

# Number of embryos for transfer after IVF and ICSI: a Cochrane review

Zabeena Pandian<sup>1,3</sup>, Allan Templeton<sup>1</sup>, Gamal Serour<sup>2</sup> and Siladitya Bhattacharya<sup>1</sup>

<sup>1</sup>Department of Obstetrics & Gynaecology, Aberdeen Maternity Hospital, Aberdeen AB25 2ZD, UK and <sup>2</sup>Egyptian IVF & ET Center, Maadi, Cairo, Egypt

<sup>3</sup>To whom correspondence should be addressed. E-mail: ogy211@abdn.ac.uk

This paper is based on a Cochrane review (Pandian Z, Bhattacharya S, Ozturk O, Serour GI, Templeton A. Number of embryos for transfer following in vitro fertilization or intra-cytoplasmic sperm injection) published in the Cochrane Library, issue 4, 2004 (updated issue 2, 2005, see [www.CochraneLibrary.net](http://www.CochraneLibrary.net) for information) reproduced with permission from The Cochrane Collaboration and John Wiley and Son Ltd. Cochrane reviews are regularly updated as new evidence emerges and in response to comments and criticisms, and The Cochrane Library should be consulted for the most recent version of the review.

**BACKGROUND:** The most common complication of IVF is multiple pregnancy, which occurs in 25% of pregnancies following the transfer of two embryos. Single embryo transfer can minimize twin pregnancies but could also lower live birth rates. Our aim was to perform a systematic review of randomized trials to determine the effectiveness of single versus double embryo transfer. **METHODS:** Cochrane Collaboration review methods were followed. Randomized controlled trials comparing single and double embryo transfers were identified by searching Medline, EMBASE and the Cochrane register of controlled trials. Contents of specialist journals and proceedings from meetings of relevant societies were hand searched. Data were pooled with Rev Man software using the Peto-modified Mantel–Hanzel method. **RESULTS:** Pooled results from four trials indicate that although double embryo transfer leads to a higher live birth rate per woman [odds ratio (OR) 1.94, 95% confidence interval (CI) 1.47–2.55] in a fresh IVF cycle, comparable results are obtained by subsequent transfer of a frozen embryo (OR 1.19, 95% CI 0.87–1.62). The multiple pregnancy rate is significantly higher (OR 62.83, 95% CI 8.52–463.57) after double embryo transfer. **CONCLUSIONS:** Single embryo transfer significantly reduces the risk of multiple pregnancy, but also decreases the chance of live birth in a fresh IVF cycle. Subsequent replacement of a single frozen embryo achieves a live birth rate comparable with double embryo transfer.

*Key words:* double embryo transfer/IVF/multiple pregnancies/single embryo transfer

## Introduction

Women undergoing treatment with IVF face an ~20-fold increased risk of twins and a 400-fold increased risk of higher order pregnancies (triplets or more) (Martin and Welch, 1998). In 2002, 36.2% out of 29 423 IVF pregnancies in the USA were multiple fetus pregnancies (SART, 2002). In Europe, where two embryo transfers are the norm in many centres, 24% of all IVF infants born in 2001 were twins (Nyboe *et al.*, 2005).

Twins are associated with higher maternal and perinatal complications including miscarriage, pregnancy-induced hypertension, ante-partum haemorrhage, gestational diabetes, operative delivery, prematurity and permanent handicap in the newborn (Seoud *et al.*, 1992; Yokoyama *et al.*, 1995). The perinatal mortality rate in IVF twin pregnancies (46.8 per 1000) is six times higher than that for singletons (Lieberman, 1998) and the risk of neurological problems, especially cerebral palsy (Stromberg *et al.*, 2002), substantially higher. Rearing of twins is also associated with practical difficulties for parents (Garel and Blondel,

1992; Doyle, 1996; Garel *et al.*, 1997), while health service costs associated with peri-natal care are formidable (Callahan *et al.*, 1994; Goldfarb *et al.*, 1996).

The principal reason behind the large number of twin pregnancies in IVF is the policy of transferring multiple embryos within the uterus. In the USA, 62% of IVF cycles involved the transfer of three or more embryos (SART, 2002) while two embryos were replaced in 32% of cycles. While the most effective way to minimize multiple pregnancy is to limit the number of embryos transferred, such a policy has to be balanced against the risk of reducing overall pregnancy rates in IVF. Previously, a large observational study demonstrated that elective transfer of two embryos resulted in a significant reduction of triplet rates (Templeton and Morris, 1998) without compromising live birth rates. As a result, a two embryo transfer policy is now common in most European centres. However, even with two embryo transfer, the risk of twins remains high at 24% (Nyboe *et al.*, 2005), and a move to

elective single embryo transfer has been proposed as the only means of limiting twins.

