional medical practice. A recent survey described the prevalence and use of complementary therapies among 82 nurse-midwives in North Carolina (Allaire 2000). Almost 20% of nurse-midwives reported use of acupuncture during pregnancy, with 6% of responders specifically recommending its use to ripen the cervix (the process of softening and dilating the cervix) and/or induce labour. In the same survey, 27 respondents (33%) reported using herbal therapies for labour stimulation. For some women with a prolonged pregnancy, an induction of labour may be perceived to intervene in the natural process of pregnancy and may drastically change their expected plan of care during pregnancy. The reasons why pregnant women are interested in using complementary therapies to ripen the cervix and/or induce labour is an important question and needs to be answered when evaluating new options of care.

Acupuncture has been used for more than two thousand years in China and Japan. The diagnosis and treatment prescribed by traditional Chinese medicine (TCM) is influenced by the systems of medicine and philosophy of ancient China. Acupuncture involves the insertion of fine needles into the skin and underlying tissues at precise points on the body. The needle can be left alone or stimulated by turning in various ways or stimulated by electricity. Electro-acupuncture involves the use of electricity to stimulate the acupuncture point. To do this a needle is inserted and a terminal is attached to the handle, the other terminal is connected to a second needle or neutral electrode. Over time, different styles of acupuncture have been practiced by acupuncturists. Acupuncture treatment is composed of needling aspects (choice or points and needling techniques), specific components relating to the style of diagnosis and treatment used, and generic non-specific needling components not specific to acupuncture such as belief, time and attention given to the patient.

In parts of Europe and Asia acupuncture has been described as a method to alleviate labour pains, and ripen the cervix. More recently it has been used to stimulate the onset of labour.

Three case series document the role of acupuncture for the induction of labour (Tsuei 1974; Tsuei 1977; Yip 1976). Induction of labour using electro-acupuncture has been reported by Yip 1976. Labour was successfully induced in 21 of the 31 women, with pregnancy duration ranging from 38 to 42 weeks. The pattern of uterine activity was similar to that of normal labour. In a second study acupuncture with and without electrical stimulation was used to induce labour in 12 pregnant women with a gestational age from 19 to 43 weeks (Tsuei 1974). The success rate was 83% and average induction to delivery time was 13.1 hours. In the third study, 34 term and post term women and seven women with an intrauterine fetal death were induced using electro-acupuncture. Labour was successfully induced in 32 (78%) women (Tsuei 1977). The limited observational studies to date suggest acupuncture for induction of labour appears safe, has no known adverse effects to the fetus, and may be effective.

Two non-randomised trials have examined whether acupuncture could initiate contractions in women at term (Kubista 1975: Theobald 1973). In the trial by Theobald (Theobald 1973), four electrodes were applied to the skin of the abdomen to induce labour in the treatment group. Treatment was given to 27 women and compared with 102 women who were controls. In the treatment group 20 (77%) women gave birth on or up to four days before the estimated date of confinement, compared with 47 (46%) in the control group. In the second trial, electro-acupuncture was administered to 35 women, and 35 women received no electro-acupuncture. An increase in the intensity of labour contraction frequency was observed in 31 women in the treatment group. In the control group, no increase in labour activity was observed (Kubista 1975).

How the intervention might work

The mechanism underlying acupuncture to induce labour is speculative at this stage but may involve stimulation of the uterus by hormonal changes or by the nervous system. In animal studies low frequency electrical stimulation of the neuro-hypophyseal system induces the secretion of oxytocin. Parasympathetic stimulation close to term has been shown to have an influence on the uterus (Bell 1972). Stimulation of acupuncture points is known to increase the discharge of thalamic nuclei and the hypothalamic anterior pituitary system (Liao 1979). It is hypothesised that acupuncture neuronal stimulation may increase uterine contractility either by central oxytocin release or by parasympathetic stimulation of the uterus (Tempfeer 1998), without influencing locally active factors such as IL-8 and PGF2 either by central oxytocin release or by parasympathetic stimulation of the uterus (Tempfeer 1998).

Why it is important to do this review

Consumers generally perceive complementary medicine to be more natural than conventional medicine and have fewer concerns about side-effects. There are reports in the literature of rare adverse reactions to acupuncture, for example pneumothorax, infection or cardiac injury (Yamashita 1999). The general advice for the treatment of conditions arising during pregnancy is to exercise caution particularly during the first trimester of pregnancy, and to avoid some acupuncture points which may stimulate uterine activity.

Treatment during the third trimester of pregnancy is thought to carry a lower risk.

This review is one of a series of reviews of methods of labour induction using a standardised protocol. For more detailed information on the rationale for this methodological approach please refer to the currently published protocol (Hofmeyr 2009).

OBJECTIVES

To determine, from the best available evidence, the effectiveness and safety of acupuncture for third trimester cervical ripening or induction of labour.

METHODS

Criteria for considering studies for this review

Types of studies

Clinical trials comparing acupuncture for cervical ripening or labour induction, with placebo/no treatment, sham acupuncture or other methods listed above it on a predefined list of methods of labour induction; the trials included some form of random allocation to either group; and they reported one or more of the prestated outcomes.

The control group in a trial of acupuncture can involve sham (mock) acupuncture where the needles are inserted away from the usual location, with the depth and needle stimulation being the same. Or alternatively, minimal acupuncture which involves needles being inserted away from the usual location, with very shallow needling and very slight stimulation, or the use of the non invasive placebo needle (Streitberger 1998).

Types of participants

Pregnant women due for third trimester induction of labour, carrying a viable fetus. We planned to use subgroup analysis for any possible differences in the effect of interventions in these groups.

Types of interventions

Acupuncture compared with placebo, no treatment, sham acupuncture or any other method above it on a predefined list of methods of labour induction, as detailed below.

To avoid duplication of data in a series of reviews on interventions for labour induction, the labour induction methods were listed in a specific order, from one to 27, as outlined below. The methods for these reviews are described in the generic protocol for cervical ripening and labour induction in late pregnancy (Hofmeyr 2009). Each review included comparisons between one of the methods (from two to 26) with only those methods above it on the list.

Thus, this review of acupuncture (20) could include comparisons with any of the following: (1) placebo/no treatment; (2) vaginal prostaglandins; (3) intracervical prostaglandins; (4) intravenous oxytocin; (5) amniotomy; (6) intravenous oxytocin with amniotomy; (7) vaginal misoprostol; (8) oral misoprostol; (9) mechanical methods including extra-amniotic Foley catheter; (10) membrane sweeping; (11) extra-amniotic prostaglandins (12) intravenous prostaglandins; (13) oral prostaglandins; (14) mifepristone; (15) oestrogens with or without amniotomy; (16) corticosteroids; (17) relaxin; (18) hyaluronidase; (19) castor oil, bath, and/or enema.

The current list is as follows:

(1) placebo/no treatment;
(2) vaginal prostaglandins (Kelly 2009);
(3) intracervical prostaglandins (Boulvain 2008);
(4) intravenous oxytocin (Alfirevic 2009);
(5) amniotomy (Bricker 2000);
(6) intravenous oxytocin with amniotomy (Howarth 2001; Bimbashi 2012);
(7) vaginal misoprostol (Hofmeyr 2010);
(8) oral misoprostol (Alfirevic 2006);
(9) mechanical methods including extra-amniotic Foley catheter (Jozwiak 2012);
(10) membrane sweeping (Boulvain 2005);
(11) extra-amniotic prostaglandins (Hutton 2001);
(12) intravenous prostaglandins (Luckas 2000);
(13) oral prostaglandins (French 2001);
(14) mifepristone (Hapangama 2009);
(15) oestrogens with or without amniotomy (Thomas 2001);
(16) corticosteroids (Kavanagh 2006b);
(17) relaxin (Kelly 2001b);
(18) hyaluronidase (Kavanagh 2006a);
(19) castor oil, bath, and/or enema (Kelly 2013);
(20) acupuncture (this review);
(21) breast stimulation (Kavanagh 2005);
(22) sexual intercourse (Kavanagh 2001);
(23) homoeopathic methods (Smith 2003);
(24) nitric oxide donors (Kelly 2011);
(25) buccal or sublingual misoprostol (Muzonzini 2004);
(26) hypnosis (*protocol in progress*);
(27) other methods for induction of labour.

Types of outcome measures

Primary outcomes

Clinically relevant outcomes for trials of methods of cervical ripening/labour induction have been prespecified by two authors of

labour induction reviews (Justus Hofmeyr and Zarko Alfirevic) (Hofmeyr 2009). Differences were settled by discussion.

Five primary outcomes were chosen as being most representative of the clinically important measures of effectiveness and complications. It was agreed that subgroup analyses would be limited to the primary outcomes:

(1) vaginal delivery not achieved within 24 hours;
(2) uterine hyperstimulation with fetal heart rate (FHR) changes;
(3) caesarean section;
(4) serious neonatal morbidity or perinatal death (e.g. seizures, birth asphyxia defined by trialists, neonatal encephalopathy, disability in childhood);
(5) serious maternal morbidity or death (e.g. uterine rupture, admission to intensive care unit, septicaemia).

Perinatal and maternal morbidity and mortality are composite outcomes. This is not an ideal solution because some components are clearly less severe than others. It is possible for one intervention to cause more deaths but less severe morbidity. However, in the context of labour induction at term this is unlikely. All these events will be rare, and a modest change in their incidence will be easier to detect if composite outcomes are presented. The incidence of individual components will be explored as secondary outcomes (see below).

Secondary outcomes

Secondary outcomes relate to measures of effectiveness, complications and satisfaction.

Measures of effectiveness:
(6) cervix unfavourable/unchanged after 12 to 24 hours;
(7) oxytocin augmentation.

Complications:
(8) uterine hyperstimulation without FHR changes;
(9) uterine rupture;
(10) epidural analgesia;
(11) instrumental vaginal delivery;
(12) meconium-stained liquor;
(13) Apgar score less than seven at five minutes;
(14) neonatal intensive care unit admission;
(15) neonatal encephalopathy;
(16) perinatal death;
(17) disability in childhood;
(18) maternal side-effects (all);
(19) maternal nausea;
(20) maternal vomiting;
(21) maternal diarrhoea;
(22) other maternal side-effects;
(23) postpartum haemorrhage (as defined by the trial authors);
(24) serious maternal complications (e.g. intensive care unit admission, septicaemia but excluding uterine rupture);
(25) maternal death.

Measures of satisfaction:
(26) woman not satisfied;
(27) caregiver not satisfied.

Acupuncture specific outcomes:
(28) use of other induction methods;
(29) time from trial intervention to the birth of the baby;
(30) length of labour.

While all the above outcomes were sought, only those with data appear in the analysis tables.

The terminology of uterine hyperstimulation is problematic (Curtis 1987). In the reviews we used the term 'uterine hyperstimulation without FHR changes' to include uterine tachysystole (more than five contractions per 10 minutes for at least 20 minutes) and uterine hypersystole/hypertonus (a contraction lasting at least two minutes) and 'uterine hyperstimulation with FHR changes' to denote uterine hyperstimulation syndrome (tachysystole or hypersystole with fetal heart rate changes such as persistent decelerations, tachycardia or decreased short term variability).

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 (23 November 2012).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly 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.

In addition, we searched PubMed (1966 to 23 November 2012), EMBASE (1980 to 23 November 2012), Dissertation Abstracts (1861 to 23 November 2012), CINAHL (1982 to 23 November 2012) and the WHO International Clinical Trials Registry Portal (

ICTRP) (23 November 2012). See Appendix 1 for search strategies used.

Searching other resources

We handsearched reference lists of trial reports and reviews.
We did not apply any language restrictions.
The search for the initial version of the review was performed simultaneously for all reviews of methods of inducing labour, as outlined in the generic protocol for these reviews (Hofmeyr 2000).

Data collection and analysis

For methods used in the previous version of this review, see Appendix 2; Appendix 3. These methods followed those described in the generic protocol (Hofmeyr 2009), which was developed in order to provide a standardised methodological approach for conducting a series of reviews examining the various methods of preparing the cervix of the uterus and inducing labour.
For this update we used the following methods when assessing the reports identified by the updated search.

Selection of studies

Two review authors C Smith (CS) and S Grant (SG) independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted a third person. When articles contained insufficient information to make a decision about eligibility, CS attempted to contact authors of the original reports to obtain further details.

Data extraction and management

Following an assessment for inclusion CS, SG independently extracted data using a data extraction form Appendix 4. A third independent person extracted data for a trial undertaken by CS and CC. We resolved discrepancies through discussion or, if required, we consulted a third person. 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 authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently (third for the Smith 2008 trial) assessed the risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions (*Higgins 2011*)*. We resolved any disagreement by discussion or by involving a third assessor.

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

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

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

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

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

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

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

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

- 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 and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion were reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or was supplied by the trial authors, we planned to re-include missing data in the analyses where possible. Trials with greater than 20% missing data were classified at a high risk of bias.

We assessed 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 we investigated the possibility of selective outcome reporting bias and what we found. We assessed the 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 had 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 high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses - *see* '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 used the mean difference if outcomes were measured in the same way between trials. We used the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We did not identify an cluster-randomised trials for inclusion in this update, but plan to include them if identified in future updates. We will include cluster-randomised trials in the analyses along with individually-randomised trials. We will adjust their sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there was little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Other unit of analysis issues

Trials with multiple arms were included and are described in the Characteristics of included studies. For example, acupuncture might be compared with sham acupuncture and with another arm where no acupuncture was delivered. If there were two acupuncture groups, data from both treatment arms were combined into one group. For studies with a sham control and no treatment control group, the shared intervention was divided evenly between

groups as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Where outcomes were repeated measures, analysis of outcomes was undertaken at the end of the intervention.

Dealing with missing data

For included studies, we noted levels of attrition. We aimed to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we carried out analyses, 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, and all participants were analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing. Studies were excluded from the analysis if there was a high level of missing data (greater than 20%).

Assessment of heterogeneity

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

Assessment of reporting biases

Had there been 10 or more studies in the meta-analysis, we planned to investigate reporting biases (such as publication bias) using funnel plots. We would have assessed funnel plot asymmetry visually. If asymmetry was suggested by a visual assessment, we proposed to perform exploratory analyses to investigate it.

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. We treated the random-effects summary as the average of the 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 would not have combined trials.

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

Subgroup analysis and investigation of heterogeneity

Had we identified substantial heterogeneity, we planned to investigate it using subgroup analyses and sensitivity analyses. We would have considered whether an overall summary was meaningful, and if it was, we would have used random-effects analysis.

Subgroup analyses were not prespecified in the earlier version of the review (Smith 2004).

We planned to carry out the following subgroup analyses:

1. nulliparity versus multiparity;
2. cervix unfavourable, versus favourable versus undefined;
3. membranes intact or ruptured;
4. classical/traditional acupuncture versus single point therapy, or auricular acupuncture.

We planned to assess subgroup differences by interaction tests available within RevMan (RevMan 2012) and report the results of subgroup analyses quoting the $\chi 2$ statistic and P value, and the interaction test I^2 value.

Sensitivity analysis

Where subgroup analysis failed to explain the heterogeneity, we planned to analyse the data using a random-effects model. A priori, we planned to perform sensitivity analysis on the results to look at the possible contribution of: (1) differences in methodological quality, with trials of high quality (low risk of bias) compared to all trials; and (2) publication bias by country. If publication bias was present, we planned to undertake a sensitivity analysis excluding trials from countries where there was a greater publication bias.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Results of the search

The original review included three trials and seven trials were excluded. This updated review includes 14 trials, and excludes eight trials. Three trials previously excluded due to no clinically relevant outcomes are now included (Martinez 2004; Romer 2000;

Tremeau 1992). One trial is currently awaiting assessment (Liu 2012).

Included studies

Study design

All studies were parallel design. Nine trials had two groups (Gaudernack 2006; Gaudet 2008; Gribel 2011; Harper 2006; Modlock 2010; Rabl 2001; Romer 2000; Selmer-Olsen 2007; Smith 2008), two trials had three groups (Asher 2009; Tremeau 1992) and one trial had five groups (Mackenzie 2011). Seven studies used sham controls (Asher 2009; Gaudet 2008; Mackenzie 2011; Modlock 2010; Romer 2000; Smith 2008; Tremeau 1992) and eight trials used standard care (Asher 2009; Gaudernack 2006; Gribel 2011; Harper 2006; Mackenzie 2011; Rabl 2001; Selmer-Olsen 2007; Tremeau 1992).

Samples sizes

Sample size of the included studies ranged from 16 (Gaudet 2008) to 553 (Romer 2000).

