Children with headache suspected of having a brain tumor: 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
Three diagnostic strategies for the management of children with headache, who were suspected of having a brain tumour, were examined. The strategies were magnetic resonance imaging (MRI), computer tomography (CT) followed by MRI for positive results (CT-MRI), and no neuroimaging with close clinical follow-up (no test).

Type of intervention
Diagnosis.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of children with headache, who were suspected of having an intracranial tumour. Migraine headaches were defined as recurrent headaches that were often pulsating, unilateral, and associated with symptoms such as nausea, light and sound sensitivity, and visual or neurologic symptoms.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data came from studies published between 1983 and 1997. No dates for the resource use data were explicitly reported. The price year was 1997.

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

Modelling
A Markov model was constructed to examine the costs and benefits of the three alternative diagnostic strategies in a hypothetical 5-year-old child with headache, but without coexisting disease. Brain tumours were defined as brain neoplasms and vascular malformations such as arteriovenous malformations. Patients with MRI findings consistent with a brain tumour were assumed to have a brain biopsy. Children with headache were divided into low-, intermediate- and high-risk groups, based on clinical predictors and on their estimated probability of having a brain neoplasm. The low-risk group included patients with non-migraine headache for more than 6 months as the sole symptom and normal neurologic examination. The intermediate-risk group included patients with migraine symptoms and a normal neurologic examination. The high-risk group included patients with headache and at least one clinical predictor of a surgical space-occupying lesion. The seven predictors include headache of less than 6 months' duration, sleep-related
headache, vomiting, confusion, absence of visual symptoms, absence of family history of migraine, and abnormal neurologic examination. The time horizon of the model was 20 years. The cycle length was not reported.

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

prior probabilities of brain tumour;
sensitivity, specificity and other characteristics of the diagnostic tests;
the proportion of children having a 1-year delay in tumour diagnosis from the initiation of clinical diagnosis;
the probability of herniation;
MRI contrast material death and severe reaction;
CT contrast material death and severe reaction;
death from sedation;
brain biopsy death and severe complication;
utility values associated with nonmedulloblastoma tumours (no residual and residual tumour) and medulloblastoma tumour (non-metastatic and metastatic);
5-year survival; and
estimated population associated with medulloblastoma, posterior fossa pilocytic astrocytoma, ependymoma, supratentorial pilocytic astrocytomas, craniopharyngioma, Grade III astrocytoma and mixed oligoastrocytomas, Grade III glial tumour and Grade IV glial tumour.

Study designs and other criteria for inclusion in the review
It was not stated whether a systematic review of the literature had been undertaken. Limited information on the design of the primary studies was reported. The mortality rates for causes other than brain tumours were derived from US statistics. Some data came from primary data derived from a hospital-based database of 315 children with headache who were imaged with MRI and CT. The utility values were estimated from a study that used the perspective of the treating physician.

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
Twenty-two studies provided the evidence.
Methods of combining primary studies
The primary studies appear to have been combined using a narrative approach.

Investigation of differences between primary studies
Not stated.

Results of the review
The prior probabilities of brain tumour were 1/10,000 (range: 0.5 - 2/10,000) in the low-risk group, 4/1,000 (range: 1 - 6/1,000) in the intermediate-risk group, and 4/100 (range: 1 - 8/100) in the high-risk group.

The sensitivity of MRI was 0.92 (range: 0.82 - 1) and the specificity was 0.99 (range: 0.81 - 1).

The sensitivity of CT was 0.81 (range: 0.65 - 1) and the specificity was 0.92 (range: 0.72 - 1).

The percentage of CT with contrast was 28% (range: 0 - 100).

The percentage of MRI with contrast was 9% (range: 0 - 100).

The percentage of CT with sedation was 6% (range: 0 - 100).

The percentage of MRI with sedation was 12% (range: 0 - 100).

The proportion of children having a 1-year delay in tumour diagnosis from the initiation of clinical diagnosis was 14% (range: 1 - 30).

The probability of herniation was 0.50% (range: 0 - 2).

The rate of death due to MRI contrast material was 0.25/1,000,000 (range: 0.1 - 0.5/1,000,000).

The rate of severe reaction due to MRI contrast material was 0.25/100,000 (range: 0.2 - 0.3/100,000).

