Potential cost-effectiveness of C-reactive protein screening followed by targeted statin therapy for the primary prevention of cardiovascular disease among patients without overt hyperlipidemia

Blake G J, Ridker P M, Kuntz K M

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
This paper examined the use of screening for C-reactive protein to target statin therapy for the primary prevention of cardiovascular disease among patients without hyperlipidaemia who are at an increased risk of cardiovascular events. The three strategies studied were:

- no C-reactive protein screening and no statin therapy (i.e. standard care);
- C-reactive protein screening followed by targeted statin therapy for patients with elevated C-reactive protein levels; and
- statin therapy for all patients.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hypothetical cohorts of adult men and women who had no overt hyperlipidaemia (low-density lipoprotein cholesterol less than 149 mg/dL). The authors reported that the base-case analysis reported in this paper was for 58-year-old men, based on the AFCAPS/TexCAPs population. (Downs et al. 1998, see 'Other Publications of Related Interest' below for bibliographic details).

Setting
It was unclear whether, if implemented, the screening would take place in a community, primary care or secondary care setting. The authors did not report the geographic setting. However, the evidence and results suggest that the study referred to practice in the USA.

Dates to which data relate
Literature published between 1994 and 2001 was used to derive the effectiveness evidence. There was no report of the resources used. The authors reported that all costs were inflated to the year 2000 using the medical care component of the Consumer Price Index.

Source of effectiveness data
The estimates for the final outcomes were derived from a review of published studies.
**Modelling**
A decision analytic Markov model was used to estimate the quality-adjusted lifetime expectancy and lifetime costs of the three strategies. All analyses were performed using DATA (Treeage Software, Williamstown). The time horizon of the model was 10 years, with cycle lengths of one year. The health states included in the model were event free, post myocardial infarction (MI), death, post stroke, and post MI and post stroke.

**Outcomes assessed in the review**
The authors chose the following outcomes:

- the risk of MI for 58-year-old persons (per 1,000 person-years) for men with low C-reactive protein, men with high C-reactive protein, women with low C-reactive protein, and women with high C-reactive protein;
- the efficacy of statin therapy for the prevention of MI (% reduction) in persons with low C-reactive protein and those with high C-reactive protein;
- the fatal MI rate for men aged 58 years and women aged 58 years;
- the yearly mortality rate post MI (per 1,000 person-years) for men aged 58 years and for women aged 58 years;
- the risk of stroke in persons aged 58 years (per 1,000 person-years) for men with low C-reactive protein, men with high C-reactive protein, women with low C-reactive protein and women with high C-reactive protein;
- the efficacy of statin therapy for the prevention of stroke (% reduction) in those with low C-reactive protein and those with high C-reactive protein;
- the fatal stroke rate for persons aged 58 years;
- the yearly mortality post stroke;
- the increased relative risk of stroke after MI;
- the efficacy of statin for stroke prevention after MI (% reduction);
- the increased relative risk of fatal stroke after MI;
- the increased relative risk of MI after stroke; and
- the increased relative risk of fatal MI after stroke.

**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
Twelve references provided the probabilities used in the model.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The literature was used to determine the following probabilities (presented as baseline; range) used in the model:

the risk of MI for 58-year-old persons (per 1,000 person-years) for men with low C-reactive protein (2.90; 0.38 - 7.06),
men with high C-reactive protein (6.30, 0.83 - 15.34), women with low C-reactive protein (1.00; 0.10 - 3.98), and
women with high C-reactive protein (2.17; 0.22 - 8.65);

the efficacy of statin therapy for the prevention of MI (% reduction) in persons with low C-reactive protein (0) and
those with high C-reactive protein (45);

the fatal MI rate for men aged 58 years (0.03 - 0.22) and women aged 58 years (0.03 - 0.22);

the yearly mortality rate post MI for persons aged 58 (per 1,000 person-years) for men (19 - 47) and women (19 - 47);

the risk of stroke in persons aged 58 years (per 1,000 person-years) for men with low C-reactive protein (1.74; 0.17 - 8.7),
men with high C-reactive protein (2.21; 0.22 - 11.31), women with low C-reactive protein (0.91; 0.17 - 5.7), and
women with high C-reactive protein (1.18; 0.22 - 7.4);

the efficacy of statin therapy for stroke prevention (% reduction) for those with low C-reactive protein (10) and those
with high C-reactive protein (10);

the fatal stroke rate for persons aged 58 years (0.1 - 0.2);

the yearly mortality post stroke (2.67);

the increased relative risk of stroke after MI (4);

the efficacy of statin for stroke prevention after MI (% reduction) (22);

the increased relative risk of fatal stroke after MI (1.50);

the increased relative risk of MI after stroke (1.40); and

the increased relative risk of fatal MI after stroke (2.36).

