Organisation and cost-effectiveness of antenatal haemoglobinopathy screening and follow up in a community-based programme

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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 main health technology assessed was a universal, community-based antenatal screening programme for the haemoglobinopathies. The laboratory tests include a full blood count, isoelectric focusing, high-performance liquid chromatography, and other confirmatory tests. In addition to the main screening programme, follow-up services were also assessed. These included counselling and post-termination support where necessary.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised women attending the antenatal clinic of a district general hospital in an inner London health district, where 45% of the population are from ethnic minority groups.

Setting
The setting was a hospital. The study was carried out at the Central Middlesex Hospital in inner London (Brent), UK.

Dates to which data relate
The effectiveness and resource data were collected retrospectively from women referred for screening during 1994. The prices used were for the year 1994 to 1995.

Source of effectiveness data
The evidence for the final outcomes was derived from a single retrospective study and a review of the literature. In addition, the authors made assumptions about the effectiveness.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness study.

Study sample
The study sample consisted of 2,101 women booking in at the antenatal clinic, whose samples were referred for screening during the study period. The authors selected the sample from an area with a relatively high prevalence of ethnic minority groups, and where the hospital had a well-established universal and community-based antenatal screening programme. It was not reported whether any sample size calculations were performed during either the
planning phase of the study, or retrospectively.

**Study design**
This was a screening test evaluation study of a group of patients undergoing a universal, community-based antenatal screening programme, which was conducted at a single centre.

**Analysis of effectiveness**
All the patients included in the study appear to have been accounted for in the analysis. The primary health outcomes used in the analysis were the number of at-risk foetuses identified, the number accepting prenatal diagnosis (PND), and the number of women terminating their pregnancy.

**Effectiveness results**
One hundred and forty-one women had abnormal haemoglobin. Twelve couples had results indicating the foetus was at risk of a major haemoglobinopathy because both partners had significant traits. Of these, four accepted the PND and one terminated the pregnancy.

**Outcomes assessed in the review**
The outcome assessed was the ratio of sickle cell disease to beta thalassaemia major.

**Study designs and other criteria for inclusion in the review**
Not stated.

**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**
Two primary studies were included in the review.

**Methods of combining primary studies**
Not stated.

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

**Results of the review**
The ratio of sickle cell disease to beta thalassaemia major was 3:1.
Methods used to derive estimates of effectiveness
The authors made assumptions about the effectiveness.

Estimates of effectiveness and key assumptions
The study identified 12 foetuses at risk. Three of these foetuses should be affected, given the 1 in 4 risk of a clinically significant haemoglobinopathy from a conception in which both partners carry a haemoglobinopathy trait. Using the 3:1 ratio, 2.25 cases of sickle cell disease and 0.75 cases of beta thalassaemia major would have been detected if the parents had pursued PND. Thus, of all the affected pregnancies, 10% of sickle cell disease and 95% of beta thalassaemia cases would have been terminated. This equates to 0.225 cases of sickle cell disease and 0.7125 cases of beta thalassaemia major per year.

Measure of benefits used in the economic analysis
The outcome measures used in the economic analysis were the number of at-risk foetuses identified, and the number of clinically significant haemoglobinopathies averted.

Direct costs
The cost information was collected for both the laboratory and the follow-up components of the programme, and the cost of treating the disease. The quantities and the unit costs were not presented separately. Both the fixed and variable elements of laboratory costs were determined. In addition, annual equivalent costs were allocated to laboratory components of the programme, reflecting the overall use of the equipment. The follow-up costs included both the fixed and variable costs for salary.

The costs averted for major haemoglobinopathies were discounted at a rate of 6%, as recommended by HM Treasury, and represented savings per case of sickle cell disease and beta thalassaemia. The quantity of resource use appears to have been measured during 1994, whilst the prices used came from 1994 to 1995. The exception was for treating the diseases, the data for which came from studies published in 1994 and 1996.

Currency
UK pounds sterling ( ).

Sensitivity analysis
A two-way sensitivity analysis was carried out to test two significant uncertainties. These were the prevalence of traits (1, 2.5, 5 and 7.5) and the proportion that were beta thalassaemia major (25, 50 and 100%). The authors also examined the impact of decreasing the cost of lifetime treatment by 50%.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' and 'Estimates of Effectiveness' sections.

