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[Intervention Review]

# Acupuncture and assisted reproductive technology

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## ABSTRACT

### Background

Acupuncture is commonly undertaken during an assisted reproductive technology (ART) cycle although its role in improving live birth and pregnancy rates is unclear.

### Objectives

To determine the effectiveness and safety of acupuncture as an adjunct to ART cycles for male and female subfertility.

### Search methods

All reports which described randomised controlled trials of acupuncture in assisted conception were obtained through searches of the Menstrual Disorders and Subfertility Group Specialised Register, CENTRAL, Ovid MEDLINE, EMBASE, CINAHL (Cumulative Index to Nursing & Allied Health Literature), AMED, [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (all from inception to July 2013), National Research Register, and the Chinese clinical trial database (all to November 2012).

### Selection criteria

Randomised controlled trials of acupuncture for couples who were undergoing ART, comparing acupuncture treatment alone or acupuncture with concurrent ART versus no treatment, placebo or sham acupuncture plus ART for the treatment of primary and secondary infertility. Women with medical illness that was deemed to contraindicate ART or acupuncture were excluded.

### Data collection and analysis

Twenty randomised controlled trials were included in the review and nine were excluded. Study selection, quality assessment and data extraction were performed independently by two review authors. Meta-analysis was performed using odds ratio (OR) and 95% confidence intervals (CI). The outcome measures were live birth rate, clinical ongoing pregnancy rate, miscarriage rate, and any reported side effects of treatment. The quality of the evidence for the primary outcome (live birth) was rated using GRADE methods.

### Main results

This updated meta-analysis showed no evidence of overall benefit of acupuncture for improving live birth rate (LBR) regardless of whether acupuncture was performed around the time of oocyte retrieval (OR 0.87, 95% CI 0.59 to 1.29, 2 studies, n = 464, I<sup>2</sup> = 0%, low quality evidence) or around the day of embryo transfer (ET) (OR 1.22, 95% CI 0.87 to 1.70, 8 studies, n = 2505, I<sup>2</sup> = 69%, low quality evidence). There was no evidence that acupuncture had any effect on pregnancy or miscarriage rates, or had significant side effects.

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**Authors' conclusions**

There is no evidence that acupuncture improves live birth or pregnancy rates in assisted conception.

**PLAIN LANGUAGE SUMMARY****Acupuncture and assisted conception**

Review question: does acupuncture improve the outcomes of assisted reproduction?

Background: one in seven couples suffer from subfertility and many will seek help in the form of assisted reproductive technology (ART). Although the use of acupuncture has gained popularity, the use of this traditional Chinese medical treatment in conjunction with ART treatments is still controversial. This review summarised the evidence from well designed studies and evaluated the effectiveness and safety of acupuncture in assisted conception.

Search date: the evidence is current to July 2013.

Study characteristics: there were 20 randomised controlled studies identified. Six studies compared acupuncture at the time of egg collection (912 women) and 14 studies compared acupuncture in assisted conception (3632 women). The studies were further divided into those which used placebo needles in their control groups versus those that had controls who did not undergo any treatment. All the studies identified involved participants undertaking in vitro fertilization (IVF); there were no studies reporting the effect of acupuncture in ovulation induction or intrauterine insemination.

Funding of included studies: no included studies had external funding.

Key results: there is no evidence of benefit for the use of acupuncture in participants undergoing assisted conception treatment around the time of embryo transfer or at egg collection in terms of improving the live birth rate, ongoing or clinical pregnancy rate. There is also no evidence that acupuncture has any effect on miscarriage rate or had significant side effects.

Quality of the evidence: overall, the results are not similar across the studies. This was due to different study designs including the use of different types of control groups that could have introduced bias. More research is needed before recommendations can be made, including studies in which some controls receive placebo needling and others receive no intervention.

## SUMMARY OF FINDINGS

### Summary of findings for the main comparison. Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture) for women undergoing ART

#### Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture) for women undergoing assisted reproductive technology (ART)

**Population:** women undergoing ART

**Intervention:** Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture)				
Live birth rate	357 per 1000	326 per 1000 (247 to 418)	OR 0.87 (0.59 to 1.29)	464 (2 studies)	⊕⊕⊕⊖ low <sup>1,2</sup>	No significant difference in live birth rate was found between the two groups

\*The basis for the **assumed risk** is the median control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** Confidence interval; **OR:** Odds ratio;

GRADE Working Group grades of evidence

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> Neither study clearly reported method of random sequence generation, one did not clearly describe method of allocation concealment

<sup>2</sup> Only two studies (n=464), wide confidence intervals.

### Summary of findings 2. Acupuncture on the day of ET versus control for women undergoing ART

#### Acupuncture on the day of embryo transfer (ET) versus control for women undergoing assisted reproductive technology (ART)

**Population:** women undergoing ART

**Intervention:** Acupuncture on the day of ET versus control (sham, placebo, no acupuncture)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Acupuncture on the day of ET versus control				
Live birth rate	281 per 1000	323 per 1000 (254 to 399)	OR 1.22 (0.87 to 1.7)	2505 (8 studies)	⊕⊕⊕⊖ low 1,2,3	No significant difference in live birth rate was found between the two groups

\*The basis for the **assumed risk** is the median control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**CI:** Confidence interval; **OR:** Odds ratio;

GRADE Working Group grades of evidence

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> Two studies did not describe method of random sequence generation; six did not clearly describe method of allocation concealment

<sup>2</sup> High statistical heterogeneity (I-squared =69%)

<sup>3</sup> Wide confidence intervals

## BACKGROUND

### Description of the condition

One in seven to 10 couples in industrialised countries suffer from subfertility (Boivin 2007; Schmidt 1995). Many will seek medical help in the form of assisted reproductive technologies (ART), including controlled ovarian stimulation (COS) with or without intrauterine insemination (IUI) and in vitro fertilisation (IVF) treatment. The use of acupuncture has increasingly gained popularity (Fisher 1994; Klein 2012; Thomas 2001) although its use as an adjuvant treatment to assisted conception is still controversial (El-Toukhy 2010; Huang 2011; Meldrum 2013).

### Description of the intervention

Acupuncture is an integral part of traditional Chinese medicine (TCM) and can be dated back at least 3000 years. In Europe, from consumer surveys (Fisher 1994; Klein 2012; Thomas 2001) between 7% and 19% of the population report using acupuncture for various reasons, and studies have shown promising results for its efficacy in adult postoperative and chemotherapy induced nausea and vomiting (Garcia 2013; Holmer 2012; NIH Consensus 1998).

In its original form, acupuncture is based on the principles of TCM and involves the insertion of fine needles into the skin along the meridians, providing a means of altering the flow of energy through the body (Vickers 1999). In a typical treatment, between four to 10 points are needed for 10 to 30 minutes. Needles can be stimulated by manual twirling or with a small electric current, as electro-acupuncture (EA). There have been few studies of the physiological effects of acupuncture on the male or female reproductive tract, although for many years acupuncture has been widely used as an adjuvant to ART. Opinion about the effectiveness of acupuncture in women undergoing assisted conception varies considerably. Some regard the traditional Chinese treatment as effective (Zheng 2012) whilst others consider acupuncture as primarily a placebo treatment (Meldrum 2013) or even as a treatment that is unscientific and futile (El-Toukhy 2010). It is, therefore, critical to examine the current evidence available using stringent methodology and analysis to evaluate the effectiveness of acupuncture in couples undertaking ART.

### How the intervention might work

The mechanisms of action of acupuncture are largely unknown. Its influence on plasma beta-endorphin levels via the hypothalamic-pituitary-adrenal (HPA) axis (Chen 2004; Stener-Victorin 2000; Stener-Victorin 2001), on uterine artery blood flow (Stener-Victorin 1996) and analgesic actions have been described (Stener-Victorin 1999).

### Why it is important to do this review

Given the controversy surrounding this topic, it is important to perform an up-to-date review so that subfertile couples, fertility practitioners and general practitioners are better informed of the benefits or harm of acupuncture in assisted conception.

## OBJECTIVES

To determine the effectiveness and safety of acupuncture as an adjunct to ART cycles for male and female subfertility.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Published and unpublished randomised controlled trials (RCTs) were included in the review. We excluded non-randomised studies (for example studies with evidence of inadequate sequence generation such as alternate days, patient numbers) as they are associated with a high risk of bias. We did not include crossover trials with no first phase data.

#### Types of participants

Participants in the trials had to meet all the following criteria to be included in the review.

#### Inclusion criteria:

- primary (subfertility in couples who have never conceived) or secondary subfertility (couples who have subfertility after previously having children);
- women undergoing ART;
- any type of acupuncture at any or all time points before, during, or after ART with the intention to improve the ART outcome.

#### Exclusion criteria:

- participants with any medical illness deemed a contraindication for ART or acupuncture treatment;
- quasi-randomised controlled trials; or
- crossover randomised controlled trials that did not provide pre-crossover data.

#### Types of interventions

RCTs comparing acupuncture treatment of participants (men or women, or both) versus no treatment, placebo or sham acupuncture during controlled ovarian stimulation (COS) with or without artificial stimulation by partner ( $\pm$  artificial insemination by husband (AIH)), IVF, or frozen-thawed embryo transfer (FET) treatment were considered.

We included studies using either traditional acupuncture, in which needles were inserted in classical meridian points, or contemporary acupuncture in which the needles were inserted in non-meridian or trigger points. The source of stimulation could be the hand, fine needle, moxibustion with warming needle, or electrical stimulation. We excluded studies of acupuncture treatment without needling, such as point injection, acupressure, laser acupuncture, tap-pricking, or cupping on pricked superficial blood vessels. We excluded trials comparing different acupuncture treatments alone.

The timing of acupuncture treatment was generally either around the time of oocyte retrieval or around the time of embryo transfer (ET) (a few days before, the day of, and a few days after).

Needling in the control groups could either be with a sham needle (for example Streitberger placebo needle, Asiamed, Pullach, Germany, where skin penetration does not occur because the tip of the needle is blunted) or normal acupuncture needles, needling an area not recommended by TCM practitioners for fertility treatment. The other type of control group had no needling treatment.

Specific interventions to be considered:

1. acupuncture + ART versus no treatment, placebo, sham acupuncture + ART; i.e. all women received ART;
2. acupuncture alone versus no treatment, placebo, sham acupuncture + ART;
3. acupuncture versus acupuncture + ART.

### Types of outcome measures

#### Primary outcomes

1. Live birth rate, defined as delivery of a live fetus after 20 completed weeks gestational age

#### Secondary outcomes

1. Ongoing pregnancy rate, defined as evidence of a gestational sac with fetal heart motion at greater than 12 weeks (12 to 18 weeks), confirmed with ultrasound
2. Clinical pregnancy rate, defined as evidence of a gestational sac with fetal heart motion measured at seven to eight weeks, confirmed with ultrasound
3. Adverse events including miscarriage, ectopic pregnancy, fetal abnormalities, side effects, ovarian hyperstimulation syndrome (OHSS) and infection

All rates were per woman randomised.

### Search methods for identification of studies

#### Electronic searches

We searched the following electronic databases, trials registers and web sites.

1. Menstrual Disorders and Subfertility Group (MDSG) Specialised Register (inception to 22.7.13).
2. Ovid Cochrane Central Register of Controlled Trials (CENTRAL) (inception to 22.7.13).
3. Ovid MEDLINE® In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® (inception to 22.7.13).
4. Ovid EMBASE (01.01.10 to 22.7.13). EMBASE was only searched for recent records as the UK Cochrane Centre has handsearched EMBASE to this point and these trials are already in CENTRAL.

5. Ovid PsycINFO (inception to 22.7.13).
6. Ovid AMED (inception to 22.7.13).

Other electronic sources of trials included:

1. Database of Abstracts of Reviews of Effects (DARE) in *The Cochrane Library* (<http://www.cochrane.org/index.htm>);
2. ClinicalTrials.gov (<http://clinicaltrials.gov/ct2/home>);
3. World Health Organization International Clinical Trials Registry Platform search portal (<http://apps.who.int/trialsearch/>);
4. OpenSige for Grey literature from Europe (<http://opensigle.inist.fr/>);
5. China Academic Journal Electronic full text Database in China National Knowledge Infrastructure;
6. Index to Chinese Periodical Literature.

There was no language restriction in these searches. The search strings are in the appendices.

#### Searching other resources

We also handsearched reference lists of articles retrieved by the search and contacted experts in the field to obtain additional data when required. We handsearched relevant journals and conference abstracts that are not covered in the MDSG register, in liaison with the Trials Search Co-ordinator.

### Data collection and analysis

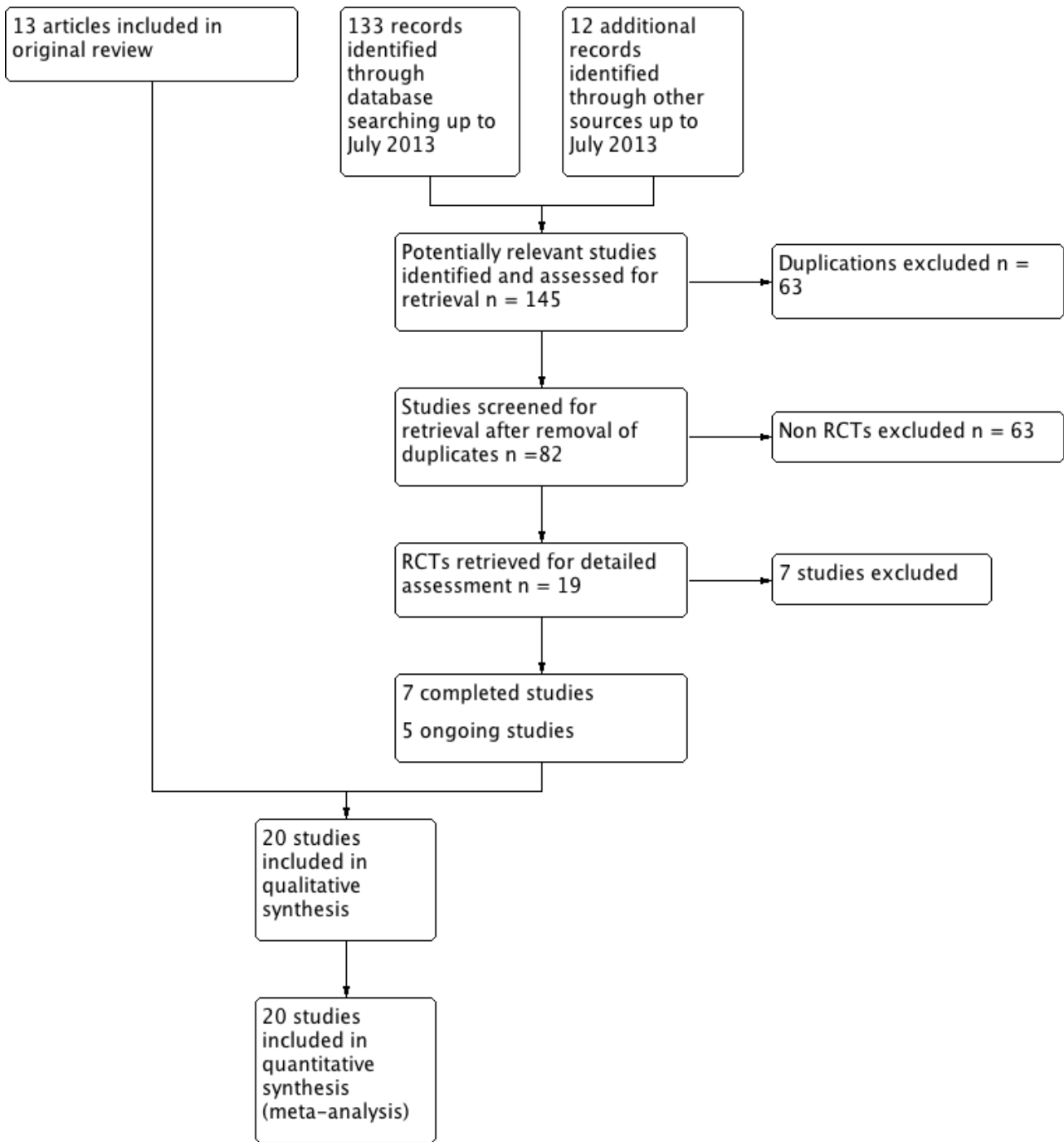
#### Selection of studies

After an initial screening of titles and abstracts that were retrieved by the search, conducted by YC and SD, the full texts of all potentially eligible studies were retrieved. Two review authors (YC and SD) independently examined these full text articles for compliance with the inclusion criteria and selected studies eligible for inclusion in the review. We corresponded with study investigators to clarify study data and eligibility. Disagreements as to study eligibility were resolved by discussion without requiring referral to a third review author (WL). Study investigators were contacted for further data on methods or results, as required.

The selection process is documented with a PRISMA flow chart in [Figure 1](#).



**Figure 1. Study selection PRISMA flow diagram.**



**Data extraction and management**

Two review authors (YC and SD) independently extracted data and assessed trial quality using forms designed according to Cochrane guidelines. Disagreements as to study eligibility were resolved by discussion without requiring referral to a third review author (WL). Where studies had multiple publications, the main trial report was used as the reference and additional details were derived from secondary papers. We corresponded with study investigators to clarify further data on methods and results.

**Assessment of risk of bias in included studies**

The included studies were assessed for risk of bias using the Cochrane risk of bias assessment tool (*Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1) to assess the following domains: random sequence generation; allocation concealment; blinding; incomplete outcome data; selective reporting; and other bias.

Two authors (YC and SD) independently assessed these six domains, with any disagreements resolved by consensus or by discussion with the third author (WL).

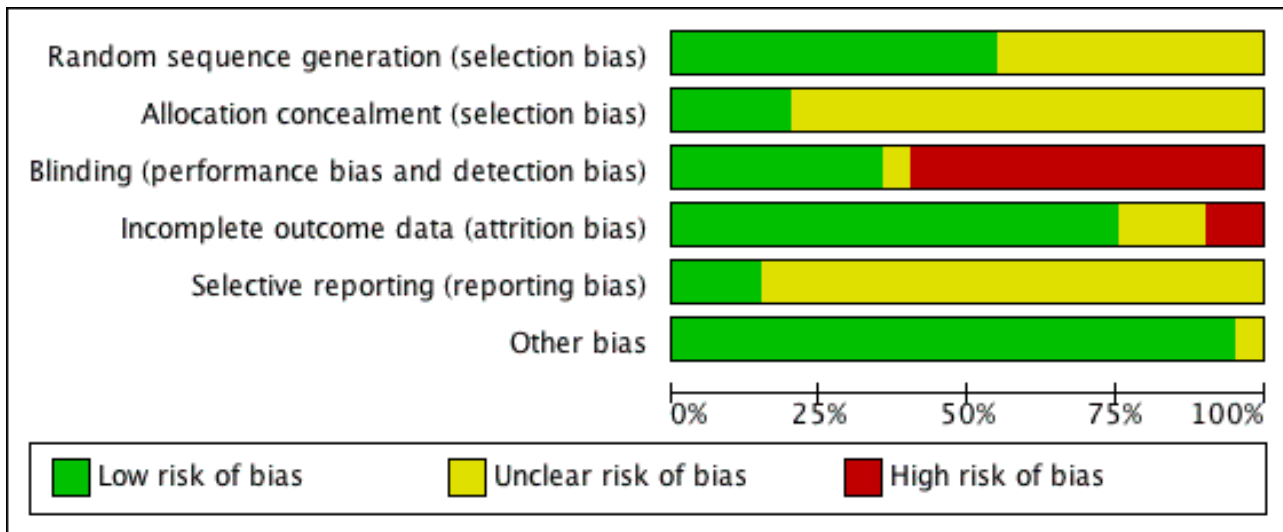
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As this was a review of surgical studies, where blinding was not possible, absence of blinding was not considered a significant source of bias. Risk of bias assessment is summarised ([Figure 2](#) and [Figure 3](#)).

**Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Andersen 2010	+	?	+	+	+	+
Benson 2006	?	?	-	?	?	+
Craig 2007	?	?	-	+	?	+
Dieterle 2006	?	?	+	+	?	+
Domar 2009	+	?	-	?	?	+
Fraterelli 2008	?	?	-	?	?	+
Gejervall 2005	+	?	-	+	?	+
Ho 2009	?	?	-	-	?	+
Humaidan 2004	?	+	+	+	?	+
Madaschi 2010	+	?	-	+	?	+
Moy 2011	+	+	+	+	?	+
Paulus 2002	+	?	-	+	?	+
Paulus 2003	+	?	+	+	?	+
Sator-K 2006	+	?	-	+	?	+
Smith 2006	+	?	?	-	?	+
So 2009	+	+	+	+	+	+
So 2010	+	+	+	+	+	+
Stener-Victorin 1999	?	?	-	+	?	?
Stener-Victorin 2003	?	?	-	+	?	+
Westergaard 2006	?	?	-	+	?	+

**Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.**



We took care to search for within trial selective reporting.

**Measures of treatment effect**

We performed statistical analysis in accordance with the guidelines and methods developed by The Cochrane Collaboration (Higgins 2011). All data were dichotomous. We expressed results for each study as odds ratio (OR) with 95% confidence interval (CI).

**Unit of analysis issues**

The unit of analysis was per participant and not per cycle. Multiple live births were counted as one live birth event.

**Dealing with missing data**

The data was analysed on an intention-to-treat basis and we have attempted to obtain missing data from the original trialists. Where these were unobtainable, imputation of individual values was undertaken for the primary outcomes only. Live births were assumed not to have occurred in participants without a reported outcome. For other outcomes, only the available data were analysed.

**Assessment of heterogeneity**

Heterogeneity was assessed using the I<sup>2</sup> statistic, according to the guidelines set out in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). An I<sup>2</sup> value greater than 50% indicated substantial heterogeneity.

**Assessment of reporting biases**

In view of the difficulty in detecting and correcting for publication bias and other reporting bias, we minimised their potential impact by ensuring a comprehensive search for eligible studies and by being aware of duplicated data. In the case where 10 or more studies were present in our analysis, we used a funnel plot to explore the possibility of a small study effect.

**Data synthesis**

Where possible, we pooled the outcomes and combined them for meta-analysis. Dichotomous data for primary and secondary outcomes in studies that were sufficiently similar were combined with RevMan software using the Peto-modified Mantel-Haenszel method and fixed-effect and random-effects models in the following comparisons.

1. Acupuncture around the time of oocyte retrieval versus control (changed for consistency).
2. Acupuncture on the day of ET versus control.

We used a fixed-effect model and examined heterogeneity between the results of different studies by inspecting the scatter in the data points, the overlap in their CIs, and more formally by checking the results of the Chi<sup>2</sup> test and the I<sup>2</sup> statistic. An I<sup>2</sup> greater than 50% was taken to indicate substantial heterogeneity and in that case a random-effects analysis was used.

**Subgroup analysis and investigation of heterogeneity**

The analysis was stratified to examine the separate evidence within the following subgroups:

- 1) studies with control groups that had sham or needling acupuncture;
- 2) studies with control groups that had no acupuncture.

**Sensitivity analysis**

None applicable

**RESULTS**

**Description of studies**

See the tables [Characteristics of included studies](#) and [Characteristics of excluded studies](#).

## Results of the search

In the original review, 16 randomised trials were identified involving acupuncture and assisted conception; 13 met the inclusion criteria and three were excluded. In the updated search, 14 further randomised trials were identified, giving a total of 30. In total, 20 trials were included and nine were excluded; see [Figure 1](#). Five ongoing studies were also identified ([ACTRN12611000226909](#); [IRCT201011275181N4](#); [NCT00317317](#); [NCT01449396](#); [NCT01608048](#)).

## Included studies

### Study design and setting

Twenty randomised controlled trials were included in this review. Four of the trial reports were abstracts ([Benson 2006](#); [Craig 2007](#); [Fraterelli 2008](#); [Paulus 2003](#)). All 20 trials had a parallel design ([Andersen 2010](#); [Benson 2006](#); [Craig 2007](#); [Dieterle 2006](#); [Domar 2009](#); [Fraterelli 2008](#); [Gejervall 2005](#); [Ho 2009](#); [Humaidan 2004](#); [Madaschi 2010](#); [Moy 2011](#); [Paulus 2002](#); [Paulus 2003](#); [Sator-K 2006](#); [Smith 2006](#); [So 2009](#); [So 2010](#); [Stener-Victorin 1999](#); [Stener-Victorin 2003](#); [Westergaard 2006](#)).

### Participants

The studies included a total of 4544 participants. All were women undergoing IVF and intracytoplasmic sperm injection (ICSI). The characteristics of the participants can be found in the table [Characteristics of included studies](#).

### Interventions

- Six of the 20 trials were designed with the primary objective of assessing the effect of acupuncture as an analgesic during oocyte retrieval, but had pregnancy rate as one of the primary outcomes ([Gejervall 2005](#); [Ho 2009](#); [Humaidan 2004](#); [Smith 2006](#); [Stener-Victorin 1999](#); [Stener-Victorin 2003](#)).
- Fourteen of the 20 trials were designed to examine the fertility outcome of acupuncture performed around the time of ET ([Andersen 2010](#); [Benson 2006](#); [Craig 2007](#); [Dieterle 2006](#); [Domar 2009](#); [Fraterelli 2008](#); [Madaschi 2010](#); [Moy 2011](#); [Paulus 2002](#); [Paulus 2003](#); [Smith 2006](#); [So 2009](#); [So 2010](#); [Westergaard 2006](#)), although two of these studies also included acupuncture two to three days after ET ([Dieterle 2006](#); [Westergaard 2006](#)).

A summary of the acupuncture points used in the various studies is provided in [Table 1](#).

### Control groups

No sham or needling:

- eight studies had a no intervention control group ([Benson 2006](#); [Craig 2007](#); [Domar 2009](#); [Fraterelli 2008](#); [Ho 2009](#); [Madaschi 2010](#); [Paulus 2002](#); [Westergaard 2006](#));
- five studies had control groups with conventional medical analgesia ([Gejervall 2005](#); [Humaidan 2004](#); [Sator-K 2006](#); [Stener-Victorin 1999](#); [Stener-Victorin 2003](#)).

With sham or needling:

- 6/20 had a sham acupuncture needle control group using Strietberger sham acupuncture needles ([Andersen 2010](#); [Moy 2011](#); [Paulus 2003](#); [Smith 2006](#); [So 2009](#); [So 2010](#)). [Smith 2006](#) needled close to but not on real acupuncture points whilst

[Andersen 2010](#), [Paulus 2003](#), [So 2009](#) and [So 2010](#) needled at the same acupoints as for the intervention group. [Moy 2011](#) had acupuncture control groups that were needled at pre-determined, non-qui lines and auricular points not used for fertility;

- one study had control groups with needling at non-acupuncture points ([Dieterle 2006](#)) using normal acupuncture needles.

### Outcomes

- 11/20 studies reported on live birth rate
- 11/20 studies reported on ongoing pregnancy rate
- 20/20 studies reported on clinical pregnancy rate
- 2/20 studies reported on multiple pregnancy rates
- 0/20 studies reported on rates of OHSS
- 9/20 studies reported on miscarriage rates
- 4/20 studies reported on side effects arising from use of acupuncture

Further details of the included studies can be found in the table [Characteristics of included studies](#).

### Excluded studies

Ten studies were excluded from the review for the following reasons:

- [Quintero 2004](#) was excluded due to the lack of first phase results in its crossover design;
- [Cui 2011](#) randomised women with polycystic ovary syndrome (PCOS) undergoing ET to either electro-acupuncture (n = 34) or the control of no treatment (n = 32). However, the description of the randomisation process showed a high risk of bias with an inadequate randomisation process, based on odd or even numbers;
- [Chen 2004](#); [Chen 2009](#); [Cui 2007](#); [Evans 2005](#); [Feliciani 2011](#); [Li 2009](#) and [Omodei 2010](#) were excluded because they were apparently not randomised.
- [Chen 2012](#) reported on supplementary analgesia and improvement of adverse reactions induced by dolantin in oocyte retrieval, which were not outcomes of interest in the review

Characteristics of excluded studies can be found in the table [Characteristics of excluded studies](#).

### Risk of bias in included studies

Risk of bias assessment focused on six main domains: random sequence generation, allocation concealment, blinding, incomplete data outcome, selective reporting and other potential bias. Details of the findings can be found in the relevant risk of bias summary figures ([Figure 2](#); [Figure 3](#)) and the [Characteristics of included studies](#) table.

### Allocation

#### Sequence generation

Eleven trials were at low risk of selection bias related to sequence generation ([Andersen 2010](#); [Domar 2009](#); [Gejervall 2005](#); [Madaschi 2010](#); [Moy 2011](#); [Paulus 2002](#); [Paulus 2003](#); [Sator-K 2006](#); [Smith 2006](#); [So 2009](#); [So 2010](#); ). The other nine trials ([Benson 2006](#); [Craig 2007](#); [Dieterle 2006](#); [Fraterelli 2008](#); [Ho 2009](#); [Humaidan 2004](#); [Stener-Victorin 1999](#); [Stener-Victorin 2003](#); [Westergaard 2006](#)) were

at an unclear risk due to a lack of detail of their methods of sequence generation.

**Allocation concealment**

Four trials were at low risk of bias for allocations concealment (Humaidan 2004; Moy 2011; So 2009; So 2010). The other sixteen trials (Andersen 2010; Benson 2006; Craig 2007; Dieterle 2006; Domar 2009; Fraterelli 2008; Gejervall 2005; Ho 2009; Madaschi 2010; Paulus 2002; Paulus 2003; Sator-K 2006; Smith 2006; Stener-Victorin 1999; Stener-Victorin 2003; Westergaard 2006) were at unclear risk of bias for allocation concealment.

**Blinding**

Due to the nature of the studies, double blinding was often not possible. Eleven trials (Benson 2006; Craig 2007; Domar 2009; Gejervall 2005; Ho 2009; Madaschi 2010; Paulus 2002; Sator-K 2006; Stener-Victorin 1999; Stener-Victorin 2003; Westergaard 2006) had no sham acupuncture intervention for the control group and so were at high risk of performance and detection bias. Five trials (Andersen 2010; Humaidan 2004; Paulus 2003; So 2009; So 2010) were low risk of performance and detection bias due to the use of sham acupuncture controls for blinding. Moy 2011 and Dieterle 2006 used an actual needling procedure on acupoints that were not considered to affect fertility and so were also low risk. Smith 2006 used sham acupuncture for the control groups but was deemed at an unclear risk of performance and detection bias as, after the 3rd session, 24 in the treatment group and 10 in the control group had guessed their allocation correctly.

**Incomplete outcome data**

Fifteen trials were at low risk of attrition bias without significant incomplete outcome data (Andersen 2010; Craig 2007; Dieterle 2006; Gejervall 2005; Humaidan 2004; Madaschi 2010; Moy 2011; Paulus 2002; Paulus 2003; Sator-K 2006; So 2009; So 2010; Stener-Victorin 1999; Stener-Victorin 2003; Westergaard 2006). In three trials the risk was unclear as they did not report on the number of participants who completed the study (Benson 2006; Domar 2009; Fraterelli 2008). Ho 2009 had a high risk of attrition bias as 12 of the 26 control group participants dropped out of the trial. Smith 2006 also had a high risk of attrition bias as 36 women (15%) were withdrawn from the trial after randomisation.

**Selective reporting**

Three trials (Andersen 2010; So 2009; So 2010) were at low risk of reporting bias as they reported live birth data as pre-stated outcomes. Seven trials (Dieterle 2006; Humaidan 2004; Madaschi 2010; Paulus 2002; Paulus 2003; Stener-Victorin 2003; Westergaard 2006) were at unclear risk of reporting bias as they reported live birth data but it was not a pre-stated outcome. The remaining 10 trials (Benson 2006; Craig 2007; Domar 2009; Fraterelli 2008; Gejervall 2005; Ho 2009; Moy 2011; Sator-K 2006; Smith 2006; Stener-Victorin 1999) did not report on live birth rate outcomes and so were also at unclear risk.

**Other potential sources of bias**

One study (Stener-Victorin 1999) was rated as at unclear risk of other potential bias, related to co-intervention in some women. The other studies were rated as at low risk of bias in this domain.

**Effects of interventions**

See: [Summary of findings for the main comparison Acupuncture around the time of oocyte retrieval versus control \(sham, placebo, no acupuncture\) for women undergoing ART](#); [Summary of findings 2 Acupuncture on the day of ET versus control for women undergoing ART](#)

Overall, 20 studies were included in the meta-analysis. The most commonly used acupuncture points were: GV 20, LI 4, SP6, and ST 29 (Table 1). A summary of the intended treatment with the various acupuncture points is given in Table 2.

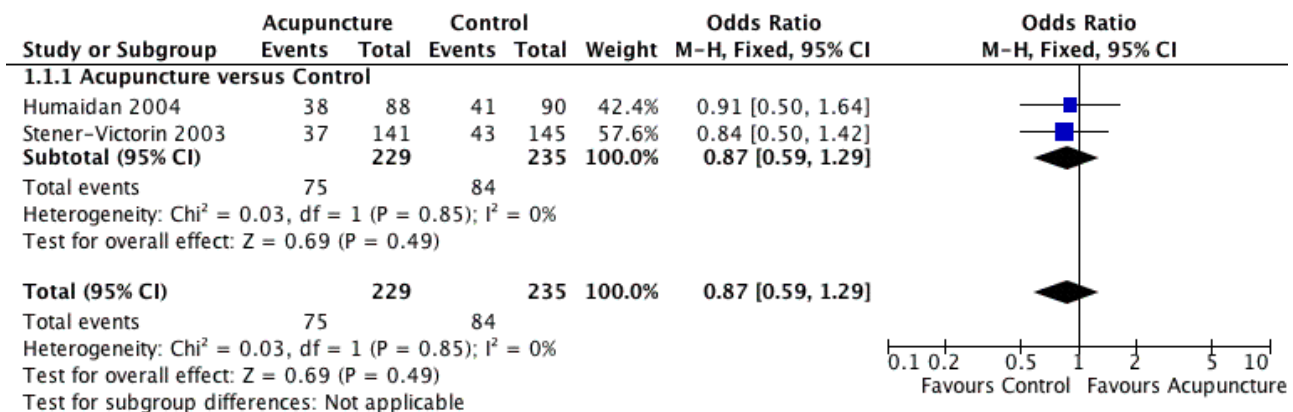
**1. Acupuncture around the time of oocyte retrieval**

None of the studies with the intervention performed around the time of oocyte retrieval had controls using sham or needling acupuncture.

**1.1 Live birth rate (LBR)**

Two studies (Humaidan 2004; Stener-Victorin 2003) reported on the LBR. There was no evidence of a difference in the LBR between the treatment group (75/229) and the control group (84/235) (OR 0.87, 95% CI 0.59 to 1.29, I<sup>2</sup> = 0%) (Analysis 1.1; Figure 4).

**Figure 4. Forest plot of comparison: 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), outcome: 1.1 Live Birth Rate.**





**1.2 Ongoing pregnancy rate**

Two trials (Humaidan 2004; Stener-Victorin 2003) reported an ongoing pregnancy rate of 78/229 in the treatment group versus 88/235 in the control group (OR 0.86, 95% CI 0.58 to 1.26,  $I^2 = 0\%$ ) (Analysis 1.2).

**1.3 Clinical pregnancy rate**

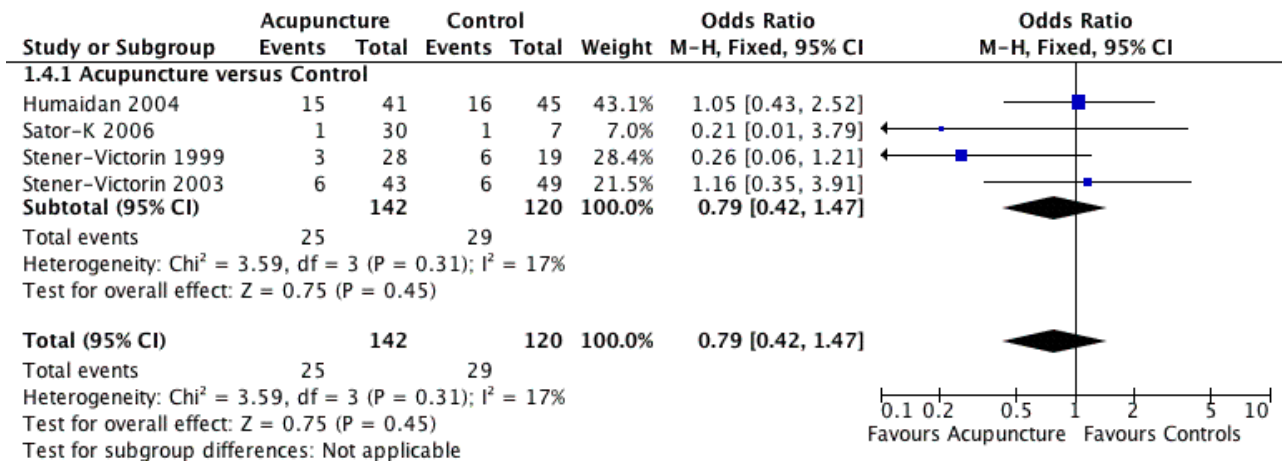
In the pooled results of six trials (Gejervall 2005; Ho 2009; Humaidan 2004; Sator-K 2006; Stener-Victorin 1999; Stener-Victorin 2003), there was no evidence of a difference in the clinical pregnancy

rate between the treatment group (174/478) and the control group 150/434 (OR 1.12, 95% CI 0.78 to 1.62,  $P = 0.53$ ,  $I^2 = 34\%$ ) (Analysis 1.3).

**1.4 Miscarriage rate**

The pooled results from four trials (Humaidan 2004; Sator-K 2006; Stener-Victorin 1999; Stener-Victorin 2003) showed no significant difference in miscarriage rates between the treatment group and control: 25/142 versus 29/120 (OR 0.79, 95% CI 0.42 to 1.47,  $I^2 = 17\%$ ) (Analysis 1.4; Figure 5).

**Figure 5. Forest plot of comparison: 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), outcome: 1.4 Miscarriage rate.**



**1.5 Multiple pregnancy**

No trials reported multiple pregnancy.

