Cost effectiveness of ovarian reserve testing in in vitro fertilization: a Markov decision-analytic model

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.

CRD summary
This study examined the cost-effectiveness of ovarian reserve testing in subfertile women aged 20 to 45 years who were undergoing in vitro fertilisation (IVF), from the perspective of the Dutch health care system. The authors concluded that basing the dose of gonadotrophin on a woman's ovarian reserve was likely to be cost-effective, but a large randomised trial was needed. The cost-effectiveness framework was conventional, which supports the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of ovarian reserve testing in subfertile women aged 20 to 45 years who were undergoing in vitro fertilisation (IVF).

Interventions
Four options were considered: no treatment; up to three cycles of IVF for women under 41 years without ovarian reserve testing; up to three cycles of IVF with gonadotrophin dose determined by ovarian reserve testing; and up to three cycles of IVF, with ovarian reserve testing after one cycle and the exclusion of those with an expected poor response.

Ovarian reserve testing categorised women as low, normal, or high responders. Gonadotrophin dose was 300 international units (IU) for low responders, 75 IU for high responders, and the standard dose of 150 IU for normal responders.

In the fourth option, after the first cycle of IVF women who produced less than four oocytes per stimulation (a poor response) received ovarian reserve testing. Those who were classified as low responders (had an expected poor response) did not receive the final two cycles of IVF.

Location/setting
Netherlands/fertility clinics.

Methods
Analytical approach:
The analysis was based on a Markov model, with a one-year time horizon. The authors stated that the analysis was carried out from the perspective of the health care system.

Effectiveness data:
The clinical data were from a selection of relevant studies. The women’s characteristics and the effects of no treatment, IVF for those under 41 years, and IVF excluding expected poor responders, came from a national Dutch prospective study performed between 2002 and 2004. The effects for IVF with varying gonadotrophin dose came from a randomised controlled trial, with a small sample. The primary input was the rate of live births with each intervention.

Monetary benefit and utility valuations:
Measure of benefit:
The cumulative rate of live births was the benefit measure.

Cost data:
The economic analysis included the costs of IVF cycles, ovarian reserve testing, and gonadotrophin dose increase or decrease. All economic data were from official Dutch sources and the authors' institution. Some unit costs were given. All costs were in Euros (EUR) and the price year was 2008.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were carried out to examine the uncertainty in the base-case findings. The ranges of values were from published sources. Conventional probability distributions were assigned to the model inputs. Confidence intervals around the incremental cost-effectiveness ratios (ICERs) and cost-effectiveness acceptability curves were calculated.

Results
The cumulative birth rates were 9.0% with no treatment, 54.8% with IVF for those under 41 years, 70.6% with IVF with varying gonadotrophin dose, and 51.9% with IVF excluding expected poor responders.

The cost per couple was zero with no treatment, EUR 6,917 with IVF for those under 41 years, EUR 6,678 with IVF with varying gonadotrophin dose, and EUR 5,892 with IVF excluding expected poor responders.

Compared with no treatment, the ICERs were EUR 15,166 with IVF for those under 41 years, EUR 10,837 with IVF with varying gonadotrophin dose, and EUR 13,743 with IVF excluding expected poor responders. IVF with varying gonadotrophin dose was dominant over the other two strategies, as they were less effective and more expensive or less cost-effective.

This dominance held in all the deterministic and first-order probabilistic sensitivity analyses. Below a threshold of EUR 10,900, no treatment was most likely to be cost-effective. If society was willing to pay more than EUR 10,900 per live birth, IVF with ovarian response testing to determine the gonadotrophin dose had the highest probability of being cost-effective.

Authors' conclusions
The authors concluded that basing the dose of gonadotrophin on a woman's ovarian reserve was likely to be cost-effective, but a large randomised trial was needed.

CRD commentary
Interventions:
The selection of the comparators was appropriate. Various ways of using the assessment of ovarian response were considered and were compared against no intervention.

Effectiveness/benefits:
The clinical data were mainly from a prospective study, conducted in the Netherlands, and this was partly described. The effect for IVF varying the gonadotrophin dose was from a clinical trial, but this had a small sample. The authors stated that no good clinical trials were available for the treatments and this was a limitation of their analysis. They also stated that the probability of live birth with no treatment was likely to be low in this study, but this should not have affected the final results. Extensive sensitivity analysis was conducted to assess the uncertainty around the key model parameters. The rate of live births is a natural outcome of IVF programmes and is often used as the summary benefit measure for fertilisation interventions.

Costs:
The cost categories and their sources were appropriate for the perspective of the Dutch health care payer. Limited resource quantities and unit costs were provided, reducing the transparency of the analysis. Statistical analyses of the costs were carried out and the impact of variations in these cost estimates was assessed. The price year was clearly
stated, allowing reflation exercises for other time periods.

Analysis and results:
The results were clearly presented. An incremental approach was used to synthesise the costs and benefits of the strategies. The time horizon was appropriate as it was the typical period required to complete a maximum of three cycles of IVF. A simplified description of the decision model was given. Valid approaches were used to assess the uncertainty around all the inputs for the model. The results of the sensitivity analyses were clearly presented. The transferability of the results was not discussed and they appear to be specific to the Netherlands.

Concluding remarks:
The cost-effectiveness framework was conventional, which supports the authors’ conclusions.

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