Study location and sources of women

Two studies were undertaken in Norway (Gaudet 2008; Selmer-Olsen 2007), two in the United States (Asher 2009; Harper 2006), and one each from Austria (Rabl 2001), Australia (Smith 2008), Brazil (Gribel 2011), Canada (Gaudet 2008), China (Long 1994), Denmark (Modlock 2010), France (Tremeau 1992), Germany (Romer 2000) the Phillipines (Martinez 2004) and the United Kingdon (Mackenzie 2011).

Participants

Six studies recruited nulliparous women only (Asher 2009; Gaudet 2008; Harper 2006; Mackenzie 2011; Romer 2000; Selmer-Olsen 2007). Six trials recruited both nulliparous and primiparous women (Gaudernack 2006; Gribel 2011; Modlock 2010; Rabl 2001; Smith 2008; Tremeau 1992). Parity was unclear in two trials (Long 1994; Martinez 2004).

Types of interventions

Eight studies used manual acupuncture only (Asher 2009; Gaudernack 2006; Modlock 2010; Rabl 2001; Romer 2000; Selmer-Olsen 2007; Smith 2008; Tremeau 1992), one trial used electro-acupuncture only (Gribel 2011), and three trials used manual and electro-acupuncture (Gaudernack 2006; Gaudet 2008; Harper 2006). Fixed points were used in nine trials (Asher 2009; Gaudet 2008; Gribel 2011; Harper 2006; Mackenzie 2011; Modlock 2010; Rabl 2001; Romer 2000; Tremeau 1992) and three trials used individualised treatment (Gaudernack 2006; Selmer-Olsen 2007; Smith 2008). There was significant variation in the acupuncture points used but included; Stomach 36 (ST36), Liver 3 (LR3), Conception Vessel 4 (CV4), Three Heater 6 (TH6), Large Intestine 4 (LI4), Gall Bladder 41 (GB41), Kidney 6 (KI6), Spleen 6 (SP6), Heart 7 (HT7), and Lung 7 (LU7), Bladder 31 (UB31), Bladder 32 (UB32), Bladder 60 (UB60) Bladder 67 (UB67), Governing Vessel (GV20).

The number of treatments varied from three trials administering one treatment (Gaudernack 2006; Mackenzie 2011; Rabl 2001), two treatments (Gaudet 2008; Modlock 2010; Selmer-Olsen 2007; Smith 2008) and five providing three of more (Asher 2009; Gribel 2011; Harper 2006; Romer 2000; Tremeau 1992).

Gaudet 2008 used a combination of manual and non active electro-stimulation for the control group.

Few details were reported in two trials (Long 1994; Martinez 2004).

Outcome measures

Few trials reported on the primary outcomes relating to this review. Nine trials reported on caesarean section (Asher 2009; Gaudet 2008; Gribel 2011; Harper 2006; Mackenzie 2011; Modlock 2010; Selmer-Olsen 2007; Smith 2008; Tremeau 1992), although all trials reported on a selection of the secondary outcomes included in this review.

Excluded studies

Eight trials were excluded; see Characteristics of excluded studies. Four trials were excluded due to insufficient reporting of randomisation (Dorr 1990; Kubista 1974; Li 1996, So 1979) and we were unable to obtain details from authors. One trial was excluded due to an evaluation of acupuncture on pain relief in labour (Bo 2006). One trial reported on women already in labour (Lyngso 2010). Two trials used a form of stimulation not relevant to this review (Aghamohammadi 2011; Dunn 1989).

Risk of bias in included studies

See Figure 1; and Figure 2 for a graphical summary of the 'Risk of bias' assessment by authors of the included studies based on the six domains of bias. One study was at a low risk of bias on all domains (Smith 2008).

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

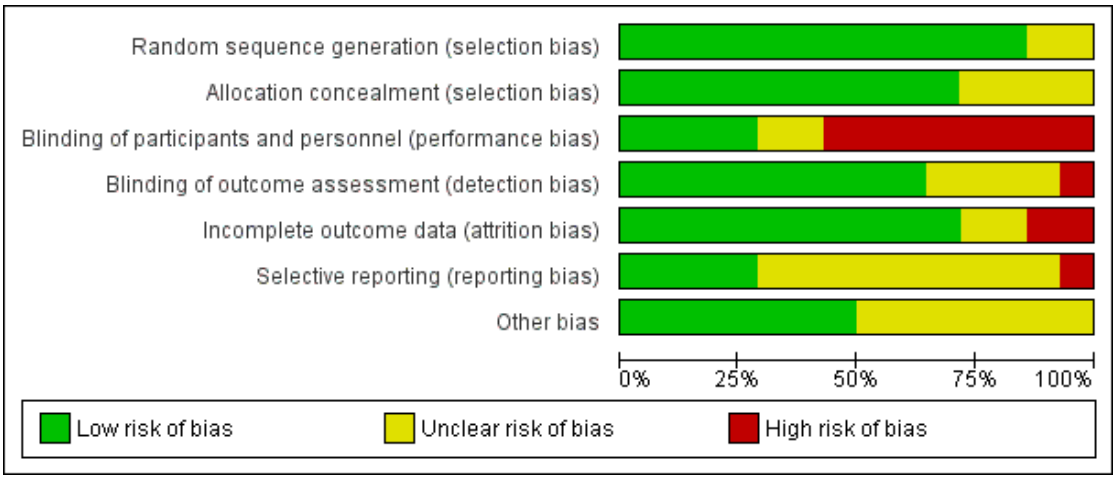
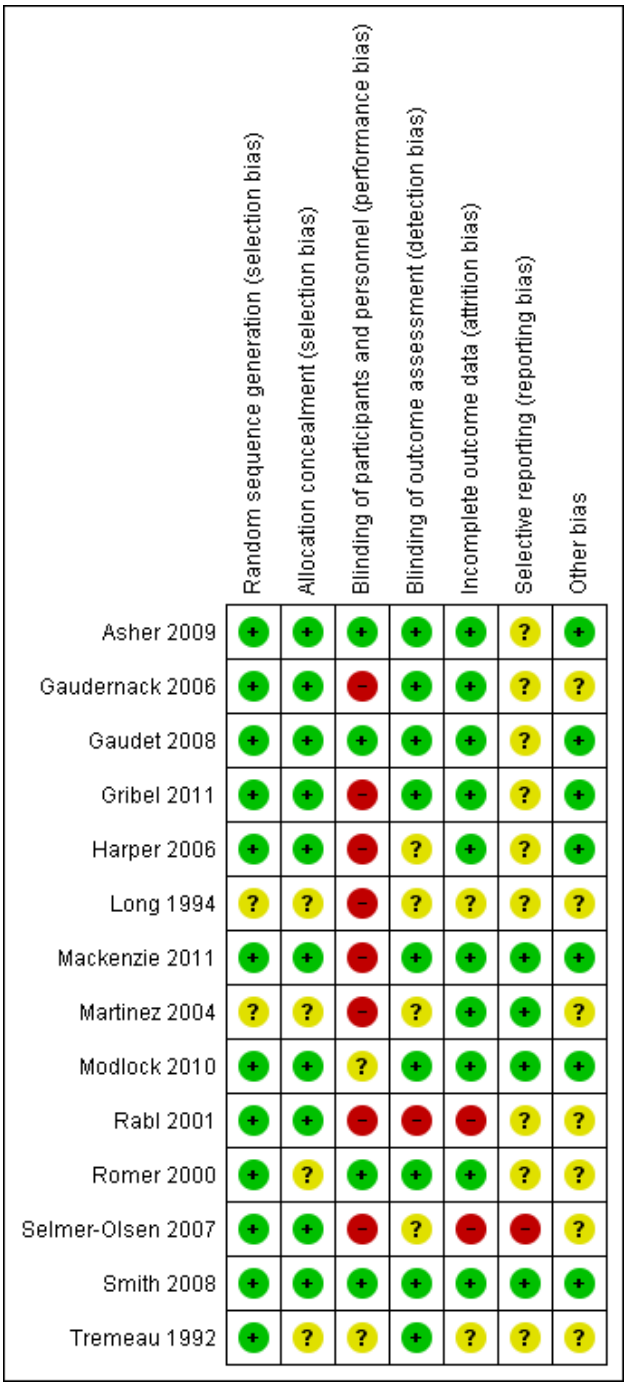


Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Twelve trials were rated at a low risk of bias for adequate generation of the randomisation sequence, generation of the randomisation schedule was unclear in two trials (Long 1994; Martinez 2004). The method of concealment was at low risk in 10 trials, with insufficient reporting in four trials (Long 1994; Martinez 2004; Romer 2000; Tremeau 1992).

Blinding

Four studies were at low risk of performance bias (Asher 2009; Gaudet 2008; Romer 2000; Smith 2008). Eight studies were assessed at a high risk of bias primarily because participants were not blind to group allocation in the studies using a standard care control. Detection bias was assessed at a low risk in nine trials (Asher 2009; Gaudernack 2006; Gaudet 2008; Gribel 2011; Mackenzie 2011; Modlock 2010; Romer 2000; Smith 2008; Tremeau 1992), one trial was assessed at high risk and four trials were assessed as unclear.

Incomplete outcome data

Ten trials were assessed at low risk of bias. Two trials were at high risk. In the Rabl trial (Rabl 2001), there were 11 (20%) post-randomisation exclusions and losses to follow-up. There was an imbalance in the post-randomisation exclusions (five in the treatment group and eight in the control group). The trial author was unable to provide outcome data on the 11 women who had been excluded from analyses. Risk was assessed as unclear in two trials.

Selective reporting

The risk of selective reporting was assessed as low in four trials (Mackenzie 2011; Martinez 2004; Modlock 2010; Smith 2008), the risk of bias was unclear in nine trials, and at high risk in one trial (Selmer-Olsen 2007).

Other potential sources of bias

The risk of bias was rated as low in seven trials (Asher 2009; Gaudernack 2006; Gaudet 2008; Gribel 2011; Harper 2006; Mackenzie 2011; Modlock 2010;Smith 2008), and unclear in the other seven trials.

Effects of interventions

This review included 14 trials of 2220 women.

We included 11 trials in the meta-analysis with data reporting on 1689 women. Because data were not available about the post-randomisation exclusions for the Rabl 2001 trial and an intention-to-treat analysis could not be undertaken, the results of this trial could not be incorporated into the meta-analysis. Primary data from the Long 1994 trial could not be obtained and no data are included in the analysis. Martinez 2004 reported on no clinically relevant outcomes.

Primary outcomes

Trials reported on two primary outcomes only: caesarean section and serious neonatal morbidity. No trial reported on vaginal delivery not achieved within 24 hours; uterine hyperstimulation with fetal heart rate (FHR) changes and serious maternal morbidity or death (e.g. uterine rupture, admission to intensive care unit, septicaemia).

1.1) Outcome: caesarean section

Data on caesarean section was reported from 9 trials with 1015 women, (Analysis 1.1).

1.1.1 Sham control

There was no difference in caesarean deliveries between groups (average risk ratio (RR) 0.95, 95% confidence interval (CI) 0.69 to 1.30, six trials, 654 women).

1.1.2 Usual care

There was no difference in caesarean deliveries between groups (average RR 0.69, 95% CI 0.40 to 1.20, six trials, 361 women; Heterogeneity: $Tau^2 = 0.18$; $I^2 = 40\%$). There was significant heterogeneity indicated by the I^2 statistic and we applied a random-effects model.The heterogeneity may be explained by the Asher 2009 and Selmer-Olsen 2007 trials, although it is unclear which aspects of the intervention may explain the heterogeneity.

1.2) Outcome: serious neonatal morbidity

1.2.1 Sham control

There was no difference in neonatal seizures between groups (RR 1.01, 95% CI 0.06 to 16.04, one trial, 364 women), Analysis 1.2.

Serious maternal morbidity or death

There were no serious outcomes or maternal death reported in one trial (Smith 2008).

Secondary outcomes

Secondary outcomes relate to measures of effectiveness, complications and satisfaction. Trials reported on cervix unfavourable/unchanged after 12 to 24 hours; oxytocin augmentation; epidural analgesia; instrumental vaginal delivery; meconium-stained liquor; Apgar score less than seven at five minutes; neonatal intensive care unit admission; perinatal death; postpartum haemorrhage; other maternal side-effects; maternal death; and woman not satisfied. The following acupuncture specific outcomes were included: use of other induction methods; time from trial intervention to the birth of the baby; and length of labour.

No trial reported on the following outcomes; uterine hyperstimulation without FHR changes; uterine rupture; neonatal encephalopathy; disability in childhood; maternal side-effects (all); maternal nausea; maternal vomiting; maternal diarrhoea; serious maternal complications; and caregiver not satisfied.

1.3) Outcome: cervical change within 12 to 24 hours

Data on cervical maturation were available from six trials with data reported in the meta-analysis from two trials, Analysis 1.3. Data were not combined but in both trials there was a greater change in the cervix for the acupuncture groups compared with the control groups, as measured by Bishop score.

1.3.1 Sham control

There was greater cervical change in Bishop score occurring within 24 hours for women receiving acupuncture compared with the sham control, mean difference (MD) 0.40. 95% CI 0.11 to 0.69, one trial, 125 women. Data from the Smith 2008 trial were not included in the meta-analysis and reported an increase in the Bishop score that did not differ between groups (RR 1.08, 95% CI 0.92 to 1.26, one trial 364 women), data not shown.

The Romer 2000 trial did not report on when the cervical change was assessed, however the authors report there was a significant change in the Bishops score (acupuncture 5.9 +/- 1.3 (mean and standard deviation (SD)), non specific acupuncture 4.0, +/- 0.9, and no acupuncture 3.6 +/- 1.0).

1.3.2 Usual care

There was an increase in cervical maturation in the acupuncture group compared with the control (MD 1.30, 95% CI 0.11 to 2.49, one trial, 67 women).

Data from the Harper 2006 trial were not included in the analysis, there was no difference in cervical dilatation on the day of admission (3.3.cm versus 2.7 cm, P = 0.28).

Data from the Tremeau 1992 trial did not include means and SDs but reported a significantly greater progression in the Bishop score for the group receiving acupuncture (2.61 points) compared with the placebo group (0.89), and the usual care group (1.08).

1.4) Outcome: oxytocin augmentation

Data on this outcome were available from seven trials and 1090 women, Analysis 1.4.

1.4.1 Sham control

There was no difference in the use of oxytocin augmentation between acupuncture and a sham control groups (RR 0.97, 95% CI 0.78 to 1.21, four trials, 833 women).

1.4.2 Usual care

There was no difference in the use of oxytocin augmentation between acupuncture and usual care groups (RR 1.08, 95% CI 0.86 to 1.34, three trials, 257 women).

1.5) Outcome: need for epidural

This outcome was reported by eight trials and 922 women, Analysis 1.5.

1.5.1 Sham control

There was no difference in the need for epidural between groups (RR 1.02, 95% CI 0.88 to 1.19, five trials, 571 women).

1.5.2 Usual care

There was no difference in the use of epidurals between groups (RR 0.92, 95% CI 0.77 to 1.11, five trials, 351 women).

1.6) Outcome: instrumental vaginal delivery

Eight trials with 961 women reported on this outcome, Analysis 1.6.

1.6.1 Sham control

There were no differences in the rate of instrumental delivery between groups (average RR 1.19, 95% CI 0.85 to 1.65, five trials, 610 women).

1.6.2 Usual care

There was significant heterogeneity indicated by the I^2 statistic and we applied a random-effects model. There was no difference between groups (RR 0.91, 95% CI 0.50 to 1.64, five trials, 351 women; Heterogeneity: $Tau^2 = 0.17$; $I^2 = 40\%$).

1.7 Outcome: meconium-stained liquor

One one trial (364 women) reported on this outcome, Analysis 1.7.

1.7.1 Sham control

There was no difference in meconium-stained liquor between groups (RR 0.81, 95% CI 0.56 to 1.16).

1.8 Outcome: Apgar score less than seven at five minutes

Data on this outcome were reported by six trials (801 women), Analysis 1.8.

1.8.1 Sham control

There was no difference in the Apgar score at five minutes between groups (RR 0.67, 95% CI 0.20 to 2.21, four trials, 559 women).

1.8.2 Usual care

There was no difference in the Apgar score at five minutes between groups (RR 0.35, 95% CI 0.01 to 8.48, three trials, 242 women).

1.9 Outcome: neonatal care admission

Three trials (186 women) reported on this outcome, Analysis 1.9.

1.9.1 Sham control

There was significant heterogeneity indicated by the I^2 statistic and we applied a random-effects model. There was no difference between groups (average RR 0.82, 95% CI 0.02 to 37.11, three trials, 141 women; Heterogeneity: $Tau^2 = 5.42$; $I^2 = 72\%$).

