**Cost-effectiveness of in vitro fertilisation and embryo transfer**


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**Record Status**
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

**Health technology**
Three different in vitro fertilisation (IVF) strategies in sub-fertile couples. The IVF strategies considered were: (1) immediate performance of three IVF cycles; (2) providing no treatment initially and then performing three IVF cycles if a pregnancy resulting in a live birth did not occur after 2.5 years; and (3) providing no treatment initially and then performing four IVF cycles if a pregnancy resulting in a live birth did not occur after 2.5 years.

**Type of intervention**
Treatment.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
Hypothetical sub-fertile couples with no previous IVF attempts.

**Setting**
Hospital. The economic study was carried out in The Netherlands.

**Dates to which data relate**
Effectiveness data were obtained from the literature published between 1995 and 1998. No dates were given for the resource use data. The price year was not explicitly specified.

**Source of effectiveness data**
The evidence for the final clinical outcomes was derived from a review of the literature.

**Modelling**
Markov models with time horizons of 3 years and Markov cycles of 28 days (the length of one menstrual cycle) were used to estimate costs and effects associated with each strategy. Couple-specific cycle success probabilities were estimated based on two prognostic models and then were used as the data inputs for the Markov models. Two separate prognostic models were used to predict the rate of conception in the absence of treatment (with the incorporation of age of the female partner, duration of sub-fertility, presence of a tubal or ovarian factor, and presence of primary or secondary sub-fertility as the prognostic factors) and IVF success rates (with the inclusion of age of the female partner, duration of sub-fertility, presence of a tubal disease, and number of previous pregnancies as the prognostic factors). It was reported that both models used in this analysis were based on patient series of over 2,000 couples and over 35,000 cycles and contained 5-6 variables. A Weibull model was used to express the course of spontaneous fertility as a function of time. The desire for a second child after the establishment of a first live birth was not considered in this analysis.
Outcomes assessed in the review
The review assessed the additional risk of getting a twin pregnancy after IVF, compared with the risk of getting a twin pregnancy after spontaneous conception. The data from the Canadian Infertility Therapy Evaluation Study was used to derive couple-specific cycle success probabilities using a prognostic model, these probabilities being incorporated into a Markov model to predict the rate of conception in the absence of treatment and IVF success rates.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 3 studies were included in the study.

Methods of combining primary studies
It appears that each study provided separate inputs for the Markov model. Couple-specific cycle success probabilities were estimated based on a published model and a Weibull model, developed by the authors and based on a published study.

Investigation of differences between primary studies
Not reported.

Results of the review
The additional risk of getting a twin pregnancy after IVF compared with the risk of getting a twin pregnancy after spontaneous conception was 25%; couple-specific cycle success probabilities were not reported.

Measure of benefits used in the economic analysis
The benefit measures used were the expected number of live births, the expected time to conception of a pregnancy resulting in a live birth, the expected number of live births resulting from IVF, and the expected number of IVF cycles performed. Benefit outcomes were not discounted in the baseline analysis, but were discounted in the sensitivity analyses (5%, 10%, 15%, and 20%).

Direct costs
Costs were discounted. Quantities were not reported separately from the costs. Cost items were reported separately. Cost analysis covered the costs of IVF, pregnancy, and a hospital stay for preterm labour, and neonatal intensive care (more related to twin pregnancies given the risk of prematurity and other complications). The perspective adopted in the cost analysis was not explicitly specified. It was not specified whether cost calculations were based on charge data or
on true costs. The sources of cost data were two studies published in 1994. The price year was not given. The cost analysis did not cover the costs of handicap care resulting from the long-term consequences of preterm delivery.

**Indirect Costs**
Not included.

**Currency**
The currency appears to have been US dollars ($).

**Sensitivity analysis**
It appears that a series of one-way sensitivity analyses was performed on the effects of decreasing the delay of IVF cycles to 1.5 years, variations in the age of the female partner from 25-40 years, the duration of sub-fertility from 1 to 5 years, the time horizon from 12 to 60 months, the discount rate of costs from 0% to 10%, and the discount rate of a live birth from 0% to 20% per year.