Initial uncertainty about single embryo transfer was based on data from observational studies suggesting relatively poor outcomes in cases where only one embryo was available for transfer. A study from Finland reported a 20.2% pregnancy rate where only one embryo was available versus 29.7% where one embryo was selected from an available pool of embryos. The cumulative pregnancy rate after frozen–thawed embryo transfers in the elective single embryo transfer group was 47.3% per oocyte retrieval. By comparison, the pregnancy rate for two embryo transfers was 29.4% per transfer and 23.9% of these were twin pregnancies (Vilksa *et al.*, 1999).

Although more treatment cycles may be needed to achieve a similar live birth rate to two embryo transfers, the lower twin pregnancy rate of single embryo transfers may make this a safer and cost-effective option (Wolner-Hanssen and Rydhstroem, 1998). The ultimate clinical decision to reduce the number of embryos for transfer will need to be based on the weight of the available evidence from randomized controlled trials.

Our aim was therefore to perform a systematic review of the literature to determine whether multiple pregnancy rates can be lowered by following a single embryo transfer policy without compromising clinical pregnancy rates.

## Methods

We identified randomized controlled trials that compared elective two embryo transfer with elective single embryo transfer. Trials that evaluated the effectiveness of two embryo transfer versus fresh single embryo transfer followed by frozen–thawed single embryo transfer were also identified. We followed the search strategy developed for the Cochrane Menstrual Disorders and Subfertility Group (MDSG). Trials were identified from the group's specialized register of controlled trials (searched June 25, 2003) and the Cochrane Central Register of Controlled Trials (Cochrane Library Issue 4, 2003). Medline and EMBASE databases were searched from 1970 to 2004 and 1985 to 2004, respectively. The following medical subject headings (MeSH) were used singly or in combination: embryo transfer, multiple pregnancy, IVF, in-vitro fertilisation, ICSI, intracytoplasmic sperm injection, infertility, sub-fertility, single/one embryo, two/double embryo, three/four/multiple embryos, effectiveness, ART, assisted reprod\$ tech\$, randomised controlled trial, clinical trial.

Hand searches included Conference proceedings of the International Federation of Fertility Societies (IFFS), American Society for Reproductive Medicine (ASRM), British Fertility Society (BFS) and European Society for Human Reproduction and Embryology (ESHRE). These were searched between 1997 and 2003 and bibliographies from the identified studies were also hand searched.

Randomized controlled trials were considered for inclusion in the review if they compared any of the following: elective two embryo transfer versus elective single embryo transfer, or the transfer of subsequent single frozen–thawed embryos. In cross-over trials, only data from the first phase (i.e. before cross-over) were used. Studies on embryo transfer at the blastocyst stage were excluded from the review.

The participants comprised subfertile women who underwent embryo transfer following IVF and/or ICSI treatment with their own gametes or as an oocyte/embryo donation recipient. Trials had to report live birth rate per woman/couple, cumulative live birth rate per

woman/couple, pregnancy rate per woman/couple and multiple pregnancy rate per woman/couple as outcome measures.

Data extraction and assessment of trial quality were performed independently by two reviewers (Z.P. and S.B.). Additional information regarding trial methodology or original data was sought from the principal author of trials. Statistical analysis was performed in accordance with the guidelines developed by the MDSG. The outcomes were pooled statistically. Results for each trial were expressed as an odds ratio (OR) with 95% confidence intervals (CIs) and combined for meta-analysis with Rev Man software using the Peto-modified Mantel–Hanzel method.

## Results

We identified four trials (Table I) where single embryo transfer was compared with double embryo transfer (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Lukassen *et al.*, 2002; Thurin *et al.*, 2004). Outcomes included cumulative live birth rate, clinical pregnancy rate, live birth rate and multiple pregnancy rate. The sample was clinically heterogeneous but all the trials included subfertile women who underwent embryo transfer following IVF and/or ICSI with their own gametes or as an oocyte/embryo donation recipient. Women included were of good prognosis, i.e. younger women without a history of multiple failed IVF cycles, and with a number of embryos available for transfer. Only one trial reported live birth rates and cumulative live birth rates after a fresh elective single embryo transfer followed by single frozen and thawed embryo transfer (Thurin *et al.*, 2004).

