

## ***Executive summary***

# **Screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia: a systematic review and cost-effectiveness analysis**

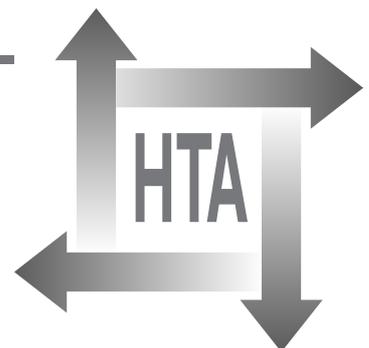
D Marks  
D Wonderling  
M Thorogood\*  
H Lambert  
SE Humphries  
HAW Neil

The London School of Hygiene and Tropical Medicine, Department of Public Health and Policy, Health Promotion Research Unit, London, UK

\* Corresponding author

---

**Health Technology Assessment  
NHS R&D HTA Programme**





## Executive summary

### Background

In the majority of people with familial hypercholesterolaemia (FH) the disorder is caused by a mutation of the low-density lipoprotein receptor gene that impairs its proper function, resulting in very high levels of plasma cholesterol. Such levels result in early and severe atherosclerosis, and hence substantial excess mortality from coronary heart disease.

Most people with FH are undiagnosed or only diagnosed after their first coronary event, but early detection and treatment with hydroxymethylglutaryl-coenzyme (HMG CoA) reductase inhibitors (statins) can reduce morbidity and mortality. The prevalence of FH in the UK population is estimated to be 1 in 500, which means that approximately 110,000 people are affected.

### Objectives

- To evaluate whether screening for FH is appropriate.
- To determine which system of screening is most acceptable and cost-effective.
- To assess the deleterious psychosocial effects of genetic and clinical screening for an asymptomatic treatable inherited condition.
- To assess whether the risks of screening outweigh potential benefits.

### Methods

#### Data sources

Relevant papers were identified through a search of the electronic databases. Additional papers referenced in the search material were identified and collected. Known researchers in the field were contacted and asked to supply information on unpublished or ongoing studies.

#### Inclusion/exclusion criteria

##### Screening and treatment

The review included studies of the mortality and morbidity associated with FH, the effectiveness and

cost of treatment (ignoring pre-statin therapies in adults), and of the effectiveness or cost of possible screening strategies for FH.

#### Psychosocial effects of screening

The search for papers on the psychological and social effects of screening for a treatable inherited condition was limited to the last 5 years because recent developments in genetic testing have changed the nature and implications of such screening tests. Papers focusing on genetic testing for FH and breast cancer were included. Papers relating to the risk of coronary heart disease with similarly modifiable outcome (non-FH) were also included.

#### Data extraction and assessment of validity

A data assessment tool was designed to assess the quality and validity of the papers which reported primary data for the social and psychological effects of screening. Available guidelines for systematically reviewing papers concentrated on quantitative methods, and were of limited relevance. An algorithm was developed which could be used for both the qualitative and quantitative literature.

#### Modelling methods

A model was constructed to investigate the relative cost and effectiveness of various forms of population screening (universal or opportunistic) and case-finding screening (screening relatives of known FH cases). All strategies involved a two-stage process: first, identifying those people with cholesterol levels sufficiently elevated to be compatible with a diagnosis of FH, and then **either** making the diagnosis based on clinical signs and a family history of coronary disease **or** carrying out genetic tests. Cost-effectiveness has been measured in terms of incremental cost per year of life gained.

### Results

#### Modelling cost-effectiveness

FH is a life-threatening condition with a long presymptomatic state. Diagnostic tests are reasonably reliable and acceptable, and treatment with statins substantially improves prognosis. Therefore,

it is appropriate to consider systematic screening for this condition.

Case finding amongst relatives of FH cases was the most cost-effective strategy, and universal systematic screening the least cost-effective. However, when targeted at young people (16 year olds) universal screening was also cost-effective. Screening patients admitted to hospital with premature myocardial infarction was also relatively cost-effective. Screening is least cost-effective in men aged over 35 years, because the gains in life expectancy are small. The modelling results would support a combination of strategies. For example, universal systematic screening at 16 years could be carried out alongside both opportunistic screening of patients with an early myocardial infarction (men aged 16–34 years, women aged 16–54 years) **and** case finding for family members of index cases (men aged 16–34 years, women aged 16–54 years).

### **Psychosocial effects of screening**

Very few papers were found that addressed the psychosocial effects of screening for a treatable inherited condition, and the quality of the papers was generally disappointing. Problems with labelling and discrimination were hypothesised, but there were few data to support these hypotheses. There was no evidence of any deleterious effect on the mental health or social functioning of adults following a diagnosis of FH, although there was some weak evidence that diagnosis in childhood aroused anxiety and created tensions within families. It is possible that diagnosis in adults may make it more difficult for them to get life insurance. Fear of discrimination was reported as a barrier to screening. Many authors called for more counselling at the time of screening, but the nature of the counselling was poorly described and there were no data to support its effectiveness.

### **Conclusions: implications for healthcare and recommendations for future research**

From the modelling exercise, it appears that a case-finding strategy (with a clinical or genetic diagnosis) to identify FH in the families of known FH patients would be cost-effective. Screening all 16 year olds using clinical methods of diagnosis appears to be similarly cost-effective, assuming that such screening is acceptable and that at least 55% of those invited for screening do attend.

There is a lack of qualitative or quantitative evidence on the psychosocial effects of screening for FH or other treatable inherited conditions, or on the effectiveness of educational and counselling interventions at the time of screening. Further research in these areas is needed.

The results of our model show that case finding in the relatives of known FH patients is probably cost-effective, as is a universal screening strategy in young people, and screening of patients admitted to hospital with premature myocardial infarction. However, primary data on the effectiveness and cost implications of screening strategies is lacking, so it is difficult to conclude with certainty that one strategy is more effective or less costly than another. Further research should concentrate on the systematic evaluation of each of these potential screening strategies.

### **Publication**

Marks D, Wonderling D, Thorogood M, Lambert H, Humphries SE, Neil HAW. Screening for hypercholesterolaemia versus case finding for familial hypercholesterol-aemia: a systematic review and cost-effectiveness analysis. *Health Technol Assess* 2000;4(29).

# 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. It was identified as a priority by the Population Screening Panel and funded as project number 95/29/04.

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. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

#### **Criteria for inclusion in the HTA monograph series**

Reports are published in the HTA monograph series if (1) they have resulted from work either prioritised by the Standing Group on Health Technology, or otherwise commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Series Editors: Andrew Stevens, Ken Stein and John Gabbay  
Monograph Editorial Manager: Melanie Corris

The editors and publisher have tried to ensure the accuracy of this report but do not accept liability for damages or losses arising from material published in this report. They would like to thank the referees for their constructive comments on the draft document.

Copies of this report can be obtained from:

The National Coordinating Centre for Health Technology Assessment,  
Mailpoint 728, Boldrewood,  
University of Southampton,  
Southampton, SO16 7PX, UK.  
Fax: +44 (0) 23 8059 5639    Email: [hta@soton.ac.uk](mailto:hta@soton.ac.uk)  
<http://www.ncchta.org>

ISSN 1366-5278