Comparing the clinical and economic effects of clinical examination, pulse oximetry, and echocardiography in newborn screening for congenital heart defects: a probabilistic cost-effectiveness model and value of information analysis

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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
Strategies for screening newborns for congenital heart defects (CHDs) were evaluated. These were clinical examination alone, clinical examination with pulse oximetry, and clinical examination with screening echocardiography.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 live born infants.

Setting
The setting was outpatient care. The economic study was carried out in the UK.

Dates to which data relate
The sources of the effectiveness data dated from 1994 to 2004, while those of resource use were from 1999 to 2001. The price year used was 2000/01.

Source of effectiveness data
In order to populate the model, the parameters included were those relating to the following:

the prevalence of defect-specific unrecognised CHDs at the point of screening and collapse before diagnosis,
the test performance characteristics (detection rates and false-positive rates), and
other probabilities (screening coverage for each of the strategies, probabilities of diagnosis without cardiovascular collapse in an affected infant given a negative screening result or no screening between 1 and 16 years, etc.).

These details were presented in one table in the paper and in two supplemental tables online.

Modelling
A decision tree with a horizon up to the time of diagnosis was developed. Details of the model, such as the clinical and epidemiological data inputs, as well as modelling assumptions, were described in the paper. As there was no randomised
comparison amongst the proposed strategies, published and unpublished observational data were used in the model.

**Sources searched to identify primary studies**
A broad range of data sources (both published and unpublished) was considered. These included a small randomised controlled trial, population-based registries, and other observational studies. These data were supplemented by expert opinion where other data sources were unavailable.

**Methods used to judge relevance and validity, and for extracting data**
Data for prevalence at screen and birth, test performance and risk of cardiovascular collapse were derived from a systematic review and from a population-based register of CHDs in the Northern Region of England. Searches for the systematic review were conducted using MEDLINE (1966 onward), EMBASE (1980 onward) and CINAHL (1982 onward)’ no other details of the review were given. Where data were not available, subjective probabilities were elicited from the consensus reached by two or three paediatric cardiologists and then translated to probability distributions.

**Measure of benefits used in the economic analysis**
The measure of benefit used was timely diagnosis per 100,000 births. This was defined as a diagnosis made preoperatively before collapse or death occurred. Timely diagnosis and diagnosis of clinically significant CHD was considered a secondary outcome.

**Direct costs**
The health service costs considered were those of screening and diagnostic tests, management of collapsed infants, staff, equipment, consumables and overheads. These costs were adjusted to 2000/01 prices but were not discounted as the model involved a 1-year time horizon. Sources included primary observations at hospitals, department of health statistics, a study of the literature and expert opinion. The unit costs were estimated from national statistics. The marginal costs were provided.

**Statistical analysis of costs**
No statistical analysis of the costs was performed.

**Indirect Costs**
No productivity costs were included.

**Currency**
UK pounds sterling (). The conversion rate (13 September 2006) was 1 = US $1.872 = EUR 1.478.

**Sensitivity analysis**
The robustness of the base-case analysis was tested through a series of one-way sensitivity analyses. Parameter uncertainty was evaluated through a probabilistic sensitivity analysis, and probability distributions to input parameters were defined. The results were displayed using cost-effectiveness acceptability curves. In addition, a value-of-information analysis was used to assess the value of perfect information, and the partial expected value of information for groups of model input parameters.

**Estimated benefits used in the economic analysis**
Timely diagnosis per 100,000 births was 34.0 for clinical diagnosis, 70.6 for pulse oximetry and 71.3 for screening echocardiography.
For the secondary outcome (timely diagnosis and diagnosis of clinically significant CHD), the result was 222.4 for clinical diagnosis, 342.2 for pulse oximetry and 427.4 for screening echocardiography.

Additional clinical information was also presented for each strategy. This comprised the expected number of life-threatening and other CHDs at birth and at screen, the number screened, the true- and false-positive screening results, the true- and false-negative screening results, the detection rates and the positive predictive values.

**Cost results**
The total costs per 100,000 births were 296,891 for clinical diagnosis, 476,193 for pulse oximetry and 3,540,388 for screening echocardiography.

