Cost-utility analysis of antihypertensive combination therapy in Japan by a Monte Carlo simulation model

Saito I, Kobayashi M, Matsushita Y, Mori A, Kawasugi K, Saruta T

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 aim was to evaluate the cost-effectiveness of antihypertensive therapy with an angiotensin-II-receptor blocker, a calcium-channel blocker, or both, in Japan. The authors concluded that the combination therapy was more favourable than monotherapy with either agent alone, irrespective of the presence of diabetes. There were a few limitations to the study and the authors’ conclusions should be considered with caution.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to evaluate the cost-effectiveness of antihypertensive therapy, using different medications, to prevent the onset of diabetes. The analysis was conducted both for females and males, and for patients with and without diabetic complications.

Interventions
The interventions were an angiotensin-II-receptor blocker (ARB) monotherapy; calcium-channel blocker (CCB) monotherapy; and ARB with CCB combination. The CCB was azelnidipine 16mg per day and the ARB was olmesartan medoxomil 20mg per day.

Location/setting
Japan/out-patient and hospital.

Methods
Analytical approach:
A lifetime Markov model was used to model the ongoing risk of coronary heart disease (CHD), stroke, and diabetic retinopathy over time and their associated costs and health outcomes. A first-order Monte Carlo simulation was used. The perspective stated by the authors was that of the payer.

Effectiveness data:
The authors assumed different systolic blood pressure decrements for each treatment strategy, but the basis for these assumptions was not reported. The relative risks of developing diabetes with ARB were extracted from randomised trials. The sources of the probabilities for the different sub-models were reported, and the authors cited a previous paper for more details (Saito, et al. 2005, see ‘Others Publications of Related Interest’ below for bibliographic details).

Monetary benefit and utility valuations:
Some of the utilities were taken from the literature (those for diabetes and stroke). Others were assumed by the authors.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs). Discounting of long-term benefits was not reported.

Cost data:
The cost categories included those of the diseases (CHD, diabetes, stroke, and death) and both out-patient and long-term costs. Medication and laboratory costs were also included. Only a few sources were reported, and most of the data
came from the Saito (2005) paper. No price year was stated, and the currency was Japanese yen (JPY). Discounting of the long-term costs was not reported.

Analysis of uncertainty:
One-way sensitivity analyses or scenario analyses were conducted for the degree of blood pressure lowering, in the combination group; testing different models for the progression of diabetes; evaluating different diabetic incidences; the relative effects of ARB in diabetes or diabetic nephropathy incidence.

**Results**
In men without diabetes, the QALYs were 16.30 for ARB, 16.16 for CCB, and 16.70 for the combination. In men with diabetes, the QALYs were 14.69 for ARB, 14.25 for CCB, and 15.15 for the combination. For women, the results showed similar trends.

In men without diabetes, the costs were JPY 6.21 million for ARB, JPY 6.07 million for CCB, and JPY 5.98 million for the combination. In men with diabetes, the costs were JPY 9.87 million for ARB, JPY 11.01 million for CCB, and JPY 9.58 million for the combination. For women, the results showed similar trends.

The combination of ARB and CCB was the dominant therapy, which means it was more effective and cheaper than the alternatives.

The sensitivity analyses showed that the combination therapy was not always cost saving, but it was always the most cost-effective strategy, and always fell below the commonly used cost-effectiveness threshold of 50,000 US dollars (JPY 5 million) per additional QALY.

**Authors' conclusions**
The authors concluded that, from a pharmacoeconomic point of view, the combination therapy of an ARB plus a CCB was more favourable than monotherapy with either agent alone, irrespective of the presence of diabetes.

**CRD commentary**
Interventions:
The interventions chosen appeared to be relevant, but it was not clear why the particular drugs from each family were selected. Also, the authors stated that other commonly used antihypertensive drug classes were omitted, such as angiotensin-converting enzyme inhibitors and thiazides.

Effectiveness/benefits:
The model translated intermediate blood pressure outcomes in millimetres of mercury (mmHg) into final events. The size of the blood pressure reduction was assumed for each regimen, and the reference or justification on which the assumptions were made was not presented. It was stated that even a 5mmHg difference between the combined therapy and the monotherapy was still cost-effective. Also, the parameter used for the reduction in the incidence of nephropathy with ARB was not described in detail. The authors did not justify their selection of the clinical-study sources and it is not clear if the best available evidence was used. It was not clear why discounting was not reported, as current guidelines for economic evaluations recommend its inclusion in long-term studies. No search strategy nor inclusion criteria for the sources were reported. The methods that were used in these studies to derive the utility estimates were not reported and it was not stated whether these methods were consistent across the studies.

Costs:
All the relevant costs appear to have been included for the stated perspective. Selected sources were described and the other data were based on assumptions or on a previous study (Saito, et al. 2005). No price year was stated and discounting was not mentioned even though the time horizon was long enough to make it relevant.

Analysis and results:
The model was clearly explained and the results were adequately reported. The impact of uncertainty was evaluated through selected one-way sensitivity analyses.
Concluding remarks:
There were a few limitations to the study and the authors’ conclusions should be considered with caution.

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