Cochrane Library

Cochrane Database of Systematic Reviews

Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women (Review)

Brown J, Buckingham K, Buckett W, Abou-Setta AM

Brown J, Buckingham K, Buckett W, Abou-Setta AM.
Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women.
Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD006107.
DOI: 10.1002/14651858.CD006107.pub4.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Julie Brown[1], Karen Buckingham[2], William Buckett[3], Ahmed M Abou-Setta[4]

[1]Liggins Institute, The University of Auckland, Auckland, New Zealand. [2]Repromed, Auckland, New Zealand. [3]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynecology, McGill University, Montreal, Canada. [4]Knowledge Synthesis Platform, George and Fay Yee Centre for Healthcare Innovation, University of Manitoba, Winnipeg, Canada

Contact address: Julie Brown, Liggins Institute, The University of Auckland, Park Rd, Grafton, Auckland, 1142, New Zealand. j.brown@auckland.ac.nz.

Editorial group: Cochrane Gynaecology and Fertility Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 3, 2016.
Review content assessed as up-to-date: 6 May 2015.

Citation: Brown J, Buckingham K, Buckett W, Abou-Setta AM. Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women. *Cochrane Database of Systematic Reviews* 2016, Issue 3. Art. No.: CD006107. DOI: 10.1002/14651858.CD006107.pub4.

ABSTRACT

Background

Many women undergoing an assisted reproductive technology (ART) cycle will not achieve a live birth. Failure at the embryo transfer stage may be due to lack of good-quality embryo/s, lack of uterine receptivity, or the transfer technique itself. Numerous methods, including the use of ultrasound guidance for proper catheter placement in the endometrial cavity, have been suggested as more effective techniques of embryo transfer. This review evaluates the efficacy of ultrasound-guided embryo transfer (UGET) compared with 'clinical touch' (CTET), which is the traditional method of embryo transfer and relies on the clinician's tactile senses to judge when the transfer catheter is in the correct position.

Objectives

To determine whether ultrasound guidance compared with clinical touch improves pregnancy outcomes in women undergoing embryo transfer during ART cycles.

Search methods

For the 2016 update of this review, we ran updated searches in the Cochrane Gynaecology and Fertility Group trials register (May 2015), the Cochrane Central Register of Controlled Trials (the Cochrane Library, May 2015), MEDLINE (2009 to May 2015), and EMBASE (2009 to May 2015). We also handsearched relevant conference proceedings: American Society for Reproductive Medicine (ASRM), European Society for Human Reproduction and Embryology (ESHRE), and International Federation of Gynecology and Obstetrics (FIGO). There were no language restrictions.

Selection criteria

We included only randomised controlled trials.

Data collection and analysis

Two review authors independently assessed eligibility and quality of trials and extracted data from those selected. We calculated odds ratio (OR) and 95% confidence interval (CI) for dichotomous outcomes. No outcomes were reported using continuous data. We assessed the overall quality of the evidence for the main findings using the GRADE working group methods.

Main results

This systematic review now has 21 included studies (four of which we added in the 2016 update), two studies awaiting assessment, and 47 excluded studies. In total, data for meta-analyses were available in 21 trials (n = 6218 women), of which only four reported live births.

UGET was associated with an increased chance of a live birth/ongoing pregnancy compared with CTET (OR 1.47, 95% CI 1.30 to 1.65; 13 trials; n = 5859 women; I^2 = 74%; low-quality evidence). Sensitivity analysis by including only trials with low risk of selection bias or by using a random-effects model did not alter the effect. We estimate that for women with a chance of a live birth/ongoing pregnancy of 23% using CTET, this would increase to between 28% and 33% using UGET. We considered the quality of the evidence using GRADE methodology to be low.

UGET was associated with an increase in the chance of a clinical pregnancy (OR 1.31, 95% CI 1.17 to 1.45; 20 trials; n = 6711 women; I^2 = 42%; moderate-quality evidence). We identified no differences between groups for the incidence of adverse events including multiple pregnancy, ectopic pregnancy, or miscarriage. These events were relatively rare, and sample sizes limited the ability to detect such differences.

Authors' conclusions

The evidence suggests ultrasound guidance improves the chance of live birth/ongoing and clinical pregnancies compared with clinical touch, without increasing the chance of multiple pregnancy, ectopic pregnancy, or miscarriage. Methodological limitations included: only four studies reporting details of both computerised randomisation techniques and adequate allocation concealment, only four studies reported on the outcome of live birth, and none of the nine studies that reported on ongoing pregnancy reported on live birth, suggesting possible reporting bias. Adequate reporting of randomisation and allocation concealment will improve the quality of future studies. The primary outcome measure of future studies should be the reporting of live births per woman randomised.

PLAIN LANGUAGE SUMMARY

Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Review question

We wanted to learn whether ultrasound-guided embryo transfer (UGET) improves pregnancy outcomes compared with clinical touch. The traditional method of embryo transfer, clinical touch relies on the clinician's tactile senses to judge when the transfer catheter is in the correct position.

Background

The inability of some women undergoing fertility treatment to achieve a live birth may be due to a number of factors, such as lack of good-quality embryo/s, problems with the uterus, or the transfer technique itself. This review looks at one aspect of the transfer technique, whether ultrasound guidance improves pregnancy outcomes compared with clinical touch (clinical judgement without any technical assistance).

Study characteristics

We found 21 randomised controlled trials that compared UGET with clinical touch in a total of 6218 women. The evidence is current to May 2015.

Key results

Live birth/ongoing pregnancies were increased for the ultrasound-guided group compared with the clinical touch group, based on low-quality evidence. We estimate that for women with a chance of a live birth/ongoing pregnancy of 23% using clinical touch, this would increase to between 28% and 33% using UGET. Data for live birth should be interpreted carefully, as differences between the studies make drawing a conclusion difficult. The evidence suggests that in studies that used the same brand of transfer catheter in both the ultrasound-guided and the clinical touch groups, ultrasound guidance was linked to an increase in the chance of a live birth. There was no evidence that the risk of harm using UGET, including miscarriage, ectopic pregnancies, and multiple pregnancies, is any different than when clinical touch is used to guide the embryo transfer.

Quality of the evidence

The quality of the evidence for live birth/ongoing pregnancy was low due to poor reporting of study methods and inconsistency in trial results.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Ultrasound guided embryo transfer versus clinical touch

Patient or population: Women undergoing embryo transfer as part of IVF or ICSI cycle
Intervention: Ultrasound guided embryo transfer
Comparison: Clinical touch

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with 'clinical touch'	Risk with ultrasound-guided embryo transfer				
Live birth and ongoing pregnancy (per woman randomised)	229 per 1000	304 per 1000 (279 to 329)	OR 1.47 (1.30 to 1.65)	5859 (13 RCTs)	⊕⊕◯◯ LOW[12]	
Live birth	210 per 1000	290 per 1000 (256 to 324)	OR 1.53 (1.29 to 1.80)	3117 (4 RCTs)	⊕⊕◯◯ LOW[23]	
Ongoing pregnancy	263 per 1000	333 per 1000 (298 to 372)	OR 1.40 (1.19 to 1.66)	2742 (9 RCTs)	⊕⊕⊕◯ MODERATE[4]	
Clinical pregnancy (per woman randomised)	267 per 1000	323 per 1000 (299 to 346)	OR 1.31 (1.17 to 1.45)	6711 (20 RCTs)	⊕⊕⊕◯ MODERATE[3]	
Multiple pregnancy (per woman randomised)	60 per 1000	67 per 1000 (53 to 85)	OR 1.13 (0.87 to 1.45)	3379 (8 RCTs)	⊕⊕⊕◯ MODERATE[3]	
Miscarriage (per woman randomised)	44 per 1000	44 per 1000 (33 to 57)	OR 0.99 (0.74 to 1.31)	4053 (11 RCTs)	⊕⊕⊕◯ MODERATE[3]	
Ectopic pregnancy (per woman randomised)	5 per 1000	3 per 1000 (1 to 7)	OR 0.64 (0.28 to 1.49)	3761 (8 RCTs)	⊕⊕⊕◯ MODERATE[3]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the median risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **ICSI:** intracytoplasmic sperm injection; **IVF:** in-vitro fertilisation; **RCT:** randomised controlled trial; **RR:** risk ratio; **OR:** odds ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Lack of clarity for the majority of the elements of risk of bias. Only four of the included studies reported on live birth. None of the studies reporting ongoing pregnancy reported live birth. Downgraded one level.
[2] $I^2 > 70\%$; downgraded one level.
[3] Lack of detail to be able to make a judgement on most of the elements of risk of bias. Downgraded one level.
[4] Lack of detail to be able to make a judgement on most of the elements of risk of bias, none of these trials reported on live birth. Downgraded one level.

BACKGROUND

Description of the condition

Since the first pregnancy using in vitro fertilisation was achieved nearly 40 years ago (Steptoe 1978), many aspects of the procedure, such as ovarian stimulation, oocyte recovery, and the in vitro techniques of fertilisation and embryo culture, have undergone major revision. In contrast, the technique of embryo transfer has remained largely unchanged. Approximately 80% of women undergoing in vitro fertilisation/intracytoplasmic sperm injection today will reach the embryo transfer stage with good-quality embryos. However, only a small proportion of these women will then go on to achieve a clinical pregnancy, and even fewer will achieve a live birth. This makes the embryo transfer phase the final and least successful step in assisted reproductive technology. Indeed, it is estimated that up to 85% of replaced embryos fail to implant, despite the selection of apparently normal embryos for transfer (Sallam 2002). This failure may be due to lack of good-quality embryo/s, lack of uterine receptivity, or the technique of embryo transfer itself.

Description of the intervention

Embryos are usually replaced into the uterine cavity through a transcervical transfer catheter between days 2 to 5 of development. Traditionally, the 'clinical touch' method has been used to guide placement of the transfer catheter to within ~10 mm from the uterine fundus prior to injection of the embryos. This method is essentially 'blind' and relies on the clinician's tactile senses to judge when the transfer catheter is in the correct position. Some clinicians transfer the embryos at a fixed distance from the external os (~6 cm), however this may not take into account variation in cervical length or uterine size, or position (retroverted). Others will conduct a 'dummy' embryo transfer to determine the length of the endometrial cavity prior to the actual embryo transfer.

Assessment of the transfer catheter position using the clinical touch method is often unreliable. This was demonstrated by Woolcott and Stanger (Woolcott 1997), who utilised transvaginal ultrasound to observe catheter placement in relation to the endometrial surface and uterine fundus during 121 embryo transfers. They noted suboptimal catheter placement in more than half of cases, with the catheter either indenting or embedded in the endometrium.

It is generally accepted that an easy, atraumatic embryo transfer is essential for successful implantation (Matorras 2002). It is possible that minimising endometrial trauma could decrease myometrial contractions, which could in turn enhance implantation. Most clinicians try to avoid having the catheter tip come into contact with the uterine fundus during embryo transfer (Kovacs 1999), as it has been suggested that this may stimulate uterine contractions (Lesny 1998), which in turn may lead to expulsion of the embryos. Indeed, it has been noted that high-frequency uterine contractions visualised by ultrasound are associated with a lower ongoing clinical pregnancy rate (Fanchin 1998).

The clinical touch method may thus be challenged as a potential cause of cycle failure as a result of (1) initiation of uterine contractility that may lead to immediate or delayed expulsion of the embryo/s, and (2) the inability to accurately identify the ideal location for deposition of embryos, especially in women with acute utero-cervical angulations, cervical stenosis, or anatomical distortion of the cervical canal and uterus.

Numerous methods to improve the technique of embryo transfer have been studied in an attempt to improve pregnancy rates, including changing the type of catheter used, performing a trial, or 'mock' transfer before the actual procedure, removing any cervical mucus prior to transfer, avoiding the use of a tenaculum, encouraging bed rest following embryo transfer, comparing full and empty bladder, as well as performing the procedure under ultrasound guidance. This review currently focuses on the role of transabdominal ultrasound.

How the intervention might work

The use of abdominal ultrasound to guide embryo transfer was first discussed by Strickler et al (Strickler 1985), who postulated that this would allow accurate and atraumatic positioning of the catheter tip near the uterine fundus, along with visualisation of the injection of the transfer fluid containing the embryos. By allowing identification of the cervical canal and endometrial cavity, ultrasound can facilitate atraumatic penetration of the catheter into the uterus, thereby minimising endometrial trauma. Moreover, its use can confirm that the catheter tip is beyond the internal os of the cervix and that placement of the embryos is at the desired level in the endometrial cavity (Lorusso 2005). This can be especially helpful in women where the uterine anatomy may be distorted by fibroids or septae (Hurley 1991). For these reasons, ultrasound-guided embryo transfers have been rated as "easier" and "cleaner" by clinicians (Prapas 2001). Disadvantages are the need for a second operator, a longer time to execute, and the inconvenience of filling the woman's bladder (Martins 2004). Another possible drawback is that in some cases moving the catheter to improve identification is required, a motion that is not needed in transfers performed by clinical touch. This manoeuvre can potentially disrupt the endometrium, thus reducing the benefits provided by ultrasound (Garcia-Velasco 2002). Another disadvantage is the possible unknown side effects of early ultrasound on the pre-implantation embryo.

Why it is important to do this review

Studies comparing transabdominal ultrasound guidance with the traditional clinical touch method have reported conflicting results in terms of pregnancy rates. Given the lack of concurrence in the literature, we decided to review the evidence systematically to evaluate this method for successful embryo transfer.

OBJECTIVES

To determine whether ultrasound guidance compared with clinical touch improves pregnancy outcomes in women undergoing embryo transfer during assisted reproductive technology cycles.

METHODS

Criteria for considering studies for this review

Types of studies

We considered all published, unpublished, and ongoing prospective randomised trials that reported data comparing outcomes of women undergoing ultrasound-guided embryo transfer (UGET) versus clinical touch embryo transfer (CTET) through the cervical route following in-vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) including frozen embryo transfers for inclusion. We excluded quasi-randomised (sampling of every n^{th} entry from a list), cross-over, and cluster randomised trials.

Types of participants

Women with any form of infertility undergoing embryo transfer via the cervical route (using either fresh or cryopreserved or donated embryos) after either IVF or ICSI and randomised to either UGET or CTET.

Types of interventions

The studies had to compare transcervical embryo transfer using transabdominal ultrasound guidance with clinical touch methods. The studies should have conducted a standard IVF/ICSI procedure, using standard protocols for controlled ovarian stimulation and transcervical replacement of embryos. Standard culture medium and catheters should have been used for culture and transfer of embryos, respectively. We included embryo transfers that involved donated gametes or embryos. There was no restriction on the number of clinicians conducting the transfers nor the type of catheters used.

We excluded studies of embryo transfer via zygote intrafallopian transfer.

Types of outcome measures

Primary outcomes

The primary outcome measure for this systematic review was live births/ongoing pregnancies per woman randomised. We defined live birth as a live fetus born after 20 completed weeks. We defined ongoing pregnancies as those continuing for at least 12 weeks after embryo transfer.

Secondary outcomes

1. Clinical pregnancies per woman randomised (as determined by heart beat detected using ultrasound)
2. Multiple birth per woman randomised
3. Miscarriage rate: miscarriage (confirmed by ultrasound and pregnancy test or histology) per woman randomised (including partial loss of multiple pregnancies)
4. Ectopic pregnancy rate: ectopic gestation per woman randomised
5. Foetal abnormalities as determined by foetal anatomy scan or after delivery per woman randomised
6. Complication rate: any adverse effects/events associated with embryo transfer per woman randomised
7. Ease of transfer as determined by clinician

Search methods for identification of studies

We searched for all published and unpublished randomised controlled trials comparing ultrasound with clinical touch, without language restriction, and in conjunction with the Cochrane Gynaecology and Fertility Group's Trials Search Co-ordinator.

Electronic searches

We searched the following electronic databases and trial registries in May 2015.

The Cochrane Gynaecology and Fertility Group Specialised Register of Controlled Trials, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (Ovid), and CINAHL (EbscoHost). We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials that appears in Section 6.4.11 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Version 5.1.0) (Higgins 2011). We combined the EMBASE, PsycINFO, and CINAHL searches with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN) (http://www.sign.ac.uk/methodology/filters.html#random) (Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6).

Other electronic sources of trials included:

- trials registers of registered and ongoing trials

- http://clinicaltrials.gov (a service of the US National Institutes of Health);
- http://who.int/trialsearch/Default.aspx (the World Health Organization International Trials Registry Platform search portal).

Searching other resources

We searched the citation lists of relevant publications and review articles published from 2009 to the present (September 2015), and handsearched the references of the included studies. We contacted commercial entities and experts in the field, where identified, to locate trials. We contacted authors where necessary for missing data on live birth rates.

We also handsearched relevant conference proceedings: American Society for Reproductive Medicine (ASRM), European Society for Human Reproduction and Embryology (ESHRE), and International Federation of Gynecology and Obstetrics (FIGO). There were no language restrictions.

Data collection and analysis

Selection of studies

After an initial screen of the titles and abstracts retrieved in the searches (by JB, a methodologist, and KB, a content expert), we retrieved the full texts of all potentially eligible studies. Two review authors (JB, KB) 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, as required, to confirm study eligibility. Disagreements as to study eligibility were resolved by consensus.

Data extraction and management

Two review authors (JB, KB) independently extracted data from the eligible studies using a data extraction form that had been developed and piloted for consistency and completeness. Any disagreements were resolved by consensus. Data extracted included study characteristics and outcome data. Where studies had multiple publications, we collated multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review, and such studies will have the same study ID with multiple references.

We corresponded with study investigators for further information on methods or data/results as required (for example live birth rates).

Assessment of risk of bias in included studies

Two review authors independently assessed the eligible studies for risk of bias using the Cochrane 'Risk of bias' assessment tool (www.cochrane-handbook.org) for the following domains: selection (random sequence generation, allocation concealment), performance (blinding of participants and personnel), detection (blinding of outcome assessors), attrition (incomplete outcome data), reporting (selective reporting), and other bias (refer to risk of bias in Characteristics of included studies). Disagreements were resolved by consensus.

We took care to search for within-trial selective reporting, such as trials failing to report specific outcomes, or reporting them in insufficient detail to allow for inclusion of data. We sought out published protocols and compared these with the data reported in the published report.

Measures of treatment effect

We performed statistical analysis in accordance with the guidelines for statistical analysis developed by the Cochrane Gynaecology and Fertility Group. The outcome of live birth/ongoing pregnancy and clinical pregnancy is considered a positive consequence of fertility treatment, therefore a higher proportion of women with a clinical pregnancy, ongoing pregnancy, or live birth is considered a benefit. Outcomes such as multiple pregnancy are a negative consequence, therefore higher numbers are considered detrimental. This should be taken into account when viewing summary graphs.

For dichotomous data, we used the number of events in the intervention and control groups to calculate the Mantel-Haenszel odds ratio with 95% confidence intervals for all outcomes. The Peto odds ratio had been used in previous versions of this review.

Unit of analysis issues

All analyses are reported per woman randomised. In studies that reported on outcome per embryo transfer, we sought verification from the primary author/s.

Dealing with missing data

We have presented data as the outcome per woman randomised. Where we could not collate such data from the paper, we sought verification from the primary author/s. Where possible, we reported data by intention-to-treat. Where data were unobtainable, we only analysed the available data.

Assessment of heterogeneity

We considered whether the clinical and methodological characteristics of the included studies were sufficiently similar for meta-analysis to provide a clinically meaningful summary. We assessed heterogeneity using the I^2 statistic. We considered an I^2 greater than 50% to indicate substantial heterogeneity (Higgins 2011).