Table II shows the summary of results. In comparison with single embryo transfer, two embryo transfer in a fresh IVF/ICSI treatment cycle led to a significantly higher pregnancy rate (OR 2.16, 95% CI 1.65–2.82;  $P < 0.00001$ ) and live birth rate per woman (OR 1.94, 95% CI 1.47–2.55, test for overall effect  $P < 0.00001$ ) (Figure 1). The multiple pregnancy rate was significantly higher in women who had double embryo transfer (OR 23.55, 95% CI 8.00–69.29;  $P < 0.00001$ ) (Figure 2). The largest and most recent trial (Thurin *et al.*, 2004) compared two policies: (i) the transfer of two fresh embryos; and (ii) the transfer of a single fresh embryo followed by a single frozen–thawed embryo. There were no significant differences in the cumulative live birth rates (OR 1.19, 95% CI 0.87–1.62,  $P = 0.3$ ) (Figure 3) or clinical pregnancy rates (OR 1.21, 95% CI 0.89–1.64,  $P = 0.2$ ) (Figure 3) between the two groups. Multiple pregnancy rates were significantly higher in women who had elective double embryo transfer (OR 62.83, 95% CI 8.52–463.57,  $P = 0.00005$ ) (Figure 2).

## Discussion

Elective single embryo transfer in a fresh IVF treatment cycle reduces multiple births but also lowers live birth and pregnancy rates in comparison with double embryo transfer. A single embryo transfer policy involving a fresh followed by a frozen embryo transfer reduces the risk of multiples while achieving a live birth rate comparable with that achieved by transferring two fresh embryos. We found no evidence of statistical heterogeneity among the trials included in this review, suggesting that variations among studies had little effect on overall conclusions.

**Table I.** Characteristics of included studies

Study	Methods	Participants	Interventions	Outcomes
Gerris (1999)	Randomized controlled trial. Concealment of allocation adequate. Good quality embryos transferred, morphology of good quality embryos defined. Protocols for ovarian stimulation, oocyte retrieval, insemination and embryo transfer clearly described. Natural progesterone used for luteal phase support. Semen prepared using mini-Percoll gradient prior to insemination. Medi-Cult medium used for embryo culture. Wallace embryo transfer catheter used for transfer. Embryo transfer performed on day 3, 64–67 h after insemination. Results expressed using 95% CI analysis.	First IVF/ICSI cycle. Female age <34 years. Average duration of infertility 3.5 years.	One embryo transfer versus two embryo transfer.	Clinical pregnancy rate, live birth rate, multiple pregnancy rate per woman/couple and implantation rates.
Martikainen (2001)	Multicentre randomized controlled trial. Computer-generated random number table, balanced in sets of 10 used. Good quality embryos transferred. Morphology of good quality embryos described clearly. Protocols for IVF/ICSI clearly defined. Effectiveness of one versus two embryo transfer in frozen replacement cycles analysed separately. All centres involved used various age limits for inclusion of women. Embryos cultured in Medi-Cult medium. IVF-500 medium or Sydney IVF medium (Cook IVF) catheters used for embryo transfer. Embryo transfer performed 46–50 h after oocyte recovery. Natural progesterone used for luteal phase support. $\chi^2$ test and two-tailed <i>t</i> -tests used for statistical analysis.	First IVF/ICSI treatment. Subfertile women with no previous failed treatment, <36 years. At least four good quality embryos should be available	One embryo versus two embryo transfer.	Clinical pregnancy rate, live birth rate, multiple pregnancy rates per woman/couple, implantation and miscarriage rates.
Lukassen (2002)	Prospective randomized controlled trial. Recruitment has been stopped. Results presented are from pilot study. Good quality embryos transferred, but morphological characteristics not defined clearly. Embryo transfer took place on day 3 after insemination.	First IVF/ICSI cycle. Female age <35 years, FSH <10 IU/l. At least one good quality embryo should be available.	One embryo transfer versus two embryo transfer.	Clinical pregnancy rate, live birth rate, multiple pregnancy rates per woman/couple.
Thurin (2004)	Randomized, multicentre trial. Computerized randomization programme used. Double blind study. Patients in single embryo transfer group who did not conceive in the fresh embryo transfer cycle, or who miscarried subsequently underwent the transfer of a single frozen and thawed embryo in a natural or a hormone-stimulated cycle. If the first frozen and thawed embryo was not viable, other embryos were thawed one by one until a viable embryo could be transferred. Intention to treat analysis performed. Statistical analysis included 95% CI.	Women <36 years who had at least two good quality embryos were included.	1. Single embryo versus two embryo transfer. 2. Single embryo transfer plus single frozen and thawed embryo versus double embryo transfer.	Clinical pregnancy rate, live birth rate, cumulative pregnancy rate, multiple pregnancy rate and miscarriage rate.

