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Review

Executive summary

Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis

D Zeuner[1]
AE Ades[1*]
J Karnon[2]
J Brown[2]
C Dezateux[1]
EN Anionwu[1]

[1] Department of Epidemiology and Public Health, Institute of Child Health, London, UK
[2] Health Economics Research Group, Brunel University, Uxbridge, UK

[*] Corresponding author

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NHS R&D HTA Programme

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Background

Antenatal haemoglobinopathy screening is intended to identify pregnancies that are at risk of an affected fetus. If the mother is identified as a carrier, testing is offered to her partner, with a view to offering prenatal diagnosis (PND) and termination of pregnancy (TOP) to carrier couples.

Neonatal testing is intended to identify newborns who are affected with sickle cell disease but not already diagnosed through PND, in order promptly to institute penicillin prophylaxis and comprehensive care, which reduce morbidity and mortality. Infants with presumed sickle cell disease are retested, and parents of affected and carrier infants are offered counselling.

Objectives of the review

The objectives were:

- to review alternative options for antenatal and neonatal haemoglobinopathy screening programmes in the UK
- to develop a decision model that compares the cost-effectiveness of universal testing and selective testing based on maternal ethnic status
- to apply the decision model to estimates of local health district ethnic composition
- to identify areas for further policy development and research.

Characterisation of alternative strategies

In a universal antenatal screening programme, all women are offered testing. In a selective programme, testing is offered to all non-north European women and to all women with a known low mean corpuscular haemoglobin (MCH) result, regardless of ethnic status. Antenatal screening for thalassaemia is therefore always universal. An alternative option, testing based exclusively on ethnicity regardless of MCH result, was examined in subsidiary analyses.

Neonatal screening would be either universal (all newborns not already diagnosed prenatally) or selective (undiagnosed babies of non-north European mothers), with selection being independent of the antenatal programme. A targeted programme, which would take account of parental carrier results to reduce the number of neonates requiring screening, was considered in subsidiary analyses. It was assumed that neonatal testing would be based on newborn heel prick samples collected on filter paper for routine phenylketonuria and congenital hypothyroidism tests. Explicit no antenatal testing and no neonatal testing policies were examined in subsidiary analyses.

Ethnic ascertainment was assumed to be part of routine antenatal booking and its costs were therefore not included in the analysis of screening, although costs were varied in sensitivity analyses.

It was assumed that the coverage of screening among ethnic minorities in a universal programme would never be less than the coverage achieved by a selective programme.

Methods

Disease progression models were developed in order to estimate the lifetime treatment costs and life expectancy of children with haemoglobinopathies and, where relevant, the effects of early diagnosis.

A computer model of the screening process was developed. For an antenatal population with any given ethnic composition, it predicted the fetal prevalence of haemoglobinopathies and calculated the costs and outcomes of each screening option.

The effectiveness of antenatal screening was measured by the expected number of women with affected fetuses who were offered choice over the outcome of a pregnancy. The number of affected live births prevented by screening was examined in subsidiary analyses. The effectiveness of neonatal screening was measured by the number of late diagnoses of sickle cell disease prevented. Costs were based on a health service perspective.

This model was applied to ethnic composition data for district health authorities in the UK, based on their 1993 boundaries. Parameter values and their ranges were identified from published and unpublished sources, informed by expert opinion. The preferred screening strategy in each district was estimated by using incremental cost-effectiveness ratios (ICERs), the additional cost of a universal compared with a selective programme per additional unit of effect.

It was assumed that districts would be willing to pay between £50,000 and £150,000 to offer an additional choice over the outcome of an affected fetus, based on an analysis of similar screening programmes, and between £10,000 and £50,000 to prevent an additional late diagnosis of sickle cell disease, based on review of other neonatal screening programmes and the estimated benefits of early diagnosis. Estimated lifetime treatment costs were used as benchmarks for affected live birth prevented ICERs in subsidiary analyses.

