
Cost-saving treatment strategies in in vitro fertilization: a combined economic evaluation of two large randomized clinical trials comparing highly purified human menopausal gonadotropin and recombinant follicle-stimulating hormone alpha

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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 objective was to assess the cost-effectiveness of highly purified menotrophin (HP-hMG) and recombinant follitropin alpha in women aged 18 to 38 years, who were experiencing tubal or unexplained infertility and being treated with in vitro fertilisation. HP-hMG was cost saving considering only treatment costs. Including maternal and neonatal costs, reduced these savings to costs due to more live births, but HP-hMG remained highly cost-effective. The methodology was good and was transparently reported. These conclusions appear to be appropriate.

Type of economic evaluation

Cost-effectiveness analysis

Study objective

The objective was to assess the cost-effectiveness of two gonadotrophin treatments in women aged 18 to 38 years, who were experiencing tubal or unexplained infertility and being treated with in vitro fertilisation (IVF).

Interventions

Highly purified (HP) menotrophin (hMG, human menopausal gonadotrophin) was compared against recombinant follitropin alpha (rFSH, follicle-stimulating hormone), using a long gonadotrophin-releasing hormone (GnRH) agonist stimulation protocol.

Location/setting

UK/secondary care.

Methods

Analytical approach:

A discrete event simulation combined individual patient data from two trials and cost data from a variety of sources. The treatment events included: stimulation, oocyte retrieval, embryo transfer, pregnancy, and live birth. The probability of fertilisation and implantation success was implicitly included. A diagram of the model was provided and the authors reported that the analysis was carried out from a health care perspective.

Effectiveness data:

The authors stated that the effectiveness of both treatments was based on a pooled, intention-to-treat analysis of patients from two prospective, randomised, multinational trials; The European and Israeli Study Group (EISG) trial, and the Menotrophin versus Recombinant FSH in vitro Fertilisation Trial (MERiT; see 'Other Publications of Related Interest' below for bibliographic details). The patients in these two trials were treated with either HP-hMG (n=491) or rFSH (n=495).

Monetary benefit and utility valuations:

Not relevant.

Measure of benefit:

The primary measure of benefit was the cost per live birth. Secondary measures included the number of live births and the number of babies born per patient initiating treatment.

Cost data:

The cost categories included drugs, hospitalisation due to ovarian hyperstimulation syndrome, patient visits, and specialist consultations. The costs of delivery and neonatal care were considered separately for singleton, twin, and triplet births. The cost and outcome consequences of failed treatments and the probability of adoption were not considered. The authors stated that the resource use data were based on established UK treatment practices or data collected in the two trials. Drug costs were obtained from the British National Formulary and hospitalisation costs were obtained from the University Hospitals of Coventry and Warwickshire. The unit costs and resource use were reported in detail, in a table. All costs were in UK pounds sterling (£) and were indexed to the year 2006.

Analysis of uncertainty:

Probabilistic sensitivity analysis assessed the uncertainty in the model. The authors stated that the values for the parameters were sampled from 95% confidence intervals (CIs) based on the probabilities of success at each stage of simulation, and from uncertainty intervals for costs, which were judged to conservatively approximate to the 95% CIs. The results were summarised using cost-effectiveness acceptability curves.

Results

The live-birth (including multiple births) rate after one fresh IVF cycle was 26.6% (95% CI 22.7 to 30.5) for HP-hMG and 20.6% (95% CI 17.0 to 24.1) for rFSH. The number of babies per 1,000 cycles was 338 for HP-hMG and 268 for rFSH. The mean IVF cost per person was £2,408 (95% CI 2,392 to 2,421) for HP-hMG and £2,660 (95% CI 2,644 to 2,678) for rFSH. The mean IVF cost per live birth was £9,058 (95% CI 7,884 to 10,676) for HP-hMG and £12,944 (95% CI 11,124 to 15,788) for rFSH. Consequently HP-hMG was less costly and more effective than rFSH.

When maternal and neonatal costs were included, the total mean costs per person were £3,936 for HP-hMG and £3,886 for rFSH. The mean cost per live birth was £14,804 (95% CI 12,753 to 17,592) for HP-hMG and £18,909 (95% CI 15,854 to 23,230) for rFSH. The incremental cost-effectiveness ratio was £824 per live birth and £710 per baby.

The probabilistic sensitivity analysis showed that the probability of being cost-effective for HP-hMG was 98.4% at a value of £20,000 per live birth, both exclusive and inclusive of neonatal and maternal costs. A one-way sensitivity analysis varying the acquisition costs of rFSH, with the cost per live birth after one cycle as the outcome, indicated that an equal cost per live birth for both gonadotrophins could not be achieved, regardless of the cost of rFSH.

Authors' conclusions

The authors concluded that HP-hMG was cost saving when only the IVF treatment costs were considered. The inclusion of maternal and neonatal costs reduced the savings to costs for HP-hMG because of the increased number of live births, but HP-hMG remained highly cost-effective.

CRD commentary

Interventions:

The interventions were well described and relevant to the secondary care setting.

Effectiveness/benefits:

The effectiveness of HP-hMG and that of rFSH were reported, but no systematic review was conducted so it is unclear whether all the relevant sources of efficacy data were captured. The measure of benefit was appropriate.

Costs:

The included costs appeared to reflect the perspective stated. The resource use data and the unit costs were well reported. The price year was adequately reported. The reporting of the costs was extremely transparent, allowing the reader to ascertain fully which resource use data and costs were included.

Analysis and results:

The model structure was presented in a diagram with all the relevant details and modelling assumptions. The authors conducted an incremental analysis and the results were adequately presented. Sensitivity analyses were conducted on the modelling assumptions and parameters, which enhances the generalisability of the findings. The authors provided a thorough discussion on the limitations and weaknesses of their study.

Concluding remarks:

The methodology was good and was clearly and transparently reported, but no systematic review was conducted to find other sources for the efficacy data. The authors' conclusions appear to be appropriate.

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Bibliographic details

Wechowski J, Connolly M, Schneider D, McEwan P, Kennedy R. Cost-saving treatment strategies in in vitro fertilization: a combined economic evaluation of two large randomized clinical trials comparing highly purified human menopausal gonadotropin and recombinant follicle-stimulating hormone alpha. *Fertility and Sterility* 2009; 91(4): 1067-1076

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Other publications of related interest

The European and Israeli Study Group on Highly Purified Menotropin versus Recombinant Follicle-Stimulating Hormone. Efficacy and safety of highly purified menotropin versus recombinant follicle-stimulating hormone in in vitro fertilization/intracytoplasmic sperm injection cycles: a randomized, comparative trial. *Fertility and Sterility* 2002; 78: 520-528.

Platteau P, Smitz J, Albano C, Sorensen P, Arce JC, Devroey P. Exogenous luteinizing hormone activity may influence the treatment outcome in in vitro fertilization but not in intracytoplasmic sperm injection cycles. *Fertility and Sterility* 2004; 81: 1401-1404.

Indexing Status

Subject indexing assigned by NLM

MeSH

Adolescent; Adult; Algorithms; Computer Simulation; Cost Savings /methods; Cost-Benefit Analysis; Double-Blind Method; Female; Fertilization in Vitro /economics /methods; Glycoprotein Hormones, alpha Subunit /economics /therapeutic use; Humans; Menotropins /economics /isolation & purification /therapeutic use; Models, Statistical; Recombinant Proteins /economics /therapeutic use; Young Adult

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