Assessment of reporting biases

We performed a comprehensive search of the literature. We have included published and unpublished data with both positive and negative findings in this review. We identified no pre-publication protocols for the included studies in our search of the trial registries. Additionally, we assessed publication bias using funnel plot techniques, Begg's rank test, Egger's regression test, and the trim-and-fill plot for outcomes that had at least 10 included trials.

Data synthesis

Where data were considered similar enough to combine, we employed a fixed-effect model as the primary analysis in the meta-analysis using Review Manager version 5.3 (RevMan 2014). We combined data for the following comparison:

- ultrasound-guided embryo transfer versus clinical touch.

Subgroup analysis and investigation of heterogeneity

Where statistical heterogeneity was found to exceed 50%, we performed subgroup analysis to try to explain the findings. We explored the use of same or different type of catheters used in the intervention or control groups.

Sensitivity analysis

We had planned to conduct sensitivity analyses to compare studies judged to have low risk of bias (those judged to be at low risk of bias for all domains of risk of bias) with those classified as having an unclear/high risk of bias. Instead, we undertook a random-effects analysis to assess sensitivity to choice of model for all outcomes where heterogeneity was greater than 50%.

Overall quality of the body of evidence: 'Summary of findings' table

We have prepared a 'Summary of findings' table using GRADEpro Guideline Development Tool software (GRADEpro GDT). This table evaluates the overall quality of the body of evidence for the main review outcomes (live birth/ongoing pregnancy, clinical pregnancy, multiple pregnancy, miscarriage and ectopic pregnancy) using GRADE (Grades of Recommendation, Assessment, Development and Evaluation) criteria (study limitations (that is risk of bias), consistency of effect, imprecision, indirectness, and publication bias). Judgements about evidence quality (high, moderate, or low) have been justified, documented, and incorporated into reporting of results for each outcome.

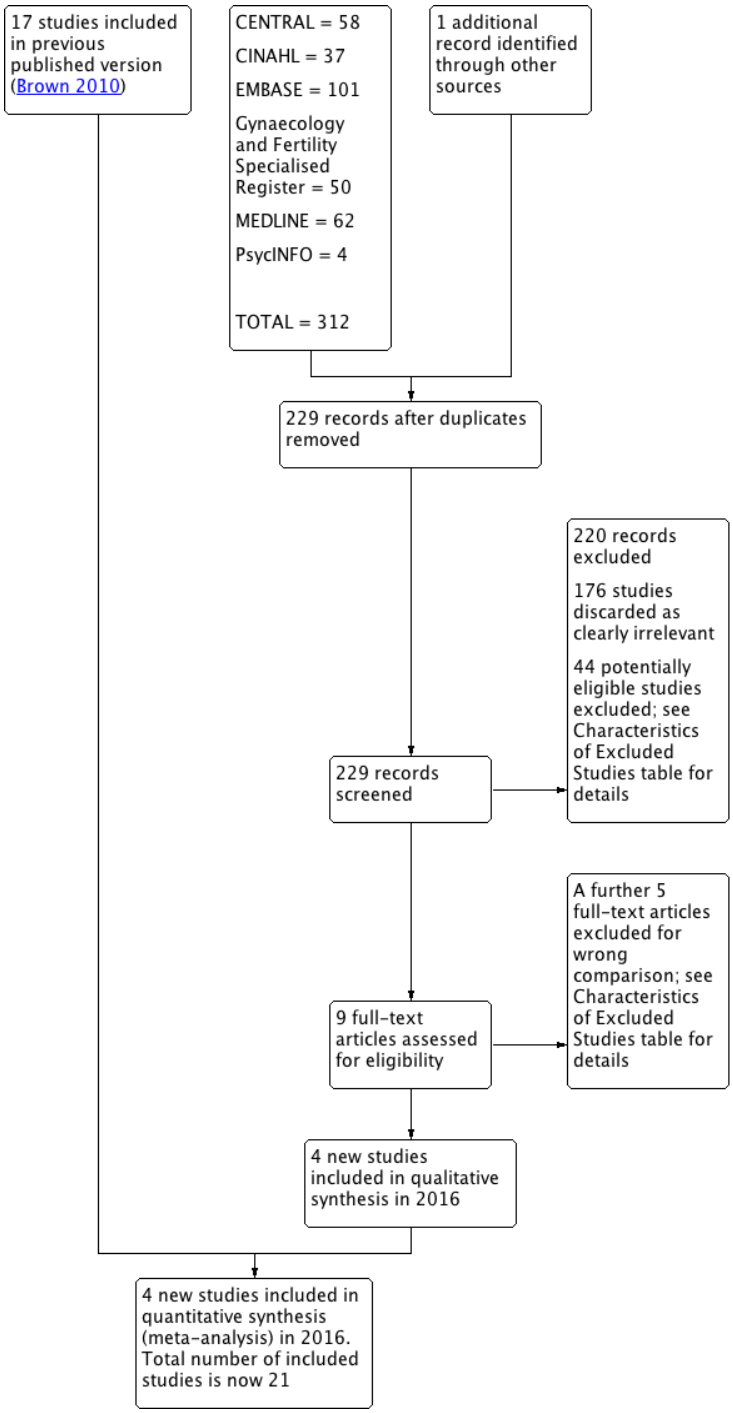
RESULTS

Description of studies

Results of the search

We identified 104 potential studies in the original search, and an additional six studies in the update in 2009. In the 2016 update, we added four new studies (Ammar 2013; Azmy 2009; Davar 2007; Maldonado 2005), and excluded five (Bodri 2011; Deep 2013; Hauzman 2012; Porat 2010; Saharkhiz 2014) (Characteristics of excluded studies). See Figure 1.

Figure 1. Study flow diagram for review update 2016.



We requested data from all authors of abstracts (Bar Hava 2003; Faure 1998; Moraga-Sanchez 2004; Weissman 2003); we received a response from Dr Bar-Harva, although no data has been forthcoming. We received no correspondence from the other authors. We requested clarification of randomisation from Dr Li but have received no response (Li 2005). Dr Blake was unable to identify the study requested; she was the head of the research department that submitted the summary but cannot identify the original authors of the study within the institution (Blake 1998). In the 2016 update of this review, we moved Blake 1998 to the excluded studies.

Included studies

We identified 23 publications associated with 21 randomised controlled trials that compared ultrasound guidance with clinical touch. We included 21 trials in the final analysis (Ammar 2013; Azmy 2009; Bar Hava 2003;Chen 2007; Coroleu 2000; Coroleu 2002; Davar 2007; Drakeley 2008; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Li 2005; Maldonado 2005; Marconi 2003; Martins 2004; Matorras 2002; Moraga-Sanchez 2004; Tang 2001; Weissman 2003; Wisanto 1989; Zakova 2008). All of the trials included in the review and final analysis were prospective randomised controlled trials.

Baseline characteristics of women

Studies emerged from a variety of centres around the world: the UK (Drakeley 2008), Spain (Coroleu 2000; Coroleu 2002; Garcia-Velasco 2002; Matorras 2002), China (Tang 2001; Li 2005), Belgium (Kosmas 2007; Wisanto 1989), Brazil (Martins 2004), Israel (Bar Hava 2003; Weissman 2003), Argentina (Marconi 2003), Taiwan (Chen 2007), Saudi Arabia (Eskander 2008), the Czech Republic (Zakova 2008), Iran (Davar 2007), Brazil (Maldonado 2005), Egypt (Ammar 2013; Azmy 2009), and Mexico/USA (Moraga-Sanchez 2004). All of the studies used transabdominal ultrasound. The 21 included studies reported on 6711 women undergoing embryo transfer.

All couples were infertile and participating in some form of fertility programme. Inclusion criteria reported in the studies was for the women to be on an in-vitro fertilisation/intracytoplasmic sperm injection (IVF/ICSI) embryo transfer programme (Bar Hava 2003; Coroleu 2000; Coroleu 2002; Li 2005; Maldonado 2005; Marconi 2003; Weissman 2003; Wisanto 1989; Davar 2007), undergoing IVF but less than 40 years of age (Marconi 2003; Matorras 2002), to be recipients of oocyte donation programme and undergoing embryo transfer of good-quality embryos (Garcia-Velasco 2002), aged 28 to 41 years undergoing IVF (including ICSI) (Ammar 2013; Li 2005; Martins 2004), or undergoing ICSI or IVF with frozen-thawed embryos. Azmy 2009 required women to be less than 38 years of age and have a body mass index equal to or less than 30 kg/m^2. Ammar 2013 required women to be between 20 and 39 years of age. Marconi 2003 and Azmy 2009 also required that women have a day 3 follicle-stimulating hormone level of less than 12 IU/ml. In Kosmas 2007, women were under 40 years of age with fresh embryos undergoing non-donor embryo transfer; exclusions were cryopreserved embryos and women with previous cervical excision for cervical dysplasia. No details of inclusion or exclusion criteria were provided by Drakeley 2008, Eskander 2008, Moraga-Sanchez 2004, and Zakova 2008.

All studies reported maternal age except Drakeley 2008, Maldonado 2005, and Moraga-Sanchez 2004 (Table 1). Thirteen trials included women who had embryo transfer related to fresh IVF/ICSI cycles (Ammar 2013; Azmy 2009; Chen 2007; Coroleu 2000; Davar 2007; Eskander 2008; Kosmas 2007; Li 2005; Marconi 2003; Martins 2004; Matorras 2002; Garcia-Velasco 2002; Wisanto 1989); one study had 56.3% fresh embryos in the ultrasound-guided group and 54% in the clinical touch group (Tang 2001); and Coroleu 2002 used frozen/thawed embryos in both groups. Drakeley 2008 included both fresh and frozen embryo transfers. Maldonado 2005 did not report if embryos were fresh or frozen. Matorras 2002 excluded women with cryopreserved embryos, having oocyte donation, or undergoing ICSI, and Tang 2001 excluded women requiring general anaesthesia or refusing to participate. No details were provided by Zakova 2008.

Seven studies reported the duration of infertility (Coroleu 2000; Li 2005; Matorras 2002; Tang 2001; Wisanto 1989; Weissman 2003; Davar 2007), and seven studies mentioned the primary causes of infertility (Ammar 2013; Coroleu 2002; Wisanto 1989; Li 2005; Matorras 2002; Tang 2001; Davar 2007). The remaining studies provided no details.

Fifteen studies provided IVF protocol information (Ammar 2013; Chen 2007; Coroleu 2000; Coroleu 2002; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Li 2005; Marconi 2003; Martins 2004; Matorras 2002; Tang 2001; Wisanto 1989; Zakova 2008; Davar 2007), and 12 described embryo transfer information (Chen 2007; Coroleu 2000; Coroleu 2002; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Li 2005; Martins 2004; Matorras 2002; Tang 2001; Wisanto 1989; Davar 2007). Seven studies described details on the embryo media (Ammar 2013; Coroleu 2000; Coroleu 2002; Li 2005; Tang 2001; Garcia-Velasco 2002; Wisanto 1989). All of the studies with the exception of Bar Hava 2003, Maldonado 2005, and Moraga-Sanchez 2004 included details of the catheter type used for embryo transfer. The distance from the fundus where the embryos were placed was not detailed by Bar Hava 2003, Kosmas 2007, Moraga-Sanchez 2004, Marconi 2003, Weissman 2003, and Zakova 2008, and two trials failed to record the number of embryos transferred (Maldonado

2005; Zakova 2008).

Twelve studies detailed ease of transfer (Azmy 2009; Coroleu 2000; Coroleu 2002; Drakeley 2008; Eskander 2008; Kosmas 2007; Matorras 2002; Tang 2001; Weissman 2003; Wisanto 1989; Zakova 2008; Davar 2007). Details regarding day of embryo transfer were not provided by Bar Hava 2003, Davar 2007, and Moraga-Sanchez 2004, and type of ultrasound machine used for the procedure was described by Azmy 2009, Chen 2007, Coroleu 2000, Coroleu 2002, Davar 2007, Drakeley 2008, Eskander 2008, Garcia-Velasco 2002, Kosmas 2007, Li 2005, Martins 2004, Matorras 2002, and Tang 2001.

Details on requirement of full bladder were provided by Ammar 2013, Azmy 2009, Coroleu 2002, Davar 2007, Drakeley 2008, Eskander 2008, Garcia-Velasco 2002, Kosmas 2007, Matorras 2002, Tang 2001, Weissman 2003, and Wisanto 1989. Bed rest post-procedure was detailed by Ammar 2013, Coroleu 2002, Davar 2007, Garcia-Velasco 2002, Kosmas 2007, Li 2005, Matorras 2002, Tang 2001, and Wisanto 1989.

For details of the transfer protocol and IVF protocol, see Table 1. For details of the transfer/replacement procedure, where reported, see Table 2. For details of day of transfer, whether women were on bed rest or not, and whether they had a full bladder or not, as well as the type of ultrasound machine used, see Table 3.

Excluded studies

We rejected 42 of the 104 potential studies outright based on the title or content of the abstract. After retrieving the remaining papers, we rejected a further 42 studies because on more detailed analysis of the content we found they were not randomised controlled trials or because they were comparing catheter types and not ultrasound guidance versus clinical touch methods of embryo transfer. Ten papers were reviews or 'letters to the editor' that did not contain any original data. We excluded a further five trials that compared transvaginal ultrasound with transabdominal ultrasound (Bodri 2011; Deep 2013; Hauzman 2012; Porat 2010), or that did not use ultrasound at the time of embryo transfer (Saharkhiz 2014). In the 2016 update, we excluded two studies that had previously been awaiting classification, as multiple attempts to contact the authors of Faure 1998 were made without reply, and we were unable to identify the authors of the Blake 1998 study. The studies were old, and the findings were unlikely to affect the results of the meta-analyses. We excluded a total of 49 studies (see Characteristics of excluded studies).

Risk of bias in included studies

See Characteristics of included studies table, Figure 2, and Figure 3.

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

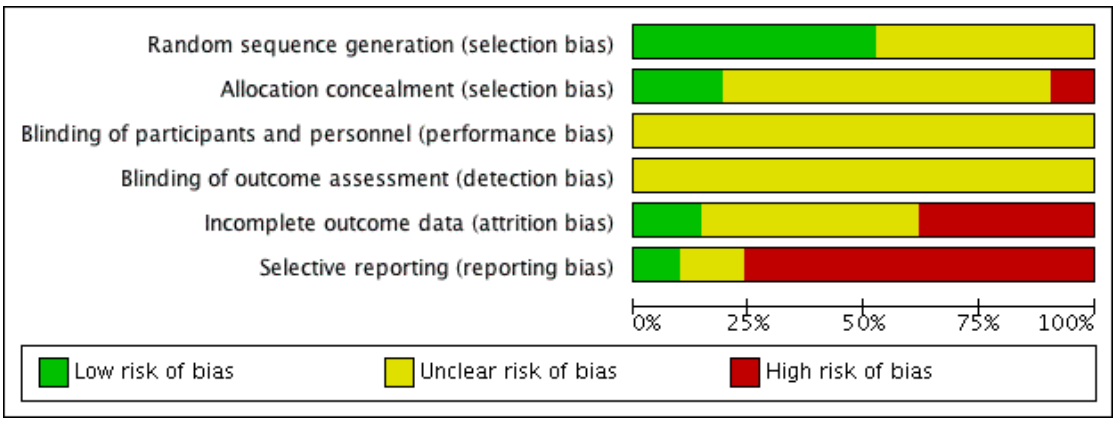
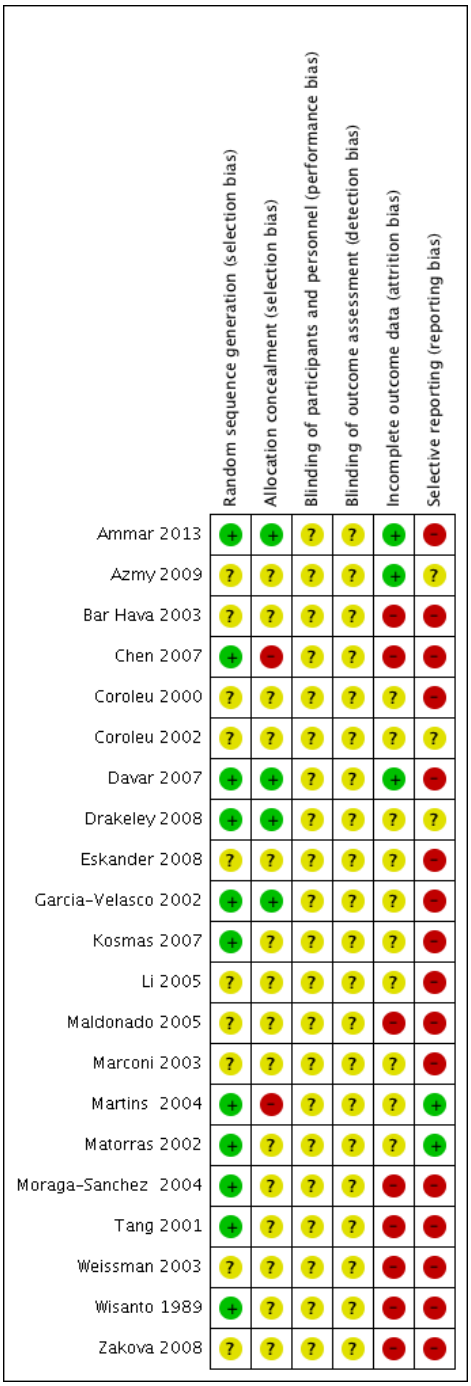


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Allocation

Nine studies used some method of computer-generated randomisation (Ammar 2013; Chen 2007; Coroleu 2002; Davar 2007; Drakeley 2008; Garcia-Velasco 2002; Kosmas 2007; Matorras 2002; Tang 2001), one study drew lots using a randomisation table on the day of oocyte retrieval (Martins 2004), and one randomised using tables of random sampling numbers (Wisanto 1989). The remaining studies provided no details of the randomisation method used.

Five studies described their process of allocation concealment (Ammar 2013; Drakeley 2008; Eskander 2008; Garcia-Velasco 2002; Davar 2007).

Blinding

None of the trials used blinding. We judged this to be unclear for performance bias, as although blinding is unlikely to affect the outcome of pregnancy, the awareness of the intervention by the clinicians involved may affect the performance of the intervention. None of the trials provided details as to whether the outcome assessors were blinded, and we judged this as unclear risk of bias.

Incomplete outcome data

Attrition and intention-to-treat analysis: Four women in the trial conducted by Wisanto 1989 were not analysed due to failure during transfer and are not included in this analysis, as their treatment changed and their outcomes are unknown. All of the remaining trials analysed the same number of women as were randomised.

Live birth rate was poorly reported, with only four of the 21 included studies reporting this primary outcome.

Selective reporting

The review authors have retrieved a wide source of data from conference papers, peer-reviewed data, and personal communication with authors. We could not identify published trial protocols for any of the included trials. In addition, 16 studies did not report on the primary outcome of live birth (Ammar 2013; Chen 2007; Coroleu 2000; Coroleu 2002; Davar 2007; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Li 2005; Marconi 2003; Matorras 2002; Moraga-Sanchez 2004; Tang 2001; Weissman 2003; Wisanto 1989; Zakova 2008).

Other potential sources of bias

We identified no other sources of bias.

