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A cost-effectiveness analysis of freeze-only or fresh embryo transfer in IVF of non-PCOS women

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STUDY QUESTION: Is a freeze-only strategy more cost-effective from a patient perspective than fresh embryo transfer (ET) after one completed In Vitro Fertilization/ Intracytoplasmic Sperm Injection (IVF/ICSI) cycle in women without polycystic ovary syndrome (PCOS)?

SUMMARY ANSWER: There is a low probability of the freeze-only strategy being cost-effective over the fresh ET strategy for non-PCOS women undergoing IVF/ICSI.

WHAT IS KNOWN ALREADY: Conventionally, IVF embryos are transferred in the same cycle in which oocytes are collected, while any remaining embryos are frozen and stored. We recently evaluated the effectiveness of a freeze-only strategy compared with a fresh ET strategy in a randomized controlled trial (RCT). There was no difference in live birth rate between the two strategies.

STUDY DESIGN, SIZE, DURATION: A cost-effectiveness analysis (CEA) was performed alongside the RCT to compare a freeze-only strategy with a fresh ET strategy in non-PCOS women undergoing IVF/ICSI. The effectiveness measure for the CEA was the live birth rate. Data on the IVF procedure, pregnancy outcomes and complications were collected from chart review; additional information was obtained using patient questionnaires, by telephone.

PARTICIPANTS/MATERIALS, SETTING, METHODS: For all patients, we measured the direct medical costs relating to treatment (cryopreservation, pregnancy follow-up, delivery), direct non-medical costs (travel, accommodation) and indirect costs (income lost). The direct cost data were calculated from resources obtained from patient records and prices were applied based on a micro-costing approach. Indirect costs were calculated based on responses to the questionnaire. Patients were followed until all embryos obtained from a single controlled ovarian hyperstimulation cycle were used or a live birth was achieved. The incremental cost-effectiveness ratio (ICER) was based on the incremental cost per couple and the incremental live birth rate of the freeze-only strategy compared with the fresh ET strategy. Probabilistic sensitivity analysis (PSA) and a cost-effectiveness acceptability curve (CEAC) were also performed.

MAIN RESULTS AND THE ROLE OF CHANCE: Between June 2015 and April 2016, 782 couples were randomized to a freeze-only ($n = 391$) or a fresh ET strategy ($n = 391$). Baseline characteristics including mean age, Body Mass Index (BMI), anti-Mullerian hormone, total dose of Follicle Stimulating Hormone (FSH), number of oocytes obtained, good quality Day 3 embryos, fertility outcomes and treatment complications were comparable between the two groups.

The live birth rate (48.6% vs. 47.3%, respectively; risk ratio, 1.03; 95% Confidence Interval [CI], 0.89, 1.19; $P = 0.78$) and the average cost per couple (3906 vs. 3512 EUR, respectively; absolute difference 393.6, 95% CI, −76.2, 863.5; $P = 0.1$) were similar in the freeze-only group versus fresh ET.

Corresponding costs per live birth were 8037 EUR versus 7425 EUR in the freeze-only versus fresh ET group, respectively. The incremental cost for the freeze-only strategy compared with fresh ET was 30 997 EUR per 1% additional live birth rate. The direct non-medical costs and indirect costs of infertility treatment strategies represented ~45–52% of the total cost.

PSA shows that the 95% CI of ICERs was −263 901 to 286 681 EUR. Out of 1000 simulations, 44% resulted in negative ICERs, including 13.0% of simulations in which the freeze-only strategy was dominant (more effective and less costly than fresh ET), and 31% of simulations in which the fresh embryo strategy was dominant. In the other 560 simulations with positive ICERs, the 95% CI of ICERs ranged from 2155 to 471 578 EUR. The CEAC shows that at a willingness to pay threshold of 300 000 EUR, the probability of the freeze-only strategy being cost-effective over the fresh ET strategy would be 58%.

LIMITATIONS, REASONS FOR CAUTION: Data were collected from a single private IVF center study in Vietnam where there is no public or insurance funding of IVF. Unit costs obtained might not be representative of other settings. Data obtained from secondary sources (medical records, financial and activity reports) could lack authenticity, and recall bias may have influenced questionnaire responses on which direct costs were based.

