Cost-effectiveness analysis of genetic screening for the Taq1B polymorphism in the secondary prevention of coronary heart disease

Kemp L K, Doran C M, Vos T, Hall W

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 study investigated the genetic testing of coronary heart disease (CHD) and stroke patients for the Taq1B polymorphism before prescribing a treatment. The impact of screening was assessed by comparing four different prescribing scenarios, depending on the results of the screening. The scenarios compared were as follows.

Scenario 1 was to prescribe statins to patients with the B2B2 genotype.

Scenario 2 was to prescribe statins to patient with either the B1B2 or B2B2 genotypes.

Scenario 3 was to prescribe statins regardless of genotype.

Scenario 4 was to prescribe statins to patients with either the B1B2 or B2B2 genotypes and to prescribe ezetimibe in the case of all other genotypes.

Type of intervention
Screening and treatment.

Economic study type
Cost-utility analysis.

Study population
The target population comprised Australian patients in the year 2000, who were aged between 35 and 84 years and who had experienced a stroke and/or CHD event. The study population was divided into ten age groups. No further exclusion or exclusion criteria were reported.

Setting
The setting was not explicitly reported. The economic study was carried out in Australia.

Dates to which data relate
The effectiveness and epidemiological data used to populate the model were obtained from studies published between 1996 and 2004. The price year was 2000.

Source of effectiveness data
The clinical parameters associated with statin effectiveness by genotype included the relative risk (RR) of stroke and CHD mortality. The RR of stroke and CHD for those treated with ezetimibe were also considered in the model. The model also included many age- and gender-dependent epidemiological parameters related to the incidence and fatality rate of CHD, ischaemic stroke and haemorrhagic stroke. However, although the sources of age- and gender-dependent
epidemiological input parameters were referenced, their values were not explicitly reported.

Modelling
A Markov model was used to estimate the long-term economic and health effects of genetic screening of CHD and stroke patients before prescribing statins. The model had been designed for the Assessing Cost-Effectiveness-Heart Disease project. The time horizon reflected the patients’ lifetime or, alternatively, it was run until patients reached the age of 100 years. Details such as the health states, cycle length and modelling assumptions were all reported.

Sources searched to identify primary studies
The effectiveness data on statin treatment by genotype were derived from a published observational study and were compared with the values reported in a meta-analysis. The RR of first-ever stroke in patients with CHD or stroke patients was derived from the Danish Monitoring of Trends and Determinants in Cardiovascular Disease study (MONICA) (Knuiman et al. 1996, 1997, 1998, see ‘Other Publications of Related Interest’ below for bibliographic details). The design of the study was not clear. The RR of stroke and CHD in those treated with ezetimibe were obtained from an unpublished meta-analysis of seven randomised controlled trials. The proportion of the overall trend in mortality assigned to incidence versus case-fatality was based on authors' assumptions.

Methods used to judge relevance and validity, and for extracting data
The process used to identify the data was not reported. No inclusion criteria for any parameters were specified. The method used to select the estimates was not discussed.

Measure of benefits used in the economic analysis
The measure of benefit used was the disability-adjusted life-years (DALYs) averted. The total number of years alive with CHD or stroke was estimated in the Markov model. The years alive were adjusted to DALYs using disability weights obtained from the Australian Board of Disease Study (Mathers et al. 1999, see ‘Other Publications of Related Interest’ below for bibliographic details). The benefits were discounted at a rate of 3%.

Direct costs
The study reported the direct costs to the health service. These were the initial cost of the genetic test, the cost of statins and ezetimibe, follow-up general practitioner consultations, tests for measuring lipid levels and liver function, and treatment costs for CHD and stroke. Resource use was derived from official sources and published studies. Aggregated treatment costs for CHD and stroke were reported, while for all other categories the unit costs and the resource quantities were reported separately. The costs were reported as the average cost per patient. All costs were appropriately adjusted for inflation using the medical component of the Consumer Price Index, and were reported for the price year 2000. The costs were appropriately discounted.

Statistical analysis of costs
No statistical analyses of the costs were conducted.

Indirect Costs
Productivity costs were not included in the analysis.

Currency
Australian dollars (AUD).

Sensitivity analysis
Parameter uncertainty was investigated through a probabilistic sensitivity analysis. All the parameters in the model were assigned prior probability distributions and the ranges used were reported. No expected-value-of-information analysis was performed. It was also reported that, for each model, a Monte Carlo simulation of 2,000 iterations was run.

