Cost-effectiveness of aromatase inhibitor co-treatment for controlled ovarian stimulation

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
The study examined the use of letrozole (an aromatase inhibitor) and FSH (not defined; presumably follicle-stimulating hormone) for controlled ovarian stimulation in patients undergoing intruterine insemination (IUI). Letrozole was given at a dose of 2.5 to 5 mg/day from cycle day 3 to 7, in conjunction with injections of recombinant FSH (rFSH) starting at 50 to 150 IU/day on day 7 of the stimulation cycle and finishing on the day of hCG administration (hCG not defined; presumably human chorionic gonadotrophin). Patients receiving FSH alone started with 50 to 150 IU/day from day 3 of the menstrual cycle.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who presented for ovarian stimulation with various infertility diagnoses, including ovarian factor, male factor, unexplained and endometriosis related.

Setting
The setting was tertiary care. The economic study was carried out in Toronto, Canada.

Dates to which data relate
The effectiveness and resource use data referred to 2003 to 2005. The price year was not stated, but the price of rFSH referred to 2005.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The resource use data were obtained prospectively from the same patient sample as that used in the effectiveness analysis.

Study sample
The authors did not report any power calculations. Patients presenting for ovarian stimulation were advised about the availability and experimental nature of letrozole, and those who consented were provided with letrozole in combination with FSH. Those who declined letrozole were provided with FSH alone. A total of 432 consecutive
patients were included in the study, with 308 consenting to receive letrozole and 124 opting not to receive letrozole. The authors did not report the exclusion of any patients. The authors reported the infertility diagnoses of the included groups and the period of time over which the study participants had been trying to conceive.

**Study design**
The study was a prospective cohort design that was based in a single study centre. Treatment assignment was solely determined by patient choice. The authors did not report any loss to follow-up. The study was not blinded.

**Analysis of effectiveness**
The analysis of effectiveness appears to have accounted for all patients included in the study (in effect, intention to treat). The primary health outcomes were the number of follicles with a diameter greater than 16 mm, the dose of FSH used per cycle and the clinical pregnancy rates. The authors stated that the two study groups were comparable in terms of their baseline characteristics.

**Effectiveness results**
The FSH alone group had a significantly higher number of mature follicles greater than 16 mm at the day of hCG administration, (p value not reported).

The pregnancy rates were similar between the two groups, with no statistically significant differences. The cumulative pregnancy rate was 27.6% in the letrozole group and 36.3% in the FSH alone group.

The total dose of FSH used was significantly higher in the FSH alone group, (p<0.0001).

**Clinical conclusions**
The authors concluded that the inclusion of letrozole may reduce the dose of FSH required but does not necessarily lead to better results in terms of efficacy.

**Measure of benefits used in the economic analysis**
The number of pregnancies was used as the measure of health benefits in the economic analysis.

**Direct costs**
The study incorporated only the costs of letrozole and FSH. These may be viewed as hospital costs. The cost of FSH was obtained from the Canadian Formulary, while the cost of letrozole was based on an author's assumption. Although discounting was not undertaken, it might not have been relevant since it was unclear if the treatment period was less than 1 year.

**Statistical analysis of costs**
The non-parametric Mann-Whitney U-test was used to analyse continuous variables that were not normally distributed. This is appropriate for cost data. A significance level of 0.05 was used. The costs were expressed in terms of the mean and standard deviation. A power calculation was not performed for the cost data.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
Canadian dollars (CAD).
**Sensitivity analysis**
A sensitivity analysis was not undertaken.

**Estimated benefits used in the economic analysis**
The total number of patients who became pregnant was 85 (28%) in the letrozole group and 45 (36%) in the FSH alone group. The difference was not statistically significant.

**Cost results**
The total costs were CAD 276,200 in the letrozole group and CAD 302,040 in the FSH alone group.

The cost per cycle was significantly higher in the FSH alone group, (p<0.0001).

**Synthesis of costs and benefits**
The study reported the average cost-effectiveness ratio of each study group in terms of the cost per pregnancy.

The average cost-effectiveness ratio was CAD 3,249.42 in the letrozole group and CAD 6712.00 in the FSH alone group.

**Authors’ conclusions**
The combination of letrozole with follicle-stimulating hormone (FSH) could be cost-effective for intrauterine insemination (IUI).

**CRD COMMENTARY - Selection of comparators**
The comparators were selected from a wide range of alternatives and so may not fully represent all relevant alternatives. Letrozole was an experimental drug in the study setting and was compared with current practice in the study centre. You should consider whether the comparison made in this study is relevant in your own setting.

**Validity of estimate of measure of effectiveness**
The measure of effectiveness was based on a prospective cohort study with treatment assignment determined by patient choice. The authors recognised this as a limitation and recommended that the study be viewed as a pilot study for a full randomised controlled trial. The authors did not comment on how representative the study sample was of the study population. The study groups were shown to be comparable at analysis, but the study design used does not control for potential confounding and bias.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. The choice of the number of pregnancies as the measure of benefit would appear reasonable.

**Validity of estimate of costs**
The authors did not specify the perspective of the study. Limited cost data were included in the analysis, thus the analysis cannot be considered a full comparison of costs. The authors did not differentiate between single and multiple pregnancies, or discuss the costs of administration of the treatments. These omissions might have affected the authors’ conclusions. The authors undertook an appropriate statistical comparison of the costs. The price year was not stated, but it can be assumed to have been 2005.
Other issues
The authors compared their findings with those from other studies in the same area. The issue of generalisability was not addressed as the authors felt that a properly designed randomised controlled trial is now required. The authors do not appear to have presented their results selectively. Their conclusions reflected the scope of the analysis and the limitations of the study design.

Implications of the study
The authors recommended that a properly designed randomised controlled trial be undertaken before any firm conclusions are drawn about the effectiveness and cost-effectiveness of adding letrozole to FSH for controlled ovarian stimulation and IUI.

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None stated.

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Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
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