The cost-effectiveness of prenatal screening for spinal muscular atrophy

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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.

CRD summary
The objective was to assess the cost-effectiveness of prenatal screening for spinal muscular atrophy (SMA). The authors concluded that universal screening for SMA was not cost-effective, but further research should be conducted in high-risk populations. There were a number of limitations to the study, but the methods and results were generally well reported. The authors' conclusions appear to reflect the evidence available at the time.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of universal prenatal screening for spinal muscular atrophy (SMA).

Interventions
Universal genetic-carrier screening was compared with no screening. Pregnant women were screened and, if they were genetic carriers, their partner was screened. If both partners were identified as carriers, amniocentesis was performed. Carrier screening was by a serum probe amplification of all exons in the SMN1 gene. Individuals with half the normal levels of SMN1 alleles were identified as carriers.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A decision model was used to synthesise the data from a variety of sources to enable a hypothetical population to be evaluated. A 100% uptake rate for each diagnosis step was assumed and if a positive foetal diagnosis was made, it was assumed that the pregnancy was terminated. The baseline population risk of SMA was assumed to be one in 10,000 people, based on a Committee on Genetics report. It was assumed that 2% of SMA cases were from a new mutation, rather than a traditional autosomal-recessive inheritance, and that these new cases occurred when at least one parent was a carrier. The time horizon included the life expectancy of both the woman and the child. The authors stated that the study took a societal perspective.

Effectiveness data:
A 90% false-negative screening rate was assumed (90% sensitivity), based on the published finding that 5% of individuals have two copies of the SMN1 gene on one chromosome. It was assumed that there were no false-positive results (100% specificity). Other clinical parameters included the proportion of SMA cases that were considered to be severe, and the miscarriage risk following amniocentesis.

Monetary benefit and utility valuations:
The utility weights were selected from a variety of published sources. The estimated maternal utility following foetal loss (either procedure-related miscarriage or pregnancy termination) was from a published study that used the Standard Gamble method and the rate was applied to the remaining life-years of the woman. The estimated maternal utility following the birth of a child with severe SMA was based on a published study that used a Likert scale and this estimate was applied for two years. After two years, the utility following foetal loss was applied for the remaining life-years. The estimated maternal utility following the birth of a child with mild SMA was assumed to be similar to that of a child with...
Down's syndrome, which was from a published study that used the Standard Gamble method.

Measure of benefit:
The primary measure of benefit was maternal quality-adjusted life-years (QALYs). The secondary measure of benefit was the cases of SMA averted. The benefits were discounted at a rate of 3% per annum.

Cost data:
The cost categories were carrier screening, foetal diagnostic testing, amniocentesis, pregnancy termination, and the lifetime cost of a child with mild or severe disease. The unit costs were from a variety of published sources. The direct and indirect costs of caring for a child with severe SMA were based on published estimates for ventilator-dependent children and those for mild SMA were based on cerebral palsy. The costs were reported in 2009 US dollars ($). The direct costs were inflated using the general Consumer Price Index and the indirect costs were inflated using the compensation index for wages and lost income. They were discounted at a rate of 3% per annum.

Analysis of uncertainty:
One-way sensitivity analyses were performed on all parameters, using reasonable ranges defined by the authors. Probabilistic sensitivity analysis, with 100,000 simulations, was conducted. The costs were assumed to have gamma distributions, with a standard deviation of 50%, and the probabilities were assumed to have beta distributions, with a standard deviation of 20%.

Results
Per 100,000 women, the total cost was $44,295,289 with prenatal SMA screening, compared with $4,714,165 without screening. The total children born with SMA was two with screening and 10 without screening. The total QALYs experienced were 2,572,954 with screening, compared with 2,572,946 without screening.

The estimated incremental cost-effectiveness ratio with screening was $4,889,675 per QALY gained, and the estimated incremental cost per SMA case averted was $4,985,028.

The univariate sensitivity analysis revealed that the results were sensitive to the prevalence of SMA. If the prevalence was one in 1,000 births, then screening could be considered cost-effective at a willingness-to-pay threshold of $100,000 per QALY. If it was one in 900 births, screening could be cost-effective at a willingness-to-pay threshold of $50,000 per QALY. Screening was dominant as it was more effective and less costly, if the prevalence was over one in 800 births.

The results were somewhat sensitive to the cost of screening, but it had to fall from $425 to $44 per test for screening to be considered cost-effective at a willingness-to-pay threshold of $100,000 per QALY. The results were not sensitive to variations in the remaining costs, utilities, and life-expectancy of a child with severe SMA.

Probabilistic sensitivity analysis found that screening was not cost-effective in 99.7% of simulations, at a willingness-to-pay threshold of $100,000.

Authors' conclusions
The authors concluded that universal prenatal screening for SMA was not cost-effective. They suggested that further research should be undertaken on the cost-effectiveness of screening in high-risk populations.

CRD commentary
Interventions:
The interventions were well described and relevant to the secondary care setting.

Effectiveness/benefits:
The clinical data were selected by the authors as the most appropriate data from available studies. It was unclear if an extensive systematic review of the evidence was conducted, as no methods were reported. It is therefore not possible to be sure that all of the available evidence was used. The authors reported that there was little evidence available and a wider search might have identified little additional evidence. The utility data appear to have been least available and the
utilities for other diseases had to be used as proxies; this limitation was highlighted by the authors. The probabilities and utilities were clearly presented in a table.

Costs:
The costs were relevant to the perspective taken and average costs for each category were presented in a table. All adjustments to the costs were appropriate and reported. The costs were presented as subtotals and no resource use was reported. It is difficult to assess how extensive the searches for the cost and resource data were. It was necessary to use lifetime costs for other diseases as proxies, and this was highlighted as a limitation by the authors.

Analysis and results:
A decision analytic model was appropriate for synthesising the data and, on the whole, it was well reported, with a diagram. Sensitivity analysis was conducted with one-way analysis results presented in a tornado diagram and probabilistic analysis results presented on a cost-effectiveness plane. The extensive sensitivity analysis highlighted some areas where uncertainty remained and could affect the conclusions, but it suggested that the circumstances required to make universal screening cost-effective were unlikely to occur, even with more thorough research. The main driver of uncertainty in the cost-effectiveness was the prevalence of SMA, which was a quite robust estimate.

Concluding remarks:
There were a number of limitations to the study, but the methods and results were generally well reported. The authors' conclusions appear to reflect the evidence available at the time.

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