WIDER IMPLICATIONS OF THE FINDINGS: In non-PCOS women undergoing IVF/ICSI, the results suggested that the freeze-only strategy was not cost-effective compared with fresh ET from a patient perspective. These findings indicate that other factors could be more important in deciding whether to use a freeze-only versus fresh ET strategy in this patient group.

STUDY FUNDING/COMPETING INTEREST(S): This study was funded by My Duc Hospital; no external funding was received. Ben Willem J. Mol is supported by an NHMRC Practioner Fellowship (GNT 1082548) and reports consultancy for Merck, ObsEva and Guerbet. Robert J. Norman has shares in an IVF company and has received support from Merck and Ferring. All other authors have no conflicts of interest to declare.

TRIAL REGISTRATION NUMBER: Not applicable.

Key words: cost-effectiveness / freeze-only / fresh embryo transfer / IVF / ICSI

Introduction

Although embryos are usually transferred in the same IVF cycle in which oocytes are collected, there is currently a shift in practice towards favoring freezing of the entire cohort of good quality embryos (Weinerman and Mainigi, 2014; Chen *et al.*, 2016; Shapiro *et al.*, 2014a, b). In such a 'freeze-only' strategy, all good quality embryos are frozen and transferred at a later stage (Doody, 2014). The good outcomes obtained using frozen embryo transfer (ET) are associated with a reduction in ovarian hyperstimulation syndrome (OHSS) and/or facilitate pre-implantation genetic testing (Devroey *et al.*, 2011; Maheshwari *et al.*, 2012; Roque, 2015). However, use of a freeze-only strategy may be more expensive due to the costs of embryo cryopreservation, endometrial priming, extra medication use and ultrasound scanning for frozen-thawed ET (Roque *et al.*, 2015a). There is uncertainty about how these additional costs could affect the potential benefits of a freeze-only policy. Thus, the cost-effectiveness of a freeze-only versus fresh ET strategy needs to be evaluated.

In a large RCT, we showed that ongoing pregnancy rates were similar after the first completed cycle using a freeze-only strategy compared with fresh ET in women without polycystic ovary syndrome (PCOS) undergoing IVF/ICSI (Vuong *et al.*, 2018). Here, we present a cost-effectiveness analysis (CEA) of the freeze-only versus ET strategy that was conducted in these patients. This analysis was conducted from a patient perspective with the costing data collected from the RCT with a following up until delivery or when no more embryos remained.

Materials and Methods

The single-center RCT was conducted in Ho Chi Minh City, Vietnam (Vuong *et al.*, 2018). The study was approved by the Medical Ethics Committee (02/15/ĐĐ-BVMĐ) and registered at www.clinicaltrials.gov (NCT02471573). The trial was conducted according to Good Clinical Practice and Declaration of Helsinki 2002 principles, including oversight by an independent Data Monitoring Committee. All patients provided written informed consent for participation in the RCT study and agreed to answer telephone questionnaires for the related CEA.

Full details of the study design have been reported previously (Vuong *et al.*, 2018). Briefly, couples were eligible if they were infertile, scheduled for IVF and had not had more than one previous IVF cycle. Women with PCOS or having oocyte donation were not eligible. All participants were treated with the same controlled ovarian hyperstimulation regimen, using a FSH/GnRH antagonist protocol.

After informed consent, participating couples were randomly assigned to a freeze-only strategy or fresh ET. In the freeze-only group, all Grade 1 and 2 embryos (Alpha Scientists in Reproductive Medicine and Embryology, 2011) were cryopreserved and a maximum of two embryos was thawed on the day of transfer in subsequent cycles.

In the fresh transfer group, a maximum of two fresh embryos was transferred on Day 3 in the stimulated cycle. Serum beta-hCG levels were measured at 2 weeks after ET, and luteal phase support was continued until 7 weeks' gestation after pregnancy was confirmed. Routine clinical care was provided for the remainder of the pregnancy and neonatal period. For the purposes of this analysis, patients were followed until all embryos obtained from a single controlled ovarian hyperstimulation cycle were used or a live birth was achieved.

