Incorporating patient-centered outcomes in the analysis of cost-effectiveness: imaging strategies for renovascular hypertension
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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 study compared imaging strategies in patients with medication-resistant hypertension (MRH). In one of the four strategies immediate improved medical therapy was administered without prior diagnostic imaging. The remaining three strategies consisted of an imaging diagnostic test - computed tomography (CT) angiography, magnetic resonance (MR) angiography or conventional angiography - followed by adequate treatment procedures (either percutaneous transluminal angiography with stent placement or improved medical therapy).

Type of intervention
Diagnosis.

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

Study population
The study population comprised a hypothetical cohort of patients with MRH with no prior diagnostic evaluation. Patients were characterised as medication-resistant hypertensive after receiving a two-drug therapy without demonstrating a decrease in blood pressure.

Setting
The setting was not explicitly stated, but it was likely to have been secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1990 and 2002. The cost data were derived from sources published between 1996 and 2002. All costs were adjusted to 1999 levels.

Source of effectiveness data
The effectiveness data were derived from a critical review and synthesis of completed studies, augmented by authors' assumptions.

Modelling
The authors constructed a decision-analytic computer model, replicating the diagnosis and treatment of renal artery stenosis in patients with suspected renovascular hypertension, in order to identify the preferred initial diagnostic strategy of renal artery stenosis. The model was constructed DATA 3.5 (TreeAge Software, Williamstown, MA). In the do nothing strategy, patients entered a Markov model that estimated blood pressure-specific incidences of myocardial infarction, stroke and chronic renal deficiencies. In the improved treatment, and in the diagnostic testing and treatment
strategies, patients entered the Markov model at the end of year 1 (which was considered to be the treatment year). The model estimated blood pressure-specific incidences of myocardial infarction, stroke and chronic renal deficiencies. The patients were followed up for life.

**Outcomes assessed in the review**

The following input parameters were included in the model:

- the incidence of renal artery stenosis,
- the sensitivity and specificity of the three imaging tests,
- the incidence of complications (e.g. contrast-induced nephropathy requiring dialysis and associated mortality rate), and
- mortality and morbidity rates associated with diagnostic conventional angiography and renal arterial stenting.

Blood pressure response to renal artery stent placement was estimated by accounting for the incidence of restenosis and the response to the addition of a third and a fourth medication in renal artery stenosis. Improvement was characterised by a diastolic blood pressure (DBP) >90 mmHg and some improvement by a DBP of 90 to 100 mmHg. Blood pressure-specific incidences of myocardial infarction stroke and chronic renal failure were measured for a DBP <90 mmHg, a DBP of 90 to 100 mmHg or when the DBP was >110 mmHg. Immediate and yearly mortality rates associated with stroke and myocardial infarction, and mortality rate associated with chronic renal failure, were also assessed.

Most of the values were derived from the literature. The authors estimated the blood pressure-specific incidences of myocardial infarction, stroke and chronic renal failure using a technique described elsewhere (see 'Other Publications of Related Interest' below for bibliographic details). Mortality rates associated with chronic renal failure were derived from survival estimates of individuals on dialysis for renovascular disease as reported in a published study (see 'Other Publications of Related Interest' below for bibliographic details).

**Study designs and other criteria for inclusion in the review**

Not stated.

**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**

Overall, the authors cited 11 primary studies as sources of the effectiveness evidence.

**Methods of combining primary studies**

It was unclear whether the authors combined the results of the primary studies.

**Investigation of differences between primary studies**

Not reported.
**Results of the review**

The incidence of renal artery stenosis was 0.20 (range: 0.10 to 0.80).

The sensitivity of CT angiography was 0.96 (range: 0.88 to 1.00) and the specificity was 0.96 (range: 0.65 to 0.97).

The sensitivity of MR angiography was 0.98 (range: 0.88 to 1.00) and the specificity was 0.94 (range: 0.75 to 1.00).

The sensitivity and specificity of conventional angiography were both 0.99 (range: 0.80 to 1.00).

The incidence rate of contrast-induced nephropathy requiring dialysis was 0.0018 (range: 0.0009 to 0.004) and the associated mortality rate was 0.545 (range: 0.25 to 1.00).

The mortality and morbidity rate associated with diagnostic conventional angiography were 0.0004 (range: 0.0002 to 0.0008) and 0.091 (range: 0.045 to 0.20), respectively.

The mortality and morbidity rates associated with renal arterial stenting were 0.0043 (range: 0.002 to 0.008) and 0.047 (range: 0.023 to 0.09), respectively.

The incidence rate of restenosis after renal artery stent placement was 0.11 (range: 0.05 to 0.20). The rate of improvement was 0.18 (range: 0.08 to 0.32) and the rate of some improvement was 0.53 (range: 0.30 to 1.00).

