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 long-term clinical and economic impact of liraglutide versus glimepiride as monotherapies in patients with type 2 diabetes mellitus. The authors concluded that liraglutide was a cost-effective alternative to glimepiride from the perspective of the US third-party payer. The methods were valid as were the sources of clinical evidence, but the cost analysis was not transparent and did not allow a full judgement of the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the long-term clinical and economic impact of liraglutide versus glimepiride as monotherapies in patients with type 2 diabetes mellitus.

Interventions
Three strategies were considered: liraglutide 1.2mg per day, liraglutide 1.8mg per day, and glimepiride 8mg per day.

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis was based on the published Center for Outcomes Research (CORE) Diabetes Model. This was a Markov model that projected the risk of complications due to diabetes over time. A 30-year time horizon was considered and the authors stated that the analysis took the perspective of the third-party payer.

Effectiveness data:
The clinical evidence on the treatment efficacy and baseline characteristics of the patient population came from a 52-week, double-dummy, placebo, randomised controlled trial (RCT); the Liraglutide Effect and Action in Diabetes (LEAD)-3 trial. This included 746 eligible patients, with 251 in the liraglutide 1.2mg group, 247 in the liraglutide 1.8mg group, and 248 in the glimepiride group. Other clinical data on diabetes complications were already incorporated in the decision model and were derived from the most relevant published epidemiological and clinical sources, such as the UK Prospective Diabetes Study. The primary endpoint was the reduction in haemoglobin A\textsubscript{1c} with the two treatments. Assumptions were needed for the long-term effects of the treatments because only 52 weeks of data were available.

Monetary benefit and utility valuations:
Not included.

Measure of benefit:
Survival was the key outcome of the model; it was not combined with the costs. Event rates were also reported.

Cost data:
The economic analysis included the costs of drugs, management of disease (medications and monitoring), and diabetes-related complications. The costs were presented as macro-categories and were derived from published sources, but the details of these were not given. All costs were in US dollars ($) and were discounted at an annual rate of 3%. The price year was 2007.

Analysis of uncertainty:
Deterministic sensitivity analyses were undertaken on the change in haemoglobin A\textsubscript{1c} (using a published 95% confidence interval), the decay curve for glimepiride, and the discount rate.

Results
After 30 years, the rate of survival was 13.6% for liraglutide 1.2mg, 16.5% for liraglutide 1.8mg, and 7.3% for glimepiride. In general, liraglutide was associated with fewer deaths and fewer complications than glimepiride. The total costs per patient were $48,456 with liraglutide 1.2mg, $45,580 with liraglutide 1.8mg, and $54,947 with glimepiride. The key cost driver was the cost associated with the management of cardiovascular events.

Both liraglutide 1.2mg and 1.8mg were less costly and more effective than glimepiride. Similar results were found after 10 and 20 years and the sensitivity analysis showed that these results were robust.

Authors' conclusions
The authors concluded that liraglutide was a cost-effective alternative to glimepiride for the treatment of patients with type 2 diabetes from the perspective of the US third-party payer.

CRD commentary
Interventions:
The authors did not provide a clear justification for the selection of the comparators, which were valid treatments for patients with type 2 diabetes mellitus. The dosages were based on the regimens used in the RCT.

Effectiveness/benefits:
The clinical analysis included recent evidence from the LEAD-3 trial in the published and validated CORE Diabetes Model, which is considered to be a key simulation of the natural history of the disease. Most of the epidemiological data were already assessed and the details of their sources were not reported. Some key information on the LEAD-3 trial was provided. An RCT, especially one that is double-blinded and directly compares treatments, is generally a valid source of evidence for treatment efficacy. Assumptions were needed for the long-term effects, but these were varied in the sensitivity analysis. Survival was a valid benefit measure, but it was not combined with the costs as a cost-consequences analysis was conducted. Other outcomes of the model, such as event rates, were appropriately reported.

Costs:
The categories of costs were appropriate for the perspective stated, but the economic analysis was not presented in detail. A breakdown of the cost items was not provided and most of the costs were reported as macro-categories. The data sources were not described and information on resource consumption was not provided. It was also not clear whether the costs of liraglutide and glimepiride were included in the total costs used to compare the two treatments. These issues should be considered when assessing the validity of the economic analysis, especially its transparency and the possibility of replicating it in other settings.

Analysis and results:
All the model outcomes were clearly presented. The authors reported the results for three time horizons (10, 20, and 30 years), but the costs and benefits were not synthesised in an appropriate cost-effectiveness analysis and a cost-consequences analysis was carried out. The issue of uncertainty was only partially investigated as the sensitivity analyses focused on a few inputs. The generalisability of the results to other settings was not explicitly addressed. The authors noted that some of the assumptions in the model might have affected their findings.

Concluding remarks:
The analysis was based on valid methods and valid sources of clinical evidence, but the cost analysis was not transparent and did not allow a full judgement of the validity of the authors’ conclusions.
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