Results

Findings relevant to both antenatal and neonatal screening

- Neither antenatal screening of north European women nor neonatal screening of their children is cost-effective

under the criteria used in the review, even under extreme assumptions about the frequency of the sickle cell trait and inter-ethnic unions.
- The rationale for universal screening is therefore based on the presumption that it will result in a higher coverage among ethnic minority women and their children.
- Lowering the failure to screen rate in a selective programme is always more cost-effective than changing to a universal policy.
- Selective screening is highly cost-effective compared with no screening.
- If costs of ethnic ascertainment and pretest counselling are included, the case for universal compared with selective screening is slightly strengthened, but the case for selective screening compared with no screening is substantially weakened.
- The use of economic criteria alone to determine whether a local screening policy should be universal or selective is not equitable: ethnic minority mothers and infants in lower-prevalence areas would receive a lower-coverage screening service than would be available to them in a high-prevalence area.

Findings relevant to antenatal screening alone

- Universal antenatal screening costs were estimated to be in the range £35,000–£145,000 per 10,000 antenatal population, and increased with prevalence. Selective screening costs were £30,000 less in low-prevalence areas and £18,000 less in high-prevalence areas.
- Adverse screening outcomes (PND-induced miscarriage, TOP with unaffected fetuses) would be very rare in both universal and selective strategies.
- If the purpose of antenatal screening was the prevention of affected live births rather than the offering of reproductive choice, universal screening would be difficult to justify in any district in the UK on the basis of costs averted, but selective screening would still be preferred to no screening.

Findings relevant to neonatal screening alone

- Universal neonatal screening was estimated to cost approximately £22,000 per 10,000 antenatal population. Selective neonatal screening costs range from less than £200 per 10,000 antenatal population to £11,500 in an area with 50% of the population from ethnic minorities.
- Antenatal screening, even if universal, would not render neonatal screening redundant at currently estimated rates of PND uptake (approximately 15% in black women). A high (80%) uptake of PND would considerably weaken the case for universal screening, but would not affect the case for selective neonatal screening in preference to no neonatal screening.
- The costs associated with neonatally identified carrier infants are small in relation to overall programme costs and do not alter the comparative cost-effectiveness of universal and selective strategies.
- The targeted screening of infants is a cost-effective alternative to selective screening, but would require robust information systems that have not yet been developed.

Conclusions

- Selective screening is cost-effective in comparison with no screening.
- Universal screening may be cost-effective in higher-prevalence districts, depending on the coverage of selective screening and economic willingness-to-pay criteria.
- On baseline assumptions, if coverage among ethnic minorities in selective screening was 5% lower than in universal screening, a universal antenatal strategy would be cost-effective at a fetal sickle cell disease prevalence above 5–12 per 10,000 antenatal population and a universal neonatal strategy would be cost-effective at a prevalence above 7–18 per 10,000.
- Based on the health districts pertaining in 1993, the model would imply that up to 15 out of 170 districts should consider universal antenatal and/or universal neonatal screening. However, if selective screening obtained a coverage only 1% lower than universal screening, the latter would be required in, at most, two districts.
- Equity considerations suggest that:
  - all districts could justifiably consider adopting explicit selective or universal strategies for antenatal and neonatal screening
  - local policy could be determined on the basis of the same economic and prevalence criteria, applied nationally
  - minimum standards for coverage of screening could be adopted and coverage monitored routinely
  - procedures for selection based on ethnicity could be standardised.

Implications and recommendations

- Research is needed to develop information protocols that can routinely deliver statistics on the coverage of antenatal and neonatal screening within ethnic groups. A pilot study in which such protocols are implemented should be considered.
- Research is needed to:
  - establish the prevalence of fetal haemoglobinopathies throughout the UK
  - ascertain the frequency and causes of: (1) the failure to offer reproductive choice to mothers with an affected fetus; and (2) the late diagnosis of haemoglobinopathies in children
  - determine the relationship between the timing of maternal carrier and couple testing and the uptake of PND and TOP.
- Medicolegal and ethical studies are needed to determine how much pretest information about antenatal and neonatal screening is required, in order that consent to testing can be considered to be informed.

Publication

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NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Population Screening Panel and funded as project number 93/33/01.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,
Mailpoint 728, Boldrewood,
University of Southampton,
Southampton, SO16 7PX, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@soton.ac.uk
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