The cost-effectiveness of C-reactive protein testing and rosuvastatin treatment for patients with normal cholesterol levels
Choudhry NK, Patrick AR, Glynn RJ, Avorn J

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.

CRD summary
This study examined the cost-effectiveness of rosuvastatin for apparently healthy men over 50 years old and women over 60 years old, with elevated high-sensitivity C-reactive protein levels (2mg/L or more), but normal low-density lipoprotein cholesterol levels (less than 130mg/dL). The authors concluded that rosuvastatin was cost-effective, especially for patients with a Framingham risk score of 10% or more. Conventional cost-effectiveness methods were used and areas of uncertainty were considered, which should ensure the validity of the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of rosuvastatin for apparently healthy men over 50 years old and women over 60 years old, with elevated high-sensitivity C-reactive protein levels of 2mg per litre or more, but normal low-density lipoprotein cholesterol levels of less than 130mg per dL.

Interventions
The test-and-treat strategy consisted of a blood test to assess the high-sensitivity C-reactive protein level, followed by rosuvastatin (20mg daily) for patients with a level of 2mg per litre or more. The comparator was no testing and no treatment, which was the usual care.

Location/setting
USA/primary and secondary care.

Methods
Analytical approach:
The analysis was based on a decision-tree model that simulated the patient management for two cohorts: men aged 50 years or older and women aged 60 years or older, both with no known cardiovascular disease. A lifetime horizon was considered and the authors stated that a societal perspective was adopted.

Effectiveness data:
Most of the clinical evidence came from the Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial (Ridker, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). Other data were identified by an extensive review of published literature. The baseline characteristics of eligible patients and the treatment effect for rosuvastatin were from the clinical trial. The key input was the efficacy of the test-and-treat strategy, which was defined as the impact of treatment on cardiovascular events (myocardial infarction, unstable angina, revascularisations, stroke, venous thromboembolism, diabetes, elevated liver enzymes, and myopathy). A key assumption was the persistence of treatment efficacy beyond the five-year observation period of the trial. Observational studies were used for the rates of some clinical events without treatment.

Monetary benefit and utility valuations:
The utility values were from the Cost-Effectiveness Analysis Registry and from studies identified by a search of MEDLINE.
Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of high-sensitivity C-reactive protein test, liver function test, rosuvastatin, treatment of cardiovascular events, and treatment of adverse events. The value of the time for both patients and informal care was considered, using average hourly wages of age-matched US workers. The costs were based on Medicare payments, average wholesale prices, and published reports. The price of branded rosuvastatin was used, until the patent expired seven years into the simulation, when the generic price was used. Hospitalisation data were from the Nationwide Inpatient Sample and other resource use data were from published studies and databases. The costs were in US dollars ($), a 3% annual discount rate was applied, and the price year was 2009.

Analysis of uncertainty:
The uncertainty was investigated in one- and two-way sensitivity analyses on selected inputs, including the efficacy of treatment, the cardiovascular risk (Framingham score), and the drug costs. Published and assumed ranges of values were considered. The cost of care for unrelated medical conditions occurring in additional years of life was considered in an alternative scenario. A probabilistic sensitivity analysis was carried out, using predetermined probability distributions for groups of model inputs; beta distributions for the probabilities and log-normal distributions for the other inputs.

Results
The total costs per patient were $19,717 with usual care and $27,616 with test-and-treat. The QALYs were 10.29 with usual care and 10.61 with test-and-treat. The incremental cost with test-and-treat over usual care was $25,198 per QALY gained ($22,160 per life-year gained).

In general, the base-case findings were robust to the variations considered in the sensitivity analyses. With the worst assumption for the efficacy of rosuvastatin from the JUPITER trial, the incremental cost per QALY rose to $57,503. Reducing the effect of treatment to last five years increased the ratio to $62,146. Restricting the test-and-treat strategy to patients with a Framingham risk score of less than 10% reduced the ratio to $14,205.

The probability of test-and-treat being cost-effective at a threshold of $50,000 per QALY was 94%.

Authors’ conclusions
The authors concluded that rosuvastatin was cost-effective, especially for patients with a Framingham risk score of 10% or more.

CRD commentary
Interventions:
The comparators were based on the strategies in the JUPITER trial. They were appropriately selected, as the proposed intervention was compared against the usual care, which was no treatment.

Effectiveness/benefits:
An appropriate approach was used to identify the relevant sources of clinical evidence. The JUPITER trial was the starting point of the analysis as it provided recent and robust evidence on the efficacy of the test-and-treat strategy. Additional data were from published sources that included administrative databases and an observational study for the natural history of disease. A standard approach was used for the long-term extrapolation of the clinical trial data. A key assumption was made for the duration of treatment efficacy and the authors pointed out that this was conservative. This assumption was varied appropriately in the sensitivity analyses. QALYs were a valid benefit measure; they not only capture the comprehensive impact of the disease on a patient’s health, but also allow cross-disease comparisons to be made. Little information was given on the instruments used to elicit preferences.

Costs:
The economic analysis appears to have been consistent with the societal perspective, as both medical costs and the value
of lost time were included. Some key unit costs were reported, but most costs, especially those for the treatment of cardiovascular conditions, were presented as category totals. This is a common method, but it reduces the transparency of the analysis and the possibility of replicating it in other settings. The data sources reflected the US health care setting, especially the Medicare payment data. The price year was reported, which will allow reflation exercises for other time periods. The cost of rosuvastatin after patent expiry appears to have been a key input for the analysis.

Analysis and results:
The projected costs and benefits of the two treatments were reported and were appropriately combined using an incremental approach. The findings were clearly reported and were assessed using the commonly quoted cost-effectiveness thresholds of $50,000 or $100,000 per QALY. Appropriate analyses were carried out to investigate the uncertainty, and the results were clearly reported. The authors acknowledged that the clinical results of the JUPITER trial were better than those of other trials of statins and it might have overestimated the true treatment effect because the trial was stopped early due to efficacy. The analysis should be considered to be US specific.

Concluding remarks:
Conventional cost-effectiveness methods were used and areas of uncertainty were considered. This should ensure the validity of the authors’ conclusions.

Bibliographic details
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