Effects of interventions

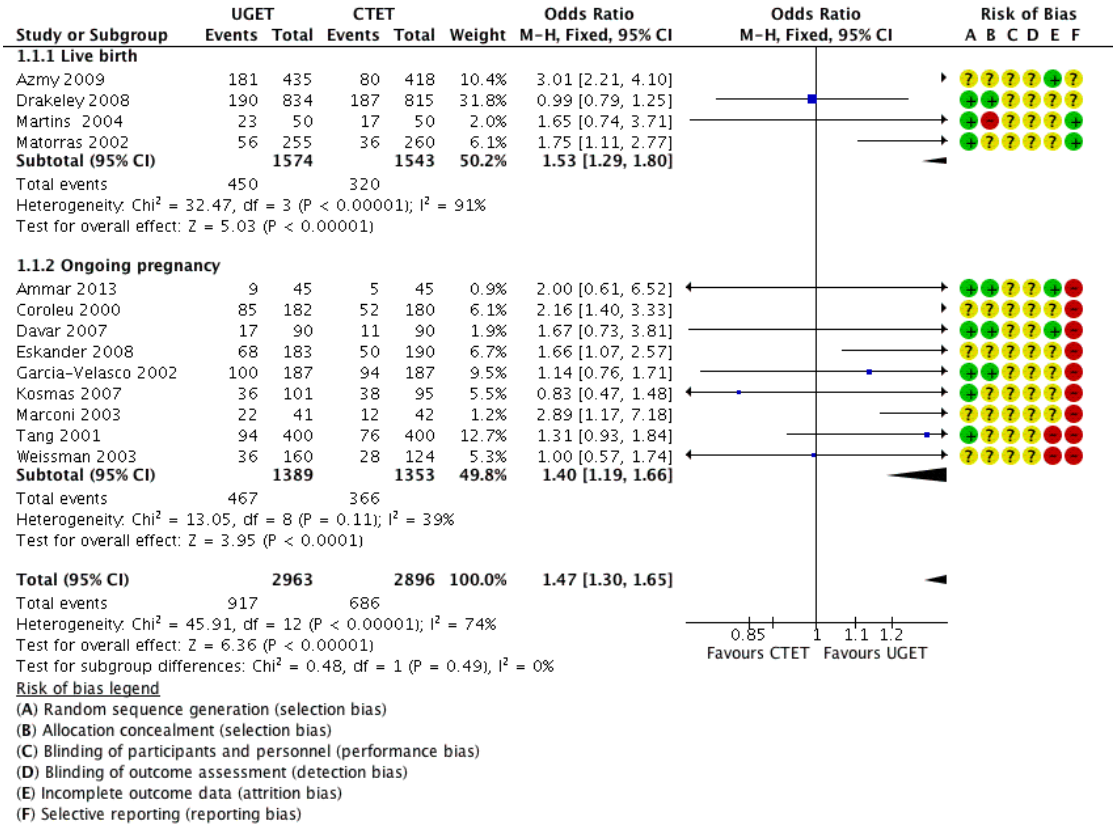
See: **Summary of findings for the main comparison** Ultrasound-guided embryo transfer versus clinical touch

1.1 Live birth/ongoing pregnancy

Thirteen trials reported on live birth/ongoing pregnancy. Four trials reported on live birth (Azmy 2009; Drakeley 2008; Martins 2004; Matorras 2002), and nine trials reported ongoing pregnancy (Ammar 2013; Coroleu 2000; Davar 2007; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Marconi 2003; Tang 2001; Weissman 2003). None of the studies reporting ongoing pregnancy reported on live birth and vice versa.

Personal communication with two authors resulted in additional data on live birth being received (Martins 2004; Matorras 2002). The use of ultrasound-guided embryo transfer (UGET) was associated with an increased chance of a live birth/ongoing pregnancy (917 out of 2963) compared with clinical touch embryo transfer (CTET) (686 out of 2896) (odds ratio (OR) 1.47, 95% confidence interval (CI) 1.30 to 1.65; 13 trials; n = 5859 women; I^2 = 74%; low-quality evidence). Sensitivity analysis using a random-effects model did not affect the overall results. The subgroup interaction test was not significant, suggesting there was no evidence of a differential effect between studies reporting live birth and those reporting ongoing pregnancy (Analysis 1.1; Figure 4). We estimate that for women with a chance of a live birth/ongoing pregnancy of 23% using CTET, this would increase to between 28% and 33% using UGET (Summary of findings for the main comparison). Using the GRADE approach, we judged the quality of the evidence to be low.

Figure 4. Forest plot of comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch', outcome: 1.1 Live birth and ongoing pregnancy (per woman randomised).



In the review protocol we stated that where there was heterogeneity we would explore it by only including trials with low risk of bias for all the domains. None of the included trials in the review had low risk of bias in all the domains. We therefore looked only at those trials that had low risk of bias for selection bias (allocation). For the outcome of live birth we excluded Azmy 2009. For the outcome of ongoing pregnancy we excluded Coroleu 2000; Eskander 2008; Marconi 2003 and Weissman 2003. The evidence of an overall benefit for UGET still remained , although the strength of the effect was diminished (OR 1.17, 95%CI 1.01 to 1.36; 8 trials, n = 3904; I^2 = 22%; analysis not shown).

For live birth (all trials included), heterogeneity was I^2 = 91%. We attempted to explore the reasons for this significant heterogeneity by looking for differences in the trial protocols.

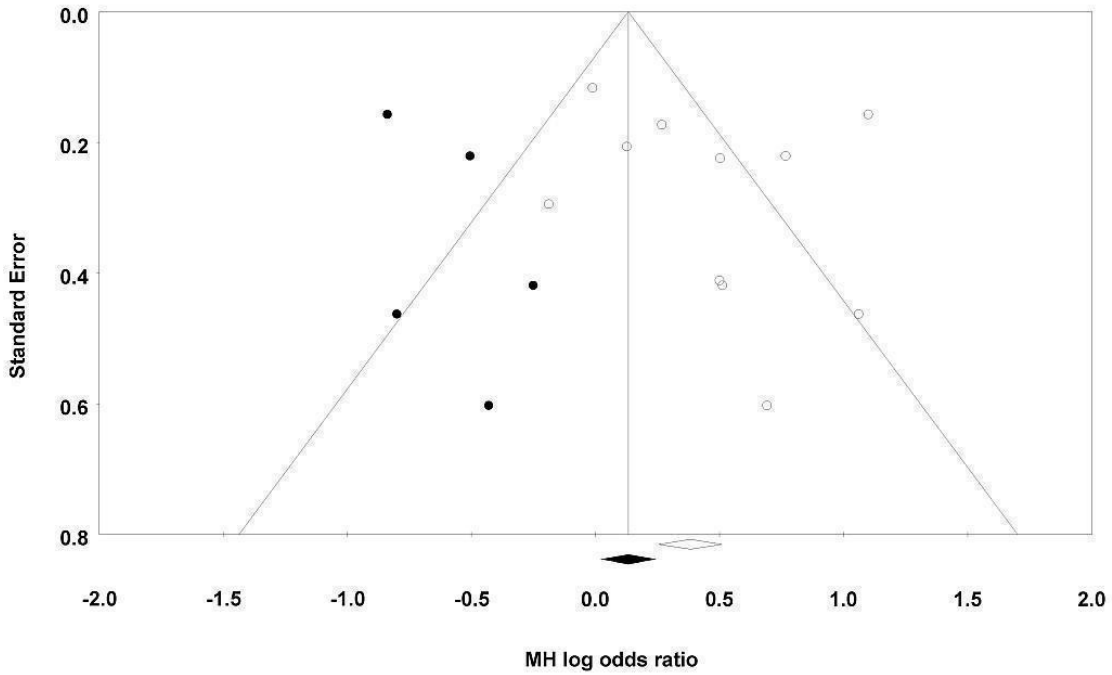
Fresh versus frozen embryos: Azmy 2009, Martins 2004, and Matorras 2002 used fresh embryos only. Drakeley 2008 reported using fresh and frozen embryos (88% fresh and 12% frozen embryos in both groups).

Type of catheter used: One of the included studies appeared to be an outlier (Drakeley 2008). We found that in this trial, the catheters used differed between the groups. In the UGET group, 97% of embryo transfers used the Cook EchoTip, 1% Wallace, and 2% Rocket catheters. In the CTET group, 2% used the Cook EchoTip, 51% the Wallace, and 47% the Rocket catheters. There was no difference in the chance of a live birth between groups (OR 0.99, 95% CI 0.79 to 1.25; 1 trial; n = 1649). Martins 2004 and Matorras 2002 used the Frydman catheter in both groups, and Azmy 2009 used the Labotect catheter in both groups. The use of UGET was associated with an increase in live birth compared to CTET where the same catheter was used in both groups (OR 2.45, 95% CI 1.92 to 3.12; 3 studies; n = 1468; I^2 = 57%). The subgroup interaction test was significant, suggesting that using the same catheter type for both intervention groups was associated with an increased chance of a live birth (Chi^2 = 23.06; I^2 = 96.4%; P < 0.00001) (Analysis 2.1). Sensitivity analysis using a random-effects model did not affect this result.

Publication bias tests did not indicate a significant probability of the presence of publication bias. Even so, the funnel plot appeared asymmetrical with a gap on the left lower corner. The trim-and-fill

plot identified that five trials (favouring CTET) would be needed to make the funnel plot symmetrical (Figure 5). With the addition of these trials, the adjusted effect estimate would still remain significant, but the magnitude of effect reduced to OR 1.14 (95% CI 1.02 to 1.28).

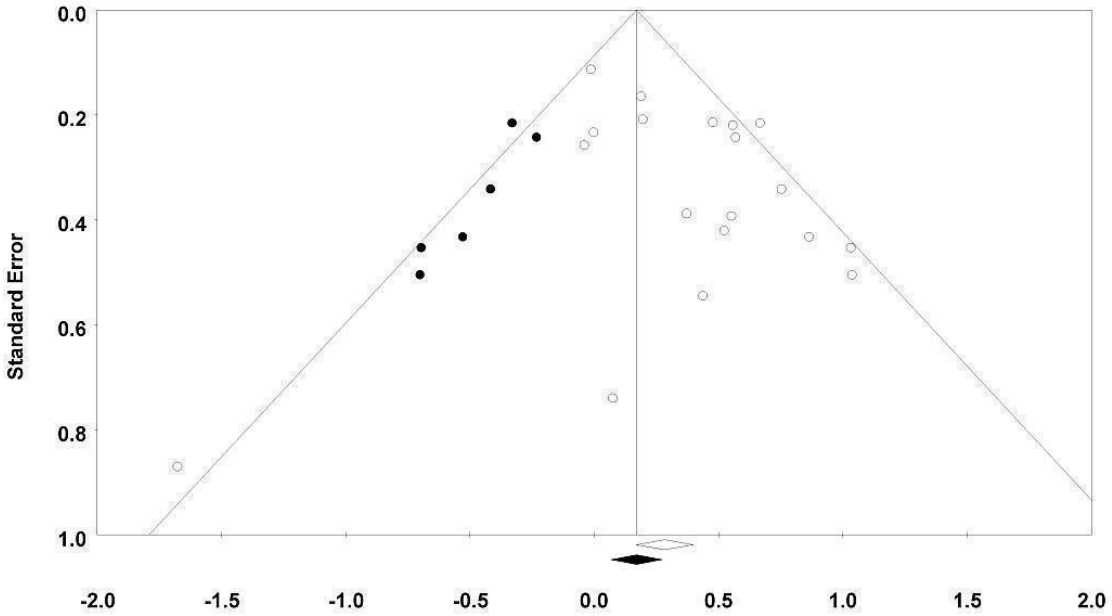
Figure 5. Live-birth/ongoing pregnancy rate trim-and-fill plot.



1.2 Clinical pregnancies

Twenty trials reported clinical pregnancies. UGET was associated with an increase in the chance of a clinical pregnancy (1118 out of 3392) compared with CTET (916 out of 3319) (OR 1.31, 95% CI 1.17 to 1.45; 20 studies; n = 6711; I^2 = 42%) (Analysis 1.2). Publication bias tests did not indicate a significant probability of the presence of publication bias. Even so, the funnel plot appeared asymmetrical with a gap on the left lower corner. The trim-and-fill plot identified that six trials (favouring CTET) would be needed to make the funnel plot symmetrical (Figure 6). With the addition of these trials, the adjusted effect estimate would still remain significant, but the magnitude of effect reduced to OR 1.19 (95% CI 1.07 to 1.32). Using GRADE methodology, we judged the quality of the evidence for clinical pregnancies to be moderate; the evidence was downgraded one level due to lack of methodological details to be able to make a judgement on risk of bias.

Figure 6. Clinical pregnancy rate trim-and-fill plot.



1.3 Multiple pregnancies

Multiple pregnancies are viewed as an adverse event, as the aim is to achieve a single live birth. Eight trials reported multiple pregnancies (Azmy 2009; Coroleu 2002; Davar 2007; Eskander 2008; Garcia-Velasco 2002; Martins 2004; Matorras 2002; Tang 2001). There was no evidence of a difference between UGET (140 out of 1693) and CTET (124 out of 1686) in the incidence of multiple pregnancies (OR 1.13, 95% CI 0.87 to 1.45; 8 trials; n = 3379; I^2 = 0%) (Analysis 1.3). Using GRADE methodology, we judged the quality of the evidence for multiple pregnancies to be moderate; the evidence was downgraded one level due to lack of methodological details to be able to make a judgement on risk of bias.

1.4 Ectopic pregnancies

There was no evidence of a difference in ectopic pregnancies per woman randomised in the eight trials reporting this outcome (Azmy 2009; Coroleu 2002; Coroleu 2002; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Matorras 2002; Tang 2001): UGET (8 out of 1885) and CTET (13 out of 1876) (OR 0.64, 95% CI 0.28 to 1.49; 8 trials; n = 3761; I^2 = 0%) (Analysis 1.5). Using GRADE methodology, we judged the quality of the evidence for ectopic pregnancies to be moderate; the evidence was downgraded one level due to lack of methodological details to be able to make a judgement on risk of bias.

1.5 Miscarriage

Eleven of the papers determined miscarriage (Ammar 2013; Azmy 2009; Coroleu 2002; Davar 2007; Eskander 2008; Garcia-Velasco 2002; Kosmas 2007; Martins 2004; Matorras 2002; Tang 2001; Weissman 2003). There was no evidence to suggest an effect on the incidence of spontaneous miscarriage between UGET (103 out of 2048) and CTET (101 out of 2005) (OR 0.99, 95% CI 0.74 to 1.31; 11 trials; n = 4053; I^2 = 0%) (Analysis 1.4). Using GRADE methodology, we judged the quality of the evidence for miscarriage to be moderate; the evidence was downgraded one level due to lack of methodological details to be able to make a judgement on risk of bias.

Publication bias tests did not indicate a significant probability of the presence of publication bias.

1.6 Blood on catheter tip

Five papers reported blood on the catheter tip as an adverse event following the transfer procedure (Coroleu 2002; Drakeley 2008; Eskander 2008; Garcia-Velasco 2002; Wisanto 1989). There was no evidence of a difference between UGET (126 out of 1397) and CTET (124 out of 1383) (OR 1.0, 95% CI 0.77 to 1.30; 5 trials; n = 2780; I^2 = 0%) (Analysis 1.6).

1.7 Difficulty in transfer

Where reported, we extracted data on transfers that were considered to be difficult. Ten trials reported this outcome (Azmy 2009; Coroleu 2000; Coroleu 2002; Davar 2007; Kosmas 2007; Matorras 2002; Tang 2001; Wisanto 1989; Weissman 2003; Zakova 2008). The studies reported that 183 out of 2173 cases were considered to be difficult in UGET compared to 258 out of 2122 for CTET; UGET was associated with a reduction in transfers that were considered to be difficult (OR 0.69, 95% CI 0.57 to 0.82; 10 trials; n = 4295; I^2 = 75%). Sensitivity analysis using random-effects model (data not shown) changed the results to a non-significant difference (OR 0.71, 95% CI 0.46 to 1.10) (Analysis 1.7). The observed difference may be due to the high number of events in the CTET group in the Azmy 2009 trial and the low event rates in the UGET group in the Matorras 2002 trial. If we remove these two trials from the meta-analysis, the results show no evidence of a difference between the UGET and CTET groups (OR 0.96, 95% CI 0.28 to 1.19; 8 trials; n = 2957), and I^2 is reduced to 0%.

Publication bias tests did not indicate a significant probability of the presence of publication bias.

There were no reports in any of the analysed papers on the outcome of foetal abnormalities either at anomaly scan or at birth.

DISCUSSION

Summary of main results

The results of this systematic review found an association between ultrasound-guided embryo transfer (UGET) and an increased chance of a live birth/ongoing pregnancy. Heterogeneity was high, with a significant proportion of weighting being attributed to one trial (Drakeley 2008).

We identified no evidence of a difference between UGET and clinical touch embryo transfer (CTET) with regards to miscarriage, multiple pregnancies, or ectopic pregnancies, and the incidence of such events was relatively small. Data on multiple pregnancies was only reported by six of the studies and may be regarded as a source of reporting bias. We have requested data from all authors with regard to this outcome, and it is recommended that future research takes this into account.

There was no evidence of a difference between transfer procedures for blood on the catheter after embryo transfer. The papers were not always explicit in identifying who was responsible for the embryo transfer and what their level of experience in the procedure was. For the outcome difficult embryo transfer, Azmy 2009 and Matorras 2002 account for the heterogeneity in the analysis.

Overall completeness and applicability of evidence

In general, the studies identified are similar enough to make meaningful comparisons. There is still a lack of data regarding live birth, which needs to be addressed in future research. The odds ratios for live birth and ongoing pregnancy are similar, and we have interpreted this as suggesting that the benefits identified for UGET over CTET for the ongoing pregnancy data are unlikely to represent selective outcome reporting.

During the searches for this review update we identified a number of trials that used transvaginal ultrasound or three-dimensional ultrasound. In subsequent updates of this review, we will include these trials for completeness.

Quality of the evidence

Overall, the included studies could be compromised by their lack of methodological quality. Only two of the studies reported using a computer-generated randomisation and adequate concealment (Drakeley 2008; Garcia-Velasco 2002). The remaining studies failed to provide adequate detail regarding methodological quality, in particular randomisation method and allocation concealment. Only four studies reported live birth, and none of the nine studies that provided data on ongoing pregnancy reported live birth.

Using GRADE methodology, we judged the quality of the evidence for the primary outcome of live birth to be low. We downgraded quality for high heterogeneity and lack of methodological detail to be able to judge the risk of bias.

For the secondary outcomes of clinical pregnancy, multiple pregnancy, ectopic pregnancy, and miscarriage, we judged the quality of the evidence to be moderate. We downgraded the quality for lack of methodological detail, which meant that we were unable to judge the risk of bias.

Potential biases in the review process

We believe that we have conducted a comprehensive and systematic search of published and unpublished trials.

However, publication bias may be an issue, with mainly positive outcomes being reported. During the literature search we identified studies that reported either no difference or a negative effect of UGET; these studies tended to be retrospective studies and were excluded for reasons of their study design. The study by Drakeley did report equivocal results between the groups (Drakeley 2008). Further, the outcomes ongoing pregnancy/live birth and clinical pregnancy rates had asymmetric funnel plots that may be the result of publication bias. Even so, the conclusions drawn from the pooled results after adjustment remained unchanged.

The review authors felt that the funnel plot for live birth/ongoing pregnancy appeared relatively asymmetrical (Figure 5) .

It has been suggested that the increase in clinical pregnancy and live birth/ongoing pregnancy may be due to a decrease in difficult transfers. The definitions of what was considered difficult varied

between the studies and may account for the heterogeneity found for this outcome. Clearer, standardised definitions are required for comparisons to be made, although the subjective nature of this outcome may influence the findings in individual studies.
The exact mechanism by which UGET increases pregnancy rates remains unclear. The main suggested explanations remain the confirmation of the catheter in the uterine cavity , 'ease of transfer' positioning of the catheter, and avoiding touching the fundus or indenting the endometrium.