**Estimated benefits used in the economic analysis**

The estimated benefits were reported for the whole population:

- treating all patients with statins resulted in 75,922 DALYs averted (95% confidence interval, CI: 46,456 to 106,659);
- treating B2B2 patients with statins resulted in 21,814 DALYs averted (95% CI: 10,169 to 32,252);
- treating B1B2 and B2B2 patients with statins resulted in 68,043 DALYs averted (95% CI: 54,618 to 93,033); and
- treating B1B2 and B2B2 patients with statins and B1B1 patients with ezetimibe resulted in 84,302 DALYs averted (95% CI: 56,215 to 114,688).

**Cost results**

The costs were reported for the whole population:

- treating all patients with statins resulted in a cost of AUD 2008 million (95% CI: 1,418 to 2,742);
- treating B2B2 patients with statins resulted in a cost of AUD 385 million (95% CI: 276 to 526);
- treating B1B2 and B2B2 patients with statins resulted in a cost of AUD 1,416 million (95% CI: 1,006 to 1,932); and
- treating B1B2 and B2B2 patients with statins and B1B1 patients with ezetimibe resulted in a cost of AUD 1,961 million (95% CI: 1,390 to 2,676).

**Synthesis of costs and benefits**

An incremental cost-effectiveness analysis was performed. The authors used a maximum willingness-to-pay threshold of AUD 50,000 per DALY averted.

Compared with treating all patients with statins, genetic screening and prescribing statins to B1B2 and B2B2 patients proved to be cost-effective in 89% of iterations and dominant 1% of the time.

Compared with treating all B1B2 and B2B2 patients with statins, treating B1B2 and B2B2 patients with statins and B1B1 patients with ezetimibe was cost-effective 98% of the time.

The sensitivity analyses demonstrated the robustness of the results on the cost-effectiveness of treatment with statins only for patients with the B1B2 or B2B2 genotypes. However, the results for the other strategies were not reported.

**Authors’ conclusions**

The most preferred strategy was to treat patients with the B1B2 or B2B2 genotype with statins and those with the B1B1 genotype with ezetimibe.

**CRD COMMENTARY - Selection of comparators**

The choice of the comparators was justified. Prescribing statins to all patients without genetic tests and regardless of the genotype would seem to represent current practice in the authors’ setting. You should decide if this represents a valid comparator in your own setting.
Validity of estimate of measure of effectiveness
The parameters were derived from published research and the most relevant clinical parameters were reported in detail. The authors did not report any search methods or inclusion criteria, nor did they provide any justification for their selection of the estimates. The parameters for the model were mainly derived from two published clinical studies and an unpublished meta-analysis. However, it is not possible to judge the validity of the data given the limited information reported in this paper.

Validity of estimate of measure of benefit
The estimation of the number of years alive with CHD or stroke was arrived at using the Markov model. Disability weights to adjust years alive to DALYs were reported and were obtained from a published study. The benefits were appropriately discounted.

Validity of estimate of costs
The study reported that the costs were collected from the perspective of the health service. Given this perspective, all the relevant categories of costs appear to have been included in the analysis. However, the treatment costs were reported as aggregate summary costs, so it is not possible to determine which costs were included in these categories (e.g. hospitalisation, overheads and administration costs). The sources of the resources used and unit costs were reported for all categories of costs. The costs were discounted at an annual rate of 3%, which would appear appropriate. Adjustments for inflation and the price year were reported. Uncertainty in the cost estimates was investigated in the sensitivity analysis. The ranges used and the results were reported in full.

Other issues
The authors did not compare their findings with those from other studies, although this may have been due to a lack of published studies in the same research area. The authors acknowledged variation in the cost data and evaluated the impact on the economic results in sensitivity analyses. However, the impact of varying prevalence data, which may differ by setting, was not evaluated in sensitivity analyses. The authors do not appear to have presented their results selectively.

The authors reported a number of limitations to their study. First, the effectiveness analysis was based on the assumption of a strong interaction between the Taq1B polymorphism and CHD mortality. However, data were obtained from a published study which was not a randomised controlled trial, thereby limiting the robustness of the evidence used. In addition, the authors presented evidence from published studies (meta-analyses) that demonstrated that Taq1B polymorphism is not correlated with the response to pravastatin treatment.

Implications of the study
The authors indicated that more research is needed to investigate the association between specific genotypes and response to statins. Subsequently, further economic evaluations will be required to evaluate the economic impact of genetic testing of patients and the provision of individually adapted therapies. The authors also explicitly drew attention to the ethical implications that may arise from not prescribing statins to patients with the B1B1 genotype, despite the possible clinical and economic benefits.

Source of funding
None stated.

Bibliographic details

Other publications of related interest
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Anticholesteremic Agents; Australia; Coronary Disease; Cost-Benefit Analysis; Genetic Screening; Pharmacogenetics; Polymorphism, Genetic; Quality-Adjusted Life Years; Risk Factors

**AccessionNumber**
22007008084

**Date bibliographic record published**
31/10/2007

**Date abstract record published**
31/10/2007