Applying some UK Prospective Diabetes Study results to Switzerland: the cost-effectiveness of intensive glycaemic control with metformin versus conventional control in overweight patients with type-2 diabetes

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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 use of metformin-based drug therapy for the intensive control of overweight patients with Type 2 diabetes.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised overweight patients with Type 2 diabetes. The specific inclusion criteria were not reported.

Setting
The setting was the community. The economic study was carried out in Switzerland.

Dates to which data relate
The effectiveness data were mainly derived from studies published in 1991 and 1998. The dates during which the resource use data were gathered were not reported. The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from published studies. The main source of data was the United Kingdom Prospective Diabetes Study (UKPDS; see Other Publications of Related Interest nos.1-2). This was a multi-centre, prospective, randomised intervention trial.

Modelling
A Markov decision model was used to simulate the occurrence of diabetes-related complications and other important events in a cohort of 1,000 patients. The time horizon of the model was 11 years (11 cycles of one year each). The patients entered the model in the state of “alive, no long-term complications” and then acute events could occur. One-year transition probabilities were calculated from the event rates reported in the UKPDS metformin sub-study (see Other Publications of Related Interest no.2).

Outcomes assessed in the review
The outcomes assessed in the review were the annual probabilities of the following events:
fatal and nonfatal myocardial infarction;
sudden death;
heart failure;
angina;
fatal and nonfatal stroke;
death from peripheral vascular disease;
amputation;
death from renal disease;
haemodialysis;
peritoneal dialysis;
kidney transplant;
retinal photocoagulation;
vitreous haemorrhage;
blindness;
cataract extraction;
death from hyperglycaemia and hypoglycaemia;
a major hypoglycaemic event;
a fatal accident; and
death from cancer, any other specified cause, or from an unknown cause.

Study designs and other criteria for inclusion in the review
The main primary study was a multi-centre, prospective, randomised intervention trial.

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
The effectiveness data were principally derived from two primary studies.
Methods of combining primary studies
Not carried out.

Investigation of differences between primary studies
Not relevant.

Results of the review
The probabilities were not reported.

Measure of benefits used in the economic analysis
The benefit measured in the economic analysis was the number of life-years gained with metformin, compared with conventional control. This was estimated by calculating the survival curves from the mortality data, which were derived from the effectiveness analysis. The benefits were both not discounted, and discounted at rates of 3 or 5%.

Direct costs
Discounting was relevant as the costs occurred over an 11-year period. The future costs were discounted at a rate of 3 or 5%. In a different model, the specification costs were not discounted. The quantities of the resources used and the unit costs were not reported. The resource/cost boundary adopted was that of the Swiss third-party payer. The categories of costs included the direct medical costs for the treatment and adverse events, presented according to the event (for example, death from renal disease). The costs of protocol-drive follow-up and investigations were excluded as it was stated that they were similar in both groups. The quantities and the unit costs were estimated using data derived from the literature (from 1994 to 1999). The price year was 1999.

Statistical analysis of costs
No statistical test of the difference of the costs was reported, although they were treated stochastically.

Indirect Costs
No indirect costs were included.

Currency
Swiss francs (Sfr). Swiss francs were converted into UK pounds sterling. The exchange rate was Sfr 2.59 = 1.00.

Sensitivity analysis
One-way sensitivity analyses were carried out on the cost and probability variables, to assess the impact of each factor on the final cost. Each parameter was varied by plus or minus 10%. Monte Carlo simulations were also conducted on the decision model. Finally, a threshold analysis was carried out on the acquisition cost of metformin.

Estimated benefits used in the economic analysis
The undiscounted life-years gained with metformin, over conventional control, were 0.43 over the 11-year follow-up period. When discounting at 3%, 0.34 life-years were gained. When discounting at 5%, 0.30 life-years were gained.

Cost results
The average undiscounted costs per patient, plus or minus the standard deviation (SD), were Sfr 13,225 (+/-23,454) in the metformin group and Sfr 14,538 (+/-28,680) in the conventional group. The cost-saving of metformin was equal to
Sfr 1,313.

The average costs per patient (+/-SD) discounted at 3% were Sfr 11,096 (+/-27,751) in the metformin group and Sfr 12,195 (+/-29,374) in the conventional group. The cost-saving of metformin was equal to Sfr 1,099.

Finally, the average costs per patient (+/-SD) per patient discounted at 5% were Sfr 9,950 (+/-27,711) in the metformin group and Sfr 10,877 (+/-30,450) in the conventional group. The cost-saving of metformin was equal to Sfr 927.

**Synthesis of costs and benefits**

The costs and the benefits were not combined. It was stated that the sensitivity analysis indicated that the cost of metformin had the greatest impact on the results, followed by the event rates, then the costs related to myocardial infarction, renal failure, and stroke. The break-even point for the annual acquisition cost of metformin was Sfr 480 per year. Above this, the use of the intensive therapy would lead to cost increases in comparison with conventional control.

**Authors’ conclusions**

Despite some limitations of the analysis, intensive control with metformin was proven to be cost-saving and life-saving, compared with conventional control, in overweight Type 2 diabetes patients in Switzerland.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparator was based on the drug therapies used in a subgroup of patients in the UKPDS, one of which was stated to be conventional. You should consider whether this represents a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence was not derived from a review of the literature. Instead, it was mainly taken from a specific study (the UKPDS trial), whose results were published in different papers (see Other Publications of Related Interest nos.1-2). The primary study used a prospective and randomised design, therefore it is likely to have provided reliable data. However, the estimated probability values were not reported. Further, the authors acknowledged that only the effect of intensive control with metformin was tested, while the effect of additional interventions (such as treatment of hyperlipidaemia, hypertension, and antioxidant therapy) was not assessed.

**Validity of estimate of measure of benefit**

The benefit measure (the life-years saved) was obtained using a decision model. This model appears to have been appropriate for simulating the treatment of diabetic patients, although the quality of live was not valued. The authors assumed that metformin would only affect the number of life-years gained during the study period (11 years) and that, at the end of the follow-up period, no future difference in treatment effect would be seen. According to the uncertainty in the literature, the benefits were both discounted (3 or 5%) and not discounted.

**Validity of estimate of costs**

The costs and the resources used were analysed using mainly estimates obtained from the literature or from assumptions made by the authors. However, several sensitivity analyses were conducted on the data assumed, and none of the assumptions made were stated to have had a major impact on the results. It would have been helpful if some of these results had been shown. The perspective from which the study was conducted was reported clearly. It appears that all the relevant categories of costs have been included in the study.

**Other issues**

The authors highlighted that the main assumption in their study was the transferability of the effectiveness data from the UK trial to the Swiss setting. However, extensive sensitivity analyses were conducted and the results appeared quite
robust. The authors also compared their findings with those from the UK setting. The authors could have reported some of the results in order to increase transparency. Their conclusions were in keeping with the population studied.

**Implications of the study**
According to the authors, the analysis showed the cost-effectiveness of intensive control with metformin, over conventional control, in overweight patients with Type 2 diabetes. However, as the authors pointed out, further country-specific clinical and economic data should be available to better assess the impact of intensive control in specific classes of diabetic patients. Finally, the claim relating to the cost-effectiveness should be viewed with caution given the uncertainty surrounding the estimates of benefit and cost, in particular, the large standard deviations in the costs.

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None stated.

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**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

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