Combined first-trimester versus second-trimester serum screening for Down syndrome: a cost analysis


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
Two strategies for screening for foetal Down syndrome (DS) were examined. Combined first-trimester screening (nuchal translucency and biochemistry for pregnancy-associated plasma protein A and free beta-human chorionic gonadotropin) was compared with second-trimester maternal serum triple screening.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 10,000 pregnant women.

Setting
The setting appears to have been secondary care. The study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1992 and 2002. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies and authors' assumptions.

Outcomes assessed in the review
The outcomes assessed from the literature were:

- the proportion of women aged 35 years and older (with respect to maternal age);
- the patient's a priori risk for foetal DS;
- the first- and second-trimester foetal DS loss rate before term; and
- the rates of sensitivity and screen positive (number of patients who screened positive divided by the number of patients screened).
Study designs and other criteria for inclusion in the review
A review of the literature does not appear to have been conducted. The design of the primary studies was unclear, but
the authors stated that some were prospective trials.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Ten primary studies were considered.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not carried out.

Results of the review
The proportion of women aged 35 years and older was 9.6%.

The patient's a priori risk for foetal DS was based on both maternal age and gestational age.

The first- and second-trimester foetal DS loss rates before term were estimated to be 30% (first-trimester) and 21%
(second-trimester), respectively.

For first-trimester screening, the sensitivity was 91% and the rate of screen positives was 5%. For second-trimester
screening, the sensitivity was 70% and the rate of screen positives was 7.5%. However, the sensitivity of second-
trimester screening was 57% in women without ultrasound dating. Also, in the second-trimester screening of women
who had never undergone ultrasound screening, the initial and final screen positive rates were 14% (initial) and 9.9%
(final), respectively.

These revised figures for women receiving second-trimester screening without prior ultrasound were used in a
sensitivity analysis of ultrasound usage rates (0% and 50%).

Methods used to derive estimates of effectiveness
The authors made some assumptions, owing to the lack of some effectiveness data.

Estimates of effectiveness and key assumptions
A singleton, viable intrauterine pregnancy was assumed at the time of screening for all 10,000 women considered in the
study. All patients underwent routine first-trimester ultrasound screening to confirm foetal number, foetal viability, and
gestational age. All patients who underwent second-trimester screening would have undergone a limited first-trimester
ultrasound screening. It was also assumed that all DS foetuses that were identified would be terminated.

**Measure of benefits used in the economic analysis**

Several output measures were calculated to assess the benefits of the two screening strategies:

- the expected number of DS cases in the whole cohort,
- the number of patients with positive screen results,
- the rate of DS cases detected,
- the yield of screening,
- the number of DS cases missed, and
- the number of DS cases live-born.

Best and worst cases were considered for second-trimester screening.

**Direct costs**

Discounting was not relevant since the costs were incurred during a short time. The unit costs were presented separately from the quantities of resources used for some items. The health services included in the economic evaluation were screening tests and live-born DS costs. The screening tests covered ultrasound, serum screening and amniocentesis/chorionic villi sampling, but not tests for other foetal chromosomal and/or structural anomalies. Live-born DS costs included all medical and non-medical services related to DS management. The cost/resource boundary of the health care payer was adopted in the analysis. Resource use data were estimated from the literature. The costs were derived from insurance reimbursement rates and published studies. The price year was 2000.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The indirect costs were not considered.

**Currency**

US dollars ($).

**Sensitivity analysis**

A univariate sensitivity analysis was conducted. This assessed the impact of variations in ultrasound rate and other base-case assumptions on the estimated costs and efficacy rates. No justification for the ranges used was provided.

**Estimated benefits used in the economic analysis**

The expected number of DS cases in the whole cohort was 21 at the time of first-trimester screening.

The number of patients with positive screen results was 500 for first-trimester screening and 500 with best-case second-trimester screening (750 with worst-case second-trimester screening).

The rate of DS cases detected was 72.9% for first-trimester screening and 62.4% with best-case second-trimester screening (55.8% with worst-case second-trimester screening).
The yield of screening was 1/26 for first-trimester screening and 1/31 with best-case second-trimester screening (1/57 with worst-case second-trimester screening).

The number of DS cases missed was 5.7 for first-trimester screening and 7.9 with best-case second-trimester screening (8.4 with worst-case second-trimester screening).

The number of DS cases live-born was 4 for first-trimester screening and 5.5 with best-case second-trimester screening (6.6 with worst-case second-trimester screening). However, it should be noted that the figures presented in the table are different from the ones described in the text. Specifically, what in the table is called a best-case scenario for second-trimester screening, is described in the text as a worst-case scenario for first-trimester screening.

Cost results
Under the base-case assumptions, the total costs of the sample of women would be $4,500,000 for first-trimester screening and $5,250,000 with best-case second-trimester screening ($6,350,000 with worst-case second-trimester screening). The lower cost was mainly attributed to the fewer amniocenteses and the higher screening rate for first-trimester screening.

Overall, the cost-savings associated with first-trimester screening over second-trimester screening were 17.3% under the worst-case scenario and 29.1% under the best-case scenario.

With less usage of first-trimester ultrasound scans, screening and the total costs of second-trimester screening were reduced, but there was an increase in live-born DS costs.

These results were, in general, confirmed in the other sensitivity analyses. The overall costs were always lower with first-trimester screening, although the cost-savings could be reduced when using assumptions that favour second-trimester screening.

Synthesis of costs and benefits
A synthesis of the costs and benefits was not conducted because the analysis focused on the costs of the screening strategies. In effect, a cost-consequences analysis appears to have been carried out.

Authors' conclusions
Combined first-trimester screening for foetal Down syndrome was more effective and less costly than traditional second-trimester screening.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators. Second-trimester screening was considered the standard approach in the USA, while first-trimester screening strategies were advocated in the UK and other European countries. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was obtained mainly from published studies. However, a review of the literature does not appear to have been undertaken. Limited information on the primary studies was provided and the authors stated that some studies were prospective trials. Other details were not provided. Thus, it is difficult to assess the validity of the primary sources. Further, the methods used to extract and combine the primary estimates were not described. Other data were based on authors' assumptions, some of which were investigated in the sensitivity analysis.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted.
Validity of estimate of costs
The authors stated explicitly which perspective was adopted in the cost analysis. As such, it appears that all the relevant categories of costs have been included in the analysis. The unit costs were presented separately from the quantities of resources used for some cost items. The costs considered in the category “live-born DS costs” were not broken down. Limited information on the source of the data was provided and most evidence came from published studies. The price year was reported, which makes reflation exercises in other settings easy. Some assumptions were varied in the sensitivity analysis, to assess the robustness of the estimated costs, but no economic data were varied. Overall, the costs were treated deterministically.

Other issues
The authors stated that their findings were consistent with those of another recently published economic evaluation of DS screening. The issue of the generalisability of the study results to other settings was not addressed explicitly and few sensitivity analyses were conducted. In general, local estimates were used, which limited the external validity of the analysis. The authors noted that their findings depended on the assumptions made. The lack of reliable data cast some doubts on the validity of their conclusions.

Implications of the study
The study results suggested that first-trimester screening for the identification of foetal DS should be made available to pregnant women in the USA because of the advantages over traditional second-trimester screening.

Source of funding
None stated.

Bibliographic details

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Other publications of related interest


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