Cost-effectiveness of pioglitazone in type 2 diabetes patients with a history of macrovascular disease: a German perspective
Scherbaum WA, Goodall G, Erny-Albrecht KM, Massi-Benedetti M, Erdmann E, Valentine WJ

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
This study examined the cost-effectiveness of adding pioglitazone to the existing treatment for adult patients with type 2 diabetes and with evidence of macrovascular disease. The authors concluded that adding pioglitazone was potentially cost-effective, in the German setting, over a patient's lifetime. The study was generally well conducted and well presented and the authors' conclusions appear to be valid.

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

Study objective
This study examined the cost-effectiveness of adding pioglitazone to the existing therapy for adult patients with type 2 diabetes and with a history of macrovascular disease, who were at high risk of cardiovascular events.

Interventions
Pioglitazone at a dosage of 15mg, 30mg, or 45mg per day was compared with the usual treatment, without pioglitazone, that could include aspirin, statins, and angiotensin-converting enzyme inhibitors.

Location/setting
Germany/out-patient primary care.

Methods
Analytical approach:
The analysis was based on an adapted version of the validated Center for Outcomes Research (CORE) Diabetes Model (Palmer, et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details), which was developed to determine the long-term health outcomes and economic consequences of interventions in diabetes. A lifetime horizon (up to 35 years) was considered. The authors stated that the perspective was that of the third-party health care payer in Germany.

Effectiveness data:
The CORE Diabetes Model was adapted to incorporate the pioglitazone treatment. The main estimates of the treatment effectiveness, which were the event rates associated with macrovascular outcomes and the annual hazard ratios, over the short term (up to three years), and the patient baseline characteristics (demographics, risk factors, and complications) were derived from the PROspective pioglitAzone Clinical Trial In macroVascular Events (PROactive). This was a multinational, prospective, double-blind, placebo, randomised controlled trial (RCT), with 5,238 patients in 321 centres. Assumptions were required to extrapolate the clinical trial data to the patient's lifetime. The key model input was the change in glycated haemoglobin (HbA_1c) with pioglitazone, compared with placebo, at one, two, and three years and its impact on diabetes-related complications.

Monetary benefit and utility valuations:
The events in the PROactive were linked to health state utilities from the Cost of Diabetes in Europe – Type 2 (CODE-2) study (Bagust, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details), where possible, and ignored if it was not possible. The remaining utilities were those from the original model publication (Palmer, et al. 2004).
Measure of benefit:
The benefits were measured in quality-adjusted life-years (QALYs) and life-years (LYs) and these were discounted at a rate of 5% per annum.

Cost data:
The direct medical costs included the drugs, patient management (screening for retinopathy, nephropathy, and foot ulcers), and diabetes-related complications. Most of the resource use data were derived from the PROactive. All unit costs were in Euros (EUR), from published German sources, and discounted at a rate of 5% per annum. The price year was 2005.

Analysis of uncertainty:
The authors performed one-way sensitivity analyses on the key model parameters, including the discount rate, time horizon, change in HbA$_1c$, event rates, utility values, and unit costs. Several scenario analyses were conducted by including the quality of life utilities for events that were not included in the CODE-2 study (base case) and a worst-case scenario was examined using the most pessimistic values for the key event utilities. A Monte Carlo simulation, with 1,000 iterations was performed, using nonparametric bootstrapping, and the results were presented in a scatter plot and as a cost-effectiveness acceptability curve.

Results
Over a patient's lifetime, treatment with pioglitazone generated 7.543 QALYs or 10.044 LYs, while placebo generated 7.422 QALYs or 9.871 LYs; a gain of 0.120 QALYs or 0.172 LYs. Total direct costs were EUR 105,433 for pioglitazone and EUR 103,834 for placebo; an additional cost of EUR 1,599. The incremental cost with pioglitazone was EUR 13,294 per QALY gained or EUR 9,281 per LY gained.

The probabilistic sensitivity analysis showed that at a willingness-to-pay of EUR 50,000 per QALY, there was a 78.2% probability of pioglitazone being cost-effective over placebo. Other sensitivity analyses showed that the incremental cost per QALY was most sensitive to the time horizon; reducing the horizon to 10 years increased (worsened) the incremental cost-effectiveness ratio to EUR 29,081.

Authors' conclusions
The authors stated that the addition of pioglitazone to the usual treatment for patients with type 2 diabetes and with a history of macrovascular disease was potentially cost-effective in the German setting.

CRD commentary
Interventions:
The basis for the selection of the comparators was clear as pioglitazone was added to the existing treatment. The authors provided only a brief definition of pioglitazone and the usual treatment for type 2 diabetes.

Effectiveness/benefits:
The treatment effectiveness was derived from a large multinational RCT. Insufficient details of this trial were reported to allow a full assessment of its validity, but it is likely that the trial was of a high standard and the results were robust. The utilities were from another validated study (CODE-2), which used the European Quality of life (EQ-5D) questionnaire. Both QALYs and LYs were appropriate, given the impact of the interventions on quality of life and survival.

Costs:
The cost categories were consistent with the perspective. The cost estimates were presented per event or health state, with associated follow-up costs, and per day, for pioglitazone, along with their sources, but the resource use was not presented separately, which reduces the transparency of the analysis. The costs were mainly from German sources. A few author assumptions were necessary, but these were clearly documented. Discounting was performed as recommended in German guidelines and alternative rates (including no discounting) were investigated in the sensitivity analysis. The price year was reported and all costs were inflated appropriately.

Analysis and results:
The adapted model, used to synthesise the costs and benefits, was appropriate and the results were generally clearly reported. The uncertainty in the base-case results was satisfactorily investigated and the main findings were well presented and appropriately discussed. The CORE Diabetes Model was validated in several settings and appears to have been an appropriate simulation for type 2 diabetes patients. It was more fully reported in the original publication (Palmer, et al. 2004). The authors compared their results against various hypothetical cost-effectiveness thresholds for other European countries, but did not compare them with those of other published economic evaluations. They acknowledged the limitations of their analysis and presented a well-balanced discussion.

Concluding remarks:
The study was well conducted and the methods and results were generally transparent. The authors’ conclusions appear to be valid.

Funding
Funded by a grant from Takeda (manufacturer of pioglitazone hydrochloride).

Bibliographic details

PubMedID
19416529

DOI
10.1186/1478-7547-7-9

Original Paper URL
http://www.resource-allocation.com/content/7/1/9/abstract/

Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
Cardiovascular Diseases; Cost-Benefit Analysis; Diabetes Mellitus, Type 2; Germany; Humans; Hypoglycemic Agents; Quality-Adjusted Life Years; Thiazolidinediones

AccessionNumber
22009102051

Date bibliographic record published
07/10/2009

Date abstract record published
24/11/2010