Cost results
The fixed costs of the screening programme were 8,203, while the variable costs were 21,253. This amounted to a total cost of 29,456. The fixed costs for the follow-up element of the programme were 2,756, while the variable costs were 11,944. This amounted to a total cost of 14,700. The annual programme costs were stated to be 42,269.

Synthesis of costs and benefits
The screening cost per at-risk foetus was 2,455 (29,456/12). If all major haemoglobinopathy cases had been averted through PND, the present net costs averted would have been 173,878 for sickle cell disease and 92,531 for beta thalassaemia. Given the estimate of 10% of sickle cell and 95% of beta thalassaemia cases averted, the present net costs
averted would be 17,388 for sickle cell disease and 87,904 for beta thalassaemia. This gives a total saving of 105,292.
Subtracting this from the programme cost (42,629) gives a net financial benefit of 62,663, although the authors stated "approximately" 61,100.

The sensitivity analysis revealed that the minimum net benefit was an extra cost of 1,350 at a trait prevalence of 1, of which 25% were beta thalassaemia. The maximum benefit was 305,000 at a prevalence of 7.5, of which 100% were beta thalassaemia. Reducing the treatment costs by 50% would only produce a net benefit greater than 0 if the prevalence were greater than 5%, of if the proportion of beta thalassaemia was greater than 50% and the prevalence was greater than 2.5%.

Authors’ conclusions
Antenatal screening with follow-up counselling can be self-financing at most prevalences of haemoglobinopathy traits. Greater savings were realised where a high proportion of the traits was beta thalassaemia. There was a net financial cost only at a prevalence below 2.5%, if these traits were mainly for sickle cell disease. Since there are other benefits, it is likely that antenatal screening would be considered cost-effective even at quite low levels of trait prevalence.

CRD COMMENTARY - Selection of comparators
The choice of no screening as comparator was justified given the prior lack of comparisons. The authors stated that no attempt has been made in this paper to compare universal and selective screening procedures.

Validity of estimate of measure of effectiveness
The choice of study design seems to have been appropriate given that the study set out to assess only one group of patients using only one health technology programme. However, there were several flaws in the analysis, which amount to a lack of account of the consequences of screening or not screening. First, the authors have implicitly assumed that the life of someone with a haemoglobinopathy has no positive value or benefit. It is not measured in terms of the quality of life or the number of life-years. Second, they have not accounted for test inaccuracy in that, unless the test preceding termination is 100% specific, an unaffected foetus could be aborted. Finally, if a test is not 100% sensitive, a foetus that was affected could be born. On balance, since preventing the abortion of unaffected foetuses would seem to be a priority, it is likely that specificity would be traded for sensitivity and affected foetuses would be born. Both this, and the account of the benefit of the lives of affected foetuses, would be likely to significantly underestimate the saving claimed.

Validity of estimate of costs
The unit costs were not reported separately from the quantities, which would reduce the generalisability of the findings. However, the generalisability may be affected to a certain degree by antenatal and neonatal screening programmes sharing resources at this centre. As the authors stated, this has major advantages in reducing the cost of maintaining access to the equipment and skills for an antenatal programme. The quantities that produced the savings, in terms of treatment avoided, were derived from published sources. This makes them difficult to validate. The sensitivity analyses, however, were carried out on appropriate parameters. Unfortunately, the authors have assumed that, by focusing on overall savings (net financial benefit), cost-effectiveness is so defined. This is erroneous. The term cost-effectiveness is only appropriate where there is increase in cost for an increase in benefit, the value of which is encompassed in the willingness to pay. They are thus missing the opportunity to analyse the sensitivity of cost-effectiveness in relation to a given willingness to pay threshold.

Other issues
The generalisability of the results was partially dealt with by carrying out a sensitivity analysis. However, this needs to be tempered slightly by the authors’ reference to shared costs with the neonatal programme, and how generalisable this is to other centres.
Implications of the study
The authors stated that these data, which have been unavailable until now, should help health service planners in their reassessment of the recommendation of the UK Standing Medical Advisory Committee. This recommended that universal antenatal screening should be established where greater than 15% of the local population are from the ethnic minorities.

It was recognised that further work is needed on costing care, likely decisions on the termination of pregnancy, and the value of earlier knowledge of significant haemoglobinopathies. Even so, these results suggested that antenatal screening is likely to be considered cost-effective at least in areas with haemoglobinopathy traits of at least 2.5%, especially if there is a high proportion for thalassaemia. However, these comments need to be considered in the light of the methodological flaws discussed.

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