1.9.2 Usual care

There was no difference between groups (RR 0.65, 95% CI 0.03 to 14.97, one trial, 45 women).

1.10 Outcome: perinatal death

One one trial (364 women) reported on this outcome, Analysis 1.10.

1.10.1 Sham control

There were no deaths in either group.

1.11 Outcome: perineal tear

One trial (91 women) reported on this outcome, Analysis 1.11.

1.11.1 Usual care

There was no difference in this outcome between groups (RR 1.22, 95% CI 0.95 to 1.56).

1.12 Outcome: maternal infection

Two trials including one three-arm trial (180 women) reported on this outcome, Analysis 1.12.

1.12.1 Sham control

There was no difference between groups (RR 1.29, 95% CI 0.43 to 3.88, one trial, 44 women).

1.12.2 Usual care

There was no difference between groups (RR 1.64, 95% CI 0.43 to 6.32, two trials, 136 women).

1.13 Outcome: fetal infection

One trial (91 women) reported on this outcome, Analysis 1.13.

1.13.1 Usual care

There were no reports of fetal infection between groups.

1.14 Outcome: postpartum bleeding greater than 500 mL

Three trials, 594 women reported on this outcome, Analysis 1.14.

1.14.1 Sham control

There was no difference between groups (RR 1.02, 95% CI 0.67 to 1.54, three trials, 542 women).

1.14.2 Usual care

There was no difference between groups (RR 0.50, 95% CI 0.10 to 2.50, one trial, 52 women).

1.15 Outcome: maternal death

One trial, 364 women reported on this outcome, Analysis 1.15.

1.15.1 Sham control

There were no maternal deaths in either group.

1.16 Outcome: time from trial entry to delivery

Three trials (161 women) reported on this outcome, Analysis 1.16.

1.16.1 Sham control

Two trials reported on this outcome (Asher 2009; Gaudet 2008). Time was reported in hours by Gaudet 2008 and in days by Asher 2009. There was no difference in time to delivery between acupuncture and the sham control (average standardised mean difference (SMD) -0.22, 95% CI -0.99 to 0.55). There was significant heterogeneity indicated by the I^2 statistic due to the differing method to record this outcome (Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 1.75$, df = 1 (P = 0.19); $I^2 = 43\%$).

1.16.2 Usual care

This outcome was measured in hours by Harper 2006 and in days by Asher 2009. No difference in time to delivery was found between groups (average SMD 0.25, 95% CI -0.77 to 1.27). There was significant heterogeneity indicated by the I^2 statistic due to the differing method to record this outcome (Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 5.98$, df = 1 (P = 0.01); $I^2 = 83\%$).

1.17 Outcome: maternal satisfaction

One trial (67 women) reported on this outcome, Analysis 1.17.

1.17.1. Usual care

There was no difference in maternal satisfaction between groups (RR 1.29, 95% CI 0.99 to 1.67).

1. 18 Outcome: need for induction methods

Seven trials 1236 women reported on this outcome, Analysis 1.18.

1.18.1 Sham control

There was no difference between groups (average RR 1.03, 95% CI 0.91 to 1.16, four trials, 977 women).

1.18.2 Usual care

There was significant heterogeneity indicated by the I^2 statistic and we applied a random-effects model (Heterogeneity: $Tau^2 = 0.06$; $I^2 = 45\%$). There was no difference between groups (RR 1.00, 95% CI 0.69 to 1.45, four trials, 259 women).

1.19 Outcome: length of labour

Four trials (761 women) reported on this outcome, Analysis 1.19.

1.19.1 Sham control

There was significant heterogeneity indicated by the I^2 statistic and we applied a random-effects model (Heterogeneity: $Tau^2 = 0.08$; $I^2 = 69\%$). There was no difference between groups (SMD -0.18, 95% CI -0.58 to 0.23, three trials, 694 women).

1.19.2 Usual care

The length of labour was shorter in the usual care group compared with acupuncture (MD 0.67, 95% CI 0.18 to 1.17, one trial, 67 women).

Data from other studies

In the Rabl trial (Rabl 2001), 11 (20%) women were post-randomisation exclusions and proceeded to have an elective induction of labour. In the acupuncture group, labour was induced for one woman because of fetal heart abnormalities and two inductions were performed due to prelabour rupture of membranes. In the control group, two women requested an elective induction of labour, three women received an induction of labour because of prelabour rupture of membranes, and in three women labour was induced due to abnormal fetal heart rate patterns. Because data were not available about the post-randomisation exclusions and an intention-to-treat analysis could not be undertaken, no results could be incorporated into this review.

Sensitivity analysis

It was proposed to undertake a sensitivity analysis on the results to look at the possible contribution of: (1) differences in methodological quality, with trials of high quality (low risk of bias) compared to all trials; and (2) publication bias by country. This was not done due to the small number of trials overall. There was one trial of high quality; there were also too few trials within comparisons to make comparisons to examine the influence of publication bias. Where there was heterogeneity, we applied a random-effects model.

Subgroup analysis

We did not undertake subgroup analysis, based on insufficient reporting of trials with the variables of interest by outcome.

DISCUSSION

Summary of main results

Findings from this review are based on comparisons between acupuncture and five sham-controlled trials, and comparisons between acupuncture with five trials using usual care controls. Evidence from 14 trials with data reporting on 2220 women suggest very limited benefit from acupuncture to induce labour. There was insufficient evidence of benefit of acupuncture compared with control for any primary endpoint. Benefit was found from individual trials of both sham and usual care controls.

There was greater cervical change occurring with 24 hours for women receiving acupuncture compared with the sham control, mean difference (MD) 0.40. 95% confidence interval (CI) 0.11 to 0.69, one trial, 125 women. Data from two studies not included in the meta-analysis found conflicting results when comparing acupuncture with a sham control (Romer 2000; Smith 2008). There was an increase in cervical maturation in the acupuncture group compared with the control (MD 1.30, 95% CI 0.11 to 2.49, one trial, 67 women). Two studies (Harper 2006; Tremeau 1992) not included in the meta-analysis also reported greater changes in the cervix for the acupuncture group compared with usual care. One trial found the length of labour was shorter in the usual care group compared with acupuncture (average MD 0.67, 95% CI 0.18 to 1.17, one trial, 67 women). Trials were characterised by heterogenous acupuncture point selection and dosage. Although there have been more trials reported since this review was last updated evaluating the role of acupuncture, there continues to be a relatively small number of trials that have provided relevant health outcomes. This limits the power of the review to detect meaningful differences between groups and analyses, suggesting these limited benefits should be interpreted with caution.

Overall completeness and applicability of evidence

Trials recruited low-risk nulliparous and primiparous women at term. The majority of trials reported that women offered the opportunity to participate in the trial agreed to participate. Smith 2008 however, reported 18% of women approached declined participation due to a lack of interest in acupuncture.

The systematic review documented wide variation in the delivery of acupuncture. This included the mode of stimulation, duration of needling, number of points used, depth of needling and duration of the trial. It is unclear how representative the treatment protocols used in the research are generalisable to acupuncture as it is usually practiced. There was insufficient reporting of the rationale of the acupuncture used in the research setting. Some trials used a fixed approach to the selection of points whilst other used a flexible approach, with selection of acupuncture points based on their clinical presentation. The variation in the duration, frequency and selection of acupuncture points suggests that the acupuncture may not have been therapeutically effective and in some cases may not represent best clinical practice. The variation may also reflect the country context in which acupuncture is practiced.

Quality of the evidence

The 'Risk of bias' tables (Figure 1; Figure 2) demonstrate that acupuncture has not been consistently subjected to consistent rigorous study. Only one trial was assessed at a low risk of bias. Since the publication of this original review the quality of reporting has improved over time. The majority of studies were at a low risk of bias in respect to randomisation. Rates of follow-up were good in the majority of trials with only two trials rated at a high risk of bias. The majority of trials were at a low risk of detection bias. Trials comparing acupuncture with usual care were rated at a high risk of bias due to the inability to blind study participants. The potential for bias however may be low given the use of objective clinical outcomes.

Only one of the sham acupuncture controlled trials used a non - penetrating needle, however these were placed at active acupuncture points and therefore may be associated with some physiological activity. The quality of the evidence is also influenced by small sample sizes, with many studies underpowered to detect changes between groups.

Potential biases in the review process

We attempted to minimise publication bias. Our search was comprehensive and we included studies identified in languages other than English. However, we cannot rule out the possibility that some studies have been missed.

Agreements and disagreements with other studies or reviews

A systematic review examining the effect of acupuncture on induction of labour and cervical maturation found all studies demonstrated labour induction by acupuncture treatment (Lim 2009). The review included 10 studies consisting of randomised controlled trials, non-randomised studies with and without controls, and a matched pair study. The review by Lim et al concluded a definitive role for acupuncture was still to be established and further research was needed. A recent systematic review of methods of induction of labour included our earlier Cochrane review (Smith 2004), and three other randomised controlled trials published since the 2004 Cochrane review (Mozurkewich 2011). The authors concluded that acupuncture for induction of labour is investigational, and no advantages have been demonstrated. Overall, all reviews identify there is insufficient evidence of a benefit from acupuncture.

AUTHORS' CONCLUSIONS

Implications for practice

There are insufficient data to demonstrate whether acupuncture is more effective than a sham control, or no treatment, or whether there is additional benefit from acupuncture when used in combination with usual care.

Implications for research

Overall, there are still only a small number of studies assessing the role of acupuncture for induction of labour. Further research is required. We suggest further research focuses on gaining a greater understanding of the specific components of acupuncture treatment in relation to working with women who are overdue. Appropriately powered randomised trials are required to examine the effectiveness of acupuncture on the clinical outcomes described in this review but following a greater understanding of the multi-components of acupuncture, or greater reflection of how acupuncture is practiced in a clinical setting.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Asher 2009

Methods	89 women were randomised to 3 groups true acupuncture (TCM) (n = 30), sham (n = 29), control (n = 30). Sample size was determined by 30 participants per group to provide 80% power to detect a 3-day difference between groups
Participants	The trial took place at a medical centre in North Carolina, USA. Women included were nulliparous, between 38 and 41 weeks of gestation, able to communicate in English, and at least 18 years old. Exclusion criteria included uncertain dating, transportation difficulties, breech presentation, or a previous inability to tolerate acupuncture
Interventions	The true acupuncture group received needles bilaterally at LI4, SP6, UB32, and UB54 alongside routine prenatal care. Needles were manually stimulated until *de qi* was attained and retained for 30 minutes. Treatments were administered for up to a maximum of 5 treatments over a 2-week period. Acupuncture was performed by 2 licensed acupuncturists. Needles were Seirin J-type (0.16 mm x 30 mm for hand and leg points, 0.24 mm x 40 mm for back points) The sham acupuncture group received invasive shallow needle insertion at non-acupuncture points on the hands, legs, and lower back, bilaterally, alongside routine prenatal care. Needles were retained for 30 minutes Patients enrolled in the true acupuncture or sham acupuncture group received treatment within 30 minutes of enrolment The control group received routine prenatal care only.
Outcomes	The primary outcome measure was time from enrolment (first acupuncture treatment) to time of delivery Secondary outcomes were rates of inpatient induction for post-term pregnancy, spontaneous rupture of membranes, caesarean section, assisted delivery, chorioamnionitis, endometritis, postpartum haemorrhage or uterine atony, maternal length of stay, intrapartum fetal distress, and neonatal outcomes (e.g. Apgar scores, post-delivery oxygen requirement)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated numbers using Stata (v8, Statacorp, College Station, TX) in equal blocks of 2 and 4
Allocation concealment (selection bias)	Low risk	Consecutively numbered, sealed, manila envelopes containing the study arm assignment were opened by the principal investigator for each participant after all entry

Asher 2009 (*Continued*)

		criteria were confirmed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Prenatal care providers and participants were masked to the treatment arm assignment if they were receiving acupuncture (TCM or sham acupuncture) but not if they were in the usual care group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All charts were reviewed by an investigator who was blinded to treatment arm assignment throughout the data abstraction process
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 woman in the sham group refused any treatments, 1 woman in the routine care group received acupuncture outside of the study. All participants were analysed
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Low risk	No imbalance at randomisation.

Gaudernack 2006

Methods	Single-blind, randomised controlled trial of acupuncture versus standard care
Participants	100 Norwegian women were randomised, 48 to the acupuncture group and 52 to the control group. The trial was undertaken in Norway, and included women with a singleton pregnancy, with spontaneous rupture of membranes, cephalic presentation and at term. Women were excluded if contractions were occurring at least every 10 minutes, lasting more than 30 seconds
Interventions	The acupuncture intervention included stimulation of acupuncture points LR3, ST36, CV4; in addition, acupuncture points were administered according to the TCM diagnosis. Total of 9 points used. Needles were retained for 20 minutes. Following treatment women left the hospital to await onset of labour Women in the control group received conventional medical treatment including prostaglandins and or oxytocin
Outcomes	Oxytocin augmentation, use of other induction agents, time from trial intervention to the birth of the baby, epidural analgesia, instrumental vaginal delivery, maternal side-effects (infection), bleeding, tears, birthweight and Apgar score < 7 at 5 minutes
Notes	There was no power calculation.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Gaudernack 2006 (*Continued*)

Random sequence generation (selection bias)	Low risk	The trial generated a computer-generated, randomisation schedule
Allocation concealment (selection bias)	Low risk	Randomisation was concealed in sealed envelopes. Allocation was undertaken by the midwife
Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not feasible for women and therapist to be blind to group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	It was unclear if the outcome assessor and analyst were blind to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 women excluded from analysis in the acupuncture group, 1 due to wrong treatment allocation and 4 had caesarean delivery. 4 women were excluded from the control due to caesarean delivery
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Unclear risk	Intention-to-treat not reported. Baseline characteristics not reported

Gaudet 2008

Methods	16 participants were randomised to receive either true acupuncture or sham acupuncture
Participants	The study took place in an obstetrics clinics in Canada. Women who were 39 + 0 and 40 + 3 weeks' gestation were approached. Inclusion criteria included nulliparity, an uncomplicated singleton gestation, provision of informed consent, a Bishop's score of < 7 prior to randomisation, and reassuring fetal status. All interested patients underwent a digital cervical examination by the research nurse prior to randomisation in order to determine the Bishop's score. If the Bishop's score was < 7, patients underwent an ultrasound to complete a biophysical profile and an amniotic fluid index. Patients were randomised if they had a biophysical profile score of 8/8 and a normal amniotic fluid index
Interventions	2 appointments for acupuncture sessions were arranged, the first within 2 to 3 days, and the second within 1 week, with an accredited physiotherapist acupuncturist The true acupuncture group received electro-acupuncture at SP6, ST43 and UB60 with manual stimulation of LI4. Patients received electro-stimulation on 4 points at 1-2 Hz for 30-45 minutes The sham acupuncture group received acupuncture at sites adjacent to the acupuncture sites. These were not known to have an effect on initiation of labour or to be located on actual acupuncture meridians. The sites used were SP6+, LI4+, ST43+, BL60+ and

Gaudet 2008 (*Continued*)

	GB36+. The locations were SP6+: above the anterior ankle joint line slightly lateral to the border of the tibia, LI4+: in the centre of the anatomical snuff box (located between the 1st and 2nd metacarpal bones), ST43+: at the joint line of the ankle superior to the web space of the 3^{rd} and 4th metatarsal bones, BL60+: inferior and posterior to the fibula head, and GB36+: also inferior and posterior to the fibula head. Sham sites were stimulated in the same order as the true acupuncture sites. Electro-stimulation was applied as in the treatment group Both groups were instructed in acupressure and encourage to apply acupressure every few hours for approximately 3 to 5 minutes, at the most important sites (LI4 and SP6 or corresponding sham sites)
Outcomes	The primary outcome was time from first acupuncture treatment to delivery. Secondary outcomes included the need for standard methods for induction of labour, duration of active labour, the need for standard pain relief, and the incidence of non-reassuring fetal heart rate in labour
Notes	Intention-to-treat analysis conducted.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was performed using a table of random numbers.
Allocation concealment (selection bias)	Low risk	Sequentially numbered sealed opaque numbers.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants blinded using sham acupuncture, clinicians administering the treatment not able to be blinded but were blinded to all obstetrical parameters. The obstetric care providers were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The trial researchers were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No participants lost.
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Low risk	No difference in baseline characteristics.

