The clinical and economic burden of nonadherence with antihypertensive and lipid-lowering therapy in hypertensive patients

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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.

CRD summary
This study examined the cost-effectiveness of antihypertensive therapy and statin therapy for hypertensive patients, with total cholesterol of 6.5mmol/L or less, considering their treatment adherence. Low adherence reduced the benefits of treatment, but therapy was still cost-effective with real-world adherence. Greater cost-effectiveness was achieved with the adherence found in clinical trials. The methods were valid and the extensive analysis of uncertainty showed that the results were robust, which supports the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of antihypertensive therapy plus statin therapy, for patients aged 40 to 79 years, who had hypertension and a total cholesterol level of 6.5mmol/L or less, and it considered their adherence to treatment.

Interventions
Three scenarios were considered: no treatment, real-world adherence to treatment, and ideal adherence to treatment. Treatment was an antihypertensive regimen plus a statin, which was 10mg atorvastatin daily. Two antihypertensive regimens were considered: amlodipine followed by perindopril and doxazosin, or atenolol followed by bendroflumethiazide and doxazosin.

Location/setting
USA/primary care.

Methods
Analytical approach:
The economic evaluation was based on a Markov model that assessed the costs and benefits of primary and secondary prevention, using antihypertensive and statin therapy, for three scenarios, which were no treatment, ideal adherence (based on a clinical trial), and real-world adherence (based on Medicaid data). A lifetime horizon was considered and the authors stated that the analysis was carried out from the perspective of the payer.

Effectiveness data:
The patients’ characteristics, clinical efficacy, and ideal adherence rate were from a randomised controlled trial; the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid-Lowering Arm (ASCOT-LLA). The real-world adherence rates were the key clinical endpoint and these and the transitions were based on filled prescription records from the California Medicaid system. The Framingham Heart Study was used to determine the long-term event rates for the model’s transition probabilities. The assumptions made, for each of the three scenarios, were reported.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years (LYs) gained and events avoided (including stroke and coronary heart disease) were the two main benefit
measures and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the costs of drugs and of emergency visits, hospitalisations, physician contacts, and follow-up for fatal and non-fatal myocardial infarction, angina, and stroke. The resource quantities and unit costs were from a previous study for emergency visits, Medicare reimbursement rates for hospitalisations, physician visits, and follow-up costs, and average wholesale acquisition prices for drugs. The costs were presented as total categories. They were in US dollars ($), for the price year 2006, and future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
A Monte Carlo simulation examined the uncertainty in the results and the distributions used were described. The mean incremental cost-effectiveness ratios (ICERs) and 95% confidence intervals were calculated. Additional sensitivity analyses considered variations in the adherence rates.

Results
The expected LYs were 14.73, the number of events was 0.74, and the mean costs per patient were $12,831, with no treatment. The LYs were 15.07, the events were 0.61, and the costs were $23,295, with real-world adherence. The LYs were 15.49, the events were 0.44, and the costs were $32,492, with ideal adherence.

The incremental cost per LY gained was $22,121 with ideal versus real-world adherence and $30,586 with real-world adherence versus no treatment. The incremental cost per event avoided was $54,364 with ideal versus real-world adherence and $81,591 with real-world adherence versus no treatment.

Relatively small confidence intervals around the ICERs were observed, and the base-case results were generally stable. Lower ICERs were associated with increasing age, for both ideal and real-world adherence compared with no treatment.

Authors’ conclusions
The authors concluded that low adherence reduced the benefits of treatment, but antihypertensive and statin therapies were still cost-effective at adherence levels seen in a real-world setting. Greater cost-effectiveness was achieved with the adherence found in clinical trials and an intervention to improve adherence could be cost-effective.

CRD commentary
Interventions:
The comparators were appropriately selected, not only because treatment was compared against no treatment, but also because two levels of treatment adherence were considered.

Effectiveness/benefits:
The data sources were selected, without a systematic review, which would have been more appropriate, but the selection was based on the authors’ knowledge of published evidence. The data sources were not fully described. A randomised controlled trial was used for the clinical efficacy and the ideal adherence rate, which appears to have been appropriate, given its high internal validity and that almost full compliance is typical of these trials. Other sources were selected to represent US clinical practice. Framingham equations are often used for this type of model. The use of two benefit measures was appropriate and might be relevant for a variety of decision makers. Events avoided are of interest to clinicians, while LYs can be compared with the benefits of other health care interventions.

Costs:
The cost categories were consistent with the economic viewpoint of the health service payer. Some detail of the cost items was provided, but some data were from a previous report and its methods were not described. The use of Medicare rates was appropriate for the perspective. The details of the probability distributions used were appropriately reported. Reflation exercises are feasible as the price year was reported.

Analysis and results:
The analytic approach used to synthesise the costs and benefits was appropriate and the results were clearly presented.
The issue of uncertainty was investigated and the findings were generally robust. A clear description of the decision model was provided. The authors stated that the cost-effectiveness of ideal adherence might have been underestimated as it was not possible to estimate the emergency costs due to stroke and these were higher with partial adherence. The model did not consider the cost of implementing a programme to increase adherence from partial to ideal. Some assumptions were needed to extrapolate the data to the long term, but these were varied in the sensitivity analyses.

**Concluding remarks:**
The methods were valid and the extensive analysis of uncertainty showed that the results were robust, which supports the authors’ conclusions.

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