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Review

Executive summary

What role for statins? A review and economic model

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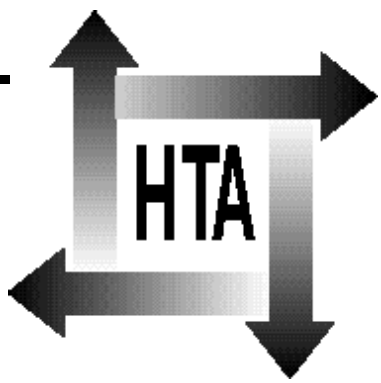

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Background

Coronary heart disease (CHD) is a major cause of morbidity and mortality in the UK. The social and health service costs are large, and CHD prevention remains a government high priority. The major preventative approach is the modification of common risk factors (tobacco smoking, high blood pressure, physical inactivity, unhealthy diet and high blood cholesterol). The statins are a new class of drugs that lower blood cholesterol. This review systematically examines the evidence for statins in the light of existing treatments and provides cost-effectiveness estimates for statins and other treatments.

Objectives

This review aimed to answer the following questions.

- By how much do low fat and other diets reduce blood cholesterol, and how effective are they in reducing CHD risk?
- Does treatment with statins reduce CHD events and are relative reductions in these events independent of the level of CHD risk?
- How effective are non-cholesterol lowering drug treatments for reducing CHD risk relative to dietary and cholesterol lowering drug treatments?
- What is the relative cost-effectiveness of different approaches to reducing cholesterol and/or CHD?

Methods

Data sources

A search of MEDLINE citations from 1993 to November 1997 was made using the standard randomised controlled trial (RCT) and meta-analysis filters. The references obtained, together with information supplied by investigators working in the field of cholesterol lowering, were used to compile a list of statin trials.

Study selection

The review included RCTs with ≥ 6 months follow-up in which clinical event outcomes were measured.

Data extraction and synthesis

A data abstraction form was developed. Effect sizes were estimated using the statistical computer package META97 and further analysis was conducted with the EGRET package using logistic regression models. Heterogeneity in fixed effects models was investigated by sensitivity analyses.

Estimates of statin effectiveness were made from pooled data. Effects of other CHD prevention treatments were taken from published meta-analyses and individual RCTs. Cost-effectiveness analyses were performed using a life-table approach which calculated the years of survival expected with and without treatment. Costs were direct costs of drugs and health service costs and were considered as gross and net (i.e. not taking account and taking account of potential NHS savings, respectively) and were presented as discounted and undiscounted. Costs per life-year gained were used as the cost-effectiveness index.

Results

Five major trials of statins were identified. Data from these and from another 18 RCTs demonstrated significant reductions in CHD events. In secondary prevention (i.e. prevention among people with evidence of cardiovascular diseases) the relative reductions in total and CHD mortality were 21% (95% CI, 14–27%) and 26% (95% CI, 17–34%), respectively. There were similar reductions for non-fatal myocardial infarctions and greater reductions for combined end-points (including revascularisation end-points). In primary prevention (i.e. among people without evidence of cardiovascular disease) there were significant reductions for combined end-points and non-fatal myocardial infarction, but not for total and CHD mortality. The primary prevention trials were too small to have adequate power to detect effects on mortality outcomes alone. Statins are effective across a wide range of levels of blood cholesterol, including levels considered normal in the UK.

Other treatments that reduce CHD risk were considered in this review. For primary prevention these were advice on smoking cessation, nicotine

replacement and antihypertensive drugs; other treatments considered for secondary prevention were advice on smoking cessation, aspirin, beta-blockers, oily fish diet and Mediterranean diet. Except for smoking interventions, these treatments have numbers needed to treat that are broadly similar to those for statins.

The cost-effectiveness of statins depends on the cost of the statin used and the CHD risk in the population treated. Gross, discounted estimates based on CHD risk in the trials considered ranged from £5400 to £13,300 per life-year gained at levels of risk expected in primary prevention, and from £3800 to £9300 at levels of risk consistent with secondary prevention. Use of low cost statins had the potential to reduce gross costs by 60%.

The cost-effectiveness of other treatments was much better than for statins. Gross discounted cost per life-year saved of aspirin (£53), bendrofluazide treatment for elderly people with hypertension (£45), low cost mixed drug antihypertensive regimens for middle-aged people (£1509), beta-blockers following myocardial infarction (£227) and Mediterranean diet following myocardial infarction (£293) were all lower than for statins.

Conclusions

Implications for health care

The evidence on efficacy supports the use of statins over a wide range of CHD risks covering both primary and secondary prevention. Although statins are less cost-effective than other treatments, there is consensus that their use in secondary prevention is acceptable because they achieve effects additional to those of other treatments. However, there is evidence that these other treatments are insufficiently used in the UK and that greater efforts are required to ensure that highly cost-effective treatments are used optimally.

The limited cost-effectiveness of statins in primary prevention indicates that their indiscriminate use might be a poor use of resources. Cost-effectiveness clearly improves with increasing baseline CHD risk. Scoring systems and guidelines have been developed to measure individual risk: most of these assume that 3% annual CHD risk marks the threshold between cost-effective and cost-ineffective use of statins. However, these scoring systems and guidelines have major weaknesses because they are derived from American data that are now out of date, and they do not consider variations between regional, ethnic or socio-economic groups.

The price of statins is a major determinant of their relative cost-effectiveness: lower cost statins are available and their use would improve cost-effectiveness to the levels of low cost antihypertensive regimens. As the price of drugs is agreed by the Department of Health, there may be a case for further examining the prices of statins, given the very large potential market for these drugs in primary prevention. Targeting statin treatment at people aged 55 years and older would further improve cost-effectiveness.

In public health terms, the major approaches to the primary prevention of CHD remain the fiscal and legislative control of tobacco, the reduction of hidden saturated fats and calories in the diet, encouraging and extending facilities available for physical activity throughout life, and the reduction of levels of poverty.

Recommendations for research

Areas of further research, which would help inform policy and practice in CHD prevention, include the following.

- Trials to examine the long-term effects of dietary modification with the oily fish or Mediterranean diet, both of which show promise but require stronger evidence of effect.
- Studies of the effects of different types of statin, and of the effects of statins in people aged 75 years and older.
- Continued surveillance of statin-treated patients for long-term adverse effects.
- Investigation of the translation of the effects of treatments found in trials to routine clinical practice.
- Evaluation of CHD risk prediction scoring systems in clinical practice (which will require longitudinal follow-up of patients to compare predicted and observed event rates) and the effects of risk scoring systems on professional and patient behaviour, risk levels and outcomes.
- Investigation of patient preferences (and their determinants) for specific types of treatment (e.g. drugs versus lifestyle modification) in primary and secondary prevention.

Publication

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NHS R&D HTA Programme

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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 Pharmaceutical Panel and funded as project number 96/14/01.

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.

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The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

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