**Estimated benefits used in the economic analysis**
The expected live birth rate was 23% for strategy A (no treatment), 54% for strategy B (immediate performance of 3 cycles IVF); 50% for strategy C (wait, then performing 3 cycles IVF); 56% for strategy D (wait, then performing 4 cycles IVF).

The corresponding values in terms of expected percentage of live births established through IVF were 0% for strategy A, 80% for strategy B, 48% for strategy C, and 53% for strategy D;

expected mean number of IVF cycles required to achieve a successful pregnancy were 0 for strategy A, 2.5 for strategy B, 1.7 for strategy C, and 2.2 for strategy D;

and the number of IVF cycles per additional live birth were 0 for strategy A, 8.1 for strategy B, 6.4 for strategy C, and 6.6 for strategy D.

The mean expected times to the conception of a pregnancy resulting in a live birth would be 13.2 months for strategy A, 5 months for strategy B, 24.1 months for strategy C, and 24.3 months for strategy D.

**Cost results**
The mean total costs per patient for the four strategies considered were not reported. The costs of IVF were estimated at $8,000 per cycle and the average costs of hospitalisation for preterm labour and subsequent neonatal care were estimated at $38,000 for women with twin pregnancies.

**Synthesis of costs and benefits**
The incremental cost per additional live birth was calculated as the measure of cost-effectiveness, resulting in the values of $85,000 for strategy B, $68,000 for strategy C, and $69,000 for the strategy D, relative to the reference strategy, A. The sensitivity analyses showed that the immediate performance of IVF was more efficient in women 25-30 years of age than in older women. Up to the age of 35 years, the number of IVF cycles needed to establish an additional live birth was lower when IVF was delayed than when it was performed immediately. Decreasing the delay in IVF treatment in the study model from 2.5 years to 1.5 years increased the cost-effectiveness such that this strategy was more cost-effective than immediate IVF for virtually every age category.

**Authors’ conclusions**
This study showed that the cost-effectiveness of IVF depends not only on the costs and expected success rates of IVF
itself but also on the couple-specific chances of treatment-independent conception.

**CRD COMMENTARY - Selection of comparators**

The "no-treatment" strategy was regarded as the comparator since the authors believed that the chance of spontaneous conception, although low, should be considered in the analysis; it may be advantageous for some couples to postpone IVF for a while to take full advantage of spontaneous conception rates. It was acknowledged that there are numerous other strategies that can be considered before IVF for a sub-fertile couple. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The internal validity of the effectiveness results can not be objectively assessed due to lack of information regarding the sources and quality of data from the literature used in the study models. Furthermore, no systematic search and quality appraisal of the primary studies in the literature appears to have been performed. It was reported that randomised clinical trials on the subject are lacking, probably because of the reluctance of couples to allow themselves to be randomised to expectant management. It was believed that in the absence of such trials, the use of current prognostic models (despite the problems associated with such models), applied conservatively, are the best source of information available for comparing IVF with expectant management. The impact of male factor infertility could not be incorporated into the study because it was not included in the prognostic model on IVF.

**Validity of estimate of measure of benefit**

The estimation of benefits was modelled. The instrument used to derive a measure of health benefit, the Markov models in association with prognostic models, was appropriate.

**Validity of estimate of costs**

Quantities were not reported separately from the costs. Adequate details of methods of cost estimation were not given. As a result, it is not clear whether all relevant cost items were included in the cost calculations. The price year was not specified. The effects of alternative procedures on indirect costs and patients' out-of-pocket expenses were not addressed. Cost results may not be generalisable to other countries or settings due to lack of sensitivity analysis on cost data.

**Other issues**

Given the apparent lack of a comprehensive review of the literature, limitations of the prognostic models, and lack of an extensive sensitivity analysis, including cost data, the study results may need to be interpreted with some degree of caution. The issue of generalisability to other settings or countries was not addressed, although some comparisons were made with other studies.

**Implications of the study**

Economic analyses in reproductive medicine should take into account the option of "no treatment" to allow for accurate comparison of the cost-effectiveness of different treatment strategies.

**Source of funding**

None stated.

**Bibliographic details**