Measure of benefits used in the economic analysis
The outcomes used in the economic analyses were the quality-adjusted life-years (QALYs) and life-years. The authors
reported that quality of life weights, taken from the literature and based on age- and gender-adjusted data, were
assigned to patients who did not have any cardiovascular event. They explained that utilities for the post MI and post
stroke states were adapted from published data and that, in the absence of published data they assumed that the utility
for the post MI and post stroke state was the product of the utilities for these two states.
Direct costs
The resource quantities and the costs were not reported separately. Health service costs appear to have been used in the analyses. The costs included statin therapy (annual cost), the C-reactive protein test, two office visits and liver function tests, the lifetime cost of MI (range given since this cost is age and gender specific), the acute cost of stroke, and the annual cost after stroke (range provided as this cost is age specific). Literature sources, combined with assumptions around usage and adherence, were used to estimate the direct cost data. A discount rate of 3% was used. The study appears to have reported the average costs. The authors reported that the costs were inflated to 2000 levels.

Statistical analysis of costs
The authors did not carry out statistical analyses of the resource use or costs.

Indirect Costs
No indirect costs were calculated. The authors reported that productivity losses associated with morbidity or premature death were not included. They also stated that they assumed that the costs of patient time were negligible, thus they were not incorporated into the analyses.

Currency
US dollars ($). No conversions were carried out.

Sensitivity analysis
A sensitivity analysis was carried out around all the probabilities, costs and utilities used in the model.

Estimated benefits used in the economic analysis
The life expectancy of men in the three treatment groups was 14.471 for no C-reactive protein screening, 14.577 for C-reactive protein screening with or without statin therapy, and 14.589 for treat all with statins. The QALYs were 12.217 (no screening), 12.323 (screening with or without statin therapy) and 12.336 (treat all with statins), respectively.

The life expectancy of women in the three treatment groups was 16.766 for C-reactive protein screening, 16.843 for C-reactive protein screening with or without statin therapy, and 16.855 for treat all with statins. The QALYs were 13.910 (no screening), 13.983 (screening with or without statin therapy) and 13.995 (treat all with statins), respectively.

Cost results
The costs for men in the three treatment groups were $9,500 for no C-reactive protein screening, $14,600 for C-reactive protein screening with or without statin therapy, and $21,100 for treat all with statins.

The costs for women in the three treatment groups were $7,500 for no C-reactive protein screening, $14,400 for C-reactive protein screening with or without statin therapy, and $22,000 for treat all with statins.

Statistical analyses of the costs were not reported, nor were confidence intervals.

The costs of any adverse events and knock-on costs were not reported.

Synthesis of costs and benefits
The costs and benefits were combined as the cost per life-year and also as the cost per QALY. Incremental analyses were performed.

C-reactive protein screening and target therapy, compared with no screening, gave an incremental cost-effectiveness ratio (ICER) of $48,100 per QALY ($48,100 per life-year) for men and $98,400 per QALY ($89,500 per life-year) per
women.

Treating all patients with statins, compared with no screening, gave an ICER of $506,100 per QALY ($535,400 per life-year) for men and $637,500 per QALY ($655,200 per life-year) per women.

Authors’ conclusions
A strategy involving C-reactive protein screening to target statin therapy for the primary prevention of cardiovascular disease among middle-aged patients without overt hyperlipidaemia could be relatively cost-effective and, in some cases, cost-saving.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for the comparator used, it would appear to represent current practice in the authors’ setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. It appears that the authors have used results from the available studies selectively. There was no report of the impact of differences between primary studies being taken into consideration when estimating effectiveness.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis. The choice of estimates was not justified.

Validity of estimate of costs
Although the authors reported that the costs were estimated from a societal perspective, no indirect costs were actually reported. It would appear that the authors felt that at least some of the indirect costs could be considered to be negligible. The individual components of most of the costs reported in the paper were not detailed, so it is not possible to state whether or not all the relevant cost components were included in the analysis. The costs were not reported separately from the quantities. Where reported, the source of the resources used or quantities appears to have been the literature. No analysis of the resources used or quantities was carried out. The costs were taken from published sources and a wide range of costs were considered in the analyses, but no further analysis was carried out. Charges were not used to proxy prices. The authors reported that the prices were inflated to 2000 US dollars using the medical care component of the Consumer Price Index.

Other issues
The authors appear to have made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their findings selectively. The study considered middle-aged patients without overt hyperlipidaemia and this was reflected in the authors’ conclusions. The authors reported that they did not assume any disutility for stain therapy. In addition, owing to the lack of reliable data, they did not model the benefits of statin therapy for the prevention of other cardiovascular outcomes.

Implications of the study
The authors suggested that further trials are required to prove the benefit of statin therapy among patients with high C-reactive protein levels.

Source of funding
None stated.

**Bibliographic details**

**PubMedID**
12727581

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Aged; C-Reactive Protein /analysis; Cardiovascular Diseases /blood /prevention & control; Cholesterol, LDL /blood; Cost-Benefit Analysis; Counseling; Diet; Female; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /therapeutic use; Male; Markov Chains; Mass Screening /economics /methods; Middle Aged; Primary Prevention; Quality-Adjusted Life Years; Risk Factors; Sensitivity and Specificity

**AccessionNumber**
22003000821

**Date bibliographic record published**
31/03/2006

**Date abstract record published**
31/03/2006