The rate of improvement after the addition of a third medication in renal artery stenosis was 0.10 (range: 0.08 to 0.30) and the rate of some improvement was 0.40 (range: 0.20 to 0.80).

The rate of improvement after the addition of a fourth medication in renal artery stenosis was 0.10 (range: 0.05 to 0.30) and the rate of some improvement was 0.05 (range: 0.025 to 0.10).

The incidence rate of myocardial infarction varied from 0.0032/year (range: 0.0015 to 0.006) when the DBP was <90 mmHg to 0.0095/year (range: 0.005 to 0.02) when the DBP was >90 mmHg. The associated immediate and yearly mortality rates were 0.15 (range: 0.07 to 0.3) and 0.0311 (range: 0.015 to 0.06), respectively.

The incidence rate of stroke varied from 0.0008/year (range: 0.0004 to 0.0016) when the DBP was <90 mmHg to 0.0072/year (range: 0.0035 to 0.014) when the DBP was >90 mmHg. The associated immediate and yearly mortality rates were 0.19 (range: 0.1 to 0.4) and 0.0201 (range: 0.01 to 0.04), respectively.

The incidence rate of chronic renal failure varied from 0.002/year (range: 0.0010 to 0.0050) when the DBP was <90 mmHg to 0.0462/year (range: 0.02 to 0.10) when the DBP was >90 mmHg. The associated mortality rate was 0.30 (range: 0.15 to 0.60).

**Methods used to derive estimates of effectiveness**

Some estimates of effectiveness were supplemented by authors' assumptions.

**Estimates of effectiveness and key assumptions**

owing to a lack of existing data in the literature, the authors assumed the sensitivity and specificity of conventional angiography were both 99%.

**Measure of benefits used in the economic analysis**

The measures of benefits used were the life-years (LYs) lived, quality-adjusted life-years (QALYs) lived and test-related disutility-adjusted QALYs.

The utilities for LYs saved were derived from two published studies that used the time trade-off technique in patients with myocardial infarction and with stroke, respectively (see ‘Other Publications of Related Interest’ below for
bibliographic details). It was reported that in combinations of conditions, the lowest quality adjustor was used. This was based on authors' assumptions and was justified appropriately.

Test-dependent short-term disutilities were derived from published studies that used risk-based assessment with the time trade-off technique in MRH patients diagnosed by MR and conventional angiography (see 'Other Publications of Related Interest' below for bibliographic details). The authors assumed that test-related disutility of CT angiography was equal to that of MR angiography, whilst acknowledging that the assumption was probably an underestimate. Test-related disutilities were incorporated into the cost-effectiveness analysis by calculating the willingness-to-pay according to a published study, and multiplying the test-related disutility by the difference between the qualities of life before and after treatment for hypertension.

Direct costs
Health service costs were included. The costs included in the analysis focused on the costs of the imaging techniques (CT, MR and conventional angiography), renal artery stent placement, myocardial infarction (per patient per year), stroke (per patient per year), dialysis (per patient per year), antihypertensive medication (with three and four antihypertensives per year) and annual clinic evaluation. The costs were either derived from actual data (1999 Medicare and Diagnosis-related group reimbursements for south-eastern Michigan) or from the literature. The unit costs were reported. The costs were discounted at an annual rate of 3%, which was appropriate as the outcomes were calculated for the patient's lifetime. All costs were reported for 1999 levels and appear to have been estimated per patient (in some cases this was explicitly stated).

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Indirect costs were reported per patient per year. The costs included were lost wages due to morbidity (myocardial infarction, stroke, chronic renal failure and hypertension), which were derived from the literature, and future earnings lost due to premature death (derived from a published study using human capital valuation of a statistical LY). The unit costs were reported. All costs were discounted at an annual rate of 3%, which was appropriate since the costs were incurred over a patient's lifetime. All costs were reported for 1999 levels.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out on all input parameters to investigate variability in the data. The type of sensitivity analysis was not explicitly stated, but it appears to have been a one-way analysis that was carried out after adjusting for quality of life and test-related disutility. The variable ranges tested were based on published data. Where data were not available in the literature, the authors conducted an analysis in which the input parameters were varied by 50% (lower limit) and 200% (upper limit) of the base-case value.

Estimated benefits used in the economic analysis
The do nothing strategy (base-case scenario) resulted in a life expectancy of 7.77 LYs, 6.08 QALYs and 6.08 quality- and test-related disutility-adjusted LYs.

Improved medical therapy resulted in a life expectancy of 9.24 LYs, 7.60 QALYs and 7.60 quality- and test-related disutility-adjusted LYs.

The CT angiography strategy resulted in a life expectancy of 9.77 LYs, 8.17 QALYs and 8.15 quality- and test-related disutility-adjusted LYs.
disutility-adjusted LYs.