**1.6 Ovarian hyperstimulation syndrome (OHSS)**

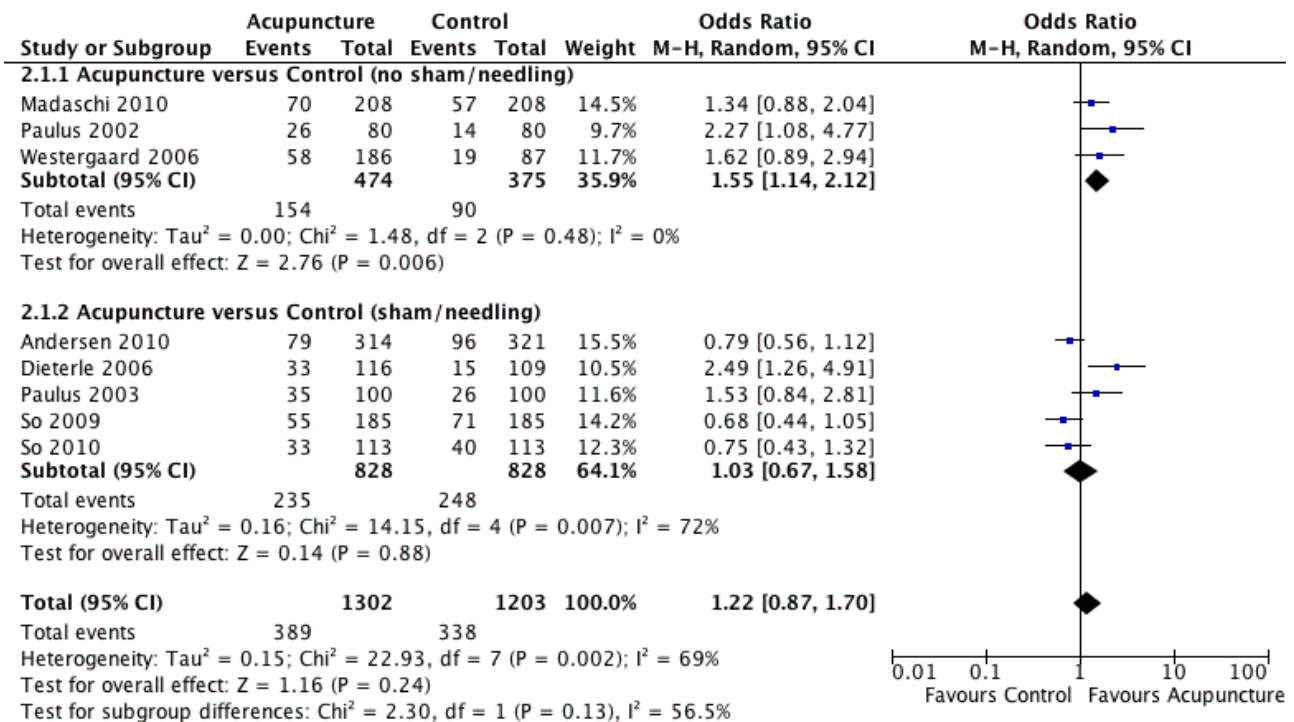
No trials reported OHSS.

**2. Acupuncture on or around the day of embryo transfer**

**2.1 Live birth rate (LBR)**

In women who had acupuncture on the day of and around ET (Andersen 2010; Dieterle 2006; Madaschi 2010; Paulus 2002; Paulus 2003; So 2009; So 2010; Westergaard 2006) (N = 2505), the overall LBR was 389/1302 compared to the controls 338/1203 (OR 1.22, 95% CI 0.87 to 1.70,  $P = 0.30$ ,  $I^2 = 69\%$ ) (Analysis 2.1; Figure 6). This was not statistically significant.

**Figure 6. Forest plot of comparison: 2 Acupuncture on and around the day of ET versus control, outcome: 2.1 Live Birth.**



In studies that had controls without sham acupuncture or needling (Madaschi 2010; Paulus 2002; Westergaard 2006), the LBR in the acupuncture group was significantly higher at 154/474 compared to 90/375 (OR 1.55, 95% CI 1.14 to 2.12,  $I^2 = 0\%$ ) in the controls. In the studies that had controls with sham acupuncture (Andersen 2010; Dieterle 2006; Paulus 2003; So 2009; So 2010) the results were 235/828 in the acupuncture group compared to 248/828 (OR 1.03, 95% CI 0.67 to 1.58,  $P = 0.88$ ,  $I^2 = 72\%$ ) in the controls. This was not statistically significant.

### 2.2 Ongoing pregnancy rate

In the pooled results of 10 trials (Andersen 2010; Craig 2007; Dieterle 2006; Fraterelli 2008; Paulus 2002; Paulus 2003; Smith 2006; So 2009; So 2010; Westergaard 2006) ( $N = 2807$ ), the overall ongoing pregnancy rate was 460/1451 in the acupuncture group compared to 427/1356 for all controls (OR 1.10, 95% CI 0.80 to 1.52,  $P = 0.56$ ,  $I^2 = 72\%$ ) (Analysis 2.2).

In studies that had controls without sham acupuncture or needling (Craig 2007; Fraterelli 2008; Paulus 2002; Westergaard 2006), the ongoing pregnancy rate in the acupuncture group was 183/514 compared to 143/410 in the controls (OR 1.08, 95% CI 0.57 to 2.07,  $P = 0.81$ ,  $I^2 = 77\%$ ). In the studies that had controls with sham acupuncture (Andersen 2010; Dieterle 2006; Paulus 2003; Smith 2006; So 2009; So 2010) the results were 277/937 in the acupuncture group compared to 284/946 in the controls (OR 1.10, 95% CI 0.74 to 1.65,  $P = 0.63$ ,  $I^2 = 73\%$ ). This was not statistically significant.

### 2.3 Clinical pregnancy rate

In the pooled results of 14 trials (Andersen 2010; Benson 2006; Craig 2007; Dieterle 2006; Domar 2009; Fraterelli 2008; Madaschi 2010; Moy 2011; Paulus 2002; Paulus 2003; Smith 2006; So 2009; So 2010; Westergaard 2006) ( $N = 3632$ ) the clinical pregnancy rate was 734/1876 in the acupuncture group compared to 658/1756 for all controls (OR 1.11, 95% CI 0.87 to 1.42,  $P = 0.39$ ,  $I^2 = 66\%$ ). This was not statistically significant (Analysis 2.3).

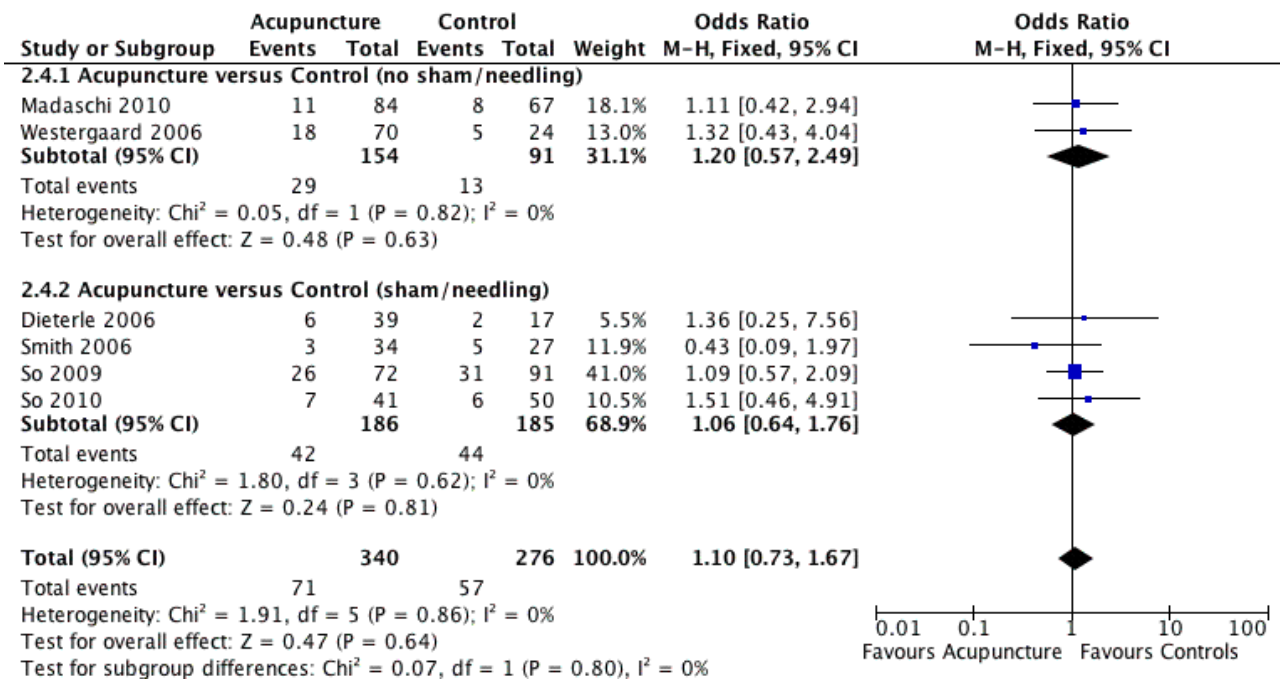
In studies that had controls without sham acupuncture or needling (Benson 2006; Craig 2007; Domar 2009; Fraterelli 2008; Madaschi 2010; Paulus 2002; Westergaard 2006) the clinical pregnancy rate in the acupuncture group was 365/853 compared to 285/736 (OR 1.21, 95% CI 0.84 to 1.73,  $P = 0.30$ ,  $I^2 = 62\%$ ). In the studies that had controls with sham acupuncture (Andersen 2010; Dieterle 2006; Moy 2011; Paulus 2003; Smith 2006; So 2009; So 2010) the results were 369/1023 compared to 373/1020 (OR 1.04, 95% CI 0.74 to 1.46,  $P = 0.83$ ,  $I^2 = 68\%$ ). This was not statistically significant.

### 2.4 Miscarriage rate

Six trials evaluated the possible impact of acupuncture on miscarriage (Dieterle 2006; Madaschi 2010; Smith 2006; So 2009; So 2010; Westergaard 2006). The miscarriage rate was 71/340 in the acupuncture group compared to 57/276 in the overall controls (OR 1.10, 95% CI 0.73 to 1.67,  $I^2 = 0\%$ ) (Analysis 2.4; Figure 7). There was no significant difference found between the two groups in the subgroup analysis.



**Figure 7. Forest plot of comparison: 2 Acupuncture on and around the day of ET versus control, outcome: 2.4 Miscarriage.**



**2.5 Multiple gestations**

Two trials reported on multiple pregnancy rates (Andersen 2010; Moy 2011); both had control groups which used sham acupuncture. There was no significant difference detected between the acupuncture (30/400) and control groups (25/395) (OR 1.32, 95% CI 0.74 to 2.35, I<sup>2</sup> = 0%) (Analysis 2.5).

**2.6 Ovarian hyperstimulation syndrome (OHSS)**

None of the 14 trials reported ovarian hyperstimulation.

**2.7 Any side effects**

So 2009 and So 2010 did not report any statistically significant difference between side effects in the 'real' and 'placebo' acupuncture groups; side effects included nausea, dizziness, fainting, tiredness, headache, chest pain and puncture site itching. However, Moy 2011 suggest a difference between the two groups in the main categories of the McGill pain score. Women in the true arm reported greater affective perception of being tired and fearful as well as more achiness.

**Assessment of heterogeneity**

Heterogeneity was generally absent or low when studies of acupuncture around the time of oocyte retrieval were pooled

However when analyses of studies of acupuncture on or around the day of embryo transfer were pooled there was high heterogeneity (I-squared >50%) for several outcomes, and we considered clinical and methodological differences between the studies that might account for this. The increased heterogeneity may be a result of the large variation in the definition of controls and acupuncture points used in the included studies (see below).

**DISCUSSION**

**Summary of main results**

This updated review reports no evidence of overall benefit of acupuncture in improving live birth rate (LBR) when acupuncture was performed around the time of oocyte retrieval or on and around the day of ET.

The subgroup analysis showed that in studies with controls without sham or needling, women who had acupuncture on and around the day of ET had a higher LBR than the controls (OR 1.55, 95% CI 1.14 to 2.12); however this evidence of benefit was not present in studies where the control group had sham acupuncture (acupuncture compared to sham controls (OR 0.93, 95% CI 0.75 to 1.15). The difference in findings between the two subgroups could possibly be due to study quality: only two RCTs, both in the sham acupuncture group, reported satisfactory methods of allocation concealment.

There was no evidence that acupuncture had an effect on miscarriage rates or other treatment side effects.

Most authors in the field assume that acupuncture has little detrimental effect. Our review reports no evidence of effect on the miscarriage rate between acupuncture groups and all controls, regardless of the timing of the intervention. This data does not prove that acupuncture is free of harm in early pregnancy and one should apply caution when giving advice to women about undergoing acupuncture in early pregnancy.

**Overall completeness and applicability of evidence**

It is generally accepted that acupuncture is relatively painless and has few side effects, although recent studies have shown that serious adverse events can occur (He et al, 2012). Before routine treatment can be accepted into mainstream medicine,

acupuncture needs to have proven efficacy. In other words, acupuncture has to be demonstrably more effective than placebo. However, the use of an appropriate placebo in this context is variable. The variety of controls used for the RCTs included in this review ranged across no intervention, placebo needling, and sham acupuncture needles. Although sham needles are regarded as an acceptable control, true patient blinding has been shown to be a challenge (Tan 2011). It is possible that acupuncture needling could elicit a placebo or true biological effect over a wide area of the body not specific to 'points'. It has been suggested that a placebo effect may positively influence reproductive outcomes through mechanisms related to stress relief (Domar 2011; Meissner 2007), although postulating the biological impact of placebo is very much outside the context of this review.

Studies included in this review also had a large variation in pregnancy rates, but most studies did not report their centre's normal pregnancy rate for comparison.

Although all 20 trials in this review examined the use of acupuncture for improving the pregnancy rate with IVF, different acupuncture points were selected to achieve the same objective and it is unclear why this is the case. In Western medicine, where the standardisation of methodology is of key importance in medical research, the absence of complete concordance of the acupuncture points in these studies is an unfamiliar concept. There is no consensus amongst practicing acupuncturists as to what constitutes a reasonable variation of the acupuncture treatment protocol. There is also no consensus as to how much experience or training an acupuncturist needs to provide effective acupuncture treatment, although courses are available that provide a license to practice the art.

At the time of writing this review, the authors knew of four further studies in the area that are ongoing (ACTRN12611000226909; IRCT201011275181N4; NCT00317317; NCT01449396).

### Quality of the evidence

The overall quality of evidence for live birth outcomes was rated as low, using GRADE methods (see [Summary of findings for the main comparison](#) and [Summary of findings 2](#)). The quality of individual studies was generally low, with over 75% failing to describe an adequate method of allocation concealment (see [Figure 2](#) and [Figure 3](#)).

### Potential biases in the review process

We made every effort to identify all potentially eligible studies, and sought additional data from study authors as necessary. However,

it is possible that there are unpublished studies that were not retrieved.

### Agreements and disagreements with other studies or reviews

Several meta-analyses have been published in the last six years in this area (Anderson 2007; Cheong 2010; El-Toukhy 2010; Manheimer 2008; Zheng 2012). Depending on the data included and when the reviews were published, researchers have reached different conclusions about the beneficial effects on acupuncture on women undergoing IVF. Such discrepancies will continue to exist unless agreed standard scientific principles and research methodologies are incorporated into future studies (MacPherson 2010).

## AUTHORS' CONCLUSIONS

### Implications for practice

We found no evidence that acupuncture improves live birth rate, ongoing pregnancy rate or clinical pregnancy rate. We also found no evidence that acupuncture increases the rate of miscarriage.

### Implications for research

Future research into the value of acupuncture in improving the pregnancy rate of women undergoing IVF treatment should incorporate basic scientific principles and methodologies. Within the realm of RCTs, studies in this area should focus on the use of 'standardised' acupuncture methods so that reasonable comparisons can be made; live birth rate should be used as the primary outcome. The use of 'sham needles' may enhance the quality of the studies performed, though further research into the biological effect of sham acupuncture is needed. Ideally, studies in this area should carefully consider how they determine the necessary treatment points, gather qualitative as well as quantitative data in parallel with a three arm study design, acupuncture, no intervention and placebo needling. They should also provide their centre's pregnancy rates during the time course of the study for comparison. It is with this comprehensive study design that any clinical benefit of acupuncture can be delineated.

## ACKNOWLEDGEMENTS

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**Zheng 2012**

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\* Indicates the major publication for the study

**CHARACTERISTICS OF STUDIES**
**Characteristics of included studies** [ordered by study ID]

**Andersen 2010**

Methods	Randomised controlled trial of fertility patients in Denmark
Participants	<p>Patients (n = 635) scheduled for embryo transfer were randomised into acupuncture according to the principles of Traditional Chinese Medicine (n = 314) or placebo acupuncture (n = 321).</p> <p>The average age of the two groups of women was 31 years and the average body mass index (BMI) was 22.5 for both groups. There were similar numbers of previous IVF/ICSI cycles and similar proportions of causes of infertility between both groups.</p>
Interventions	Needle acupuncture or placebo acupuncture using Strietberger placebo needle for 25 minutes before and after embryo transfer; performed by nurses who were professional acupuncturists or by nurses who had received instruction and training by the acupuncturists prior to the trial
Outcomes	Ongoing pregnancy rate, implantation and pregnancy rates, live birth rates
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)
Notes	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generation – LOW RISK - 'the sequence of cluster randomization was based on a computer-generated list'
Allocation concealment (selection bias)	Unclear risk	'nurses did the randomization with the sealed envelope technique'
Blinding (performance bias and detection bias) All outcomes	Low risk	Sequence allocation was performed by nurses and the procedure was performed blinded to patients and the clinician performing ET
Incomplete outcome data (attrition bias) All outcomes	Low risk	No patients lost to follow up
Selective reporting (reporting bias)	Low risk	None known
Other bias	Low risk	None known

**Benson 2006**

Methods	Randomised controlled trial of fertility patients in US; abstract only
Participants	<p>Patients (n = 258) who had been scheduled for ET were randomised into needle acupuncture (n = 53), laser acupuncture (n = 53), sham laser acupuncture (n = 52), relaxation treatment (n = 50) and no treatment (n = 50). For the purpose of this meta-analysis, only the results from the needle acupuncture and no treatment groups were used.</p> <p>There were no details on the demographics as abstract only available</p>
Interventions	Needle acupuncture performed for 25 minutes before and after embryo transfer versus no intervention control group. There were no details on the qualifications of the acupuncturists as abstract only available
Outcomes	Clinical pregnancy rate
Assisted conception protocols	Protocol breakdown not provided
Notes	Emailed authors for LBR but no reply

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Abstract only; sequence generation not stated.
Allocation concealment (selection bias)	Unclear risk	Abstract only; allocation concealment not stated.
Blinding (performance bias and detection bias) All outcomes	High risk	No sham needle group used, therefore blinding not possible
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	258 participants randomized but authors did not state the number of participants that completed the study.
Selective reporting (reporting bias)	Unclear risk	Did not report live birth
Other bias	Low risk	None known

**Craig 2007**

Methods	Multicentre randomised control trial undertaken in the US; abstract only
Participants	<p>107 patients undergoing IVF randomised women into two groups: one with acupuncture treatment (n = 48) and one without (n = 46).</p> <p>There were no details on demographics as this report was presented as an abstract</p>
Interventions	Acupuncture performed for 25 minutes before and after embryo transfer, against no intervention control group. There were no details on the qualifications of the acupuncturists as abstract only available.

