Diagnosis of subtle ovulation disorders in subfertile women with regular menstrual cycles: cost-effective clinical practice?


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
Using one of three strategies in the diagnosis of subtle ovulation disorders (SOD) in women with regular menstrual cycles attending fertility clinics. Three diagnostic strategies were compared: pre-selection strategy in which patients were selected by screening for progesterone serum levels in the luteal phase; maximal strategy involving trying to identify all fertility reducing factors in the patient group, which in the case of diagnosing SOD required extensive cycle monitoring, combining hormone assays with sonographic findings in a so-called 'extensive cycle analysis' (ECA), applied to all patients with a regular menstrual cycle of 24-36 days' duration; and ultrasound-only strategy, in which abnormalities such as a luteinised unruptured follicle cycle, or ovulation of a follicle of a reduced size, would be seen, but hormonal events would remain obscure.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Women with regular menstrual cycles attending a fertility clinic.

Setting
Hospital. The economic study was conducted in The Netherlands.

Dates to which data relate
No dates were specified for the effectiveness and resource use data. Cost data related to 1991. The price year adopted in the study was not explicitly specified.

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

Link between effectiveness and cost data
Costing was performed on the same patient sample as that used in the effectiveness analysis, and was then applied to an hypothetical cohort of 100 patients.

Study sample
Power calculations were not reported as being used to determine the sample size. The sample consisted of 177 women.
with regular menstrual cycles eligible for screening for luteal progesterone and referred to the authors' fertility clinic in a 12-week period. Extensive cycle analyses (ECA) were performed on 50 patients who had a low progesterone cycle (a level of 32 nmol/l not reached in two cycles).

**Study design**
This was a cohort study, carried out in a hospital. The time frame of the study was 12 weeks. Loss to follow-up was not reported.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat. The main health outcome used in the analysis was the presence of a subtle ovulation disorder (SOD).

**Effectiveness results**
The serial progesterone measurements were normal (a level of 32 nmol/l obtained on at least 1 occasion) in 82% of women and were low in 18%. For the 18%, the second progesterone measurements were normal for 5%, too low for 8.5% and not repeated for 4.5% because of severe sperm abnormalities. Of the 8.5%, an extended cycle analysis found 4.25% normal and 4.25% (based on a 50% incidence of SOD in 50 patients) with subtle ovulation disorders.

**Clinical conclusions**
Regardless of how subtle ovulation disorders are diagnosed, treatment strategies with proven efficacy are lacking.

**Methods used to derive estimates of effectiveness**
Estimates of effectiveness were also based on the authors’ assumptions.

**Estimates of effectiveness and key assumptions**
The three strategies were assumed to be able to identify all cases of SOD in the population.

**Measure of benefits used in the economic analysis**
The benefit measure was the diagnosis of subtle ovulation disorder (SOD).

**Direct costs**
Costs were not discounted. Some quantities were reported separately from the costs. Direct medical costs (wages for medical and laboratory staff, expenses for analyser machines and reagents, additional costs for housing, energy and maintenance) and indirect medical costs (personnel for administration and desk tasks, computers, telephone costs, housing and maintenance) were considered. The transportation cost was included as an element of non-medical costs. The perspective adopted in the cost analysis was that of society. Costs were derived from an investigation of real costs of diagnostic procedures in the University Hospital Utrecht, which was performed in 1991 by the Department of Administration and Information.

**Indirect Costs**
Costs were not discounted. Some quantities were reported separately from the costs. Costs to patients from loss of productivity when travelling to and staying at the hospital were considered. Results from the same 1991 study were used, when the non-medical costs were calculated for an average Dutch population. The perspective adopted in the cost analysis was that of society.
Currency
European currency units (ECU): 1 ECU = DFl 2.23 = 0.65.

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
The strategies under investigation detect all cases of SOD in the population.

Cost results
The ultrasound-only strategy was associated with total medical costs of ECU 38,424 (with an extra non-medical cost of ECU 19,300) for 100 cycles. The corresponding values for the maximal diagnosis strategy were ECU 76,987 (with an extra non-medical cost of ECU 31,700) and for the pre-selection strategy were ECU 12,906 (with an extra non-medical cost of ECU 18,000).

Synthesis of costs and benefits
The total medical costs of diagnosing one SOD were calculated as measures of cost-effectiveness:

maximal diagnosis strategy, ECU9,057 (total costs, including non-medical indirect costs ECU 12,787);
ultrasound-only strategy, ECU 4,520 (total costs ECU 6,791);
pre-selection strategy, ECU3,036 (total costs ECU 6,868).

Authors’ conclusions
Although the pre-selection and ultrasound strategies were the least expensive approaches, they still resulted in high costs to establish a diagnosis. In the authors’ opinion, these costs are not in balance with the possible, but still unclear and unproven, advantages.

CRD COMMENTARY - Selection of comparators
The pre-selection strategy, as a most likely low cost strategy, was implicitly regarded as the comparator (measuring progesterone concentrations in the diagnostic work-up of women attending a fertility clinic is common practice). You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
The internal validity of the effectiveness results cannot be guaranteed since they were based on the authors’ assumptions. As the authors acknowledged, some of the SOD cases can be missed by the pre-selection or the ultrasound-only strategies, which inevitably would affect their cost-effectiveness.

Validity of estimate of costs
Some quantities were reported separately from the costs. Adequate details of the methods of cost estimation were given. The price year adopted in the economic analysis was not reported. The authors acknowledged the fact that non-medical costs may differ greatly between countries and patient populations.

Other issues
The authors’ conclusions were justified given the uncertainties surrounding the study results. The issue of
generalisability to other settings or countries was not fully addressed, although appropriate comparisons were made with other studies.

**Implications of the study**

As the real significance of SOD diagnosis for the prognosis of the patient to become pregnant without treatment remains unclear, and as no randomised trials on treatment effectiveness have as yet been undertaken, it is questionable whether this approach is worthwhile.

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