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Title **Second-Line Therapy for Patients With Diabetes Inadequately Controlled on Metformin: A Systematic Review and Cost-Effectiveness Analysis**

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Aim

To systematically review the clinical evidence pertaining to second-line antidiabetes drugs for patients with type 2 diabetes inadequately controlled on metformin monotherapy; and based on the results of the systematic review, conduct a cost-effectiveness analysis.

Conclusions and results

We identified evidence for 8 classes of second-line antidiabetes therapies in adults with type 2 diabetes inadequately controlled with metformin monotherapy. The methodological quality of the evidence was generally low. All agents achieved statistically significant reductions in A1C, and there were no statistically significant differences between drug classes. A modest increase in body weight was observed with most second-line therapies. We found little evidence regarding the effect of second-line antidiabetes drugs on the long-term complications of diabetes or mortality. Sulfonylureas were the most cost-effective second-line therapy in patients inadequately controlled on metformin, due primarily to their lower cost compared to insulin and newer agents. Cost-effectiveness results were robust to variations in model inputs and assumptions. Sulfonylureas are equally efficacious as other agents when used as second-line treatment after inadequate control with metformin monotherapy, and represent the most cost-effective treatment option.

Methods

The literature search included electronic databases, grey literature, reference lists, conference abstracts, and stakeholder consultation. Mixed treatment comparison and pairwise meta-analyses were conducted to pool trial results, when appropriate. Numerous sensitivity analyses were performed to examine robustness of meta-analytic results. We used the United Kingdom Prospective Diabetes Study Outcomes Model to forecast diabetes-related complications and cost consequences. Treatment effect estimates were obtained from the systematic review of clinical evidence. Other inputs for the model were derived from published and unpublished sources. We performed numerous sensitivity analyses to examine the robustness of results to variation in model inputs and assumptions.

Written by CADTH, Canada