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
3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statins) therapy in patients aged 75 to 84 with a history of myocardial infarction.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
A hypothetical cohort of patients aged between 75 and 84 with a history of myocardial infarction.

Setting
Hospital. The economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness data were obtained from the literature published between 1990 and 1998. The resource use data mentioned in the paper were based on routine recommendations and authors' assumptions. The price year was 1998.

Source of effectiveness data
The evidence for the final outcome was based on a literature review and assumptions made by the authors.

Modelling
A Markov model was developed using DATA 3.5 software to estimate the costs and effects associated with each preventive strategy for hypothetical patients randomly assigned to one of the two strategies. The model had six health states and a lifetime time horizon. The model was not configured to deal with multiple events because such sequences of events occur infrequently enough to have a small effect on the overall analysis. Some health states such as congestive heart failure were not modelled explicitly but were averaged into the mortality estimates and quality of life weights.

Outcomes assessed in the review
The outcomes extracted from the literature were as follows:

mortality risk ratios, including mortality from all causes other than myocardial infarction and stroke;
one-year mortality after recurrent myocardial infarction (excluding in-hospital mortality);

annual mortality more than 1 year after recurrent myocardial infarction;

one-year mortality after stroke;

annual mortality more than 1 year after stroke;

in hospital mortality rates after recurrent myocardial infarction;

annual event rates (for patients in the baseline state), including reinfarction, and stroke;

relative risk reduction by statin for reinfarction and stroke;

utilities, including baseline state, one year or less after recurrent myocardial infarction, more than one year after recurrent myocardial infarction, one year or less after stroke, and more than one year after stroke.

Study designs and other criteria for inclusion in the review
This study relied directly on data from randomised, controlled trials to model statin efficacy. Mortality rates after stroke were based on published data from a county community stroke project. All of the data used to determine transition probabilities were population-based and specific to patients older than 75 years of age, with the exception of data from a clinical trial of patients up to 75 years of age.

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 16 studies were included.

Methods of combining primary studies
Most of the input values were based on individual studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The base case outcome results were as follows:

mortality risk ratios, including mortality from all causes other than myocardial infarction and stroke, 1.52;

one-year mortality after recurrent myocardial infarction (excluding in-hospital mortality), 5.09 at 80 years of age and 3.98 at 90 years of age;
annual mortality more than 1 year after recurrent myocardial infarction, 4.08 (the value representing biased toward statin therapy was 7.04);

one-year mortality after stroke, 7.09 at 80 years of age and 7.80 at 90 years of age;

annual mortality more than 1 year after stroke, 2.44 at 80 years of age and 1.12 at 90 years of age;

in hospital mortality rates after recurrent myocardial infarction, 0.18 at 80 years of age and 0.27 at 90 years of age;

annual event rates (for patients in the baseline state) for reinfection, 0.081 (0.037 representing biased toward statin therapy), and stroke, 0.028 (0.021 representing biased against statin therapy);

relative risk reduction by statin for reinfection, 33% (53% representing biased toward statin therapy and 4% representing biased against statin therapy), and stroke 40% (62% representing biased toward statin therapy and 4% representing biased against statin therapy);

utilities, including baseline state, 0.87; more than one year after recurrent myocardial infarction, 0.87; and more than one year after stroke, 0.83.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also based on assumptions made by the authors.

Estimates of effectiveness and key assumptions
Best and worst-case values used in the sensitivity analysis for the clinical probabilities where data were not available were based on the authors' assumptions.

The base case utility values for the following states were based on the authors' assumptions:

one year or less after recurrent myocardial infarction, 0.80;

one year or less after stroke, 0.76.

The best and worst-case values used in sensitivity analysis for all utility values were based on the authors' assumptions where data were not available. Because the study did not model multiple strokes or recurrent myocardial infarction, the model was based on the assumption that patients discontinued statin therapy after their first stroke or recurrent myocardial infarction. It was also assumed that patients in the baseline state who were receiving statin therapy continued to accrue the benefits associated with this therapy for the duration of their time in the baseline state. The authors limited the benefits of statin therapy to the first 5 years in the baseline states. The base-case model assumed no disutility associated with statin use. However, in sensitivity analysis a utility decrement of 0.013 was considered for patients taking statins.

Measure of benefits used in the economic analysis
Number of life-years saved and quality-adjusted life-years (QALYs) gained were used as measures of benefit. For the purpose of calibration, the authors initially created a two-state (alive or dead) Markov model, with mortality rates based on the 10-year survival curve after acute myocardial infarction for patients aged between 75 and 84 years of age. The life expectancy of patients in the calibration model was then used as a benchmark to calibrate life expectancy for patients in the usual care strategy of the full six-state model.

