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Corifollitropin alfa versus follitropin beta: an economic analysis alongside a randomized controlled trial in women undergoing IVF/ICSI

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Abstract This cost-effectiveness analysis was conducted from the patient's perspective alongside a randomized controlled trial comparing corifollitropin alfa with follitropin beta for a single stimulation cycle. Only unit costs paid by patients are included in this analysis. The incremental cost-effectiveness ratio was calculated. One-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were also performed. Baseline characteristics (except for the number of follicles and frozen embryos), treatment outcomes and complications were similar in the two groups. The live birth rate was comparable between the two groups, but the mean total cost per patient was higher for the corifollitropin alfa strategy (€4293) compared with the follitropin beta strategy (€4086). Costs per live birth were €13,726 and €12,511, respectively. The difference in effect between corifollitropin alfa and collitropin beta was three fewer live births, and the difference in costs was €24,048. The probability of live birth after the first and second embryo transfers and the proportion of patients who had no more frozen embryos available after non-achievement of live birth in the first or second transfer influenced the comparative cost-effectiveness of the two strategies. PSA showed that a corifollitropin alfa strategy would be rejected in up to 27.4% of scenarios. Follitropin beta 300 IU/day was more cost-effective than corifollitropin alfa 150 μg in women aged 35–42 years weighing ≥50 kg undergoing in-vitro fertilzation/intracytoplasmic sperm injection.

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KEYWORDS: cost-effectiveness, corifollitropin alfa, follitropin beta, IVF, ICSI

Introduction

Ovarian stimulation with gonadotropins is an essential step in each cycle of in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI). Corifollitropin alfa has been developed recently to overcome issues with the short half-life and rapid metabolic clearance of traditional agents (including human menopausal gonadotropins and recombinant follicle-stimulating hormone). The prolonged activity of corifollitropin alfa, which requires only one dose over 7 days, could reduce the dropout rate and increase the success of assisted reproductive technologies (ART) (Verberg et al., 2008).

Several randomized controlled trials (RCT) and meta-analyses show that there is no significant difference in fertility, pregnancy and obstetric outcomes between women who underwent ovarian stimulation with corifollitropin alfa compared with follitropin beta, both in Western populations and Asian patients aged ≥35–42 years and weighing ≥50 kg (Boostanfar et al., 2015; Corifollitropin Alfa Dose-finding Study, 2008; Corifollitropin Alfa Ensure Study, 2010; Devroey et al., 2009; Griesinger et al., 2016a, 2016b; Vuong et al., 2017).

The cost per cycle of ovarian stimulation was determined based on data from the PURSUE study, which was conducted in Spain (a high-income country) and only included direct costs associated with the stimulation phase (Barrenetxea et al., 2018). However, the literature shows that there is currently great diversity in the IVF funding and reimbursement policies within Europe, the USA, Australia and New Zealand (Chambers et al., 2009, 2012; Connolly et al., 2010), while patients in low- or middle-income countries have to self-fund infertility treatments (Dyer and Patel, 2012). Moreover, the direct non-medical costs and indirect costs of infertility treatment strategies, not always reported or discussed in patients' treatment decisions, represent approximately 45–52% of the total treatment cost (Le et al., 2018). Therefore, the findings of this study will provide evidence on the cost-effectiveness of corifollitropin alfa versus follitropin beta from the patient's perspective where ART treatment is not publicly funded.

As far as is known, this is the first cost-effectiveness analysis (CEA) to be conducted from the patient's perspective and used data from an RCT, the Asian PURSUE study (Vuong et al., 2017), with follow-up until delivery or until no more embryos remained.

Materials and methods

Study design, participants and treatments

This CEA was based on data from patients treated with corifollitropin alfa compared with follitropin beta (standard treatment) in a single-centre RCT in Ho Chi Minh City, Vietnam (Ethical Approval No.: 03/15/ĐĐ-BVMĐ; NCT02466204) (Vuong et al., 2017). All patients provided written informed consent before enrolment in the RCT. Full study details and treatment outcomes have been reported previously (Vuong et al., 2017).

In the decision analytic model, it is assumed that all patients who fulfilled the inclusion criteria were randomized to undergo ovarian stimulation using a gonadotrophin-releasing hormone (GnRH) antagonist protocol with a single dose of corifollitropin alfa 150 μg on Day 2 or 3 of the menstrual cycle, or follitropin beta (recombinant FSH) 300 IU/day for 7 days starting on Day 2 or 3 of the menstrual cycle.

From Day 8 of stimulation, participants in the two groups could be continued with a daily subcutaneous dose of follitropin beta (maximum 300 IU/day) up to the day before administration of human chorionic gonadotrophin or GnRH agonist. Oocyte retrieval followed by ICSI was performed ~34–36 h later according to the study site's clinical practice regulations. Two or three embryos were transferred 3 days after oocyte retrieval.