**Craig 2007** (Continued)

Outcomes	Ongoing and clinical pregnancy rate	
Assisted conception protocols	Protocol breakdown not provided	
Notes	No information provided by authors	
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Random sequence generation (selection bias)	Unclear risk	Abstract only; sequence generation not stated
Allocation concealment (selection bias)	Unclear risk	Abstract only; allocation concealment not stated.
Blinding (performance bias and detection bias) All outcomes	High risk	No sham acupuncture control used
Incomplete outcome data (attrition bias) All outcomes	Low risk	107 participants randomized, 94 completed the study. 10 IVF cycles cancelled, 3 patients withdrew.
Selective reporting (reporting bias)	Unclear risk	Did not report live birth
Other bias	Low risk	None known

**Dieterle 2006**

Methods	Randomised controlled trial, fertility patients in clinic in Germany	
Participants	<p>225 patients randomised: 116 to treatment and 109 to placebo. Treatment included placing Chinese herbs in patients' ears. No losses to follow up. Placebo treatment at sites that will not affect fertility, but physicians who were performing ET were blinded.</p> <p>The average age (<math>\pm</math> SD) of the study group (<math>n = 116</math>) was 35.1 years (<math>\pm 3.8</math>) compared to 34.7 years (<math>\pm 4</math>) for the placebo group (<math>n = 109</math>). There were no statistical differences in the body mass index (BMI), causes of subfertility, and number of previous cycles between the study and control groups.</p>	
Interventions	Treatment included acupuncture + Chinese herbs in ears versus control group of acupuncture at sites that are not believed to affect fertility. The intervention was performed for 30 minutes after embryo transfer and again 3 days later. All acupuncture was performed by the same practitioner	
Outcomes	Live birth rate, clinical pregnancy rates and ongoing clinical pregnancy rates	
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)	
Notes	Placebo group did not have drugs placed in ears	
<b>Risk of bias</b>		



**Dieterle 2006** (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated in the manuscript
Allocation concealment (selection bias)	Unclear risk	'randomised with sealed randomization envelopes' but not stated if these envelopes were opaque or sequentially numbered.
Blinding (performance bias and detection bias) All outcomes	Low risk	Use of placebo treatment in control group
Incomplete outcome data (attrition bias) All outcomes	Low risk	225 participants randomized; none lost to follow up.
Selective reporting (reporting bias)	Unclear risk	Not known whether LBR a pre-stated outcome
Other bias	Low risk	None known

**Domar 2009**

Methods	Randomised controlled trial of fertility patients in the US
Participants	150 patients recruited and randomised to either needle acupuncture (n = 78) and no treatment (n=68). The average age of the two groups of women was 36 years, with similar numbers of previous IVF cycles in the two groups.
Interventions	Acupuncture performed by an acupuncturist 25 minutes before and after embryo transfer versus no treatment control
Outcomes	Clinical pregnancy rate
Assisted conception protocols	Protocol breakdown not provided
Notes	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'randomisation was accomplished by using a computer-generated random numbers table'
Allocation concealment (selection bias)	Unclear risk	Not stated in the manuscript
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible to blind as control group had no intervention
Incomplete outcome data (attrition bias)	Unclear risk	146 participants randomized but number completed not reported.

**Domar 2009** (Continued)

All outcomes

Selective reporting (reporting bias)	Unclear risk	No LBR outcomes reported.
Other bias	Low risk	None known

**Fraterelli 2008**

Methods	Randomised controlled trial of fertility patients in the US; abstract only	
Participants	1000 patients randomised to five arms: needle acupuncture (n = 200), laser acupuncture (n = 202), sham laser acupuncture (n = 198), relaxation (n = 203) and non-treatment group (n = 197).  No demographics breakdown given but stated no difference between groups	
Interventions	Two treatment arms (laser and needle acupuncture) and three control arms (sham laser acupuncture, relaxation and non-treatment). For the purpose of this meta-analysis, only the results from the needle acupuncture and no treatment groups were used	
Outcomes	Chemical and clinical pregnancy rate	
Assisted conception protocols	Protocol breakdown not provided	
Notes	Only needle acupuncture versus control are relevant to this review	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Abstract only, no randomisation details given
Allocation concealment (selection bias)	Unclear risk	Abstract only, no details given
Blinding (performance bias and detection bias) All outcomes	High risk	Control group received no treatment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	not stated if all participants randomized completed the study
Selective reporting (reporting bias)	Unclear risk	No LBR outcomes reported.
Other bias	Low risk	None known

**Gejervall 2005**

Methods	Open, randomised single-centre trial performed at the IVF unit of Reproductive Medicine at Sahlgrenska University Hospital in Goteborg
Participants	<p>There were 160 women randomised in the study: 80 to the EA (electro-acupuncture) group and 80 to the CA (conventional acupuncture) group.</p> <p>The average age of the women (<math>\pm</math> SD) in the control group (<math>n = 80</math>) was 33.9 years (<math>\pm 3.7</math>) compared to 33.2 years (<math>\pm 3.6</math>) in the intervention group; the average number of IVF cycles performed was 1.56 (<math>\pm 0.93</math>) compared to 1.48 (<math>\pm 0.93</math>). The majority of women had male factor or unexplained subfertility.</p>
Interventions	The study compared electro-acupuncture at the time of oocyte retrieval (EA group) with conventional analgesia (intravenous alfentanil). Both groups also had a paracervical block performed. Electro-acupuncture was performed by midwives who had been trained in the IVF unit.
Outcomes	<p>Wellbeing was evaluated with the State Trait Anxiety Inventory (STAI). Pain and subjective expectations and experiences were recorded on a visual analogue scale (VAS). Time and drug consumption were recorded</p> <p>Pregnancy rate was recorded as secondary outcome</p>
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)
Notes	Study designed to assess effectiveness of acupuncture as an analgesic

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'randomisation was performed by the study coordinator according to a computerized list'
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding (performance bias and detection bias) All outcomes	High risk	Conventional analgesia of I.V. alfentanil used as control analgesia. Therefore both participants and personnel not blinded. Not stated if assessor was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	160 women randomized; 2 lost to follow up.
Selective reporting (reporting bias)	Unclear risk	No LBR outcome reported.
Other bias	Low risk	None

**Ho 2009**

Methods	Randomised study performed at the IVF centre of China Medical University Hospital in Taiwan
Participants	<p>A total of 44 women were enrolled in the study: 30 were randomised to acupuncture group and 14 to the control (no-acupuncture group).</p> <p>The two groups were described as comparable for demographics including age and cause of infertility</p>

**Ho 2009** (Continued)

Interventions	The study compared electro-acupuncture (twice a week for two weeks, from cycle day 2 to the day prior to oocyte retrieval) with no acupuncture around the time of oocyte retrieval
Outcomes	Outcome measures studied were clinical pregnancy and the pulsatility index (PI) of left and right uterine arteries
Assisted conception protocols	Protocol breakdown not provided
Notes	The study was designed to assess the impact of acupuncture on uterine artery blood flow and clinical pregnancy rate

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	'randomly assigned to one of the two groups by selection of a sealed envelope.'
Blinding (performance bias and detection bias) All outcomes	High risk	Control group received no treatment
Incomplete outcome data (attrition bias) All outcomes	High risk	30 randomised to acupuncture group, and 26 to control group (but 12 in the control group dropped out), leaving 30 in the acupuncture group and only 14 in the control group.
Selective reporting (reporting bias)	Unclear risk	No LBR outcome data reported.
Other bias	Low risk	None known

**Humaidan 2004**

Methods	Randomised trial of fertility patients in Denmark
Participants	200 patients randomised to either electro-acupuncture (n = 100) or conventional analgesia (n = 100) at the time of oocyte retrieval. Both groups also received a para-cervical block.
Interventions	Electro-acupuncture at the time of oocyte retrieval, given by specially trained nurses, versus conventional analgesia control (benzodiazepine, alfentanil)
Outcomes	VAS scale Clinical pregnancy rate
Assisted conception protocols	Protocol breakdown not provided
Notes	Study designed to assess effectiveness of acupuncture as an analgesic

**Risk of bias**

**Humaidan 2004** (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Details not stated
Allocation concealment (selection bias)	Low risk	Adequate: randomisation using sealed unlabelled envelopes containing a study number
Blinding (performance bias and detection bias) All outcomes	Low risk	'doctors and patients are blinded to the arm of treatment'.
Incomplete outcome data (attrition bias) All outcomes	Low risk	160 participants randomized; 8 in total withdrew from the study.
Selective reporting (reporting bias)	Unclear risk	LBR not a pre-stated outcome
Other bias	Low risk	None known

**Madaschi 2010**

Methods	Randomised controlled trial of fertility patients in Brazil	
Participants	416 patients stratified according to age and then randomised to either acupuncture group (n = 208) or control with no acupuncture (n = 208)	
Interventions	Needle acupuncture 25 minutes before and after embryo transfer versus no acupuncture control. Intervention performed by the same practitioner in all cases  There was no statistically significant difference between the two groups for demographic characteristics. The average age ( $\pm$ SD) in the acupuncture group was 35.3 ( $\pm$ 4.7) compared to 34.6 ( $\pm$ 4.6) in the control group ( $p = 0.103$ ). The average BMI in the acupuncture group was 22.4 ( $\pm$ 3.8) compared to 22.4 ( $\pm$ 2.9) in the control group ( $P = 0.951$ )  The main causes of subfertility were ovarian disorders and male factor with no statistical significance between both groups for any cause of subfertility	
Outcomes	Pregnancy rate, implantation rate, abortion rate and live birth rate	
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)	
Notes		

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'patients were randomized before the beginning of the ovarian stimulation according to computer generated randomized numbers'
Allocation concealment (selection bias)	Unclear risk	method of allocation concealment not reported

**Madaschi 2010** (Continued)

Blinding (performance bias and detection bias) All outcomes	High risk	Control group had no treatment. It was not stated if the clinicians or the assessors of the study were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	416 participants were randomized; no drop out noted.
Selective reporting (reporting bias)	Unclear risk	LBR not a prestated outcome.
Other bias	Low risk	None

**Moy 2011**

Methods	Randomized controlled trial of fertility patients in US	
Participants	160 patients undergoing IVF ± ICSI were randomised to either true acupuncture (n = 87) or sham acupuncture (n = 74)  The average age (± SD) in the true acupuncture group was 33.3 (± 0.307) years compared to 33.16 (± 0.334) years in the sham acupuncture group. There was no statistically significant difference in BMI or infertility diagnosis between the two groups, with the leading causes of infertility being male factor, ovarian dysfunction and unexplained.	
Interventions	True (needle) acupuncture performed by hospital employed licensed acupuncturists versus sham placebo acupuncture. Both interventions performed for 25 minutes before and after embryo transfer	
Outcomes	Clinical pregnancy rate and clinical symptoms during embryo transfer	
Assisted conception protocols	Protocol breakdown not provided	
Notes		

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	patients were randomized using a 'random number generator'
Allocation concealment (selection bias)	Low risk	Use of 'sealed, sequentially numbered, opaque envelopes'.
Blinding (performance bias and detection bias) All outcomes	Low risk	Control group was allocated to Sham acupuncture. The physicians and patients were blinded to the randomization until the conclusion of the study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	160 participants were randomized; 1 lost to follow up
Selective reporting (reporting bias)	Unclear risk	LBR outcome data not reported.

**Moy 2011** (Continued)

Other bias	Low risk	None
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**Paulus 2002**

Methods	Randomised controlled trial in fertility clinic in Germany
Participants	<p>160 patients randomised: 80 to treatment and 80 to no intervention control.</p> <p>The age of the women (<math>\pm</math> SD) in the control group (<math>n = 80</math>) was 32.1 years (<math>\pm 3.9</math>) compared to 32.8 years (<math>\pm 4.1</math>) in the acupuncture group (<math>n = 80</math>). In the control group the average number of previous cycles was 2.0 (<math>\pm 2.0</math>) versus 2.1 (<math>\pm 2.1</math>) in the treatment group.</p> <p>Most women had tubal disease, followed by male factor infertility then polycystic ovarian disease. These were in equal portions in both the study and control groups.</p>
Interventions	Acupuncture performed by "well-trained examiners" 25 min before and after embryo transfer for treatment group; auricular acupuncture also performed on the treatment group
Outcomes	Clinical pregnancy rates
Assisted conception protocols	Protocol breakdown not given
Notes	Same authors as <a href="#">Paulus 2003</a> but different group of patients

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated how the allocation was carried out.
Blinding (performance bias and detection bias) All outcomes	High risk	Control group had no treatment. Not stated if clinicians or assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	160 randomised; no drop out.
Selective reporting (reporting bias)	Unclear risk	Not known whether LBR a prestated outcome
Other bias	Low risk	None

**Paulus 2003**

Methods	Randomised placebo-controlled trial; abstract only
Participants	Patients were divided into two groups by random selection: embryo transfer with verum acupuncture ( $n = 100$ ) and embryo transfer with placebo needling ( $n = 100$ ).

**Paulus 2003** (Continued)

No demographic details presented

Interventions	Acupuncture or sham acupuncture performed for 25 minutes before and after embryo transfer. In the control group (n=100) a placebo needle set was used without penetrating the skin, but at the same acupoints and after the same scheme
Outcomes	Clinical pregnancy rates
Assisted conception protocols	Protocol breakdown not given
Notes	Only included women with good embryos

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer generated randomisation
Allocation concealment (selection bias)	Unclear risk	Abstract only, not stated
Blinding (performance bias and detection bias) All outcomes	Low risk	Control group had placebo needling.
Incomplete outcome data (attrition bias) All outcomes	Low risk	100 participants were randomized. No drop out reported.
Selective reporting (reporting bias)	Unclear risk	Not known whether LBR a prestated outcome
Other bias	Low risk	None

**Sator-K 2006**

Methods	Randomised controlled trial in fertility clinic in Austria
Participants	<p>Patients were randomised in proportions of 1:1:1 to treatment with electro-acupuncture (n = 32), auricular acupuncture without electrical stimulation (n = 32) or a control group without needles or electrical stimulation (n = 30).</p> <p>The mean ages (<math>\pm</math> SD) of the women undergoing IVF treatment in the group receiving electro-acupuncture with remifentanil (EA), acupuncture with remifentanil (A), and remifentanil with placebo (CO) were 33.3 years (<math>\pm</math> 1.7), 34.2 years (<math>\pm</math> 1.1) and 33.9 years (<math>\pm</math> 1.9), respectively. There were no differences in the number of failed cycles or causes of subfertility.</p>
Interventions	EA, or EA with electrical stimulation or control of conventional analgesia (remifentanil) at the time of oocyte retrieval
Outcomes	Pain intensity and subjective well being were assessed using a visual analogue scale Nausea and tiredness were also assessed using a visual rating scale Analgesic drug requirements during the entire study period



**Sator-K 2006** (Continued)

Assisted conception protocols      Protocol breakdown not provided

Notes      Study designed to assess effectiveness of acupuncture as an analgesic

Each P-Stim™ was programmed by an independent technician for electrical stimulation or no stimulation before the study. To ensure blinding of the investigator, each P-Stim™ was packed in a non-transparent case in which the respective permanent needles or adhesive tapes were also included. The packages were numbered consecutively, according to the randomisation list. Patients and investigators were blinded to the randomisation

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer generated sequence randomisation
Allocation concealment (selection bias)	Unclear risk	'Randomisation was concealed until at least 30 patients were randomized.' 'Patients and investigators were blinded to the randomisation'. Method of allocation concealment not clearly reported
Blinding (performance bias and detection bias) All outcomes	High risk	Control group had traditional I.V. pain relief.
Incomplete outcome data (attrition bias) All outcomes	Low risk	94 were randomized. 1 drop out.
Selective reporting (reporting bias)	Unclear risk	LBR outcome not reported.
Other bias	Low risk	None known

**Smith 2006**

Methods	Randomised controlled trial in fertility clinic in Australia
Participants	228 randomised, 36 excluded: 110 in treatment group and 118 in control group.  The average age of the control group ( $\pm$ SD) was 35.9 years ( $\pm$ 4.7) versus 36.1 years ( $\pm$ 4.8) in the study group; there were no differences in the number of previous treatment cycles, BMI, duration of subfertility.
Interventions	All women had 3 sessions: day 9 of stimulation, immediately before ET, and immediately after ET. For the sham acupuncture group a sham needle was used close to but not on the treatment point
Outcomes	Clinical pregnancy rates
Assisted conception protocols	Protocol breakdown not provided
Notes	After 3rd session, 24 in treatment group and 10 in control group guessed their allocation group correctly

**Smith 2006** (Continued)

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	'randomization was in balanced, variable blocks of random size prepared by a researcher not involved in the trial'.
Allocation concealment (selection bias)	Unclear risk	Not stated specifically
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Control groups had placebo needles (Streitberger) although after the 3 <sup>rd</sup> session, 24 in the treatment group and 10 in the control group guessed their allocation group correctly.
Incomplete outcome data (attrition bias) All outcomes	High risk	228 subjects were randomized. 36 women had to be withdrawn (15%).
Selective reporting (reporting bias)	Unclear risk	LBR data not reported.
Other bias	Low risk	None known

**So 2009**

Methods	Randomised controlled trial of fertility patients in Hong Kong	
Participants	<p>370 patients undergoing assisted reproductive treatment randomised to either acupuncture (n = 185) or placebo acupuncture arms (n = 185).</p> <p>The median age (interquartile range) in the acupuncture and placebo groups respectively was 36 (33 - 38) and 36 (34 - 38). Mean BMI (<math>\pm</math> SD) was similar at 21.6 (<math>\pm</math> 2.1) and 21.7 (<math>\pm</math> 2.7) kg/m<sup>2</sup> for acupuncture and placebo groups respectively.</p> <p>Both groups were comparable in terms of duration of infertility, cause of infertility, previous experience of acupuncture and smoking habit</p>	
Interventions	Needle acupuncture or placebo needle acupuncture for 25 minutes before and after embryo transfer. Intervention performed by a certified Chinese acupuncturist with a degree in Chinese Medicine and 3 years experience	
Outcomes	Pregnancy rate, clinical pregnancy rate, live birth rate, miscarriage rate	
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)	
Notes		

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomized by a computer generated randomization list

**So 2009** (Continued)

Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes from the list used. 'The sequence of randomization was concealed until interventions were assigned.'
Blinding (performance bias and detection bias) All outcomes	Low risk	'patients, clinical staff involved in the care of patients and embryologist were blinded to the treatment group assigned'. The codes were only revealed after the completion of the entire study. Control group also had placebo needles.
Incomplete outcome data (attrition bias) All outcomes	Low risk	370 participants randomized; all completed the study.
Selective reporting (reporting bias)	Low risk	None known.
Other bias	Low risk	None known

**So 2010**

Methods	Randomised controlled trial of fertility patients undergoing frozen embryo transfer in Hong Kong	
Participants	226 patients randomised to either real (n = 113) or placebo acupuncture (n=113).  The median age at thawing was 36 (34 - 38) and 36 (34 - 39) years for real and placebo acupuncture respectively. The BMI, duration and cause of infertility and previous experience of acupuncture were also comparable between the two groups.	
Interventions	Needle acupuncture according to TCM principles or placebo acupuncture with Streitberger's sham placebo needles. Intervention performed by a certified Chinese acupuncturist with a degree in Chinese Medicine and 3 years experience	
Outcomes	Overall pregnancy rate, clinical pregnancy rate, ongoing pregnancy rate, live birth rate	
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)	
Notes	More patients in placebo group correctly guessed their randomisation compared to the true acupuncture group	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	participants were randomized by a computer generated randomization list
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes from the list was used. 'The sequence of randomization was concealed until interventions were assigned.'
Blinding (performance bias and detection bias) All outcomes	Low risk	'patients, clinical staff involved in the care of patients and embryologist were blinded to the treatment group assigned'. The codes were only revealed after the completion of the entire study. Control group also had placebo needles.
Incomplete outcome data (attrition bias) All outcomes	Low risk	226 participants randomized. All completed the study.

