Natural cycles for in-vitro fertilization: cost-effectiveness analysis and factors influencing outcome

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
Natural cycles (intervention) versus stimulated cycles (comparator) for in-vitro fertilization (IVF) in infertile patients who had previously undergone IVF treatment using gonadotrophin stimulation.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Infertile patients with regular menstrual cycles (25-35 days) who had demonstrated fertilization in a previous stimulated IVF cycle without becoming pregnant. Patients were aged less than 38 years and with day 3 follicle stimulating hormone (FSH) less than 15 IU.

Setting
Hospital. The economic study was carried out in Hamilton, Ontario, Canada.

Dates to which data relate
The dates during which the effectiveness data for the natural cycles in the single study were collected were not specified. The data related to live birth per cycle as the benefit measure adopted in the study were obtained from studies published between 1989 and 1995. No dates were specified for the resource use and price data.

Source of effectiveness data
Effectiveness data were derived from a single study (for the intervention) and a review of previously published studies (for the comparator).

Link between effectiveness and cost data
The costing was undertaken separately from the patient sample used for the effectiveness analysis. The costs were based on standard prices at the institution (cost per cycle).

Study sample
Power calculations were not used to determine the sample size. Regarding each cycle as an independent event, a total of 240 natural cycles were included in the study.
Study design
Case series, carried out in a single centre. Duration of follow-up was until live birth.

Analysis of effectiveness
The analysis was based on intention to treat. The primary health outcome used was live birth rate per natural cycle, the oocyte yield using either a single-bore needle or a double-bore needle, percentage of cycles cancelled, comparison between cycles with and without successful retrieval, with and without fertilization, and with and without pregnancy after embryo transfer.

Effectiveness results
Live birth rate per natural cycle was 3.8% (9/240). The oocyte yield in terms of average number of oocytes recovered using a single-bore needle was 0.7 (SD, 0.5) as opposed to 1.0 (0.4) for a double-bore needle, P<0.001. The percentage of cycles cancelled was 35%. Comparison between cycles with and without successful retrieval showed no significant differences. Comparison between cycles with and without fertilization showed no significant differences except in terms of concentration of spermatozoa based on semen testing, according to which the cycles without fertilization had significantly lower concentration both before and after preparation (P<0.05 for both cases). Comparison between cycles with and without pregnancy after embryo transfer showed no significant differences.

Clinical conclusions
The aspiration and flushing technique with the double-bore needle is desirable in the natural cycle to minimize failures at oocyte retrieval, but does not appear to be as crucial a requirement for stimulated cycles. Fertilization rate can be improved by selecting patients for treatment on the basis of semen testing.

Outcomes assessed in the review
The review assessed live birth rate per cycle for the natural and stimulated cycle.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

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
Six studies were included.

Methods of combining primary studies
The live birth rate per cycle attributed to the natural cycle was the result of a crude aggregate. The corresponding rate attributed to the stimulated cycle was obtained from one study published in 1994.
Investigation of differences between primary studies
Not reported.

Results of the review
The live birth rate per cycle related to the natural cycle and reported from different studies ranged from 2.7% to 18.1%. The live birth rate per cycle attributed to the natural cycle was 6.8% (based on a crude aggregate) versus 16.1% for the stimulated cycle (14.3% delivery rate per stimulated cycle plus 1.8% for the additional contribution from one thawed embryo transfer cycle).

Measure of benefits used in the economic analysis
The benefit measure employed in the economic analysis was live birth rate per cycle.

Direct costs
There was no report of quantities or costs components for the intervention. For the intervention, only the total cost per natural cycle was reported. For the comparator, the cost components were the costs of fertility drugs, embryo cryopreservation, and one embryo transfer with thawed embryos. The cost boundary adopted was that of the hospital and the consumer. The cost analysis was based on standard prices for the services provided in the home institution. No dates were reported for the prices used. Adjustments in direct costs for natural cycles were made to account for reductions from incomplete cycles resulting from cancellations or failure at various stages prior to embryo transfer.

Indirect Costs
Not reported.

Currency
Canadian dollars (Can$).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
The live birth rate per cycle attributed to the natural cycle was 6.8% versus 16.1% for the stimulated cycle (14.3% delivery rate per stimulated cycle plus 1.8% for the additional contribution from one thawed embryo transfer cycle).

Cost results
The total cost per natural cycle in the study institution was Can$1,200 versus Can$5,680 for the stimulated cycle.

Synthesis of costs and benefits
The total cost per live birth and the incremental cost per live birth were used as the measure of synthesis of costs and benefits. The total cost per live birth using the intervention was Can$17,647. The total cost for one live birth using the comparator was Can$35,000. The incremental cost per live birth when using the comparator compared to the intervention was estimated to be Can$48,000.

Authors' conclusions
The authors concluded that "So far the results with natural cycles are encouraging and indicate that this approach to infertility treatment should be considered more seriously. Natural cycles are more cost-effective than stimulated cycles.
which incur an incremental cost per live birth of Can$48,000. Natural cycles offer a low-cost alternative that may be more accessible to patients. However, more studies are required to identify the factors that predict a successful outcome, so that the therapy can be offered only to those patients who are likely to derive maximal benefit”.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.

**Validity of estimate of measure of benefit**
The internal validity of benefit results may be weakened by the apparent lack of a systematic and comprehensive review of the literature and quality assessment of the primary studies included in the analysis. No justification was given for the aggregation of a set of studies in the estimation of the measure of benefit (live birth per natural cycle) rather than the result of the authors’ own single study. The study adopted an ad-hoc approach in using the benefit results obtained in the authors’ own study and the results reported in the literature.

**Validity of estimate of costs**
Resource quantities were not reported separately from the costs and insufficient details of the methods of cost estimation were given.

**Other issues**
In view of the lack of a systematic review of the literature and quality assessment of the primary studies included in the analysis, as well as the absence of both sensitivity analysis and statistical analysis of the costs, the results need to be treated with some caution. Given the fact that the authors regarded patients convenience as one of the advantages of the natural cycle, the study would have been more appropriately conducted in the framework of cost-utility analysis rather than cost-effectiveness analysis. The issue of the generalisability of the results to other settings or countries was not fully addressed.

**Source of funding**
None stated

**Bibliographic details**

**PubMedID**
8582968

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Cost-Benefit Analysis; Equipment Design; Female; Fertilization in Vitro /economics; Humans; Menstrual Cycle; Needles; Oocytes; Pregnancy Rate; Specimen Handling /instrumentation; Treatment Outcome

**AccessionNumber**
21995000976

**Date bibliographic record published**
31/07/1999

**Date abstract record published**
31/07/1999