The rate of death due to CT contrast material was 0.9/100,000 (range: 0.3 - 2.6/100,000).

The rate of severe reaction due to CT contrast material was 31/100,000 (range: 2 - 62/100,000).

The rate of death from sedation was 1/1,000,000 (range: 0.5 - 2/1,000,000).

The rate of death due to brain biopsy was 0.5% (range: 0.1 - 1).

The rate of severe complications associated with brain biopsy was 3% (range: 0.5 - 3).

The utility values associated with nonmedulloblastoma tumours were 0.93 (range: 0.8 - 1) for no residual tumour and 0.51 (range: 0.3 - 0.7) for residual tumour.

The utility values associated with medulloblastoma tumour were 0.76 (range: 0.6 to 1) for non-metastatic tumour and 0.31 (range: 0.1 - 0.5) for metastatic tumour.

The 5-year survival and estimated population associated with medulloblastoma (proportion of total brain tumours 20%) were 59% and 82%, respectively, with local neoplasm with no metastasis, and 36% and 18% with metastatic cancer.

The 5-year survival and estimated population associated with posterior fossa pilocytic astrocytoma (20%) were 95% and 69%, respectively, with total excision, and 80% and 31% with partial excision.

The 5-year survival and estimated population associated with ependymoma (10%) were 75% and 47%, respectively, with local cancer with gross total resection, and 0 - 2% and 53% with residual disease after resection.
The 5-year survival and estimated population associated with supratentorial pilocytic astrocytomas (10%) were 99% and 22%, respectively, with total excision, and 95% and 78% with subtotal excision.

The 5-year survival rate was 95% with craniopharyngioma (10%), 52% with Grade III astrocytoma and mixed oligoastrocytomas (10%), 25% with Grade III glial tumour (10%), and 10% with Grade IV glial tumour (10%).

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

Estimates of effectiveness and key assumptions
Conditional independence between CT and MRI was assumed for the case where a positive CT examination was followed by a MRI test. Further, quality of life weights and disease-specific mortality rates were assumed to persist only for the first 5 years after diagnosis, after which time the child was assumed to be cured.

Measure of benefits used in the economic analysis
The summary benefit measure was the estimated number of quality-adjusted life-years (QALYs). These were calculated combining quality of life data and the expected survival obtained from the decision model. An annual discount rate of 3% was applied.

Direct costs
Discounting was relevant since the costs were incurred during a long timeframe, and an annual discount rate of 3% was applied. The unit costs were presented separately from the quantities of resources used for some items only. The health services included in the economic evaluation were radiological and non-radiological procedures, treatment of severe adverse reactions to contrast material or sedation, and favourable or unfavourable prognosis brain tumours (including hospitalisation, surgery, chemotherapy, radiation therapy, laboratories, pharmacy, imaging, and follow-up visits). Fixed, variable and overhead costs were considered. The authors stated that the cost/resource boundary of the study was that of society, although it was unclear whether all the relevant categories of costs had been included as the costs were presented as macro-categories. The costs were estimated using data derived from the Boston Children's Hospital cost accounting system. The source of the resource data was not explicitly reported, although some estimates were derived from the literature. The price year was 1997.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Indirect costs do not appear to have been included.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were carried out to test the robustness of the estimated cost per QALY to variations in all model inputs. The authors stated that plausible ranges of values were considered.

Estimated benefits used in the economic analysis
In the low-risk group (prior probability 0.01%), the estimated QALYs were 15.0285 with no imaging, 15.02776 with
In the intermediate-risk group (prior probability 0.4%), the estimated QALYs were 15.00349 with no imaging, 15.00378 with MRI, and 15.00431 with CT-MRI.

In the high-risk group (prior probability 4%), the estimated QALYs were 14.77259 with no imaging, 14.78248 with MRI, and 14.78116 with CT-MRI.

In the high-risk group (prior probability 8%), the estimated QALYs were 14.51604 with no imaging, 14.53658 with MRI, and 14.53321 with CT-MRI.

Cost results
In the low-risk group (prior probability 0.01%), the estimated costs were $7 with no imaging, $861 with MRI, and $1,304 with CT-MRI.

