Children with suspected craniosynostosis: a cost-effectiveness analysis of diagnostic strategies
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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 technologies studied were radiography (followed by three-dimensional computed tomography (3D CT) if abnormalities were found), and 3D CT, in the diagnosis of children with suspected craniosynostosis.

Type of intervention
Diagnosis.

Economic study type
Cost-utility analysis.

Study population
The study population comprised children with suspected craniosynostosis.

Setting
The setting was hospital. The economic study was performed in the USA.

Dates to which data relate
The data collected for the effectiveness analysis were derived from previous studies and medical literature published between 1960 and 2000. The date for resource quantities was not stated. The date to which the cost of all imaging studies related was 1999. The date to which other costs were estimated was not stated.

Source of effectiveness data
The effectiveness data were based on a review of the literature.

Modelling
A decision analytic Markov model was used to derive the outcomes and costs of the three strategies considered. Three risk groups of children were considered:

- a low-risk group, i.e. completely healthy children;
- an intermediate-risk group, i.e. healthy children with head deformity; and
- a high-risk group, i.e. children with syndromic craniofacial disorders (Crouzon's, Appert's, or Pfeiffer's syndrome).

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

- pre-test probability of synostosis (i.e. prevalence) for the three risk groups considered in the analysis (low, intermediate and high-risk groups);
- the sensitivity and specificity of radiographs in studies of good quality;
- the sensitivity and specificity of radiographs in studies of poor quality;
- the sensitivity and specificity of 3D CT in good quality studies with experienced reviewers;
- the sensitivity and specificity of 3D CT in good quality studies with less experienced reviewers;
- the sensitivity and specificity of CT in poor quality studies;
- the probability of death risk from sedation; and
- the probability of death risk from surgery.

**Study designs and other criteria for inclusion in the review**
No inclusion criteria were stated.

**Sources searched to identify primary studies**
Published medical literature, including medical publications from 1960 to 1999, was used as the source for data for the effectiveness analysis.

**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**
Sixteen studies were included as sources of effectiveness evidence. The types of primary studies included in the review were not reported.

**Methods of combining primary studies**
It was not clearly stated how the authors used the results of the primary studies to obtain the estimates of effectiveness. They reported that the baseline values for the outcomes were the best available literature estimates.

**Investigation of differences between primary studies**
The authors mentioned the existence of differences in the quality of the studies and the level of expertise of the reviewer, which affected the results of these studies. The authors reported evidence that studies of poor quality, or which were carried out by less experienced reviewers, showed a significant decrease in the sensitivity and specificity of 3D CT and radiography.

**Results of the review**
The results of the review were as follows:
The pre-test probabilities of synostosis were 34/100,000 for the low-risk group, 8.7/1,000 for the intermediate-risk group, and 90/100 for the high-risk group.

The sensitivity and specificity of radiographs in good quality studies were, respectively, 80 and 95.

The sensitivity and specificity of radiographs in studies of poor quality were 60 and 78, respectively.

The sensitivity and specificity of 3D CT in good quality studies with experienced reviewers were 96.4 and 100, respectively.

The sensitivity and specificity of 3D CT in good quality studies with less experienced reviewers were, respectively, 96.4 and 83.3.

The sensitivity and specificity of CT in poor quality studies were 73 and 78, respectively.

The probability of death risk from sedation was 1/1,000,000.

The probability of death risk from surgery was 0.5%.

Methods used to derive estimates of effectiveness
An author's assumption was used to derive the utility value for patients with undiagnosed craniosynostosis.

Estimates of effectiveness and key assumptions
A utility value of 0.95 was assumed for patients with undiagnosed craniosynostosis.

Measure of benefits used in the economic analysis
The measure of benefit was number of quality-adjusted life years (QALYs) gained. The quality-of-life weight (utility) was obtained from the treating physician's perspective. The utility values of early diagnosis and treatment of craniosynostosis versus delayed diagnosis and treatment of craniosynostosis were incorporated in a Markov model.

