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
Four noninvasive screening tests for the identification of Down syndrome (DS) were examined:

- second-trimester expanded alpha-fetoprotein (XAFP) screen;
- first-trimester ultrasound screening test of nuchal translucency (NT);
- first-trimester serum screening (SS) test using pregnancy-associated plasma protein A (PAPP-A); and
- combined first-trimester NT plus SS (NT+SS).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis.

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

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1988 and 2002. Resource use and the costs were estimated from studies published between 1995 and 2000. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies.

Modelling
A decision tree model was constructed to assess the clinical and economic outcomes associated with the four alternative screening strategies in a hypothetical cohort of 4 million births per year. The structure of the tree was reported.

Outcomes assessed in the review
The outcomes assessed were the sensitivities of the four screening strategies and the following probability values:

- risk of DS in the first, second and third trimesters;
- loss from amniocentesis;
- loss from chorionic villus sampling;
- the proportion of women accepting an invasive procedure; and
- the proportions of women seeking prenatal care in the first, second, or third trimester.

Utility values associated with procedural-related loss and a DS child were also estimated from a study that used the standard gamble approach.

**Study designs and other criteria for inclusion in the review**

No inclusion or exclusion criteria for the primary studies were reported.

**Sources searched to identify primary studies**

The English language literature was searched using the terms "NT", "aneuploidy", "serum screen", "Down syndrome", "biochemical screen", "obstetric ultrasound", "MSAFP", "PAPP-A", "free beta", "amniocentesis" and "chorionic villus sampling".

**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**

Twenty-three primary studies provided the evidence.

**Methods of combining primary studies**

The sensitivities associated with the NT and SS approaches were obtained by calculating a weighted average of the rates reported in the primary studies (8 for NT and 5 for SS). The number of patients included in each of these primary studies was reported. The methods used to combine the other estimates were not reported.

**Investigation of differences between primary studies**

Not stated.

**Results of the review**

The sensitivity was 0.70 with NT (false-positive rate of 0.043), 0.60 with first-trimester SS (false-positive rate of 0.05), 0.80 with NT+SS, and 0.60 with second-trimester SS (0.50 for women of 35 years and 0.89 for women older than 35 years).

The risk of DS was 0.002 in the first trimester, 0.0014 in the second trimester, and 0.001 in the third trimester.

The rate of loss from amniocentesis was 0.005.
The rate of loss from chorionic villus sampling was 0.008.

The proportion of women accepting an invasive procedure was 0.70.

The proportions of women seeking prenatal care was 75% in the first trimester, 18% in the second trimester, and 7% in the third trimester.

The utility value associated with a procedural-related loss was 0.92 and that for a DS child was 0.81.

**Measure of benefits used in the economic analysis**
The summary benefits measures were the number of DS cases identified for the cost-effectiveness analysis, the quality-adjusted life-years (QALY) for the cost-utility analysis, and the economic value of a DS case for the cost-benefit analysis. Life expectancy used to calculate the QALYs was discounted at an annual rate of 3%. All measures were obtained from the decision model. The ratio of procedural-related loss by DS cases was also reported.

**Direct costs**
An annual discount rate of 3% was used as the costs were incurred during a long timeframe. The unit costs were presented but only in macro-categories, while the quantities of resources used were not reported. A breakdown of the cost items was not provided. The health services included in the economic evaluation were diagnostic tests, genetic counsellor consultation, invasive tests and pregnancy termination. The cost/resource boundary of society was adopted. The cost of DS was also considered, but its source and items were unclear. The costs and quantities were derived mainly from published studies. All the costs were presented in 2002 values using the Consumer Price Index.

**Statistical analysis of costs**
The costs appear to have been treated deterministically in the base-case analysis.

**Indirect Costs**
It was unclear whether the indirect costs were considered in the analysis, as the cost items considered in the category "cost of Down syndrome" were not reported.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate sensitivity analyses were conducted to assess the robustness of the results of the analysis. Some key baseline model inputs were varied, using published and assumed ranges of values. Threshold analyses were also conducted when the ranges of outputs crossed above or below different thresholds of cost-effectiveness.

**Estimated benefits used in the economic analysis**
In the cost-effectiveness analysis, the estimated number of DS cases identified was 3,833 with the NT+SS approach, 3,413 with NT, 2,993 with SS, and 2,446 with XAFP.

The ratio of procedural-related loss by DS cases was 0.22 with the NT+SS approach, 0.33 with NT, and 0.58 with SS.

In the cost-benefit analysis, the economic value of a DS case was $577,248.