Agreements and disagreements with other studies or reviews

The evidence of this review is congruent with other published evidence, including two systematic reviews with meta-analyses of randomised controlled trials, both of which found a benefit for live birth and clinical pregnancy with UGET compared with CTET (Abou-Setta 2007; Teixeira 2015).

AUTHORS' CONCLUSIONS

Implications for practice

The evidence suggests that, where personnel and resources are available, the chance of an ongoing pregnancy or live birth is better with UGET than with CTET.

Implications for research

The studies highlight a lack of data for the primary outcome measure (live birth) of the systematic review. It is suggested that future research should report on the live birth rate per woman randomised as an outcome measure that is of importance to the target population. Sample size calculations suggest that 759 women in each arm would be sufficient to detect an 8 per cent difference in live birth with 95% power and α 0.5. The same type of transfer catheter should be used in the intervention and control groups where possible to avoid confounding variables.

ACKNOWLEDGEMENTS

We wish to acknowledge the peer reviewers and the staff at the Cochrane Gynaecology and Fertility Group for their contribution to this review.

REFERENCES

References to studies included in this review

Ammar 2013 *{published data only}*
Ammar AR, Mousa KS, Rabei NH, Galal A. Effect of ultrasound guided embryo transfer on pregnancy rates. *New York Science Journal* 2013;**6**(12):79–83.

Azmy 2009 *{unpublished data only}*
Al-Shemi M. *Ultrasound Guided Versus Blind Touch Embryo Transfer Among Patients Undergoing Intra Cytoplasm Sperm Injection [Protocol for Thesis]*. Faculty of Medicine, Ain Shams University, Egypt, 2008.
* Azmy O, Taha T, Bibars M, Refaat M. Ultrasound guided versus blind touch embryo transfer: the Egyptian experience. Proceedings of the 15th World Conference of IVF and 4th Congress of IVM. 2009:9–12.

Bar Hava 2003 *{published data only}*
Bar-Hava I, Meltzer S, Rabinson J, Ayash I, Sega S, Tur-Kaspa I. Ultrasound guided versus blind tactile embryo transfer: a prospective randomised study. *Human Reproduction* 2003;**18 (suppl 1)**(7):xviii7.

Chen 2007 *{published data only}*
Chen S-C, Lai T-H, Lee F-K. The influence of abdominal ultrasound-guided embryo transfer on pregnancy rate: a preliminary report. *Fertility and Sterility* 2007;**87**(5): 1235–7.

Coroleu 2000 *{published data only}*
Coroleu B, Carreras O, Veiga A, Martell A, Martinez F, Belil I, et al. Embryo transfer under ultrasound guidance improves pregnancy rates after in-vitro fertilization. *Human Reproduction* 2000;**15**(3):616–20.

Coroleu 2002 *{published data only}*
Coroleu B, Barri P, Carreras O, Martinez F, Veiga A, Balasch J. The usefulness of ultrasound guidance in frozen-thawed embryo transfer: a prospective randomised clinical trial. *Human Reproduction* 2002;**17**(11):2885–90.

Davar 2007 *{published data only}*
Davar R, Ghandi S, Tayebi N. Does transabdominal ultrasound-guided embryo transfer improve pregnancy rates in ART cycles?. *Iranian Journal of Reproductive Medicine* 2007;**5**(3):95–8.

Drakeley 2008 *{published and unpublished data}*
* Drakeley A, Jorgensen A, Sklavounos J, Aust T, Gazvani R, Williamson P, et al. A randomized controlled clinical trial of 2295 ultrasound-guided embryo transfers. *Human Reproduction* 2008;**23**(5):1101–6.
Drakeley AJ, Lunt R, Aust T, Williamson P, Gazvani R, Sklavounos J, et al. A randomized trial of 2250 women having ultrasound guided embryo transfer. *Human Reproduction* 2006;**21**((suppl 1)):i82.

Eskander 2008 *{published data only}*
Eskandar M, Abou-Setta A, Almushait M, El-Amin M,

Mohamad S. Ultrasound guidance during embryo transfer: a prospective, single-operator, randomized controlled trial. *Fertility and Sterility* 2008;**90**(4):1187–90.

Garcia-Velasco 2002 *{published data only}*
Garcia-Velasco J, Isaza V, Martinez-Salazar J, Landazabal A, Requena A, Remohi J, et al. Transabdominal ultrasound-guided embryo transfer does not increase pregnancy rates in oocyte recipients. *Fertility and Sterility* 2002;**78**(3):534–9.

Kosmas 2007 *{published data only}*
Kosmas IP, Janssens R, De Munck L, Al Turki HF, Tournaye H, Van Steirteghem AC, et al. Ultrasound guidance during embryo transfer does not offer any benefit in clinical outcome: a randomized controlled trial. *Human Reproduction* 2007;**22**(5):1327–34.

Li 2005 *{published data only}*
Li R, Lu L, Hao G, Zhong K, Cai Z, Wang W. Abdominal ultrasound guided embryo transfer improves clinical pregnancy rates after in vitro fertilization: experiences from 330 clinical investigations. *Journal of Assisted Reproduction and Genetics* 2005;**22**(1):3–8.

Maldonado 2005 *{published data only}*
Maldonado LG, Ajzen Sa, Busato WC, Iaconelli A Jr, Bibancos M, Borges E Jr. Impact of previous hysterosonometry on embryo transfer. *Fertility and Sterility* 2005;**84**:S364.

Marconi 2003 *{published data only}*
Marconi G, Young E Jr, Vilela M, Bello A, Young E Sr, Sueldo C. Prospective randomized comparison of an ultrasound-guided embryo transfer versus a blind catheter placement. *Fertility and Sterility* 2003;**80**(suppl 3):S130.

Martins 2004 *{published and unpublished data}*
Martins A, Baruffi R, Mauri A, Petersen C, Oliveira J, Contart P, et al. Ultrasound guidance is not necessary during easy embryo transfers. *Journal of Assisted Reproduction and Genetics* 2004;**21**(12):421–5.

Matorras 2002 *{published and unpublished data}*
Matorras R, Urquijo E, Mendoza R, Corcostegui B, Exposito A, Rodriguez-Escudero F. Ultrasound-guided embryo transfer improves pregnancy rates and increases the frequency of easy transfers. *Human Reproduction* 2002;**17**(7):1762–6.

Moraga-Sanchez 2004 *{published data only}*
Moraga-Sanchez M, Llata E, Resendiz V, Haliscak R, Galache-Vega P, Ayup S, et al. Ultrasound influence and 30 second wait in embryo transfer. *Human Reproduction* 2004; **19**:i127.

Tang 2001 *{published data only}*
Tang O, Ng E, So W, Ho P. Ultrasound guided embryo transfer: a prospective randomized controlled trial. *Human Reproduction* 2001;**16**(11):2310–5.

Weissman 2003 *{published and unpublished data}*
Weissman A, Farhi J, Steinfeld Z, Mustafi R, Nahum H, Levran D. A prospective randomized study of ultrasound-guided embryo transfer. *Fertility and Sterility* 2003;**80 (Suppl 1)**:S122.

Wisanto 1989 *{published data only}*
Wisanto A, Janssens R, Desacht J, Camus M, Devroey P, Van Steirtegham AC. Performance of different embryo transfer catheters in a human in vitro fertilization program. *Fertility and Sterility* 1989;**52**(1):79–84.

Zakova 2008 *{published data only}*
Zakova J, Crha L, Ventruba P, Lobsova E, Huser M. Does ultrasound-guided embryo transfer improve pregnancy rate in in vitro fertilization?. *Human Reproduction* 2008;**23 (Supplement 1)**:i135.

References to studies excluded from this review

Al-Shawaf 1993 *{published data only}*
Al-Shawaf T, Yang D, Al-Magid Y, Seaton A, Iketubosin F, Craft I. Ultrasonic monitoring during replacement of frozen/thawed embryos in natural and hormone replacement cycles. *Human Reproduction* 1993;**8**(12): 2068–74.

Al-Shawaf 1993b *{published data only}*
Al-Shawaf T, Dave R, Harper J, Linehan D, Riley P, Craft I. Transfer of embryos into the uterus: How much do technical factors affect pregnancy rates?. *Journal of Assisted Reproduction and Genetics* 1993;**10**(1):31–6.

Anderson 2002 *{published data only}*
Anderson RE, Nugent NL, Gregg AT, Nunn SL, Behr BR. Transvaginal ultrasound-guided embryo transfer improves outcome in patients with previous failed in vitro fertilization cycles. *Fertility and Sterility* 2002;**77**(4):769–74.

Baba 2000 *{published data only}*
Baba K, Ishihara O, Hayashi N, Saioh M, Taya J, Kinoshita K. Three dimensional ultrasound in embryo transfer. *Ultrasound in Obsterics and Gynecology* 2000;**16**:372–3.

Blake 1998 *{unpublished data only}*
Blake. Unpublished. Personal communicaton 1998.

Bodri 2011 *{published data only}*
Bodri D, Colodron M, Garcia D, Obradors Am Vernaeve V, Coll O. Transvaginal versus transabdominal ultrasound guidance for embryo transfer in donor oocyte recipients: a randomized clinical trial. *Fertility and Sterility* 2011;**95**(7): 2263–8.

Broussin 1998 *{published data only}*
Broussin B, Jayot S, Subtil D, Parneix I, Audebert A, Dubecq F, et al. Difficult embryo transfer: the ultrasonography contribution. *Fertilite Contraception Sexualite* 1998;**26**(7-8):492–7.

Coroleu 2002a *{published data only}*
Coroleu B, Barri PN, Carreras O, Martinez F, Parriego M, Hereter L, Parera N, Veiga A, Balasch J. The influence of the depth of embryo placement into the uterine cavity on implantation rates after IVF: a controlled, ultrasound-guided study. *Human Reproduction* 2002;**17**(2):341–6.

Cruickshank 2003 *{published data only}*
* Cruickshank B, Fasciani A, Di Berardino A, Hannam TG, Casper RF, Greenblatt E. The ultrasound guided embryo transfer significantly increases the ongoing pregnancy

rates when a 'laminar flow' pattern is observed. *Human Reproduction* 2003;**18**((Suppl 1) Issue 6):Xviii6.

Deep 2013 ***{published data only}***
Deep JP, Li Y, Liu H. The effect of embryo transfer on IVF treatment: Comparing the trans-vaginal versus transabdominal ultrasound approach. *Journal of Minimally Invasive Gynecology* 2013;**1**:S42–3.

Englert 1986 ***{published data only}***
Englert Y, Puissant F, Camus M, Van Hoeck J, Leroy F. Clinical study on embryo transfer after human in vitro fertilisation. *Journal of In Vitro Fertilization and Embryo Transfer* 1986;**3**(4):243–6.

Eskander 2007 ***{published data only}***
Eskander M, Abou-Setta A. Ultrasound-guided embryo transfer is superior to clinical touch alone: A single operator randomized controlled trial. *Fertility and Sterility* 2007;**88 (suppl 1)**:S326–7.

Faure 1998 ***{published data only}***
Faure JM, Dechaud H, Deschamps F, Arnal F, Humeau C, Hedon B. Ultrasound guided embryo transfer. Effects on implantation and pregnancy rates. *Fertility and Sterility* 1998:S26.

Flisser 2006 ***{published data only}***
Flisser E, Grifo JA, Krey L, Noyes N. Transabdominal ultrasound-assisted embryo transfer and pregnancy outcome. *Fertility and Sterility* 2006;**85**(2):353–7.

Garcia-Velasco 2001 ***{published data only}***
Garcia-Velasco J, Martinez-Salazar J, Isaza A, Landazabal A, Requena A, Simon C. Does ultrasound guidance at embryo transfers improve pregnancy rates in oocyte recipients?. *Fertility and Sterility* 2001;**76**:75–6.

Garzo 2006 ***{published data only}***
Garzo G. Embryo transfer technique. *Clinical Obstetrics and Gynecology* 2006;**49**(1):117–22.

Gergely 2005 ***{published data only}***
Gergely R, DeUgarte C, Danzer H, Surrey M, Hill D, DeCherney A. Three dimensional/four dimensional ultrasound-guided embryo transfer using the maximal implantation potential point. *Fertility and Sterility* 2005;**84** (2):500–3.

Ghazzawi 1999 ***{published data only}***
Ghazzawi I, Hassani S, Karaki R, Souso S. Transfer technique and catheter choice influence the incidence of transcervical embryo expulsion and the outcome of IVF. *Human Reproduction* 1999;**14**(3):677–82.

Hauzman 2012 ***{published data only}***
Hauzman E, Kohls G, Barrio A, Martinez Salazar J, Iglesias C, Garcia-Velasco JA. Comparison of embryo transfer in egg donation recipients with transvaginal and transabdominal ultrasound: A randomized pilot study. *Human Reproduction* 2013;**28**:i241.

Hurley 1991 ***{published data only}***
Hurley V, Osborn J, Leoni M, Leeton J. Ultrasound-guided embryo transfer: a controlled trial. *Fertility and Sterility* 1991;**55**(3):559–62.

Kan 1999 ***{published data only}***
Kan AKS, Abdalla HI, Gafar AH, Nappi L, Ogunyemi BO, Thomas A, Ola-ojo OO. Embryo transfer: ultrasound-guided versus clinical touch. *Human Reproduction* 1999;**14** (5):1259–61.

Karande 2002 ***{published data only}***
Karande V, Hazlett D, Vietzke M, Cleicher N. A prospective randomized comparison of the Wallace catheter and the Cook Echo-Tip catheter for ultrasound guided embryo transfer. *Fertility and Sterility* 2002;**77**(4):826–30.

Kojima 2001 ***{published data only}***
Kojima K, Nomiyama M, Kumamoto T, Matsmoto Y, Iwasaka T. Transvaginal ultrasound guided embryo transfer improves pregnancy and implantation rates after IVF. *Human Reproduction* 2001;**16**(12):2578–82.

Kolankaya 2001 ***{published data only}***
Kolankaya A, Enginsu ME, Camlibel TF, Sarikamis B, Kurt E, Yildiz K, Hunerli C. Ultrasound guided embryo transfer improves pregnancy rates. *Human Reproduction* 2001;**16**((Suppl 1)):155.

Kosmas 2006a ***{published data only}***
Kosmas IP, Janssens R, De Munck L, Al Turki HF, Tournaye H, Van Steirteghem AC, et al. Ultrasound guidance during embryo transfer does not offer any benefit in clinical outcome: a randomized controlled trial. *Human Reproduction* 2006;**21**(6):i101.

Kreiner 2000 ***{published data only}***
Kreiner D, Moschella J, Carlson N, Jelicks J, Bolkas M, Moodie G, et al. Pregnancy rates of a two step ultrasound guided embryo transfer 1-112 cm from the top of the uterine cavity. *Fertility and Sterility* 2000;**74**(3 (suppl 1)): S206.

Lenz 1987a ***{published data only}***
Lenz S, Leeton J, Rogers P, Trouson A. Transfundal transfer of embryos using ultrasound. *Journal of In Vitro Fertilization and Embryo Transfer* 1987;**4**(1):13–7.

Lenz 1987b ***{published data only}***
Lenz S, Leeton J. Evaluating the possibility of uterine transfer by ultrasonically guided transabdominal puncture. *Journal of In Vitro Fertilization and Embryo Transfer* 1987;**4** (1):18–22.

Leong 1986 ***{published data only}***
Leong M, Leung C, Tucker M, Wong C, Chan H. Ultrasound assisted embryo transfer. *Journal of In Vitro Fertilization and Embryo Transfer* 1986;**3**(6):383–5.

Lesny 1998 ***{published data only}***
Lesny P, Killick SR, Tetlow RL, Robinson J, Maguiness SD. Embryo transfer - can we learn anything new from the observation of junctional zone contractions?. *Human Reproduction* 1998;**13**(6):1540–6.

Letterie 2005 ***{published data only}***
Letterie GS. Three-dimensional ultrasound-guided embryo transfer: A preliminary study. *American Journal of Obstetrics and Gynecology* 2005;**192**:1983–8.

Lindheim 1999 *{published data only}*
Lindheim SR, Cohen MA, Sauer MV. Ultrasound guided embryo transfer significantly improves pregnancy rates in women undergoing oocyte donation. *International Journal of Gynecology and Obstetrics* 1999;**66**:281–4.

Lorusso 2005 *{published data only}*
Lorusso F, Depalo R, Bettocchi S, Vacca M, Vimercati A, Selvaggi L. Outcome of in vitro fertilization after transabdominal ultrasound-assisted embryo transfer with a full or empty bladder. *Fertility and Sterility* 2005;**84**(4): 1046–8.

Martinez 2001 *{published data only}*
Martinez F, Coroleu B, Parriego M, Carreras O, Belil I, Parera N, Hereter L, Buxaderas R, Barri PN. Ultrasound-guided embryo transfer: immediate withdrawal of the catheter versus a 30 second wait. *Human Reproduction* 2001;**16**(5):871–4.

Parsons 1987 *{published data only}*
Parsons JH, Bolton VN, Wilson L, Campbell S. Pregnancies following in vitro fertilization and ultrasound-directed surgical embryo transfer by perurethral and transvaginal techniques. *Fertility and Sterility* 1987;**48**(4):691–3.

Porat 2010 *{published data only}*
Porat N, Boehnlein LM, Schouweiler CM, Kang J, Lindheim SR. Interim analysis of a randomized clinical trial comparing abdominal versus transvaginal ultrasound-guided embryo transfer. *The Journal of Obstetrics and Gynaecology Research* 2010;**36**(2):384–92.

Prapas 1995 *{published data only}*
Prapas Y, Prapas N, Hatziparasidou A, Prapa S, Nijs M, Vanderzwalmen P, et al. The echoguide embryo transfer maximises the IVF results. *Acta Europaea Fertilitatis* 1995; **26**(3):113–5.

Prapas 2001 *{published data only}*
Prapas Y, Prapas N, Hatziparasidou A, Vanderzwalmen P, Nijs M, Prapa S, et al. Ultrasound-guided embryo transfer maximizes the IVF results on day 3 and day 4 embryo transfer but has no impact on day 5. *Human Reproduction* 2001;**16**(9):1904–8.

Saharkhiz 2014 *{published data only}*
Saharkhiz N, Nikbakht R, Salehpour S. Comparison between conventional blind embryo transfer and embryo transfer based on previously measured uterine length. *International Journal of Fertility and Sterility* 2014;**8**(3): 249–54.

Sallam 2001 *{published data only}*
Sallam H, Agameya A, Rahman A, Ezzeldin F, Sallam A. Ultrasound measurement of the uterocervical angle before embryo transfer: a prospective controlled study. Human Reproduction. 2001; Vol. 16, issue abstract book 1:126.

Sallam 2002a *{published data only}*
Sallam HN, Agameya AF, Rahman AF, Ezzeldin F, Sallam AN. Ultrasound measurement of the uterocervical angle before embryo transfer: a prospective controlled study. *Human Reproduction* 2002;**17**(7):1767–772.

Sasy 2003 *{published data only}*
Sasy M, Salem W, Fattah A, Ashraf M, Abozaid T, Khan I, et al. Comparison between ultrasound-guided embryo transfer and tubal embryo transfer after intracytoplasmic sperm injection. *Middle East Fertility Society Journal* 2003;**8** (3):223–8.

Scholtes 1994 *{published data only}*
Scholtes M, Roozenburg B, Verhoeff, Zeilmaker G. A randomised trial of transcervical intrafallopian transfer of pronucleate embryos controlled by ultrasound versus intrauterine transfer of four to eight cell embryos. *Fertility and Sterility* 1994;**61**(1):102–4.

