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Impact of an educational intervention and insurance coverage on patients' preferences to transfer multiple embryos


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Abstract Multiple gestations resulting from IVF continue to be a major problem associated with maternal/neonatal morbidity and mortality including preterm labour/delivery, pre-eclampsia and post-partum haemorrhage. A prospective survey at a university IVF clinic evaluated the effect of education and insurance coverage on patients' preferences for single-embryo transfer (SET) versus double-embryo transfer (DET). Patients undergoing IVF treatment from September 2008 to October 2009 were included. The main outcome measure was patients' preference of SET versus DET. Patients were sent an educational handout describing maternal and fetal risks of twin gestation. A total of 163 patients (32.6% response rate) returned the pre- and post-education surveys regarding preferences for SET versus DET based on three different IVF insurance coverage scenarios (no coverage, two cycles covered and unlimited coverage). There were statistically significant differences in the preference for SET before and after education across all insurance scenarios (scenario 1, 42.0% versus 61.1%; scenario 2, 50.6% versus 71.0%; and scenario 3, 61.7% versus 79.6%; $P < 0.001$ for all scenarios). Before education, patients preferred SET more in the unlimited coverage scenario (61.7%) versus no coverage (42.0%; $P < 0.001$). An educational handout and increasing the amount of insurance coverage significantly increased a patient's preference for SET. 

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Introduction

Risk of multiple gestation including twins continues to be a significant challenge in treating patients with infertility (Moise et al., 1998). The incidence of twin pregnancies after IVF has been reported to be around 30% compared with a 1% risk in natural conception (Kiely and Kiely, 2001). Twin gestations carry significant risks for both mother and neonate. Maternal risks include pre-eclampsia, gestational diabetes, anaemia, post-partum haemorrhage and Caesarean section. Neonatal risks include growth restriction, prematurity, neonatal intensive care admission, cerebral palsy and developmental delay (Adashi et al., 2003; Practice Committee of American Society for Reproductive Medicine, 2006). There is also a significant cost to the healthcare system for pre-term delivery, with over half of all healthcare dollars spent on newborns going towards infants born <37 weeks (Newton et al., 2007).

A successful strategy to combat the risk of multiple gestations with IVF therapy is to transfer a single embryo (Thurin et al., 2004). One study showed equivalent pregnancy rates when comparing SET versus DET, with a 3.2% risk of twins in SET compared with DET, which had a 62% chance of twins (Criniti et al., 2005). Another study showed similar results when comparing SET versus DET (Ryan et al., 2007). A previous retrospective analysis at the current study centre demonstrated similar pregnancy rates (55.1% versus 55.4%) with DET versus SET in women <38 years of age with a multiple birth rate of 30% versus 0% (Mann et al., 2009). Despite the evidence of success rates with SET and a low risk of twins, some patients and physicians still prefer to transfer two embryos. According to national data during the study period, patients aged <38 years had on average 2.3 embryos transferred resulting in 31.4% conceiving with twins, and at the study centre patients aged <38 years had on average 2.0 embryos transferred resulting in 27.2% conceiving with twins (Centres for Disease Control and Prevention, 2009).

Several studies have evaluated educational tools to help patients better understand the risks of multiple gestation including discussion sessions, an educational DVD and handouts (Hope and Rombauts, 2010; Murray et al., 2004; Ryan et al., 2007). The effects of education from these studies on a patient's preference for SET versus DET have been contradictory. There are multiple reasons for patients preferring DET versus SET including insurance coverage/financial status, lack of knowledge about the risks of a twin pregnancy and misperceptions about the success rates with SET (Grobman et al., 2001; Hojgaard et al., 2007; Pinborg et al., 2003).

As pregnancy rates at the study centre appear to be similar between DET versus SET, with the only difference being the incidence of multiple births, the goal of the current investigation was to determine if: (i) education regarding the risks of twins to both fetal and maternal wellbeing; and (ii) level of insurance coverage would influence a couple's preference for SET versus DET. The hypothesis was that, with education, patients would prefer SET over DET and the effect would be greater as a patient's insurance coverage improved.