**So 2010** (Continued)

Selective reporting (reporting bias)	Low risk	LBR available.
Other bias	Low risk	None known

**Stener-Victorin 1999**

Methods	Randomised controlled trial, conducted in Sweden	
Participants	150 women undergoing IVF and ET were randomised to receive either electro-acupuncture and a paracervical block or alfentanil analgesia and a paracervical block.  The mean ages (range) of the study and control groups were 33.3 years (25 to 42) and 34.4 years (25 to 46). There was no difference in the two groups in terms of the cause of subfertility and the number of previous cycles.	
Interventions	Acupuncture was performed at least 30 min before oocyte aspiration and PCB was placed at the start of the procedure and terminated directly after oocyte aspiration	
Outcomes	VAS, level of stress, implantation and pregnancy rates	
Assisted conception protocols	Protocol breakdown not provided	
Notes	Study designed to assess effectiveness of acupuncture as an analgesic	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Each centre randomized its patients using sealed, unlabelled envelopes" - no further details
Allocation concealment (selection bias)	Unclear risk	'sealed unlabelled envelope'
Blinding (performance bias and detection bias) All outcomes	High risk	Control group had traditional analgesia and t (Alfentanil + para cervical block) therefore blinding nor possible for clinicians or participants.
Incomplete outcome data (attrition bias) All outcomes	Low risk	150 women were randomized. 1 drop out.
Selective reporting (reporting bias)	Unclear risk	LBR data not reported.
Other bias	Unclear risk	"There is a possible bias in the study in that some of the women in the EA group were administered additional alfentanil during oocyte aspiration."

**Stener-Victorin 2003**

Methods	Randomised, controlled multi-centre trial in Sweden	
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**Acupuncture and assisted reproductive technology (Review)**

**Stener-Victorin 2003** (Continued)

Participants	<p>Women were randomised to either electro-acupuncture and a paracervical block or alfentanil and a paracervical block, as analgesia at the time of oocyte retrieval.</p> <p>The mean age (range) in the study group was 32.9 years (22 to 38) and for the control group it was 32.9 years (25 to 38). The causes of infertility and number of IVF attempts did not differ between the two groups.</p>
Interventions	<p>Women were given EA and a PCB of lidocaine hydrochloride during oocyte aspiration. Those women randomised to the alfentanil group were given alfentanil and a PCB during oocyte aspiration. The acupuncture stimulation began at least 30 min before oocyte aspiration</p>
Outcomes	<p>VAS were used for pain assessment</p> <p>Other variables recorded included abdominal pain, pain during placement of PCB, time of discomfort, adequacy of analgesia, stress level, nausea.</p> <p>IVF outcomes were pregnancy rate (number of pregnancies per embryo transfer), implantation rate (number of gestational sacs per number of transferred oocytes) and on-going pregnancies (number of pregnancies per embryo transfer after the 16th week of gestation)</p>
Assisted conception protocols	<p>Protocol breakdown not provided</p>
Notes	<p>Stopped after interim analysis as results show no difference between two groups. Study designed to assess effectiveness of acupuncture as an analgesic</p>

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	not stated
Allocation concealment (selection bias)	Unclear risk	'sealed unlabeled envelopes'
Blinding (performance bias and detection bias) All outcomes	High risk	Control group had paracervical block + Alfentanil and therefore blinding nor possible for clinicians or participants.
Incomplete outcome data (attrition bias) All outcomes	Low risk	286 randomized; 5 in the acupuncture group and 7 in the control group dropped out.
Selective reporting (reporting bias)	Unclear risk	Not known whether LBR a pre-stated outcome
Other bias	Low risk	None

**Westergaard 2006**

Methods	<p>Randomised controlled trial with patients from private clinic in Denmark</p>
Participants	<p>273 women randomised: 87 allocated to no acupuncture and 95 to acupuncture on ET day only; 91 to acupuncture on ET and ET+2 days; 27 excluded,</p>

**Westergaard 2006** (Continued)

The average ages of the three groups of women were: 37 years (27 to 45) in the control (n = 87) group, 37 years (24 to 45) in the group who had acupuncture on the day of ET (n = 95), and 37 years (27 to 45) for those with repeated acupuncture (ET + 2) (n = 91). There was no difference in the BMI between the three groups and about 67% of women had one or more attempts of IVF in the three groups.

The main causes of subfertility were described as male factor or unexplained

Interventions	Acupuncture was performed by specially trained nurses on patients undergoing ET on the day of ET, ET +2 and not on controls
Outcomes	Clinical pregnancy rate on ultrasound
Assisted conception protocols	Standard, long protocol GnRH down-regulation and the follicle stimulating hormone (FSH) or human menopausal gonadotrophin (hMG)
Notes	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation procedure handled by nurse not involved in study
Allocation concealment (selection bias)	Unclear risk	'drawing of sealed envelope' - no further details reported
Blinding (performance bias and detection bias) All outcomes	High risk	Control group had paracervical block, so blinding of the participants and personnel not possible.
Incomplete outcome data (attrition bias) All outcomes	Low risk	300 participants randomized. 27 dropped out leaving 273 participants for analysis.
Selective reporting (reporting bias)	Unclear risk	LBR data not pre-stated outcome.
Other bias	Low risk	none

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

Study	Reason for exclusion
<a href="#">Chen 2004</a>	No reply to written and electronic request; study design, allocation concealment and outcomes unclear
<a href="#">Chen 2009</a>	No reply to electronic request; study design, methods and results not known
<a href="#">Chen 2012</a>	No outcomes of interest
<a href="#">Cui 2007</a>	No reply to electronic request; study design, methods and results not known
<a href="#">Cui 2011</a>	Inadequate randomisation process in study design, based on odd and even numbers

Study	Reason for exclusion
Evans 2005	Lack details on pregnancy outcome, study design, allocation concealment and type of randomisation; no reply to written or electronic letters
Feliciani 2011	No reply to electronic request; study numbers, randomisation process and outcomes unclear
Li 2009	No reply to electronic request; study design, methods and results not known
Omodei 2010	No reply to electronic request; study design, allocation concealment and outcomes unclear
Quintero 2004	Lacks details on allocation concealment and randomisation, no reply to requests for details; crossover design

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

#### ACTRN12611000226909

Trial name or title	Acupuncture compared to sham acupuncture and standard care to improve live birth rates for women undergoing IVF: a randomised controlled trial
Methods	Parallel design, randomised controlled trial
Participants	Women aged less than 43 years, undergoing a fresh IVF or ICSI cycle, and restricted to women with the potential for a lower live birth rate defined as > 2 previous unsuccessful embryo transfers (fresh or frozen), and unsuccessful clinical pregnancies of quality embryos deemed by the embryologist to have been suitable for freezing by standard criteria
Interventions	Needle or sham acupuncture for 1 hr on day 6-8 of the IVF cycle, plus two treatments on the day of the embryo transfer, 30 minutes before and after embryo transfer. Compared to no treatment control
Outcomes	<p>Primary outcome: live birth - defined as the delivery of one or more living infants, greater than 20 weeks gestation or 400 grams or more birth weight.</p> <p>Secondary outcomes:</p> <ol style="list-style-type: none"> <li>1. clinical pregnancy defined as demonstration of fetal heart activity on ultrasound scan</li> <li>2. miscarriage defined as a non viable pregnancy prior to 12 weeks gestation</li> <li>3. quality of life</li> <li>4. self efficacy</li> </ol>
Starting date	Registration: 02/03/2011
Contact information	<p>Caroline Smith</p> <p>Centre for Complementary Medicine Research University of Western Sydney Locked Bag 1797 Penrith South DC NSW 2751, Australia</p>
Notes	

**IRCT201011275181N4**

Trial name or title	Effects of acupuncture on outcome of in vitro fertilization and intracytoplasmic sperm injection (IVF/ICSI) in women with polycystic ovarian -
Methods	Parallel design, triple blind, randomised controlled trial
Participants	Inclusion criteria: women with the diagnosis of PCO (Rotterdam criteria) admitted to the clinic for IVF or ICSI treatments of infertility
Interventions	Intervention group 1: acupuncture based on Traditional Chinese Medicine, 5 sessions of thirty minutes. Intervention 2: Control group: (placebo) the same needles are used in 5 sessions of thirty minutes
Outcomes	<p>Primary outcomes:</p> <p>Embryo quality. Timepoint: 2 days after embryo transfer. Method of measurement: diagnosed by Embryologist and with embryological criteria.</p> <p>Oocyte fertilisation rate. Timepoint: first day after embryo transfer. Method of measurement: diagnosed by embryologist and with embryological criteria</p> <p>Oocyte metaphase 2. Timepoint: before and after embryo transfer. Method of measurement: diagnosed by embryologist and with embryological criteria</p> <p>Secondary outcomes:</p> <p>Biochemical pregnancy. Timepoint: 2 weeks after embryo transfer. Method of measurement: B-hCG</p> <p>Clinical pregnancy. Timepoint: 4 weeks after embryo transfer. Method of measurement: sac observed in vaginal sonography</p> <p>Miscarriage. Timepoint: &lt;12 weeks after embryo transfer. Method of measurement: vaginal sonography</p> <p>Take home baby. Timepoint: 9 months after embryo transfer. Method of measurement: Delivery</p>
Starting date	Registration 13/04/2011
Contact information	Rashidi Batool Address: Tehran University of Medical Sciences, Valieasr Hospital and Imam Khomeini Hospital Tehran Islamic Republic of Iran
Notes	

**NCT00317317**

Trial name or title	The Effect of Acupuncture on Infertility With In-Vitro Fertilization (IVF) Patients
Methods	Parallel design, single-blinded randomised controlled trial
Participants	Inclusion criteria: - Undergoing in vitro fertilisation protocol (both IVF and intracytoplasmic sperm injection - ICSI)



**NCT00317317** (Continued)

- Acupuncture naïve
- Basal FSH <10
- Minimum age 21 years

Interventions	Acupuncture
Outcomes	Primary outcome: Clinical pregnancy rate  Secondary outcomes: <ul style="list-style-type: none"> <li>- B-endorphin levels</li> <li>- Miscarriage rate</li> <li>- Stress measurement</li> <li>- Take home baby rate</li> </ul>
Starting date	Registration: 20/06/2006
Contact information	Grant Zhang, Ph.D.  Center For Integrative Medicine, University of Maryland
Notes	

**NCT01449396**

Trial name or title	Chinese Traditional Medicine Contribution to Improve In-vitro Fertilization (IVF) Results: Acupuncture in Embryo Transfer
Methods	Parallel design, double-blinded, randomised controlled trial
Participants	Inclusion criteria: <ul style="list-style-type: none"> <li>- 18 to 35 years old</li> <li>- BMI 20-25</li> <li>- Medical indication of intracytoplasmic sperm injection (ICSI) treatment to treat sterility</li> <li>- No previous in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) treatments</li> <li>- No previous experience of acupuncture treatments</li> <li>- Make cause of sterility</li> <li>- At least one high quality embryo on the day of uterine transfer</li> </ul>
Interventions	Acupuncture versus bed rest
Outcomes	Primary outcome: pregnancy rate  Secondary outcomes: <ul style="list-style-type: none"> <li>- Analysis of the results of assisted reproductive cycle</li> <li>- Determination of serum prolactin and 24h urine cortisol</li> </ul>

**NCT01449396** (Continued)

- Endometrial vascularisation study
- Rating preconceived ideas about acupuncture

Starting date	Registered: 04/10/2011
Contact information	Monica Romeu romeu_monvil@gva.es
Notes	

**NCT01608048**

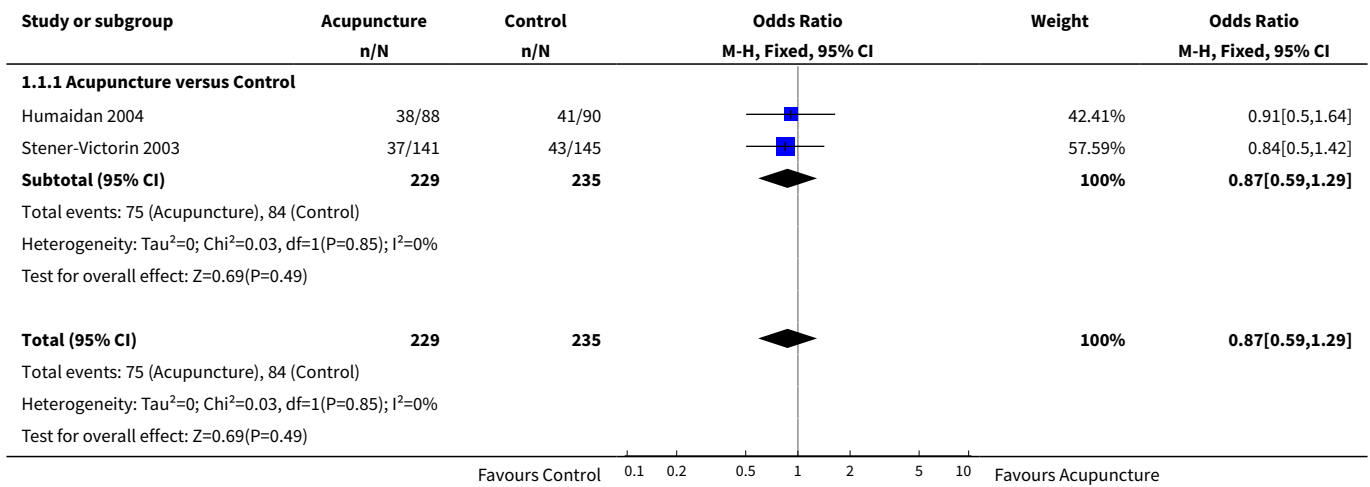
Trial name or title	Transcutaneous Electrical Acupoint Stimulation to Improve Pregnancy Rates for Women Undergoing in Vitro Fertilization
Methods	Single blind RCT
Participants	Women undergoing IVF
Interventions	Transcutaneous electrical acupoint stimulation vs no acupuncture
Outcomes	Live birth, clinical pregnancy
Starting date	May 2012
Contact information	Cui Hong Zheng, Doctor ph: 86-27-83663275 email: 635342693@qq.com
Notes	

**DATA AND ANALYSES**
**Comparison 1. Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture)**

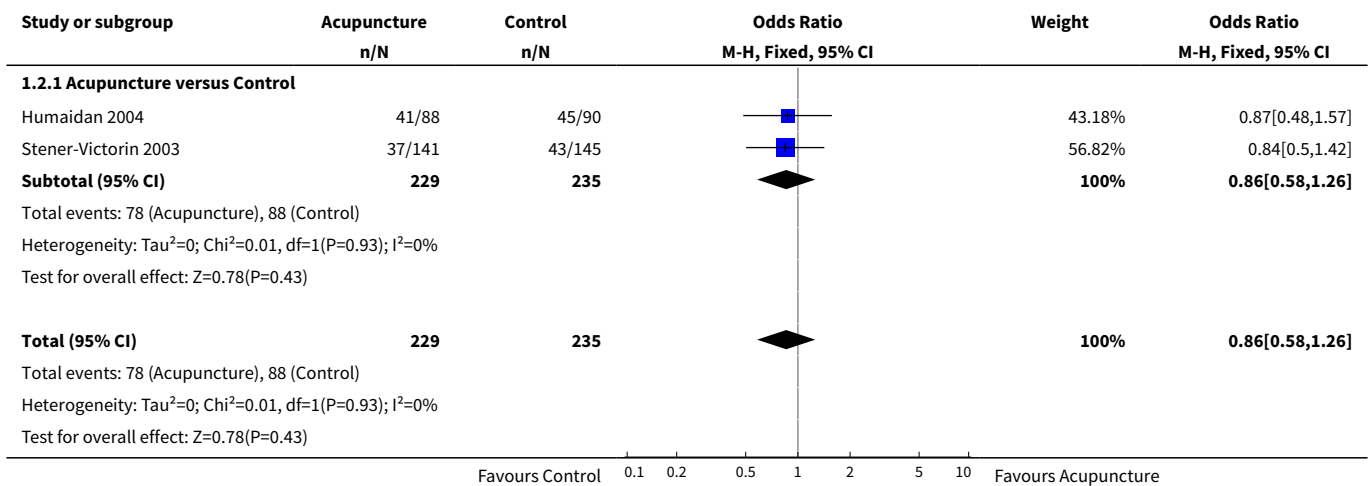
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
<b>1 Live Birth Rate</b>	2	464	Odds Ratio (M-H, Fixed, 95% CI)	0.87 [0.59, 1.29]
1.1 Acupuncture versus Control	2	464	Odds Ratio (M-H, Fixed, 95% CI)	0.87 [0.59, 1.29]
<b>2 Ongoing Pregnancy Rate</b>	2	464	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.58, 1.26]
2.1 Acupuncture versus Control	2	464	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.58, 1.26]
<b>3 Clinical Pregnancy Rate</b>	6	912	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.78, 1.62]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Acupuncture versus Control	6	912	Odds Ratio (M-H, Random, 95% CI)	1.12 [0.78, 1.62]
4 Miscarriage rate	4	262	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.42, 1.47]
4.1 Acupuncture versus Control	4	262	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.42, 1.47]

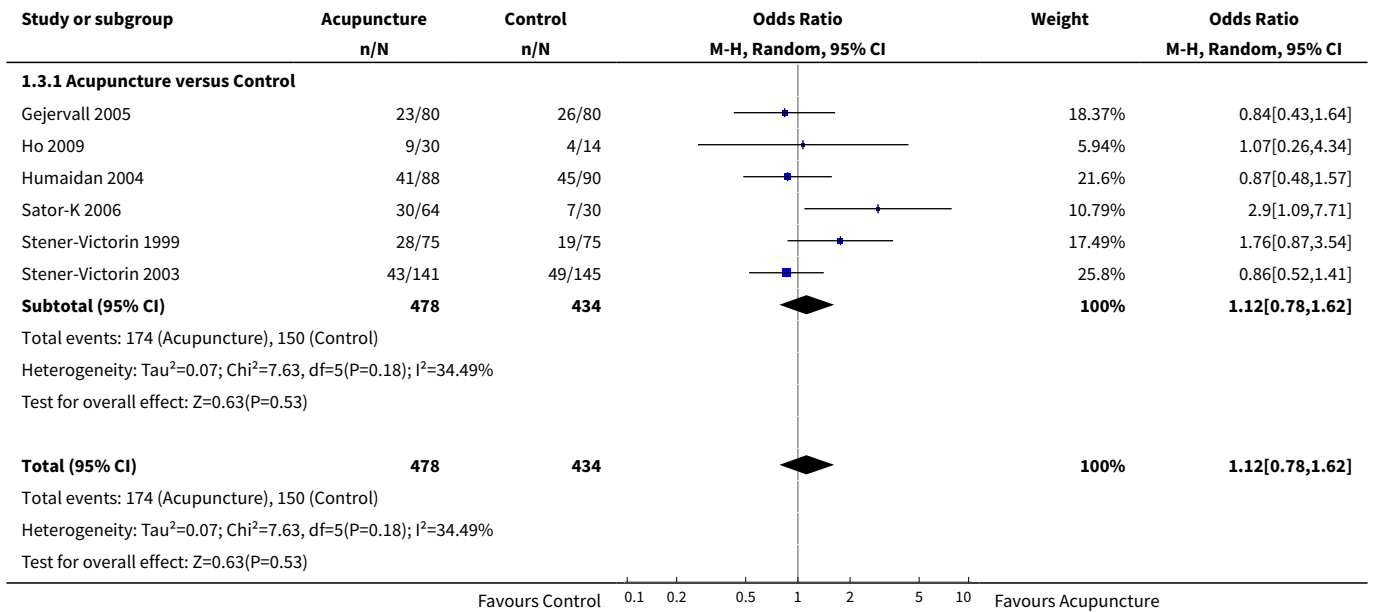
**Analysis 1.1. Comparison 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), Outcome 1 Live Birth Rate.**