Costing method and outcome measures

The CEA was performed from a patient perspective and was limited to costs from randomization to delivery. A CEA analysis was chosen because current literature and Health Technology Assessment guidelines recommend that even when there is no significant difference in outcomes (as was the case for our RCT), a CEA should be performed because the aim is to

evaluate effectiveness rather than efficacy (Ramsey *et al.*, 2015). The effectiveness measure for this analysis was the live birth rate.

Healthcare utilization relating to treatment (including examination, luteal support drug, embryo freezing and thawing, complications, pregnancy follow-up and delivery) and treatment complications (OHSS, miscarriage, abortion, ectopic pregnancy, gestational hypertension and pre-eclampsia, antepartum hemorrhage, and gestational diabetes mellitus) were determined from patient medical records. Financial and activity reports from the fiscal year 2016 were used to apply fees to each resource used, which allowed direct costs to be determined (Supplementary Table S1). Direct non-medical costs (travel costs, accommodation costs) and indirect costs (income lost) data were based on a previous review (Tai *et al.*, 2016). These were determined based on responses to a patient questionnaire (Supplementary Data) that was developed specifically for this study and administered by trained interviewers over the telephone, with responses recorded in a standardized form for later conversion to direct non-medical costs and indirect costs. Travel expenses were calculated by multiplying the distance with the number of visits and the fuel price, which varied by transportation type. Income lost due to the visits was calculated by multiplying the time spent at visits with the number of visits and the couples' income converted to an hourly rate. Accommodation costs were calculated based on the duration of use and cost of paid accommodation (Supplementary Table S1).

All costs were calculated in Vietnamese Dong (in VND) and converted to EURO (EUR) at the 2016 exchange rate of 24 395 VND to1 EURO (Van, 2016). Inflation adjustment was not applicable because prices in Vietnam did not change over the study period. Also, the mean values of direct and indirect costs per patient did not change from the first to the last transfer cycle (up to four cycles).

Statistical analyses

All analyses were conducted on an intention-to-treat basis. Clinical and costing data were stored in Microsoft Excel and were analyzed using the R statistical package (R version 3.3.1, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as the mean and SD, and categorical variables were summarized as frequencies and percentages. Rates were calculated for dichotomous variables and compared by calculating relative risks and 95% CI values.

Between-group differences in non-continuous and continuous variables were assessed using the Fisher's exact test and Student's *t*-test, respectively. *P*-values < 0.05 were considered to indicate statistical significance.

The incremental CEA was performed along with the CEA. The incremental cost-effectiveness ratio (ICER) was based on the incremental cost per couple and the incremental live birth rate of the freeze-only strategy compared with the fresh ET strategy. The incremental cost per couple reflects the additional cost to a couple if they undergo a freeze-only treatment rather than fresh ET treatment. The incremental effectiveness reflects an additional percentage of live birth rate when the freeze-only strategy is used instead of the fresh ET strategy.

Sensitivity analyses

We performed probabilistic sensitivity analysis (PSA) with Monte Carlo simulation by bootstrapping 1000 trials using Microsoft Excel 2013. A cost-effectiveness plane was used to calculate the incremental cost per couple and the incremental effectiveness as the result of the PSA. A cost-effectiveness acceptability curve (CEAC) was generated to represent the probability that the freeze-only strategy was cost-effective at a specific willingness to pay (WTP) threshold.

Results

Participants

Between June 2015 and April 2016, 782 infertile couples in a RCT were randomized to the freeze-only or fresh ET group (391 for each arm). There was an additional year of follow-up after completion of the RCT (to May 2017) to allow collection of live birth data from all ETs resulting from a single controlled ovarian hyperstimulation cycle.

Baseline characteristics were comparable between the two groups (Vuong *et al.*, 2018). There were no between-group differences in fertility outcomes and treatment complications (Table I).

Costing data were missing for 78 couples, including 28 unreachable couples and 50 couples who refused to provide data. The average cost per couple was calculated from the available cost data for 704 couples (352 in each treatment group; 90% of the total study sample). It was assumed that the average cost per couple for those with unavailable data would be the same as for couples with available cost data, allowing total costs for all patients with effectiveness data (782 couples, 391 couples in each group) to be estimated.

