Prenatal cystic fibrosis screening in Mexican Americans: an economic 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
The use of a prenatal genetic sequential screening programme for cystic fibrosis (CF), compared with no screening strategy, in Mexican American gravid women.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised Mexican American pregnant women with single gestations who were seeking prenatal care with known partners of the same ethnic background. This was the first pregnancy (and therefore first screening) for both the women and their partners, but there was no independent reason for undergoing amniocentesis, such as advanced maternal age. Aside from different carrier frequency and prevalence of CF, Hispanic American individuals differ from individuals from white populations in CF alleles, and this alters the sensitivity of the CF screening tests. In addition, Hispanic American individuals have different cultural beliefs concerning the acceptance of amniocentesis and the termination of a pregnancy in the case of a foetal anomaly.

Setting
The setting was secondary care. The economic evaluation was conducted in the University of Texas, Houston (TX), USA.

Dates to which data relate
Both the effectiveness and cost data were taken from literature published between 1994 and 2002. The costs were probably uplifted to 2002 prices, but this was explicitly stated only for one cost component.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A model was used to evaluate the cost and expected outcome in terms of the number of CF cases found with a prenatal sequential screening strategy and with no screening. The model was formed as a decision tree. It was assumed that the woman was tested first. Her partner was examined if she tested positive for carrier status. If both partners proved to be carriers then, following the woman's consent, an amniocentesis was performed as the foetal diagnostic test. If the foetus tested positive for CF disease, there was the option of pregnancy termination, if the woman agreed.
Outcomes assessed in the review
The outcomes assessed in the review referred specifically to the Mexican American population. The outcomes assessed were:

the carrier frequency and the prevalence of CF,

the detection rate of carrier status (i.e. sensitivity of the screening test), and

the acceptance rates for amniocentesis and pregnancy termination.

Study designs and other criteria for inclusion in the review
The review included all published references concerning CF screening in Mexican American women. No further details of other inclusion or exclusion criteria were provided.

Sources searched to identify primary studies
The authors searched PubMed.

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
Approximately 5 primary studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not reported.

Results of the review
The carrier frequency of CF in Mexican individuals was 1 in 46 (22%).

The prevalence of CF in Hispanic individuals was 1 in 8,500.

The detection rate in Hispanic individuals was 57%.

The acceptance rates for amniocentesis and pregnancy termination were both 75%.

Methods used to derive estimates of effectiveness
The authors made some assumptions about the structure of the model.

Estimates of effectiveness and key assumptions
The authors assumed the following:

- Female and male partners shared the same ethnic makeup and risk factors;
- The standard mutation panel was used for screening both women and their partners;
- Screening was offered in time to consider prenatal diagnosis if the couple was found to be at risk;
- Serum samples were collected when blood was drawn for other tests in the first prenatal visit;
- If screening was declined, or if the result was negative, the pregnancy resulted in a normal term delivery;
- There were no false-positive results for disease or carrier status, and the false-negative rate was considered under the heading of test sensitivity;
- Foetal diagnosis by amniocentesis was 100% accurate.

**Measure of benefits used in the economic analysis**
The measure of benefit implicitly used in the analysis was the net benefit per case of CF averted. This is the difference between the cost of care saved and the direct cost of the intervention.

**Direct costs**
The perspective adopted in the economic analysis was that of a third-party payer. Most of the costs relevant to this perspective were included in the analysis. These comprised the costs of CF screening, amniocentesis and termination, and the costs of caring for a child with CF. Genetic counselling costs were included in the amniocentesis package. The cost data were derived from literature published between 1994 and 2002. The total costs resulting from the adoption of the screening strategy were derived through modelling.

The quantities and the costs were not analysed separately in relation to the health care cost of a child with CF. In terms of the screening programme, discounting was not relevant since the costs were incurred during less than one year. The cost of caring for a child with CF, as adopted from the literature, was inflated at an annual rate of 3% to the 2002 price. However, it was not reported whether the initial value of this cost was discounted, or the time during which this cost was incurred. The year to which the rest of the costs referred was not explicitly reported.