**Table II.** Summary of results

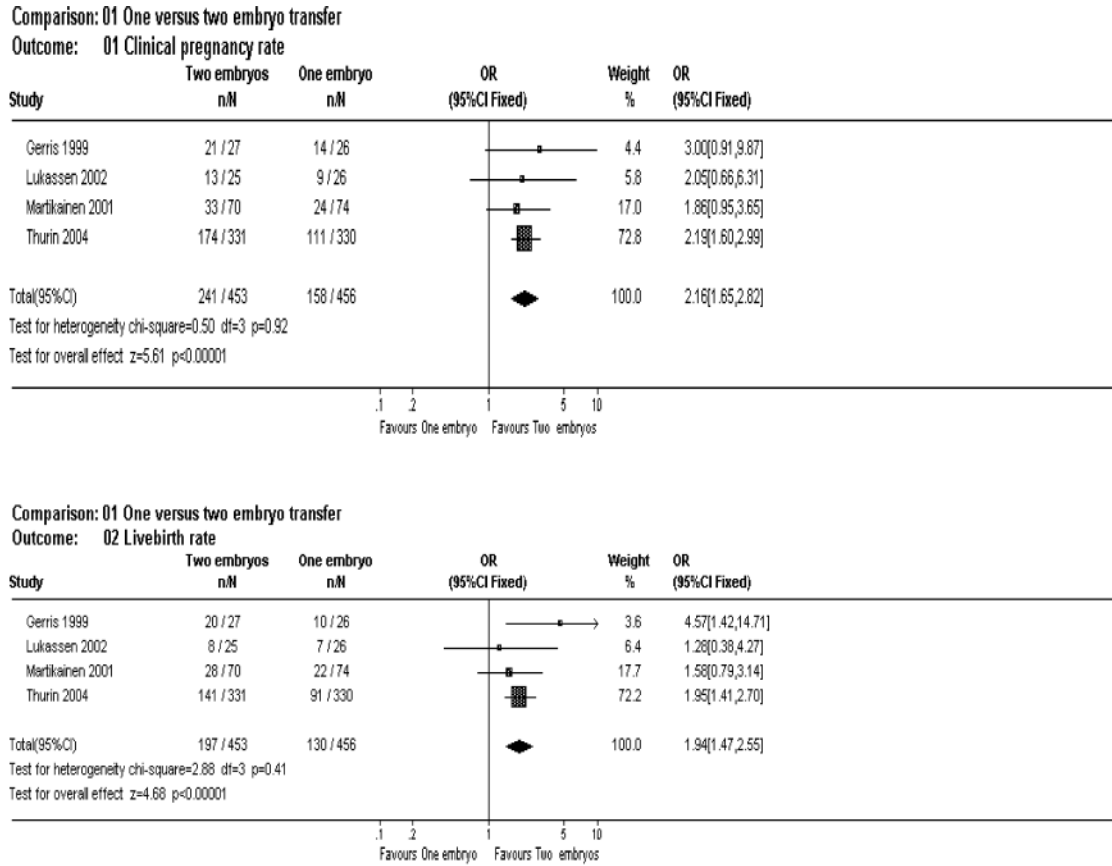
Comparison	Effect size, OR (95% CI)
eDET versus eSET	2.16 (1.65–2.82) <sup>a</sup>
	1.94 (1.47–2.55) <sup>b</sup>
	23.55 (8.00–69.29) <sup>c</sup>
	1.73 (0.95–3.15) <sup>d</sup>
eDET versus eSET + 1FZET	1.21 (0.89–1.64) <sup>a</sup>
	1.19 (0.87, 1.62) <sup>b</sup>
	62.83 (8.52–463.57) <sup>c</sup>
	0.89 (0.52–1.53) <sup>d</sup>

<sup>a</sup>Pregnancy rate per woman.<sup>b</sup>Live birth rate per woman.<sup>c</sup>Multiple pregnancy rate per woman.<sup>d</sup>Miscarriage rate per woman.