Patients who received initial therapy with corifollitropin alfa experienced fresh embryo transfer [fET(+)] (n=195) or skipped the fresh embryo transfer [fET(-)] (n=61). Among patients who underwent fET(+) (n=134), there were 32 live births [LB(+)], 67 treatment failures with no more embryos

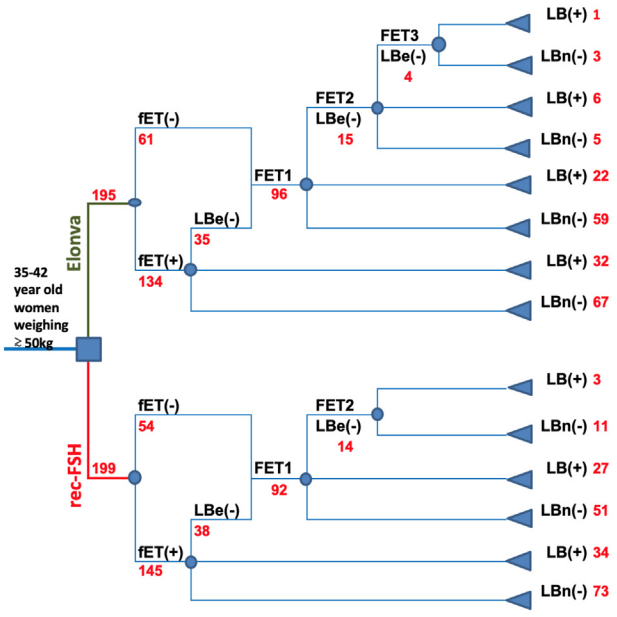

Figure 1 Decision analytic model for economic evaluation of corifollitropin alfa (Elonva) compared with follitropin beta (rec-FSH). ET, embryo transfer; fET(+), fresh embryo transfer; fET(-), fresh embryo tranfer skipped; FET1, first frozen embryo transfer; FET2, second frozen embryo transfer; FET3, third frozen embryo transfer; LB(+), live birth; LBe(-), no live birth but still have embryo(s); LBn(-), no live birth and no more embryos.

[LBn(-)], and 35 treatment failures with remaining embryo (s) [LBe(-)]. Patients in the fET(-) group and LBe(-) group experienced first frozen embryo transfer (FET1) (n = 35 + 61 = 96). Of these, there were 22 LB(+), 59 LBn(-) and 15 LBe(-). These patterns were repeated at second and third frozen embryo transfer (FET2 and FET3). A similar model was used in patients randomized to follitropin beta, with one fresh embryo transfer and two frozen embryo transfers (Figure 1). Rates of maternal and fetal outcomes after one completed cycle of ICSI were monitored for 2 years after randomization of patients in the PURSUE study.

Although treatment outcomes were similar in the two treatment groups, Health Technology Assessment guidelines suggest that a CEA should be conducted for assessment of effectiveness rather than efficacy (Briggs and O'Brien, 2001). Data for the CEA were collected after completion of the RCT. A course of treatment was defined as from the start of IVF-related treatment to delivery or use of all embryos. Direct medical costs were calculated based on 2016 prices, and the resource use data were extracted from patients' medical records and the 2016 financial and activity reports (Table S1, see online supplementary material). Direct non-medical costs and indirect costs were determined retrospectively by telephone interviews with each patient (Tai et al., 2016). Questionnaire responses were then converted into direct non-medical costs (travel costs, accommodation costs) and indirect costs (opportunity cost). Travel expenses were calculated by multiplying the distance, number of visits and fuel price based on the mode of transportation, while accommodation costs were determined by the duration of stay multiplied by the per-night cost. Opportunity cost (lost income) was estimated based on the number of visits, duration of visits and patient's income (Table S1, see online supplementary material). The costs [initially collected in Vietnamese Dong (VND)] were converted to 2016€ at the exchange rate of 24,395 VND to 1€ (Van, 2016). Costs and outcomes were not discounted or adjusted for inflation as prices were unchanged over the 1-year timeframe of data collection. The main effectiveness outcome measure in this analysis was the live birth rate.

Data were input into Excel (Microsoft Corp., Redmond, WA, USA), then exported to R Version 3.3.1 for analysis. Mean and standard deviation values were used to summarize continuous variables, while frequencies and percentages were used for categorical variables; 95% confidence interval values were also reported.