Gribel 2011

Methods	72 multiparous or nulliparous pregnant women were randomised to receive either acupuncture or misoprostol
Participants	The study took place in a maternity hospital in Brazil. Women were included if they had a Bishop score < 7, single cephalic presentation with gestational age confirmed by ultrasound, with normal ranges for reactive cardiotocography, amniotic fluid volume, blood pressure (< 110 and < 160 mmHg), controlled diabetes, and estimated fetal weight. Women with contraindications for vaginal delivery
Interventions	The acupuncture group received acupuncture at :LI4, ST36, LR3, SP6, UB23 and UB32. Points were bilaterally electro-stimulated using two distinct frequencies (5 and 50 Hz) that alternated every 7 pulses for 30 minutes. Electro-acupuncture was performed using a (DIAN series # NS AH1405) pulse generator. The electric current intensity was slowly increased until it could be felt by each patient, although without discomfort (30 min) in the ventral (in lied down position with 30_ dorsal elevation) and in the dorsal points (in the sit down position). Stimulation was performed every 7 hours in 1 to up to 3 sessions in a 24 hour period of hospitalisation to all 6 points. Needles were 0.25 x 30. Only 1 physician, with 10 years experience in providing acupuncture to pregnant women, provided the acupuncture The control group received misoprostol (25 mg intravaginally; every 6 hours; up to 4 tablets) within 24 hours
Outcomes	Primary outcome: successful induction of vaginal delivery within 24 hours Secondary outcomes: labour induction; induction and labour duration, caesarian section rate; and initial and final Bishop score (defined as the scores at the end of the protocol, or at the beginning of labour). Labour was defined as 2 to 3 30-40 duration, contractions every 10 minutes for more than 60 minutes, with a 2 or 3 cm dilation of cervix in multiparous or nulliparous women, patient satisfaction
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated, Internet-based block randomisation.
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and clinicians were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded (information attained through email correspondence with the author)

Gribel 2011 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	3 patients from the misoprostol group were excluded, 2 refused to participate and 1 used a dosage different to the study protocol. 2 patients were excluded from the acupuncture group as they used misoprostol during their hospital stay. These participants excluded after randomisation were not included in the final analysis
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Low risk	No imbalance at randomisation.

Harper 2006

Methods	Single-blind, randomised controlled trial of acupuncture versus standard care. Group assignment was made by the principal investigator after entry criteria were confirmed
Participants	56 women were randomised to the trial. The trial was undertaken in an outpatient clinic at the University of North Carolina, USA. Women were included if they were primiparous, with a Bishops score < 7, between 39 and 4 days to 41 weeks, with a cephalic presentation. Women were excluded if they had a contraindication to vaginal delivery, uncertain dating or an inability to tolerate acupuncture
Interventions	The intervention group involved acupuncture administered for 3 out of 4 consecutive days from the first day of enrolment. A Licensed TCM acupuncturist administered the acupuncture. Acupuncture was administered bilaterally to LI4, SP6, UB31 and 32. Electro-acupuncture was administered to the sacrum UB31 and 32 points with current at 2Hz during the 30-minute treatment. needles retained for 30 minutes The control group received routine care (not specified).
Outcomes	Caesarean section, cervical change, time from administration of acupuncture to delivery, mode of delivery spontaneous onset of labour, neonatal complications
Notes	Pre trial power analysis undertaken.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The trial generated a computer-generated randomisation schedule
Allocation concealment (selection bias)	Low risk	Randomisation was concealed in sealed envelopes.

Harper 2006 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	It was not feasible for women and therapist to be blind to group allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was unclear if the outcome assessor and analyst were blind to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up.
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Low risk	No imbalance at randomisation.

Long 1994

Methods	This trial compared pregnant women receiving auricular acupressure and rivanol with a control group who received rivanol only
Participants	400 women were recruited from China. No other details provided
Interventions	Auricular acupuncture was applied to points: Inner genitals, Sympathetic, Shenmen, Liver, Yuanzhong and Adrenal gland, using a white mustard seed or a pill with adhesive plaster. The points were pressed by the woman until the points felt warm, distention and a numb sensation was generated. The control group received 1% rivanol
Outcomes	Time to induce labour, amount of bleeding, length of labour, and mental state of woman
Notes	Contact was attempted with the author, advised the author had retired, and no contact could be established

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Women were equally divided into the 2 groups, no further details provide
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Women would not be blind to their group allocation.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated.

Long 1994 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated.
Selective reporting (reporting bias)	Unclear risk	Not stated.
Other bias	Unclear risk	Not stated.

Mackenzie 2011

Methods	This was a double-blind manual, electro- and sham acupuncture study comparing acupuncture with a control group for analgesia for labour induction
Participants	Nulliparous women from the United Kingdon with a singleton pregnancy and fetal cephalic presentation with intact membranes undergoing labour induction using vaginal prostaglandins and low amniotomy were eligible for the study. Women with a previous experience of acupuncture were excluded
Interventions	105 women were randomised to receive manual acupuncture, electro-acupuncture or sham acupuncture or sham electro-acupuncture or no treatment. In the manual acupuncture and electro-acupuncture group the following points were needled: LI4, SP6, UB60, UB67. Serin needles (0.20 x 30-0.30 x 50 mm) were inserted to a depth of 15-20 mm with *de qi* sensation attained. In the manual group needles were stimulated intermittently and irregularly by hand for 30 minutes. In the electro-acupuncture group, points were stimulated by an electrical stimulator with 2-Hz pulses of 0.5 millisecond duration for 30 minutes, sufficient to cause non-painful muscle contractions. In the sham acupuncture group, needles were inserted at sites adjacent to the specific acupuncture points to a depth of 1-1.5 mm only and insufficient to provoke an unusual sensation. The sham electro-acupuncture group were connected to a electrical stimulator but the current was not activated Intrapartum care was provided by the routine delivery suite staff. Subsequent pain management including aromatherapy, TENS and parenteral opioids, and regional blockade was provided when requested or recommended by the attending midwife or obstetrician
Outcomes	The primary outcome was the rate of intrapartum epidural analgesia requirement. Other outcomes included caesarean section, instrumental deliver, length of labour, Apgar scores
Notes	A power calculation was done based on the reduction in epidural rates

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers were generated using a computer program (RALLOC, Stata Corporation, Singleton, TX, USA) and randomisation was stratified by the acupuncturist

Mackenzie 2011 (*Continued*)

Allocation concealment (selection bias)	Low risk	Allocations were concealed in numbered sealed opaque envelopes opened only after consent and immediately before treatment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Study allocation was concealed from all except the acupuncturist, who was not involved with intrapartum management (double blind) Women randomised to the 'no-treatment' control group were aware of their treatment group (single blind) Great care was taken to conceal treatment allocation from those providing intrapartum care
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Attempts to ensure outcome assessment was blind to group allocation The randomisation code was only revealed after completion of the clinical study
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participant data were included in the analysis. 2 protocol violations, 1 woman randomised to control group received acupuncture, and a second woman was randomised to electro-acupuncture but withdrew from the study before the acupuncture was administered
Selective reporting (reporting bias)	Low risk	All outcomes reported as per outcomes stated on trial registry
Other bias	Low risk	No imbalance at randomisation.

Martinez 2004

Methods	Acupuncture versus no treatment to examine the effect on uterine contractions
Participants	The Obstetrics Out-patient Department of the university hospital in the Phillipines 50 pregnant women who were term, singleton, not in labour, and with uncomplicated course of pregnancy were included in the study. Exclusion criteria: women who were in the active phase of labour, who had previous caesarean section, premature rupture of membranes, concomitant medical illness, or allergy to metals, such as chromium or zinc
Interventions	Spleen 6 (point Sanyinjiao) is on the lower leg approximately 3 inches proximal to the centre of the medial malleolus was stimulated bilaterally. SP6 was pierced on both sides of the lower extremities. Two minutes were allotted for each patient for the insertion of the acupuncture needle. The control group received no intervention

Martinez 2004 (*Continued*)

Outcomes	The frequency, intensity, duration, and interval of uterine contractions were measured for 20 minutes. No outcomes relevant to the review were reported
Notes	The trial did not report on any outcomes relevant to this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Partcipant and clinician not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete data, no losses.
Selective reporting (reporting bias)	Low risk	Single outcome collected relating to uterine contractions.
Other bias	Unclear risk	No imbalance at randomisation.

Modlock 2010

Methods	Acupuncture versus sham non invasive acupuncture.
Participants	The study was undertaken in Aarhus University Hospital, and Herning Hospital, Denmark, 1/2/2007-31/5/2008 125 healthy pregnant women at gestational week 41+6 were recruited to the study Exclusion criteria: woman did not speak or understand the Danish language; multiple pregnancy; PROM or contractions at 4- to 5-minute intervals and increasing in intensity; previous caesarean section; diseases of the mother or unborn child (diabetes, pre-eclampsia, diseases of the heart, liver or kidneys, HIV/AIDS, malformation of the pelvis, psychological disorders, intrauterine growth restriction, hydrocephalus, suspected macrosomia, fetal malposition, antepartum stillbirth, treatment with anticoagulants, skin infections, allergy to metal, or major complications at previous delivery such as low Apgar score

Interventions	Acupuncture was administered to points BL67, LI4, SP6, GV20. The control used the park sham needle (non invasive) at real acupuncture points BL67, LI4, SP6, GV20 The Park supporting device was used to hold the needle in place for both groups The intervention was delivered by trained midwives. The intervention was administered over 30 minutes, needles were stimulated every 10 minutes. Treatment commenced at 8.00am, and if the primary endpoint had not occurred by this time the treatment was repeated at 2.30pm
Outcomes	The primary outcome was achieved if the participant had undergone delivery or was in active labour, defined as rupture of fetal membranes and/or contractions at 4- to 5-minute (or more frequent) intervals and increasing in intensity within 24 hours Secondary outcomes were: the cervical dilatation was sufficient for amniotomy, cervical length and dilatation, length of labour, time from randomisation to start of active labour, postpartum bleeding, use of epidural, augmentation of contractions and instrumental delivery, as well as neonatal outcomes such as Apgar score and umbilical pH value when available
Notes	Power analysis undertaken.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Central computer-generated.
Allocation concealment (selection bias)	Low risk	Phone service.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Acupuncturist not blind. Blinding failed in 6 cases, 2 informed by partners (evenly distributed by group) . 4 randomisations and administration of treatment was undertaken by the same midwife. Most women did not know which group they were in
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Principal investigator and nurses gathering data were blind to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 lost to follow-up in the acupuncture group, and 2 lost to follow-up in the control group. 12 protocol violations in the acupuncture group, and 7 in the control group

Selective reporting (reporting bias)	Low risk	All outcomes reported as per entry on trial registry.
Other bias	Low risk	No imbalance at randomisation.

Rabl 2001

Methods	Women were randomised to acupuncture or no acupuncture.
Participants	56 women were randomised to the trial in Austria. Inclusion criteria were EDC confirmed by ultrasound, uncomplicated pregnancy, singleton pregnancy with cephalic presentation. Exclusion criteria were cervical dilatation greater than 3 cm, premature rupture of membranes, previous caesarean section, maternal complications, e.g. pre-eclampsia, fetal growth retardation. Women were randomised at term
Interventions	All women were examined at term and at 2-day intervals thereafter. Fetal heart rate was monitored, the cervical length was measured by ultrasound, cervical mucus was obtained for fetal fibronectin test and the cervical status was assessed for the Bishops score. Women received acupuncture at term and at 2-day intervals thereafter Acupuncture points - LI4, and SP6 were bilaterally inserted. *De qi* needling sensation was achieved. Needles were left in for 20 minutes. If the woman was undelivered 10 days after her EDC labour was induced The control group received routine care.
Outcomes	The change in cervical length over time, time from the first fibronectin test to delivery, time period from EDC to time of delivery, number of postdate indications, length of first and second stage of labour, need for oxytocin augmentation and mode of delivery
Notes	No sample-size calculation. Eleven (20%) women were excluded and follow-up data were not available on these women. Intention-to-treat analysis was reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The trial used a central randomisation service, with computer-generated sequence of random numbers
Allocation concealment (selection bias)	Low risk	Computer generation.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study participants were not blind to their group allocation. The care providers were blind to the woman's study group
Blinding of outcome assessment (detection bias) All outcomes	High risk	The outcome assessors and statistician were not blind to group allocation

Rabl 2001 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	There were 11 (20%) post-randomisation exclusions and losses to follow-up
Selective reporting (reporting bias)	Unclear risk	No study protocol available.
Other bias	Unclear risk	Limited reporting, and unable to assess.

Romer 2000

Methods	Randomised controlled trial of acupuncture,and control using non specific acupuncture to examine the effect on cervical maturation and duration of labour. A non-randomised usual care group was recruited to the study
Participants	553 women were randomised to the trial at a Uni-centre hospital in Mannheim, Germany. Women were primiparous, with exclusion criteria stated as multiple pregnancy, placenta previa, planned caesarean section, any bleeding after 28 weeks, and any coagulation disorder
Interventions	Acupuncture was administered weekly from 36 weeks until delivery. For the treatment group, fixed acu-points were administered including: ST36, SP6, GB34, BL67.Control acupuncture used non specific acupuncture including GC20, PC6, HT7. Points were needled using tonifying techniques, with a treatment duration of 20 minutes
Outcomes	Bishop score, length of cervix, duration of labour.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation using random table numbers.
Allocation concealment (selection bias)	Unclear risk	No other details available.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants allocated to acupuncture or the non specific acupuncture group were blind to their group allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessor blind to group allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no drop outs.

Romer 2000 (*Continued*)

Selective reporting (reporting bias)	Unclear risk	No details available.
Other bias	Unclear risk	No details available.

Selmer-Olsen 2007

Methods	This was a randomised controlled trial to assess the effect of acupuncture on the onset of labour and the need for induction after prelabour rupture of membranes. Women were randomised to receive acupuncture or standard care
Participants	The study took place in a hospital in Norway between 2004 and 2006. 106 women were included who were nulliparous with an uneventful singleton cephalic pregnancy between 37 and 42 weeks, with confirmed rupture of membranes without contractions of the uterus
Interventions	All women in the acupuncture group were needled at CV4. There were than diagnosed into 3 TCM categories based on their constitution. For Spleen qi deficiency, points were UB20, SP6 and ST36. For Liver qi stagnation, points were UB18, LR3, and LI4. For Kidney qi deficiency, points were UB23 and KI3. The following additional points could be used when appropriate, GVl 4, GV20, HT7, UB15, LU7, UB32, PC6, TH6. De qi was attained on all points. All Bladder channel points were needled bilaterally, the rest unilaterally. Single use needles (length: 2.5 and 4 cm) were retained for 30 minutes. Women were offered an additional treatment the following day if they were not in labour The control group received standard care. Standard care for nulliparas was expectant management at home for approximately 48 hours if cardiotocogram, temperature and amniotic fluid are normal, checked on a daily basis. To avoid infection, no digital examination was performed before onset of labour or induction
Outcomes	Time from PROM to active phase of labour. The active phase of labour was defined as a cervix dilatation of 3 cm and at least 2 uterine contractions in 10 minutes. The incidence of induction and additional outcomes of birth (Apgar score, epidural, oxytocin, caesarian sections, instrumental delivery) were reported. Self-reported physical well-being was registered using a 100-mm Visual Analogue Scale at randomisation and when they reached the active phase
Notes	It is unclear who conducted the differential diagnosis to determine treatment and what instrument was used to guide the diagnosis and maximise inter-rater reliability

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Internet based block randomisation.
Allocation concealment (selection bias)	Low risk	Concealed centrally.

Selmer-Olsen 2007 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and clinicians were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	It was not stated if assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	5 participants were lost to follow-up, and 1 participant refused further participation. 4 participants were excluded after randomisation, 1 had meconium-stained waters, 1 did not return questionnaire, 2 had intact membranes. These participants were not included in the analysis
Selective reporting (reporting bias)	High risk	The outcomes of Apgar score, epidural, instrumental delivery, caesarean sections, inductions, dilatation, oxytocin were reported but no between group analysis was conducted
Other bias	Unclear risk	Baseline characteristics were not reported.