All the trials included in this review (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Lukassen *et al.*, 2002; Thurin *et al.*, 2004) reported higher live birth rates per woman with double embryo transfer after fresh IVF treatment. This difference was not sustained in the largest trial on 660 women (Thurin *et al.*, 2004) when the outcome of a fresh as well as the first frozen and thawed single embryo transfers was considered. Multiple pregnancy rates per woman/couple were significantly lower in women who underwent single

embryo transfer in all four trials that were included in this comparison.

The results are based on relatively few trials (the total number of patients from four studies were 456 in the single embryo transfer group and 453 in the double embryo transfer group) and are dominated by a single trial (Thurin *et al.*, 2004). Even though there was no statistical heterogeneity among the trials, it is impossible to exclude an element of clinical heterogeneity. All the trials included ‘good prognosis’ women, i.e. younger women without a history of multiple failed IVF cycles and with a number of embryos available for transfer. The age criteria, however, were different for the included studies. Three trials (Gerris *et al.*, 1999; Lukassen *et al.*, 2002; Thurin *et al.*, 2004) had an upper age limit of 34, 35 and 36 years, respectively. In a multicentre trial (Martikainen *et al.*, 2001) that was included in this comparison, one centre did not take female age into account. The other centres in the trial included women younger than 36 years who were undergoing their first treatment cycle. In all four trials, only ‘good quality’ embryos were transferred. Three trials (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Thurin *et al.*, 2004) defined a ‘top quality embryo’ in explicit terms but their criteria varied in each case. Embryo transfer was performed on day 3 in three trials (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Lukassen *et al.*, 2002). One trial included women who had embryo transfer on 2, 3 or 5 days



† Elective single embryo transfer

\* Elective double embryo transfer

**Figure 1.** Elective single embryo transfer (eSET) versus elective double embryo transfer (eDET). Clinical pregnancy and live birth rates.

after oocyte retrieval (Thurin *et al.*, 2004). Ovarian stimulation protocols, oocyte retrieval and embryo transfer techniques, including embryo culture media and sperm preparations, were clearly described in three trials (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Thurin *et al.*, 2004), but not in the fourth (Lukassen *et al.*, 2002). Again there were variations in the techniques used.

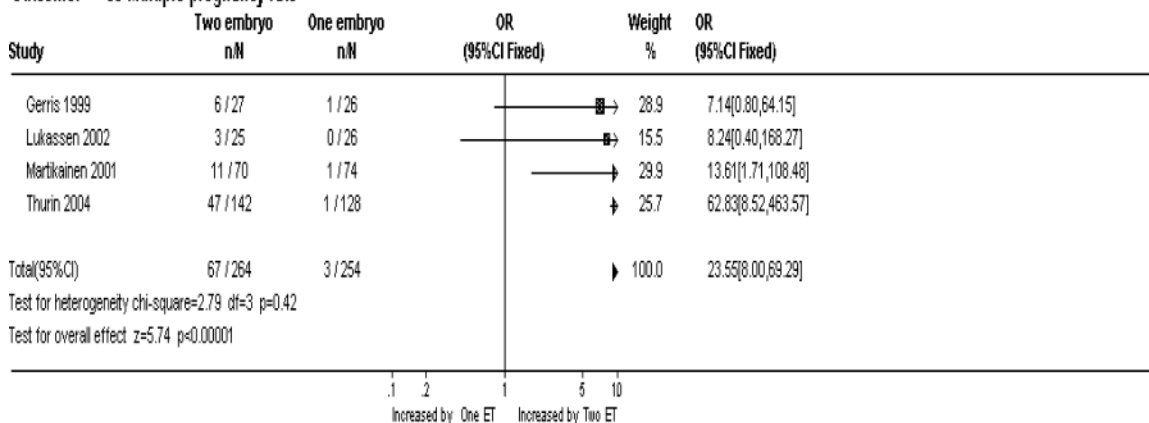
The methodological quality of the trials was variable. Two used computer-generated randomization (Martikainen *et al.*, 2001; Thurin *et al.*, 2004). The others (Gerris *et al.*, 1999; Lukassen *et al.*, 2002) did not describe the method of randomization. Three studies randomized women just before embryo transfer (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Thurin *et al.*, 2004). One did not mention the timing of randomization (Lukassen *et al.*, 2002). Only one study explicitly described measures used for concealment of allocation (Gerris *et al.*, 1999). Three studies included explicit descriptions of methods of statistical analysis (Gerris *et al.*, 1999; Martikainen *et al.*, 2001; Thurin *et al.*, 2004). Intention to treat analysis was performed in a single trial (Thurin *et al.*, 2004) which also was the only one to enforce double blinding. This trial included a power calculation and complete trial flow chart showing the number of withdrawals including cancellations, dropouts and women lost to follow-up (Thurin *et al.*, 2004).