Materials and methods

This study was conducted at the Centre for Advanced Reproductive Services at the University of Connecticut Health Centre. Institutional Review Board approval for this study was obtained in April 2008 (ref No. 08-266-3). All couples in which the woman was between 21 and 38 years old undergoing their first IVF cycle from September 2008 until October 2009 were invited to participate in the study. Couples who had previously undergone IVF were excluded because they may have been exposed to education regarding the risks of multiple gestations during previous cycles.

All couples were mailed an introductory letter explaining the purpose and process of the study along with one copy of a pre-education survey, an educational handout and a post-education survey. If the couples chose to participate in the study, they were asked to fill out the anonymous pre-survey to obtain the demographic information including age, race, number of children and prior infertility treatments. This survey was similar to a questionnaire used for a prior study (Hope and Rombauts, 2010). The pre-survey also evaluated the couple's perceived financial status and gave hypothetical insurance coverage scenarios and asked for the patient's preference for SET versus DET. The survey stated that transferring one blastocyst entails a 50% chance of pregnancy with a 5% chance of twins, while transferring two multicellular embryos entails a 50% chance of pregnancy with a 33% chance of twins. Couples were then asked to state their preference between one blastocyst versus two multicellular embryos assuming: scenario 1: they had to pay \$15,000 out-of-pocket for each cycle; scenario 2: insurance would cover up to two cycles; and scenario 3: insurance would cover unlimited cycles (see Addendum). The patients were asked to review an educational handout reviewing the risks of a twin gestation (Supplementary Addendum, available online only). At the study centre, scenario 2 is the usual scenario as most patients have insurance coverage for up to two IVF cycles since it is a mandated insurance fertility coverage state. After reviewing the educational handout, the couple then filled out the post-education survey, which was similar to the pre-education survey. The surveys were then returned and the answers were recorded and analysed. The primary outcome was the couple's preference for SET over DET before and after education. The secondary outcome was how this decision was influenced by the level of insurance coverage.

Statistical analysis

Power analysis was performed and based on a 0.05 two-sided significance level. A sample size of 162 subjects would provide 67% power to detect a significant increase in the desire for a singleton gestation following appropriate education from 69% to 86% (Ryan et al., 2007).

All variables were analysed using Statistical Package for the Social Sciences software (release 6.0; SPSS, Chicago, IL, USA). Categorical data were compared using the chi-squared or Fisher's exact tests where appropriate. The McNemar test for change was used to compare patients' preference for SET before and after education. A logistic

regression analysis was performed to determine if patient demographics influenced the preference for SET. A binomial test was used to determine if the number of patients who changed their preference from DET to SET depending on insurance coverage was significant. A P -value <0.05 was considered significant, in cases where multiple analyses were performed the alpha values were Bonferroni corrected.

Results

A total of 500 couples were mailed the surveys and educational handout for the study. A total of 163 couples (32.6%) returned and completed the pre- and post-education surveys. One couple was excluded for history of a prior IVF cycle. All of the questions were completed for the 162 surveys included in the analysis. Demographic information on the couples who completed the survey is presented in **Table 1**. A logistic regression analysis was performed to determine if any of the demographics contributed to a patient's preference for SET versus DET and showed no statistical significance. A preliminary analysis was performed after 162 patients were enrolled which showed a statistically significant difference among the different insurance

coverage scenarios as well as between pre- and post-education results ($P < 0.001$).

Patients were asked their preference for a singleton versus twin gestation should they be successful in conceiving with IVF. The data are presented in **Table 2**. After education, a statistically significant number of patients changed their preference to a singleton gestation ($P < 0.001$).

When comparing preference for SET between scenario 1 (no IVF insurance coverage) and scenario 3 (unlimited IVF insurance coverage), significantly more patients chose SET in scenario 3 than in the scenario 1 in both the pre- and post-education surveys (**Table 3**).

Discussion

The results of this investigation demonstrate the efficacy of an educational tool when counselling patients on the risks of twin gestation in preparation for the decision to transfer one or more embryos during IVF. The results show a significant decline in preference for DET versus SET with education in all groups regardless of IVF insurance coverage status. As far as is known, no studies have looked at this data prospectively and also compared patients' preferences based on insurance coverage for IVF. The results show an educational tool can help change a patient's preference to SET. Of interest, more couples preferred SET in the unlimited coverage scenario 3 compared with the other two scenarios. This shows the significance of IVF insurance coverage in influencing the number of embryos to transfer, confirming a previously reported retrospective study (Stillman et al., 2009).