Fisher's exact test and Student's t-test were used to assess between-group differences in non-continuous and continuous variables, respectively. The incremental cost-effectiveness ratio (ICER) was calculated to compare the cost-effectiveness of corifollitropin alfa with follitropin beta. P-values <0.05 were considered to indicate statistical significance.

One-way sensitivity analysis (OSA) and probabilistic sensitivity analysis (PSA) were used in Excel 2013 to test the sensitivity of ICER to changes in each clinical and cost parameter. OSA was performed using a Tornado diagram based on the assumption that each factor varied from its

Table 1 Clinical parameters after one completed cycle of in-vitro fertilization/intracytoplasmic sperm injection.

	Corifollitropin alfa (n=195)	Follitropin beta (n=199)	Between-group difference (95% CI)	Risk ratio for corifollitropin alfa versus follitropin beta (95% CI)	P-value
Examination, n	4.71 (0.67)	5.79 (0.63)	1.08 (-1.21 to -0.96)		<0.001
Duration of stimulation, days	9.88 (1.52)	8.99 (1.22)	0.89 (0.61 to 1.16)		<0.001
Ultrasound, n	2.71 (0.67)	3.79 (0.63)	1.08 (-1.21 to -0.96)		<0.001
Additional dose, IU	610.26 (494.87)	603.02 (355.46)	7.24 (-78.28 to 92.76)		0.868
Oocytes retrieved, n	11.55 (5.81)	10.88 (5.80)	0.67 (-0.48 to 1.82)		0.250
Fertility outcomes					
Total fresh ET cycles, n (%)	134 (68.7)	145 (72.9)	-4.2 (-13.6 to 5.3)	0.94 (0.83 to 1.07)	0.365
Total FET cycles, n (%)	111 (56.9)	106 (53.3)	3.6 (-6.7 to 14.0)	1.07 (0.89 to 1.28)	0.466
Embryos transferred, n	2.24 (0.72)	2.27 (0.61)	-0.03 (-0.17 to 0.10)		0.616
Good embryos transferred, n	1.75 (0.83)	1.89 (0.74)	-0.06 (-0.30 to 0.02)		0.077
Average number of ETs	1.23 (0.53)	1.21 (0.44)	0.02 (-0.08 to 0.12)		0.701
Live birth, n (%)	47 (24.6)	51 (25.6)	-1.0 (-10.6 to 7.5)	0.93 (0.65 to 1.31)	0.815
Singleton	33 (17.3)	42 (21.1)	-3.8 (-12.4 to 4.1)	0.80 (0.53 to 1.21)	0.353
Twins	14 (7.3)	9 (4.5)	-2.8 (-2.5 to 7.8)	1.59 (0.70 to 3.58)	0.363
Moderate/severe OHSS, n (%)	2 (1.0)	1 (0.5)	0.5 (-1.0 to 2.7)	2.04 (0.19 to 22.33)	0.550
Delivery in weeks, n (%)					
<24	1 (0.5)	0 (0.0)	0.5 (-1.0 to 2.0)	-	0.992
24 to <32	0 (0.0)	1 (0.5)	-0.5 (-2.0 to 1.0)	-	0.999
32 to <37	5 (2.6)	5 (2.5)	0.1 (-3.2 to 3.2)	1.02 (0.30 to 3.47)	0.974
≥37	42 (21.5)	45 (22.6)	-0.9 (-9.8 to 7.6)	0.95 (0.66 to 1.38)	0.797

CI, confidence interval; ET, embryo transfer; FET, frozen embryo transfer; OHSS, ovarian hyperstimulation syndrome.
Values are mean (standard deviation) or n of patients (%).

Table 2 Estimated cost data for one completed in-vitro fertilization/intracytoplasmic sperm injection cycle per couple.[a]