Direct costs
Resource quantities and costs were not reported separately. The direct costs reported in the study were the direct and total costs of skull radiography; 3D CT; sedation; CT plus sedation; and surgery. The total costs of the imaging studies included the technical and professional fee. Total costs of no imaging, radiography and CT were calculated for each one of the three risk groups analysed in the study. The estimation of the costs was based on actual data. The costs of the imaging studies were estimated using the 1999 Ohio Medicaid fee schedule. The other costs were estimated from the Cincinnati Children's Hospital Medical Center cost accounting system. The costs used for the case-base study were those related with Medicaid reimbursement.

Discounting was not carried out. However, it would have been relevant, as the period considered for the outcomes was 20 years. Although surgery is usually performed early in life, it was not stated that the costs were incurred over a period of less than two years. The price year was 1999 for the costs related to the imaging studies. The date for the remaining cost was not stated.

Statistical analysis of costs
No statistical analysis of costs was performed.

Indirect Costs
Indirect costs were not reported.
Currency
US dollars ($).

Sensitivity analysis
The authors performed sensitivity analysis by varying the model estimates to determine the robustness of the model. The ranges over which sensitivity analyses were conducted were stated by the authors to be ‘clinically plausible’; no further justification or source being given.

The ranges analysed for pre-test probabilities of synostosis were: 31 - 48/100,000 for the low-risk group, 7 - 10/1,000 for the intermediate-risk group, and 80 - 100/100 for the high-risk group.

The ranges analysed for the sensitivity and specificity of radiographs in good quality studies were, respectively, 57 - 80, and 54 - 100.

The ranges of sensitivity and specificity of radiographs in studies of poor quality were 40 - 80, and 56 - 100, respectively.

The ranges analysed for the sensitivity and specificity of 3D CT in good quality studies with experienced reviewers were 92.9 - 96.4, and 95 - 100, respectively.

The ranges analysed for the sensitivity and specificity of 3D CT in good quality studies with less experienced reviewers were, respectively, 89.3 - 100, and 43.3 - 100.

The ranges analysed for the sensitivity and specificity of CT in poor quality studies were 53 - 83, and 30 - 81.8, respectively.

The range analysed for the probability of death risk from sedation was 0.5 - 2/1,000,000.

The range analysed for the probability of death risk from surgery was 0.1% - 1%.

The areas of uncertainty investigated were variability in data and generalisability of results.

For the costs, the ranges analysed were: 20 - 100 for skull radiography; 150 - 300 for 3D CT; 0 - 150 for sedation; 150 - 450 for CT plus sedation.

One-way and two-way sensitivity analyses were performed. Some of the break-even points were reported.

Estimated benefits used in the economic analysis
In the low-risk group, 15.03702 QALYs were gained with no imaging, 15.03711 with radiography, and 15.03714 with CT.

In the intermediate group, the number of QALYs gained with no imaging was 15.03334, with radiography 15.03578, and with CT 15.03639.

The number of QALYs gained in the high-risk group was 14.641 with no imaging, 14.893 with radiography, and 14.956 with CT.

The period considered in estimating the QALY gains was 20 years.

Cost results
The total costs, as obtained from the medical centre cost estimates were: skull radiography, $76; 3D CT, $191; sedation, $121; CT plus sedation, $312; and surgery, $12,000.
In the low-risk group, the total cost of no imaging was $80, the total cost of radiography was $134, and the total cost of CT was $345. In the intermediate-risk group, the total costs were $80 for no imaging, $213 for radiography, and $441 for CT.

In the high-risk group, the total costs for no imaging were $80, for radiography $8,636, and for CT $10,752.