In the intermediate-risk group (prior probability 0.4%), the estimated costs were $269 with no imaging, $1,150 with MRI, and $1,588 with CT-MRI.

In the high-risk group (prior probability 4%), the estimated costs were $2,694 with no imaging, $3,819 with MRI, and $4,212 with CT-MRI.

In the high-risk group (prior probability 8%), the estimated costs were $5,389 with no imaging, $6,775 with MRI, and $7,117 with CT-MRI.

Synthesis of costs and benefits
An incremental cost-utility analysis was carried out to combine the costs and benefits of the alternative diagnostic strategies. The analysis showed that no test dominated both MRI and CT-MRI in the low-risk group. In the intermediate-risk group, no test dominated (extended dominance) MRI, while the incremental cost per QALY gained with CT-MRI over no imaging was $1,600,000. In the high-risk group, CT-MRI was dominated by MRI, and the incremental cost per QALY gained with MRI over no imaging was $113,800 with a prior probability 4% and $67,000 with a prior probability of 8%.

The sensitivity analysis showed that, in general, substantial variations in base-case values were required for the diagnostic strategies to be cost-effective. In particular, lower costs per QALY were observed as the increasing number of brain tumour predictors increased the prior probability. MRI was ruled out by dominance or extended dominance if its specificity was lower than 97%. CT was no longer dominated if its specificity was greater than 97%. However, the base-case results were not sensitive to variations in the sensitivity of CT or MRI. Extending the time horizon of the study showed a decrease in the cost per QALY gained ($65,000 after 60 years). MRI became more cost-effective ($80,000 per QALY) when its cost equalled the cost of doing a CT examination.

Authors' conclusions
Magnetic resonance imaging (MRI) was reasonably cost-effectiveness in children with headache who were at high risk of having a brain tumour. Conversely, the strategy of no imaging with close clinical follow-up was cost-saving in children with a low risk of brain tumour. In the intermediate-risk group, computed tomography (CT)-MRI maximised the QALYs gained but at a cost that was too high. The authors pointed out that the accurate selection of patients and diagnostic strategy could maximise the benefits of the intervention at reasonable costs.

CRD COMMENTARY - Selection of comparators
The selection of the comparators reflected the actual diagnostic pattern (no test and close clinical follow-up), while MRI alone and CT-MRI represented two alternative diagnostic strategies for the management of children with headache. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on data derived from the literature. However, it was not stated explicitly whether a systematic review of the literature had been undertaken to identify primary studies. Limited information on the design and characteristics of the primary sources was reported. The methods of extracting and combining the primary estimates were not described, and the issue of comparability of the primary studies was not addressed. Therefore, it appears difficult to examine the validity of the studies. Some assumptions were also made. The authors investigated the impact of variations in all clinical inputs in the sensitivity analysis.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate since they detect the impact of the intervention on life expectancy and quality of life, which are relevant aspects of care in the case of children with brain tumour. The source of utility values was reported and physicians’ preferences were used to elicit utility weights. Discounting was applied, as recommended in US guidelines. QALYs are comparable with the benefits of other health care interventions.

Validity of estimate of costs
The authors stated that a societal perspective was adopted in the study. However, it appears that only direct medical costs have been included in the study. Indeed, the costs were estimated from a hospital database. A detailed breakdown of the cost items was not provided and the costs were presented as macro-categories. Since not all of the unit costs were reported separately from the quantities, it appears difficult to replicate the study. The costs were treated deterministically but some estimates were varied in the sensitivity analysis. The source of the resource use data was unclear. The price year was reported, which will simplify reflation exercises in other settings.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. It was stated that the cost-effectiveness of diagnostic tests could be different in countries with different neuroimaging costs and equipment availability. The study referred to children with headache suspected of having brain tumour and this was reflected in the authors’ conclusions.

Implications of the study
The authors proposed a diagnostic algorithm to support the use of neuroimaging diagnostic tests only in children with a high risk of brain tumour, with close clinical follow-up being recommended for those with a low risk of brain tumour. They also noted that future studies to compare the diagnostic yield of CT and MRI, as well as to define other clinical risk groups, are required.

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Other publications of related interest

Frishberg BM. The utility of neuroimaging in the evaluation of headache in patient with normal neurologic...

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