	Average cost per couple (€)		Absolute between-group difference (95% CI)	*P*-value[b]
	Corifollitropin alfa (*n*=195)	Follitropin beta (*n*=199)		
Direct medical costs	**3836.2 (839.5)**	**3574.9 (816.8)**	**261.3 (97.2 to 425.4)**	**0.002**
Examination	26.6 (6.6)	37.3 (6.2)	-10.7 (-12.0 to -9.4)	
Ultrasound	22.2 (5.5)	31.1 (5.2)	-8.9 (10.0 to -7.9)	
Screening test	164.0	164.0	0.0	
Stimulation drug	1361.1 (213.6)	1136.3 (182.7)	224.8 (185.4 to 264.2)	
Luteal support drug	151.7 (97.5)	110.4 (80.6)	41.3 (23.5 to 59.0)	
IVF/ICSI	1188.8	1188.8	0.0	
Embryo freezing	270.8 (204.5)	257.5 (196.0)	13.3 (-26.4 to 53.0)	
Embryo thawing	198.3 (239.7)	190.8 (234.0)	7.5 (-39.4 to 54.4)	
Complications	10.1 (56.8)	14.8 (75.4)	-4.7 (-18.0 to 8.5)	
Drug during pregnancy	67.8 (97.3)	66.4 (96.7)	1.4 (-17.9 to 20.6)	
Test during pregnancy	141.3 (202.6)	138.4 (201.6)	2.8 (-37.2 to 42.9)	
Delivery	233.5 (351.3)	238.9 (352.7)	-5.4 (-75.1 to 64.3)	
Direct non-medical costs	**257.9 (267.6)**	**252.0 (261.9)**	**5.9(-46.5 to 58.4)**	**0.825**
Travel	40.4 (80.2)	41.9 (79.5)	-1.5 (-17.4 to 14.3)	
Accommodation	217.6 (277.7)	210.1 (272.1)	7.5 (-47.0 to 61.9)	
Indirect costs	**199.6 (293.3)**	**259.6 (448.1)**	**-60.1 (-135.0 to 14.9)**	**0.116**
Opportunity	199.6 (293.3)	259.6 (448.1)	-60.1 (-135.0 to 14.9)	
Total cost	**4293.7 (1103.6)**	**4086.5 (1103.5)**	**207.2 (-11.5 to 425.8)**	**0.063**

CI, confidence interval; ICSI, intracytoplasmic sperm injection; IVF, in-vitro fertilization.
Values are mean (standard deviation).

Table 3 Estimated cost data per couple following fresh embryo transfer and frozen embryo transfer.

	Average cost per couple (€)	
	Corifollitropin alfa (*n*=195)	Follitropin beta (*n*=199)
Fresh embryo transfer		
Direct medical costs	3836.2 (839.50)	3574.88 (816.76)
Direct non-medical costs	282.33 (287.25)	282.92 (305.03)
Indirect costs	199.58 (293.32)	259.63 (448.10)
Total cost	4318.08 (1111.82)	4117.43 (1055.33)
First frozen embryo transfer		
Direct medical costs	4224.6 (768.91)	3971.03 (715.86)
Direct non-medical costs	352.3 (378.54)	310.92 (322.61)
Indirect costs	228.03 (345.55)	229.88 (260.50)
Total cost	4804.97 (1106.15)	4511.83 (932.22)
Second frozen embryo transfer		
Direct medical costs	4764.84 (814.66)	4318.72 (599.65)
Direct non-medical costs	321.77 (319.96)	264.17 (255.84)
Indirect costs	300.96 (456.58)	210.35 (238.16)
Total cost	5387.57 (1185.71)	4793.24 (825.08)
Third frozen embryo transfer		
Direct medical costs	4730.29 (557.72)	
Direct non-medical costs	607.28 (277.42)	
Indirect costs	92.23 (75.84)	
Total cost	5429.81 (483.28)	

Values are mean (standard deviation).

Table 4 Incremental cost-effectiveness ratio of both strategies at various embryo transfer stages.

Subgroup	Corifollitropin alfa	Follitropin beta	ΔC or ΔE	ICER (ΔC/ΔE)
Fresh ET	*n*=134	*n*=145		
Total cost	842,026	819,369	22,657	-11,328
Live birth	32	34	-2	
Mean cost per live birth	26,313	24,099		
FET1	*n*=96	*n*=92		
Total cost	442,057	415,088	26,969	-5393
Live birth	22	27	-5	
Mean cost per live birth	20,093	15,374		
FET2	*n*=15	*n*=14		
Total cost	80,814	67,105	13,709	4569
Live birth	6	3	3	
Mean cost per live birth	13,469	22,368		
FET3	*n*=4	NA		
Total cost	21,719	NA	NA	NA
Live birth	1	NA	NA	
Mean cost per live birth	21,719	NA		
One completed cycle				
Total cost	837,267	813,219	24,048	-8016
Live birth	61	64	-3	
Mean cost per live birth	13,726	12,511		

Fresh ET, fresh embryo transfer; FET1, first frozen embryo transfer; FET2, second frozen embryo transfer; FET3, third frozen embryo transfer; ΔC, incremental cost; ΔE, incremental effectiveness; ICER, incremental cost-effectiveness ratio.

base-case value by ±10% while other factors were unchanged. The results indicate the range of ICER based on a change to a single variable. A larger range of ICER reflects more sensitive factors. PSA with Monte Carlo simulation (using 1000 resamples) was performed to address the uncertainty around the mean estimates of incremental costs and effects. A cost-effectiveness acceptability curve was generated to represent the probability that the corifollitropin alfa strategy was cost-effective at a specific willingness-to-pay (WTP) threshold.