Cost and cost-effectiveness

The mean (±SD) total cost per couple was not significantly different in the freeze-only group and the fresh ET groups (Table II: 3905.8 ± 2458.6 vs. 3512.1 ± 3755.7, respectively; absolute difference 393.6, 95% CI, −76.2, 863.5; $P = 0.1$). The mean of direct medical cost was higher in the freeze-only group while the mean of direct non-medical costs and indirect costs associated with the freeze-only strategy were similar to those for the fresh ET strategy (Table II).

The estimated total cost per couple that underwent the freeze-only strategy was 3906 EUR, and 3512 EUR for the fresh ET strategy (Cohen's *d* was 0.127). The small effect size showed that the estimated cost per couple did not differ for the freeze-only versus the fresh ET strategy. The estimated cost per live birth was 8037 EUR for the freeze-only strategy versus 7425 EUR for a fresh ET strategy. The incremental cost per 1% additional live birth rate for the freeze-only versus fresh ET strategy was 30 997 EUR.

Sensitivity analyses

The cost-effectiveness plane (C–E plane) (Fig. 1) represents the results of the PSA based on 1000 simulated trials, in which the uncertainty of the ICER was evaluated. Accordingly, the 95% CI of the ICER ranged from −263 901 to 286 681 EUR. Out of 1000 simulations, 44.0% resulted in negative ICERs. The trials with negative ICERs comprised 13.0% of the total, of which the freeze-only strategy was dominant, as shown in the south-east quadrant (II), and 31% in which the freeze-only strategy dominated (less effective and more costly), as shown in the north-west quadrant (IV). In the other 560 simulations with positive ICERs, the 95% CI of ICERs ranged from 2155 to 471 578. Owing to the wide range of ICERs, a further analysis was conducted (as recommended by Black, 1990), which showed the high probability better effectiveness with the freeze-only strategy at an increased cost (47% of the simulated trials, north-east quadrant, I).

Table I Fertility outcomes and treatment complications after one completed IVF/ICSI cycle in women without polycystic ovary syndrome.

	Freeze-only ($n = 391$)	Fresh ET ($n = 391$)	Between-group difference, % (95% CI)	Risk ratio for freeze-only versus fresh ET (95% CI)	*P*-value†
Mean number of ETs	1.4 ± 0.6	1.5 ± 0.7			0.13
ET cycles, *n* (%)					
1	391 (100)	391 (100)			–
2	157 (40.2)	172 (44.0)			0.31
3	31 (7.9)	45 (11.5)			0.12
4	3 (0.8)	7 (1.8)			0.34
Fertility outcomes—*n* (%)					
Live birth	190 (48.6)	185 (47.3)	1.3 (−6, 8.5)	1.03 (0.89, 1.19)	0.78
Singleton	142 (36.3)	134 (34.3)	2 (−4.9, 9)	1.06 (0.88, 1.28)	0.6
Twins	48 (12.3)	51 (13.0)	−0.8 (−5.7, 4.1)	0.94 (0.65, 1.36)	0.83
Treatment complications—*n* (%)					
Ectopic pregnancy	10 (2.6)	19 (4.9)	−2.3 (−5.2, 0.6)	0.53 (0.25, 1.12)	0.13
Miscarriage	47 (12)	38 (9.7)	2.3 (−2.3, 6.9)	1.24 (0.83, 1.85)	0.36
Moderate/severe OHSS	3 (0.8)	4 (1.0)	−0.3 (−1.8, 1.3)	0.75 (0.17, 3.33)	1
Obstetric complications—*n* (%)					
Hypertension	7 (1.8)	10 (2.6)	−0.8 (−3.1, 1.5)	0.7 (0.27, 1.82)	0.63
Diabetes	10 (2.6)	12 (3.1)	−0.5 (−3.1, 2.1)	0.83 (0.36, 1.91)	0.83

Plus-minus values are mean ± SD.
† Wilcoxon test for mean number of embryo transfers (ETs); all others Fisher's exact test and Student's *t*-test; A *P*-values < 0.05 was considered statistically significant.
ET, embryo transfer; OHSS, ovarian hyperstimulation syndrome.