**Synthesis of costs and benefits**

Cost and benefit results were combined into cost-utility ratios. The ratios calculated were the cost per QALY gained, either with radiography or with CT, when compared with no imaging. These cost-effectiveness ratios were calculated for low-risk, intermediate risk and high-risk groups. In the low-risk group the cost-effectiveness ratios were $568,100 for radiography, and $8,827,700 for CT, when compared with no imaging. In the intermediate-risk group, the cost-effectiveness ratio for radiography, when compared with no imaging, was $54,600, and for CT was $374,200. In the high-risk group, CT had extended dominance over the other alternatives, with a cost-effectiveness ratio equal to $33,500, when compared to no imaging.

When analysing costs of imaging strategies for the intermediate risk group, break-even points were found when the cost of radiography was $194 (a higher cost of radiography implied that 3D CT was the preferred strategy) and when the cost of 3D CT was $51 (a cost higher than this implied that radiography was the preferred strategy). When utility values were analysed, it was found that, as the utility decreased (i.e. undiagnosed synostosis implied worse quality of life), the cost per QALY gained decreased for the radiographic and 3D CT strategies, with a more marked decrease for 3D CT.

Sensitivity analysis showed that lower prevalence of the disease, and lower sensitivity and specificity of radiography or 3D CT (obtained with studies of poor quality or with less experienced reviewers), made the cost per QALY of radiography or of 3D CT increase. Changes in the sensitivity and specificity of one of the imaging strategies influenced the cost per QALY in the other strategy. When 3D CT specificity was equal to or less than 95%, radiography became the preferred strategy because it dominated 3D CT. However, the lower the 3D CT specificity, the higher the radiographic cost per QALY gained, because the abnormal findings on conventional radiography were followed by 3D CT.

**Authors' conclusions**

The authors concluded that there was controversy in the strategy chosen depending on the different levels of risk of craniosynostosis considered. In the high-risk group CT was the most effective strategy, with the lower cost per QALY, because of the high prevalence of craniosynostosis within this group. In the intermediate-risk group, radiography had the lower cost per QALY gained; although 3D CT was the most effective strategy within this group, it implied a higher cost. In the low-risk group radiography or 3D CT should not be considered due to the high cost per QALY gained. As the authors stated, the cost-effectiveness ratios of the high-risk group 3D CT ($33,800 per QALY gained) and the intermediate-risk group radiography ($54,600 per QALY gained) presented favourable results in comparison with other well-accepted diagnostic strategies.

**CRD COMMENTARY - Selection of comparators**

Although no specific justification was given for the choice of the comparator, it would appear to be an accepted alternative strategy due to the different risk groups considered at analysis.

**Validity of estimate of measure of effectiveness**

The authors did not state that a systematic review of the literature had been undertaken. It was not stated how the estimates of effectiveness were derived from the primary studies. The authors reported that the best available literature estimates were chosen as baseline values, but they did not report the methods used to obtain these estimates. However, they provided evidence that differences in the quality of the studies and in the level of expertise of the reviewers affected the clinical outcomes obtained in the primary studies.
Validity of estimate of measure of benefit
The instrument used to derive the measure of health benefit (the number of QALYs gained) was a Markov model, which, given the nature of the study, seemed appropriate. Although, the horizon considered covered a 20 year-period, no discounting of health benefit was performed, though it may have been required.

Validity of estimate of costs
Although the authors adopted a societal perspective for the analysis, indirect costs (lost productivity or psychological effects produced for a noticeably misshapen forehead and face) were not included in the analysis. Resource quantities and costs were not reported separately, which limits the generalisability of results to other settings. The price year was not clearly stated. Discounting was not conducted, and, although many of the direct costs may have been incurred within the first two years, this was not explicitly stated by the authors and therefore may not in fact be the case.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but did not address the issue of the generalisability of results to other settings. The results do not appear to have been presented selectively. The authors did not report any limitations to their study.

Implications of the study
Children with suspected craniosynostosis should be selected according to their risk group before choosing the most appropriate evaluation strategy, so as to maximise clinical and economic outcomes for these patients. The authors recommended further investigation, such as large prospective cohort studies with other well-defined craniosynostosis disorders, in order to study other clinical risk groups and to determine their prevalence of craniosynostosis.

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