Efficacy of treatment for unexplained infertility

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
Treatment for unexplained infertility.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Female patients for whom the results of a standard infertility evaluation were normal. Women with stage I or stage II endometriosis were also included.

Setting
Clinical practices. The economic study was conducted in the USA.

Dates to which data relate
The main effectiveness data were obtained from a review of studies previously published between 1985 and 1998. The dates to which resource use and cost data related were not reported. The price year was not stated.

Source of effectiveness data
Effectiveness data were derived from a review of previously published studies.

Modelling
No modelling was undertaken.

Outcomes assessed in the review
The outcomes assessed included the number of initiated cycles for each treatment, the number of clinical pregnancies, and quality-adjusted pregnancy rates.

Study designs and other criteria for inclusion in the review
Studies with the following study design were included: observational studies with no control, non-randomised studies with control and prospective, randomised studies.
Sources searched to identify primary studies
MEDLINE was searched and retrieved papers were scanned for further references.

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

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

Number of primary studies included
45 studies were included.

Methods of combining primary studies
Narrative method.

Investigation of differences between primary studies
Each study was assigned a "quality" score based on its strengths and weaknesses. The score was a sum of points assigned to each of six categories of study methodology: study design, patient population, sample size, multicentre versus single site, definition of pregnancy, and clarity of outcome. The actual point scores for the studies reviewed ranged from 6 to 19 (minimum and maximum values:6 and 20). The mean score was 12.7 (+/- 3.2).

Results of the review
The number of pregnancies per initiated cycle were estimated to be 4% (15/378) for IUI alone, 6% (37/617) for CC alone, 6.7% (21/315) for CC+IUI, 7.7% (139/1,806) for hMG alone, 18% (207/1,133) for hMG+IUI, 22.5% (378/683) for IVF and 26% (158/607) for GIFT. The pregnancy rate without treatment was 1.8%. If only randomized studies were included, the pregnancy rate without treatment was 3.8%. Correcting for differences in study quality, pregnancy rates were estimated to be 3.8% (IUI alone), 5.6% (CC alone), 8.3% (CC+IUI), 7.7% (hMG alone), 17.1% (hMG+IUI), 20.7% (IVF) and 27% (GIFT). The quality-adjusted pregnancy rate was 1.3% or 4.1% if only randomised studies were included.

Measure of benefits used in the economic analysis
The measure of benefits was the incremental quality-adjusted pregnancy rate over baseline for CC+IUI, hMG+IUI, GIFT and IVF.

Direct costs
It was not reported whether costs were discounted or not. Quantities and costs were not reported separately. Treatment costs were included in the analysis. Average costs per treatment cycle were based on average costs in the communities represented by the investigators. The quantity/cost boundary adopted was that of the health service. The price year was not stated.

Statistical analysis of costs
Not reported.

Indirect Costs
Not included.
Currency
US dollars ($).

Sensitivity analysis
Not reported.

Estimated benefits used in the economic analysis
Incremental quality-adjusted pregnancy rates compared to a baseline rate of 1.3% were estimated to be 7% for CC+IUI, 15.8% for hMG+IUI, 25.7% for GIFT, and 19.4% for IVF. Incremental quality-adjusted pregnancy rates compared to a baseline rate of 4.1% were estimated to be 4.2%, 13%, 22.9%, and 16.6%, respectively.

Cost results
Average costs per treatment cycle were $500 (CC+IUI), $2,500 (hMG+IUI), $9,000 (GIFT) and $10,000 (IVF).

Synthesis of costs and benefits
The cost per incremental pregnancy associated with a baseline pregnancy rates of 1.3% was estimated to be $7,143 (CC+IUI), $15,823 (hMG+IUI), $38,911 (GIFT) and $46,391 (IVF). The cost per incremental pregnancy associated with a baseline pregnancy rate of 4.1% was estimated to be $11,905 (CC+IUI), $19,230 (hMG+IUI), $43,668 (GIFT) and $54,217 (IVF).

Authors’ conclusions
CC + IUI is a cost-effective treatment for unexplained infertility. If this treatment fails, hMG + IUI and assisted reproduction are efficacious therapeutic options.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparators is clear. Ovarian superovulation (using clomiphene citrate - CC or hMG), IUI, GIFT, IVF and expectant observation with timed intercourse are the principal treatments for unexplained infertility. You, as a user of this database, should consider whether these treatment procedures are relevant to your own setting.

Validity of estimate of measure of benefit
The estimate of measure of benefit used in the economic analysis is likely to be internally valid. The data do not appear to have been used selectively. As noted by the authors, this retrospective analysis of data retrieved from the literature may suffer from potential biases. Pregnancy rates from IVF and GIFT may be biased downward because of adverse selection of patients who have failed to conceive from hMG+IUI. Furthermore, there may be upward publication bias in the reporting of pregnancy rates from both hMG+IUI and assisted reproduction, as those practices experiencing low pregnancy rates would be less likely to report their results. One must also be cautious in evaluating the reported pregnancy rates from hMG+IUI in the absence of randomised trials which include an untreated control group.

Validity of estimate of costs
Resource quantities were not reported separately from the prices. Important cost items do not appear to have been omitted. However, the costing methodology was not reported in detail. As no statistical analysis was conducted and the estimates were based on average costs in the communities represented by the investigators, the cost figures need to be treated with a degree of caution.

Other issues
The authors’ conclusions are likely to be justified given the uncertainties in the data. The issue of generalisability to other settings or countries was not addressed. As stated by the authors, costs per delivery may vary across individual centres, depending on their particular treatment protocols, associated with costs and delivery rates. Moreover, costs per
pregnancy in contemporary IVF practice may be significantly lower in many centres than those reported in this study, as pregnancy rates from hMG+IUI in recent years have appeared to reach a plateau, whereas those from IVF are increasing in many centres. Appropriate comparisons were made with other studies in terms of pregnancy rates, birth rates and costs per delivery.

**Implications of the study**

Further analysis is required within the context of a randomized controlled clinical trials.

**Source of funding**

None stated.

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**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Cost-Benefit Analysis; Female; Fertilization in Vitro; Gamete Intrafallopian Transfer; Humans; Infertility /etiology /therapy; Insemination, Artificial; Pregnancy; Pregnancy Rate; Randomized Controlled Trials as Topic; Retrospective Studies; Superovulation

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