Newborn screening with tandem mass spectrometry: examining its cost-effectiveness in the Wisconsin newborn screening panel

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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 use of tandem mass spectrometry (MS/MS) in the screening of newborns for medium-chain acyl-CoA dehydrogenase deficiency (MCAD).

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of unselected newborns.

Setting
The setting was a hospital. The model parameters were based on UK and United States studies.

Dates to which data relate
The effectiveness data were derived from studies published between 1995 and 2001. The resource use data were mainly obtained from studies published in 1997 and 1999. The price year was 2001.

Source of effectiveness data
The effectiveness evidence came from published studies, augmented by the authors’ assumptions.

Modelling
A decision tree was used to assess the costs and benefits of the MS/MS screening strategy versus no screening. The tree was populated using the authors’ assumptions and published data.

Outcomes assessed in the review
The model parameters estimated in the review were:

the MCAD diagnosis rate before screening;
the death rate;
the severe and mild neurological impairment rates;
the rate of acute complications only;
the rate of asymptomatic diagnosis;
MCAD incidence post-screening;
the sensitivity and specificity of MS/MS;
the mortality reduction with screening;
the life expectancy with severe neurological impairment;
the quality of life, both with severe and mild neurological impairment; and
the age-adjusted quality-adjusted life-years (QALYs).

Study designs and other criteria for inclusion in the review
Not stated. One of the primary studies was the overview of the Wisconsin Newborn Screening Program. Another was a MS/MS screening panel conducted by the UK NHS in 1997 (Pollitt et al., see Other Publications of Related Interest).

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
The effectiveness evidence was obtained from 13 primary studies.

Methods of combining primary studies
The authors used data from the available studies selectively. They stated that they chose conservative estimates for the base-case, which would tend to underestimate the cost-effectiveness of MS/MS screening for MCAD.

Investigation of differences between primary studies
Not stated.

Results of the review
The base-case results are reported below, along with best estimates for two variables for the sensitivity analyses.

The MCAD diagnosis rate before screening was 2.5 in 100,000.
The death rate was 0.40 in 100,000.
The severe neurological impairment rate was 0.13 in 100,000.
The mild neurological impairment rate was 0.13 in 100,000.

The rate of acute complications only was 1.23 in 100,000.

The rate of asymptomatic diagnosis was 0.63 in 100,000. The percentage of symptomatic cases undiagnosed was 0%. The best estimate was 37%.

The MCAD incidence post-screening was 4.4 in 100,000.

The sensitivity of MS/MS was 90% and the specificity was 99.9%.

The mortality reduction with screening was 60%. The best estimate was 90%.

The life expectancy with severe neurological impairment was 65 years.

The quality of life with severe neurological impairment was 0.06.

The quality of life with mild neurological impairment was 0.67.

Various values (not reported) were used for the age-adjusted QALYs.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to identify the most conservative scenario for the study intervention.

**Estimates of effectiveness and key assumptions**
The authors assumed that all undiagnosed MCAD cases in the absence of screening were asymptomatic. They also assumed that the distribution of outcomes for Wisconsin cases diagnosed in the absence of screening, with death and neurological impairment occurring at one year of age, was similar. Also, further morbidity or mortality later in life relative to a prior metabolic decompensation was excluded. It was also assumed that infants with asymptomatic MCAD would have a normal life expectancy.

**Measure of benefits used in the economic analysis**
The QALYs were used as the benefit measure in the economic analysis. A 3% annual discount rate was applied since the time horizon of the analysis was lifetime. The quality of life weights used to calculate QALYs for mild neurological impairment were based on ratings of this health state by teenagers formerly of extremely low birth weight. The valuation tool was the standard gamble. The weights for severe neurological impairment were based on the Health Utility Index 3 scores for patients with severe dementia. The QALY values were then adjusted according to age-specific weights, as described by Erickson et al. (see Other Publications of Related Interest).