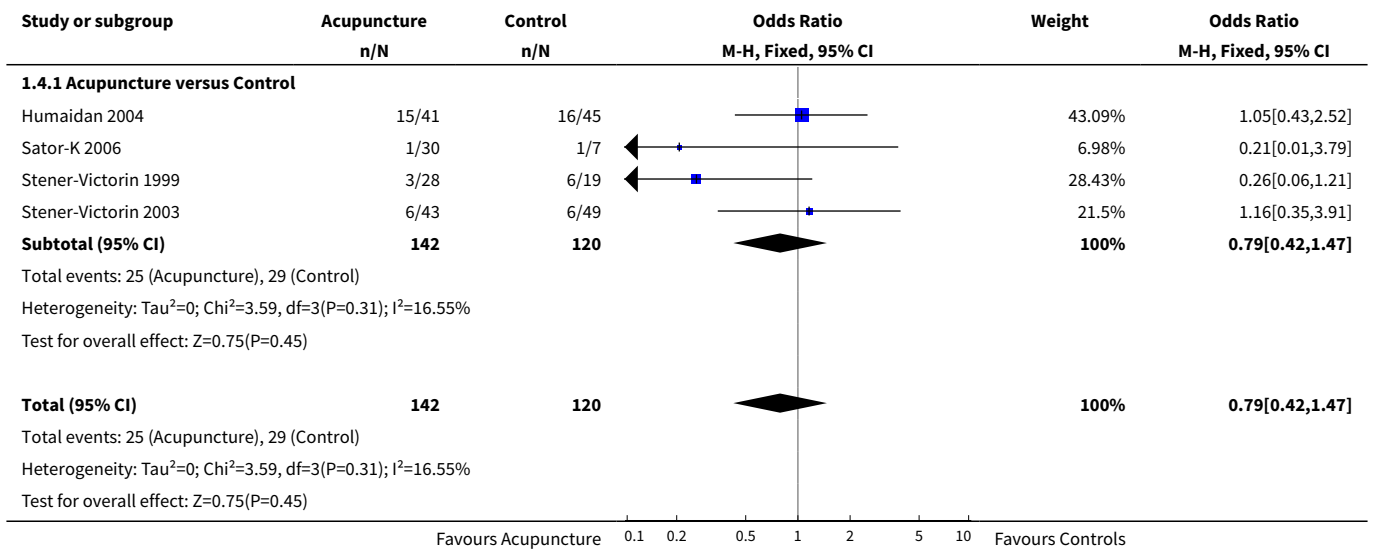
**Analysis 1.2. Comparison 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), Outcome 2 Ongoing Pregnancy Rate.**



**Analysis 1.3. Comparison 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), Outcome 3 Clinical Pregnancy Rate.**



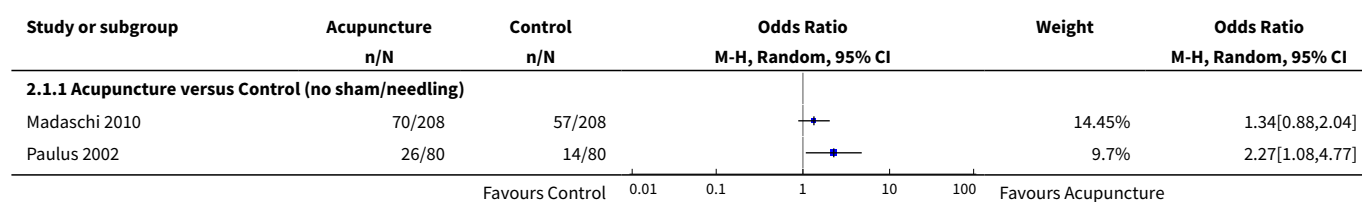
**Analysis 1.4. Comparison 1 Acupuncture around the time of oocyte retrieval versus control (sham, placebo, no acupuncture), Outcome 4 Miscarriage rate.**

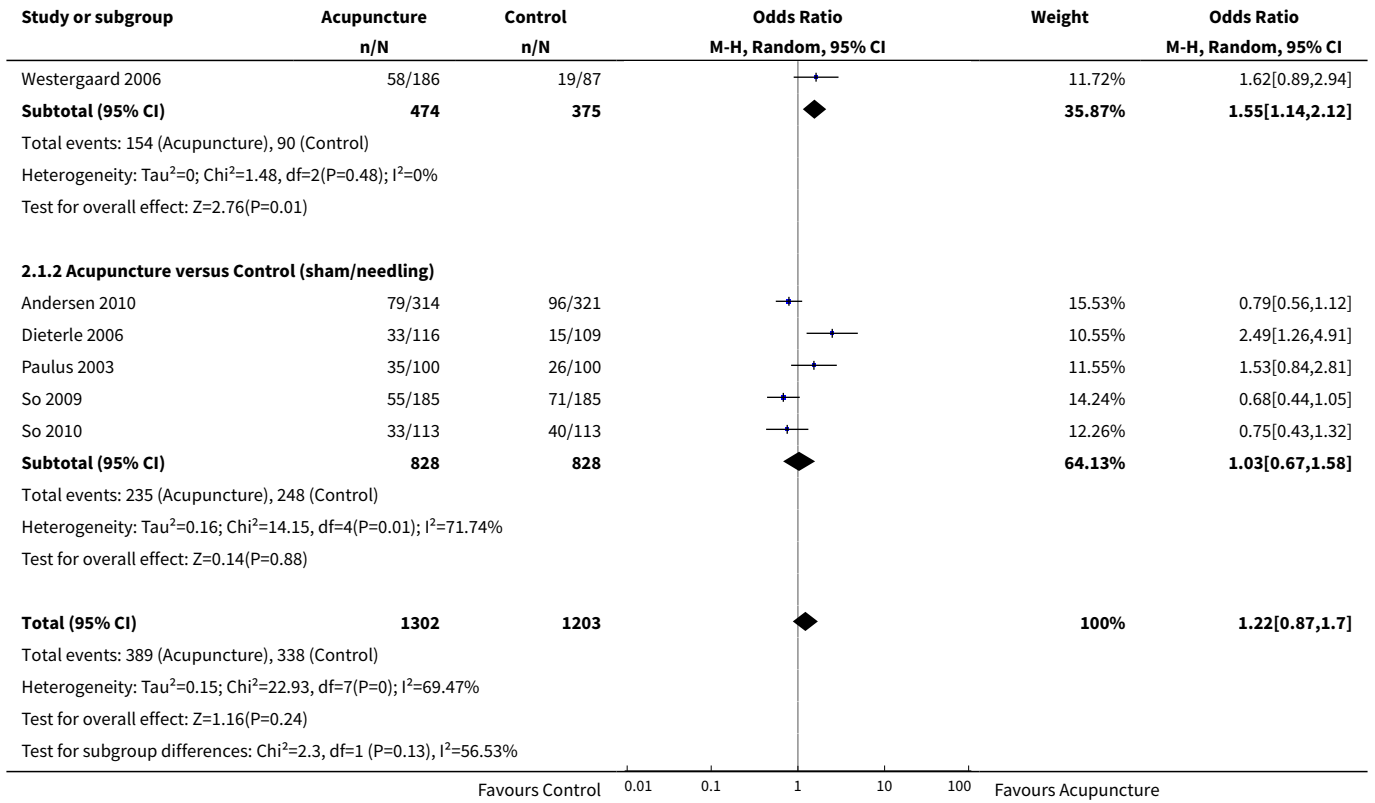


**Comparison 2. Acupuncture on and around the day of ET versus control**

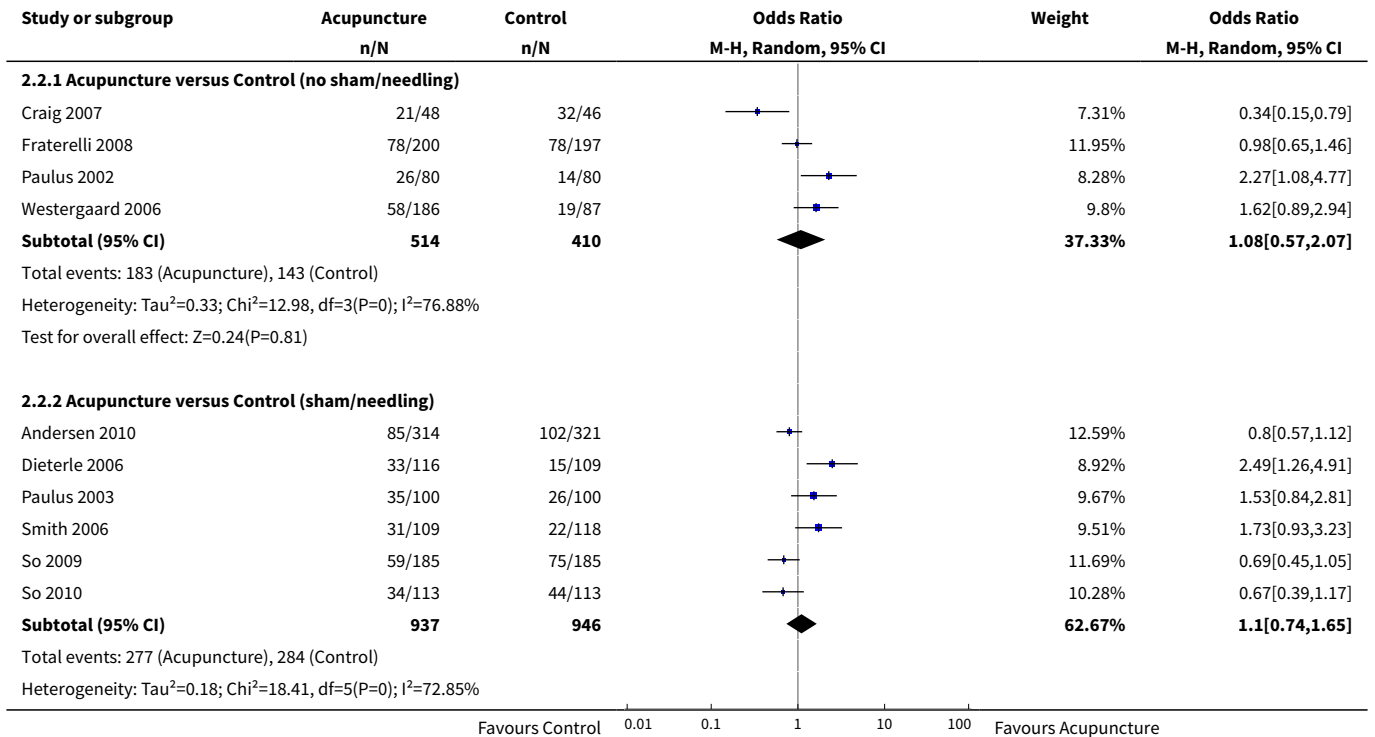
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
<b>1 Live Birth</b>	8	2505	Odds Ratio (M-H, Random, 95% CI)	1.22 [0.87, 1.70]
1.1 Acupuncture versus Control (no sham/needling)	3	849	Odds Ratio (M-H, Random, 95% CI)	1.55 [1.14, 2.12]
1.2 Acupuncture versus Control (sham/needling)	5	1656	Odds Ratio (M-H, Random, 95% CI)	1.03 [0.67, 1.58]
<b>2 Ongoing pregnancy</b>	10	2807	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.80, 1.52]
2.1 Acupuncture versus Control (no sham/needling)	4	924	Odds Ratio (M-H, Random, 95% CI)	1.08 [0.57, 2.07]
2.2 Acupuncture versus Control (sham/needling)	6	1883	Odds Ratio (M-H, Random, 95% CI)	1.10 [0.74, 1.65]
<b>3 Clinical pregnancy</b>	14	3632	Odds Ratio (M-H, Random, 95% CI)	1.11 [0.87, 1.42]
3.1 Acupuncture versus Control (no sham/needling)	7	1589	Odds Ratio (M-H, Random, 95% CI)	1.21 [0.84, 1.73]
3.2 Acupuncture versus Control (sham/needling)	7	2043	Odds Ratio (M-H, Random, 95% CI)	1.04 [0.74, 1.46]
<b>4 Miscarriage</b>	6	616	Odds Ratio (M-H, Fixed, 95% CI)	1.10 [0.73, 1.67]
4.1 Acupuncture versus Control (no sham/needling)	2	245	Odds Ratio (M-H, Fixed, 95% CI)	1.20 [0.57, 2.49]
4.2 Acupuncture versus Control (sham/needling)	4	371	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.64, 1.76]
<b>5 Multiple gestation</b>	2	795	Odds Ratio (M-H, Fixed, 95% CI)	1.32 [0.74, 2.35]
5.1 Acupuncture versus Control (sham/needling)	2	795	Odds Ratio (M-H, Fixed, 95% CI)	1.32 [0.74, 2.35]

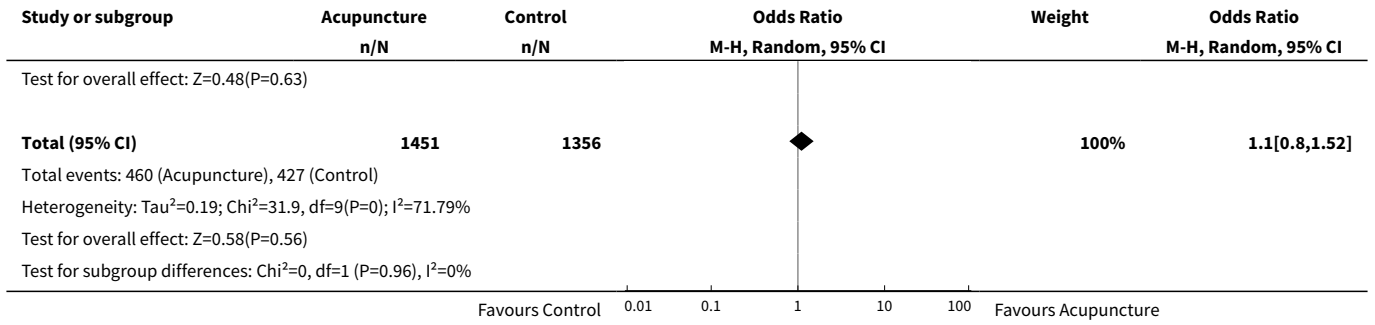
**Analysis 2.1. Comparison 2 Acupuncture on and around the day of ET versus control, Outcome 1 Live Birth.**