Shamonki 2005 *{published data only}*
Shamonki MI, Spandorfer SD, Rosenwaks Z. Ultrasound-guided embryo transfer and the accuracy of trial embryo transfer. *Human Reproduction* 2005;**20**(3):709–16.

Silberstein 2005 *{published data only}*
Silberstein T, Trimarchi JR, Shackelton R, Weitzen S, Frankfurter D, Plosker S. Ultrasound guided mid-uterine cavity embryo transfer is associated with a decreased incidence of retained embryos in the transfer catheter. *Fertility and Sterility* 2005;**84**(5):1510–2.

Strickler 1985 *{published data only}*
Strickler RC, Christianson C, Crane JP, Curato A, Knight AB, Yang V. Ultrasound guidance for human embryo transfer. *Fertility and Sterility* 1985;**43**(1):54–61.

Wood 2000 *{published data only}*
Wood EG, Batzer F, Go KJ, Gutmann JN, Corson SL. Ultrasound-guided soft catheter embryo transfers will improve pregnancy rates in in-vitro fertilization. *Human Reproduction* 2000;**15**(1):107–12.

Woolcott 1997 *{published data only}*
Woolcott R, Stanger J. Potentially important variables identified by transvaginal ultrasound-guided embryo transfer. *Human Reproduction* 1997;**12**(5):963–6.

Yovich 1985 *{published data only}*
Yovich J, Turner S, Murphy A. Embryo transfer technique as a cause of ectopic pregnancies in in-vitro fertilization. *Fertility and Sterility* 1985;**44**(3):318–21.

Additional references

Abou-Setta 2007
Abou-Setta AM, Mansour RT, Al-Inany HG, Aboulghar MM, Aboulghar MA, Serour GI. Among women undergoing embryo transfer is the probability of pregnancy and live birth improved with ultrasound guidance over clinical touch alone? A systematic review and meta-analysis of prospective randomised controlled trials. *Fertility and Sterility* 2007;**88**(2):333–41.

Fanchin 1998
Fanchin R, Righini C, Olivennes F, Taylor S, de Ziegler D, Frydman R. Uterine contractions at the time of embryo transfer alter pregnancy rates after in vitro fertilization. *Human Reproduction* 1998;**13**:1968–74.

GRADEpro GDT [Computer program]
McMaster University (developed by Evidence Prime Inc). Available from gradepro.org. GRADEpro GDT: GRADEpro Guideline Development Tool. McMaster University (developed by Evidence Prime Inc). Available from gradepro.org, 2015.

Higgins 2011
Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Kovacs 1999
Kovacs GT. What factors are important for successful embryo transfer after in-vitro fertilization?. *Human Reproduction* 1999;**14**:590–2.

RevMan 2014 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Sallam 2002
Sallam HN, Saad-el-Din S. Performing embryo transfer under ultrasound guidance - A meta analysis of randomized trials. *Fertility and Sterility* 2002;**78**(3 (Suppl 1)):S46.

Steptoe 1978
Steptoe PC, Edwards RG. Birth after the reimplantation of a human embryo. *The Lancet* 1978;**2**:366.

Teixeira 2015
Teixeira DM, Dassuncao LA, Vieira CV, Barbosa MA, Coelho Neto MA, Nastri CO, et al. Ultrasound guidance during embryo transfer: a systemtic review and meta-analysis of randomised controlled trials. *Ultrasound in Obstetrics and Gynecology* 2015;**45**(2):139–48.

References to other published versions of this review

Brown 2010
Brown J, Buckingham K, Abou-Setta AM, Buckett W. Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women. *Cochrane Database of Systematic Reviews* 2010, Issue 1.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Ammar 2013

Methods	Randomised controlled trial, single centre
Participants	90 infertile women from Egypt Inclusion criteria: Women undergoing ICSI. Age 20 to 39 years, male factor infertility, ovarian factor, and unexplained infertility Exclusion criteria: Tubal factor infertility, endometriosis, FSH concentration > 16 IU/mL on cycle day 3, less than 2 embryos grade A, difficult embryo transfer that needs cervical dilatation, tenaculum, or anaesthesia Setting: Maternity hospital, Egypt Timing: September 2009 to August 2011
Interventions	Ultrasound-guided embryo transfer Clinical touch
Outcomes	Primary outcomes were not prespecified. Outcomes listed as clinical pregnancy, ongoing pregnancy, and miscarriage
Notes	Sample size calculation - Not reported ITT analysis - Yes Funding - No details of funding reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised by computer-generated random number table
Allocation concealment (selection bias)	Low risk	A nurse not involved with the recruitment kept the randomisation table
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women randomised were analysed

Ammar 2013 (*Continued*)

Selective reporting (reporting bias)	High risk	All outcomes listed in the methods were reported on. Live birthrate not reported

Azmy 2009

Methods	Randomised controlled trial
Participants	853 women undergoing ICSI Inclusion: < 38 years, ≤ BMI 30 kg/m^2, basal FSH ≤ 12 IU/mL, embryo quality was ≥ grade B on day 3 and number of fresh embryos replaced was ≤ 3 Setting: ART unit in Cairo, Egypt Timing: Not stated
Interventions	Ultrasound-guided embryo transfer (n = 435) versus Clinical touch (n = 418)
Outcomes	Live birth, other outcomes were not prespecified but ease of transfer, implantation rate, miscarriage rate, multiple pregnancy rate, ectopic pregnancy rate, preterm birth, chemical pregnancy rate
Notes	No power calculation ITT analysis: All women randomised appear to be analysed Funding - no details

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	'randomised'. No details
Allocation concealment (selection bias)	Unclear risk	No details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women randomised appear to be analysed
Selective reporting (reporting bias)	Unclear risk	Outcomes are not clearly prespecified

Bar Hava 2003

Methods	Prospective randomised trial, no details of randomisation method. No details of allocation concealment
Participants	131 women participating in this Israeli study attending an IVF programme. Age 31 +/- 5.5 for UGET and 33.2 +/- 6.0 for clinical touch. No details of inclusion or exclusion criteria
Interventions	Ultrasound-guided embryo transfer (n = 65) versus clinical touch (n = 66)
Outcomes	Pregnancy and implantation rates
Notes	Unable to extract pregnancy data directly from abstract, authors contacted and awaiting response

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details of randomisation
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	No pre-publication protocol identified
Selective reporting (reporting bias)	High risk	Did not follow up to live birth. No adverse events reported

Chen 2007

Methods	Randomised by means of a computer-generated random number sequence
Participants	50 women undergoing IVF in Taiwan Inclusion: At least 1 grade 2 embryo available for transfer; embryo to be transferred at the 8-cell stage Exclusion: Woman age $\geq$ 40 years; cleaved embryos with less than 8 cells; patient history of 3 previous failed assisted conception cycles; anticipated difficulty in the transfer
Interventions	UGET = 27 women Clinical touch = 23 women

Chen 2007 (*Continued*)

Outcomes	Clinical pregnancy
Notes	Clinical pregnancy confirmed by ultrasound scan showing at least 1 sac in the uterine cavity 2 weeks after the positive pregnancy test

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised by means of a computer-generated random number sequence
Allocation concealment (selection bias)	High risk	No details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	No details of follow up to live birth. Does not appear to be any attrition
Selective reporting (reporting bias)	High risk	No details of adverse events or live birth/ongoing pregnancies

Coroleu 2000

Methods	Prospective randomised trial. No details of randomisation procedure
Participants	Study conducted in Spain. 362 women on the IVF embryo transfer programme Mean age 34.6 +/- 4.0 (UGET), 34.5 +/- 4.1 (clinical touch) Main causes of infertility were male and tubal for both UGET and clinical touch groups. No details on duration of infertility No details of exclusion criteria
Interventions	Ultrasound-guided embryo transfer (n = 182) versus clinical touch (n = 180)
Outcomes	Embryos retrieved and transferred, pregnancy rate, ongoing pregnancies, pregnancy by embryos transferred, ease of transfer, number of clinical pregnancies, implantation rate, adverse events
Notes	Published data only

Risk of bias

Coroleu 2000 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details of randomisation
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-study protocol identified
Selective reporting (reporting bias)	High risk	No details of follow up to live birth, although adverse events were included

Coroleu 2002

Methods	Prospective randomised trial. Randomised on day of transfer using computer-generated randomisation table
Participants	Study conducted in Spain. 184 women Inclusion: on the IVF embryo transfer programme who had their own cryopreserved pre-embryos Exclusion: Oocyte donation cycles were excluded Mean age: 36.6 +/- 3.4 (UGET), 36.2 +/- 3.0 (clinical touch) Main causes of infertility were male and tubal for both UGET and clinical touch groups Duration of infertility was 6.0 +/- 2.3 years for UGET, 5.6 +/- 1.8 years for clinical touch
Interventions	Ultrasound-guided embryo transfer (n = 93) versus clinical touch (n = 91)
Outcomes	Embryos retrieved and replaced, ease of transfer, clinical pregnancies, implantation rate, adverse events
Notes	Published data only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details of randomisation

Coroleu 2002 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-study protocol identified
Selective reporting (reporting bias)	Unclear risk	No details of follow up to live birth, although adverse events were included

Davar 2007

Methods	Randomised controlled trial, single centre
Participants	180 infertile women (20 to 39 years) undergoing treatment with IVF and ICSI. Only first embryo transfers were included No other details of inclusion or exclusion Setting: Centre for Infertility, Yazd, Iran Timing: 2005 to 2006
Interventions	Fresh embryos transferred in all women Transabdominal ultrasound-guided embryo transfer with full bladder (n = 90) versus Clinical touch embryo transfer (n = 90)
Outcomes	Ease of transfer, clinical pregnancy, ongoing pregnancy, implantation rate, number of embryos transferred, miscarriage rate
Notes	Sample size calculation - no details ITT analysis - data available for all women randomised No details on funding

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	'computer-generated random table'
Allocation concealment (selection bias)	Low risk	The randomisation table was made and kept by a nurse who was not involved in the recruitment of the women

Davar 2007 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported, but unlikely to have occurred. Although blinding for this intervention is unlikely to affect the outcome for the woman, it might influence the researcher's performance
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Low risk	All women randomised appear to have been analysed
Selective reporting (reporting bias)	High risk	No details on live birth were reported

Drakeley 2008

Methods	Randomised controlled trial
Participants	No details of inclusion or exclusion No details of mean age or main reasons for or duration of infertility Setting : Women attending a centre for reproductive medicine in the UK Timing: February 2003 to May 2005
Interventions	Some women had more than 1 attempt at embryo transfer during the trial, therefore we used the data for first attempts only, as this reflects per woman randomised Ultrasound-guided embryo transfer = 834 Clinical touch = 816
Outcomes	Biochemical and clinical pregnancy and live birth; blood on catheter tip; ease of transfer; types of catheter
Notes	Biochemical pregnancy defined as positive beta-hCG, clinical pregnancy defined as the observation of foetal heart on ultrasound at 7 weeks gestation Sample size calculation - Yes based on pregnancy rates ITT analysis - Yes Funding - UK government, NHS

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation with random block size using computer randomisation software. Randomisation stratified for age and fresh/frozen embryos

Drakeley 2008 (*Continued*)

Allocation concealment (selection bias)	Low risk	Randomisation codes were prepared independently from the authors by the hospital research and development office and allocations sealed in 4 different-coloured, sequentially numbered envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported, but unlikely to have occurred. Although blinding for this intervention is unlikely to affect the outcome for the woman, it might influence the researcher's performance
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Analysis by ITT, follow to live birth, no details of adverse events such as miscarriage
Selective reporting (reporting bias)	Unclear risk	Adverse events such as miscarriage or multiple pregnancies are not included

Eskander 2008

Methods	Randomisation was performed using dark, sealed envelopes
Participants	373 women undergoing embryo transfer in an assisted reproduction unit in Saudi Arabia Inclusion: Criteria not specified. Authors note that they used broad criteria so as to truly represent the patient population Exclusion: No details
Interventions	Ultrasound-guided embryo transfer (n = 183) versus clinical touch (n = 190)
Outcomes	Live birth, ongoing pregnancy, clinical pregnancy rates per woman randomised
Notes	Live birth - delivery of living foetus after > 28 weeks Clinical pregnancy - positive hCG measurement 2 weeks after transfer and viable gestational sac with foetal heartbeat at 3 weeks on ultrasound Ongoing pregnancy - > 14 weeks gestation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details of randomisation process
Allocation concealment (selection bias)	Unclear risk	Dark, sealed envelopes used, but no details on sequential numbering or on where allocation was performed

Eskander 2008 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-study protocol identified
Selective reporting (reporting bias)	High risk	Unable to separate live birth from ongoing pregnancies. Data includes adverse effects of importance

Garcia-Velasco 2002

Methods	Prospective randomised trial
Participants	Study conducted in Spain on 374 infertile women Mean age UGET 37.8 +/- 0.3, mean age clinical touch 38.2 +/- 0.4 Main causes of infertility were male and age-related factors. No details on duration of infertility Inclusion: Recipients of oocyte donation programme and be undergoing embryo transfer of good-quality embryos
Interventions	Ultrasound-guided embryo transfer (n = 187) versus clinical touch (n = 187)
Outcomes	Embryos transferred, clinical pregnancies, implantation rate, adverse events
Notes	Published data only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised using permuted blocks
Allocation concealment (selection bias)	Low risk	Adequate opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention

Garcia-Velasco 2002 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-study protocol identified
Selective reporting (reporting bias)	High risk	Not followed up to live birth

Kosmas 2007

Methods	Prospective randomised trial. Randomisation was computer generated
Participants	Study conducted in Belgium on 196 women. Women undergoing IVF or ICSI. Aged less than 40 years who had undergone fresh, non-donor embryo transfer. BMI 20 to 30 kg/m^2. Women with previous cervical surgery for cervical intraepithelial neoplasia excluded. Mean age UGET 32.05 +/- 4.31 years, clinical touch group 32.31 +/- 3.92 years. Over 80% of women were undergoing ICSI Mean duration of infertility for the UGET group was 3.19 +/- 2.25 years, and the main cause of infertility was male factor (54%). Mean duration of infertility for the clinical touch group was 3.37 +/- 2.67 years, and the main cause of infertility was male factor (65.3%)
Interventions	Ultrasound-guided embryo transfer (n = 150) Clinical touch embryo transfer (n = 150)
Outcomes	Embryos transferred, implantation rates and pregnancy rates, adverse events, difficulty of transfer
Notes	Pregnancy rate - rising hCG level 2 weeks after embryo transfer Clinical pregnancy - pregnancy sac with a positive heartbeat at 7-week scan

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised using computer-generated sequence
Allocation concealment (selection bias)	Unclear risk	Randomisation list was kept in the embryo transfer room. Participant allocation was done by an accompanying nurse not involved in the study
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention

Kosmas 2007 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	ITT analysis. A power calculation suggested a sample of 772 was required to detect a difference. After an interim analysis found no difference between the groups; recruitment was halted at n = 300. There was no loss to follow-up
Selective reporting (reporting bias)	High risk	Not followed up to live birth. Details of adverse events included, although not mentioned in methods section

Li 2005

Methods	Prospective randomised trial. Randomly divided on day of transfer
Participants	330 infertile Chinese women Mean age UGET group 32.2 +/- 3.9 years, clinical touch group 32.5 +/- 4.2 Main cause of infertility was tubal and male factors in both groups, duration of infertility was 5.8 +/- 2.1 years for UGET and 5.6 +/- 1.6 years for clinical touch Inclusion: 28 to 41 years of age undergoing treatment with IVF (including ICSI) No details of exclusion criteria
Interventions	Ultrasound-guided embryo transfer (n = 178) versus clinical touch (n = 152)
Outcomes	Embryos transferred, clinical pregnancies, implantation rate
Notes	Published data only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomly divided on day of transfer, no details
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-publication protocol identified
Selective reporting (reporting bias)	High risk	Did not follow up to live birth, no adverse events reported

Maldonado 2005

Methods	Randomised controlled trial
Participants	26 Brazilian women Inclusion criteria: Women attending clinic for infertility Exclusion criteria: No details Setting: Fertility centre in Brazil Timing: Not stated
Interventions	Ultrasound-guided embryo transfer no hysterosonometry (n = 13) versus Hysterosonometry followed by clinical touch embryo transfer (n = 13)
Outcomes	Not prespecified in the conference abstract
Notes	Sample size calculation - No ITT analysis - Unclear as conference abstract Funding - Not reported in abstract

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	'randomised', no other details
Allocation concealment (selection bias)	Unclear risk	No details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	Conference abstract, no details of attrition provided

Maldonado 2005 (*Continued*)

Selective reporting (reporting bias)	High risk	Conference abstract only, no full paper identified. Outcomes were not prespecified

Marconi 2003

Methods	Prospective randomised trial. No details of randomisation method or allocation concealment
Participants	Argentinian study of 83 women undergoing IVF treatment at a university-affiliated IVF unit. All women were under the age of 38 and day 3 FSH < 12 IU/mL, mean age UGET 31.8 +/- 2.67, clinical touch group 32.5 +/- 3.88. No details on exclusion criteria
Interventions	Ultrasound-guided embryo transfer (n = 41) versus clinical touch (n = 42)
Outcomes	Pregnancy rate, ongoing pregnancy rate
Notes	Published data only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	'Randomised' but no details
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-publication protocol identified
Selective reporting (reporting bias)	High risk	Not followed to live birth, no adverse events

Martins 2004

Methods	Prospective randomised trial. Randomisation was done by drawing lots using a randomisation table on the day of oocyte retrieval
Participants	Study conducted in Brazil on 100 women participating in an ICSI program who were submitted to mock transfer during a cycle preceding the process and were considered likely to have an easy transfer No exclusion details Mean age UGET group 32.1 +/- 4.1, mean age clinical touch group 32.0 +/- 3.2 No details on cause or duration of infertility
Interventions	Ultrasound-guided embryo transfer (n = 50) versus clinical touch (n = 50)
Outcomes	Embryos transferred, clinical pregnancies, implantation rate, abortion rate
Notes	Published data only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised by drawing lots
Allocation concealment (selection bias)	High risk	Inadequate
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-publication protocol identified
Selective reporting (reporting bias)	Low risk	Main outcomes reported on

Matorras 2002

Methods	Prospective randomised trial. Randomisation was computer-generated random table, took place on the morning of embryo transfer
Participants	Study conducted in Spain on 515 women Inclusion: less than 40 years of age undergoing IVF Exclusion: cryopreserved embryos, oocyte donation, ICSI Mean age 33.98 +/- 3.12 (UGET), 34.21 +/- 2.98 (clinical touch) Main causes of infertility were male and tubal for both UGET and clinical touch groups

Matorras 2002 (*Continued*)

	Duration of infertility was 4.7 +/- 2.48 years for UGET and 5.10 +/- 2.81 years for clinical touch	
Interventions	Ultrasound-guided embryo transfer (n = 255) versus clinical touch (n = 260)	
Outcomes	Fertilisation rate, embryos replaced, ease of transfer, clinical pregnancies, implantation rate, adverse events	
Notes	Published data only	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random table
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No pre-publication protocol identified
Selective reporting (reporting bias)	Low risk	Main outcomes discussed

Moraga-Sanchez 2004

Methods	Prospective randomised trial. No details of randomisation method or allocation concealment	
Participants	Mexican/USA study of 67 women. No details of inclusion or exclusion	
Interventions	Ultrasound-guided embryo transfer (n = 33) versus clinical touch (n = 34)	
Outcomes	Pregnancy and implantation rates	
Notes	Conference abstract only. Authors contacted, no response	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Moraga-Sanchez 2004 (*Continued*)

