The cost effectiveness of prenatal ultrasound screening for trisomy 21  
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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.

**Health technology**
Four prenatal screening strategies for the detection of trisomy 21 were examined.

Strategy 1 was serum screening in the second trimester, followed by amniocentesis for those with a positive test.

Strategy 2 was nuchal translucency screening (NTS) in the first trimester, followed by chorionic villus sampling (CVS) for those with a positive test.

Strategy 3 was NTS and maternal serum screening in the first trimester, followed by CVS for those with a positive test.

Strategy 4 was NTS and maternal serum screening for high-risk women (age-related) in the first trimester, with maternal serum screening in the second trimester for other women.

**Type of intervention**
Screening.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
The study population comprised pregnant women.

**Setting**
The setting was secondary care. The economic study was carried out in Australia.

**Dates to which data relate**
The effectiveness and some resource use data came from studies published between 1997 and 2002. The price year was 2001.

**Source of effectiveness data**
The effectiveness evidence was derived from a synthesis of completed studies and author’s assumptions.

**Modelling**
A decision model, based on published work, was used to compare the costs and benefits of the alternative screening strategies in a cohort of pregnant women in Australia. Details of the models and its assumptions had already been reported (Medical Service Advisory Committee, see Other Publications of Related Interest). The model started with a cohort of births and calculated the number of affected and unaffected births screened in a given trimester. The model took the spontaneous foetal loss rate into consideration. According to the model, CVS or amniocentesis was offered to
women who had a risk in excess of 1:250 in the second trimester and 1:300 in the first trimester, either determined through screening or because of the risk associated with maternal age.

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

- the number of births in Australia in 2001;
- the detection rate for triple-marker serum screening in the second trimester (alpha-fetoprotein, total human chorionic gonadotropin, inhibin A);
- the detection rate with NTS;
- the false-positive rate of NTS;
- the proportion of women accepting or declining amniocentesis; and
- the foetal loss associated with amniocentesis.

**Study designs and other criteria for inclusion in the review**
It appears that a systematic review of the literature has not been undertaken to identify relevant studies. Most of the evidence came from a published study (Medical Services Advisory Committee, see Other Publications of Related Interest), which included information on the model and a systematic review. Details of the design of other sources of evidence were not provided.

**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**
Approximately four primary studies provided the evidence.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The number of births in Australia in 2001 was approximately 260,000.

The detection rate for triple-marker serum screening in the second trimester was no more than 64%, with a 5% false-
positive rate.

The rate of foetal loss associated with amniocentesis was 0.9% (95% confidence interval, CI: 0.6 - 1.2).

The detection rate with NTS was 77% (95% CI: 72 - 82).

The false-positive rate of NTS was 5%.

The proportion of women accepting amniocentesis was 85% and the proportion declining was 15%.

Methods used to derive estimates of effectiveness
The author made some assumptions that were used in the decision model.

Estimates of effectiveness and key assumptions
The proportion of women accepting CVS was 85% and the proportion declining was 15%. The rate of termination was 90%. The rate of spontaneous miscarriage was 40%. The rate of foetal loss between the time when a second trimester serum screen would be done and term was 23%. A combination of NTS, double-serum markers and age increased the detection rate to 86.4%.

Measure of benefits used in the economic analysis
The summary benefit measures used were the numbers of cases detected and live trisomy 21 births. Both measures were derived using a modelling approach. No discounting was applied.

Direct costs
Discounting was not relevant since the costs were incurred during a short timeframe. The unit costs were presented separately from the quantities of resources used for most items. The health services included in the economic evaluation were screening tests, antenatal diagnoses, termination and miscarriages, and counselling at each stage. The cost/resource boundary of the third-party payer appears to have been adopted. The costs were estimated on the basis of reimbursement fees. The resource use data were based on current screening and diagnostic patterns, which were mostly derived from the literature. The price year was 2001.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
Australian dollars (Aus$).

Sensitivity analysis
A sensitivity analysis was carried out to examine the impact of variations in model inputs on the estimated cost-effectiveness ratios. The author stated that each parameter was varied individually and in combination. The ranges of values used in the sensitivity analysis and their sources were not reported clearly, although some alternative values came from the literature. A probabilistic sensitivity analysis was carried out using a Monte Carlo simulation to examine the impact of changes in the detection rate. The effect of using different rates of substitution of ultrasound scan with NTS was explored.
**Estimated benefits used in the economic analysis**
The benefits were estimated for the cohort of 260,000 pregnancies in Australia in 2001. Strategies 3 and 4 could have been grouped, although it was not clear.