Table II Estimated cost data for one completed IVF/ICSI cycle per couple.

	Average * cost per couple (± SD); €		Absolute between-group difference (95% CI)	*P*-value†
	Freeze-only ($n = 391$)	Fresh ET ($n = 391$)		
Direct medical costs	***2138.5 ± 747.6***	***1684.1 ± 823.4***	***454.3 (337.9; 570.7)***	***<0.001***
Examination	197.7 ± 122.1	179.5 ± 137.1	18.2 (−0.9; 37.4)	0.063
Luteal support drug	263.8 ± 242.7	216.5 ± 223.3	47.3 (12.8; 81.8)	0.007
Embryo freezing	448.6 ± 107.2	364.3 ± 167.3	84.3 (63.5; 105.1)	<0.001
Embryo thawing	558.3 ± 229.5	251.4 ± 252.8	306.9 (271.1; 342.5)	<0.001
Complications	23.2 ± 126.6	21.7 ± 109.7	1.5 (−16.0; 19.0)	0.865
Drug during pregnancy	94.8 ± 97.3	105.5 ± 107.2	−10.7 (−25.8; 4.5)	0.167
Tests during pregnancy	189.6 ± 195.5	201.3 ± 211.2	−11.7 (−41.9; 18.36)	0.444
Delivery	362.5 ± 369.0	344.0 ± 362.6	18.52 (−35.6; 72.66)	0.502
Direct non-medical costs	***726.6 ± 905.4***	***640.1 ± 889.1***	***86.4 (−46.35; 219.2)***	***0.202***
Travel expense	145.8 ± 198.4	120.5 ± 176.3	25.3 (−2.4; 53.1)	0.074
Accommodation	580.8 ± 932.7	519.7 ± 906.5	61.1 (−74.9; 197.2)	0.378
Indirect costs	***1040.7 ± 2065.1***	***1187.8 ± 3444.7***	***−147.1 (−567.6; 273.34)***	***0.492***
Total cost	**3905.8 ± 2458.6**	**3512.1 ± 3755.7**	**393.6 (−76.2; 863.5)**	**0.100**

Plus-minus values are mean ± SD.
†Student's *t*-test; a *P*-value < 0.05 was considered statistically significant.
*Costing data were missing for 78 couples. Based on the cost data for 704 couples (352 couples in each treatment group; 90% of the total study sample), costs for the total sample of 782 couples (391 couples in each treatment) were estimated.

