In vitro fertilization (IVF) versus gonadotropins followed by IVF as treatment for primary infertility: a cost-based decision 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.

Health technology
Immediate in vitro fertilisation (IVF) was compared with gonadotropins followed by IVF as treatment for primary infertility.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 women under 35 years of age who were undergoing treatment for unexplained infertility. Patients entering either treatment arm were assumed to have already had three failed cycles of clomiphene citrate with intrauterine insemination.

Setting
The setting was unclear. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was derived from papers published between 1994 and 2003. The cost data were derived from papers published between 1994 and 2000. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a synthesis of published studies.

Modelling
A decision tree model was constructed to incorporate the cost and success of each infertility regimen, as well as the pregnancy-associated costs of singleton or multiple gestations and the risk and cost of cerebral palsy. Women were exposed to 6 cycles of infertility treatment (3 with gonadotropins and 3 with IVF) in the standard treatment with gonadotropins prior to IVF arm, as opposed to 3 cycles in the immediate IVF arm.

Outcomes assessed in the review
The following parameters were obtained from a review:

the probability of treatment success;
the probability associated with a singleton, twin or high-order multiple pregnancy (HOMP);
the likelihood of cerebral palsy associated with each plurality of gestation.

**Study designs and other criteria for inclusion in the review**
The review appears to have been ad hoc and no inclusion criteria were discussed.

**Sources searched to identify primary studies**
MEDLINE was searched from January 1991 to March 2003 for primary studies. Further information was obtained through a manual search of the reference lists of retrieved articles and through the Society for Assisted Reproductive Technology registry.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
Four primary studies were included in the review.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The live birth rate per cycle was 42% in the IVF arm (with 3 cycles of treatment) and 14% in the gonadotropins prior to IVF arm (with 6 cycles of treatment).

The probabilities associated with a singleton, twin or HOMP were:

in the IVF arm, 66.1% for singleton, 33.1% for twin, and 0.8% for HOMP; and

in the gonadotropins prior to IVF arm, 72.2% for singleton, 27.7% for twin, and 8.8% for HOMP.

It should be noted that in table 1 in the paper, the live birth rates for singleton and for HOMP were not consistent with the corresponding percentage of live births. It appears that 59,753 singleton births and 3,612 HOMP births in the gonadotropins arm accounted for 68.2% (instead of 72.2%) and 4.1% (instead of 8.8%) of live births, respectively, in this arm.

The likelihood of cerebral palsy was 0.1% for singleton, 0.9% for twin and 3.1% for HOMP.

**Measure of benefits used in the economic analysis**
The outcome measure used in the economic analysis was live births.
**Direct costs**
The direct costs included the costs of IVF and gonadotropin therapies and the cost of pregnancy. In addition, antepartum and intrapartum medical costs associated with different pregnancy pluralities were analysed. The costs of IVF and gonadotropin therapies were derived from a study that calculated all costs for each treatment, including those due to personnel, equipment, materials and medication (Goverde et al. 2000, see Other Publications of Related Interest- below for bibliographic details). The costs of pregnancy, stratified by plurality, were derived from a study that calculated comprehensive inpatient hospital charges for both the mother and infant (Callahan et al. 1994, see Other Publications of Related Interest- below for bibliographic details). The antepartum and intrapartum medical costs associated with different pregnancy pluralities and the medical cost of cerebral palsy were derived from published studies (Callahan et al 1994, Yokoyama et al. 1995, and Waizmann et al. 1992, see Other Publications of Related Interest- below for bibliographic details). Costs derived before 2003 were adjusted for inflation according to the medical care component of the Consumer Price Index to reflect 2003 dollars. The authors did not mention whether discounting was carried out, and it was unclear what timeframe was covered by the cycles within the model.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A one-way sensitivity analysis was carried out to test the sensitivity of the base-case results to changes in the probability and cost variables. A two-way sensitivity analysis was performed to determine the point at which the IVF algorithm is equal in cost per live birth to the gonadotropin algorithm for varying probability of IVF and gonadotropin birth rates.

**Estimated benefits used in the economic analysis**
For the hypothetical cohort of 100,000 couples, the IVF arm resulted in 80,489 live births (53,203 singletons, 26,642 twins and 644 HOMP), compared with 87,590 live births (59,753 singleton, 24,225 twin and 3,612 HOMP) in the gonadotropin arm.

**Cost results**
The treatment cost per cycle was $15,000 in the IVF arm and $3,000 in the gonadotropins prior to IVF arm.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating the cost per live birth. The cost per live birth was $61,930 in the IVF arm and $58,401 in the gonadotropins prior to IVF arm.

Sensitivity analyses showed that relatively small adjustments in the base-case pregnancy rates associated with IVF and gonadotropin therapy, as well as the base-case costs associated with both treatments, might shift the cost per live birth analysis to favour immediate IVF.

**Authors’ conclusions**
After considering the risk and cost of high-order multiple pregnancy (HOMP), immediate in vitro fertilisation (IVF) was more costly per live birth than a trial of gonadotropins prior to IVF.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. It represented current practice at the time of the study. You should decide if this represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The estimate of measure of effectiveness was based on a synthesis of published studies. No systematic review of the literature was undertaken. Although this is common practice with models, it does not always ensure that the best data available are used in the model. The authors appear to have used the data from the available studies selectively. The authors did not consider the impact of differences between the studies when estimating effectiveness.

Validity of estimate of measure of benefit
The measure of benefit used was the number of live births. This was derived from the effectiveness analysis. When the authors reported the effectiveness and benefits of gonadotropins prior to IVF, there was some inconsistency.

Validity of estimate of costs
The authors reported that the study had been conducted from the perspective of a medical system. As such, all the categories of costs relevant to that perspective appear to have been included in the analysis. The costs and the quantities were not reported separately, which could be an obstacle to reworking the analysis in other settings. The costs were treated deterministically, but sensitivity analyses were conducted to assess the robustness of the estimates used. Appropriate adjustments for inflation were performed and the price year was reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability was addressed. The authors stated that one issue of the study was that women were exposed to different numbers of treatment cycles in the two arms. This might have affected the results, although the authors stated that this reflected actual clinical practice. The authors reported that standard effectiveness outcomes, such as quality-adjusted life-years, were not employed because their use in certain pregnancy situations could be difficult to interpret. In addition, the quality-adjusted life-years with regard to achieving pregnancy in the context of greater pregnancy and neonatal complications was not well known.

Implications of the study
The study implied that immediate IVF would become less costly per live birth when IVF was more likely to achieve birth (55.1%) or was cheaper ($11,432) than the base-case assumptions. The authors recommended that further research in the area of quality-adjusted life-years with regard to treatment for primary fertility would allow further refinement of a cost-effectiveness model.

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None stated.

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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