**Statistical analysis of costs**
The costs were treated deterministically. No statistical analysis of the costs was performed.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and two-way sensitivity analyses were carried out to examine the robustness of the results. The parameters examined in the one-way analysis were the screening test cost, the test sensitivity, and the acceptance rates for amniocentesis and pregnancy termination. The two-way analyses were performed by simultaneously varying the screening test cost and the test sensitivity, and the screening test cost and the acceptance rate for pregnancy termination. The range of values used covered the total possible range (0% to 100%) for the acceptance rates. A wide range of values (from 0 to an upper realistic value) was used for the other parameters examined. Threshold analyses were also performed.
conducted to determine under what conditions the screening strategy would be cost-effective.

**Estimated benefits used in the economic analysis**
The total number of CF cases averted due to the screening strategy was not reported. The total cost of the screening programme per case averted was $1,234,568. The direct cost of screening per case averted was $1,000,000. Thus, the net benefit was -$234,568.

**Cost results**
See the 'Estimated Benefits ...' section.

**Synthesis of costs and benefits**
The net cost of averting a case of CF was $250,000. One-way sensitivity analyses showed that the results were generally robust for a wide range of assumptions. The exception was a test sensitivity of 90%, which would result in the screening strategy providing net savings (a test with this sensitivity was not available in Mexican American women at the time of the study). Such a high degree of test sensitivity would, in practice, require a higher screening test cost. However, it was reported that the two-way sensitivity analysis showed that if the test sensitivity was greater than 90%, a screening test cost of less than $100,000 would result in net savings (described as cost beneficial). In addition, there was a range of acceptance rates for amniocentesis where the screening was shown to be cost-beneficial, with the screening test cost being lower than $40,000 at the same time. The threshold analysis revealed that if the baseline assumptions were held constant, the test needed to be priced below $53,000 to be cost beneficial. Under the most favourable assumptions for screening, the test needed to cost less than $100,000 for it to be cost beneficial.

**Authors' conclusions**
The prenatal screening strategy for cystic fibrosis (CF) in Mexican American women was not cost beneficial (it resulted in net costs and not savings) over a wide range of assumptions.

**CRD COMMENTARY - Selection of comparators**
The screening strategy was evaluated in terms of the net costs or benefits derived from its implementation, so that the implicit comparator was no screening. This allowed the active value of the intervention to be estimated.

**Validity of estimate of measure of effectiveness**
The authors stated that a review of the literature had been conducted. However, the methods and conduct of the review were not reported. It was not stated whether the effectiveness data from the primary studies were combined, or whether the impact of differences between the primary studies was explored. The authors made key assumptions concerning the model structure, but not the effectiveness estimates.

**Validity of estimate of measure of benefit**
The measure of benefit was the net benefit (the difference between the cost of care saved and the cost of the intervention). The authors stated that this does not cover quality of life issues, or any measure of health benefit for that matter.

**Validity of estimate of costs**
All the categories of cost relevant to the perspective adopted were included in the analysis, with the exception of the cost likely to arise after amniocentesis, in the case of miscarriage. The quantities and the costs were not reported separately, but this would be appropriate mainly at the estimation of the health care cost of a child with CF. A sensitivity analysis was conducted, examining only the impact of the screening test cost on the results. Discounting was not relevant in relation to the costs of the screening strategy, but it was probably relevant in the case of the health care
cost of a child with CF. However, this cost was adopted from the literature and it was not reported whether it had been discounted. The year to which the prices referred was explicitly stated only for this latter cost (health care cost of a child with CF).

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of the generalisability of the results to other settings was not addressed. The authors appear to have presented their results in full. One limitation of the study, according to the authors, was that they did not attempt to capture the indirect costs and quantify, in monetary values, quality of life issues. Essentially, a third-party payer perspective was taken and the authors' conclusions and study implications must be assessed with that in mind. Thus, the authors' conclusions reflected the scope of the analysis.

Implications of the study
According to the authors, the role of the cost analysis was not to determine whether the screening strategy should be implemented, but only to contribute to the decision-making, along with other scientific, policy, ethical and moral issues. They suggested that the genetic screening programme defined the target population and the frequency and severity of the disease within particular ethnic groups. In addition, recommendations from the American College of Obstetricians and Gynaecologists and the American College of Medical Genetics should be revised.

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