**Synthesis of costs and benefits**
The cost per additional timely diagnosis was 4,894 for pulse oximetry compared with clinical examination, and 4,496,666 for screening echocardiography compared with pulse oximetry. These figures decreased to 1,489 and 36,013, respectively, when using the secondary outcome.

The results were sensitive to the detection rates for screening echocardiography and age at screening, but were robust to assumptions about antenatal detection rates when using published ranges, the availability of diagnostic echocardiography and the coverage of screening echocardiography. The probability that pulse oximetry was cost-effective was over 0.90 if decision-makers were willing to pay between 10,000 and 100,000 for a timely diagnosis.

The maximum monetary value of further research for an arbitrary cost-effectiveness threshold of 50,000 per timely diagnosis was 744,000 for the primary outcome and 14,450,000 for the secondary outcomes. Key determinants of cost-effectiveness with a maximum value of future research were detection rates of pulse oximetry, screening echocardiography, and screening test costs. Disbenefits associated with false-positive screens were not evaluated.

**Authors' conclusions**
The addition of pulse oximetry to clinical examination is likely to be a cost-effective strategy for screening newborns for congenital heart defects (CHDs). Screening echocardiography is unlikely to be cost-effective, unless the detection of all clinically significant CHDs is considered beneficial and a 5% false-positive rate acceptable.

**CRD COMMENTARY - Selection of comparators**
The authors justified the evaluation of feasible new technologies such as pulse oximetry and echocardiography in order to improve current screening strategies based on clinical examination alone (baseline comparator in the authors' setting). You should decide if these are appropriate technologies in your own setting.

**Validity of estimate of measure of effectiveness**
Parameters were derived both from published and unpublished results, as well as from expert opinion. Though some synthesis was performed and occasionally described, it was unclear what methods were used to do so. In common with other modelling studies, there was only a brief description of the databases searched, and no details of the search strategies, retrieved studies, or inclusion or exclusion criteria of the studies. Nevertheless, the authors seem to have used adequate data sources for the parameters.

**Validity of estimate of measure of benefit**
The estimation of benefit (timely diagnosis) was appropriately derived using the decision model. The authors acknowledged the limitations of not capturing the disbenefits associated with false-positive screens; these were mainly due to lack of field data and methodology relating to health-related quality of life in newborns.

**Validity of estimate of costs**
From the health service perspective adopted, the most relevant cost categories seem to have been included. An omission that would mainly affect echocardiography, owing to its higher false-positive rate, was the cost of false-positive infants. The resource quantities and prices were taken from published sources. The price year and adjustments were adequately reported, and data were not discounted because of the 1-year time horizon. The sources of the unit costs included primary observations in the authors' setting, published national sources and expert opinion. The costs and the quantities were, in the main, reported separately.

**Other issues**
The authors made no comparisons with other studies. In addition, the generalisability to other settings was not addressed. As the authors stated, owing to the limitations of the data, the model relied extensively on expert opinion. A further stated limitation was the lack of information on the dependence of age at screening and test performance.

**Implications of the study**
The authors stated that there appears to be scope to improve the effectiveness of newborn screening policies for CHDs by implementing a combined strategy of pulse oximetry and clinical examination. Nevertheless, before implementing this strategy in clinical practice, the development of protocols to specify the measurement of oxygen saturation and the proper investigation of positive screening results, as well as considering the benefit of identifying respiratory and neurological abnormalities also, is important. Further research, aimed at reducing uncertainties surrounding the use of pulse oximetry as a population screening strategy, is about to be commissioned as a result of this study.

**Source of funding**
Funded by the National Health Service Health Technology Assessment Programme.

**Bibliographic details**

**PubMedID**
17493305

**DOI**
10.1017/S0266462307070304

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cost-Benefit Analysis; Echocardiography; Great Britain; Heart Defects, Congenital /diagnosis; Humans; Infant, Newborn; Neonatal Screening /economics /methods; Oximetry /methods; State Medicine

**AccessionNumber**
22007008112

**Date bibliographic record published**
31/07/2007

**Date abstract record published**
31/07/2007