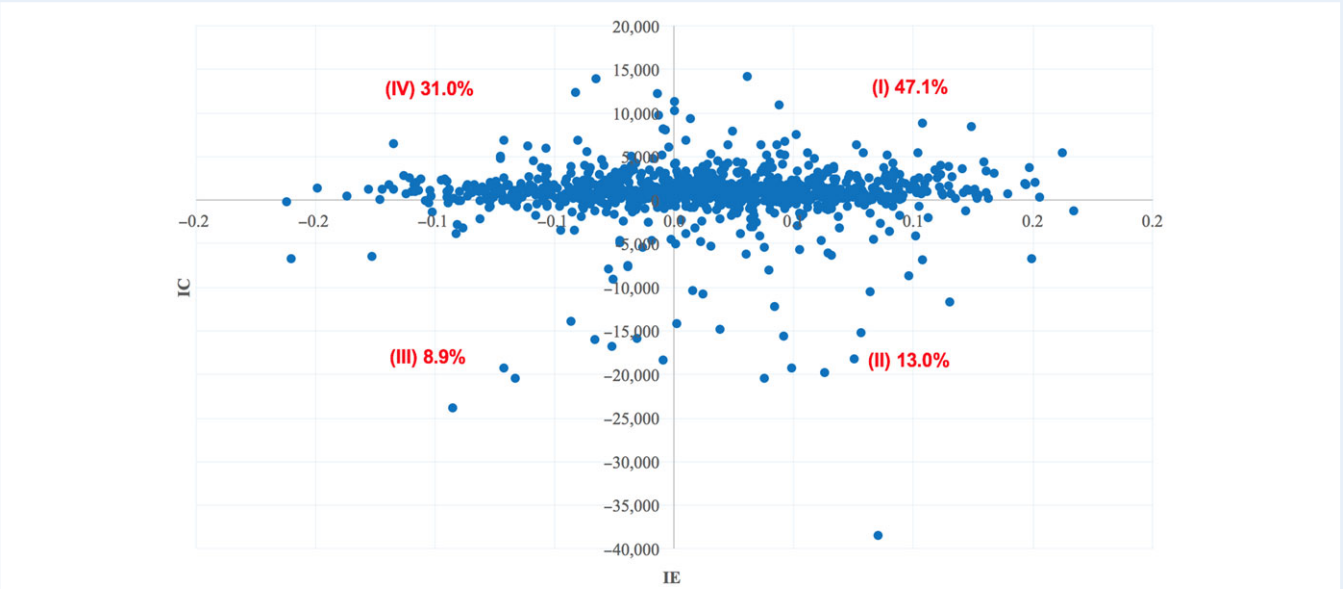

Figure 1 Cost-Effectiveness Plane: Scatter plot showing the mean differences in costs per patient (incremental cost) and in the live birth rates (incremental effectiveness). Note: This Cost-Effectiveness Plane represents for the Probabilistic Sensitivity Analysis through bootstrapping 1000 trials. IC: incremental cost, €; IE: incremental effectiveness, %. (I) North-East quadrant: trials in which Freeze-only strategy increased effectiveness at increased cost. ICERs in these trials have positive values. (II) South-East quadrant: trials in which Freeze-only strategy increased effectiveness at decreased cost. ICERs in these trials have negative values. (III) South-West quadrant: trials in which Freeze-only strategy decreased effectiveness at decreased cost. ICERs in these trials have positive values. (IV) North-West quadrant: trials in which Freeze-only strategy decreased effectiveness at increased cost. ICERs in these trials have negative values.

