A cost per live birth comparison of HMG and rFSH randomized trials

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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
The aim was to assess the cost-effectiveness of two gonadotrophin treatments, highly purified human menopausal gonadotrophin (HP-HMG) and recombinant follicle stimulating hormone (rFSH), follitropin, alpha in women being treated with in-vitro fertilisation. The authors concluded that HP-HMG improved live birth rates and had lower costs compared with rFSH alpha. The methods were satisfactory and the authors’ conclusions appear to be appropriate for the analysis reported.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of two leading gonadotrophin treatments in women treated with in-vitro fertilisation (IVF).

Interventions
Highly purified human menopausal gonadotrophin (HP-HMG) was compared with recombinant follicle stimulating hormone (rFSH), follitropin, alpha. Due to reported differences in dosing for rFSH in clinical trials and practice, two dosing scenarios were considered: a high-dose scenario in which the average weighted mean dose was 2,491 international units (IU) of HP-HMG compared with 2,434 IU of rFSH alpha; and a low-dose scenario in which the median dose was 2,500 IU of HP-HMG compared with 2,200 IU of rFSH alpha.

Location/setting
Belgium/secondary care.

Methods
Analytical approach:
A simulated decision tree was used to combine the effectiveness and cost data from a variety of sources. Despite the inclusion of health states the model was time independent. Health events included: start fresh treatment; cryopreserved cycle; live birth; and treatment withdrawal. Withdrawal from treatment could occur when there was: cancellation of fresh cycle; unsuccessful fertilisation; unsuccessful embryo implantation; or miscarriage following diagnosis of a clinical pregnancy. The model explored cost and outcomes over two IVF cycles: cycle one involved one fresh cycle for all patients; cycle two involved either another fresh cycle or one cryopreserved cycle, dependent on the probability of cryopreserved embryos being available. The authors reported that the analysis was carried out from the perspective of the Belgium health service Rijksinstituut voor Ziekte-en Invaliditeitsverzekering (RIZIV).

Effectiveness data:
The relative risk of a live birth for HP-HMG compared with rFSH alpha was based on a published meta-analysis of seven studies that all used long-agonist protocols (Coomarasamy, et al. 2008, see 'Other Publications of Related Interest' below for bibliographic details). Other clinical data included the ovarian hyperstimulation syndrome (OHSS) for each treatment, miscarriage rates, and success of cryopreserved embryos. These were from published studies or national statistics from the Belgian Register for Assisted Procreation.

Monetary benefit and utility valuations:
Not relevant.
Measure of benefit:
The primary measure of benefit was live birth. The live birth rate for each treatment was reported.

Cost data:
The direct cost categories included drug costs, costs due to OHSS, miscarriage, cost of IVF (oocyte retrieval, laboratory procedures, embryo transfer, and freezing, storing, and thawing of embryos) and three clinical consultations. Cost data were from a single study centre, published references, and expert opinion. The unit costs and resource quantities were reported in detail. Costs were reported in Euros (EUR) and indexed to 2007 values, using the inflation rate.

Analysis of uncertainty:
Uncertainty in the model was explored using Monte Carlo first-order micro-simulation where 50,000 patients with different baseline characteristics were passed through the model. Second-order Monte Carlo probabilistic sensitivity analysis (PSA) was also conducted, where probability distributions were assigned to the parameter estimates. The results were summarised using 95% confidence intervals.

Results
Extensive results were presented.

For one fresh cycle only: In the deterministic analysis, the cost per live birth was EUR 10,288 for HP-HMG, EUR 13,515 for high-dose rFSH alpha and EUR 13,017 for low-dose rFSH alpha. In the first-order micro-simulation, the cost per live birth was EUR 10,167 (95% CI 9,358 to 11,479) for HP-HMG, EUR 13,338 (95% CI 12,256 to 14,965) for high-dose rFSH alpha, and EUR 12,954 (95% CI 11,482 to 14,747) for low-dose rFSH alpha. In the PSA, the cost per live birth was EUR 10,293 (95% CI 9,953 to 10,660) for HP-HMG, EUR 13,520 (95% CI 13,106 to 13,974) for high-dose rFSH alpha, and EUR 13,020 (95% CI 12,616 to 13,469) for low-dose rFSH alpha.

For one fresh cycle and one cryopreserved cycle: In the deterministic analysis, the average cost per live birth was EUR 9,996 for HP-HMG, EUR 13,009 for high-dose rFSH alpha, and EUR 12,535 for low-dose rFSH alpha. In the first-order micro-simulation, the cost per live birth was EUR 10,055 (95% CI 9,243 to 10,843) for HP-HMG, EUR 12,862 (95% CI 11,854 to 13,992) for high-dose rFSH alpha, and EUR 12,653 (95% CI 11,467 to 14,103) for low-dose rFSH alpha. In the PSA, the cost per live birth was EUR 9,999 (95% CI 9,668 to 10,351) for HP-HMG, EUR 13,012 (95% CI 12,159 to 12,946) for low-dose rFSH alpha.

Authors' conclusions
The authors concluded that HP-HMG resulted in improved live birth rates, lower average costs per fresh cycle, lower average cumulative costs for one fresh and one cryopreserved cycle, and lower average costs per live birth compared with rFSH alpha.

CRD commentary
Interventions:
The interventions were well described and appeared to represent the relevant comparators in the setting.

Effectiveness/benefits:
The clinical estimates and their sources were clearly reported. The authors suggested in the discussion that a systematic review had been conducted, but presented no evidence to support the statement and so it was unclear whether all relevant sources of data were considered. The authors identified a further meta-analysis (Al-Inany, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details) that compared HMG and rFSH where the live birth rate was higher with HMG (OR 1.20, 95% CI 1.01 to 1.42); it was unclear why the authors chose not to include the results of this meta-analysis in their own analysis.

Costs:
The costs were relevant to the perspective taken. The unit costs and resource quantities were well reported, but many costs were based on experiences in a single study centre, which may have limited the generalisability to other settings. The adjustments to the cost data were reported and were appropriate. A number of costs (which included nursing consultation costs, costs of ongoing pregnancies, deliveries, counselling services due to withdrawals, and adoption costs)
were excluded as irrelevant to the Belgium perspective, but these might be relevant to other health service perspectives.

**Analysis and results:**
The model was appropriate for the disease and the methods were well reported. The three types of analysis (deterministic, first-order simulation, and second-order simulation) allowed uncertainty to be addressed comprehensively. The reporting of the results as cost per delivery and cost per live birth was appropriate and given in full.

**Concluding remarks:**
The methods were satisfactory and well reported. The authors' conclusions appear to be appropriate for the analysis reported.

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**Other publications of related interest**


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