Clomifene citrate and intrauterine insemination as first-line treatments for unexplained infertility: are they cost-effective?


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 clomiphene citrate and intra-uterine insemination, as first-line treatments for couples with unexplained infertility. The authors concluded that both treatments were unlikely to be cost-effective. On the whole, the methods seem to have been appropriate and were relatively well reported. The authors’ conclusions seem valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of clomiphene citrate and intra-uterine insemination, as first-line treatments for couples with unexplained infertility.

Interventions
The three interventions were clomiphene citrate, intra-uterine insemination, and expectant management. Clomiphene citrate was given as an oral dose of 50mg between days two and six of each treatment cycle, with the couple advised to have intercourse on cycle days 12 to 18. Intra-uterine insemination included the monitoring of mid-morning urinary luteinising hormone concentrations from day 12 of the cycle, with a single insemination performed 20 to 30 hours after detecting a surge in the hormone. Expectant management included general advice for regular intercourse.

Location/setting
UK (Scotland)/hospital.

Methods
Analytical approach:
The economic evaluation was undertaken alongside a clinical trial. The time horizon was six months. The authors reported that the perspective was that of the UK NHS.

Effectiveness data:
The effectiveness data came from a multi-centre randomised controlled trial (RCT; Bhattacharya, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). The sample size was 580 couples. An intention-to-treat approach was taken, with four couples lost to follow-up. The main clinical effectiveness estimate was the number of live births.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was the live birth rate.

Cost data:
The analysis included the costs associated with staff, consumables, equipment, and overheads. Resource use and cost data were obtained by questionnaires completed at the five sites participating in the RCT. Equipment costs were
calculated using equivalent annual costing techniques. All costs were reported in 2006 UK pounds sterling (£).

**Analysis of uncertainty:**
The analysis of uncertainty included an assessment of the impact of changes in some of the cost estimates on the cost-effectiveness results. Confidence intervals around these cost estimates were generated, using bootstrapping techniques. Probabilistic sensitivity analysis was used to estimate a cost-effectiveness acceptability curve for each intervention. A threshold analysis was performed examining how variations in the live birth rates for clomiphene citrate and intra-uterine insemination affected the cost-effectiveness results.

**Results**
The live birth rate was 17% for expectant management, 13% for clomiphene citrate, and 22% for intra-uterine insemination. The mean treatment cost per patient was £11.88 for expectant management, £349.96 for clomiphene citrate, and £331.27 for intra-uterine insemination. The incremental cost-effectiveness ratio (ICER) for intra-uterine insemination versus expectant management was £5,604 per live birth; while clomiphene citrate was dominated by intra-uterine insemination as it was more costly and less effective.

The sensitivity analysis showed clomiphene citrate was dominated regardless of changes in the cost estimates. The cost-effectiveness acceptability curves indicated that, at a willingness to pay of £30,000 per live birth, expectant management had a 15% chance of being cost-effective and intra-uterine insemination had an 80% chance of being cost-effective.

**Authors' conclusions**
The authors concluded that intra-uterine insemination and clomiphene citrate were unlikely to be cost-effective for the first-line treatment of unexplained infertility.

**CRD commentary**

**Interventions:**
The interventions were well described and the comparator was appropriate as it was the usual practice in the authors’ setting.

**Effectiveness/benefits:**
The effectiveness data were from a multi-centre RCT. Relatively few details of the trial were reported, making it difficult to comment on the validity of the data. The live birth rate was an appropriate measure of benefit, given the interventions studied, but the follow-up was reported to be six months, making it unclear when the birth rate was determined.

**Costs:**
The authors reported the perspective and relevant costs appear to have been included. The source of the resource use and cost estimates was reported and seems to have been appropriate for the setting.

**Analysis and results:**
The benefits and costs were appropriately combined in an incremental analysis, the results of which were reported and discussed. The uncertainty was investigated using valid approaches and the results were discussed. The authors reported that some of the sensitivity analysis results appeared counter-intuitive due to the uncertainties in the effectiveness data. They noted a number of limitations to their analysis, including the exclusion of secondary outcomes, such as the psychological effects on the couples.

**Concluding remarks:**
On the whole, the methods seem to have been appropriate and were relatively well reported. The authors conclusions seem correct.

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