Cost-benefit analysis of targeted ultrasonography for prenatal detection of spina bifida in patients with an elevated concentration of second-trimester maternal serum alpha-fetoprotein

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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
The health intervention examined was targeted ultrasonography (TU) for the prenatal detection of spina bifida (SB) in pregnant women with an elevated concentration of maternal serum alpha-fetoprotein in the second trimester (high-risk patients).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a group of 100 hypothetical pregnant women with elevated concentration of maternal serum alpha-fetoprotein (greater than or equal to 2 or greater than or equal to 2.5 multiples of the median) in the second trimester.

Setting
The setting of the study was not reported. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1987 and 1997. No dates for resource use were reported. The price year was 1998.

Source of effectiveness data
The effectiveness evidence came from a review of published studies and from the authors' assumptions.

Modelling
An analytic model was used to calculate the cost-effectiveness of the two diagnostic strategies. The authors reported the formula and labelled it as the cost-benefit formula.

Outcomes assessed in the review
The primary health outcomes assessed in the review were the sensitivity and false-positive rates of TU. The number of pregnancies that would be screened by maternal serum alpha-fetoprotein in the second trimester in the USA, and the frequency of pregnant women with elevated concentration of maternal serum alpha-fetoprotein in the second trimester,
were also estimated from published studies.

**Study designs and other criteria for inclusion in the review**
Only English-language studies using "cranial" signs for the detection of SB in the second trimester and reporting detection rate (which could alternatively have been calculated from the presented data) were included.

**Sources searched to identify primary studies**
MEDLINE was searched for primary studies.

**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**
Seventeen primary studies were included in the review. A further two primary studies were also used for the remaining outcome measures referring to US data.

**Methods of combining primary studies**
The primary studies were combined by calculating the average value.

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

**Results of the review**
The sensitivity values ranged from 92 to 100% (average 97.3%).

The false-positive rates of TU ranged from 0 to 3% (average 0.5%).

The number of pregnancies that would be screened by maternal serum alpha-fetoprotein in the second trimester, in the USA, was about 2.5 million.

The frequency of pregnant women with elevated concentration of maternal serum alpha-fetoprotein in the second trimester was approximately 3%.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to derive the effectiveness estimates.

**Estimates of effectiveness and key assumptions**
It was assumed that the prevalence of SB was 1%, that AMNIO would virtually detect all cases of SB, and that the abortion rates for prenatally diagnosed cases with SB ranged from 50 to 100%.

**Measure of benefits used in the economic analysis**
The main benefit measure used in the economic analysis was the detection rate, which was evaluated in the effectiveness study. The analytical model used to calculate the cost-effectiveness of the two diagnostic strategies permitted the number of foetal losses, and the number of foetuses that may have SB in the USA, to be assessed.

**Direct costs**
The economic evaluation took into account the costs of TU, AMNIO and the lifetime care of all live infants with SB. The unit costs were reported separately from the quantities of resources used. The cost/resource boundary adopted in the study was that of society. Discounting was not conducted, but it could have been relevant since the lifetime costs of caring for infants with SB were included. The diagnostic costs were estimated using 'Medrisk' tables, which, in turn, were based on nationwide reimbursement data derived from health insurance companies, health maintenance organisations and other managed care organisations. The direct cost components of lifetime care of neonates born with SB was based on a publication on birth defects and was adjusted for inflation (2.5% per year). Resource use was likely to have been estimated on the basis of the authors' assumptions. The price year was 1998.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were included in the economic evaluation because a societal perspective was adopted. The lifetime productivity losses due to early death or disability were evaluated from a published study on birth defects, as for the direct costs. Details on how the costs and resource consumption were calculated were not reported. The price year was 1998.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted to assess the robustness of the study results to variations in the prevalence of SB. The range used (1:50 to 1:200) was derived from published studies. The analytical model was manipulated in a subject-specific sensitivity analysis to calculate the minimum accuracy of TU for TU being cheaper than AMNIO. Risk factors were assessed in white patients, black patients and diabetic patients, accounting for a risk of SB ranging from 1:380 to 1:10.

**Estimated benefits used in the economic analysis**
There were 300 foetal losses with universal AMNIO and 32 with TU. However, there would be 75 undetected cases of SB with TU at a worst-case assumed sensitivity value of 90%. According to the calculation, about 75,000 foetuses (of a total of 4 million annual births in the USA) may have SB.

**Cost results**
The total costs were $90 - 214 million with AMNIO and $54 - 165 million with TU, depending on the abortion rate (range: 50 - 100%).