Individually, none of the trials apart from the largest (Thurin *et al.*, 2004) showed a statistically significant difference in

pregnancy and live birth rates between elective single embryo transfer and elective double embryo transfer. Collectively, the combined OR based on 909 women favoured elective double embryo transfer in women undergoing a single fresh cycle of treatment with IVF. A potential advantage of elective single embryo transfer is that it offers an opportunity of freezing surplus embryos and utilizing these in successive treatments after thawing. Two of the trials presented data relating to outcome after transfer of single frozen and thawed embryos in a small group of women (Martikainen *et al.*, 2001; Thurin *et al.*, 2004). In the first (Martikainen *et al.*, 2001), the outcome is similar in the elective single embryo transfer and elective double embryo transfer groups. However, the original randomization was not adhered to for frozen transfers (elective single embryo transfer and single frozen and thawed embryo transfer or subsequent single frozen and thawed embryo transfers), making these data impossible to interpret. The Scandinavian trial (Thurin *et al.*, 2004) provides the most comprehensive data available so far. Even so, this trial does not allow for the possibility of frozen and thawed double embryo transfers or repeated (more than once) frozen and thawed single embryo transfers. Crucially, in the current IVF climate, it does not provide data on acceptability or costs.

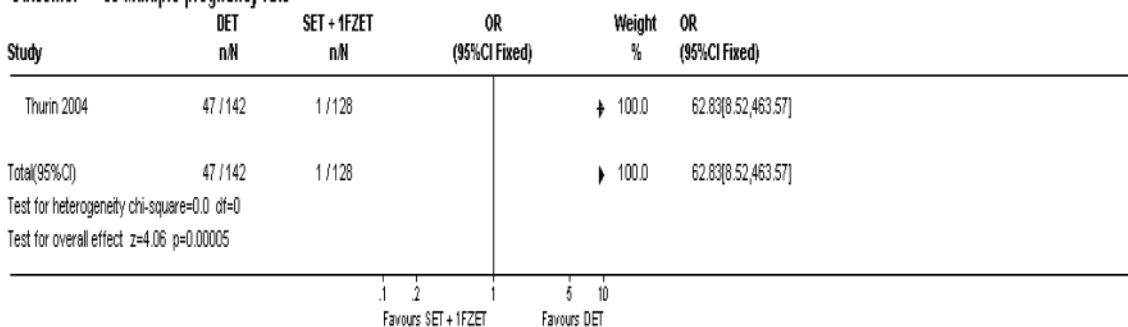
Comparison: 01 One versus two embryo transfer

Outcome: 03 Multiple pregnancy rate



Comparison: 03 SET + 1FZET versus DET

Outcome: 03 Multiple pregnancy rate



† Elective single embryo transfer

\* Elective double embryo transfer

\*\* Single frozen and thawed embryo transfer

**Figure 2.** Elective single embryo transfer (eSET) versus elective double embryo transfer (eDET) and eSET + single frozen and thawed embryo transfer (1FZET) versus eDET. Multiple pregnancy rate.

It will not come as a surprise to clinicians that a blanket policy of fresh elective single embryo transfer will minimize multiple pregnancy rates but also lower pregnancy rates per fresh IVF cycle. For such a policy to work, it needs to be selective in terms of identifying women at risk of twins (Vilksa *et al.*, 1999). These women should ideally be younger than 35, in their first or second cycles of IVF, use fresh non-donor eggs or embryos and have a number of good quality embryos for future use. It is also important that success is defined in terms of cumulative live birth rates per oocyte retrieval and includes the outcomes of fresh as well as frozen embryo transfers (Templeton, 2000; Thurin *et al.*, 2004).

