Cost-effectiveness study of clomiphene citrate versus anastrozole for inducing ovulation in infertile adult patients in a public hospital, La Raza in Mexico City

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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 evaluate the cost-effectiveness of clomiphene citrate versus anastrozole for the induction of ovulation in infertile adult women. The authors concluded that clomiphene citrate was the most cost-effective intervention. This conclusion should be treated with extreme caution as it was inappropriately based on average, rather than incremental, cost-effectiveness ratios.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to evaluate the cost-effectiveness of clomiphene citrate versus anastrozole for the induction of ovulation in infertile adult women.

Interventions
The interventions were clomiphene citrate, at doses of 50mg to 150mg per day, and anastrozole, at a dose of 1mg per day. Each intervention was administered from day five to day nine of the patient's menstrual cycle, for six months, followed by six months of rescue therapy using recombinant follicle-stimulating hormone.

Location/setting
Mexico/secondary care.

Methods
Analytical approach:
The authors reported that a decision-analytic Markov model was used to assess the costs and outcomes for each of the two interventions. The time horizon was one year and the authors reported that a hospital perspective was adopted.

Effectiveness data:
The authors undertook a small pilot study and a systematic review of the literature. They searched PubMed, Scopus, and the Cochrane Library for controlled clinical trials published between 2000 and 2009. The key search terms and inclusion and exclusion criteria were reported. Treatment efficacy was from a meta-analysis of the results of the pilot study and two trials found by the literature review. Treatments were considered successful if patients reached ovulation with progesterone concentrations above 10 nanograms per mL.

Monetary benefit and utility valuations:
The sources for the utility estimates were not reported.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained.

Cost data:
The direct costs were those of drugs, medical consultations, diagnostic tests, and hospitalisations. The indirect costs were those of transport, absence from work (for both patients and carers), and out-of-pocket expenses. The resource use was collected in the pilot study, either from medical records or patient questionnaires. The unit costs were from the NHS Economic Evaluation Database (NHS EED)
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hospital's finance department or national fee schedules. The price year was 2009. All costs were converted into US dollars ($), at the rate of $1 equalled 13.02 Mexican pesos.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken, varying the parameters by ±5% of their base-case value.

Results
The average cost per patient was $1,644 with clomiphene citrate and $1,816 with anastrozole.

The average cost-utility for clomiphene citrate was $405 per QALY, and that for anastrozole was $457 per QALY. The incremental cost-utility ratio for anastrozole, compared with clomiphene citrate, was $52 per QALY gained.

These results were not sensitive to changes in the cost inputs.

Authors’ conclusions
The authors concluded that clomiphene citrate was the most cost-effective intervention for female infertility due to anovulation.

CRD commentary
Interventions:
The interventions were reported clearly. They were valid interventions for the setting, but it was not clear whether they included all the options.

Effectiveness/benefits:
The clinical and effectiveness data were from a small, non-randomised study and two trials identified by a systematic review. The pilot study included only 30 patients (with five patients in the anastrozole group) and its results should be treated with caution. The authors combined these results with those from two trials, with a total of 364 patients. The meta-analysis combined data based on the number of cycles. The authors appropriately reported the methods of their systematic review and it is likely that all relevant studies were included. A quality assessment of these trials was not reported, making it difficult to assess their validity and hence the validity of the model inputs. The measure of benefit was stated to be quality-adjusted life-years, but the utility derivation and values were not reported, severely limiting the analysis.

Costs:
The perspective was reported to be that of the hospital, but indirect costs, such as out-of-pocket expenses, work loss, and transport costs, were included and it appears that a societal perspective was adopted. For this societal perspective, all the major relevant cost categories were analysed. The authors appropriately reported the sources for the unit costs and resource use. The price year, time horizon, and currency were appropriately reported. As the pilot study supplied the resource use, the generalisability of the findings may be limited.

Analysis and results:
The costs and effectiveness data were synthesised using a decision-analytic Markov model. Appropriate details of this model were reported, including a diagram. The authors’ conclusion that clomiphene citrate was cost-effective, compared with anastrozole, was based on the average cost-utility ratios, rather than the incremental cost-utility ratio. The incremental ratio for anastrozole, compared with clomiphene citrate, was $52 per QALY gained, suggesting that anastrozole was highly cost-effective. The uncertainty in the model was assessed in a limited one-way sensitivity analysis. This went some way towards evaluating the uncertainty, but a probabilistic sensitivity analysis could have captured the overall model uncertainty. The authors reported that the main limitation to their study was the small number of patients included in their pilot study.

Concluding remarks:
The conclusions of this study should be treated with extreme caution. The authors’ conclusion that clomiphene citrate was cost-effective, compared with anastrozole, was based on average cost-utility ratios, rather than the incremental cost-utility ratio, and this was inappropriate.
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