Random sequence generation (selection bias)	Low risk	'Randomised', no details
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	Conference abstract not fully published
Selective reporting (reporting bias)	High risk	No details of follow up to live birth. No details of adverse events

Tang 2001

Methods	Prospective randomised trial. Randomised by computer-generated random number table on day of transfer
Participants	Study conducted in China on 800 infertile women Mean age UGET 34.2 +/- 4.1, clinical touch 34.4 +/- 3.5 years Main cause of infertility was tubal and male. Duration of infertility was 6.6 +/- 2.9 years for UGET and 6.6 +/- 2.8 for clinical touch Inclusion: ICSI, frozen thawed, treated for IVF Exclusion: Required general anaesthesia or refused to participate 441 fresh embryo transfer and 359 frozen-thawed embryo transfer
Interventions	Ultrasound-guided embryo transfer (n = 400) versus clinical touch (n = 400)
Outcomes	Ease of transfer, clinical pregnancies, implantation rate, adverse events, ongoing pregnancy
Notes	Published data only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomised by computer-generated random number table
Allocation concealment (selection bias)	Unclear risk	Unclear, no details

Tang 2001 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	No pre-published protocol identified
Selective reporting (reporting bias)	High risk	Not followed up to live birth, although some adverse events were described

Weissman 2003

Methods	Prospective randomised trial, no details of method of randomisation or of allocation concealment
Participants	Israeli study of 155 women attending an IVF unit. Mean age of women was 34.6 +/- 5.9 in the UGET group and 33.6 +/- 6.2 years in the clinical touch group from the conference abstract and 34.9 +/- 5.6 (UGET) and 34.0 +/- 6.2 (clinical touch) from personal communication No details of inclusion or exclusion criteria
Interventions	Ultrasound-guided embryo transfer (n = 88 conference abstract and total of 160 from personal communication) versus clinical touch (n = 67 conference abstract and total of 124 from personal communication)
Outcomes	Pregnancy and implantation rates, miscarriage rates, and difficulty of transfer
Notes	Conference abstract. Authors contacted for further details. Through personal communication some data provided that was for a larger sample size than in the conference abstract. Updated data is presented in the analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No details of randomisation process
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention

Weissman 2003 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	Conference abstract, not fully published
Selective reporting (reporting bias)	High risk	Not followed up to live birth

Wisanto 1989

Methods	Prospective randomised trial. Randomisation using tables of random sampling numbers
Participants	200 women undergoing fresh embryo transfer for infertility No exclusion details Mean age 32.8 +/- 5 for UGET, 32.2 +/- 4.4 for clinical touch Main cause of infertility was tubal
Interventions	Ultrasound-guided embryo transfer (n = 100) versus clinical touch (n = 100)
Outcomes	Pregnancy rates, adverse events, ease of transfer
Notes	Study was a trial comparing 3 catheter types, only part of the study compared ultrasound guidance and clinical touch, the data for this has been abstracted separately from the rest of the study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Tables of randomly selected numbers
Allocation concealment (selection bias)	Unclear risk	Unclear, no details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	Conference abstract, not fully published
Selective reporting (reporting bias)	High risk	Not followed up to live birth

Zakova 2008

Methods	Randomised to 2 groups - no details
Participants	Women attending medical centre in the Czech Republic; no details of inclusion or exclusion criteria, infertility causes or duration
Interventions	UGET = 308 Clinical touch = 309
Outcomes	Clinical pregnancies
Notes	No definitions

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised to 2 groups - no details
Allocation concealment (selection bias)	Unclear risk	No details
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No details, but unlikely. Unlikely to affect participant outcomes, but may affect clinical performance of intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No details
Incomplete outcome data (attrition bias) All outcomes	High risk	Conference abstract, not fully published
Selective reporting (reporting bias)	High risk	No details of live birth or adverse events except ease of transfer

ART: assisted reproductive technology
hCG: human chorionic gonadotropin
BMI: body mass index
FSH: follicle-stimulating hormone
ICSI: intracytoplasmic sperm injection
ITT: intention-to-treat
IVF: in-vitro fertilisation
NHS: National Health Service
UGET: ultrasound-guided embryo transfer

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

Study	Reason for exclusion
Al-Shawaf 1993	Retrospective study of ultrasonic monitoring did not compare ultrasound guidance and clinical touch
Al-Shawaf 1993b	Transfer of embryos into the uterus, however randomisation was on the basis of availability of the sonographer and was therefore rejected
Anderson 2002	Retrospective study and did not compare with clinical touch
Baba 2000	Three-dimensional ultrasound in embryo transfer but not randomised trial
Blake 1998	No details found regarding this study
Bodri 2011	Comparison was abdominal versus transvaginal ultrasound, therefore both groups had ultrasound-guided embryo transfer
Broussin 1998	Retrospective study not compared with clinical touch
Coroleu 2002a	Randomised trial comparing implantation differences but not comparing with clinical touch
Cruickshank 2003	Cohort study, not a randomised trial
Deep 2013	Comparison was abdominal versus transvaginal ultrasound, therefore both groups had ultrasound-guided embryo transfer
Englert 1986	Characteristics of replacement procedure, however did not compare with ultrasound transfer
Eskander 2007	Conference proceeding superceded by full publication
Faure 1998	Abstract only. Attempts to contact authors on multiple occasions. No response received
Flisser 2006	Transabdominal ultrasound-assisted transfer, but design was retrospective
Garcia-Velasco 2001	Study excluded because of duplication of data with Garcia-Velasco 2002
Garzo 2006	Paper is a review of transfer techniques not a clinical trial
Gergely 2005	Used ultrasound guidance for embryo transfer, but study was retrospective
Ghazzawi 1999	Paper reports on catheter type, not comparing ultrasound guidance and clinical touch
Hauzman 2012	Comparison was abdominal versus transvaginal ultrasound, therefore both groups had ultrasound-guided embryo transfer
Hurley 1991	Randomised trial of ultrasound versus clinical touch. However, randomisation for this study was based on availability of authors

(*Continued*)

Kan 1999	Prospective controlled study of ultrasound versus clinical touch, but randomisation was dependent upon the availability of ultrasound
Karande 2002	Randomised comparison of catheter types using ultrasound but not comparing it with clinical touch
Kojima 2001	Retrospective study using ultrasound
Kolankaya 2001	Not a randomised trial, retrospective analysis
Kosmas 2006a	Conference abstract superceded by full publication
Kreiner 2000	Prospective randomised trial using ultrasound to replace embryos at a specific point, does not compare with clinical touch
Lenz 1987a	Transfundal transfer of embryos using ultrasound. Not a randomised trial and not comparing with clinical touch
Lenz 1987b	Transfundal transfer of embryos using ultrasound. Not a randomised trial and not comparing with clinical touch
Leong 1986	Describes technique, not a randomised trial
Lesny 1998	Study was based on mock transfers without embryos
Letterie 2005	Compares 2D and 3D ultrasound transfer, not a randomised controlled trial
Lindheim 1999	Retrospective analysis of women undergoing ultrasound-guided embryo transfer
Lorusso 2005	Randomised trial but not comparing ultrasound with clinical touch
Martinez 2001	Randomised trial of ultrasound-guided embryo transfer, however main outcome was immediate withdrawal versus a 30-second delay
Parsons 1987	Paper of case reports of ultrasound-directed surgical embryo transfer. Not randomised trial
Porat 2010	Comparison was abdominal versus transvaginal ultrasound, therefore both groups had ultrasound-guided embryo transfer
Prapas 1995	Ultrasound-guided embryo transfer, study was not a randomised trial and choice of transfer type was dependent on the room available for the procedure
Prapas 2001	Ultrasound-guided embryo transfer, study was not a randomised trial and choice of transfer type was dependent on the room available for the procedure
Saharkhiz 2014	There was no ultrasound guidance at the time of embryo transfer in the intervention group. Ultrasound had been previously performed to measure uterine length

(*Continued*)

Sallam 2001	Ultrasound measurement of the uterocervical angle before embryo transfer, study rejected as allocation was done alternately, not randomised
Sallam 2002a	Ultrasound measurement of the uterocervical angle before embryo transfer, study rejected as allocation was done alternately, not randomised
Sasy 2003	Retrospective study comparing ultrasound-guided embryo transfer and tubal embryo transfer
Scholtes 1994	Randomised trial of transcervical intrafallopian transfer of pronucleate embryos controlled by ultrasound versus intrauterine transfer of 4- to 8-cell embryos. Randomisation was dependent on day of the week menstrual bleeding started. Also not compared with clinical touch
Shamonki 2005	Study looking at accuracy of transfer, not a randomised trial
Silberstein 2005	Ultrasound-guided mid-uterine cavity embryo transfer, retrospective analysis of effectiveness, but did not compare with clinical touch
Strickler 1985	Ultrasound guidance for human embryo transfer, not a randomised trial
Wood 2000	Retrospective analysis of ultrasound and embryo transfers
Woolcott 1997	Evaluating transvaginal ultrasound-guided embryo transfer, not a randomised controlled trial and not compared with clinical touch
Yovich 1985	Evaluating embryo transfer technique, but does not compare ultrasound with clinical touch

DATA AND ANALYSES

Comparison 1. Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Live birth and ongoing pregnancy (per woman randomised)	13	5859	Odds Ratio (M-H, Fixed, 95% CI)	1.47 [1.30, 1.65]
1.1 Live birth	4	3117	Odds Ratio (M-H, Fixed, 95% CI)	1.53 [1.29, 1.80]
1.2 Ongoing pregnancy	9	2742	Odds Ratio (M-H, Fixed, 95% CI)	1.40 [1.19, 1.66]
2 Clinical pregnancies (per woman randomised)	20	6711	Odds Ratio (M-H, Fixed, 95% CI)	1.31 [1.17, 1.45]
3 Multiple pregnancies (per woman randomised)	8	3379	Odds Ratio (M-H, Fixed, 95% CI)	1.13 [0.87, 1.45]
4 Miscarriage (per woman randomised)	11	4053	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.74, 1.31]
5 Ectopic pregnancy (per woman randomised)	8	3761	Odds Ratio (M-H, Fixed, 95% CI)	0.64 [0.28, 1.49]
6 Blood on catheter	5	2780	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.77, 1.30]
7 Not considered an easy transfer	10	4295	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.57, 0.82]

Comparison 2. Additional analyses - Live birth and type of catheter

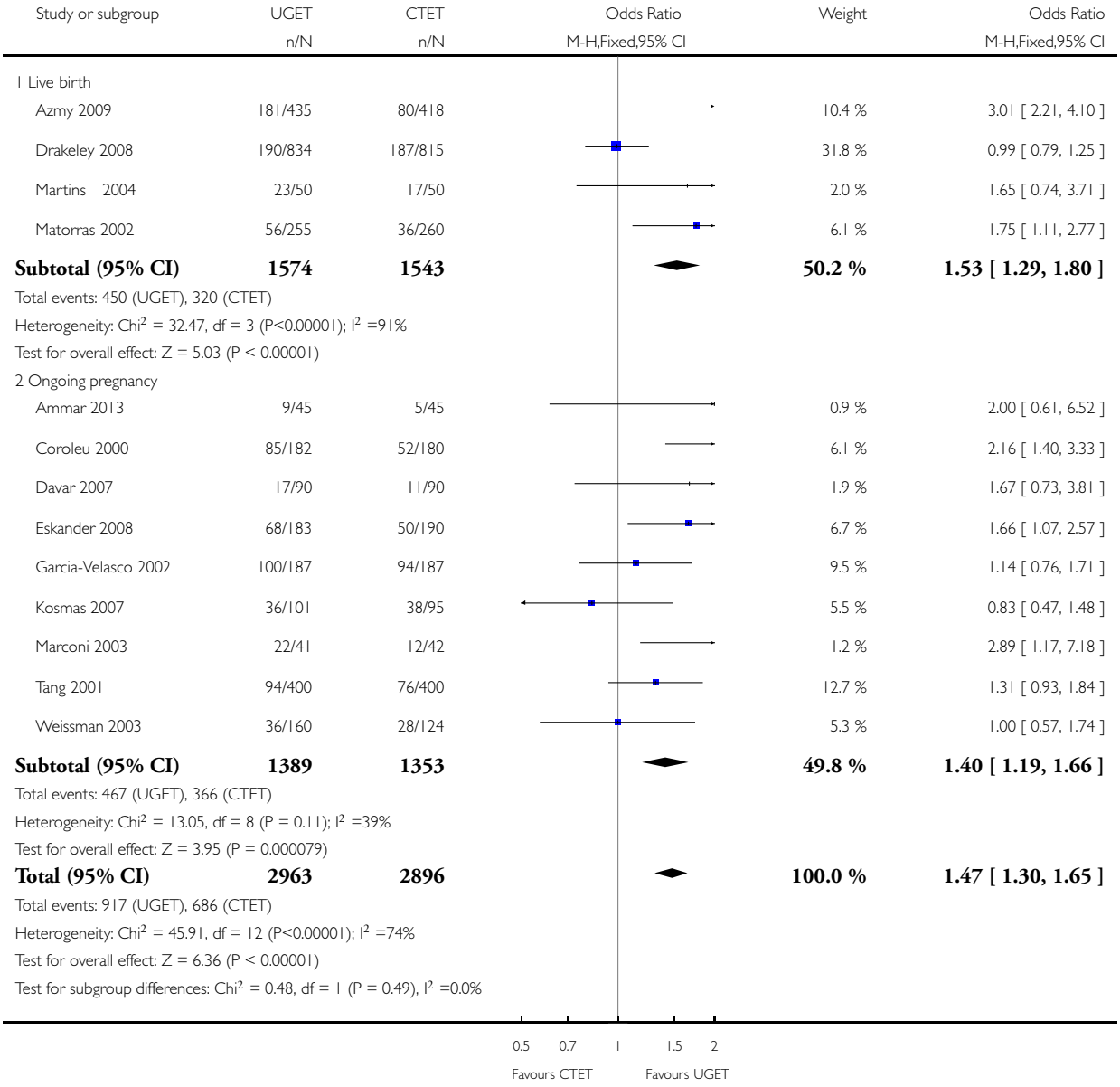
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Type of catheter	4	3117	Odds Ratio (M-H, Fixed, 95% CI)	1.53 [1.29, 1.80]
1.1 Different catheters used between groups	1	1649	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.79, 1.25]
1.2 Same catheter both groups	3	1468	Odds Ratio (M-H, Fixed, 95% CI)	2.45 [1.92, 3.12]

Analysis 1.1. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 1 Live birth and ongoing pregnancy (per woman randomised).

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 1 Live birth and ongoing pregnancy (per woman randomised)

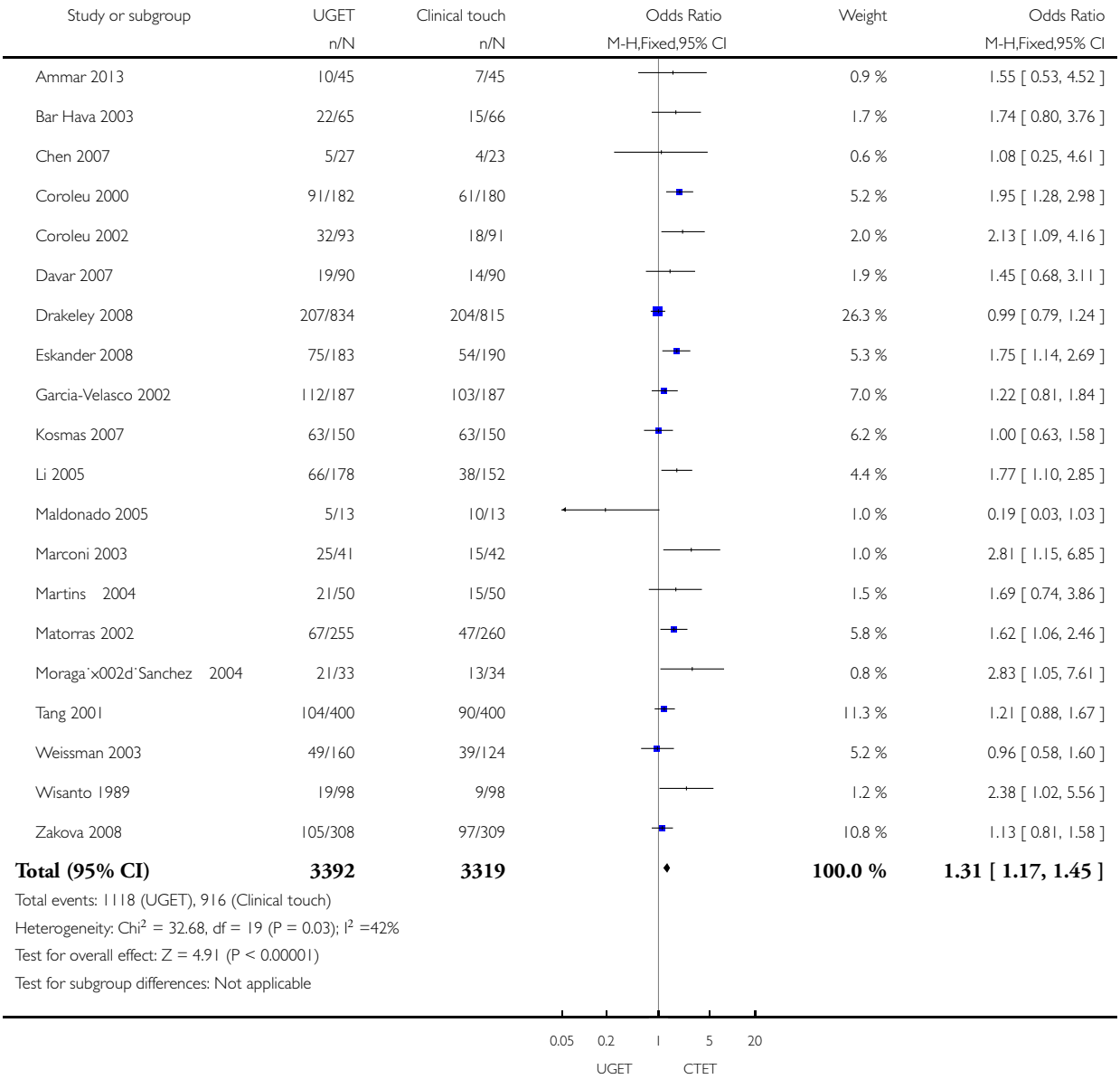


Analysis 1.2. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 2 Clinical pregnancies (per woman randomised).

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 2 Clinical pregnancies (per woman randomised)



Analysis 1.3. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 3 Multiple pregnancies (per woman randomised).

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 3 Multiple pregnancies (per woman randomised)

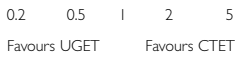
Study or subgroup	UGET n/N	Clinical touch n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Azmy 2009	48/435	50/418		40.5 %	0.91 [0.60, 1.39]
Coroleu 2002	6/93	6/91		5.1 %	0.98 [0.30, 3.15]
Davar 2007	0/90	0/90			Not estimable
Eskander 2008	3/183	2/190		1.7 %	1.57 [0.26, 9.49]
Garcia-Velasco 2002	24/187	25/187		19.4 %	0.95 [0.52, 1.74]
Martins 2004	6/50	7/50		5.5 %	0.84 [0.26, 2.70]
Matorras 2002	22/255	14/260		11.3 %	1.66 [0.83, 3.32]
Tang 2001	31/400	20/400		16.5 %	1.60 [0.89, 2.85]
Total (95% CI)	**1693**	**1686**		**100.0 %**	**1.13 [0.87, 1.45]**

Total events: 140 (UGET), 124 (Clinical touch)

Heterogeneity: Chi^2 = 4.27, df = 6 (P = 0.64); I^2 =0.0%

Test for overall effect: Z = 0.93 (P = 0.35)

Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 4 Miscarriage (per woman randomised).