Some patients may have a strong preference for twins as a way to complete their family more quickly (Murray et al., 2004). Also, some physicians may have their own preference when counselling patients regarding SET versus DET (Gleicher and Barad, 2006). Regardless of the physician's preference, patients need to be informed of the risks of multiple gestations (Buckett and Tan, 2004). The current study supports the use of education to influence a patient's preference for SET. An educational DVD has also been shown to have an effect on changing a patient's preference from DET to SET (Hope and Rombauts, 2010). The current study also supports the results from Ryan et al. (2007), which showed a significant increase in patients desiring SET after an educational pamphlet was given about risk of twins. Murray et al. (2004) evaluated an extra information leaflet to educate patients on risks of multiple gestation and pregnancy rates with SET and showed no significant effect from education on the risks of multiple gestation for a patient's preference of SET versus DET, contrary to the current results. A likely explanation for this discrepancy is that the current survey indicated no difference in pregnancy

Table 1 Demographic information.

Variable	Population (n = 163)
Female age (years)	32.1 ± 3.3
Race	
Caucasian	130 (79.8)
Hispanic	13 (8.0)
Asian	12 (7.4)
African American	8 (4.9)
Parity	
Nulliparous	128 (78.5)
One child	27 (16.6)
Two or more children	8 (4.9)
Prior IVF treatment	
No	162 (99.4)
Yes	1 (0.6)
Perceived financial status	
Struggling	2 (1.2)
Managing	55 (33.7)
Secure	104 (63.8)
Well-off	2 (1.2)

Values are mean ± SD or n (%).

Table 2 Preference of singleton versus twin gestation should a couple conceive.

Preference	Pre-education (n = 162)	Post-education (n = 162)	P-value
Singleton gestation	60 (37.0)	109 (67.3)	<0.001
Twin gestation	33 (20.4)	19 (11.7)	<0.001
No preference	69 (42.6)	34 (21.0)	<0.001

Values are mean ± SD or n (%). Comparisons analysed using the McNemar test for change.

Table 3 Preference for single-embryo transfer for each insurance scenario.

Scenario	Preference for single-embryo transfer		P-value
	Pre-education (n = 162)	Post-education (n = 162)	
Scenario 1: Out-of-pocket IVF expense	68 (42.0) ^a	99 (61.1) ^b	<0.001
Scenario 2: Two IVF cycles covered	82 (50.6)	115 (71.0)	<0.001
Scenario 3: Unlimited IVF coverage	100 (61.7) ^c	129 (79.6) ^d	<0.001

Values are n (%). Comparisons analysed using the McNemar test for change.

^{a-d}Comparisons of a versus c, and b versus d were statistically significant ($P < 0.001$).

rates between transferring one versus two embryos whereas the investigation by Murray et al. (2004) reported a lower pregnancy rate with the transfer of a single embryo. When they asked if patients would choose SET if the pregnancy rates were the same as DET, over 80% of the couples stated they would elect for SET. Also, in their initial power analysis it was assumed that 20% of the baseline population would prefer SET; however, even after education, only 3.7% of all subjects in the study indicated they would prefer SET, possibly due to the fact the pregnancy rates were lower in the single-embryo group (Murray et al., 2004).

Some centres have used financial incentives in order to increase the number of patients electing SET. One investigation (Marek et al., 2005) showed that patients with a financial incentive elected SET more often than patients without a financial incentive (64.5% versus 26.8%). Newton et al. (2007) evaluated factors associated with SET preference and showed younger age and education significantly decreased a patient's preference for a twin gestation. The current results differed from the results of Newton et al. (2007) in that financial circumstances did not play a role in their patients' decisions. This difference may be due to the fact that the study by Newton et al. (2007) was conducted in Canada and 78% of women had some IVF insurance coverage and the cost of IVF may be significantly less than in the current population (Newton et al., 2007).