**Synthesis of costs and benefits**
An average cost-effectiveness analysis was conducted to combine the costs and benefits of the two diagnostic strategies. However, the data on the costs and effectiveness were mixed in the analytical model, in order to reach the three objectives of the study.
Objective 1 - the (cost-benefit) analysis showed that the minimum sensitivity value of TU at a baseline prevalence rate of 1%, such that the costs of TU were less than or equal to the costs of performing universal AMNIO in high-risk patients, was 76%. It ranged from 88% at a prevalence rate of 1:50 to 51% at a prevalence rate of 1:200.

Objective 2 - the average value of TU sensitivity derived from the literature was 97.3%. This was well above the minimum required for TU to be cheaper than universal AMNIO. Consequently, with worst-case assumptions (sensitivity of 90% and a false-positive rate of 10%), the cost per diagnosed SB case was $120,000 with universal AMNIO and $44,000 with TU.

Objective 3 - the authors stated that TU would lead to a saving of $36 - 49 million in comparison with AMNIO, depending on the abortion rate (range: 50 - 100%).

The subject-specific sensitivity analysis showed that the required sensitivity values ranged from 18.3 to 96.8% for white women, from 3 to 93.3% for black women, and from 26 to 97.7% for diabetic women.

Authors' conclusions
Targeted ultrasonography (TU) was more cost-effective than universal amniocentesis (AMNIO) from a societal perspective. The observed accuracy of TU was far above the minimum accuracy rate required for TU to be cheaper than AMNIO, except among pregnant women with both diabetes and maternal serum alpha-fetoprotein elevations of at least 4 multiples of median. This conclusion was robust to variations in the spina bifida (SB) prevalence rate. However, the analysis showed that TU resulted in 75 undetected cases of SB in the cohort of 4 million newborns in the USA.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Universal AMNIO was selected since it represented the standard diagnostic approach for high-risk pregnant patients in the study setting. You should decide whether it is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from a formal review of the literature. The inclusion criteria and the database searched were reported. The primary study data were combined by calculating the average value, but it was unclear whether the authors considered the differences across the primary studies when estimating the effectiveness. Details of the primary studies, and their design, were not reported. The authors also made some assumptions to calculate the cost-effectiveness ratios, and some of these assumptions were investigated in the sensitivity analyses. The overall validity of the effectiveness results should be high.

Validity of estimate of measure of benefit
The number of cases of SB detected with the two diagnostic strategies was used as the benefit measure. This is fairly specific to the diagnostic intervention evaluated and is hardly comparable with the benefits of other technologies. However, the authors commented that reliable data on quality of life for SB were not available.

Validity of estimate of costs
The perspective adopted in the study was explicitly reported. It appears that all the relevant categories of costs have been included in the analysis. The indirect costs were appropriately evaluated. The unit costs of the diagnostic strategies were reported, as well as the source of the data. The price year was given, thus facilitating reflation exercises in other settings. However, the lifetime costs of caring for infants with SB were derived from a published study and a total figure was reported without any detail of the cost calculation. Discounting would have been relevant, but was not mentioned. It was unclear whether discounting was carried out in the previous study. The costs were treated deterministically and no sensitivity analyses were conducted on the costs or quantities. Consequently, the cost estimates were specific to the study setting. The authors stated that their analysis did not consider the costs of genetic counselling and abortion, which would have occurred in either strategy.
Other issues
The authors did not compare the estimated cost-effectiveness of the diagnostic strategies with that obtained in other studies. In terms of the generalisability of the study results to other settings, the authors stated that their conclusion should be valid in other contexts because the literature review showed that the accuracy of TU does not vary substantially. Further, several sensitivity analyses were conducted to take into consideration the uncertainty around the effectiveness estimates and assumptions used in the analysis. The study referred to pregnant women with elevated concentration of maternal serum alpha-fetoprotein in the second trimester, and this was reflected in the conclusions of the analysis. The authors discussed the arguments favouring and critiquing the use of TU in place of AMNIO. The study was described as a cost-benefit analysis by the authors, which does not conform to the definitions of cost-benefit analysis in the NHS EED, but it appears that a difference in the total costs of the two diagnostic strategies was actually calculated.

Implications of the study
The study suggests that routine TU may be recommended, instead of universal AMNIO, as first option for the detection of SB in pregnant women with an elevated concentration of maternal serum alpha-fetoprotein in the second trimester, in the USA.

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