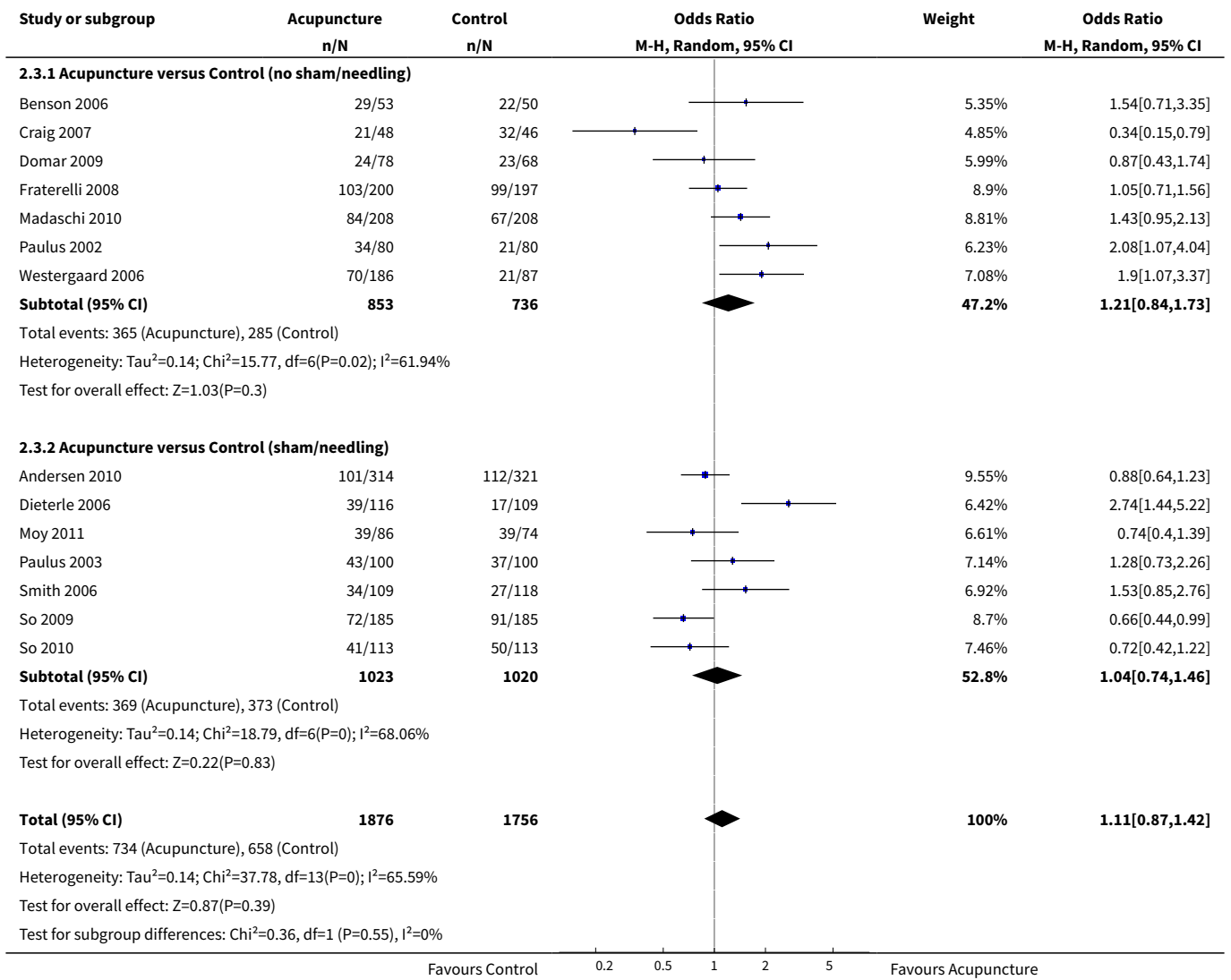


**Analysis 2.2. Comparison 2 Acupuncture on and around the day of ET versus control, Outcome 2 Ongoing pregnancy.**

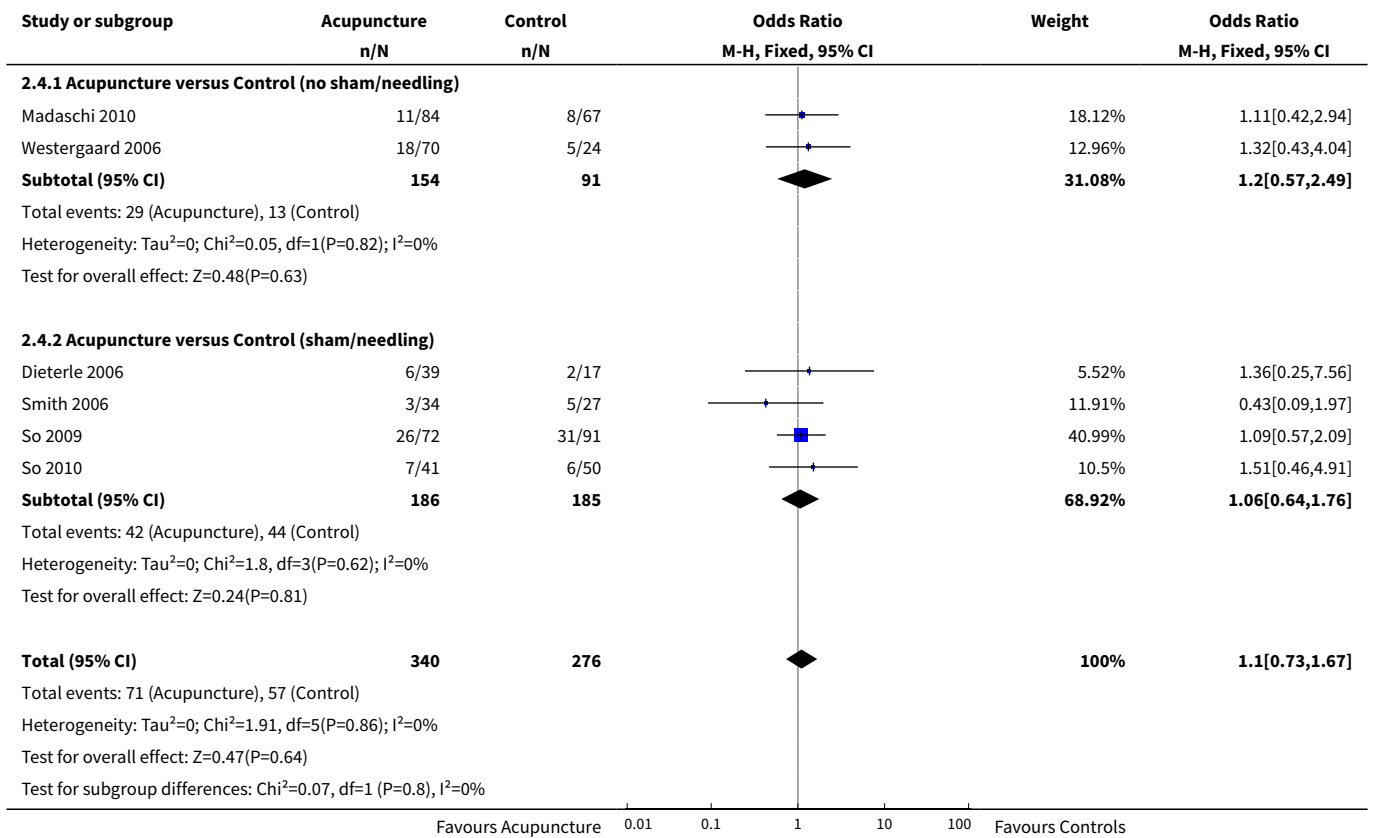




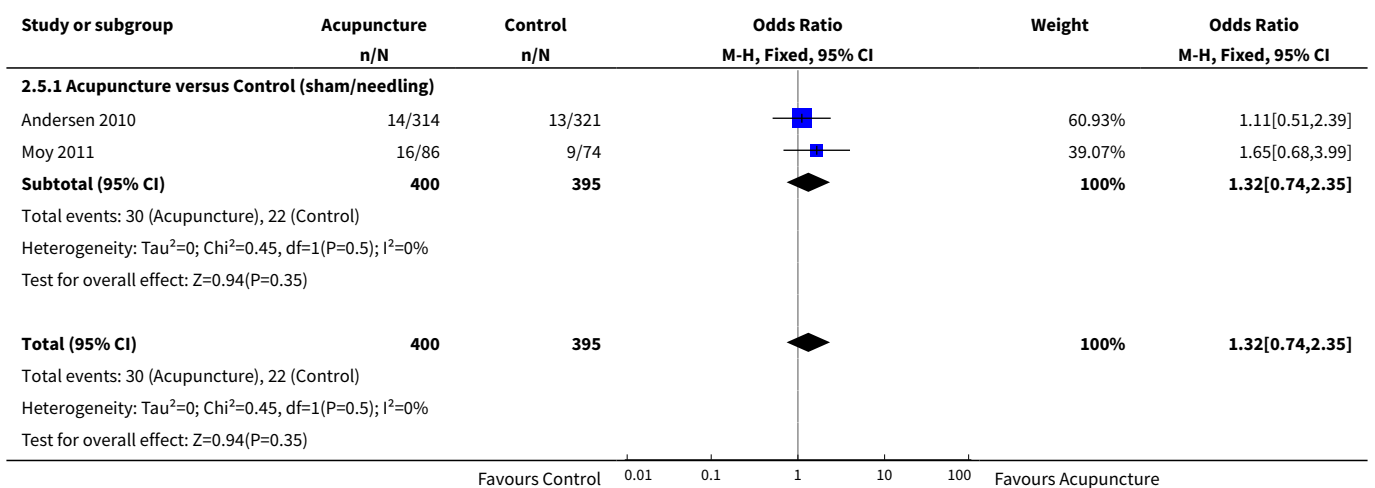
**Analysis 2.3. Comparison 2 Acupuncture on and around the day of ET versus control, Outcome 3 Clinical pregnancy.**



**Analysis 2.4. Comparison 2 Acupuncture on and around the day of ET versus control, Outcome 4 Miscarriage.**



**Analysis 2.5. Comparison 2 Acupuncture on and around the day of ET versus control, Outcome 5 Multiple gestation.**





## ADDITIONAL TABLES

**Table 1. Table 1. Summary of acupuncture points used.**

Acupuncture points	Craig 2007	Wester- gaard 2006	Di- eter- le 2006	Paulus 2002 Paulus 2003 An- der- sen 2010; Do- mar 2009	Madaschilo 2010 2009	Moy 2011	Smith 2006	So 2009	So 2010	Sten- er-Vic- torin 1999	Sten- er-Vic- torin 2003	Gejer- vall 2005	Hu- maid- an 2004	Sa- tor-K 2006
Cv6 (Qi Hai)	Y (be- fore ET)					Y								
Cx6 (Neiguan)	Y			Y			Y							
DU 20 (bai hui)						Y								
GV 20 (Baihui)	Y	Y (around ET and ET + 2)		Y	Y		Y	Y		Y	Y	Y	Y	Y
Liv 2 (Xingjian)														
Liv 3 (Taichong)	Y			Y		Y	Y							
LI 4 (Hegu)	Y	Y (ET + 2)	Y (ET + 3)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
LI 10 (Shoushanli)												Y		
LR 3 (Taichong)		Y			Y	Y		Y						
LU 7 (lieque)				Y										

**Table 1. Table 1. Summary of acupuncture points used.** (Continued)

SP 6 (Sanyinjiao)	Y	Y (ET + 2)	Y (ET + 3)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
SP 8 (Diji)	Y	Y	Y	Y	Y		Y	Y	Y					
SP 10 (Xuehai)	Y		Y	Y	Y		Y	Y	Y	Y				
ST28						Y								
ST29 (Guilai)	Y	Y (ET and ET + 2)	Y	Y	Y		Y	Y	Y		Y	Y	Y	
ST36 (Zushanli)	Y		Y (ET + 3)	Y	Y		Y	Y	Y	Y	Y	Y	Y	
PC6 (Neiguan)		Y	Y		Y				Y					
Ren 3 (Zhongji)		Y (ET + 2)												
RN 4 (Guanyuan)			Y			Y								
RN6 (Qihai)			Y			Y								
K3 (Tai Xi)	Y (after ET)													
K13 (Taxiu)			Y (ET + 3)											
K1 11(Henggu)	Y											Y		
TE 5 (Weiguan)													Y	
EX-CA 1 (Zigong)						Y								

**Table 2. Table 2. Summary of the treatment intended for the respective acupuncture points**

Acupuncture points	Intended treatment
Cx6 (Neiguan)	<p>Location: 2 cun above the transverse crease of the wrist, between the tendons of muscle palmaris longus and muscle flexor radialis.</p> <p>Indications            Cardiac pain, palpitation, stuffy chest, pain in the hypochondriac region, stomach ache, nausea, vomiting, hiccups, mental disorders, epilepsy, insomnia, febrile diseases, irritability, malaria, contracture and pain in elbow and arm.</p> <p>Traditional action            Opens the chest, regulates heart Qi and blood, regulates and clears the Triple Burner, calms the mind, regulates the terminal Yin, harmonizes the stomach.</p>
GV 20 (Baihui)	<p>Location: on the midline of the head, 7 cun directly above the posterior hairline, approximately on the midpoint of the line connecting the apexes of the two auricles.</p> <p>Indications            Headache, vertigo, tinnitus, nasal obstruction, aphasia by apoplexy, coma, mental disorders, prolapse of the rectum and the uterus.</p> <p>Traditional action            Clears the mind, lifts the spirits, tonifies yang, strengthens the ascending function of the spleen, eliminates interior wind, promotes resuscitation.</p>
Liv 2 (Xingjian)	<p>Location: on the dorsum of the foot between the 1st and 2nd toes, proximal to the margin of the web at the junction of the red and white skin.</p> <p>Point associations:            Ying Spring point            Fire point</p> <p>Actions and effects:            Generally, clears LV Fire - extreme irritability, red face, eyes, tongue.            Clears heat from the lower Jiao - burning urination.            Useful for "true heat, false cold" - lack of Qi flow to the extremities (cold hands or feet).</p>
Liv 3 (Taichong)	<p>Location: on the dorsum of the foot in a depression distal to the junctions of the 1st and 2nd metatarsal bones.</p> <p>Point associations:            Shu Stream point            Earth point            Yuan source point</p> <p>Actions and effects:            Generally, resolves stagnation and tonifies Yin - balancing for all LV pathologies.            LV Qi Stagnation, LV Yang Rising - headaches, dizziness, canker sores.            Eye issues - blurred vision, red, swollen, painful eyes.            Menstrual issues from deficient blood, Yin, Qi, LV Qi stagnation - dysmenorrhea, amenorrhoea, PMS, breast tenderness.            Genital issues - pain and swelling, hernia, impotence, seminal emission.            Stagnation in the middle warmer - subcostal tension, chest or flank pain, swellings in the axillary region.            Digestive issues from LV attacking ST/SP - nausea, vomiting, constipation, diarrhoea with undigested food.            Calming point - anger, irritability, insomnia, anxiety.            With LI 4, four gates treatment - powerfully effects the flow of Qi and blood in the body.</p>

**Table 2. Table 2. Summary of the treatment intended for the respective acupuncture points** (Continued)

	<p>Location: On the dorsum of the foot in a depression distal to the junctions of the 1st and 2nd metatarsal bones.</p> <p>Point associations: Shu Stream point Earth point Yuan source point</p> <p>Actions and effects: Generally, resolves stagnation and tonifies Yin - balancing for all LV pathologies. LV Qi Stagnation / LV Yang Rising - headaches, dizziness, canker sores. Eye issues - blurred vision, red, swollen, painful eyes. Menstrual issues from deficient blood, Yin, Qi a/or LV Qi stagnation - dysmenorrhea, amenorrhoea, PMS, breast tenderness. Genital issues - pain and swelling, hernia, impotence, seminal emission. Stagnation in the middle warmer - subcostal tension, chest/flank pain, swellings in the axillary region. Digestive issues from LV attacking ST/SP - nausea, vomiting, constipation, diarrhoea with undigested food. Calming point - anger, irritability, insomnia, anxiety. With LI 4, four gates treatment - powerfully effects the flow of Qi and blood in the body.</p>
LI 4 (Hegu)	<p>Location: in the middle of the 2nd metacarpal bone on the radial side.</p> <p>Precautions: no moxa, no needle in pregnancy.</p> <p>Point associations: Yuan source point Entry point Command point for face, nose, mouth and jaw</p> <p>Actions and effects: Releases the exterior for wind-cold or wind-heat syndromes. Strengthens the wei qi, improves immunity. Regulates the sweat glands, for excessive sweating tonify LI 4 then disperse KD 7 and vice versa. Any problem on the face - sense organs, mouth, teeth, jaw, toothache, allergies, rhinitis, hay fever, acne, eye problems, etc. Toothache use both LI 4 &amp; ST 44 - LI for the lower jaw &amp; ST for the upper jaw. Headache, especially frontal, sinus (yangming area). Chronic pain. Influence the circulation of Qi and blood - use the four gates, LI 4 &amp; LV 3 to strongly move the Qi and blood in the body clearing stagnation and alleviating pain. Promote labor or for retained placenta.</p>
LI 10 (Shoushanli)	<p>Location: 2 cm below LI 11 on the LI 5 to LI 11 line.</p> <p>Actions and effects: The following relationships exist between the ST and the LI and can be used to treat ST, LI and SI organ problems. SI: LI 8 &amp; ST 39. LI: LI 9 &amp; ST 37. ST: LI 10 &amp; ST 36. Shoulder, elbow and wrist pain issues, general aches in these areas. Less dispersive and more tonifying than other LI points. Epigastric and abdominal pain, ulcers, vomiting.</p> <p>Location: 2 cm below LI 11 on the LI 5 to LI 11 line.</p>
SP 6 (Sanyinjiao)	<p>Location: 3 cm directly above the tip of the medial malleolus on the posterior border of the tibia.</p>

**Table 2. Table 2. Summary of the treatment intended for the respective acupuncture points** (Continued)

	<p>Precautions: no needle in pregnancy</p> <p>Point associations: Intersection point of the SP, LV and KD (3 leg yin meridians)</p> <p>Actions and effects: Tonify Yin and blood, all spleen disorders. Digestive disorders, sinking or prolapse. Gynecological issues, male sexual issues, difficult labor (expel fetus). Bleeding disorders, cool blood in hot skin diseases. Insomnia and other anxiety related emotions.</p>
SP 8 (Diji)	<p>Location: 3 cm below SP 9 on line connecting SP 9 and the tip of the medial malleolus.</p> <p>Point associations: Xi Cleft point.</p> <p>Actions and effects: Xi Cleft point - acute and painful menstrual issues due to blood stagnation - clotting, fibroids, dysmenorrhoea. Male infertility.</p>
SP 10 (Xuehai)	<p>Location: with knee flexed, 2 cm above the superior medial border of the patella on the bulge of the medial portion of quadriceps femoris (vastus medialis).</p> <p>Actions and effects: Any gynaecological issues originating from blood, heat, stasis and/or deficiency - irregular menstruation, cramping, PMS. Skin problems from damp-heat or hot blood.</p>
ST29 (Guilai)	<p>Location: 2 cm lateral to the AML level with CV 3.</p> <p>Actions and effects: Excess or cold/deficient disorders of the lower warmer - amenorrhoea, irregular menstruation, qi stagnation/masses. Running Piglet disorder.</p>
ST36 (Zushanli)	<p>Location: 3 cm below ST 35, one finger width lateral from the anterior border of the tibia.</p> <p>Point associations: He Sea point Lower Lower He Sea point of the ST Earth point Sea of Water and Grain point Command point of the abdomen</p> <p>Actions and effects: Tonify deficient Qi or blood. Tonify Wei Qi. All issues involving the stomach or the spleen. Clear disorders along the course of the channel - breast problems, lower leg pain. Earth as the mother of Metal - will support lung function in cases of asthma, wheezing, dyspnoea. Psychological/Emotional disorders - PMS, depression, nervousness.</p>
PC6 (Neiguan)	<p>Location: 2 cm above the wrist crease between the tendons of palmaris longus and flexor carpi radialis.</p> <p>Point associations:</p>

**Table 2. Table 2. Summary of the treatment intended for the respective acupuncture points** (Continued)

	<p>Luo Connecting point Yin Wei Master point coupled with SP 4</p> <p>Actions and effects: Similar to PC 3 but more for chronic heart symptoms from Qi stagnation. Opens and relaxes the chest, chest tightness, asthma, angina, palpitations. Insomnia, other spirit disorders of an excess or deficient nature, mania, nervousness, stress, poor memory. Nausea, seasickness, motion sickness, vomiting, epigastric pain. Carpal tunnel syndrome.</p>
Ren 3 (Zhongji)	<p>Location (zhongji): 1 cm superior to qugu. Regulates LR, warms KI, irregular menses.</p>
RN 4 (Guanyuan)	<p>Location: 1.5 cm lateral to the Du meridian, at the level of the lower border of the spinous process of the 5th lumbar vertebra.</p> <p>Indications Low back pain, abdominal distension, diarrhoea, enuresis, sciatica, frequent urination.</p> <p>Traditional action Strengthens the lower back, removes obstructions from the channel.</p>
RN6 (Qihai)	<p>Location: 1.5 cm lateral to the Du meridian, at the level of the lower border of the spinous process of the third lumbar vertebra.</p> <p>Indications Low back pain, irregular menstruation, dysmenorrhoea, asthma.</p> <p>Traditional action Strengthens lower back, removes obstructions from channel, regulates Qi and blood.</p>
KI 3 (Taixi)	<p>Location: in the depression between the medial malleolus and tendo calcaneus, at the level with the tip of the medial malleolus.</p> <p>Indications Sore throat, toothache, deafness, tinnitus, dizziness, spitting of blood, asthma, thirst, irregular menstruation, insomnia, nocturnal emission, impotence, frequency of micturition, pain in the lower back.</p> <p>Traditional action Tonifies the kidneys, benefits essence, strengthens the lower back and knees, regulates the uterus.</p>
KI 11 (Henggu)	<p>Location: 1.5 cm posterior to Wuchu (UB 5), 1.5 cm lateral to the Du meridian.</p> <p>Indications Headache, blurring of vision, nasal obstruction.</p> <p>Traditional action Clears heat and eliminates vexation, brightens the eyes and opens the portals.</p>
TE 5 (Weiguan)	<p>Location: 1.5 cm lateral to the lower border of the spinous process of the eighth thoracic vertebra.</p> <p>Indications Diabetes, vomiting, abdominal pain, pain in the chest and hypochondriac region.</p> <p>Traditional action Relieves stagnation of blood.</p>

## APPENDICES

### Appendix 1. MDSG search string

Menstrual Disorders and Subfertility Database Search strategy for IRS911

All reports which described randomised controlled trials of acupuncture in assisted conception were identified using the following search strategy.

