Cost effectiveness of statin therapy for the primary prevention of coronary heart disease in Ireland
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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 use of statin therapy for the primary prevention of coronary heart disease (CHD) in Ireland was compared with no statin therapy. The study evaluated the use of all available statins (including generics) at a dose sufficiently high to achieve a 30 to 40% reduction in low-density lipoprotein cholesterol. The seven statins studied were atorvastatin, rosuvastatin, fluvastatin, simvastatin (generic), simvastatin, pravastatin (generic) and pravastatin.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The hypothetical target population comprised individuals aged 40 years and older from the general population initially free of CHD, who had a 10-year risk of a fatal cardiovascular event of at least 5%.

Setting
The setting was primary and secondary care. The economic study was conducted in Ireland.

Dates to which data relate
The effectiveness evidence dated from 1990 to 2005. The resource use data were from 2001. The price year was 2005.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.

Modelling
A Markov state-transition model was used to evaluate the costs and quality-adjusted life expectancy. A primary prevention strategy was compared with no primary prevention for each of the statins evaluated. The patients were initially distributed across seven health states. The health states were well, acute myocardial infarction (AMI), angina, coronary artery bypass grafting, percutaneous transluminal angioplasty, stroke and death. Patient outcome was represented in the model in terms of their probability of dying, progressing to AMI, or remaining well. The time horizon of the model was not reported clearly but it appears to have been the patient’s lifetime. The duration of each cycle was 1 year. The model was based on the assumption that if patients in the control arm suffered an AMI, they would then commence a statin for secondary prevention of cardiovascular disease, as recommended by European guidelines. It was also assumed that patients would be treated until they died or until the age of 65. An additional assumption was that the efficacy of all statins would be similar for both men and women to that of pravastatin, as
demonstrated in the West of Scotland Coronary Prevention Study (WOSCOPS) (which included only men).

**Outcomes assessed in the review**
The outcomes assessed were:

- the probability of AMI and death according to age;
- differences in the relative risk of AMI for patients treated with statins compared with those not receiving treatment;
- age-specific cardiac mortality of AMI survivors; and
- statin effect on this mortality and the secondary AMI rates.

**Study designs and other criteria for inclusion in the review**
Few details of the inclusion criteria for this review were reported. The probability of AMI and death according to age was taken from Irish lifetables. Differences in the relative risk of AMI for patients treated with statins versus those not receiving treatment were taken from the WOSCOPS, a primary prevention trial. Age-specific cardiac mortality of AMI survivors was derived, based on regression modelling from the Framingham study. Statin effect on this mortality and the secondary AMI rates were calculated using the relative risk of death and AMI observed in the Scandinavian Simvastatin Survival Study (4S study), a secondary prevention trial.

**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**
The authors included 10 references as sources of effectiveness evidence.

**Methods of combining primary studies**
A narrative method was used to combine the primary studies.

**Investigation of differences between primary studies**
No differences between the primary studies were investigated.

**Results of the review**
The authors did not state the actual parameters used.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the quality-adjusted life-years (QALYs). Sources and values for the QALY weights were reported, but no details of the methodology used were reported.
Direct costs
The results were presented from two perspectives, the GMS and DP schemes. The DP scheme includes a 50% mark-up and results in higher drug prices. Resources used for patients at risk of CHD were general practitioner visits and laboratory tests, as well as the cost of an AMI event. The drug costs were also included. The costs were appropriately discounted given the long-term horizon of the study. The quantities and the costs were not analysed separately, and their estimation was derived through modelling. The quantity and cost data came from both authors' assumptions and a published paper. The price year was 2005. Rflation was used when required.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
No indirect costs were included.

Currency
Euros (EUR).

Sensitivity analysis
A probabilistic sensitivity analysis was performed, and the costs and probabilities of outcomes were varied using Monte Carlo simulation (n=10,000). Ninety-five per cent confidence intervals were used where available; where not available, the costs and probabilities were varied by +/- 50%. Acceptability curves were also produced to evaluate the probability of statins being cost-effective at different cost-effectiveness thresholds.