Smith 2008

Methods	Randomised controlled trial of acupuncture versus sham acupuncture sessions to estimate the effectiveness of acupuncture to induce labour
Participants	The study took place in a Women's and Children's Hospital in Australia between 1998 and 2005. 364 women aged greater than 16 years with a singleton pregnancy and cephalic presentation scheduled for a post term induction were recruited to the study. Women were excluded if they were in active labour with regular uterine contractions, or if there were contraindications to labour or vaginal birth, or if they presented with spontaneous prelabour rupture of membranes
Interventions	The acupuncture group received acupuncture at LI4, SP6, UB31, UB32, ST36 and LR3. Any underlying pathology from a TCM framework was examined and treated with addition points, e.g. KI7, UB20, UB21, LR3. Needles were retained for 30-40 minutes with strong stimulation and *de qi*. Seirin 1-2 inch needles were used with a 32 gauge (0.25 mm) diameter The sham group received the same treatment in terms of timing and duration, but with minimal insertion and stimulation. Sham points were selected on the sacral area, hand, foot, a point below the knee and lower leg, at points that were not acupuncture points. Treatments were administered over a 2-day period before the planned induction

Outcomes	The primary outcome was the need for induction, a reduction in the need for prostaglandins, oxytocin, and artificial rupture of membranes, change in Bishop score, time of intervention to time of delivery, and length of active labour Secondary: methods of pain relief, mode of birth, Apgar scores less than 7 at 5 minutes, admission of the mother and neonate from the labour ward to the postnatal ward together, meconium, non-reassuring fetal heart rate tracing, neonatal jaundice requiring phototherapy, neonatal seizures, acceptability of treatment by the mother, Bishop score, labour agentry scale of control in childbirth, likes and dislikes regarding participation in the trial
Notes	Intention-to-treat analysis was conducted. Sample size calculation reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A computer-generated randomisation schedule created by an independent statistician in variable block size and stratified by parity (nulliparous and multiparous) and incorporated into a telephone randomisation service
Allocation concealment (selection bias)	Low risk	A central telephone randomisation service was available 7 days a week at the recruiting hospital
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants were blinded to allocation by use of sham control. Caregivers were blind to the women's study group. The treatment allocation was known only to the acupuncturist administering the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Data collection was done by someone not involved in the administration of the intervention and the analyst was blind until the end of data analysis
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients received at least 1 session in both groups, 11 participants in the acupuncture group received only 1 treatment and 15 women in the sham acupuncture group. Reasons given were problems with childcare, feeling too tired, and lack of transportation to the trial centre. All participants were included in the analysis

Smith 2008 (*Continued*)

Selective reporting (reporting bias)	Low risk	All outcomes reported as per trial registration.
Other bias	Low risk	Women in the sham group were older and there were also differences in the categorisation of the Bishop score. The authors adjusted the primary outcomes for maternal age and the raw Bishop score

Tremeau 1992

Methods	Randomised controlled trial examining the effect of acupuncture on cervical maturation. Parallel design of acupuncture versus usual care and sham acupuncture
Participants	128 women met the entry criteria and were randomised. Participants were recruited from a maternity hospital in France. Women were 37-38 weeks pregnant with a Bishops score of less than 4. Exclusion criteria included; at risk of premature delivery, planned caesarean section, placenta previa, receiving concurrent treatments such as yoga, homeopathy, acupuncture
Interventions	Acupuncture points were selected based on those used to increase cervical maturation including: CV2, CV3, CV4, Liv3, BL60, GB34, ST36, LI4, SP6, BL67. The acupuncture control was pricked with needles at sites 1 cm from the bilateral acu-point, and 1 cm from the med line points, and a third group received usual care Three treatment sessions were administered, with electro-stimulation for 20 minutes
Outcomes	The Bishops score was assessed 48 hours after the last acupuncture session, duration of labour, time to 2 cm cervical dilatation
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers.
Allocation concealment (selection bias)	Unclear risk	Not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details were reported on whether the integrity of blinding between acupuncture and the sham group was maintained
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The outcome assessment was undertaken by a clinician blind to group

Tremeau 1992 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	16% of women did not complete the protocol due to spontaneous labour before the second examination, 2 women declined the second examination and 1 woman did not return for acupuncture
Selective reporting (reporting bias)	Unclear risk	Limited reporting unable to assess.
Other bias	Unclear risk	No imbalance in baseline characteristics.

EDC: estimated date of confinement
PROM: premature rupture of membranes
TCM: traditional Chinese medicine
TENS: transcutaneous nerve stimulation

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

Study	Reason for exclusion
Aghamohammadi 2011	This was a randomised double-blind study comparing TENS versus sham TENS on LI4 and SP6 in 64 nulliparous women who were in first stage of active labour. Labour time was found to be significantly shorter in the TENS group as was the need for oxytocin to augment labour. The trial was excluded as it did not meet the inclusion criteria of an acupuncture intervention - no needles were used and it did not have a primary outcome that met our inclusion criteria
Bo 2006	This study evaluated the role of acupuncture primarily during labour on pain relief. No data on induction outcomes were reported
Dorr 1990	The evidence regarding the clinical effectiveness of this technique is limited. This controlled clinical trial undertaken in Czechoslovakia consisted of women between 39 to 43 weeks with a cervical score greater than 5 (with no regular uterine contractions). Sixteen women received acupuncture. In 1 group electrical acupuncture commenced after the discharge of amniotic fluid (up to 4 hours); in the other group, stimulation began 6 or more hours after the discharge of amniotic fluid. Spontaneous vaginal delivery was achieved in 13 women
Dunn 1989	This comparison between electrical acupuncture stimulation or placebo acupuncture assessed the onset of uterine contractions in 20 postdate pregnant women. There was evidence of strong contractions in the treatment group. TENS does not meet the eligibility criteria for the review
Kubista 1974	This study reported on 60 pregnant women who received acupuncture (ST36, KI8, GB34 and UB 62) compared to a control of 60 pregnant women from the same clinic with a primary outcome of length of labour. The study was not randomised
Li 1996	This study was a quasi-randomised trial and was excluded.

(*Continued*)

Lyngso 2010	This trial included women who were already in labour and was therefore excluded
So 1979	A controlled clinical trial was undertaken at a hospital in Hong Kong. 60 women were allocated to 3 groups: electro-acupuncture (stimulation of SP6 and LI4); acupuncture at these same points on 1 side of the body only; and thirdly, sham acupuncture. No data were available on the results of the trial

TENS: transcutaneous nerve stimulation

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

Liu 2012

Methods	Single blind randomised controlled trial of electro-acupuncture on labour
Participants	38 women.
Interventions	Women randomised to electro-acupuncture, 37 to sham acupuncture and 36 to a control
Outcomes	Blood pressure, heart rate, postpartum bleeding, Apgar score, length of labour
Notes	Chinese manuscript, awaiting translation.

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

Fabio 2007

Trial name or title	Efficacy of acupuncture on induction of labour.
Methods	Randomised controlled trial.
Participants	Women at 40 + 2 - 40 + 4 gestational age.
Interventions	Acupuncture versus placebo. Acupuncture administered daily from 40 + 4 for 7 days
Outcomes	To evaluate the efficacy of acupuncture administered daily from 40 weeks + 4 days of gestation for induction of labour respect with placebo, to evaluate safety of acupuncture
Starting date	November 2007. Completed January 2009.
Contact information	Facchinetti Fabio, University of Modena and Reggio Emilia, Italy
Notes	The purpose of this study is to evaluate the efficacy and safety of acupuncture for the induction of labour in pregnant women at the 40 weeks + 4 days of gestation

DATA AND ANALYSES

Comparison 1. Acupuncture versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Acupuncture versus sham control	6	654	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.69, 1.30]
1.2 Acupuncture versus usual care	6	361	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.40, 1.20]
2 Neontal seizure	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Acupuncture versus sham	1	364	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.06, 16.04]
3 Cervical maturity within 24 hours (Bishop score)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Acupuncture versus sham acupuncture	1	125	Mean Difference (IV, Fixed, 95% CI)	0.40 [0.11, 0.69]
3.2 Acupuncture versus usual care	1	67	Mean Difference (IV, Fixed, 95% CI)	1.30 [0.11, 2.49]
4 Oxytocin augmentation	7		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Acupuncture versus sham	4	833	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.78, 1.21]
4.2 Acupuncture versus usual care	3	257	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.86, 1.34]
5 Need for epidural	8		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Acupuncture versus sham acupuncture	5	571	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.88, 1.19]
5.2 Acupuncture versus usual care	5	351	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.77, 1.11]
6 Instrumental vaginal delivery	8		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 Acupuncture versus sham	5	610	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.85, 1.65]
6.2 Acupuncture versus usual care	5	351	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.50, 1.64]
7 Meconium-stained liquor	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Acupuncture versus sham	1	364	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.56, 1.16]
8 Apgar score less than 7	6		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
8.1 Acupuncture versus sham	4	559	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.20, 2.21]
8.2 Acupuncture versus usual care	3	242	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.01, 8.48]
9 Neonatal care admission	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 Acupuncture versus sham	3	141	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.02, 37.11]
9.2 Acupuncture versus usual care	1	45	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.03, 14.97]
10 Perinatal death	1	364	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
10.1 Acupuncture versus sham	1	364	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Perineal tear	1	91	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.95, 1.56]
11.1 Acupuncture versus usual care	1	91	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.95, 1.56]
12 Maternal infection	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

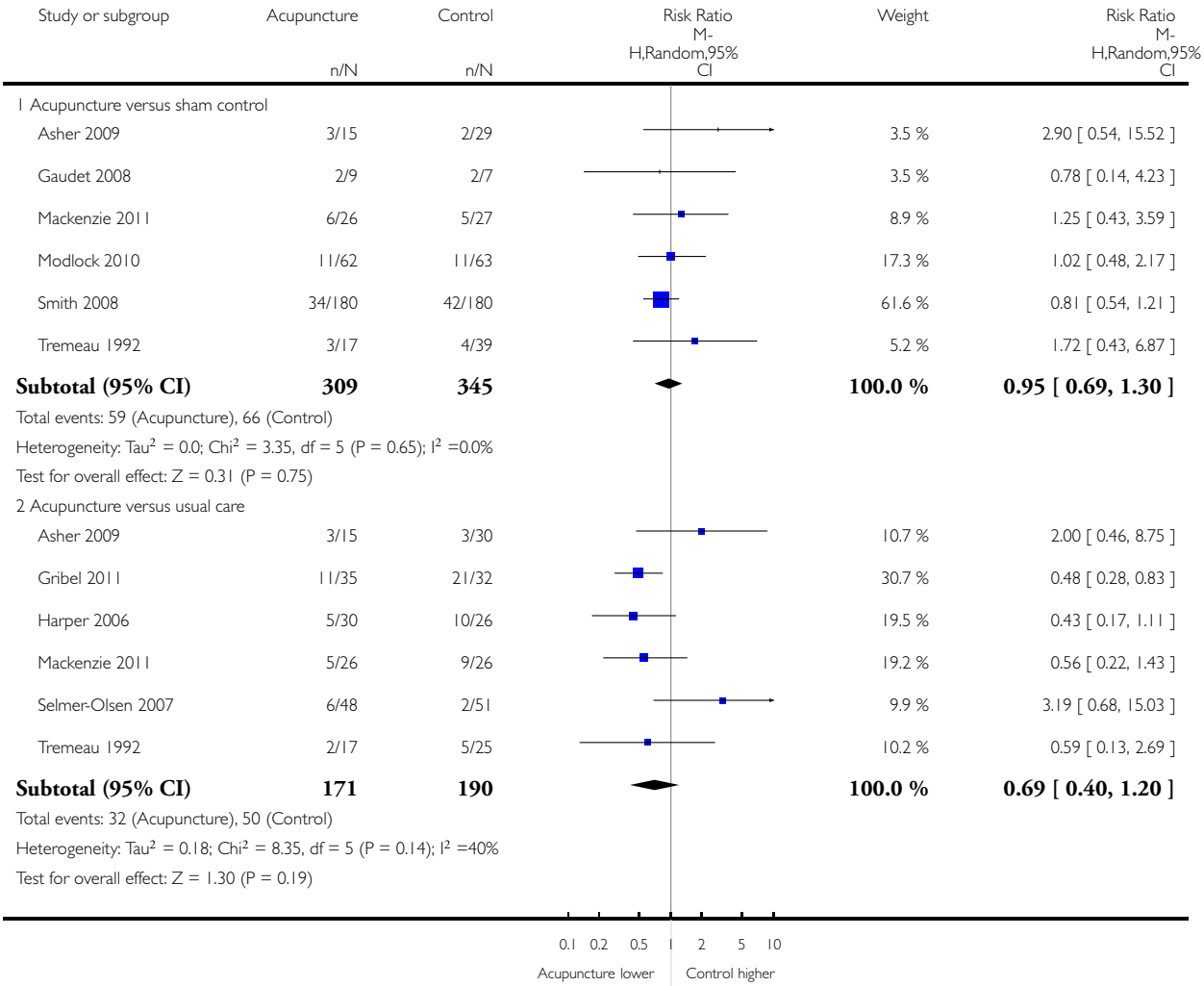
12.1 Acupuncture versus usual care	2	136	Risk Ratio (M-H, Fixed, 95% CI)	1.64 [0.43, 6.32]
12.2 Acupuncture versus sham	1	44	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.43, 3.88]
13 Fetal infection	1	91	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
13.1 Acupuncture versus usual care	1	91	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Postpartum bleeding > 500 mL	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
14.1 Acupuncture versus sham	3	542	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.67, 1.54]
14.2 Acupuncture versus usual care	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.10, 2.50]
15 Maternal death	1	364	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
15.1 Acupuncture versus sham	1	364	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
16 Time from trial entry to birth of baby (days; hours)	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 Acupuncture versus sham acupuncture	2	61	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.99, 0.55]
16.2 Acupuncture versus usual care	2	100	Std. Mean Difference (IV, Random, 95% CI)	0.25 [-0.77, 1.27]
17 Maternal satisfaction	1	67	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.99, 1.67]
17.1 Acupuncture versus usual care	1	67	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [0.99, 1.67]
18 Need for induction methods	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
18.1 Acupuncture versus sham	4	977	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.91, 1.16]
18.2 Acupuncture versus usual care	4	259	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.69, 1.45]
19 Length of labour	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
19.1 Acupuncture versus sham	3	694	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.58, 0.23]
19.2 Acupuncture versus usual care	1	67	Std. Mean Difference (IV, Random, 95% CI)	0.67 [0.18, 1.17]

Analysis 1.1. Comparison 1 Acupuncture versus control, Outcome 1 Caesarean section.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 1 Caesarean section

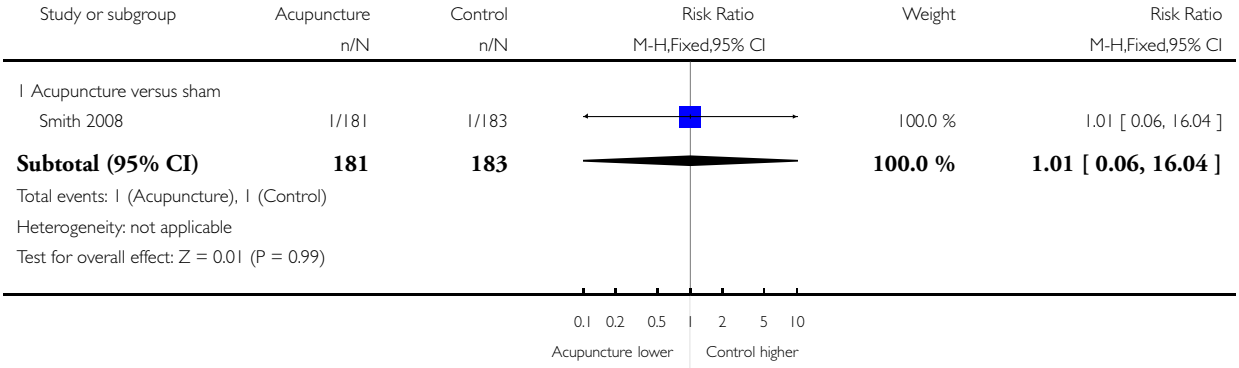


Analysis 1.2. Comparison 1 Acupuncture versus control, Outcome 2 Neontal seizure.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 2 Neontal seizure

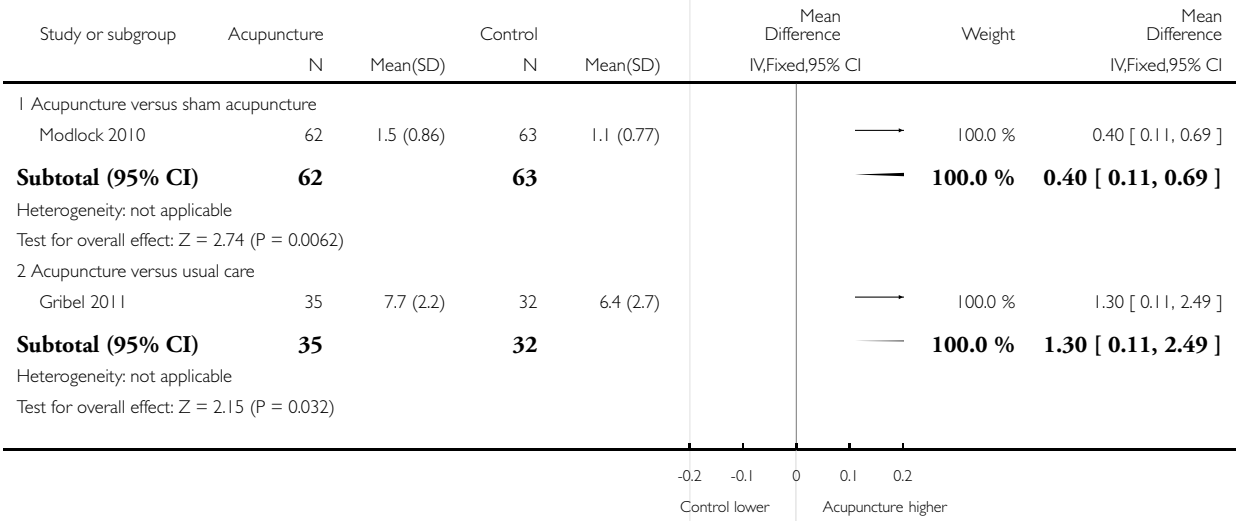


Analysis 1.3. Comparison 1 Acupuncture versus control, Outcome 3 Cervical maturity within 24 hours (Bishop score).