Direct costs
Costs were discounted. Some quantities were reported separately from the costs. Cost items were reported separately. The cost analysis covered the costs of hospitalisation for non-fatal and fatal myocardial infarction, hospitalisation for stroke, post-stroke institutional care, annual drug use, office visits, and liver function panel. The perspective adopted in
the cost analysis was reported to have been that of society. Cost data (wholesale sale prices or reimbursements or charges) were obtained from studies or reports published between 1996 and 1999. Costs were inflated to 1998 US dollars using the medical care component of the Consumer Price Index. Standard deviations of cost were used to define upper and lower bounds for sensitivity analyses. The cost analysis did not include costs for coronary artery bypass grafting or percutaneous transluminal coronary angioplasty, even though statin therapy has been shown to reduce the frequency of these procedures in patients between 65 and 75 years of age. \(<\text{INDIRECT COSTS}>\) Indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A set of one-way and two-way sensitivity analyses was performed on input parameters. Monte Carlo simulation was conducted to vary transition probabilities, costs, and utilities simultaneously (probabilistic sensitivity analysis).

**Estimated benefits used in the economic analysis**
The mean undiscounted life expectancy was 5.81 years for patients receiving usual care and 6.17 years for those taking HMG-CoA reductase inhibitors. It was estimated that the average patient aged 75 to 84 would experience 4.41 discounted QALYs if they received usual care and 4.66 QALYs with the use of statins, for a gain of 0.25 QALY with statin use. The applied discount rate was 3% (0 - 5% in sensitivity analysis).

**Cost results**
The applied discount rate was 3% (0 - 5% in sensitivity analysis). Total discounted costs were $3,249 for usual care and $8,078 for statin therapy, yielding an incremental cost of $4,829.

**Synthesis of costs and benefits**
The incremental cost-utility of statin therapy compared with usual care in patients aged between 75 and 84 years of age with a previous myocardial infarction was $18,800 per quality-adjusted life-year. The corresponding value in terms of cost per year of life saved was $17,200. In the probabilistic sensitivity analysis, the 25th, 50th, and 75th percentiles of the incremental cost-utility ratios were $15,900, $24,700, and $39,800 per QALY, respectively. The sensitivity analyses confirmed the robustness of the base-case results.

**Authors' conclusions**
The cost-effectiveness ratios of statin therapy in older patients with previous myocardial infarction are reasonable under a wide variety of assumptions about drug efficacy, drug cost, and rates of cardiac and cerebrovascular events. Pending the results of randomised, controlled trials of secondary prevention in patients in this age group, statin therapy seems to be as cost-effective as many routinely accepted medical interventions in this setting.

**CRD COMMENTARY - Selection of comparators**
The strategy of usual care was explicitly regarded as the comparator. You, as a database user, should consider which preventive strategy is widely used in your own setting.

**Validity of estimate of measure of benefit**
The internal validity of the effectiveness results is likely to be high given that the statin efficacy data were based on randomised trials, mortality rates were mainly based on population-based studies, and uncertainties in the data were addressed by sensitivity analysis. However, the criteria used to ensure the validity of primary studies (such as blinding methods adopted in the studies), the methods used to judge the relevance, and validity of data and investigations of
differences among the primary studies were not reported. It was acknowledged that the study analysis was limited by the lack of data from randomised trials showing the efficacy of statin therapy in patients aged between 75 and 84 years of age.

Validity of estimate of measure of benefit:

The estimation of benefits was modelled. The Markov model used to derive a measure of health benefit appears to have been appropriate. Benefits were discounted at 3% and was also subject to sensitivity analyses (varied between 0 and 5%). Discounting of benefits might be different in other settings or countries. It was reported that additional benefits of statin therapy not factored into the analysis (such as a reduction in coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, and coronary heart disease death other than fatal myocardial infarction) would have made the study results more favourable.

Validity of estimate of costs
Positive aspects of the cost analysis likely to have contributed to its validity were that some quantities were reported separately from the costs, adequate details of methods of cost estimation were given and it appears that all important direct cost elements were included in the cost analysis. Moreover, the price year and perspective adopted in the cost analysis were specified, adjustment was made for inflation and sensitivity analysis was performed on cost parameters. However, the following characteristics may have had an adverse effect. The cost calculations do not seem to have been based on true costs rather than charges or reimbursements, and the effects of alternative procedures on indirect costs were not addressed, although it was claimed that the perspective was societal. Costs were discounted at 3% and the sensitivity analysis investigated the effect of varying the rate between 0 and 5%. This does not apply to the UK setting.

Other issues
The authors’ conclusions appear to be justified given the extensive sensitivity analyses performed. The issue of generalisability to other settings or countries was not explicitly addressed, although it may have been accounted for through the ranges considered for the values incorporated in the sensitivity analyses. Some comparisons were made with other studies. It was acknowledged that the study model did not describe the full range of health states that such a cohort of patients might experience. However, it was deemed that the most important health states, with their associated costs and effects, were captured in the model.

Implications of the study
Until data from randomised, controlled trials that include patients in this age group are available, this study can act as a data-driven basis for policy decisions about drug therapy in this large and growing population of patients.

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Other publications of related interest
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