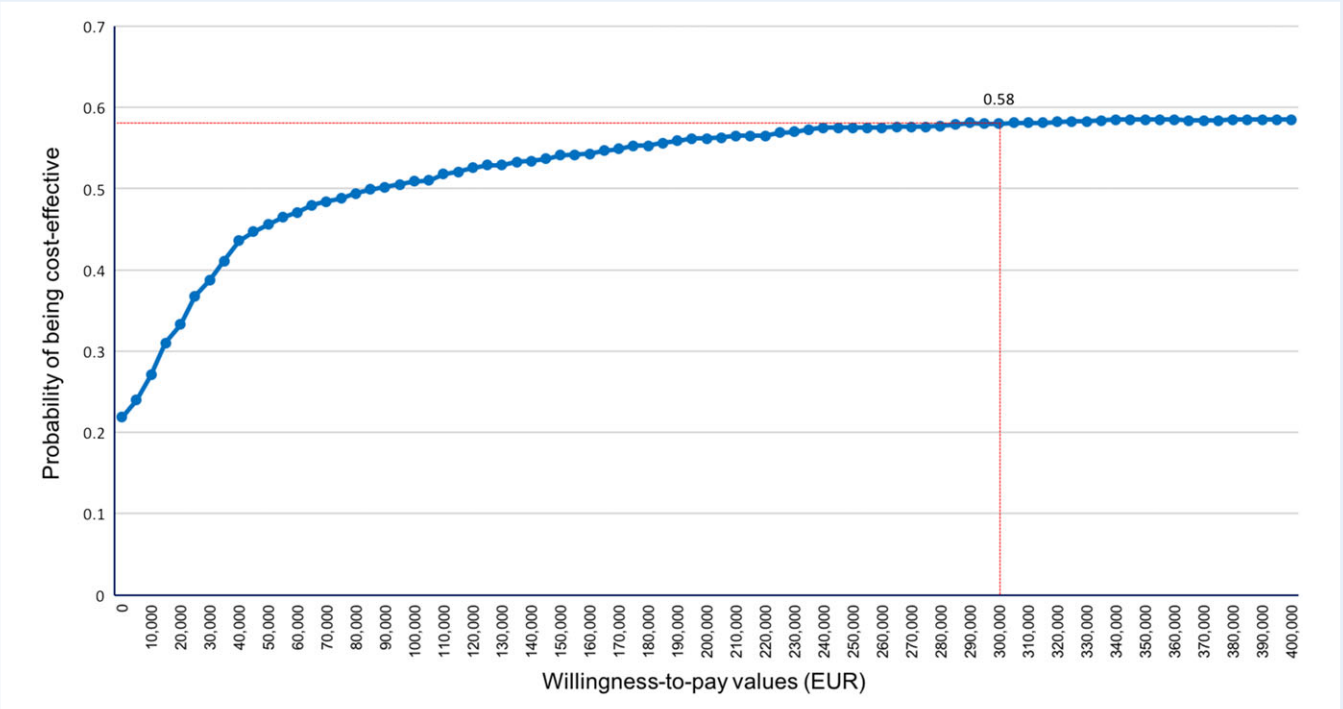

Figure 2 Cost-effectiveness acceptability curves for a freeze-only versus fresh embryo transfer strategy.

CEAC

Figure 2 presents a CEAC, which shows the probability of the freeze-only strategy being cost-effective over the fresh ET strategy according to the WTP thresholds. The data show that, at the WTP threshold of 300 000 EUR, the probability of the freeze-only strategy being cost-effective over the fresh ET strategy would be 58%.

Discussion

This analysis examined the cost-effectiveness of a freeze-only versus fresh ET strategy from a patient perspective in the context of a low or middle-income country with no public or insurance funding for ART. The results of the parent RCT had not shown any significant differences in effectiveness (live birth rate) between the two strategies. Findings from this analysis indicate there is a low probability of the freeze-only strategy being cost-effective over the fresh ET strategy, and at the WTP threshold of 300 000 EUR, the probability of the freeze-only strategy being cost-effective over the fresh ET strategy would be 58%.

This CEA was based on our previous RCT (Vuong *et al.*, 2018) which provides the highest level of evidence on which to base answers to clinical questions. The live birth rate was chosen as the effectiveness measure because the ultimate goal of IVF for patients is the birth of a healthy child rather than the time to success (Romundstad *et al.*, 2015). We reported both direct and indirect costs during treatment. The direct non-medical costs and indirect costs of infertility treatment strategies represent ~45–52% of the total cost. These are not always reported or discussed in patients' treatment decisions. Our findings demonstrate there is considerable uncertainty regarding the cost-effectiveness of the freeze-only strategy compared with fresh ET. The most important finding was that even with a WTP of 300 000 EUR, the probability of the freeze-only strategy being cost-effective was only 58%.

The results need to be interpreted in the context of a number of potential limitations. Data were obtained from secondary sources (medical records, financial and activity reports) and might, therefore, lack authenticity. Recall bias might be a limiting factor for the data collected via the telephone questionnaire, although the CEA was conducted soon after completion of the treatment. In addition, extrapolating available cost data to the small subset of patients (10%) who had missing cost data could have introduced inaccuracies to our analyses. However, we felt that it was better to use the full effectiveness dataset generated in the robust RCT and extrapolate cost data than to remove patients with missing cost data from the analysis altogether. Another limitation is that unit costs were estimated using prices from one private IVF center. Therefore, policymakers, healthcare providers, and couples should consider country-specific prices and assumptions before generalizing these results to different settings. The important factors that could influence the relative cost-effectiveness of a freeze-only versus fresh transfer strategy include the rate of complications (i.e. OHSS, preterm birth, perinatal outcomes). A freeze-only strategy is an appropriate approach to minimize or eliminate these complications, which could impact on the relative cost-effectiveness of the two strategies in a more diverse population in a clinical setting. Finally, this analysis was conducted from a patient perspective, rather than that of the healthcare system. In Vietnam, there is no public funding or health insurance cover for IVF treatment. Therefore, there are no healthcare system data on which to base a cost analysis. Given that patients have to pay all costs for IVF, this is the most relevant perspective for the setting in which the data were collected. This could limit the generalizability of the findings to other healthcare settings that have a different payer paradigm.