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 3 Cervical maturity within 24 hours (Bishop score)



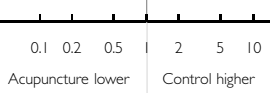
Analysis 1.4. Comparison 1 Acupuncture versus control, Outcome 4 Oxytocin augmentation.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 4 Oxytocin augmentation

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Acupuncture versus sham					
Gaudet 2008	6/9	5/7		6.3 %	0.93 [0.48, 1.80]
Modlock 2010	26/62	22/63		24.3 %	1.20 [0.77, 1.88]
Romer 2000	15/329	17/224		22.6 %	0.60 [0.31, 1.18]
Smith 2008	46/73	40/66		46.8 %	1.04 [0.80, 1.35]
Subtotal (95% CI)	**473**	**360**		**100.0 %**	**0.97 [0.78, 1.21]**
Total events: 93 (Acupuncture), 84 (Control)					
Heterogeneity: Chi^2 = 3.08, df = 3 (P = 0.38); I^2 =3%					
Test for overall effect: Z = 0.25 (P = 0.81)					
2 Acupuncture versus usual care					
Gaudernack 2006	25/43	31/48		44.6 %	0.90 [0.65, 1.25]
Gribel 2011	13/35	7/32		11.1 %	1.70 [0.78, 3.72]
Selmer-Olsen 2007	31/48	30/51		44.3 %	1.10 [0.80, 1.50]
Subtotal (95% CI)	**126**	**131**		**100.0 %**	**1.08 [0.86, 1.34]**
Total events: 69 (Acupuncture), 68 (Control)					
Heterogeneity: Chi^2 = 2.45, df = 2 (P = 0.29); I^2 =18%					
Test for overall effect: Z = 0.65 (P = 0.52)					

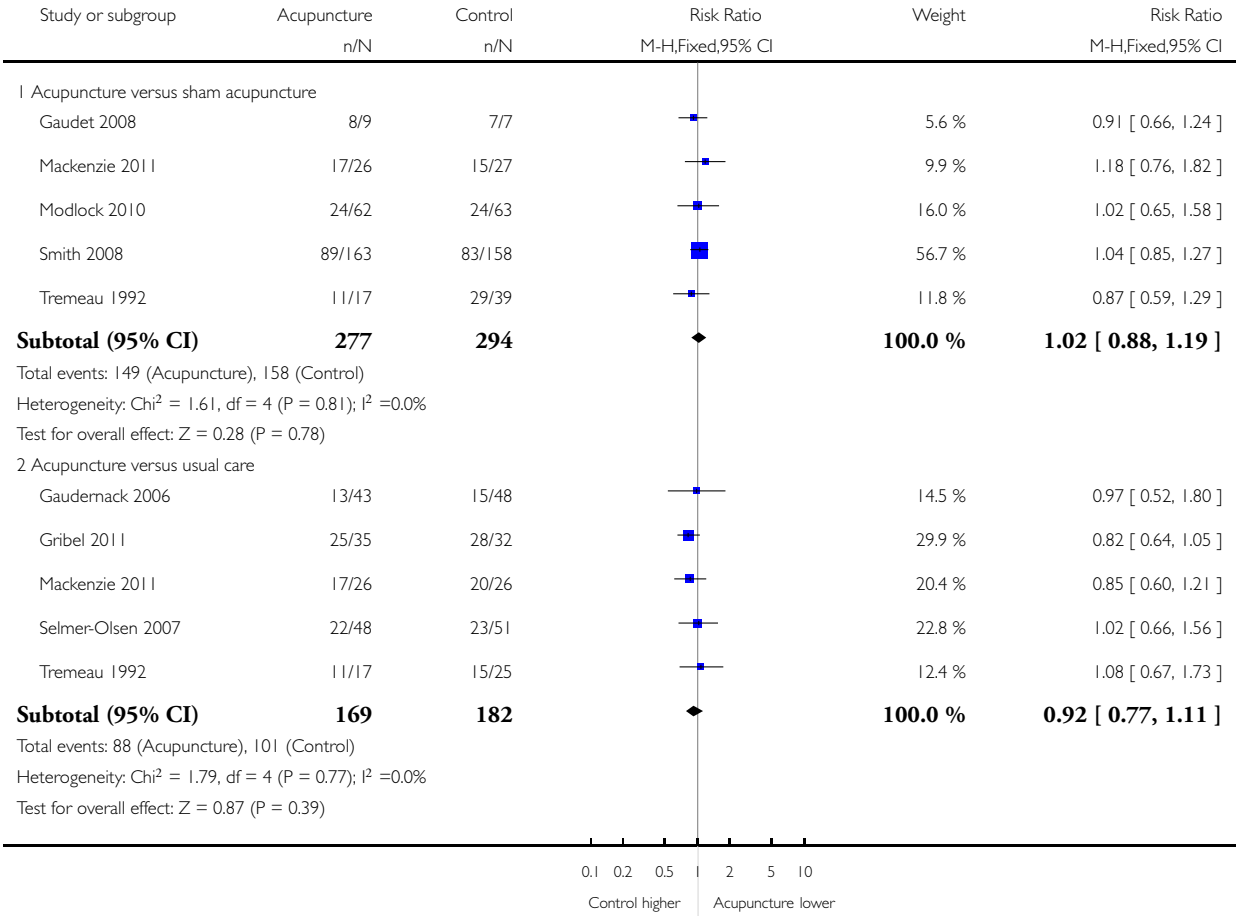


Analysis 1.5. Comparison 1 Acupuncture versus control, Outcome 5 Need for epidural.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 5 Need for epidural

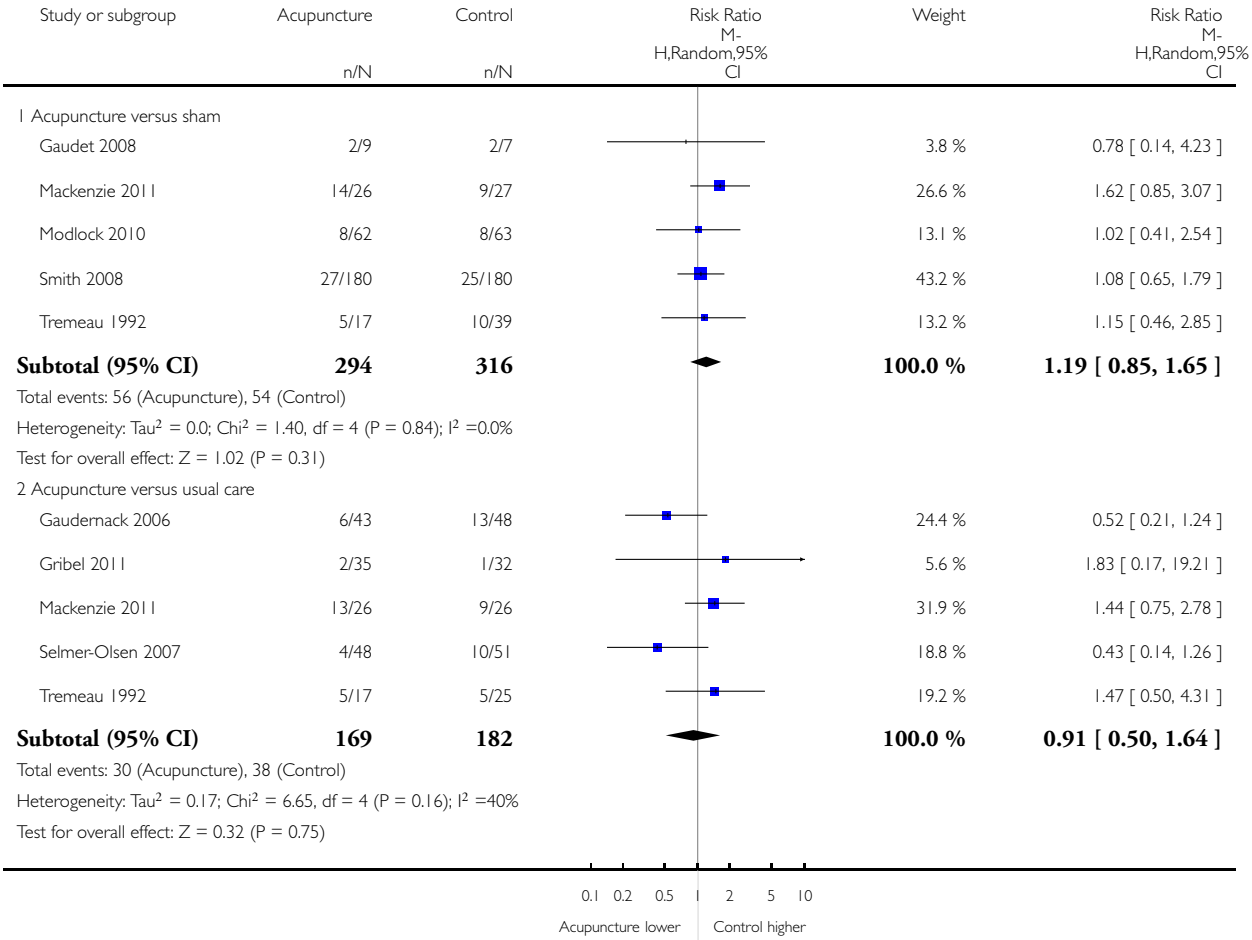


Analysis 1.6. Comparison 1 Acupuncture versus control, Outcome 6 Instrumental vaginal delivery.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 6 Instrumental vaginal delivery

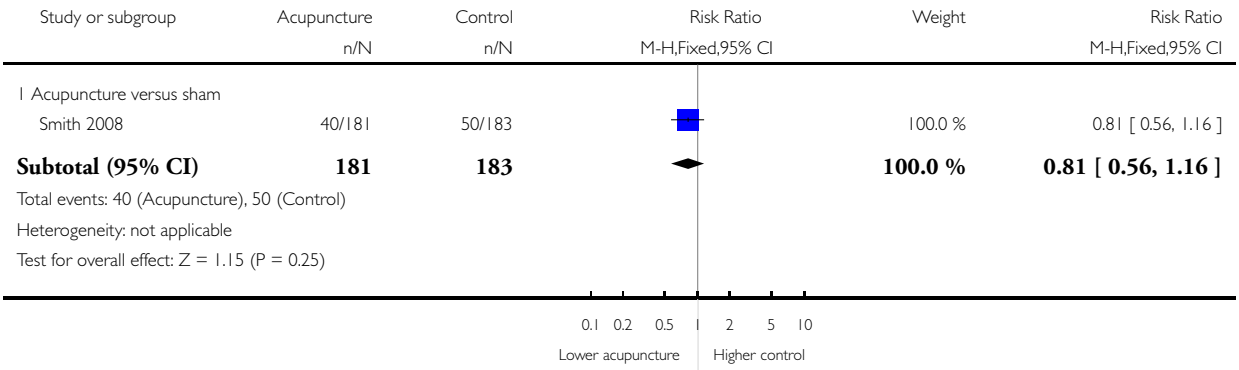


Analysis 1.7. Comparison 1 Acupuncture versus control, Outcome 7 Meconium-stained liquor.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 7 Meconium-stained liquor

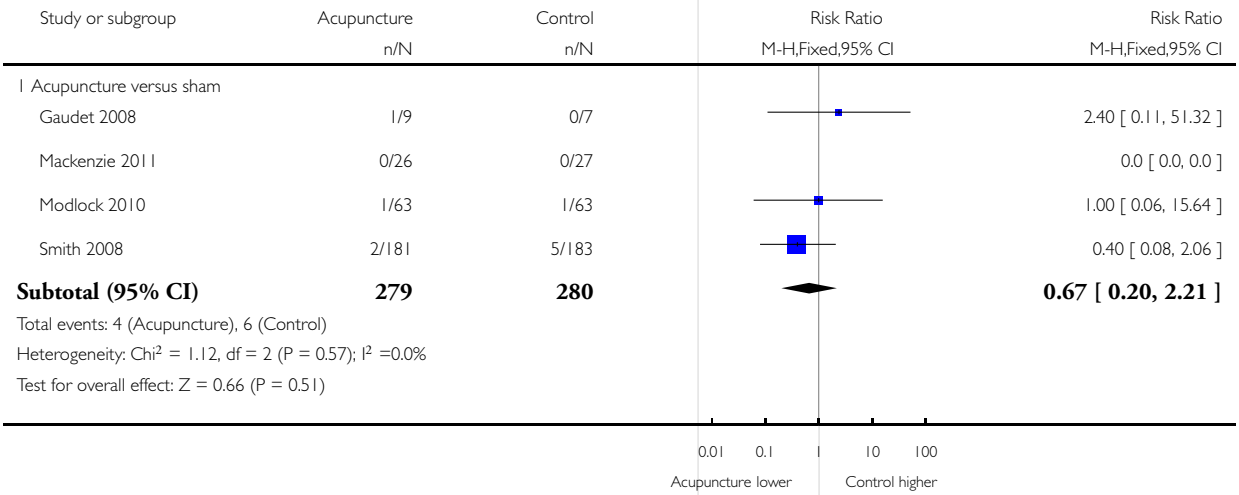


Analysis 1.8. Comparison 1 Acupuncture versus control, Outcome 8 Apgar score less than 7.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

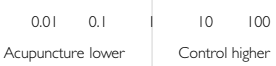
Outcome: 8 Apgar score less than 7



(*Continued . . .*)

(. . . *Continued*)

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Acupuncture versus usual care				
Gaudernack 2006	0/43	0/48		0.0 [0.0, 0.0]
Mackenzie 2011	0/26	0/26		0.0 [0.0, 0.0]
Selmer-Olsen 2007	0/48	1/51		0.35 [0.01, 8.48]
Subtotal (95% CI)	**117**	**125**		**0.35 [0.01, 8.48]**
Total events: 0 (Acupuncture), 1 (Control)				
Heterogeneity: Chi^2 = 0.0, df = 0 (P = 1.00); I^2 =0.0%				
Test for overall effect: Z = 0.64 (P = 0.52)				



Analysis 1.9. Comparison 1 Acupuncture versus control, Outcome 9 Neonatal care admission.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 9 Neonatal care admission

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Acupuncture versus sham				
Asher 2009	0/15	0/29		0.0 [0.0, 0.0]
Gaudet 2008	3/9	0/7		5.60 [0.34, 93.35]
Smith 2008	0/45	3/36		0.11 [0.01, 2.15]
Subtotal (95% CI)	**69**	**72**		**0.82 [0.02, 37.11]**
Total events: 3 (Acupuncture), 3 (Control)				
Heterogeneity: Tau^2 = 5.42; Chi^2 = 3.52, df = 1 (P = 0.06); I^2 =72%				
Test for overall effect: Z = 0.10 (P = 0.92)				
2 Acupuncture versus usual care				
Asher 2009	0/15	1/30		0.65 [0.03, 14.97]
Subtotal (95% CI)	**15**	**30**		**0.65 [0.03, 14.97]**

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Total events: 0 (Acupuncture), 1 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.27 (P = 0.79)				

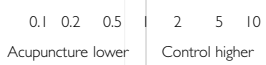
Analysis 1.10. Comparison 1 Acupuncture versus control, Outcome 10 Perinatal death.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 10 Perinatal death

Study or subgroup	acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Acupuncture versus sham				
Smith 2008	0/181	0/183		0.0 [0.0, 0.0]
Total (95% CI)	**181**	**183**		**0.0 [0.0, 0.0]**
Total events: 0 (acupuncture), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%				

