Cost-effectiveness of irbesartan 300 mg given early versus late in patients with hypertension and a history of type 2 diabetes and renal disease: a Canadian perspective
Coyle D, Rodby R, Soroka S, Levin A, Muirhead N, de Cotret P R, Chen R, Palmer A

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
The authors evaluated the cost-effectiveness of early and late use of irbesartan in the development of renal disease, in addition to conventional therapy, for hypertensive patients with type 2 diabetes. The authors concluded that the early initiation of irbesartan was the most cost-effective option for this population in Canada. Despite a couple of methodological uncertainties, the authors’ conclusions appear to be reasonable.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the cost-effectiveness of early and late addition of the angiotensin II receptor antagonist (AIIRA) irbesartan to conventional treatment for the management of hypertensive patients with type 2 diabetes and early renal disease.

Interventions
Three treatment strategies were evaluated. In the early irbesartan treatment strategy, when patients started to develop microalbuminuria, 300mg per day of irbesartan was added to their conventional treatment (medications for diabetes or hypertension without AIIRAs). In the late irbesartan treatment strategy, irbesartan was added to the conventional treatment, at the same dose, but after patients had developed advanced overt nephropathy (AON). The conventional treatment strategy consisted of commonly used antihypertensive medications.

Location/setting
Canada/primary care.

Methods
Analytical approach:
The progression of microalbuminuria in hypertensive patients with type 2 diabetes until their death was modelled using a Markov model over a 25-year time horizon by combining data from two previous trials (IRMA-2 and IDNT trials). The authors stated that the perspective was that of the Canadian health and social care system.

Effectiveness data:
The disease progression probabilities were derived from two randomised control trials (RCTs), with 1,715 patients in the IDNT trial and 201 patients in the IRMA-2 trial. Baseline and relative risk of mortality data came from Canadian statistics and a Danish study.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The measure of benefit was life-years gained (LYG) and these were discounted at an annual rate of 5%.

Cost data:
The cost categories included the costs of irbesartan and ancillary drug therapies, patient management, dialysis and...
transplantation, and managing a cardiovascular event. The estimates of the costs of additional therapies were based on the IRMA-2 and IDNT trials. The resource use for patient management was determined by an expert panel of Canadian physicians. The other resource use and cost data were derived from the two trials and from other published studies. The costs were presented in Canadian dollars (CAD). The price year was 2006 and all costs were discounted at an annual rate of 5%.

**Analysis of uncertainty:**

One-way sensitivity analyses were conducted on the transition probabilities, key model parameters and the discount rate. A threshold analysis was conducted to identify the critical values of all input parameters associated with the disease progression, while assuming a maximum willingness-to-pay of CAN $50,000 per LYG. Parameter uncertainty was also investigated through probabilistic sensitivity analysis using Monte Carlo simulations. A range of incremental cost-effectiveness ratios was presented to show the results of the sensitivity analysis.

**Results**

The early irbesartan strategy dominated the other two strategies as it was less costly and more effective. It resulted in 0.45 LYG and a cost-saving of CAN 54,100 compared with the late irbesartan strategy.

The one-way sensitivity analysis demonstrated that these results were only sensitive to increased mortality risk due to development of overt nephropathy (ON) and the time taken to progress from early ON to AON. The threshold analysis demonstrated that the results were robust at the assumed willingness-to-pay. The probabilistic analysis revealed that the early irbesartan strategy had a probability of over 99% of being the most cost-effective strategy at a willingness-to-pay for a LYG of CAN 0 up to $100,000. Similarly the late irbesartan strategy had a probability of over 99% of being more cost-effective than conventional treatment.

**Authors' conclusions**

The authors concluded that, in Canada, the early addition of irbesartan to conventional treatment for hypertensive patients with type 2 diabetes at the initial stage of microalbuminuria, before it progressed to AON, resulted in cost-savings and increased life expectancy when compared with conventional treatment or initiation of irbesartan after the development of AON.

**CRD commentary**

**Interventions:**
The interventions were clearly reported including the dosage. The study was thorough in its coverage of alternative interventions, including current practice in its setting.

**Effectiveness/benefits:**
The effectiveness data were derived from two clinically comparable RCTs. However, the selection of these studies was not justified. The full details of the trials were not reported in this paper; and a full assessment of their internal validity was therefore not possible. Life-years gained is a useful measure of benefit given the risk of death from the disease progression. However, the relative importance of quality of life outcomes should be considered.

**Costs:**
The costs appeared to reflect the perspective stated. With the exception of some costs and quantities which were not reported separately, most of the cost data were adequately reported, along with adjustments, including discounting and the price year. An extensive probabilistic sensitivity analysis around the cost estimates and one-way sensitivity analysis around the discount rate demonstrated that these estimates were robust. They were also appropriate for the study setting.

**Analysis and results:**
The model structure, relevant details and modelling assumptions were clearly reported. The authors conducted an incremental analysis and the results were adequately presented. The methods used throughout the economic evaluation and the sensitivity analysis were adequately reported. An extensive sensitivity analysis was conducted on modelling parameters, which enhanced the generalisability of the findings and showed the robustness of the results. The authors outlined a number of possible limitations to the study and their impact on the results.
Concluding remarks:
Apart from a couple of methodological uncertainties, the authors presented a fairly transparent analysis and their conclusions appear to be reasonable.

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