Keywords CONTAINS "ART" or "assisted reproduction" or "assisted reproduction techniques" or "IVF" or "ICSI" or "in vitro fertilisation" or "in-vitro fertilisation techniques" or "in vitro fertilization" or "in vitro maturation" or "intracytoplasmic sperm injection" or "subfertility" or "Infertility" or "IUI" or "Intrauterine Insemination" or "\*\*Embryo Transfer" or "ET" or Title CONTAINS "ART" or "assisted reproduction" or "assisted reproduction techniques" or "IVF" or "ICSI" or "in vitro fertilisation" or "in-vitro fertilisation techniques" or "in vitro fertilization" or "in vitro maturation" or "intracytoplasmic sperm injection" or "subfertility" or "Infertility" or "IUI" or "Intrauterine Insemination" or "\*\*Embryo Transfer" or "ET"

AND

Keywords CONTAINS "acupoint" or "acupressure" or "acupressure-acupuncture therapy" or "acupuncture" or "electro-acupuncture" or "electroacupuncture" or "moxibustion" or "Tui Na" or "ear electroacupuncture" or "ear point pressing" or Title CONTAINS "acupoint" or "acupressure" or "acupressure-acupuncture therapy" or "acupuncture" or "electro-acupuncture" or "electroacupuncture" or "moxibustion" or "Tui Na" or "ear electroacupuncture" or "ear point pressing"

### Appendix 2. MEDLINE

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1950 to Present>

- 1 exp reproduction techniques/ (101304)
- 2 exp fertility agents/ (24722)
- 3 (in vitro adj5 fertili\$).tw. (16577)
- 4 ivf.tw. (12990)
- 5 icsi.tw. (4184)
- 6 (intracytoplas\$ adj5 sperm\$).tw. (4102)
- 7 subfertil\$.tw. (2853)
- 8 (sperm\$ adj5 inject\$).tw. (5040)
- 9 suzi.tw. (101)
- 10 (subzon\$ adj5 sperm\$).tw. (110)
- 11 (zona adj5 dissect\$).tw. (111)
- 12 pzd.tw. (61)
- 13 (ovar\$ adj5 hyperstim\$).tw. (3208)
- 14 ohss.tw. (899)
- 15 (oocyt\$ adj5 retriev\$).tw. (3100)
- 16 (oocyt\$ adj5 pickup).tw. (48)
- 17 (sperm\$ adj5 prepa\$).tw. (1589)
- 18 (acrosom\$ adj5 sperm\$).tw. (4519)

- 19 (sperm\$ adj5 stimul\$).tw. (2014)
- 20 (sperm\$ adj5 pentox\$).tw. (114)
- 21 (sperm\$ adj5 caff\$).tw. (143)
- 22 (sperm\$ adj5 kalli\$).tw. (59)
- 23 (sperm\$ adj5 swimup\$).tw. (4)
- 24 (sperm adj5 percol\$).tw. (239)
- 25 (embry\$ adj5 biops\$).tw. (563)
- 26 (cocult\$ adj5 embry\$).tw. (401)
- 27 (cocult\$ adj5 trophobl\$).tw. (33)
- 28 (luteal phase adj5 support).tw. (210)
- 29 (sperm\$ adj5 cryopreserv\$).tw. (1809)
- 30 (frozen adj5 embry\$).tw. (1648)
- 31 (antisperm\$ adj5 antibod\$).tw. (1061)
- 32 (sperm\$ adj5 antibod\$).tw. (2406)
- 33 (artific\$ adj5 inseminat\$).tw. (4842)
- 34 (cervi\$ adj5 inseminat\$).tw. (201)
- 35 (fallopian tub\$ adj5 perfus\$).tw. (30)
- 36 (luteal adj5 defect\$).tw. (375)
- 37 (luteal adj5 dysfunct\$).tw. (82)
- 38 (ovulat\$ adj5 induc\$).tw. (6757)
- 39 (intraut\$ adj5 inseminat\$).tw. (1569)
- 40 (ectop\$ adj5 preg\$).tw. (7399)
- 41 (tub\$ adj5 preg\$).tw. (4499)
- 42 inseminat\$.tw. (12887)
- 43 varicoc\$.tw. (3433)
- 44 fertility/ (28979)
- 45 fertilization/ (11655)
- 46 insemination/ (630)
- 47 ovum implantation/ (8013)
- 48 Ovarian Hyperstimulation Syndrome/ (1424)
- 49 (embry\$ adj5 transf\$).tw. (16430)



- 50 or/1-49 (198724)
- 51 acupuncture/ (944)
- 52 exp acupuncture therapy/ (14092)
- 53 electroacupuncture/ (1949)
- 54 meridians/ (341)
- 55 acupuncture points/ (2977)
- 56 acupunctur\$.tw. (12149)
- 57 (electroacupunctur\$ or electro-acupunctur\$).tw. (2370)
- 58 acupoint\$.tw. (1825)
- 59 ((meridian or non-meridian or trigger) adj10 point\$).tw. (1359)
- 60 exp Moxibustion/ (887)
- 61 (moxabustion or moxibustion or moxa\$).tw. (2215)
- 62 or/51-61 (19443)
- 63 randomised controlled trial.pt. (307764)
- 64 controlled clinical trial.pt. (83549)
- 65 randomized.ab. (220349)
- 66 placebo.tw. (132278)
- 67 clinical trials as topic.sh. (153325)
- 68 randomly.ab. (163109)
- 69 trial.ti. (95112)
- 70 (crossover or cross-over or cross over).tw. (50660)
- 71 or/63-70 (747590)
- 72 exp animals/ not humans.sh. (3606997)
- 73 71 not 72 (691399)
- 74 50 and 62 and 73 (54)
- 75 (200710\$ or 200711\$ or 200712\$).ed. (201896)
- 76 (2008\$ or 2009\$ or 2010\$).ed. (2609966)
- 77 75 or 76 (2811862)
- 78 74 and 77 (23)

### Appendix 3. CENTRAL

Database: EBM Reviews - Cochrane Central Register of Controlled Trials

- 1 exp reproduction techniques/ (2310)
- 2 exp fertility agents/ (1423)
- 3 (in vitro adj5 fertili\$).tw. (1280)
- 4 ivf.tw. (1749)
- 5 icsi.tw. (600)
- 6 (intracytoplas\$ adj5 sperm\$).tw. (385)
- 7 subfertil\$.tw. (124)
- 8 (sperm\$ adj5 inject\$).tw. (431)
- 9 suzi.tw. (13)
- 10 (subzon\$ adj5 sperm\$).tw. (19)
- 11 (zona adj5 dissect\$).tw. (23)
- 12 pzd.tw. (6)
- 13 (ovar\$ adj5 hyperstim\$).tw. (506)
- 14 ohss.tw. (138)
- 15 (oocyt\$ adj5 retriev\$).tw. (547)
- 16 (oocyt\$ adj5 pickup).tw. (7)
- 17 (sperm\$ adj5 prepa\$).tw. (98)
- 18 (acrosom\$ adj5 sperm\$).tw. (54)
- 19 (sperm\$ adj5 stimul\$).tw. (113)
- 20 (sperm\$ adj5 pentox\$).tw. (45)
- 21 (sperm\$ adj5 caff\$).tw. (7)
- 22 (sperm\$ adj5 kalli\$).tw. (16)
- 23 (sperm\$ adj5 swimup\$).tw. (0)
- 24 (sperm adj5 percol\$).tw. (38)
- 25 (embry\$ adj5 biops\$).tw. (26)
- 26 (cocult\$ adj5 embry\$).tw. (20)
- 27 (cocult\$ adj5 trophobl\$).tw. (0)
- 28 (luteal phase adj5 support).tw. (122)
- 29 (sperm\$ adj5 cryopreserv\$).tw. (59)
- 30 (frozen adj5 embry\$).tw. (114)
- 31 (antisperm\$ adj5 antibod\$).tw. (48)

- 32 (sperm\$ adj5 antibod\$).tw. (49)
- 33 (artific\$ adj5 inseminat\$).tw. (54)
- 34 (cervi\$ adj5 inseminat\$).tw. (19)
- 35 (fallopian tub\$ adj5 perfus\$).tw. (23)
- 36 (luteal adj5 defect\$).tw. (34)
- 37 (luteal adj5 dysfunct\$).tw. (10)
- 38 (ovulat\$ adj5 induc\$).tw. (535)
- 39 (intraut\$ adj5 inseminat\$).tw. (368)
- 40 (ectop\$ adj5 preg\$).tw. (170)
- 41 (tub\$ adj5 preg\$).tw. (139)
- 42 inseminat\$.tw. (599)
- 43 varicoc\$.tw. (106)
- 44 fertility/ (101)
- 45 fertilization/ (127)
- 46 insemination/ (3)
- 47 ovum implantation/ (313)
- 48 Ovarian Hyperstimulation Syndrome/ (121)
- 49 (embry\$ adj5 transf\$).tw. (1050)
- 50 or/1-49 (5752)
- 51 acupuncture/ (100)
- 52 exp acupuncture therapy/ (1824)
- 53 electroacupuncture/ (299)
- 54 meridians/ (25)
- 55 acupuncture points/ (662)
- 56 acupunctur\$.tw. (3825)
- 57 (electroacupunctur\$ or electro-acupunctur\$).tw. (559)
- 58 acupoint\$.tw. (687)
- 59 ((meridian or non-meridian or trigger) adj10 point\$).tw. (256)
- 60 exp Moxibustion/ (117)
- 61 (moxabustion or moxibustion or moxa\$).tw. (513)
- 62 or/51-61 (5069)

63 50 and 62 (34)

64 limit 63 to yr="2007 -Current" (13)

#### **Appendix 4. EMBASE**

Database: EBM Reviews - Cochrane Central Register of Controlled Trials

1 exp reproduction techniques/ (2310)

2 exp fertility agents/ (1423)

3 (in vitro adj5 fertili\$).tw. (1280)

4 ivf.tw. (1749)

5 icsi.tw. (600)

6 (intracytoplas\$ adj5 sperm\$).tw. (385)

7 subfertil\$.tw. (124)

8 (sperm\$ adj5 inject\$).tw. (431)

9 suzi.tw. (13)

10 (subzon\$ adj5 sperm\$).tw. (19)

11 (zona adj5 dissect\$).tw. (23)

12 pzd.tw. (6)

13 (ovar\$ adj5 hyperstim\$).tw. (506)

14 ohss.tw. (138)

15 (oocyt\$ adj5 retriev\$).tw. (547)

16 (oocyt\$ adj5 pickup).tw. (7)

17 (sperm\$ adj5 prepa\$).tw. (98)

18 (acrosom\$ adj5 sperm\$).tw. (54)

19 (sperm\$ adj5 stimul\$).tw. (113)

20 (sperm\$ adj5 pentox\$).tw. (45)

21 (sperm\$ adj5 caff\$).tw. (7)

22 (sperm\$ adj5 kalli\$).tw. (16)

23 (sperm\$ adj5 swimup\$).tw. (0)

24 (sperm adj5 percol\$).tw. (38)

25 (embry\$ adj5 biops\$).tw. (26)

26 (cocult\$ adj5 embry\$).tw. (20)

27 (cocult\$ adj5 trophobl\$).tw. (0)

- 
- 28 (luteal phase adj5 support).tw. (122)
- 29 (sperm\$ adj5 cryopreserv\$).tw. (59)
- 30 (frozen adj5 embryo\$).tw. (114)
- 31 (antisperm\$ adj5 antibod\$).tw. (48)
- 32 (sperm\$ adj5 antibod\$).tw. (49)
- 33 (artific\$ adj5 inseminat\$).tw. (54)
- 34 (cervi\$ adj5 inseminat\$).tw. (19)
- 35 (fallopian tub\$ adj5 perfus\$).tw. (23)
- 36 (luteal adj5 defect\$).tw. (34)
- 37 (luteal adj5 dysfunct\$).tw. (10)
- 38 (ovulat\$ adj5 induc\$).tw. (535)
- 39 (intraut\$ adj5 inseminat\$).tw. (368)
- 40 (ectop\$ adj5 preg\$).tw. (170)
- 41 (tub\$ adj5 preg\$).tw. (139)
- 42 inseminat\$.tw. (599)
- 43 varicoc\$.tw. (106)
- 44 fertility/ (101)
- 45 fertilization/ (127)
- 46 insemination/ (3)
- 47 ovum implantation/ (313)
- 48 Ovarian Hyperstimulation Syndrome/ (121)
- 49 (embry\$ adj5 transf\$).tw. (1050)
- 50 or/1-49 (5752)
- 51 acupuncture/ (100)
- 52 exp acupuncture therapy/ (1824)
- 53 electroacupuncture/ (299)
- 54 meridians/ (25)
- 55 acupuncture points/ (662)
- 56 acupunctur\$.tw. (3825)
- 57 (electroacupunctur\$ or electro-acupunctur\$).tw. (559)
- 58 acupoint\$.tw. (687)

59 ((meridian or non-meridian or trigger) adj10 point\$).tw. (256)

60 exp Moxibustion/ (117)

61 (moxabustion or moxibustion or moxa\$).tw. (513)

62 or/51-61 (5069)

63 50 and 62 (34)

64 limit 63 to yr="2007 -Current" (13)

### Appendix 5. AMED

Database: AMED (Allied and Complementary Medicine)

1 (IVF or ICSI or IUI).tw. (29)

2 "embryo transfer".tw. (3)

3 ("in vitro fertilisation" or "in vitro fertilization").tw. (22)

4 ("intrauterine insemination" or "intracytoplasmic sperm injection").tw. (10)

5 exp Infertility female/ (122)

6 exp acupuncture therapy/ (5986)

7 acupuncture.tw. (8055)

8 exp Moxibustion/ (419)

9 (moxibustion or moxabustion or moxa\$).tw. (498)

10 or/6-9 (8837)

11 or/1-5 (149)

12 10 and 11 (31)

13 limit 12 to yr="2007 -Current" (13)

### Appendix 6. CINHAL

1 Controlled study/ or randomised controlled trial/

2 (drug\$ adj5 compar\$).ti,ab,hw,tn,mf.

3 placebo/

4 random\$.ti,ab,hw,tn,mf.

5 latin square.ti,ab,hw,tn,mf.

6 crossover.ti,ab,hw,tn,mf.

7 cross-over.ti,ab,hw,tn,mf.

8 placebo\$.ti,ab,hw,tn,mf.

9 ((doubl\$ or singl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).ti,ab,hw,tn,mf.

10 (comparative adj5 trial\$).ti,ab,hw,tn,mf.

11 (clinical adj5 trial\$).ti,ab,hw,tn,mf.

12 or/1-11

13 animal/ not (human/ and animal/)

14 12 not 13

15 exp reproduction techniques/

16 exp fertility agents/

17 (in vitro adj5 fertili\$).tw.

18 ivf.tw.

19 icsi.tw.

20 (intracytoplas\$ adj5 sperm\$).tw.

### Acupuncture and assisted reproductive technology (Review)

- 21 subfertil\$.tw.  
 22 (sperm\$ adj5 inject\$).tw.  
 23 suzi.tw.  
 24 (subzon\$ adj5 sperm\$).tw.  
 25 (zona adj5 sperm\$).tw.  
 26 (zona adj5 dissect\$).tw.  
 27 pzd.tw.  
 28 (ovar\$ adj5 hyperstim\$).tw.  
 29 ohss.tw.  
 30 (oocyt\$ adj5 retriev\$).tw.  
 31 (oocyt\$ adj5 pickup).tw.  
 32 (sperm\$ adj5 prepa\$).tw.  
 33 (acrosom\$ adj5 sperm\$).tw.  
 34 (sperm\$ adj5 stimul\$).tw.  
 35 (sperm\$ adj5 pentox\$).tw.  
 36 (sperm\$ adj5 caff\$).tw.  
 37 (sperm\$ adj5 kalli\$).tw.  
 38 (sperm\$ adj5 swimup\$).tw.  
 39 (sperm adj5 percol\$).tw.  
 40 (embry\$ adj5 biops\$).tw.  
 41 (cocult\$ adj5 embry\$).tw.  
 42 (cocult\$ adj5 trophobl\$).tw.  
 43 (luteal phase adj5 support).tw.  
 44 (sperm\$ adj5 cryopreserv\$).tw.  
 45 (frozen adj5 embry\$).tw.  
 46 (antisperm\$ adj5 antibod\$).tw.  
 47 (sperm\$ adj5 antibod\$).tw.  
 48 (artific\$ adj5 inseminat\$).tw.  
 49 (cervi\$ adj5 inseminat\$).tw.  
 50 (fallopian tub\$ adj5 perfus\$).tw.  
 51 (luteal adj5 defect\$).tw.  
 52 (luteal adj5 dysfunct\$).tw.  
 53 (ovulat\$ adj5 induc\$).tw.  
 54 (intraut\$ adj5 inseminat\$).tw.  
 55 (ectop\$ adj5 preg\$).tw.  
 56 (tub\$ adj5 preg\$).tw.  
 57 inseminat\$.tw.  
 58 varicoc\$.tw.  
 59 fertility/  
 60 fertilization/  
 61 insemination/  
 62 ovum implantation/  
 63 Ovarian Hyperstimulation Syndrome/  
 64 (embry\$ adj5 transf\$).tw.  
 65 or/15-64  
 66 65 and 14  
 67 acupuncture/ or electroacupuncture/ or meridians/ or acupuncture points/  
 68 acupunctur\$.tw.  
 69 (electroacupunctur\$ or electro-acupunctur\$).tw.  
 70 acupoint\$.tw.  
 71 ((meridian or non-meridian or trigger) adj10 point\$).tw.  
 72 exp MOXIBUSTION/  
 73 (moxibustion or moxabustion or moxa).tw.  
 74 or/67-73  
 75 66 and 74  
 76 from 75 keep 1-8

## Appendix 7. PsycINFO

Database: PsycINFO

- 1 (IVF or ICSI or IUI).tw. (305)

- 2 "embryo transfer".tw. (74)
- 3 ("in vitro fertilisation" or "in vitro fertilization").tw. (405)
- 4 ("intrauterine insemination" or "intracytoplasmic sperm injection").tw. (28)
- 5 exp Reproductive Technology/ (1025)
- 6 exp Infertility/ (1378)
- 7 or/1-6 (2241)
- 8 exp Acupuncture/ (850)
- 9 acupuncture.tw. (1164)
- 10 Moxibustion.tw. (19)
- 11 (moxibustion or moxabustion or moxa\$).tw. (24)
- 12 acupressure.tw. (76)
- 13 electroacupuncture.tw. (1)
- 14 acu\$ point\$.tw. (97)
- 15 or/8-14 (1306)
- 16 7 and 15 (3)

## WHAT'S NEW

Date	Event	Description
23 July 2013	New citation required but conclusions have not changed	Seven new studies included in this update ( <a href="#">Andersen 2010</a> ; <a href="#">Fraterelli 2008</a> ; <a href="#">Ho 2009</a> ; <a href="#">Madaschi 2010</a> ; <a href="#">Moy 2011</a> ; <a href="#">So 2009</a> ; <a href="#">So 2010</a> )
23 July 2013	New search has been performed	Updated review

## HISTORY

Protocol first published: Issue 1, 2008  
 Review first published: Issue 4, 2008

Date	Event	Description
13 June 2008	Amended	Converted to new review format.
13 October 2007	New citation required and conclusions have changed	Substantive amendment



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## CONTRIBUTIONS OF AUTHORS

Ying Cheong developed the selection criteria, wrote the review and performed the analysis. Ernest Ng co-authored the review. William Ledger acted as a moderator for the meta-analysis and co-wrote the review. Sarah Dix performed the analysis, and co-wrote the review.

## DECLARATIONS OF INTEREST

Ernest Ng is an author for [So 2009](#) and [So 2010](#).

## SOURCES OF SUPPORT

### Internal sources

- None, Not specified.

### External sources

- Cochrane Menstrual and Subfertility Group, New Zealand.  
Support of search strategy, advice, refereeing and proof reading

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the 2013 update the following changes were made.

A third comparison was added - acupuncture versus acupuncture + ART.

Ongoing pregnancy and clinical pregnancy rates were moved from primary to secondary outcomes.

The methodology section was rewritten with subheadings.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Acupuncture Therapy; \*Live Birth; \*Pregnancy Rate; \*Reproductive Techniques, Assisted; Embryo Transfer; Oocyte Retrieval; Randomized Controlled Trials as Topic; Time Factors

### MeSH check words

Female; Humans; Male; Pregnancy