The cost-effectiveness of doxazosin for the treatment of hypertension in type II diabetic patients in the UK and Italy

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 doxazosin for the treatment of hypertension in Type II diabetes.

Type of intervention
Treatment and prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with Type II diabetes and hypertension in the UK and Italy.

Setting
The setting was the community. The economic study was carried out in the UK and Italy.

Dates to which data relate
The dates during which the effectiveness data and resource use estimates were obtained were not provided. The unit prices for both UK and Italy were from 1999.

Source of effectiveness data
The risk rates were taken from a single study, namely the UK Prospective Diabetes Study (UKPDS, see Other Publications of Related Interest no.1), and were adjusted for age and lipid levels using the Framingham risk equations (see Other Publications of Related Interest no.2). Patient characteristics of the modelled patient cohorts were also taken from the UKPDS study.

Link between effectiveness and cost data
The costing was not undertaken on the same patient sample as that used for the clinical study. The costing was based on assumptions derived from Delphi panels.

Modelling
A Markov model evaluating hypothetical cohorts of 100,000 patients was used to simulate and synthesise costs and consequences for the choice of antihypertensive treatment.

Outcomes assessed in the review
The outcomes of interest to this analysis were absolute risk rate of angina, stroke, myocardial infarction (MI), heart failure, peripheral vascular disease (PVD) and all-cause mortality.

**Study designs and other criteria for inclusion in the review**
Not reported.

**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**
Nine studies were reviewed, but only a single study was used to estimate the lipid-lowering impact of doxazosin, namely the Treatment of Mild Hypertension Study. The impact of lower lipid levels on the risk rates for the clinical outcomes were then estimated. The UKPDS was used to derive risk rates for the other treatment strategies.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The absolute risk rates of macrovascular complications for the tight control group were as follows (rates taken from UKPDS, see Other Publications of Related Interest no.1):

- angina, 0.0079 (95% confidence interval, CI: 0.0037 - 0.016);
- stroke, 0.0065 (95% CI: 0.0028 - 0.014);
- MI, 0.0186 (95% CI: 0.011 - 0.030);
- heart failure, 0.0036 (95% CI: 0.0011 - 0.010);
- PVD, 0.0014 (95% CI: 0.00015 - 0.0071); and
- all-cause mortality, 0.0224 (95% CI: 0.014 - 0.034).

The absolute risk rates of macrovascular complications for the less tight control group were as follows (rates taken from UKPDS):

- angina, 0.0075 (95% CI: 0.0034 - 0.016);
- stroke, 0.0116 (95% CI: 0.0062 - 0.021);
MI, 0.0235 (95% CI: 0.015 - 0.035); heart failure, 0.0081 (95% CI: 0.0038 - 0.016); PVD, 0.0027 (95% CI: 0.00064 - 0.0091); and all-cause mortality, 0.0272 (95% CI: 0.018 - 0.040)

The absolute risk rates of macrovascular complications for the doxazosin group were based on estimates from 'tight control', but were adjusted for the additional lipid-lowering effect of doxazosin. The following rates were presented without CIs:

angina, 0.00691;
stroke, 0.00647;
MI, 0.01466;
heart failure, 0.00351;
PVD, 0.00137; and all-cause mortality, 0.01792.

Methods used to derive estimates of effectiveness
The authors made assumptions about the treatment effect on the basis of the results from the UKPDS (see Other Publications of Related Interest no.1).

Estimates of effectiveness and key assumptions
The authors made several assumptions:

all the antihypertensive agent combinations studied were equally effective at achieving blood-pressure control;
all the drug regimens achieved a blood-pressure reduction equal to that of tight control in UKPDS, or 144/82 mmHg;
patients on minimal drug therapy showed a reduction in blood-pressure equal to that of less tight control in UKPDS, or 157/87 mmHg;
the duration of treatment and follow-up was 10 years.

Measure of benefits used in the economic analysis
The measure of benefit was the number of life-years saved.

Direct costs
The costs estimated for each health state in the model included the costs of laboratory tests, surgical procedures, hospitalisations, rehabilitative care, physician visits and medication use. The utilisation of these resources was established through interviews with a Delphi panel. The average resource use for each patient was then calculated. The resource quantities were not given. The unit costs were not provided, but were taken from 1999. The costs were discounted at a rate of 6%.

Statistical analysis of costs
Not reported.

**Indirect Costs**
Indirect costs were not included.

**Currency**
UK pounds sterling (£) and Italian lira (L).

**Sensitivity analysis**
The authors conducted both univariate and multivariate sensitivity analyses on the results. A range of estimates for drug costs and lipid levels was explored, as were discount rates of 0 and 6%. Further, a probabilistic sensitivity analysis was conducted in which the probabilities of developing macrovascular complications and the lipid levels were assigned a truncated normal distribution and varied within the 95% CI. Medication costs were simultaneously varied over a 10% range.