The MR angiography strategy resulted in a life expectancy of 9.78 LYs, 8.18 QALYs and 8.17 quality- and test-related disutility-adjusted LYs.

The conventional angiography strategy resulted in a life expectancy of 10.31 LYs, 8.87 QALYs and 8.85 quality- and test-related disutility-adjusted LYs.

Cost results
When only direct medical costs were included, the do nothing strategy (base-case scenario) resulted in a cost of $69,459, the improved medical therapy strategy in a cost of $85,502, the CT angiography strategy in a cost of $83,856, the MR angiography strategy in a cost of $80,807, and the conventional angiography strategy in a cost of $87,050.

When indirect costs were also included, the do nothing strategy resulted in a cost of $2,178,098, the improved medical therapy strategy in a cost of $2,139,787, the CT angiography strategy in a cost of $2,148,768, the MR angiography strategy in a cost of $2,148,768, and the conventional angiography strategy in a cost of $2,130,680.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was performed. A strategy was assumed to be cost-effective if it resulted in an incremental cost-effectiveness ratio of less than $50,000 per additional QALY.

When only direct costs were taken into account, MR angiography proved to be the most cost-effective strategy in comparison with the base-case scenario with an incremental cost of approximately $6,000 per additional QALY (test-related disutilities were also included). After the inclusion of indirect costs, all strategies dominated the base-case scenario and conventional strategy dominated all other strategies. When the three imaging strategies were compared with the improved medical treatment strategy, CT angiography and MR angiography proved to be cost-effective with a cost of $16,000 per additional QALY.

The results of the sensitivity analysis demonstrated that conventional angiography remained a cost-effective alternative and generally dominated MR angiography, except when the probability of stenosis was less than 3%.

Authors’ conclusions
Management strategies involving imaging diagnostic tests were more effective in saving lives than the other two approaches for the diagnosis and treatment of medication-resistant hypertension (MRH) at an "extremely reasonable cost". Magnetic resonance (MR) angiography was the dominant strategy when only direct costs were considered, while conventional angiography was the dominant strategy when indirect costs were also taken into account.

CRD COMMENTARY - Selection of comparators
The authors chose the do nothing strategy (no further diagnostic imaging and no further medical therapy) as the comparator for the analysis. They discussed the existence of alternative management strategies in detail, reporting also that conventional angiography is thought to be the ‘gold’ standard for the diagnosis of renal artery stenosis. You should decide if these strategies represent a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The authors reported that they carried out a critical analysis of the literature but they did not conduct a systematic review of the literature. The sources searched, inclusion criteria and data extraction methodology were not reported. It is therefore possible that data from the available studies could have been used selectively. The authors did not note any differences between the studies or report on the methods used to combine estimates, if in fact a synthesis took place. Given the level of reporting it is difficult to judge the quality of the parameters used as model inputs. However, the authors performed several sensitivity analyses in relation to the efficacy estimates and this should improve the
reliability and generalisability of the study findings.

**Validity of estimate of measure of benefit**
The measures of benefits used in the economic analysis were the LYs lived, QALYs lived and test-related disutility-adjusted QALYs. The authors referred the reader to published studies concerning the methods and data used to derive these measures of benefits. The use of QALYs enables comparisons with other health care programmes.

**Validity of estimate of costs**
The analysis of the costs was performed from the perspectives of the health care system and of society. All the relevant costs appear to have been included in the analysis. However, the costs and the quantities were not reported separately which means that the analysis could not be easily reworked for other settings. The costs were treated deterministically, but sensitivity analyses were conducted to assess the robustness of the estimates used. The unit costs, price year and discounting were all reported, all of which improve the generalisability of the results.

**Other issues**
The authors did not make appropriate comparisons of their findings with those from other studies. However, this may have been due to a lack of published literature in this specific area. The authors did, however, summarise the results, study design and methods of relevant published studies, stressing the differences between these and their own study. The issue of generalisability was not addressed. The authors do not appear to have presented the results selectively. The study involved patients with MRH this was reflected in the authors’ conclusions.

The authors reported a number of limitations of their study. First, test-related disutilities might have been an underestimate as they were derived from a study on patients with peripheral vascular disease and not on patients with renovascular hypertension. Second, the model did not include other diagnostic methods such as Doppler sonography or captopril scintigraphy, although the authors suggested that the fact that they had incorporated a clinical decision rule with a predictive value close to that of these diagnostic methods counterbalanced their absence from the model. The absence of surgical interventions from the model was adequately justified.

**Implications of the study**
The authors did not make any explicit recommendations for changes in policy or practice, stressing the fact that the adoption of a cost-effective strategy depends on the perspective of the decision-maker and also the available infrastructure of each health service. The authors did not identify further research although the discussion highlighted some areas where more information is needed.

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