Cost effectiveness of DNA diagnosis for four monogenic diseases

van der Riet A A, van Hout B A, Rutten F F

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
Use of DNA diagnosis for carrier screening or prenatal diagnosis in the retrospective genetic counselling (triggered by previous information) of couples at risk of having a monogenic disease and who sought genetic counselling because of their reproductive plans. Four diseases were considered: cystic fibrosis (CF), Duchenne muscular dystrophy, myotonic dystrophy, and fragile X syndrome.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Couples at risk of having monogenic diseases and who sought genetic counselling because of their reproductive plans.

Setting
Hospital. The economic study was carried out in the Netherlands.

Dates to which data relate
Effectiveness data were based on literature published between 1972 and 1995. Resource use data and their collection dates were not reported. The price year was 1994.

Source of effectiveness data
Effectiveness data were derived from a literature review and assumptions made by the authors.

Modelling
A decision tree was developed to estimates the costs and benefits associated with each strategy.

Outcomes assessed in the review
The outcomes assessed were the percentage of at risk couples choosing (further) offspring, carrier screening, prenatal diagnosis, and termination of pregnancy when the fetus was affected. Outcomes were separately reported for two groups of couples: those with a greater than 10% risk of an affected child and those with a less than 10% risk of having an affected child. The percentage of all CF mutations identified, the risk of infertility, and the risk of induced abortion after chorionic villus sampling were also reported.
Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 13 studies were directly used as references for the clinical probabilities incorporated in the model. Reference was made to a further 4 studies to support some descriptive claims.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The values for the clinical probabilities were:

No form of carrier or prenatal diagnosis available.

Couples with a greater than 10% risk of an affected child:
50% for all diseases considered except CF; and
30% (range: 30 - 70%) for CF.

Couples with a less than 10% risk of an affected child:
80% for all diseases considered.

DNA diagnosis available:
percentage of at risk couple choosing carrier screening, 100% (>10% risk) and 90% (< 10% risk);
percentage of at risk couples choosing (further) offspring, 85% (range: 60 - 100%);
percentage of at risk couples choosing prenatal diagnosis, 90% (range: 60 - 100%); and
termination of pregnancy when the fetus is affected, 99%.

In addition, the percentage of all CF mutations identified after analysis of the 10 most frequent mutations was 85%, the risk of infertility was 10%, and the risk of induced abortion after chorionic villus sampling was 1%.
Methods used to derive estimates of effectiveness
Estimates of effectiveness were also based on the authors' assumptions.

Estimates of effectiveness and key assumptions
The percentage of at risk couples (with a less than 10% risk of having an affected child) choosing carrier screening was 90% (range: 60 - 100%). The efficacy of DNA diagnosis in identifying DMD mutation in female carriers or male fetuses in families where the mutation was already known was 96.5%.

Measure of benefits used in the economic analysis
The measures of benefits used were the incremental number of couples achieving pregnancy, number of healthy children, number of affected children, and number of terminated pregnancies compared to the pedigree analysis for 100 counselling couples in distinct risk groups.

Direct costs
Costs were discounted. Quantities were not reported separately from the costs but cost items were reported separately. Cost analysis covered the costs of DNA test, deliveries, abortions, curettage, and lifetime costs of CF, DMD, congenital myotonic dystrophy (CMD), and fragile X syndrome. The perspective adopted in the cost analysis was that of the health system. The profile of resource use data related to three of the monogenic diseases (except for CF) was supplied by expert panels. The average costs of a test in four major DNA laboratories in the Netherlands were used for the costs of carrier screening and prenatal screening. Dutch tariffs were used for delivery and abortion costs. The sources of cost data for the treatment of the monogenic diseases were global "burden of illness" studies in 1994 or a published study in 1996. The date of the price data was 1994.

Indirect Costs
Indirect costs were not considered.

Currency
Dutch guilders (Dfl). The 1994 exchange rate was US$1= Dfl 1.82.

Sensitivity analysis
A series of one-way sensitivity analyses was performed on all baseline assumptions and threshold values were identified for the sensitive parameters.

Estimated benefits used in the economic analysis
For CF, the effects of DNA diagnosis, compared to the pedigree analysis for 100 counselling couples, when prior risk of parents being carriers (children affected) was 1 (1:4), were as follows:

incremental number of couples achieving pregnancy, 55;

healthy children, 40.7;

affected children prevented, 5.2; and

terminated pregnancies, 19.2

Values were also reported for all other diseases and risk categories.
Cost results
The incremental costs of DNA diagnosis per counselling couple compared to pedigree analysis were positive for three risk categories for CF disease were:

1:45 risk of parents being carriers (1:180 prior risk of an affected child) : Dfl42
1:60 risk of parents being carriers (1:240 prior risk of an affected child): Dfl854
1:120 risk of parents being carriers (1:240 prior risk of an affected child): Dfl 2075

For CF with risk category 1 (1:4), and for all other diseases and risk categories, incremental costs were negative, ranging from Dfl 16,956 to Dfl 321,417. The discount rate was 5%.

Synthesis of costs and benefits
Costs and benefits were not combined since the use of DNA diagnosis was the dominant strategy in most risk categories. The sensitivity analysis established that in most cases the positive benefits and cost savings associated with the intervention did not change.

Authors' conclusions
DNA diagnosis appears to be quite cost-effective in the diseases considered here.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.

Validity of estimate of measure of benefit
The internal validity of the effectiveness results cannot be assessed due to lack of information regarding the methodology adopted in the literature review. The benefits were estimated using decision-modelling techniques, which appears to be appropriate for the study question.

Validity of estimate of costs
Some details of the methods of cost estimation were given. However, quantities were not reported separately from the costs. Only health care costs were considered, excluding costs to patients and others in society. A discount rate of 5% was applied which might differ from the rates used in other countries. Cost results might not be generalisable to other settings.

Other issues
The authors' conclusions seem to be justified given the relatively comprehensive sensitivity analysis performed, which also addressed the issue of generalisability to other settings or countries. Comparisons with other studies were not made.

Implications of the study
Two implications were noted by the authors from this study:

(1) in terms of the cost-effectiveness of the intervention, an investigation can be initiated on a broader application of this counselling service not only to couples seeking genetic counselling but through "actively searching for families with high risk profiles (for example, by testing the mentally disabled for fra(X))";

(2) on the basis of this study, the Dutch authorities decided "to incorporate this activity into the package of health care
services available to all those publicly insured in The Netherlands”.

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