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 4 Miscarriage (per woman randomised)

Study or subgroup	UGET n/N	Clinical touch n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Ammar 2013	1/45	2/45		2.0 %	0.49 [0.04, 5.59]
Azmy 2009	43/435	38/418		36.4 %	1.10 [0.69, 1.74]
Coroleu 2002	7/93	4/91		3.9 %	1.77 [0.50, 6.27]
Davar 2007	2/90	3/90		3.1 %	0.66 [0.11, 4.04]
Eskander 2008	5/183	4/190		4.0 %	1.31 [0.35, 4.94]
Garcia-Velasco 2002	12/187	10/187		9.7 %	1.21 [0.51, 2.88]
Kosmas 2007	4/150	6/150		6.1 %	0.66 [0.18, 2.38]
Martins 2004	2/50	7/50		7.0 %	0.26 [0.05, 1.30]
Matorras 2002	10/255	10/260		9.9 %	1.02 [0.42, 2.49]
Tang 2001	8/400	10/400		10.2 %	0.80 [0.31, 2.04]
Weissman 2003	9/160	7/124		7.7 %	1.00 [0.36, 2.75]
Total (95% CI)	**2048**	**2005**		**100.0 %**	**0.99 [0.74, 1.31]**

Total events: 103 (UGET), 101 (Clinical touch)

Heterogeneity: Chi^2 = 5.17, df = 10 (P = 0.88); I^2 =0.0%

Test for overall effect: Z = 0.10 (P = 0.92)

Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 5 Ectopic pregnancy (per woman randomised).

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 5 Ectopic pregnancy (per woman randomised)

Study or subgroup	UGET n/N	Clinical touch n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Azmy 2009	0/435	0/418			Not estimable
Coroleu 2000	1/182	1/180		7.2 %	0.99 [0.06, 15.93]
Coroleu 2002	0/93	0/91			Not estimable
Eskander 2008	1/183	0/190		3.5 %	3.13 [0.13, 77.37]
Garcia-Velasco 2002	0/187	5/187		39.4 %	0.09 [0.00, 1.61]
Kosmas 2007	2/150	2/150		14.2 %	1.00 [0.14, 7.19]
Matorras 2002	2/255	1/260		7.1 %	2.05 [0.18, 22.72]
Tang 2001	2/400	4/400		28.6 %	0.50 [0.09, 2.73]
Total (95% CI)	**1885**	**1876**		**100.0 %**	**0.64 [0.28, 1.49]**

Total events: 8 (UGET), 13 (Clinical touch)

Heterogeneity: $Chi^2 = 3.99$, df = 5 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 1.03 (P = 0.30)

Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 6 Blood on catheter.

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 6 Blood on catheter

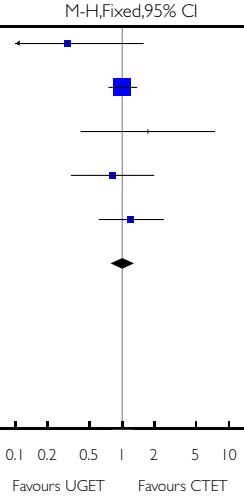
Study or subgroup	UGET n/N	Clinical touch n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Coroleu 2002	2/93	6/91		5.3 %	0.31 [0.06, 1.58]
Drakeley 2008	89/834	86/815		69.9 %	1.01 [0.74, 1.39]
Eskander 2008	5/183	3/190		2.6 %	1.75 [0.41, 7.43]
Garcia-Velasco 2002	9/187	11/187		9.4 %	0.81 [0.33, 2.00]
Wisanto 1989	21/100	18/100		12.8 %	1.21 [0.60, 2.44]
Total (95% CI)	**1397**	**1383**		**100.0 %**	**1.00 [0.77, 1.30]**

Total events: 126 (UGET), 124 (Clinical touch)

Heterogeneity: $Chi^2 = 3.05$, df = 4 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 0.00 (P = 1.0)

Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1 Ultrasound-guided embryo transfer versus 'clinical touch', Outcome 7 Not considered an easy transfer.

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 1 Ultrasound-guided embryo transfer versus 'clinical touch'

Outcome: 7 Not considered an easy transfer

Study or subgroup	UGET n/N	Clinical touch n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Azmy 2009	31/435	88/418		34.4 %	0.34 [0.23, 0.50]
Coroleu 2000	3/182	5/180		1.9 %	0.59 [0.14, 2.45]
Coroleu 2002	6/93	11/91		4.3 %	0.53 [0.21, 1.38]
Davar 2007	8/90	12/90		4.6 %	0.67 [0.29, 1.55]
Kosmas 2007	7/150	9/150		3.4 %	0.78 [0.30, 2.03]
Matorras 2002	1/255	18/260		6.8 %	0.06 [0.01, 0.42]
Tang 2001	65/400	72/400		27.6 %	0.90 [0.67, 1.23]
Weissman 2003	24/160	11/124		4.7 %	1.69 [0.86, 3.32]
Wisanto 1989	6/100	7/100		2.7 %	0.86 [0.30, 2.46]
Zakova 2008	32/308	25/309		9.6 %	1.28 [0.78, 2.11]
Total (95% CI)	**2173**	**2122**		**100.0 %**	**0.69 [0.57, 0.82]**

Total events: 183 (UGET), 258 (Clinical touch)

Heterogeneity: Chi^2 = 35.34, df = 9 (P = 0.00005); I^2 =75%

Test for overall effect: Z = 4.12 (P = 0.000038)

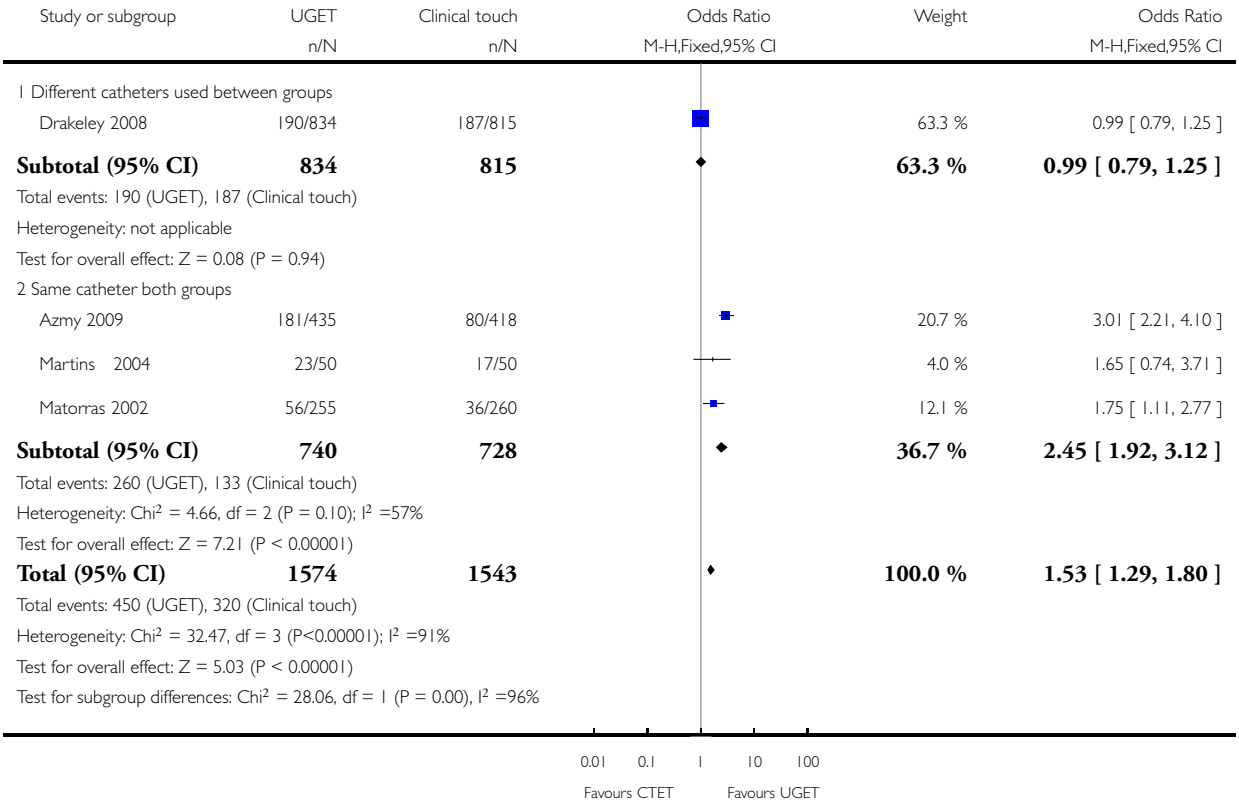
Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Additional analyses - Live birth and type of catheter, Outcome 1 Type of catheter.

Review: Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women

Comparison: 2 Additional analyses - Live birth and type of catheter

Outcome: 1 Type of catheter



ADDITIONAL TABLES

Table 1. Additional data

Study ID	Frozen or fresh	IVF protocol	Embryo transfer protocol	Age of women
Ammar 2013	Fresh embryos	Long protocol, pituitary down-regulation with triptorelin (0.1 mg SC) daily starting from day 21 of cycle and	Dorsolithotomy position and sterile speculum inserted into vagina. When cervix was visualised it was washed with	29.0 +/- 5.0 in UGET group and 30.0 +/- 5.0 in clinical touch group

Table 1. Additional data (*Continued*)

		decreased to 0.05 mg/day with the onset of menstruation. HMG started on day 2 of menstrual cycle (150 to 300 IU/day) When 3 or more follicles were > 18 mm in diameter, 10,000 IU of hCG given IM. Oocytes retrieved 36 hours later	a sponge soaked with the transfer media Catheter removed after 10 seconds of releasing embryos	
Azmy 2009	Fresh embryos	No details	No details	32.4 +/- 4.1 in UGET group and 33.2 +/- 3.6 in clinical touch group
Zakova 2008	No details	Standard procedure for institution	No details	32.7 +/- 4.2 in UGET group and 32.5 +/- 4.4 in clinical touch group
Drakeley 2008	Fresh and frozen embryos used	No details	No details	No details of mean age
Eskander 2008	Fresh transfer from both groups	Down-regulation with GnRH agonist protocol followed by ovarian stimulation with recombinant FSH or hMG, or both, until the day of hCG administration. When the leading follicle reached > 18 mm, hCG was given and oocyte retrieval performed 34 to 36 hours later. Luteal phase support provided by daily P vaginal suppositories	Standardised procedure not described	32.41 +/- 5.47 in UGET group and 31.69 +/- 5.46 in clinical touch group
Chen 2007	Fresh transfers from both groups	Down-regulated with the a GnRH analogue. On day 3 of the treatment cycle, recombinant FSH at a dose of 225 to 300 IU/day combined with hMG 150 IU/day administered for 3 days. From day 6 follitropin alfa (Gonal-F) 300 IU/day administered for 4 days. HCG admin-	External genitalia and cervix prepared	34 +/- 3.6 in UGET group and 32.6 +/- 3.6 in clinical touch group

Table 1. Additional data (*Continued*)

		istered when leading follicles > 18 mm diameter and at least 2 other follicles > 14 mm diameter. Luteal phase support through micronised P beginning on the day of embryo retrieval		
Coroleu 2002	100% frozen from each group	Leuprolide acetate for pituitary suppression. A 'flare up' protocol was used in women with poor response and/or basal FSH > 10.5 IU/L (leuprolide acetate + hMG). HCG administered when 2 or more follicles > 18 mm in diameter were present. Oocyte aspiration 35 to 37 hours post hCG injection. Embryo transfer protocol: women given IM triptorelin (Decapeptyl) on days 20 to 22 of menstrual cycle. At onset of menses or 14 to 16 days after Decapeptyl and with estradiol levels < 50 pg/ml estradiol valerate 8 mg/day given for 13 days. On day 14, 200 mg vaginal micronised progesterone 3 times per day	Lithotomy position, cervix exposed using bivalve speculum; exocervix cleaned with phosphate-buffered saline; endocervical mucus removed with sterile Teflon catheter	36.6 +/- 3.4 for UGET group and 36.2 +/- 3.0 for clinical touch group
Coroleu 2000	Fresh embryos	Leuprolide (0.5 mg/day SC) down-regulation, routine ovarian stimulation (Neo Fertinorm; Serono, Madrid, Spain)	Lithotomy position, cervix exposed using bivalve speculum; exocervix cleaned with phosphate-buffered saline; endocervical mucus removed with sterile Teflon catheter	34.6 +/- 4.0 in UGET group and 34.5 +/- 4.1 in clinical touch group
Davar 2007	Fresh embryo	Treated with a long protocol. Down-regulated with buserelin acetate (0.5 mg SC per day) from	Full bladder in UGET group. Dorsolithotomy position, cervix washed with a sponge soaked in	29.39 +/- 4.2 in UGET group and 30.21 +/- 5.1 in clinical touch group

Table 1. Additional data (*Continued*)

		day 21. Stimulated with hMG from day 2 of menstrual cycle 150 to 300 IU/day. When 3 follicles > 18 mm were observed, women received 10,000 IU hCG and oocyctes retrieved 36 hours later	transfer medium. Cervix mucus aspirated from the external os	
Tang 2001	56.3% fresh embryos in UGET group, 54% fresh embryos in clinical touch group	Buserelin (150 micrograms, intra-nasally, four times daily) down-regulation from day 21. HMG started on day 2 of the treatment cycle, hCG given when leading follicle greater than or equal to 18 mm and at least 3 follicles greater than or equal to 15 mm in diameter. For frozen transfers, embryo transfer based on natural cycles, clomiphene citrate-induced cycles, or controlled cycles using pituitary down-regulation followed by HRT depending on woman's ovulatory history	Lithotomy position, cervix exposed using bivalve speculum; cervix cleansed with sterile saline and then culture medium	34.2 +/- 4.1 for UGET group and 34.4 +/- 3.5 for clinical touch group
Wisanto 1989	Fresh embryos	74% of UGET group and 60% of clinical touch group received buserelin, hMG; 26% of UGET group and 40% clinical touch group received clomiphene citrate, hMG	Indomethacin suppositories 100 mg given 30 mins pre-transfer. Lithotomy position, exocervix cleaned with cotton swab and culture medium containing HEPES (Sigma; St Louis, MO)	32.8 +/- 5 for UGET group and 32.2 +/- 4.4 for clinical touch group
Maldonado 2005	Not stated	Not stated	Not stated	Not stated
Martins 2004	Fresh embryos	Nafarelin acetate 400 micrograms/day intra-nasally down-regulation from the 21st day of cycle to day of hCG. FSH given 14 days after use of nafarelin (150 to	Lithotomy position, cervix exposed using bivalve speculum, mucus and secretions removed with culture medium	32.1 +/- 4.1 in UGET group and 32.0 +/- 3.2 in clinical touch group

Table 1. Additional data (*Continued*)

		450 IU for 7 days). HCG administered when minimum of 2 follicles have a minimum diameter of 17 mm		
Matorras 2002	Fresh embryos	Nafarelin acetate SC daily down-regulation from day 20 to 22; recombinant FSH started on day 2 of treatment cycle, hCG 10, 000 IU administered IM when at least 3 follicles > 18 mm. Luteal phase supported with micronised progesterone	Lithotomy position, cervix exposed using bivalve speculum, exocervix cleansed with Ham's F-10 medium (Invitrogen Corp; UK). Mucus not removed	33.98 +/- 3.12 in UGET group and 34.21 +/- 2.98 in clinical touch group
Garcia-Velasco 2002	Fresh embryos	Recipients: pituitary desensitisation with IM leuprorelin. HRT given to all women from day 1	Cervix cleansed with sterile saline and endocervical mucus aspirated	37.8 +/- 0.3 in UGET group and 38.2 +/- 0.4 in clinical touch group
Kosmas 2007	Fresh, non-donor embryos	Down-regulation with agonist and antagonist protocols. Ovarian stimulation with various forms of urinary and recombinant FSH. OPU performed 36 hrs after administration of hCG 10,000 units when at least 3 follicles ≥ 17 mm. Vaginal progesterone given for luteal support	Woman placed in dorsal lithotomy position and cervix visualised with bivalve speculum. Pericervical area and cervix cleaned with gauze moistened with 0.5 M NaCl. Endocervical mucus removed with aseptic gauze	32.05 +/- 4.3 for UGET group and 32.31 +/- 3.92 for clinical touch group
Bar Hava 2003	No details	No details	No details	31.6 +/- 5.5 in UGET group and 33.2 +/- 6.0 in clinical touch group
Weissman 2003	No details	No details	No details	34.9 +/- 5.6 for UGET group and 34.0 +/- 6.2 for clinical touch (personal communication)
Li 2005	Fresh embryo	Regular regimen: IM GnRH on day 21 of cycle, then FSH (150 to	Lithotomy position, cervix exposed using bivalve speculum, cervix	32.2 +/- 3.9 in UGET group and 32.5 +/- 4.2 in clinical touch group

Table 1. Additional data (*Continued*)

		300 IU/day) on days 3 to 5 of next cycle. HCG given when leading follicles > 18 mm diameter 'Mini-dose' regimen: Oral contraceptives for at least 21 days, then 3 days later triptorelin (Decapeptyl) 0.1 mg given daily. FSH 150 to 300 IU/day given on days 2 to 3 of menstrual cycle. 10,000 IU of hCG injected when leading follicle > 18 mm 'Oral contraceptives + GnRHa': Oral contraceptives for 21 to 28 days and in last 7 days. Decapeptyl 0.1 mg daily. On days 2 to 3 of menstrual cycle FSH 75 to 150 IU/day then 10,000 IU hCG when lead follicle > 18 mm	cleansed with saline	
Moraga-Sanchez 2004	No details	No details	No details	No details
Marconi 2003	Fresh embryo	rFSH from either day 2 or 3 at 225 IU SC daily. GnRH antagonist at 0.25 mg SC daily given when largest follicle reached 14 to 15 mm diameter. HCG 10,000 IU administered when leading follicle was at least 18 mm in diameter 35 to 36 hrs prior to oocyte retrieval	No details	31.8 +/- 2.67 in UGET group and 32.5 +/- 3.88 in clinical touch group

FSH: follicle-stimulating hormone
GnRHa: gonadotropin-releasing hormone agonist
hCG: human chorionic gonadotropin
hMG: human menopausal gonadotropin
HRT: hormone replacement therapy
IM: intramuscularly
IVF: in-vitro fertilisation
OPU: ovum pick-up
P: progesterone

QDS: 4 times a day
rFSH: recombinant follicle-stimulating hormone
SC: subcutaneously
UGET: ultrasound-guided embryo transfer