Strengths of this study include the prospective design and anonymous participation. Anonymous participation allows the subject to answer the questions on the survey honestly without worry about whether their answers would have an influence on their treatment plan. The study evaluated different economic constraints including the patient's financial status and insurance coverage. The study also compared the same group before and after education. As far as is known, this is the first study to look simultaneously at how both education and level of insurance coverage might influence a couple's decision regarding the number of embryos to transfer.

Limitations of the study include a response rate of 32.6% to the survey, which may have biased the results. The level of prior education was not evaluated and this has been shown to affect a patient's preference for SET (Newton et al., 2007). The current study excluded patients who had a prior IVF cycle and it is possible that patients with failed IVF cycles may prefer the transfer of more than one embryo to improve pregnancy rates. The survey did not ask about embryo quality and grading, which may result in a couple wanting to transfer more than one embryo. At the study centre, patients should have three excellent-quality multicellular embryos in order to stay in culture until the

blastocyst stage. If these patients do not meet this criterion, they are encouraged to transfer to two multicellular embryos by their physician.

Further research on selecting good candidates for SET and selecting the best embryo for SET needs to be done. Based on these results, it is important to educate patients on the risk of multiples and a simple tool such as a handout can influence a patient's decision to have SET. It is hoped that, if other IVF centres are not using some form of education that discusses the risk of multiple gestations when counselling couples on the number of embryos to transfer, this study may provide another reason to start.

In conclusion, this study suggests that two important influences on a patient's preference to transfer a single embryo are education and IVF insurance coverage. It demonstrates that education regarding the risks of multiple gestations significantly increases the number of women who preferred SET. It also demonstrates that, with more comprehensive insurance coverage for IVF, there was a significant increase in the number of women who preferred SET. Both of these observations were seen when patients were educated that pregnancy rates were equivalent with the transfer of one versus two embryos. These findings have important implications for practice and underscore the significance of thorough patient education regarding pregnancy rates with SET versus DET and the risks of multiple gestations. They also suggest that if the insurance industry increased its level of reimbursement for IVF, the number of women who prefer to transfer multiple embryos during IVF could be significantly reduced, thereby reducing both the higher maternal and neonatal morbidity and mortality rates associated with multiple gestations. This increase in reimbursement may ultimately reduce the overall financial burden for insurance companies and the healthcare system overall.

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Appendix A. Addendum

Patient insurance coverage scenarios and question of preference of single- versus double-embryo transfer for the pre- and post-education surveys.

Scenario 1. If you had to pay \$15,000 out of pocket for each cycle of IVF, which of the following options would you prefer? Please select one option from each row.

(✓)	Option 1: Single-embryo transfer	or	(✓)	Option 2: Two-embryo transfer
	One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one out of twenty (5%) chance of having twins			One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one of three (33%) chance of having twins

Scenario 2. If insurance would cover up to two cycles of IVF at no cost to you, which of the following options would you prefer? Please select one option from each row.

(✓)	Option 1: Single-embryo transfer	or	(✓)	Option 2: Two-embryo transfer
	One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one out of twenty (5%) chance of having twins			One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one of three (33%) chance of having twins

Scenario 3. If insurance would cover unlimited cycles of IVF at no cost to you, which of the following options would you prefer? Please select one option from each row.

(✓)	Option 1: Single-embryo transfer	or	(✓)	Option 2: Two-embryo transfer
	One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one out of twenty (5%) chance of having twins			One out of two (50%) chance of becoming pregnant and, if you were pregnant, a one of three (33%) chance of having twins

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.rbmo.2012.04.006>.

References

Adashi, E.Y., Barri, P.N., Berkowitz, R., Braude, P., Bryan, E., Carr, J., Cohen, J., Collins, J., Devroey, P., Frydman, R., Gardner, D., Germond, M., Gervis, J., Gianaroli, L., Hamberger, L., Howles, C., Jones Jr., H., Lunenfeld, B., Pope, A., Reynolds, M., Rosenwaks,

Z., Shieve, L.A., Serour, G.I., Shenfield, F., Templeton, A., van Steirteghem, A., Veeck, L., Wennerholm, U.B., 2003. Infertility therapy-associated multiple pregnancies (births): an ongoing epidemic. *Reprod. Biomed Online* 7, 515–542.