Estimated benefits used in the economic analysis
The total benefits and incremental benefits were not reported. The results were reported as incremental cost-effectiveness ratios (ICERs).

Cost results
The total costs and incremental costs were not reported. The results were reported as ICERs.

Synthesis of costs and benefits
The cost per QALY gained for the GMS and DP schemes, respectively, were:

- with atorvastatin, 17,900/QALY and 24,500/QALY;
- with rosuvastatin, 18,500/QALY and 25,500/QALY;
- with fluvastatin, 18,700/QALY and 25,800/QALY;
- with simvastatin (generic), 20,910/QALY and 29,999/QALY;
- with simvastatin, 27,300/QALY and 38,700/QALY;
- with pravastatin (generic), 26,752/QALY and 38,999/QALY; and
- with pravastatin, 33,800/QALY and 48,500/QALY.

All strategies were compared with a no primary prevention strategy, and no incremental analyses were conducted.
amongst them.

The probabilistic sensitivity analysis was run using the cost of atorvastatin for GMS patients. This showed that 80% of the patients had an ICER that fell below the cost-effectiveness threshold of EUR 46,500/QALY (or <\= 30,000/QALY).

Authors' conclusions
The majority of statins are cost-effective in the primary prevention of patients at high risk of developing coronary heart disease (CHD) under the general medical services (GMS) scheme, with atorvastatin 10 mg being the most cost-effective and pravastatin 40 mg falling outside of the threshold. "Due to drug cost, statins are more cost effective under the GMS scheme as compared with the drug payment (DP) scheme where pravastatin, generic pravastatin and simvastatin fall outside the cost-effectiveness threshold."

CRD COMMENTARY - Selection of comparators
All drugs of the statin family available in Ireland seem to have been included and compared with a no primary prevention strategy. Both branded and generic statins were evaluated, which seems to have been appropriate given the study question.

Validity of estimate of measure of effectiveness
Primary prevention effectiveness was extrapolated from only one trial performed in the West of Scotland with pravastatin, and the effects observed in the trial were extrapolated to all statins. No systematic review of the literature appears to have been carried out to synthesise different primary prevention trials. As the authors stated, this represents a limitation to this study. Only the effects on AMI were evaluated; other beneficial or harmful side effects of statins were excluded.

Validity of estimate of measure of benefit
A similar statement applies to this section. The benefits were derived through modelling and, as is usual practice in modelling studies, quality of life weights do not seem to have come from a systematic review but rather from a few selected sources.

Validity of estimate of costs
Few costs were included in the analysis (general practitioner visits, laboratory tests, drug costs and AMI event costs). Other events potentially related to statin use, such as adverse events or other beneficial events, do not seem to have been included. The unit costs were not reported separately from the resource quantities, making it difficult to extrapolate the results to other settings. Resource use was taken from authors' assumptions and one reference in the case of AMI. Discounting was appropriately performed given the long-term horizon of the study. The date to which the prices referred was recorded, and this increases the reproducibility of the results.

Other issues
The authors did not compare their results with those from other studies. The issue of generalisability to other settings was not addressed, but the conclusions reflected the scope of the analysis. The authors stated that the study was subject to certain limitations, namely that the WOSCOPS only included men and it was therefore assumed that women derived similar benefits from statins. The authors assumed that the efficacy observed in randomised clinical trials would be seen in the general population. Finally, the efficacy of all statins was assumed to be similar to that of pravastatin. This does not take any other mechanism of action that may positively influence patient outcome, such as reduction in arterial inflammation, into consideration.

Implications of the study
Though generally accepted, generic prescription did not optimise cost-effectiveness in this study, as the pricing of the
generic preparations was not sufficiently low to allow them to compete favourably with atorvastatin, rosuvastatin or
fluvastatin. Further evidence is required to support the use of a more intensive lipid lowering strategy in primary
prevention. In addition, recent strategies, such as more intensive statin therapy in patients with established CHD, are not
yet supported for primary prevention.

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