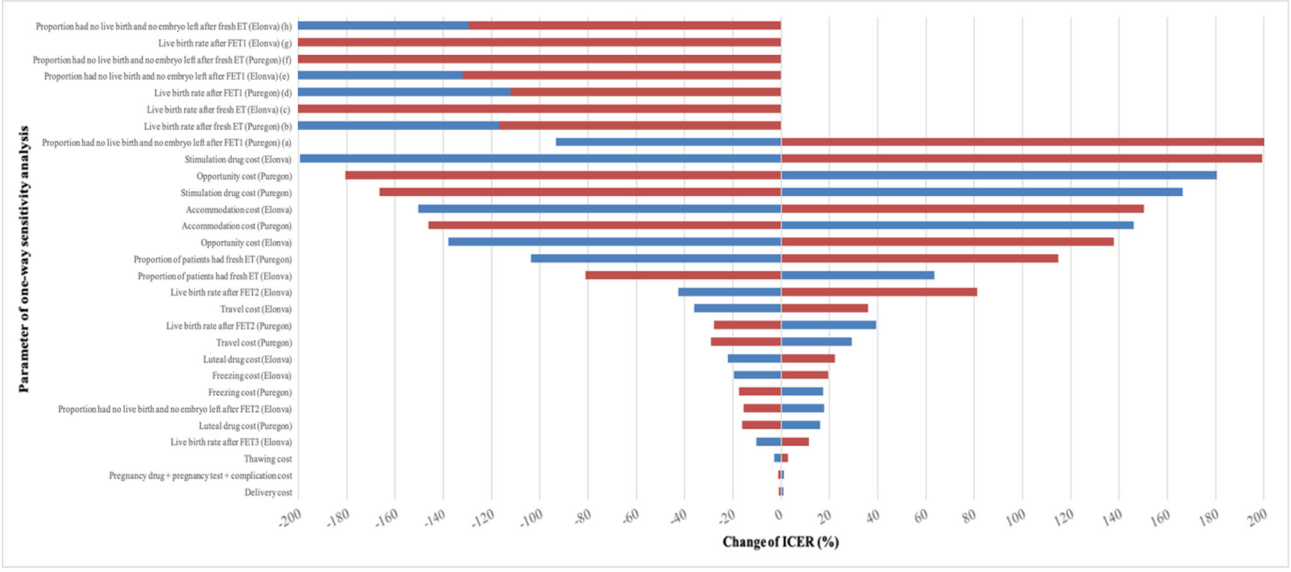

Figure 2 Tornado diagram of one-way sensitivity analysis of the incremental cost-effectiveness ratio (ICER) (range of input parameter: base-case value ± 10%). a, ICER increases 4-fold when the variable increases by 10%; b, ICER decreases 4.4-fold when the variable decreases by 10%; c, ICER decreases 4.4-fold when the variable increases by 10%; d, ICER decreases 5.9-fold when the variable decreases by 10%; e, ICER decreases 5.7-fold when the variable decreases by 10%; f, ICER decreases 9-fold when the variable increases by 10%; g, ICER decreases 13-fold when the variable increases by 10%; h, ICER decreases 15.6-fold when the variable decreases by 10%.

Results

From 19 June 2015 to 10 August 2016, 400 infertile couples were assigned at random to receive corifollitropin alfa or follitropin beta (n=200 in each treatment group). Baseline characteristics (except for the number of follicles and frozen embryos), treatment outcomes and complications were similar in both groups (Table 1). Cost data were missing for six patients: four patients could not be contacted and two refused to provide data. As such, 394 couples (195 in the corifollitropin alfa group and 199 in the follitropin beta group; 98.5% of the total study sample) were included in the CEA. Effectiveness data were available for all 400 patients.

The live birth rate was comparable between the two groups and the mean total cost per patient was not significantly different [corifollitropin alfa €4293 versus follitropin beta €4086; P=0.063) (Table 2). Most direct medical costs were higher in the corifollitropin alfa group, while the mean indirect costs and direct non-medical costs associated with the corifollitropin alfa strategy were similar to those for the follitropin beta strategy (Table 2). Table 3 depicts the estimated cost data per couple for fresh embryo transfer and frozen embryo transfer, and Table 4 reveals ICER of both strategies at the various embryo transfer stages. The total cost was higher for the corifollitropin alfa group compared with the follitropin beta group.

Cost per live birth was €13,726 with corifollitropin alfa compared with €12,511 with follitropin beta. The difference in effect between corifollitropin alfa and collitropin beta was three fewer live births, and the difference in costs was €24,048.