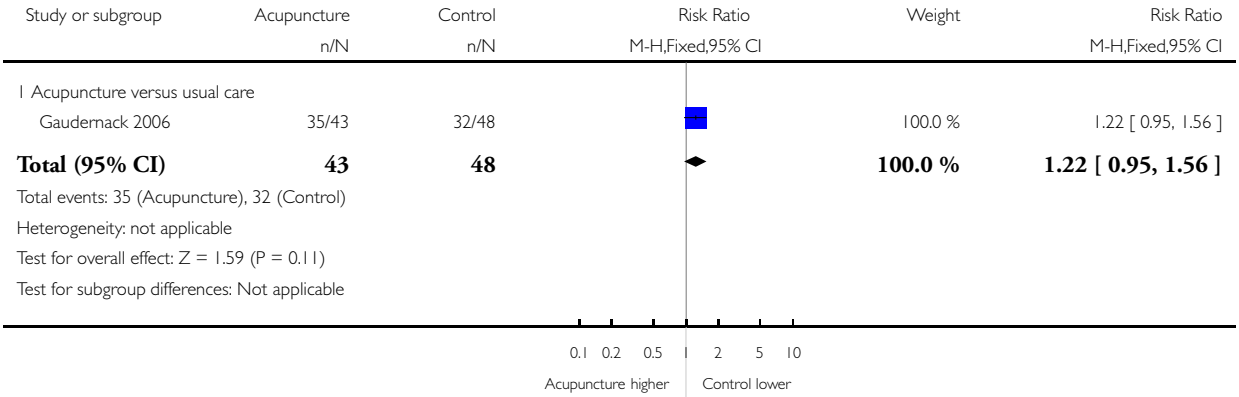


Analysis 1.11. Comparison 1 Acupuncture versus control, Outcome 11 Perineal tear.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 11 Perineal tear

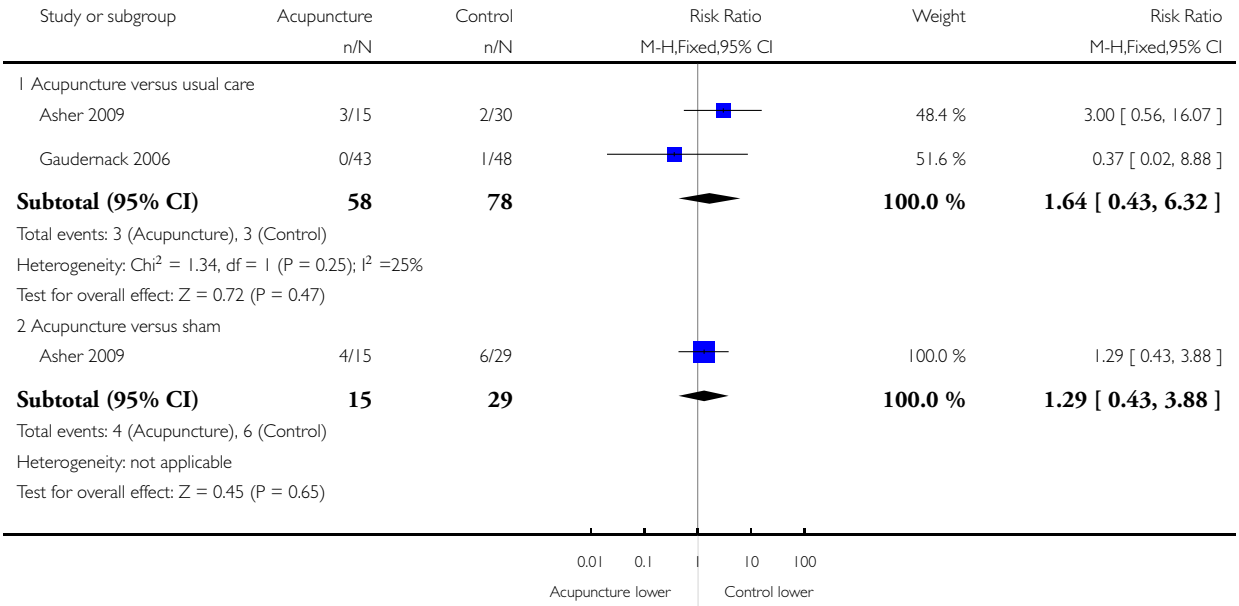


Analysis 1.12. Comparison 1 Acupuncture versus control, Outcome 12 Maternal infection.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 12 Maternal infection



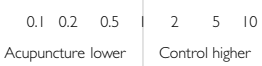
Analysis 1.13. Comparison 1 Acupuncture versus control, Outcome 13 Fetal infection.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 13 Fetal infection

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Acupuncture versus usual care				
Gaudernack 2006	0/43	0/48		0.0 [0.0, 0.0]
Total (95% CI)	**43**	**48**		**0.0 [0.0, 0.0]**
Total events: 0 (Acupuncture), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%				



Analysis 1.14. Comparison 1 Acupuncture versus control, Outcome 14 Postpartum bleeding > 500 mL.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 14 Postpartum bleeding > 500 mL

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Acupuncture versus sham					
Mackenzie 2011	3/26	3/27		8.0 %	1.04 [0.23, 4.69]
Modlock 2010	15/62	13/63		35.1 %	1.17 [0.61, 2.26]
Smith 2008	19/181	21/183		56.9 %	0.91 [0.51, 1.64]
Subtotal (95% CI)	**269**	**273**		**100.0 %**	**1.02 [0.67, 1.54]**
Total events: 37 (Acupuncture), 37 (Control)					
Heterogeneity: Chi^2 = 0.31, df = 2 (P = 0.86); I^2 =0.0%					
Test for overall effect: Z = 0.07 (P = 0.94)					
2 Acupuncture versus usual care					
Mackenzie 2011	2/26	4/26		100.0 %	0.50 [0.10, 2.50]
Subtotal (95% CI)	**26**	**26**		**100.0 %**	**0.50 [0.10, 2.50]**
Total events: 2 (Acupuncture), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.84 (P = 0.40)					

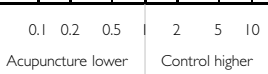
Analysis 1.15. Comparison 1 Acupuncture versus control, Outcome 15 Maternal death.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 15 Maternal death

Study or subgroup	Acupuncture n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Acupuncture versus sham				
Smith 2008	0/181	0/183		0.0 [0.0, 0.0]
Total (95% CI)	**181**	**183**		**0.0 [0.0, 0.0]**
Total events: 0 (Acupuncture), 0 (Control)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.0 (P < 0.00001)				
Test for subgroup differences: Chi^2 = 0.0, df = -1 (P = 0.0), I^2 =0.0%				



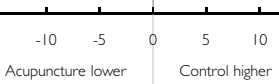
Analysis 1.16. Comparison 1 Acupuncture versus control, Outcome 16 Time from trial entry to birth of baby (days; hours).

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 16 Time from trial entry to birth of baby (days; hours)

Study or subgroup	Acupuncture N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Acupuncture versus sham acupuncture							
Asher 2009	15	12.2 (3.7)	30	11.9 (3.8)		63.4 %	0.08 [-0.54, 0.70]
Gaudet 2008	9	146 (91.6)	7	208 (61)		36.6 %	-0.73 [-1.76, 0.30]
Subtotal (95% CI)	**24**		**37**			**100.0 %**	**-0.22 [-0.99, 0.55]**
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 1.75$, df = 1 (P = 0.19); $I^2 = 43\%$							
Test for overall effect: Z = 0.56 (P = 0.58)							
2 Acupuncture versus usual care							
Asher 2009	15	12.2 (3.6)	29	9.3 (3.6)		48.3 %	0.79 [0.14, 1.44]
Harper 2006	30	124 (82.7)	26	145 (82.7)		51.7 %	-0.25 [-0.78, 0.28]
Subtotal (95% CI)	**45**		**55**			**100.0 %**	**0.25 [-0.77, 1.27]**
Heterogeneity: $Tau^2 = 0.45$; $Chi^2 = 5.98$, df = 1 (P = 0.01); $I^2 = 83\%$							
Test for overall effect: Z = 0.49 (P = 0.63)							

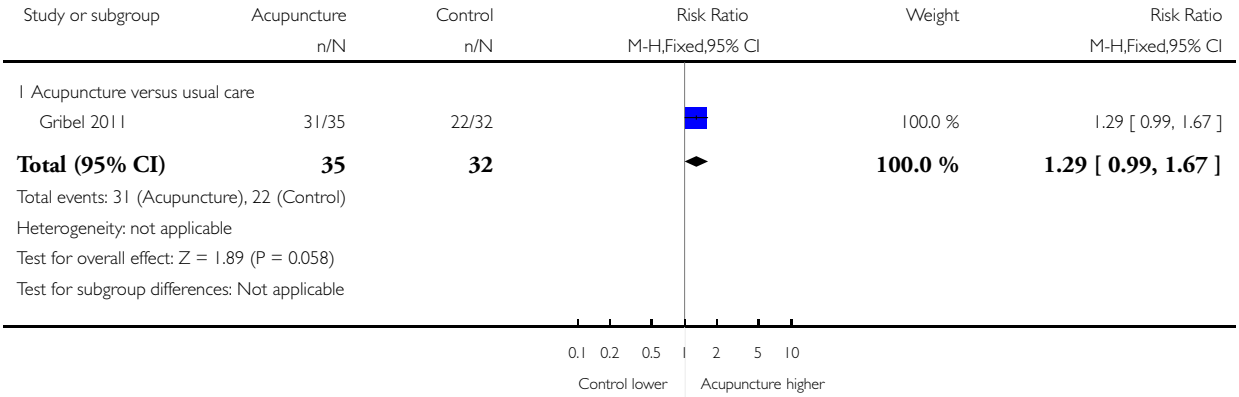


Analysis 1.17. Comparison 1 Acupuncture versus control, Outcome 17 Maternal satisfaction.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 17 Maternal satisfaction

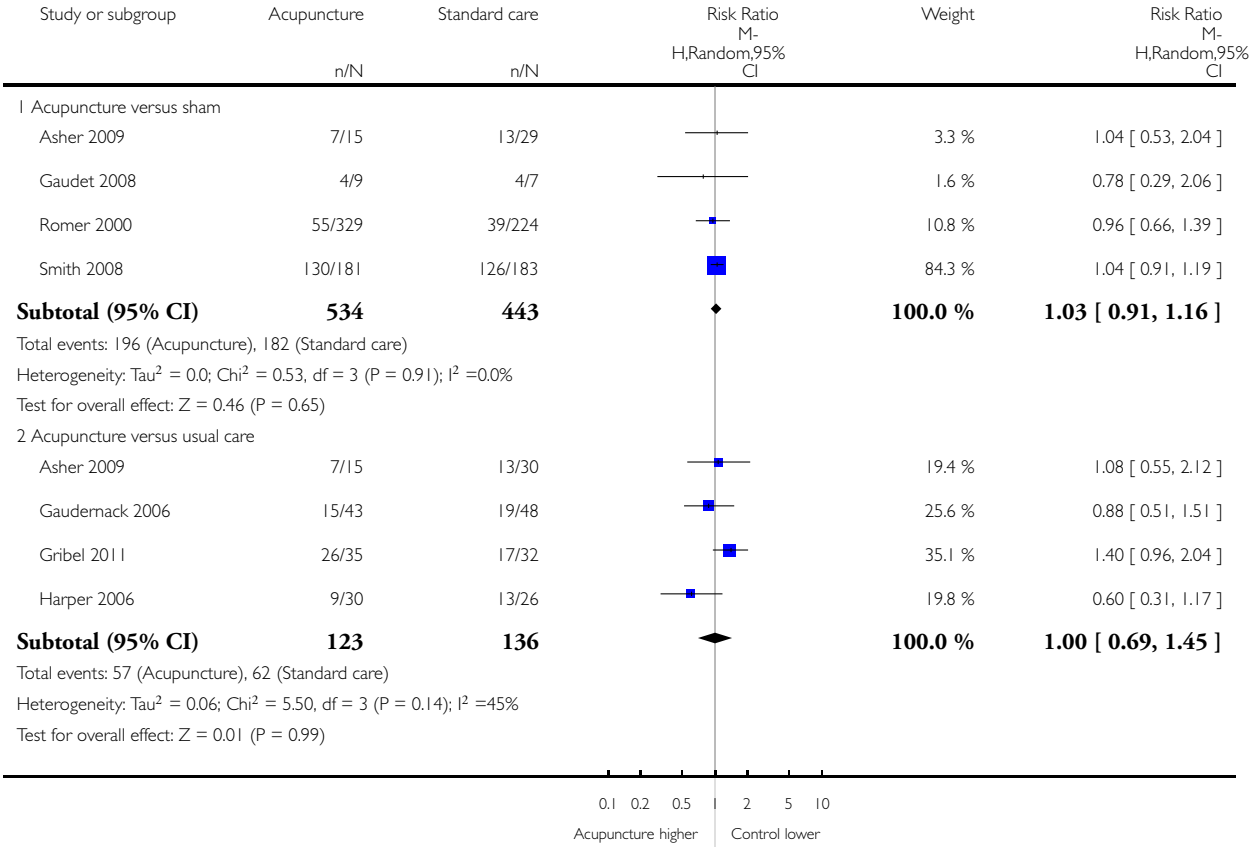


Analysis 1.18. Comparison 1 Acupuncture versus control, Outcome 18 Need for induction methods.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 18 Need for induction methods

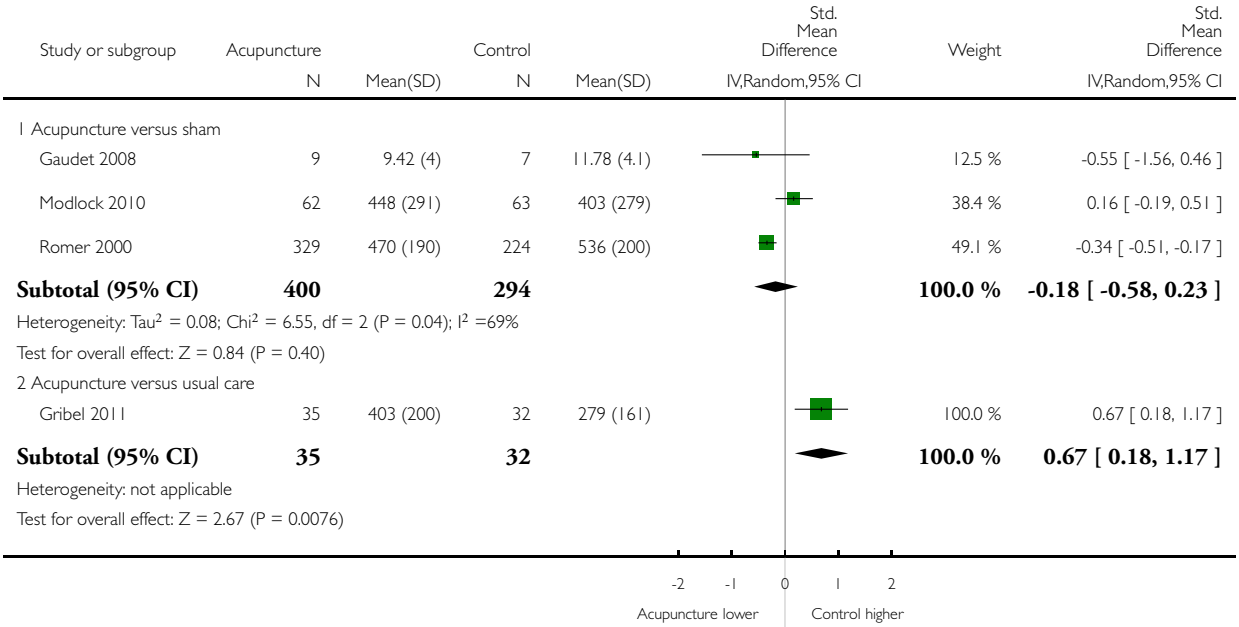


Analysis 1.19. Comparison 1 Acupuncture versus control, Outcome 19 Length of labour.