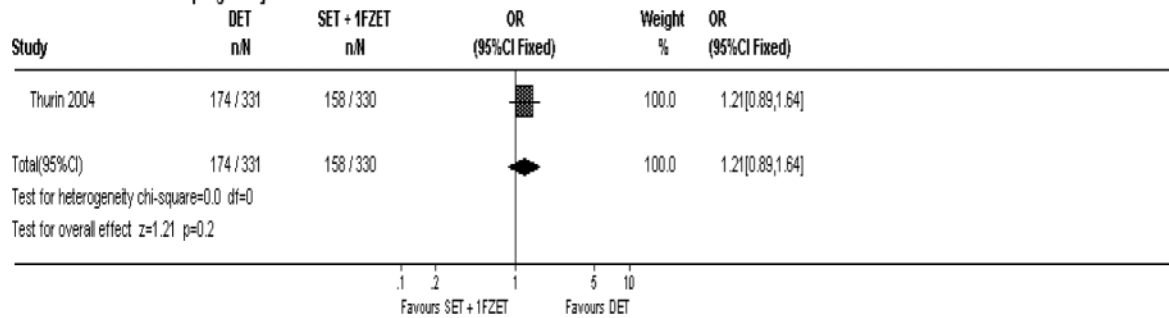
The feasibility and success of an elective single embryo transfer policy is limited by various national laws governing IVF treatment and funding issues. The new legislation in Sweden which enforces the routine use of single embryo transfer in eligible couples has led to a general implementation of

single embryo transfer (ESHRE Campus Report, 2001). Elsewhere, if IVF is to be accessed in the private sector, patients might prefer multiple embryo transfer in order to maximize the chances of a live birth(s) at their first attempt. Single embryo transfer has worked well in European settings where IVF is subsidized. The existing system in other countries such as the USA and UK, whereby many couples pay for IVF, but not for neonatal care, is apt to discourage some couples from accepting elective single embryo transfer.

Currently, single embryo transfers are rare, accounting for only 6.2% of all fresh transfers in the USA (SART, 2002) and 12% of fresh transfers in Europe. Within Europe, there are enormous variations in practice, with rates varying from 30.5% in Finland to 7.3% in the UK (Nyboe *et al.*, 2005). This review demonstrates that it is possible for elective single embryo transfer to reduce risks in IVF without diminishing the chances of success, but debate continues about its feasibility in different

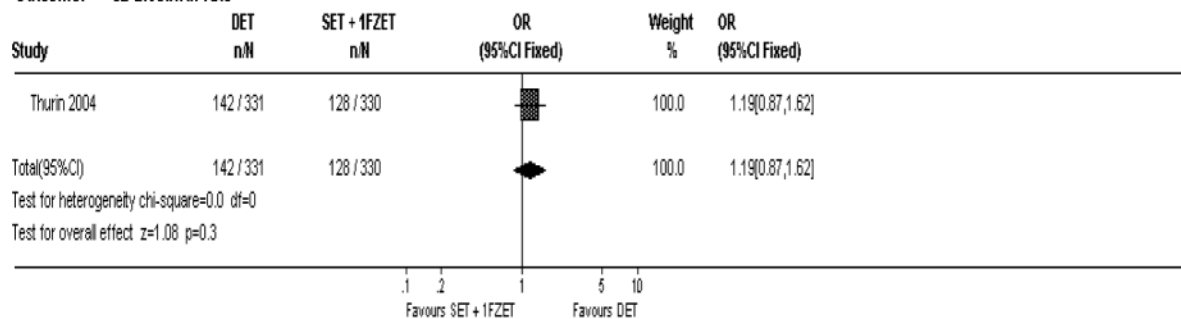
Comparison: 03 SET + 1FZET versus DET

Outcome: 01 Clinical pregnancy rate



Comparison: 03 SET + 1FZET versus DET

Outcome: 02 Livebirth rate



† Elective single embryo transfer

\* Elective double embryo transfer

\*\* Single frozen and thawed embryo transfer

**Figure 3.** Elective single embryo transfer (eSET) + single frozen and thawed embryo transfer (1FZET) versus elective double embryo transfer (eDET). Clinical pregnancy and live birth rates.

clinical settings. Despite awareness of the risks of twins, consumers as well as service providers remain uncertain about adopting a single embryo transfer policy in routine clinical practice and continue to question its clinical and cost effectiveness. In order to answer these lingering doubts, there is a need for further large multi-centre randomized trials with a duration of follow-up incorporating fresh as well as frozen embryo replacements assessing not just clinical effectiveness, but also cost effectiveness and acceptability.