ICER varied four- to 15-fold in response to changes in several parameters (Figure 2). Of these, the probability of live birth after the first and second embryo transfers, and the proportion of patients who had no more frozen embryos available after non-achievement of live birth in the first or second transfers had the greatest influence on ICER. Other factors (e.g. accommodation, stimulation drug and opportunity costs) modified ICER to a lesser extent.

Figure 3 illustrates the incremental cost-effectiveness plane for the cost and effectiveness data bootstrapped from the Asian PURSUE study. PSA scatter plots represent uncertainty in ICER estimates on the incremental cost-effectiveness plane divided into four quadrants: north-east quadrant (I) with higher costs and higher effectiveness; south-east quadrant (II) with lower costs and higher effectiveness; south-west quadrant (III) with lower costs and lower effectiveness; and north-west quadrant (IV) with higher costs and lower effectiveness (Black, 1990). Approximately 26.1% of scenarios were in Quadrant I, 20.4% were in Quadrant II, 26.1% were in Quadrant III and 27.4% were in Quadrant IV (Figure 3).

Figure 4 shows that, at a WTP threshold of €1950 (GDP per capita in 2016) for an additional live birth, there is 22.1% chance that corifollitropin alfa is cost-effective. At a WTP threshold of €12,500 (cost per live birth in follitropin beta group) and €13,700 (cost per live birth in corifollitropin alfa

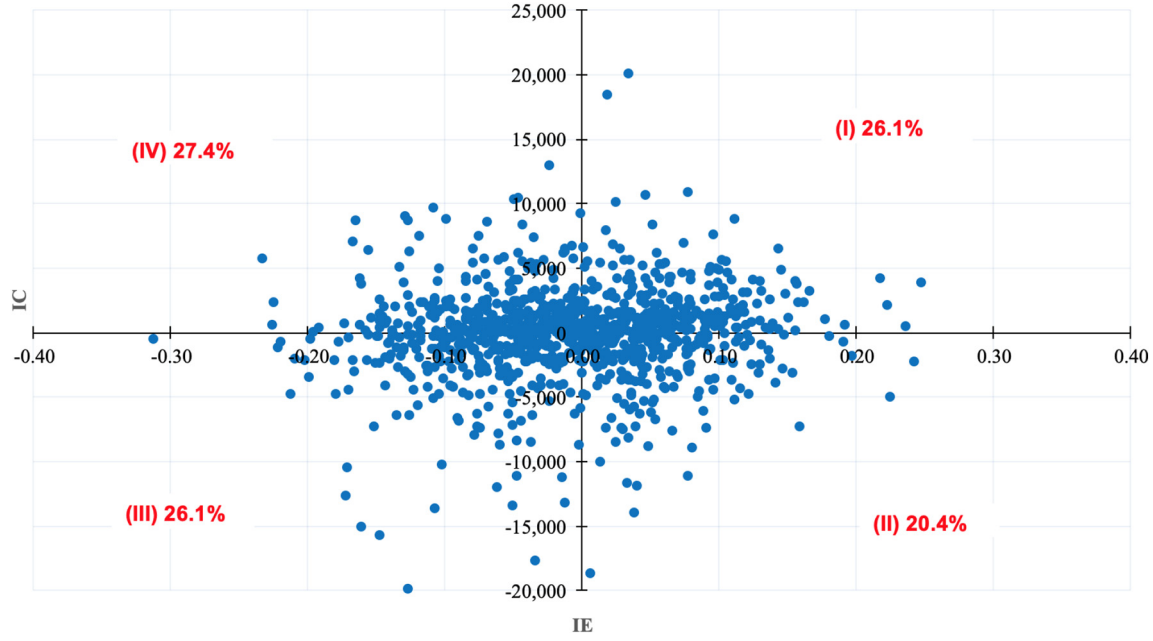

Figure 3 Probabilistic sensitivity analysis (PSA) scatter plots showing the mean differences in costs per patient [incremental cost (IC)] and live birth rate as a percentage [incremental effectiveness (IE)]. Note: the cost-effectiveness plane shows the PSA based on bootstrapping 1000 trials. (I) North-east quadrant: trials in which the corifollitropin alfa strategy had greater effectiveness than the follitropin beta strategy at higher cost [positive incremental cost-effectiveness ratio (ICER) values]. (II) South-east quadrant: trials in which the corifollitropin alfa strategy had greater effectiveness than the follitropin beta strategy at lower cost (negative ICER values). (III) South-west quadrant: trials in which the corifollitropin alfa strategy had lower effectiveness than the follitropin beta strategy and lower cost (positive ICER values). (IV) North-west quadrant: trials in which the corifollitropin alfa strategy had lower effectiveness than the follitropin beta strategy and higher cost (negative ICER values).