The number of cases detected was 0 with no screening, 346 with serum screening (second trimester), 534 with NTS, and 599 with NTS plus serum testing (first trimester).

The number of live trisomy 21 births was 416 with no screening, 212 with serum screening (second trimester), 171 with NTS, and 141 with NTS plus serum testing (first trimester).

**Cost results**
The costs were estimated for the cohort of 260,000 pregnancies in Australia in 2001.

The expected costs of screening (in million) were Aus$21.3 with serum screening (second trimester), Aus$33.8 with NTS, and Aus$48.1 with NTS plus serum testing (first trimester).

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative screening strategies.

The average cost per case detected was Aus$61,700 with serum screening (second trimester), Aus$63,300 with NTS, and Aus$80,200 with NTS plus serum screening (first trimester).

The average cost per live trisomy 21 birth avoided was Aus$117,100 with serum screening (second trimester), Aus$201,700 with NTS, and Aus$345,500 with NTS plus serum screening (first trimester).

The incremental cost per extra case detected was Aus$61,700 with serum screening (second trimester) over no screening, Aus$66,300 with NTS over serum screening (second trimester), Aus$218,600 with NTS plus serum screening (first trimester) over NTS, and Aus$105,500 with NTS plus serum screening (first trimester) over serum screening (second trimester).

The incremental cost per extra live trisomy 21 birth avoided was Aus$104,800 with serum screening (second trimester) over no screening, Aus$301,400 with NTS over serum screening (second trimester), Aus$476,200 with NTS plus serum screening (first trimester) over NTS, and Aus$374,800 with NTS plus serum screening (first trimester) over serum screening (second trimester).

The sensitivity analysis showed that the results were sensitive only to the extent of substitution for dating ultrasound and the assumed detection rate for NTS.

With 100% substitution, the incremental cost per extra case detected and trisomy 21 birth averted for the combination of NTS and serum screening in the first trimester, compared with serum screening in the second trimester, was less than 50% of the primary results.

The probabilistic sensitivity analysis showed that variation in the detection rates led to an incremental cost per extra case detected for the NTS and serum screening combination, compared with second trimester serum screening alone, of Aus$121,554 (95% CI: 104,109 - 141,664).

**Authors' conclusions**
The incorporation of nuchal translucency thickness (NTS) into existing services provided in early pregnancy (thus reducing the additional cost of NTS) would make this screening option for the detection of trisomy 21 more attractive from the perspective of the service payer.
CRD COMMENTARY - Selection of comparators
The selection of the comparators was appropriate as all the relevant screening strategies were considered in the analysis. However, strategies 3 and 4 could have been grouped in a single category (NTS plus serum screening in the first trimester), because there was no distinction between the two possible screening options in the results of the analysis. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from published evidence, as well as from author's assumptions when published data were not available or were unclear. Most of the clinical data used in the model were derived from a published report (MSAC 2002), where some key details of the analysis were reported. In fact, the information on the other sources of estimates was limited. The approach used to extract and then combine the primary estimates was not described. Likewise, it was unclear whether the primary studies were comparable. The issue of uncertainty in some estimates was addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
The author discussed the choice of the benefit measures. They highlighted the difficulties in using a broader definition of benefits, which could have included reassurance, emotional and psychological effects associated with the prevention of the birth of a disabled child. However, the use of cases detected and live trisomy 21 births reduces the possibility of comparing them with the benefits of other health care interventions.

Validity of estimate of costs
The cost analysis included all categories of costs relevant from the perspective of the payer. However, the unit costs were presented separately from the quantities of resources used only for some items. The source of the data was reported and only reimbursement rates were considered. The resource use data were derived from typical screening patterns. The costs were specific to the study setting. It was stated that sensitivity analyses had been carried out on all of the inputs, but the author did not discuss the impact of variations of cost estimated on the final results of the analysis. Only changes in the substitution rate of NTS were reported. The price year was reported, which enhances the possibility of reflating the results of the analysis.

Other issues
The author compared the findings with those from a study published in the UK, stating that the differences observed between the studies were explained by the different cost assumptions. Thus, the author highlighted the need for caution when extrapolating the results of the study to other settings, owing to differences in the reimbursement rates, nature of medical practice, and medical incomes. The study referred to pregnant women undergoing screening for the detection of trisomy 21 and this was reflected in the author's conclusions.

Implications of the study
The author stressed that even if the additional unit costs of NTS were high, some decision-makers may want to pay for the benefits of this more accurate screening option.

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This study is part of a review commissioned by the Commonwealth Department of Health and Ageing on behalf of the Medical Services Advisory Committee.

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Other publications of related interest


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