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Review

Executive summary

Neonatal screening for inborn errors of metabolism: cost, yield and outcome

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Health Technology Assessment
NHS R&D HTA Programme

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Objectives

- To systematically review the literature on inborn errors of metabolism, neonatal screening technology and screening programmes in order to analyse the costs and benefits of introducing screening based on tandem mass-spectrometry (tandem MS) for a wide range of disorders of amino acid and organic acid metabolism in the UK.

- To evaluate screening for cystic fibrosis, Duchenne muscular dystrophy and other disorders which are tested on an individual basis.

How the research was conducted

Systematic searches were carried out of the literature on inborn errors of metabolism, neonatal screening programmes, tandem MS-based neonatal screening technology, economic evaluations of neonatal screening programmes and psychological aspects of neonatal screening. Background material on the biology of inherited metabolic disease, the basic philosophy, and the history and current status of the UK screening programme was also collected. Relevant papers in the grey literature and recent publications were identified by hand-searching. Each paper was graded. For each disease an aggregate grade for the state of knowledge in six key areas was awarded.

Additional data were prospectively collected on activity and costs in UK neonatal screening laboratories, and expert clinical opinion on current treatment modalities and outcomes. These data were used to construct a decision-analysis model of neonatal screening technologies, comparing tandem MS with the existing phenylketonuria screening methods. This model determined the cost per additional case identified and, for each disease, the additional treatment costs per case, and the cost per life-year saved. All costs and benefits were discounted at 6% per annum. One-way sensitivity analysis was performed showing the effect of varying the discount rate, the incidence rate of each disorder, the number of neonates screened and the cost of tandem MS, on the cost per life-year gained.

Research findings

The UK screening programmes for phenylketonuria and congenital hypothyroidism have largely achieved the expected objectives and are cost-effective. Current concerns are the difficulty of maintaining adequate coverage, perceived organisational weaknesses, and a lack of overview.

For many of the organic acid disorders it was necessary to rely on data obtained from clinically-diagnosed cases. Many of these diseases can be treated very effectively and a sensitive screening test was available for most of the diseases.

Except for cystic fibrosis, there have been no randomised controlled trials of the overall effectiveness of neonatal screening.

Despite the anxiety generated by the screening process, there is strong parental support for screening. The effects of diagnosis through screening on subsequent reproductive behaviour is less clear.

Conflicts exist between current concepts and the traditional principles of screening. The availability of effective treatment is not an absolute prerequisite: early diagnosis is of value to the family concerned and, to the extent that is leads to increased use of prenatal diagnosis, may help to reduce the overall burden of disease. Neonatal screening is also of value in diseases which present early but with non-specific symptoms. Indeed, almost all of the diseases considered could merit neonatal screening.

The majority of economic evaluations failed to incorporate the health benefits from screening, and therefore failed to address the value of the information which the screening programmes provided to parents.

The marginal cost of changing from present technology to tandem MS would be approximately £0.60 per baby at a workload of 100,000 samples a year, and £0.87 at 50,000 samples per year. The ability to screen for a wider range of diseases would lead to the identification of some 20 additional cases per 100,000 infants screened, giving a laboratory cost per additional diagnosis of £3000 at an annual workload of 100,000 babies per year.

This compares with average, approximate laboratory costs of £6000 for diagnosing a case of phenylketonuria and £4000 for congenital hypothyroidism, and costs including specimen collection of £27,000 and £15,000, respectively.

The overall marginal costs of screening for additional disorders will include the additional costs of earlier treatment of all patients and the additional lifetime costs of treatment of those patients who would have died in the absence of screening, e.g. for the fatty acid oxidation defects. For a population with 100,000 births per year, short-term costs are estimated at £18,000 per year with long-term costs rising eventually to £174,000 per year. There are likely to be substantial cost-savings to set against these treatment costs.

The health benefits of diagnosis by neonatal screening range from prevention of mental retardation, severe neurological disease, or physical deformity, to avoidance of sudden death. The model only included the mortality health benefits and did not incorporate a measure of quality of life or the non-health benefits of screening. The results can be viewed as conservative estimates of the total benefits of screening for each disease. The data on the treatment efficacy and life expectancy with treatment are largely based on clinical opinion, and may therefore be open to challenge. However, there are so few cases of each of these diseases that it is unrealistic to look for an alternative source of data. The estimated treatment cost per life-year saved ranged from £8339 for tyrosinaemia type I to £31 for medium-chain acyl-CoA dehydrogenase deficiency.

The case for screening for cystic fibrosis has been examined in some detail. The cost is small relative to the total cost of the disease, there are recognised short-term benefits and emerging evidence of long-term benefits from very early treatment.

Main recommendations

- The existing programmes for phenylketonuria and congenital hypothyroidism should be continued, but consideration should be given to strengthening the organisation by the establishment of a national multidisciplinary forum to give guidance on performance criteria, organisational matters and monitor the impact of introducing new screens.

- The Welsh scheme for Duchenne muscular dystrophy should be continued on a research basis and the findings used to inform decisions on introducing screening elsewhere.

- Performance data should be collected from the current UK screening programmes for cystic fibrosis. Expansion of screening for this disease should be encouraged.

- There appears to be a strong case for introducing tandem MS-based screening. Screening should be limited to clearly-defined diseases where specificity is known to be adequate and there are satisfactory confirmatory tests. Given the technical complexity of the method, the large number of diseases covered, and limited experience of applying tandem MS-based screening to UK populations, a 3-year pilot study is proposed as detailed in the main text of the report.

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.

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.

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