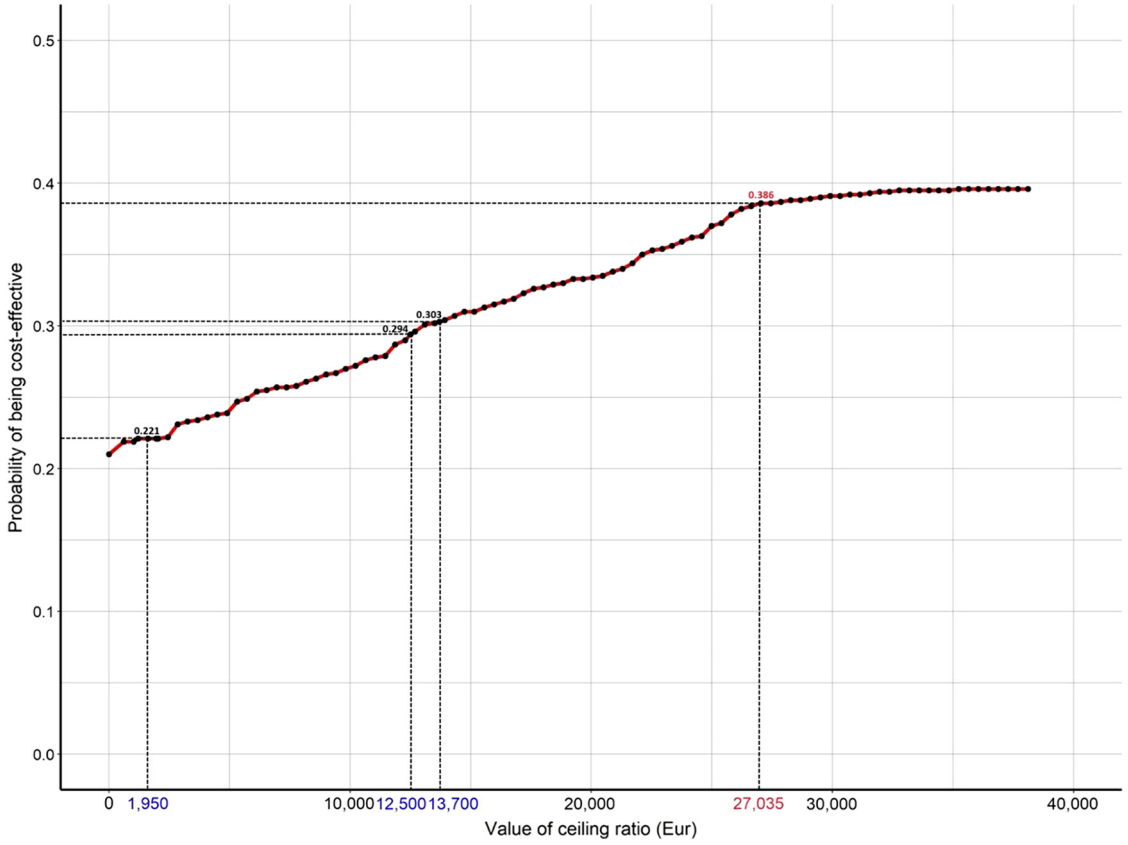

Figure 4 Cost-effectiveness acceptability curves for corifollitropin alfa strategy versus follitropin beta strategy.

group), the probabilities of being cost-effective are 29.4% and 30.3%, respectively. The probability that the corifollitropin alfa strategy is cost-effective is approximately 38.6% at a WTP threshold of €27,035 EUR (approximately 13.8 times higher than GDP per capita), with little change in probability as the WTP threshold increased further.

Discussion

The results of this CEA, conducted from the patient's perspective in conjunction with an RCT (Vuong et al., 2017), showed that a corifollitropin-based strategy for ovarian stimulation in IVS/ICSI was not cost-effective in Vietnam compared with a strategy based on follitropin beta. It is important to note that Vietnam is classified as a low–middle income country and there has been a lack of financial support from the public and private sectors for ART. ICER was most sensitive to changes in the live birth rate after first and second embryo transfers, and the proportion of patients who had no more frozen embryos available after non-achievment of live birth in the first or second transfers. Overall, the probability of corifollitropin alfa being cost-effective in the population and conditions of the analysis was only 20.4%.

The association between the patient-centred CEA and the RCT (Vuong et al., 2017) may have some advantages when using advanced analysis methods (e.g. OSA, PSA). Firstly, all outcomes in the RCT closely reflected daily practice, and RCT data provide the strongest empirical evidence of comparative treatment efficacy. The most important outcome for patients undergoing IVF/ICSI is the cumulative live birth rate (meaning they get to take a new baby home), rather than the time to success (Romundstad et al., 2015). Secondly, costing data in this analysis included indirect, as well as direct, costs. The indirect costs of infertility treatment strategies are often neglected or unexpected, and might influence a patient's decision about proceeding with treatment. Furthermore, useful information was obtained about which factors had the greatest influence on ICER.