Table 2. Replacement procedure

Study ID	Medium type	Distance from fundus	Ease of transfer	Type of catheter	Number of embryos
Ammar 2013	G-1^{TM} version 3 (Vitrolife, Goteborg, Sweden)	1.5 cm	No details	Labotect catheter	Maximum of 3
Azmy 2009	No details	10 to 15 mm	There were no difficult transfers in either group	Soft catheter (Labotect embryo transfer catheter set)	2.23 +/- 0.5 for UGET group and 2.34 +/- 0.6 for clinical touch group
Davar 2007	No details	1.5 cm	8.9% of UGET group versus 13.3% of clinical touch group were difficult transfers	An ultrasoft catheter	2.11 +/- 0.6 for UGET group and 2.29 +/- 0.6 for clinical touch group
Zakova 2008	No details	No details	89.5% in UGET group and 91.8% in clinical touch group were ideal transfers	Cook SoftPass EchoTip in the UGET group; Cook Sydney IVF Embryo Transfer Catheter Set in the clinical touch group	No details
Drakeley 2008	No details	15 mm from the endometrial fundus in the sagittal plane in the UGET group; 6 cm from the external cervical os in the clinical touch group	Ease of transfer not compared between groups; overall data provided only	Cook SoftPass EchoTip in the UGET group; soft non-echogenic Wallace or Rocket Embryon catheters in the clinical touch group	1.89 +/- 0.35 for UGET group and clinical touch group
Eskander 2008	No details	Approximately 2 cm from fundus in both groups	No significant differences between groups in the incidence of easy transfers	Cook	3.36 +/- 1.07 for UGET group and 3.32 +/- 1.04 for clinical touch group

Table 2. Replacement procedure *(Continued)*

Chen 2007	No details	UGET = within 1 cm of the fundus; clinical touch based on judgement but as close to the fundus as possible without touching	No details	Frydman soft catheter	5.0 +/- 1.6 for UGET group and 4.5 +/- 1.7 for clinical touch group
Coroleu 2000	50% synthetic serum substitute (Irvine Scientific) plus IVF50 for early cleavage or G2.2 (Scandinavian IVF Science) for blastocysts. Quantity: 30 microliters for both groups	UGET = 1.5 cm; clinical touch based on judgement ("as close to fundus without touching")	98.3% in UGET group and 97.2% in clinical touch group were easy and very easy	Edwards Wallace	2.9 +/- 0.8 for UGET group and 2.8 +/- 0.8 for clinical touch group
Coroleu 2002	50% synthetic serum substitute and IVF50 medium. Quantity: 30 microliters	UGET = 1.5 to 2.0 cm, clinical touch = 1.5 to 2.0 cm as predicted from ultrasonic measurement of uterine cavity performed within 3 months of embryo transfer	93.5% in UGET group and 87.9% in clinical touch group were very easy, easy or moderate	Edwards Wallace	2.1 +/- 0.8 for UGET group and 2.2 +/- 0.9 for clinical touch group
Maldonado 2005	Not stated	The catheter tip was placed above the half point of the endometrial cavity	Not stated	Not stated	Not stated
Matorras 2002	No details	1 cm in both groups	96.9% in UGET group and 80.8% in clinical touch group were easy	Frydman	3.54 +/- 1.07 for UGET group and 3.4 +/- 1.20 for clinical touch group
Tang 2001	IVF-20/-100 (Scandi- navian IVF Science, Sweden). Quantity: 5 microliters	6 cm from external os and < 1 cm from fundus in both groups	26.6% in UGET group and 23.8% in clinical touch group were easy	Jansen-Anderson	2.2 +/- 0.6 for UGET group and 2.3 +/- 0.6 for clinical touch group
Garcia-Velasco 2001	No details	UGET = 1.5 cm; clinical touch = judgement	No details	Delphin	3.2 +/- 0.04 for UGET group and 3.2 +/- 0.04 for clini-

Table 2. Replacement procedure (*Continued*)

					cal touch group
Wisanto 1989	Earle's culture medium (Gibco Europe Ltd, Paisley, Scotland). Quantity: 10 to 25 microlitres	1 cm in both groups	UGET 6% were difficult and 2% failed; clinical touch 7% were difficult and 2% failed	TDT (Prodimed; Neuilly-en-Thelle, France)	2.4 +/- 0.7 for UGET group and 2.6 +/- 0.7 for clinical touch group
Martins 2004	No details. Quantity: < 30 microliters culture medium	UGET group = 0.5 to 1.0 cm from fundus; clinical touch group = distance estimated from mock transfer	No details	Frydman	2.6 +/- 0.9 for UGET group and 2.3 +/- 0.6 for clinical touch group
Kosmas 2007	No details	15 mm from the uterine fundus in the UGET group; 6 cm from the cervical os in the clinical touch group	95. 3% in UGET group and 94% in clinical touch group were considered easy	Cook K-J-SPPE EchoTip in UGET group; Cook K-Soft in clinical touch group	1.49 +/- 0.61 for UGET group and 1.43 +/- 0.57 for clinical touch group
Bar Hava 2003	No details	No details	No details	No details	2.2 +/- 1.0 for UGET group and 2.0 +/- 1.2 for clinical touch group
Weissman 2003	No details	No details	15% in UGET group and 8% in clinical touch group were difficult	Cook	2.63 +/- 0.9 for UGET group and 2.51 +/- 0.9 for clinical touch group
Li 2005	HTF Medium	UGET group = 1.5 to 2.0 cm; clinical touch group = clinical judgement ("inserted into the uterine cavity about 6 cm. The embryos were slowly released according to clinicians' judgement")	No details	Wallace all using outer sheath	2.3 +/- 0.53 for UGET group and 2.2 +/- 0.46 for clinical touch group
Moraga-Sanchez 2004	No details	No details	No details	No details	At least 1 embryo of good quality

Table 2. Replacement procedure *(Continued)*

Marconi 2003	No details	No details	No details	Cook EchoTip for UGET group and Frydman for clinical touch group	3.48 +/- 0.67 for UGET group and 3.65 +/- 0.69 for clinical touch group

UGET: ultrasound-guided embryo transfer

Table 3. Other data

Study ID	Day of embryo transfer	Bed rest	Full bladder	USS machine used
Ammar 2013	Day 2	30 minutes after procedure	Advised for women in the UGET group	No details
Azmy 2009	Day 3	No details	Advised for women in the UGET group	3.5 MHz transabdominal probe (Medison, SonoAce 3200, Korea)
Davar 2007	Not clearly stated	30 minutes after procedure	Yes, only for UGET group	Hitachi, Japan, 2000, EZU-PC3A, 220V and 3.5 MHz
Zakova 2008	Day 3 or 4	No details	No details	No details
Drakeley 2008	Day 2 in both groups	No details	Yes, for both groups	Hitachi EUB-525
Eskander 2008	Day 3	No details	Yes, for both groups	2101 Falcon 3.5 MHz probe; BK Medical; Herlev, Denmark
Chen 2007	Day 3	No details	No details	3.5 MHz, Aloka SSD-500
Garcia-Velasco 2002	Day 2 UGET 113/187, clinical touch 118/187; Day 3 UGET 62/187, clinical touch 59/187; Day 6 UGET 12/187, clinical touch 10/187	30 minutes for UGET and clinical touch	Required for both UGET and clinical touch	3.5 MHz, Aloka SSD 1400
Wisanto 1989	48 to 60 hours after retrieval	Yes, 4 hours for both groups	Yes, for both groups	No details
Tang 2001	48 hours after retrieval in both UGET and clinical touch groups	Not required	Required for UGET but not for clinical touch group	3.5 MHz, Aloka SSD - 620

Table 3. Other data (*Continued*)

Coroleu 2000	Day 2 or 3 with cleaved embryos and day 5 or 6 with blastocysts. 93% of UGET transferred on days 2 or 3, 91% of clinical touch transferred on days 2 or 3	No details	No details	Toshiba TOSBEE (SSA-240A) convex 3.75 MHz
Coroleu 2002	UGET day 2 (15%) and day 3 (85%); clinical touch day 2 (11%) and day 3 (89%)	30 minutes for both groups	Required for UGET but not for clinical touch group	Toshiba TOSBEE (SSA-240A) convex 3.75 MHz
Maldonado 2005	Day 3	No details	No details	No details
Martins 2004	All embryos were transferred on day 2 in both groups, any additional embryos were cryopreserved at the end of the second day	No details	No details	3.5 MHz, Aloka SSD 1100
Matorras 2002	85.9% of UGET took place on day 2 to 3, 87.7% of clinical touch transfers took place on days 2 to 3	10 to 15 minutes in both groups	Required for UGET but not for clinical touch group	3.5 MHz, Aloka SSD 1200
Kosmas 2007	Day 3 or 5	Yes, 2 hours prior to leaving hospital	Full bladder not a prerequisite	3.5 MHz, Aloka 3500
Bar Hava 2003	No details	No details	No details	No details
Weissman 2003	Day 2 to 3 transfers in both UGET and clinical touch groups	No details	Yes, in both groups	No details
Moraga-Sanchez 2004	No details	No details	No details	No details
Li 2005	Days of embryo culture in vitro UGET 2.45 +/- 0.4, clinical touch 2.42 +/- 0.2	Minimum 6 hours in both UGET and clinical touch groups	No details	3.5 MHz, Aloka SSD 1400
Marconi 2003	Day 3 post aspiration in both groups	No details	No details	No details

UGET: ultrasound-guided embryo transfer

APPENDICES

Appendix 1. Gynaecology and Fertility Group key words

Keywords CONTAINS “Embryo Transfer” or “embryo transfer techniques” or “Embryo Transfer-uterine” or “frozen embryo transfer” or “frozen-thawed embryo transfer” or “ET” or “FET” or “embryo placement” or “Embryo transfer-tubal” or “embryos transferred” or “blastocyst transfer” or Title CONTAINS “embryo placement” or “Embryo transfer-tubal” or “embryos transferred” or “blastocyst transfer” or “Embryo Transfer” or “embryo transfer techniques” or “Embryo Transfer-uterine” or “frozen embryo transfer” or “frozen-thawed embryo transfer” or “ET” or “FET”
AND
Keywords CONTAINS “ultrasonography” or “ultrasound” or “ultrasound guidance” or “ultrasound guided” or “ultrasound guided embryo transfer” or “ultrasound, pelvic” or “sonographic” or “imaging” or “sonographic” or “sonohysterogram” or “sonohysterography” or “hysterosonography” or Title CONTAINS “ultrasonography” or “ultrasound” or “ultrasound guidance” or “ultrasound guided” or “ultrasound guided embryo transfer” or “ultrasound, pelvic” or “sonographic” or “imaging” or “sonographic” or “sonohysterogram” or “sonohysterography” or “hysterosonography”

Appendix 2. CENTRAL search strategy

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <March 2015>
Search Strategy:
---
1 exp embryo transfer/ (827)
2 ivf-et.tw. (316)
3 (embryo$ adj2 transfer$).tw. (1403)
4 (blastocyst$ adj2 transfer$).tw. (148)
5 (embryo$ adj2 place$).tw. (12)
6 (embryo$ adj2 replac$).tw. (89)
7 (embryo$ adj2 position$).tw. (3)
8 or/1-7 (1825)
9 ultrasonography/ or endosonography/ or ultrasonography, interventional/ (1759)
10 ultrasonogra$.tw. (3567)
11 ultrasound$.tw. (8863)
12 sonograph$.tw. (1495)
13 sonogram$.tw. (70)
14 (echograph$ or echogram$).tw. (174)
15 hysterosono$.tw. (12)
16 endosonogra$.tw. (92)
17 or/9-16 (13257)
18 8 and 17 (204)
19 limit 18 to yr=“2009 -Current” (57)

Appendix 3. MEDLINE search strategy

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---
1 exp embryo transfer/ (13099)
2 ivf-et.tw. (1899)
3 (embryo$ adj2 transfer$).tw. (12109)
4 (blastocyst$ adj2 transfer$).tw. (1083)
5 (embryo$ adj2 place$).tw. (1029)

6 (embryo$ adj2 replac$).tw. (603)
7 (embryo$ adj2 position$).tw. (186)
8 or/1-7 (20203)
9 ultrasonography/ or endosonography/ or ultrasonography, interventional/ (87377)
10 ultrasonogra$.tw. (81827)
11 ultrasound$.tw. (165388)
12 sonograph$.tw. (44691)
13 sonogram$.tw. (3346)
14 (echograph$ or echogram$).tw. (9315)
15 hysterosono$.tw. (111)
16 endosonogra$.tw. (2116)
17 or/9-16 (297635)
18 8 and 17 (1630)
19 randomized controlled trial.pt. (392819)
20 controlled clinical trial.pt. (89297)
21 randomized.ab. (318332)
22 randomised.ab. (63190)
23 placebo.tw. (166071)
24 clinical trials as topic.sh. (172401)
25 randomly.ab. (229693)
26 trial.ti. (137331)
27 (crossover or cross-over or cross over).tw. (63850)
28 or/19-27 (999407)
29 exp animals/ not humans.sh. (4028808)
30 28 not 29 (921377)
31 18 and 30 (198)
32 (2009$ or 2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$).ed. (6001613)
33 (2009$ or 2010$ or 2011$ or 2012$ or 2013$ or 2014$ or 2015$).dp. (5814773)
34 32 or 33 (6674457)
35 31 and 34 (62)

Appendix 4. EMBASE search strategy

Database: Embase <1980 to 2015 Week 18>
Search Strategy:
---
1 exp embryo transfer/ (21998)
2 (embryo$ adj2 transfer$).tw. (16959)
3 ivf-et.tw. (2510)
4 (blastocyst$ adj2 transfer$).tw. (1836)
5 (embryo$ adj2 place$).tw. (1228)
6 (embryo$ adj2 replace$).tw. (829)
7 (embryo$ adj2 position$).tw. (196)
8 or/1-7 (28966)
9 transvaginal echography/ (12976)
10 ultrasound$.tw. (234070)
11 ultrasonogr$.tw. (105392)
12 sonograph$.tw. (57508)
13 sonogram$.tw. (3974)
14 (echograph$ or echogram$).tw. (10994)
15 hysterosono$.tw. (143)
16 or/9-15 (366886)

17 Clinical Trial/ (843553)
18 Randomized Controlled Trial/ (369125)
19 exp randomization/ (66088)
20 Single Blind Procedure/ (20079)
21 Double Blind Procedure/ (119899)
22 Crossover Procedure/ (42594)
23 Placebo/ (255278)
24 Randomi?ed controlled trial$.tw. (114897)
25 Rct.tw. (16728)
26 random allocation.tw. (1402)
27 randomly allocated.tw. (22147)
28 allocated randomly.tw. (2011)
29 (allocated adj2 random).tw. (721)
30 Single blind$.tw. (15643)
31 Double blind$.tw. (149839)
32 ((treble or triple) adj blind$).tw. (440)
33 placebo$.tw. (212811)
34 prospective study/ (287679)
35 or/17-34 (1452441)
36 case study/ (31373)
37 case report.tw. (279675)
38 abstract report/ or letter/ (921238)
39 or/36-38 (1226085)
40 35 not 39 (1413427)
41 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5260646)
42 40 not 41 (1358099)
43 8 and 16 and 42 (443)
44 (2013$ or 2014$ or 2015$).em. (3872912)
45 (2013$ or 2014$ or 2015$).dp. (528499)
46 44 or 45 (3873631)
47 43 and 46 (101)

Appendix 5. PsycINFO search strategy

Database: PsycINFO <1806 to April Week 4 2015>
Search Strategy:
---
1 exp Infertility/ or exp Reproductive Technology/ or exp Embryo/ (4150)
2 (embryo$ adj2 transfer$).tw. (123)
3 (blastocyst$ adj2 transfer$).tw. (4)
4 (embryo$ adj2 place$).tw. (18)
5 (embryo$ adj2 replac$).tw. (7)
6 or/1-5 (4200)
7 exp Ultrasound/ (1096)
8 ultrasonogra$.tw. (763)
9 ultrasound$.tw. (2486)
10 sonograph$.tw. (551)
11 sonogram$.tw. (66)
12 (echograph$ or echogram$).tw. (57)
13 or/7-12 (3796)
14 6 and 13 (24)
15 random.tw. (43430)

16 control.tw. (337122)
17 double-blind.tw. (18791)
18 clinical trials/ (8613)
19 placebo/ (4057)
20 exp Treatment/ (613111)
21 or/15-20 (940087)
22 14 and 21 (11)
23 limit 22 to yr="2009 -Current" (4)

Appendix 6. CINAHL search strategy

CINAHL search strategy for JB604 06.05.15

#	Query	Results
S31	S18 AND S30	37
S30	S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29	957,665
S29	TX allocat* random*	4,263
S28	(MH "Quantitative Studies")	13,366
S27	(MH "Placebos")	9,206
S26	TX placebo*	33,746
S25	TX random* allocat*	4,263
S24	(MH "Random Assignment")	39,076
S23	TX randomi* control* trial*	86,804
S22	TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))	765,707
S21	TX clinic* n1 trial*	171,460
S20	PT Clinical trial	77,813
S19	(MH "Clinical Trials+")	186,869
S18	S8 AND S17	135
S17	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16	71,153

(*Continued*)

S16	TX endosonogra*	2,392
S15	TX hysterosono*	9
S14	TX (echograph* or echogram*)	208
S13	TX sonogram*	242
S12	TX sonograph*	6,497
S11	TX ultrasound	29,600
S10	TX ultrasonogra*	59,808
S9	(MM "Ultrasonography") OR (MM "Endosonography")	10,870
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7	1,938
S7	TX (embryo* N2 replac*)	13
S6	TX (embryo* N2 place*)	22
S5	TX (blastocyst* N2 transfer*)	52
S4	TX (embryo* N2 transfer*)	771
S3	(MM "Embryo Transfer")	262
S2	TX embryo* N3 transfer*	777
S1	(MM "Fertilization in Vitro")	1,450

WHAT'S NEW

Last assessed as up-to-date: 6 May 2015.

Date	Event	Description
1 March 2016	New search has been performed	New searches run in May 2015 and four new studies added (Ammar 2013, Azmy 2009, Davar 2007, Maldonado 2005). Five studies were excluded (Bodri 2011, Deep 2013, Hauzman 2012, Porat 2010, Saharkhiz 2014).

(*Continued*)

1 March 2016	New citation required but conclusions have not changed	The addition of new studies did not lead to a change in the conclusions of this review

HISTORY

Protocol first published: Issue 3, 2006

Review first published: Issue 1, 2007

Date	Event	Description
22 June 2009	New search has been performed	Five new studies have been added to the review and the review style altered to the RevMan 5 requirements
22 June 2009	New citation required and conclusions have changed	The conclusions of the updated review have altered with the addition of five newly identified randomised controlled trials, and the review has been amended as a consequence
6 November 2008	Amended	Converted to new review format.
14 November 2006	New citation required and conclusions have changed	Substantive amendment.

CONTRIBUTIONS OF AUTHORS

Julie Brown took the lead in writing the review and update and was involved in all aspects of review design, search, data extraction, and summary.

Karen Buckingham was a co-author of the review and was involved in the design, data extraction, and summary. She is a clinical expert in the field.

William Buckett and Ahmed Abou-Setta helped review the manuscript and are experienced in the specialised field.

DECLARATIONS OF INTEREST

Ahmed Abou-Setta and William Buckett are both authors of separate, complementary systematic reviews on the topic of ultrasound guidance versus clinical touch during embryo transfer.

SOURCES OF SUPPORT

Internal sources

- Liggins Institute, The University of Auckland, New Zealand.

Infrastructure support to update this review

- Department of Obstetrics and Gynaecology, The University of Auckland, New Zealand.

Infrastructure support to update this review

External sources

- None, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As per the Cochrane Gynaecology and Fertility Group's new guidelines, the Peto odds ratio has been replaced with the Mantel-Haenszel odds ratio.

We have removed the secondary outcome of multiple pregnancy rate - multiple pregnancy (twins, triplets, or higher, order specified if possible) per clinical pregnancy, confirmed by ultrasound or delivery.

INDEX TERMS

Medical Subject Headings (MeSH)

*Ultrasonography, Interventional; Embryo Transfer [adverse effects; *methods]; Palpation [adverse effects; *methods]; Randomized Controlled Trials as Topic; Treatment Outcome

MeSH check words

Female; Humans; Pregnancy