Review: Acupuncture for induction of labour

Comparison: 1 Acupuncture versus control

Outcome: 19 Length of labour



APPENDICES

Appendix 1. Search Strategies

PubMed

1. exp Acupuncture Therapy (10724)
2. exp Medicine, East Asian Traditional (3238)
3. exp Acupuncture/ (15070)
4. (acupuncture or acupressure or acupoint* or electroacupuncture or electro-acupuncture or TENS
5. 1 OR 2 OR 3 OR 4 (32010)
6. exp induction of labour (1496)
7. exp labour (21925)
8. labo?r
9. 6 OR 7 OR 8
10. 5 AND 9 (101)

11. randomized controlled trial.pt.
12. controlled clinical trial.pt.
13. randomized.ab.
14. placebo.ab.
15. drug therapy.fs.
16. randomly.ab.
17. trial.ab.
18. groups.ab.
19. 11 or 12 or 13 or14 or 15 or 16 or 17 or 18
20. 10 AND 20 (31)

CINAHL Plus search strategy

1. (MH "Acupuncture+") OR (MH "Acupuncture Points") OR (MH "Acupuncture, Ear") OR (MH "Acupuncturists") OR (MH "Acupuncture Analgesia")
2. electroacupuncture OR electro-acupuncture
3. acupressure OR acupoint* OR TENS
4. #1 OR #2 OR #3 (10,266)
5. (MH "Labor, Induced+") OR (MH "Labor Stage, First") OR (MH "Labor Stage, Second") OR (MH "Labor Stage, Third") OR (MH "Labor Support")
6. Caesarean OR Pregnancy OR uterine cervix ripening OR Prostaglandin OR intravaginal drug administration OR Oxytocin OR misoprostol OR labo*r induction OR induction of labo*r
7. #5 OR #6 (113,359)
8. (MM "Randomized Controlled Trials") OR (MM "Clinical Trials+")
9. randomized controlled trial.pt. OR controlled clinical trial.pt. OR randomized.ab. OR placebo.ab. OR drug therapy.fs. OR randomly.ab. OR trial.ab. OR groups.ab.
10. #8 OR #9 (146,052)
11. #4 AND #7 AND #10 (118)

Embase search strategy

1. exp acupuncture analgesia/
2. acupuncture.mp.
3. exp acupuncture/
4. exp acupuncture needle/
5. electroacupuncture OR electro-acupuncture
6. acupressure OR acupoint* OR TENS
7. 1 OR 2 OR 3 OR 4 OR 5 OR 6 (39862)
8. cesarean section/ or pregnancy/ or prostaglandin/ or intravaginal drug administration/ or oxytocin/ or uterine cervix ripening/ or prostaglandin E2/ or misoprostol/ or labor induction/ or induction of labour.mp. or prostaglandin derivative/ (732108)
9. 7 AND 8 (1165)
10. Limited to Human and yr=2012 (59)
11. Randomization.mp/ or controlled clinical trial.pt. / or double blind procedure/ or randomized controlled trials.mp or (topic)/ or random allocation.mp. / or double blind method.sh. / or meta analysis/ or single-blind method.sh. / or single blind procedure/ or clinical trial.pt.
12. 11 AND 9 (16)

Dissertations and Theses A&I (ProQuest)

Acupuncture AND [labour OR labor] in Title, Subject, Abstract

WHO International Clinical Trials Registry Platform (ICTRP)

Acupuncture AND (labour OR labor)

Appendix 2. Methods used to assess trials included in previous versions of this review

Prior to 2001, data extraction was conducted centrally using the methods outlined below, for all reviews on interventions for labour induction.

From 2001, the data extraction was no longer conducted centrally. This meant that the data extraction was carried out by the reviewers of the primary reviews if new trials were found when the search strategy was rerun, and the reviews updated.

The following methods were used to assess Gaudernack 2006; Harper 2006; Rabl 2001.

A strategy was developed to deal with the large volume and complexity of trial data relating to labour induction. Many methods have been studied, examining the effects of these methods when induction of labour was undertaken in a variety of clinical groups e.g. restricted to primiparous women or those with ruptured membranes. Most trials are intervention-driven, comparing two or more methods in various categories of women. Clinicians and parents need the data arranged according to the clinical characteristics of the women undergoing induction of labour, to be able to choose which method is best for a particular clinical scenario. To extract these data from several hundred trial reports in a single step would be very difficult. We therefore developed a two-stage method of data extraction. The initial data extraction was done in a series of primary reviews arranged by methods of induction of labour, following a standardised methodology. The intention was then to extract them from the primary reviews into a series of secondary reviews, arranged by the clinical characteristics of the women undergoing induction of labour.

To avoid duplication of data in the primary reviews, the labour induction methods were listed in a specific order, from one to 25. Each primary review included comparisons between one of the methods (from two to 25) with only those methods above it on the list. Thus, the review of intravenous oxytocin (4) included only comparisons with intracervical prostaglandins (3), vaginal prostaglandins (2) or placebo (1). Methods identified in the future will be added to the end of the list. The current list is as follows:

(1) placebo/no treatment;
(2) vaginal prostaglandins (Kelly 2003);
(3) intracervical prostaglandins (Boulvain 2008);
(4) intravenous oxytocin (Kelly 2001a);
(5) amniotomy (Bricker 2000);
(6) intravenous oxytocin with amniotomy (Howarth 2001);
(7) vaginal misoprostol (Hofmeyr 2003);
(8) oral misoprostol (Alfirevic 2006);
(9) mechanical methods including extra-amniotic Foley catheter (Boulvain 2001);
(10) membrane sweeping (Boulvain 2005);
(11) extra-amniotic prostaglandins (Hutton 2001);
(12) intravenous prostaglandins (Luckas 2000);
(13) oral prostaglandins (French 2001);
(14) mifepristone (Neilson 2000);
(15) oestrogens with or without amniotomy (Thomas 2001);
(16) corticosteroids (Kavanagh 2006b);
(17) relaxin (Kelly 2001b);
(18) hyaluronidase (Kavanagh 2006a);
(19) castor oil, bath, and/or enema (Kelly 2001);
(20) acupuncture (Smith 2004);
(21) breast stimulation (Kavanagh 2005);
(22) sexual intercourse (Kavanagh 2001);
(23) homoeopathic methods (Smith 2003);
(24) nitric oxide (Kelly 2011);
(25) buccal or sublingual misoprostol (Muzonzini 2004);
(26) other methods for induction of labour.

The primary reviews were analysed by the following subgroups:

(1) previous caesarean section or not;
(2) nulliparity or multiparity;

(3) membranes intact or ruptured;
(4) cervix favourable, unfavourable or undefined.
The secondary reviews would have included all methods of labour induction for each of the categories of women for which subgroup analysis has been done in the primary reviews. There would have thus been six secondary reviews, of methods of labour induction in the following groups of women:
(1) nulliparous, intact membranes (unfavourable cervix, favourable cervix, cervix not defined);
(2) nulliparous, ruptured membranes (unfavourable cervix, favourable cervix, cervix not defined);
(3) multiparous, intact membranes (unfavourable cervix, favourable cervix, cervix not defined);
(4) multiparous, ruptured membranes (unfavourable cervix, favourable cervix, cervix not defined);
(5) previous caesarean section, intact membranes (unfavourable cervix, favourable cervix, cervix not defined);
(6) previous caesarean section, ruptured membranes (unfavourable cervix, favourable cervix, cervix not defined).
Each time a primary review was updated with new data, those secondary reviews which included data which have changed, would also have been updated.
The trials included in the primary reviews were extracted from an initial set of trials covering all interventions used in induction of labour (see above for details of search strategy). The data extraction process was conducted centrally. This was co-ordinated from the Clinical Effectiveness Support Unit (CESU) at the Royal College of Obstetricians and Gynaecologists, UK, in co-operation with the Pregnancy and Childbirth Group of the Cochrane Collaboration. This process allowed the data extraction process to be standardised across all the reviews.
The trials were initially reviewed on eligibility criteria, using a standardised form and the basic selection criteria specified above. Following this, data were extracted to a standardised data extraction form which was piloted for consistency and completeness. The pilot process involved the researchers at the CESU and previous reviewers in the area of induction of labour.
Information was extracted regarding the methodological quality of trials on a number of levels. This process was completed without consideration of trial results. Assessment of selection bias examined the process involved in the generation of the random sequence and the method of allocation concealment separately. These were then judged as adequate or inadequate using the criteria described in Appendix 3 for the purpose of the reviews.
Performance bias was examined with regards to whom was blinded in the trials i.e. patient, caregiver, outcome assessor or analyst. In many trials the caregiver, assessor and analyst were the same party. Details of the feasibility and appropriateness of blinding at all levels was sought.
Predefined subgroup analyses were: previous caesarean section or not; nulliparity or multiparity; membranes intact or ruptured, and cervix unfavourable, favourable or undefined. Only those outcomes with data appear in the analysis tables.
Individual outcome data were included in the analysis if they met the pre-stated criteria in 'Types of outcome measures'. Included trial data were processed as described in the Cochrane Reviewers' Handbook (Clarke 2002). Data extracted from the trials were analysed on an intention-to-treat basis (when this was not done in the original report, re-analysis was performed if possible). Where data were missing, clarification was sought from the original authors. If the attrition was such that it might significantly affect the results, these data were excluded from the analysis. This decision rested with the reviewers of primary reviews and is clearly documented. If missing data become available, they will be included in the analyses.
Data were extracted from all eligible trials to examine how issues of quality influence effect size in a sensitivity analysis. In trials where reporting was poor, methodological issues were reported as unclear or clarification sought.
Once the data had been extracted, they were distributed to individual reviewers for entry onto the Review Manager computer software (RevMan 2000), checked for accuracy, and analysed as above using the RevMan software. For dichotomous data, relative risks and 95% confidence intervals were calculated, and in the absence of heterogeneity, results were pooled using a fixed-effect model.
The predefined criteria for sensitivity analysis included all aspects of quality assessment as mentioned above, including aspects of selection, performance and attrition bias.
Primary analysis was limited to the prespecified outcomes and subgroup analyses. In the event of differences in unspecified outcomes or subgroups being found, these were analysed post hoc, but clearly identified as such to avoid drawing unjustified conclusions.
In 2012 the methods and software for carrying out reviews were updated, as a result of which new reviews and updates, where appropriate, used these new methods (Higgins 2011; RevMan 2012), which are described in the Methods section of all the individual new and updated reviews.

Appendix 3. Methodological quality of trials

Methodological item	Adequate	Inadequate
Generation of random sequence	Computer generated sequence, random number tables, lot drawing, coin tossing, shuffling cards, throwing dice	Case number, date of birth, date of admission, alternation.
Concealment of allocation	Central randomisation, coded drug boxes, sequentially sealed opaque envelopes	Open allocation sequence, any procedure based on inadequate generation

Appendix 4. Data extraction form

The Cochrane Pregnancy and Childbirth Group
Review title: Acupuncture for induction of labour

Review ID:	**Study ID**:	**Reference ID:**
Person extracting data:	**Date of date extraction:**	**Year of study publication:**
Title:		
Author:		
Reference:		

Study design

Type of study design (cluster RCT; block randomisation; stratified randomisation; multi-arm; factorial etc):

Unit of randomisation:

Participants and setting

Describe setting: **Inclusion criteria:**

Intervention

Comparison
Outcomes:

Study methods

Risk of bias

Adequate sequence generation Was the allocation sequence adequately generated?	Yes / Unclear / No
Allocation concealment Was allocation concealment adequate?	Yes / Unclear / No Describe:
Blinding Was knowledge of the allocated intervention adequately prevented during the study?	Participant: Yes / Unclear / No Clinician: Yes / Unclear / No Outcome assessor : Yes / Unclear / No Describe:
Incomplete outcome data addressed Were complete outcome data adequately addressed?	Yes / Unclear / No Describe any loss of participants to follow-up at each data collection point: Describe any exclusion of participants after randomisation: Was the analysis intention to treat? If not has the data been able to be re-included?

(*Continued*)

Free of selective reporting bias Are reports of study free of suggestions of selective reporting bias?	Yes / Unclear / No Describe:
Free of other bias Was the study apparently free of other problems that could put it at high risk of bias?	Yes / Unclear / No If the study was stopped early, explain the reasons: Describe any baseline in balance: Describe any differential diagnosis:

Additional information requested

Outcomes for main analysis

	Outcome Measures (Dichotomous)	Total number of participants in study = 101			
		Intervention group total no. in study =		Comparison group Total no. in study =	
		events	Total	events	total
	Primary:				
1	vaginal delivery not achieved within 24 hours;				
2	uterine hyperstimulation with fetal heart rate (FHR) changes;				
3	caesarean section;				
4	serious neonatal morbidity or perinatal death (e.g. seizures, birth asphyxia defined by trialists, neonatal encephalopathy, disability				

(*Continued*)

	in childhood);				
5	serious maternal morbidity or death (e.g. uterine rupture, admission to intensive care unit, septicaemia)				
	Secondary:				
6	cervix unfavourable/ unchanged after 12 to 24 hours;				
7	oxytocin augmentation.				
8	uterine hyperstimulation without FHR changes;				
9	uterine rupture				
10	epidural analgesia;				
11	instrumental vaginal delivery;				
12	meconium-stained liquor;				
13	Apgar score less than seven at five minutes;				
14	neonatal intensive care unit admission;				
15	neonatal encephalopathy;				
16	perinatal death;				
17	disability in childhood;				
18	maternal side-effects (all);				
19	maternal nausea;				

(*Continued*)

20	maternal vomiting					
21	maternal diarrhoea;					
22	other maternal side-effects;					
23	postpartum haemorrhage (as defined by the trial authors);					
24	serious maternal complications (e.g. intensive care unit admission, septicaemia but excluding uterine rupture);					
25	maternal death					

	Outcome Measures (Continuous)	Total number of participants in study =					
		Intervention group Total no. in study =			Control group Total no. in study =		
		total	mean	SD	total	mean	SD
	Secondary						
1	woman not satisfied;						
2	care giver not satisfied						
3	use of other induction methods;						
4	time from trial intervention to the birth of the baby;						

(*Continued*)

5	length of labour						

Outcomes for subgroup analyses
previous caesarean section or not;
nulliparity or multiparity;
membranes intact or ruptured, and cervix unfavourable, favourable or undefined. Other subgroup analyses will examine the effects of different styles of acupuncture (for example classical/traditional acupuncture versus single point therapy, or auricular acupuncture), as well as the type of control group.

	Outcome Measures (Dichotomous)	Total number of participants in study =			
		Intervention group Total no. in study =		**Control group** Total no. in study =	
		events	Total	events	total
	Primary:				
1					
2					
	Secondary:				
3					
4					
5					

	Outcome Measures (Continuous)	Total number of participants in study =

(*Continued*)

		Intervention group Total no. in study =			**Control group** Total no. in study =		
		total	mean	SD	total	mean	SD
	Primary:		**Median**	**IQR**			
1							
2							
	Secondary:						
3							
4							
5							

General conclusions

Very brief summary of study authors main findings/conclusions:

Exclusion after data extraction

Reasons for exclusion: (study design? participants? interventions/ outcomes? attrition? bias?)

WHAT'S NEW

Last assessed as up-to-date: 14 December 2012.

Date	Event	Description
7 February 2013	New citation required and conclusions have changed	Eleven trials have been added since the last update. Conclusions have changed for one outcome: need for induction methods. There is now no difference in the use of additional induction methods between acupuncture and standard care groups
23 November 2012	New search has been performed	Search updated and 18 trial reports identified.

HISTORY

Protocol first published: Issue 2, 2000

Review first published: Issue 1, 2001

Date	Event	Description
23 May 2012	Amended	Search updated. Fifteen reports added to Studies awaiting classification.
10 November 2008	Amended	Contact details updated.
13 August 2008	Amended	Corrected typing mistake in the Plain language summary.
8 February 2008	New search has been performed	Search updated. We identified nine new trial reports for eight trials, two of which have been included (Gaudernack 2006; Harper 2006a), three excluded (Bo 2006; Martinez 2004a; So 1979), one is awaiting assessment (Coeytaux 2007) and two are ongoing (Lorentzen 2006; Modlock 2006)
8 February 2008	Amended	Converted to new review format.
31 October 2003	New search has been performed	Search updated. We identified one new trial that met the inclusion criteria (Rabl 2001) and two new trials which we excluded (Dorr 1990;Romer 2000a).

CONTRIBUTIONS OF AUTHORS

Caroline Smith conceptualised and took the lead in writing the protocol and the original review. She performed initial searches of databases for trials, was involved in selecting trials for inclusion, performed data extraction and quality assessment of the included trials, was responsible for statistical analysis and interpretation of the data, and wrote the first draft of this update.

Caroline Crowther was involved with selecting trials for inclusion, performed data extraction and quality assessment of the included trials, interpretation of the data and commented on drafts of the protocol and the original review and drafts of this update.

Suzanne Grant was involved with selecting trials for inclusion, performed data extraction and quality assessment of the included trials, interpretation of the data and commented on drafts of this updated review.

DECLARATIONS OF INTEREST

Caroline Smith and Caroline Crowther are both authors on one of the included trials (Smith 2008), and so a third independent person assessed and extracted data for this trial.

SOURCES OF SUPPORT

Internal sources

- University of Western Sydney, Australia.
- University of Adelaide, Australia.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Methods updated to current Cochrane Pregnancy and Childbirth Group standard text.

INDEX TERMS

Medical Subject Headings (MeSH)

*Acupuncture Therapy; Cervical Ripening; Labor, Induced [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Female; Humans; Pregnancy