Cost-effectiveness of recombinant follicle-stimulating hormone (FSH) versus human FSH in intrauterine insemination cycles: a statistical model-derived analysis

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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.

CRD summary
This study examined the cost-effectiveness of recombinant versus human follicle-stimulating hormone (FSH) in intra-uterine insemination cycles in infertile patients. The authors concluded that human FSH was more cost-effective than recombinant FSH. The study appears to have been based on valid methodology, but was not extensively reported, especially on the clinical side. Thus, caution is required when interpreting the authors' conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the cost-effectiveness of recombinant versus human follicle-stimulating hormone (FSH) in intra-uterine insemination cycles in infertile patients considering the high acquisition cost of recombinant FSH.

Interventions
The two protocols of stimulation in intra-uterine insemination cycles were human and recombinant FSH.

Location/setting
Italy/fertility clinic.

Methods
Analytical approach:
This economic evaluation was based on a single study, which was modelled using two approaches: in the first model, all probabilities of cancelled cycles, pregnancies, deliveries, and miscarriages were derived from the single study, to assess the cost-effectiveness of a complete cycle; in the second model, after a cancelled cycle, no pregnancy, and miscarriage, patients started a new cycle (up to four) or stopped treatment. The time horizon of the analysis was not explicitly reported. The authors did not state the economic perspective.

Effectiveness data:
The clinical data came from a randomised controlled trial (RCT) that was published by the authors of this study (with others). The sample size was 65 patients, with 31 in the human FSH group and 34 in the recombinant FSH group. Other study characteristics were not reported. The key clinical endpoint was the pregnancy rate.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The summary benefit measure was the pregnancy rate.

Cost data:
The economic analysis included only the costs of the drugs, which were derived from the Italian formulary. The quantities of ampoules used were based on resource consumption in the clinical trial. Costs were in Euros (EUR) and the price year was 2001.

Analysis of uncertainty:
The issue of uncertainty was investigated using two approaches. In a deterministic one-way sensitivity analysis, an arbitrary range of recombinant FSH costs and the available confidence interval for pregnancy rates were tested. In a Monte Carlo simulation, 10,000 iterations were used to generate cost-effectiveness acceptability curves according to different thresholds of willingness to pay.

**Results**

In the first model, recombinant FSH was associated with an additional cost of EUR 97.8 per patient and a gain of 0.008 benefits, resulting in an incremental cost-effectiveness ratio (ICER) of EUR 13,727 per additional pregnancy. In the second model the additional cost was EUR 219.9, the benefit gain was 0.0201, and the ICER was EUR 10,934. According to the authors’ judgment based on previous studies, these ICERs were too high suggesting that the extra cost of recombinant FSH per pregnancy, was not worthwhile.

The sensitivity analysis showed that better findings for recombinant FSH were achieved when its cost was reduced or its efficacy increased. However, substantial changes were required to alter the conclusions on the cost-effectiveness of the two strategies. The probabilistic analysis suggested that, at a willingness-to-pay threshold of EUR 0, human FSH was cost-effective in 73% of simulations for the first model and in 96% of simulations for the second model.

**Authors’ conclusions**

The authors concluded that human FSH was more cost-effective than recombinant FSH in infertile patients. The authors stated that further RCTs should be carried out to provide reliable data on the comparative efficacy of the two protocols.

**CRD commentary**

**Interventions:**

The selection of the comparators was appropriate because the two available formulations of the same FSH were compared. This comparison has been widely investigated.

**Effectiveness/benefits:**

The clinical data were derived from a RCT, which is generally considered to be a valid source of evidence given its robust design. However, the study was published elsewhere and, except for the sample size, no information was provided on the study features, such as the patient demographics, length of follow-up, type of analysis, and use of power calculations or other statistical tests. This means that an objective assessment of the internal validity of the study is not possible. The benefit measure was derived directly from the clinical trial and was a commonly used outcome of fertilisation techniques.

**Costs:**

The economic viewpoint of the study was not stated and only the costs of medications were included. The authors stated that 2001 prices were used, but the use of more recent (2006) costs would further improve the cost advantage in favour of human FSH. The source of costs reflected official prices in Italy. Resource use reflected the treatment patterns in the RCT. Variations in the costs of medications were considered in the sensitivity analysis.

**Analysis and results:**

The costs and benefits were appropriately combined and presented. Both average and incremental cost-effectiveness ratios were calculated. The issue of uncertainty was satisfactorily addressed, using both a deterministic and a probabilistic approach. The results of these alternative analyses were clearly reported. The authors presented two cost-effectiveness models, and the second model resembled closely a real-world setting where multiple cycles of intra-uterine insemination are generally required.

**Concluding remarks:**

The study appears to have been based on valid methodology, but was not extensively reported, especially on the clinical side. Thus, caution is required when interpreting the authors’ conclusions.
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