Despite these advantages, a number of limitations need to be considered when interpreting these data. Due to the nature of cost data collected from the secondary sources and telephone interviews, there is potential for information recall bias (although the CEA was conducted as soon as possible after completion of the RCT). In addition, the RCT on which this analysis was based was conducted in a private hospital where the costs and service prices are much higher than in public facilities. Therefore, cost adjustments would be necessary when applying this model to data from patients treated in government-funded hospitals. Similarly, the data may not be applicable to healthcare systems in other countries.

The finding that the cost per live birth for an ovarian stimulation strategy based on corifollitropin alfa treatment was higher than that for follitropin-beta-based treatment

(€13,726 versus €12,511, respectively) differs from a previous cost-minimization analysis (CMA) of the two approaches (Barrenetxea et al., 2018). In addition to a difference in design (CMA versus CEA), the other study was conducted in a different setting (Spain; a high-income country) and did not include direct non-medical and indirect cost data. Furthermore, total costs in the Spanish study were considered in both the private and public sectors, whereas the present data were collected from one single private IVF centre. In addition, OSA and PSA were performed in this study to help understand the data, rather than CEA alone.

Although statistically total costs were higher in the corifollitropin alfa group, values were numerically higher with corifollitropin alfa versus follitropin beta. Costs for stimulation drugs and luteal support agents are the main parameters that contributed to higher direct medical costs with corifollitropin alfa compared with follitropin beta (Table 2). In contrast, examination and ultrasound costs were lower in the corifollitropin alfa group; this may have been because fewer patient visits are needed, as a single injection of corifollitropin alfa can replace 7 days of gonadotropin treatment with follitropin beta.

In this analysis, indirect non-medical costs (e.g. travel, accommodation) and indirect costs (e.g. income lost) varied between individuals. Patients may have stayed at more expensive hotels, taken less expensive forms of transport, or simply had a lower income. However, direct non-medical and indirect costs did not differ significantly between the two groups (Table 2).

OSA was performed using a Tornado diagram based on the assumption that each factor varied from its base-case value by ±10% while other factors were unchanged. The results indicate the range of ICER based on a change to a single variable. Greater range in ICER shows factors that have more influence on this parameter. The probability of live birth after the first and second embryo transfers and the proportion of patients who had no more frozen embryos available after non-achievement of live birth in the first or second transfer influenced the comparative cost-effectiveness of the two strategies. However, this approach is still limited because only one parameter changes at a time. In fact, all parameters could change simultaneously to any value within their range. Therefore, PSA was used to examine the change in ICER over 1000 trials in which all parameters changed contemporaneously. This showed that the probability of a corifollitropin alfa strategy being accepted was 14.6%, whereas it would be rejected in up to 27.4% of scenarios. This means that the comparative cost-effectiveness of the corifollitropin alfa and follitropin beta strategies in the remaining scenarios (approximately 53%) is less clear. In these settings, it would be interesting to know how much a patient might be willing to pay for corifollitropin alfa in order to achieve a 1% increase in the live birth rate; this is an important area for future study.

When more than 40% of the total health expenditure is required to be funded by patients as out-of-pocket payments, this is considered a source of financial health-related catastrophe and impoverishment (Lee and Shaw, 2014). The financial impact of fertility treatment is particularly problematic in low- and middle-income countries where these are fully self-funded (Dyer and Patel, 2012). In contrast, most high-income countries have publicly funded ART options (Connolly et al., 2010). Therefore, in low- or middle-income countries, the decision to use corifollitropin alfa or follitropin beta for ovarian stimulation could have an important influence on the rates of financial hardship and treatment discontinuation.

In conclusion, in women aged 35–42 years weighing ≥50 kg undergoing one IVF/ICSI cycle in Vietnam, an ovarian stimulation strategy based on follitropin beta 300 IU/day was more cost-effective than a strategy based on corifollitropin alfa 150 μg. ICER of corifollitropin alfa was influenced to the greatest extent by the probability of live birth after the first and second embryo transfers, and the proportion of patients who had no more frozen embryos available after non-achievement of live birth in the first or second transfer. These factors need to be considered when making a decision about the use of corifollitropin alfa versus follitropin beta strategies. Furthermore, to confirm the health economic impact of a corifollitropin alfa strategy based on the level of out-of-pocket payments, it is important to take average income per capita and WTP into account before changing ART practice.

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