In the cost-utility analysis, the number of QALYs gained was not reported.
Cost results
For a hypothetical cohort of 4 millions births per year, the total costs (in millions) were $1,532 with the NT+SS approach, $1,183 with NT, $1,176 with SS, and $1,088 with XAFP.

Synthesis of costs and benefits
In the cost-effectiveness analysis, the incremental cost per additional DS case identified in comparison with baseline XAFP was $319,934 with the NT+SS approach, $98,381 with NT, and $160,266 with SS. All these values were well below the hypothetical threshold of $577,248, which was the estimated cost of a DS case to society.

In the cost-benefit analysis, the benefit-to-cost-ratio was 1.57 with the NT+SS strategy, 5.21 with NT, and 4.85 with SS. Therefore, the costs of all first-trimester screening strategies were less than the savings of avoiding a DS case.

The incremental cost per QALY gained over baseline XAFP was $128,338 with NT and $100,437 with the NT+SS approach.

SS dominated XAFP, which was both more costly and less effective.

The results of the sensitivity analysis showed that when the sensitivity of NT varied from 0.5 to 0.9, the cost per DS foetus identified ranged from $1,494,450 to $1,586 for NT screening and from $610,680 to $195,976 for the combined strategy when compared with baseline XAFP.

When the sensitivity of SS was varied from 0.4 to 0.8, the cost per DS case identified ranged from $429,642 to $219,570 for the combined strategy.

The threshold analysis showed that SS was dominated by XAFP at a sensitivity of less than 0.47 and, in turn, dominated XAFP when its sensitivity was greater than 0.78.

Plausible variations in other model inputs did not vary substantially the base-case results.

Authors' conclusions
The nuchal transparency screen (NT) and first-trimester serum screen (SS), used either alone or in combination, could be a cost-effective strategy for the diagnosis of Down syndrome (DS) in pregnant women.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Baseline XAFP was appropriately selected as the standard approach for the diagnosis of DS cases in pregnant women. All the other first-trimester strategies were then selected to cover all possible noninvasive diagnostic strategies. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from published studies. A review of the literature was undertaken for some inputs, which were calculated from the weighted average of primary estimated obtained from the literature. Other inputs came from studies that were identified selectively. However, no information on the design of the primary studies was provided. Thus, the validity of the sources was unclear. To deal with the issue of uncertainty, some key model inputs were varied in the sensitivity analysis. The authors noted that some inputs were derived from small studies. Similarly, the utility weights used in the analysis were derived from a sample of 534 women and could not be representative of larger samples. It was also noted that the disutility associated with a false-positive result was not modelled.

Validity of estimate of measure of benefit
In each type of economic study the most appropriate benefit measure appears to have been used (namely, QALYs, DS cases detected, and economic value of a DS case). Discounting was applied when the future benefits were considered.
The source of the economic benefit of a DS case was unclear and it was not stated how it was calculated.

Validity of estimate of costs
The authors stated that a societal perspective was adopted, but a detailed breakdown of the costs was not provided. The economic data were estimated from the literature and no information on the methods used was provided. The resource use data were not reported. The overall cost calculation was not transparent. The costs were treated deterministically and the cost estimates were not varied in the sensitivity analysis. The role of the cost of DS case in the whole analysis was not entirely clear, as it was used as the summary benefit measure in the cost-benefit analysis. Discounting was mentioned, but it was not stated to which categories of costs it was applied. The authors noted that if universal first-trimester screening strategies were performed in the USA, the start-up costs (which were not considered in the study) would be substantial.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address explicitly the issue of the generalisability of the study results to other settings. Overall, few sensitivity analyses were conducted. The authors noted that some costs, such as start-up expenses, were not considered and, similarly, some benefits related to improved gestational dating were not included in the analysis.

Implications of the study
The study results supported the widespread use of first-trimester screening for DS. However, the authors noted that it would take several years to create the capacity able to perform universal first-trimester screening for DS in the USA.

Source of funding
Supported in part by the National Institute of Child Health and Human Development (grant number HD01262) and by the Agency for Healthcare Research and Quality (grant number T32 H500086).

Bibliographic details

PubMedID
12439512

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Cost-Benefit Analysis; Down Syndrome /diagnosis /ultrasonography; Female; Fetal Blood /metabolism; Humans; Mass Screening /economics /methods; Neck /ultrasonography; Pregnancy; Pregnancy Trimester, First; Pregnancy Trimester, Second; Ultrasonography, Prenatal /economics; alpha-Fetoproteins /analysis
AccessionNumber
22003000035

Date bibliographic record published
28/02/2005

Date abstract record published
28/02/2005