Cost effectiveness of saxagliptin and metformin versus sulfonylurea and metformin in the treatment of type 2 diabetes mellitus in Germany: a Cardiff Diabetes Model analysis

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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.

CRD summary
The objective was to assess the cost-effectiveness of saxagliptin and metformin, compared with sulphonylurea (glipizide) and metformin, for the second-line treatment of patients with type-2 diabetes mellitus. The authors concluded that saxagliptin might be associated with improved outcomes, at a cost that was acceptable in Germany. The methods and reporting were good. The authors’ conclusion reflects the evidence presented.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of saxagliptin and metformin, compared with sulphonylurea (glipizide) and metformin, for the second-line treatment of patients with type 2 diabetes. The patient characteristics were based on patients in a recent multinational randomised trial, 85% of whom were European.

Interventions
Saxagliptin with metformin was compared with sulphonylurea (glipizide) with metformin. Both therapies were given after the failure of metformin alone. If either second-line therapy failed, metformin plus insulin was given as third-line therapy. A glycated haemoglobin level of 7% was used as the threshold for moving from first- to second-line therapy, and 7.5% was used for moving to third-line therapy.

Location/setting
Germany/primary care.

Methods
Analytical approach:
A published state-transition model (the Cardiff Diabetes Model) was adapted to estimate the cost-effectiveness of the treatment pathways, over 40 years. The model assessed three lines of treatment, which differed in second-line therapy only. The authors stated that the perspective was that of the German National Sick Fund.

Effectiveness data:
The key effectiveness measures were the changes in glycated haemoglobin and body weight, and the occurrence of hypoglycaemia. The data for metformin as first-line therapy were from a systematic review; those for the two second-line therapies were from a head-to-head multinational randomised trial; and those for the third-line therapy were from a meta-analysis. Disease progression was based on evidence from the UK Prospective Diabetes Study (UKPDS) 68.

Monetary benefit and utility valuations:
The model used age-specific utility values, to which decrements were applied for complications. The initial utility values were published EQ-5D estimates for UK patients, with no complications. Most of the utility decrements were from the UKPDS 62. The relationship between the patient’s fear of hypoglycaemia and utility was modelled using published equations.

Measure of benefit:
The primary measure of benefit was quality-adjusted life-years (QALYs). Future effects were discounted at a rate of
3% per annum.

Cost data:
The cost categories were drugs, fatal events, cases of severe hypoglycaemia, and care in hospital and by general physicians. The costs of drug therapy were based on official price lists, with weighting by the defined daily dose and average consumption. Other costs were based on published literature; German sources were generally used. The costs were presented in Euros (EUR) and adjusted to 2009 values using the consumer price index. Future costs were discounted at a rate of 3% per annum.

Analysis of uncertainty:
The authors conducted one-way, two-way, and probabilistic sensitivity analyses to assess the impact of uncertainty on the results. These results were presented in tornado charts, and a cost-effectiveness acceptability curve of the probability that the intervention was most cost-effective, over a range of willingness-to-pay thresholds.

Results
Second-line metformin with saxagliptin therapy was expected to cost EUR 38,163, compared with EUR 36,550 for metformin with sulphonylurea; an incremental cost of EUR 1,613 with saxagliptin. Saxagliptin was expected to result in 13.42 QALYs, compared with 13.31 QALYs for sulphonylurea; an incremental QALY gain of 0.12 with saxagliptin.

The incremental cost effectiveness ratio was EUR 13,931 per QALY gained with saxagliptin, compared with sulphonylurea.

The sensitivity analysis showed that the results were sensitive to varying the weight convergence, age, utilities, and the timing of second-line treatment.

The probabilistic incremental cost-effectiveness ratio was EUR 10,329. The cost-effectiveness acceptability curve showed that saxagliptin was cost-effective in around 50% of simulations at a threshold of EUR 12,000, and around 60% at thresholds of EUR 30,000 to EUR 100,000.

Authors' conclusions
The authors concluded that saxagliptin might be associated with improved outcomes, at a cost that was acceptable in Germany.

CRD commentary
Interventions:
The key details of the treatment options were reported, but no dosages were supplied. The second-line treatments were stated to be consistent with German guidelines, and combinations of metformin and sulphonylurea were commonly used as second-line therapy. Other options were mentioned and might be relevant in other settings; the exclusion of relevant comparators can affect the cost-effectiveness results.

Effectiveness/benefits:
The effectiveness data were clearly reported and were from sources with good designs. The methods of identifying and selecting these sources were not described, but the authors stated that the trial used as the main source was the only trial of German patients that was available. Key details of this trial and the patient characteristics were reported. The authors gave reasons for their selection of adverse events. The methods used to derive the estimates from the UKPDS were not described. The QALY estimates were clearly reported and appropriately derived and discounted, but they were from UK sources, which could differ from other populations.

Costs:
The cost categories were consistent with the stated perspective, and the sources for the cost data were described in detail, in the text and in tables. The methods used to identify the cost estimates, from the literature, were not described, so it is not clear whether the best available evidence was used. The costs were clearly reported and appropriately adjusted and discounted; adjustment using the health care component of the consumer price index would have been more appropriate as health care inflation can be higher than general inflation. The costs were specific to Germany.
Analysis and results:
The model was described, and an incremental analysis was completed, which was the most appropriate method to assess the relative cost-effectiveness of the treatments. The reporting of the results was sufficient. The authors comprehensively assessed the impact of parameter uncertainty and presented the results fully and appropriately. They concluded that the results were robust, but the analysis indicated that the results were sensitive to variations in several parameters and assumptions, and these might be particularly relevant in other settings.

Concluding remarks:
The methods and reporting were good. The authors’ conclusion reflects the evidence presented.

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