**Estimated benefits used in the economic analysis**
The average treatment effect of regimens that substituted doxazosin in a combination regime was 0.36 and 0.71 additional life-years, compared with patients in the tightly and less tightly controlled treatment groups, respectively.

**Cost results**
The total, expected aggregated costs over a 10-year treatment period ranged from 7,599 for atenolol, frusemide and nifedipine, to 9,886 for captopril, doxazosin and nifedipine (11.5 million L to 14.2 million L). The least costly intervention was the less tightly controlled regime. Substituting doxazosin for either atenolol, frusemide or nifedipine in the 'tightly controlled' regimes increased the total costs by between 795 (659,196 L) and 1,741 (3,318,470 L).

**Synthesis of costs and benefits**
The incremental costs per life-year saved by substituting doxazosin with components of other treatment regimes were given. Not all the results were presented as it was only necessary to compare any therapy containing doxazosin with the next most costly therapy, which would be something other than minimal drug therapy. However, since all of these therapies were assumed to give the same benefit, the cheapest, i.e. atenolol, frusemide and nifedipine, would always be chosen. Minimal drug therapy would never be chosen because it gave less benefit and cost more, i.e. it was dominated by atenolol, frusemide and nifedipine.

Doxazosin substituted for frusemide in the regime of atenolol, frusemide and nifedipine gave an incremental cost-effectiveness ratio (ICER) of 4,783 (8,949,417 L).

The authors commented that the results from the sensitivity analysis were "relatively insensitive to the varied parameters and did not substantially affect the cost-effectiveness ratios or the rank-order of the results", but they did not present them.

**Authors' conclusions**
The use of doxazosin in antihypertensive treatment strategies reduced morbidity and mortality in Type II diabetic patients at a favourable cost-effectiveness ratio.

**CRD COMMENTARY - Selection of comparators**
The antihypertensive agents used in combination to achieve reduced levels of blood-pressure in the UKPDS were atenolol or captopril, frusemide and nifedipine. These are extensively used in the routine management of hypertension.
for patients with Type II diabetes and seemed appropriate for the economic analysis.

**Validity of estimate of measure of effectiveness**
The authors made several, explicit assumptions in their evaluation. They assumed that desired blood pressure levels would be achieved on a 'tight control' regime for all patients, but only 29% in the UKPDS achieved these desired levels. It is unclear whether the authors took this 'success rate' into consideration in their model and reduced effectiveness estimates appropriately. The authors also assumed that all combinations of antihypertensive agents were equally effective at achieving desired blood pressure levels, but this was not substantiated by clinical data. The authors acknowledged that the assumptions of effectiveness were based on the UKPDS, which primarily included Caucasians, and combined these with survival functions from the Framingham heart study, which also included predominantly Caucasians. Generalisability to other populations may not, therefore, be straightforward and should be judged on an ad-hoc basis.

**Validity of estimate of measure of benefit**
The number of life-years gained is a useful measure of benefit since it allows comparison with the effects of other technologies. It does not, however, account for quality of life or individual preferences over different health attributes.

**Validity of estimate of costs**
The cost estimates were based entirely on expert opinion through the use of Delphi panels. This is a less robust method than prospective data collection alongside a study. Only direct costs were included in the analysis. The costs were appropriately discounted. Although the method of estimating costs was given, the results in terms of resource quantities and unit costs were not, which affects the generalisability of the study. The authors presented the appropriate ICER, although they presented redundant and possibly misleading comparisons. It would also have been helpful to have seen the 95% CIs for the ICERs presented in the paper, in order to assess the precision of the estimates. Furthermore, the results of the sensitivity analysis were not presented, and this would have been useful.

**Other issues**
The authors pointed out that this is the first economic evaluation to be published on doxazosin, and comparison with other studies was therefore not possible. They also highlighted the limitations of the clinical data and the assumptions made in terms of relevance to other clinical settings.

**Implications of the study**
The authors recommended that adding doxazosin to combination treatments for hypertension should be strongly considered in Type II diabetes patients in the UK and Italy. In order to make this decision, one must compare the cost-effectiveness with other technologies, bearing in mind the study limitations already mentioned.

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None stated.

**Bibliographic details**

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**Other publications of related interest**


**MeSH**
Antihypertensive Agents /economics /therapeutic use; Cost-Benefit Analysis; Diabetes Mellitus, Type 2 /complications /economics; Diabetic Angiopathies /drug therapy /economics; Doxazosin /economics /therapeutic use; Drug Therapy, Combination; Female; Great Britain; Humans; Hypertension /drug therapy /economics; Italy; Lipids /blood; Male; Middle Aged; Risk Assessment

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