Preimplantation genetic screening in older women: a cost-effectiveness analysis
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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
This study examined the cost-effectiveness of traditional in vitro fertilisation (IVF) with prenatal amniocentesis in comparison with IVF with pre-implantation genetic screening in infertile women with advanced age for pregnancy. The authors concluded that traditional IVF was the most cost-effective strategy. On the whole, the study was based on robust methodology that considered various aspects of uncertainty, but the issues related to the comparability of the clinical sources reduced the validity of the authors' conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the cost-effectiveness of traditional in vitro fertilisation (IVF) with prenatal diagnosis, in comparison with IVF with pre-implantation genetic screening (PGS), in infertile women with advanced age for pregnancy (38 to 40 years or 41 to 42 years).

Interventions
IVF consisted of a total of two fresh cycles, with a possible frozen cycle for each fresh one. Prenatal diagnosis in traditional IVF consisted of amniocentesis, with the option of a subsequent pregnancy termination. The pre-implantation screening was fluorescence in situ hybridisation (FISH), which tested a selection of chromosomes (13, 15, 16, 18, 21, 22, X, and Y) for aneuploidy (too many or too few chromosomes). All women undergoing PGS also underwent amniocentesis.

Location/setting
USA/out-patient infertility clinics.

Methods
Analytical approach:
This economic evaluation was based on a decision analytic model with a time horizon from embryo implantation to delivery. The authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical evidence came from a selection of known, relevant studies. For example, the probability of miscarriage and the pregnancy rate with PGS plus IVF was taken from a published randomised controlled trial (RCT) that included women aged 40.1 years ±2.4. The data for IVF alone and other clinical data (for example, abnormal amniocentesis) came from the 2003 report of the Centers for Disease Control (CDC), supplemental surveillance reports, and the authors' institution (the University of California at San Francisco). The key clinical endpoint was the pregnancy rate.

Monetary benefit and utility valuations:
Not included.

Measure of benefit:
The probability of having a healthy newborn was the summary benefit measure.

Cost data:
The economic analysis included both the direct and indirect costs of IVF, PGS, manual vacuum aspiration,
amniocentesis, and dilatation and evacuation. The indirect costs were the loss of productivity for patients due to treatments. All the economic data (unit costs and resource quantities) were derived from published studies and supplemented by information from a website of a centre that routinely performed PGS. When only charges were available, a 0.48 cost-to-charge ratio was applied. The costs were in US dollars ($) and the price year was 2006.

Analysis of uncertainty:
A series of one- and two-way sensitivity analyses was carried out, varying model inputs arbitrarily to 0.5 and two times their baseline values. Published estimates for non-randomised studies were also used to generate plausible ranges of variations. A Monte Carlo simulation was undertaken by assigning triangular distributions to the model inputs in a hypothetical sample of 18,660 (the total number of IVF cycles performed in the US) women aged 38 to 40 years and in another hypothetical sample of 8,185 women over 40 years, and using specific estimates for each age group from the 2003 CDC reports.

Results
In the cohort of women aged 38 to 40 years, the rate of live births was 37.8% with IVF alone and 21.7% with PGS plus IVF. The total costs per woman were $25,700 with either strategy. The average cost per healthy birth was $68,026 with IVF alone and $118,713 with PGS plus IVF.

The sensitivity analysis showed that IVF alone remained the preferred strategy in most deterministic scenarios and in 96.2% of probabilistic simulations. The most influential model inputs were the pregnancy rates after PGS. If this rate was improved to 36.6% (19.5% in the base case), PGS plus IVF was the preferred strategy.

In the cohort of women aged 41 to 42 years, the rate of live births was 20.7% with IVF alone and 21.7% with PGS plus IVF. The total costs per woman were $25,200 with IVF alone and $25,700 with PGS plus IVF. The average cost per healthy birth was $122,000 with IVF alone and $118,713 with PGS.

The sensitivity analysis showed that these findings were sensitive to a number of inputs and the probability of IVF alone being cost-effective was 51.7%. In most scenarios, the two procedures were similarly cost-effective.

Authors' conclusions
The authors concluded that traditional IVF was the most cost-effective strategy and that there was insufficient evidence to support the use of PGS, as reported in published guidelines.

CRD commentary
Interventions:
The two strategies were appropriately selected and reflected the current (IVF alone) and alternative (with PGS) patterns of care in the authors' setting.

Effectiveness/benefits:
Selected sources of data were used to provide the clinical inputs. A large, validated database was used for most clinical inputs for IVF alone and other model parameters, while the clinical data for PGS were taken from a RCT. A systematic approach to identifying the valid sources of data would have been more appropriate. The use of mixed sources may raise issues regarding the comparability of these data. The authors acknowledged that, while data from the CDC database were highly representative of the US health care system, the RCT was conducted in Europe and some differences might exist. Also the patient populations were not perfectly comparable in terms of their age and other characteristics. The benefit measure was specific to the interventions studied. The rate of live births is a common endpoint of treatments for infertility, but it is not comparable with the benefits of other health care interventions.

Costs:
The analysis of costs included all the relevant items, for the societal viewpoint. The costs were presented as macro-categories and were not broken down into individual items. A clear distinction between the direct and indirect costs was not provided. Only limited details of resource consumption were given. These issues reduce the transparency of the economic analysis.
Analysis and results:
The results of the analysis were appropriately reported. The synthesis of the costs and benefits was based on an average approach, but an incremental analysis would have been useful. A diagram of the decision tree used to simulate the patient management was provided. The issue of uncertainty was extensively investigated and well presented.

Concluding remarks:
On the whole, the study was based on robust methodology that considered various aspects of uncertainty, but the issues related to the comparability of the clinical sources reduced the validity of the authors’ conclusions.

Funding
Not stated.

Bibliographic details
Mersereau JE, Plunkett BA, Cedars MI. Preimplantation genetic screening in older women: a cost-effectiveness analysis. Fertility and Sterility 2008; 90(3): 592-598

PubMedID
18001724

DOI
10.1016/j.fertnstert.2007.07.1307

Original Paper URL
http://www.fertstert.org/article/S0015-0282(07)02942-1/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Age Distribution; Cost-Benefit Analysis; Female; Genetic Counseling /economics /statistics & numerical data; Genetic Testing /economics /statistics & numerical data; Humans; Infertility, Female /economics /epidemiology /therapy; Live Birth /economics /epidemiology; Pregnancy; Preimplantation Diagnosis /economics /statistics & numerical data; Treatment Outcome; United States /epidemiology; Women's Health /economics

AccessionNumber
22008101922

Date bibliographic record published
02/03/2009

Date abstract record published
27/01/2010