The incremental cost of the freeze-only strategy compared with the fresh ET strategy for a 1% additional live birth rate was very high (30 977 EUR) owing to a very small difference in live birth rate, the measure of effectiveness of the treatments (48.6% vs. 47.3%). Our study differs from those of Matheus Roque and colleagues, both in perspective (patient vs. hospital) and patient demographics (low to middle vs. upper middle-income level) (Roque *et al.*, 2015a). In addition, they did not include direct non-medical costs and indirect costs, or undertake PSA or CEAC.

Direct non-medical costs and indirect costs may have been more similar in the two groups because treatment was provided in the context of an RCT, and these costs could differ when the freeze-only and fresh transfer strategies are implemented in clinical practice. It is also possible that the between-group differences in costs observed occurred by chance, given the increased likelihood of similarity in the RCT.

According to the World Health Organization (WHO), there could be inequity in healthcare when the proportion of out-of-pocket payments (OOPs) as a share of total health expenditure is >40% (WHO, 2009; Lee and Shaw, 2014). High OOP also contribute to high patient expenditure on health and therefore can result in patients becoming impoverished. While most high-income countries offer ART procedures that are fully or partially funded by the government (Connolly *et al.*, 2010), patients in low- or middle-income countries usually have to self-fund infertility treatments (Dyer and Patel, 2012). This variation in OOPs between countries is likely to impact on patients (e.g. financial hardship, treatment discontinuation). Therefore, patients and/or healthcare providers must consider the balance between costs and success, the level of OOP required, and budget planning before making any decision about whether to use a freeze-only or fresh ET strategy.

The cumulative twin birth rate after transfer of a maximum of two embryos in our RCT was 12.6%. Twin pregnancies are associated with a higher rate of maternal and neonatal complications, including pre-eclampsia, post-partum hemorrhage and preterm birth (Aisien *et al.*, 2000; Sumathipala *et al.*, 2002; Obiechina *et al.*, 2011; Smits and Monden, 2011; Practice Committee of American Society for Reproductive Medicine, 2012), which are known risk factors for morbidity in mothers and their off-spring (Tobias *et al.*, 2016), and are associated with substantial financial costs to families and society (Callahan *et al.*, 1994; Collins, 2007). Our data show that the average cost per couple for twin delivery (5067 EUR) was ~1.28 times higher than the average cost for a singleton birth (3949 EUR). The increased healthcare costs for multiple births may be linked to a longer duration of hospital stay, temporary income lost during bed rest, and increased admission to the neonatal intensive care unit. These data are often not included in cost analyses. The fact that freezing of embryos does not affect the live birth rate (Dieamant *et al.*, 2017; Shi *et al.*, 2018; Vuong *et al.*, 2018) raises the possibility of performing a fresh single ET followed by additional frozen-thawed transfer of single embryos if required. The single ET approach could help to avoid multiple

gestations and facilitate patient counseling regarding risks associated with the transfer of more than one embryo.

Conclusion

This CEA of data from a RCT shows that there is a low probability of the freeze-only strategy being more cost-effective than the fresh ET strategy from a patient perspective for non-PCOS women undergoing IVF/ICSI in a low- or middle-income country. These findings also suggest that factors in addition to cost need to be taken into consideration when deciding whether to use a freeze-only versus fresh ET strategy in non-PCOS patients.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

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Authors' roles

Khoa D. Le was involved in study design, execution, analysis, manuscript drafting, and critical discussion. Ben Willem J. Mol was involved in study design, execution, provided critical revision for important intellectual content. Lan N. Vuong, Tuong M. Ho, Vinh Q. Dang, Robert J. Norman (R.J.N) were involved in the execution, critical discussion. Toan D. Pham was involved in clinical data analysis, critical discussion. Clarabelle Pham was involved in cost-effectiveness analysis, critical discussion. All authors approved the final version to be published.

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Conflict of interest

Ben Willem J. Mol reports consultancy for Merck, ObsEva, and Guerbet. Robert J. Norman has shares in an IVF company and has received support from Merck and Ferring. All other authors have nothing to declare.

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