## References

- Assisted Reproductive Technology Success Rates for 2002 (2004) National Summary and Fertility Clinic Reports. US Department of Health and Human Services, Centers for Disease Control and Prevention, Washington, DC.
- Callahan TL, Hall JE, Ettner SL et al. (1994) The economic impact of multiple gestation pregnancies and the contribution of assisted reproduction techniques to their incidence. *N Engl J Med* 331,244–249.
- Doyle P (1996) The outcome of multiple pregnancy. *Hum Reprod* 11,110–120.
- ESHRE Campus Report (2001) Prevention of twin pregnancies after IVF/ICSI by single embryo transfer. *Hum Reprod* 16,790–800.
- Garel M and Blondel B (1992) Assessment at one year of the psychological consequences of having triplets. *Hum Reprod* 7,729–732.
- Garel M, Salobir C and Blondel B (1997) Psychological consequences of having triplets: a four-year follow up study. *Fertil Steril* 67,1162–1165.
- Gerris J, De Neubourg D, Mangelschots K et al (1999) Prevention of twin pregnancy after in-vitro fertilization or intracytoplasmic sperm injection based on strict embryo criteria: a prospective randomized clinical trial. *Hum Reprod* 14,2581–2587.
- Goldfarb J, Kinzer DJ, Boyle M and Kurit D (1996) Attitudes of in vitro fertilisation and intrauterine insemination couples towards multiple gestation pregnancy and multifetal pregnancy reduction. *Fertil Steril* 65,815–820.
- Lieberman B (1998) An embryo too many? *Hum Reprod* 13,2664–2666.
- Lukassen HGM, Braat DDM, Zeilhuis, Adang EM and Kremer JAM (2002) 2×1 versus 1×2, a randomized study. *Hum Reprod Abstracts* V,0064.
- Martikainen H, Tiitinen A, Candido T et al (2001) One versus two embryo transfer after IVF and ICSI: a randomized study. *Hum Reprod* 16, 1900–1903.
- Martin PM and Welch HG (1998) Probabilities for singleton and multiple pregnancies after in vitro fertilization. *Fertil Steril* 70,478–481.
- Nyboe Anderson A, Gianaroli, Felberbaum R, de Mouzon J and Nygren KG (2005) The European IVF monitoring programme (EIM) for the European Society of Human Reproduction and Embryology (ESHRE) Assisted reproductive technology in Europe, 2001. Results generated from European registers by ESHRE. *Human Reprod* 20,1158–1176.
- Seoud MA, Toner JP, Kruithoff C and Muasher SJ (1992) Outcome of twin, triplet and quadruplet in-vitro fertilisation pregnancies: the Norfolk experience. *Fertil Steril* 57,825–834.

- Stromberg B, Dahlquist G, Ericson A, Finnstrom O, Koster M and Stjernqvist K (2002) Neurological sequelae in children born after in vitro fertilisation: a population based study. *Lancet* 359,461–465.
- Templeton A (2000) Avoiding multiple pregnancies in ART. Replace as many embryos as you like—one at a time. *Hum Reprod* 15,1662–1665.
- Templeton A and Morris JK (1998) Reducing the risk of multiple births by transfer of two embryos after in vitro fertilization. *N Engl J Med* 339,573–577.
- Thurin A, Hausken J, Hillensjo T, Jablonowska B, Pinborg A, Strandell A and Bergh C (2004) Elective single embryo transfer in IVF, a randomized study. Abstracts of the 20th Annual meeting of the ESHRE, Germany, June 2004, 0–70, i60.
- Vilksa S, Tiitinen A, Hydén-Granskog C et al. (1999) Elective transfer of one embryo results in an acceptable pregnancy rate and eliminates the risk of multiple birth. *Hum Reprod* 14,2392–2395.
- Wolner-Hanssen P and Rydhstroem H (1998) Cost effectiveness analysis of in-vitro fertilization: estimated cost per successful pregnancy after transfer of one or two embryos. *Hum Reprod* 13,88–94.
- Yokoyama Y, Shimizu T and Hayakawa K (1995) Incidence of handicaps in multiple births and associated factors. *Acta Genet Med Gemellol* 44,81–91.

*Submitted on May 10, 2005; accepted on May 19, 2005*