**Direct costs**
A 3% discount rate was used since the lifetime costs were estimated in the analysis. The unit costs were reported, but the quantities of resource consumption were not and would, therefore, have to be inferred from the model. The health service costs included in the economic evaluation were for the screening test, positive test confirmation, carnitine supplements to age 18, follow-up and routine hospital admissions. The screening costs were for the MS/MS instrument, personnel, consumables, data management operations, departmental indirect expenses, and laboratory overhead and programme start-up. The follow-up costs included testing, visits and staff time to age 18. The cost-savings were calculated on the basis of the avoided costs of neurological impairment and medical costs of fatal and acutely ill cases. The cost/resource boundary adopted was not explicitly stated, but it was probably that of the health service. The hospital costs were estimated using charge data from the Healthcare Cost and Utilisation Project, adjusted by a national cost-to-charge ratio of 0.6. Other costs were derived from the Wisconsin Newborn Screening Program. The data on resource consumption were derived from assumptions and published studies. All of the costs were inflated to 2001 prices using the Consumer Price Index.
Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not included in the cost analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were conducted because of the uncertainty around the model inputs used in the analysis. While the base-case was constructed on conservative assumptions, a more realistic case (best-case) was simulated in the sensitivity analysis, where some cost and effectiveness parameters were varied. All the model parameters were also varied individually in one-way sensitivity analyses, to assess the impact of each item on the results of the analysis.

Estimated benefits used in the economic analysis
The total QALYs gained from screening in comparison with no screening were 9.6.

Cost results
The total costs of screening were $526,079 and the total cost-savings were $124,200. Consequently, the net cost of screening relative to no screening was $401,879.

Synthesis of costs and benefits
An incremental cost-utility analysis was conducted to combine the costs and QALYs of the screening programme. The incremental cost per QALY gained with MS/MS screening, compared with no screening, was $41,862. Under the best-case assumptions, the incremental cost per QALY gained was $6,008. One-way sensitivity analyses showed that the model inputs that most affected the study results were the effectiveness of early diagnosis and treatment, the incremental cost of the MS/MS screening test, the screening test sensitivity, and the overall disease incidence. For MS/MS screening to cost more than $50,000/QALY, the effectiveness of early diagnosis and treatment would need to be less than 36%, the incremental testing costs would have to rise above $13.05/infant, and the test sensitivity would need to fall below 28%.

Authors' conclusions
Even under conservative assumptions, the use of tandem mass spectrometry (MS/MS) for the screening of newborns proved to be as cost-effective as other well-accepted medical interventions. Under more realistic assumptions, the screening strategy became even more cost-effective.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. No screening was selected as this represented the routine practice and the aim of the study was to assess the active value of the screening intervention. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used published data, but a formal review of the literature was not undertaken. The authors did not state whether they took into account differences between the primary studies when estimating the effectiveness,
and they chose the estimates selectively. The authors carried out a conservative analysis in the base-case. The incidence rates appear to be higher in the UK. The paper of Pollitt et al. (see Other Publications of Related Interest) may contain better UK estimates. Estimates were then changed in the sensitivity analyses, which were conducted to investigate the robustness of the effectiveness estimates used in the analysis.

**Validity of estimate of measure of benefit**
The benefit measure used in the economic analysis was the QALY. This was calculated using data derived from published studies through a decision model. Appropriate discounting was conducted. The use of QALYs enables the comparison with other health care benefits. The QALY values were adjusted for unrelated co-morbidities.

**Validity of estimate of costs**
The perspective adopted in the study was not reported and several categories of costs were included in the analysis. A study published in the UK was the main source of the cost data, in addition to the Wisconsin Newborn Screening Program. The resource use data were mainly derived from assumptions and two studies. The unit costs were reported, but few details on resource consumption were provided. The price year was stated, thus facilitating reflation exercises in other settings. All of the costs were inflated to 2001 prices. Appropriate discounting was performed as the lifetime costs were estimated.

**Other issues**
The authors did not compare their findings with those from other published studies, probably due to the lack of available studies. The study focused on deriving results specifically for Wisconsin and did not consider generalisability explicitly. However, sensitivity analyses were performed, which aid generalisability. The authors commented on some limitations of their analysis. First, the evidence on both the costs and on the effectiveness came from different sources, due to the lack of comprehensive studies. Second, the analysis focused only on MCAD disease, assuming that the intervention would be cost-effective for the remaining 13 fatty acid oxidation and organic acidemia disorders included in the Wisconsin Newborn Screening Program, although the follow-up costs of the other diseases may be substantial. Third, the analysis did not consider the impact on a family's quality of life of a diagnosis of MCAD made on the basis of the screening.

**Implications of the study**
The study suggests that MS/MS screening for MCAD may be cost-effective in newborns, allowing for the prevention of neonatal deaths in the USA.

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**Other publications of related interest**


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