Bucket, W., Tan, S.L., 2004. What is the most relevant standard of success in assisted reproduction? The importance of informed choice. *Hum. Reprod.* 19, 1043–1045.

Centers for Disease Control and Prevention. 2009. 2007 Assisted Reproductive Technology Success Rates. National Summary and Fertility Clinic Reports. Atlanta: US Department of Health and Human Services; Centers for Disease Control and Prevention.

Criniti, A., Thyer, A., Chow, G., Lin, P., Klein, N., Soules, M., 2005. Elective single blastocyst transfer reduces twin rates without compromising pregnancy rates. *Fertil. Steril.* 84, 1613–1619.

Gleicher, N., Barad, D., 2006. The relative myth of elective single embryo transfer. *Hum. Reprod.* 21, 1337–1344.

Grobman, W.A., Milad, M.P., Stout, J., Klock, S.C., 2001. Patient perceptions of multiple gestations: an assessment of knowledge and risk aversion. *Am. J. Obstet. Gynecol.* 185, 920–924.

Hojgaard, A., Ottosen, L.D., Kesmodel, U., Ingerslev, H.J., 2007. Patient attitudes towards twin pregnancies and single embryo transfer—a questionnaire study. *Hum. Reprod.* 22, 2673–2678.

Hope, N., Rombauts, L., 2010. Can an educational DVD improve the acceptability of elective single embryo transfer? A randomized controlled study. *Fertil. Steril.* 94, 489–495.

Kiely, J.L., Kiely, M., 2001. Epidemiological trends in multiple births in the United States, 1971–1998. *Twin Res.* 4, 131–133.

Mann, J.E.A., Siano, L., Benadiva, C., Nulsen, J., Engmann, L., 2009. Good-prognosis patients not meeting embryologic criteria for a single blastocyst transfer (SBT) have similar pregnancy rates but higher rate of multiples than those receiving a SBT. *Fertil. Steril.* 92, S151.

Marek, D.M.J., Chantlis, S., Kaufmann, R., Lynch, D., Meintjes, M., 2005. The effect of a comprehensive incentive program on patient participation in elective single blastocyst transfers. *Fertil. Steril.* 84, S85–S86.

Practice Committee of American Society for Reproductive Medicine, 2006. Multiple pregnancy associated with infertility therapy. *Fertil. Steril.* 86, S106–S110.

Moise, J., Laor, A., Armon, Y., Gur, I., Gale, R., 1998. The outcome of twin pregnancies after IVF. *Hum. Reprod.* 13, 1702–1705.

Murray, S., Shetty, A., Rattray, A., Taylor, V., Bhattacharya, S., 2004. A randomized comparison of alternative methods of information provision on the acceptability of elective single embryo transfer. *Hum. Reprod.* 19, 911–916.

Newton, C.R., McBride, J., Feyles, V., Tekpetey, F., Power, S., 2007. Factors affecting patients' attitudes toward single- and multiple-embryo transfer. *Fertil. Steril.* 87, 269–278.

Pinborg, A., Loft, A., Schmidt, L., Andersen, A.N., 2003. Attitudes of IVF/ICSI-twin mothers towards twins and single embryo transfer. *Hum. Reprod.* 18, 621–627.

Ryan, G.L., Sparks, A.E., Sipe, C.S., Syrop, C.H., Dokras, A., van Voorhis, B.J., 2007. A mandatory single blastocyst transfer policy with educational campaign in a United States IVF program reduces multiple gestation rates without sacrificing pregnancy rates. *Fertil. Steril.* 88, 354–360.

Stillman, R.J., Richter, K.S., Banks, N.K., Graham, J.R., 2009. Elective single embryo transfer: a 6-year progressive implementation of 784 single blastocyst transfers and the influence of payment method on patient choice. *Fertil. Steril.* 92, 1895–1906.

Thurin, A., Hausken, J., Hillensjo, T., Jablonowska, B., Pinborg, A., Strandell, A., Bergh, C., 2004. Elective single-embryo transfer versus double-embryo transfer in in vitro fertilization. *N. Engl. J. Med.* 351, 2392–2402.

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