Glucose-lowering drugs added to existing therapies and risks of mortality and cardiovascular disease in type 2 diabetes: Network meta-analysis of randomized trials

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Background

The optimal treatment strategy to reduce premature death and cardiovascular disease in type 2 diabetes is relatively uncertain. Recent trials have compared treatments with placebo and evaluated effects on mortality. However, few trials are available to compare different glucose-lowering therapies on mortality and cardiovascular outcomes.

Objectives

To compare the effects of glucose lowering drugs regardless of background therapy on preventing mortality and cardiovascular events and avoiding hypoglycemia for patients with type 2 diabetes.

Methods

- Study selection: Randomized trials comparing glucose-lowering drugs in addition to background treatment for adults with type 2 diabetes.
- Data sources: Electronic databases (CENTRAL, Medline, and Embase) to June 2016.
- Data analysis: Systematic review and random-effects network meta-analysis.
- Outcomes: All-cause and cardiovascular mortality, myocardial infarction, stroke, heart failure, hypoglycemia.

Results

- 238 trials involving 187,134 patients.
- SGLT-2 inhibitors more effective at reducing mortality than thiazolidinediones (odds ratio 0.71, 0.54-0.94), metformin (0.66, 0.44-0.98), sulfonylureas (0.61, 0.44-0.85), and basal insulin (0.39, 0.17-0.90) and were similarly effective to GLP-1 receptor agonists (0.83, 0.65-1.06).
- GLP-1 receptor agonists more effective at lowering mortality than sulfonylureas (0.73, 0.55-0.99). SGLT-2 inhibitors more effective at preventing cardiovascular death than thiazolidinediones (0.67, 0.48-0.95), DPP-4 inhibitors (0.65, 0.49-0.87), and sulfonylureas (0.51, 0.30-0.88), and possibly more effective than GLP-1 receptor agonists (0.76, 0.57-1.00).
- No drug class other than SGLT-2 inhibitors reduced odds of cardiovascular death.
- No drug class prevented stroke or myocardial infarction.
- SGLT-2 inhibitors more effective than DPP-4 inhibitors, metformin and thiazolidinediones for preventing heart failure.
- All drug classes except SGLT-2 inhibitors incurred higher odds of hypoglycemia than placebo.

Conclusion

SGLT-2 inhibitors appear to be the most effective and safest glucose lowering drug class to prevent all-cause and cardiovascular death in patients with type 2 diabetes.

Figure 1. Network of available treatment comparisons in randomized trials

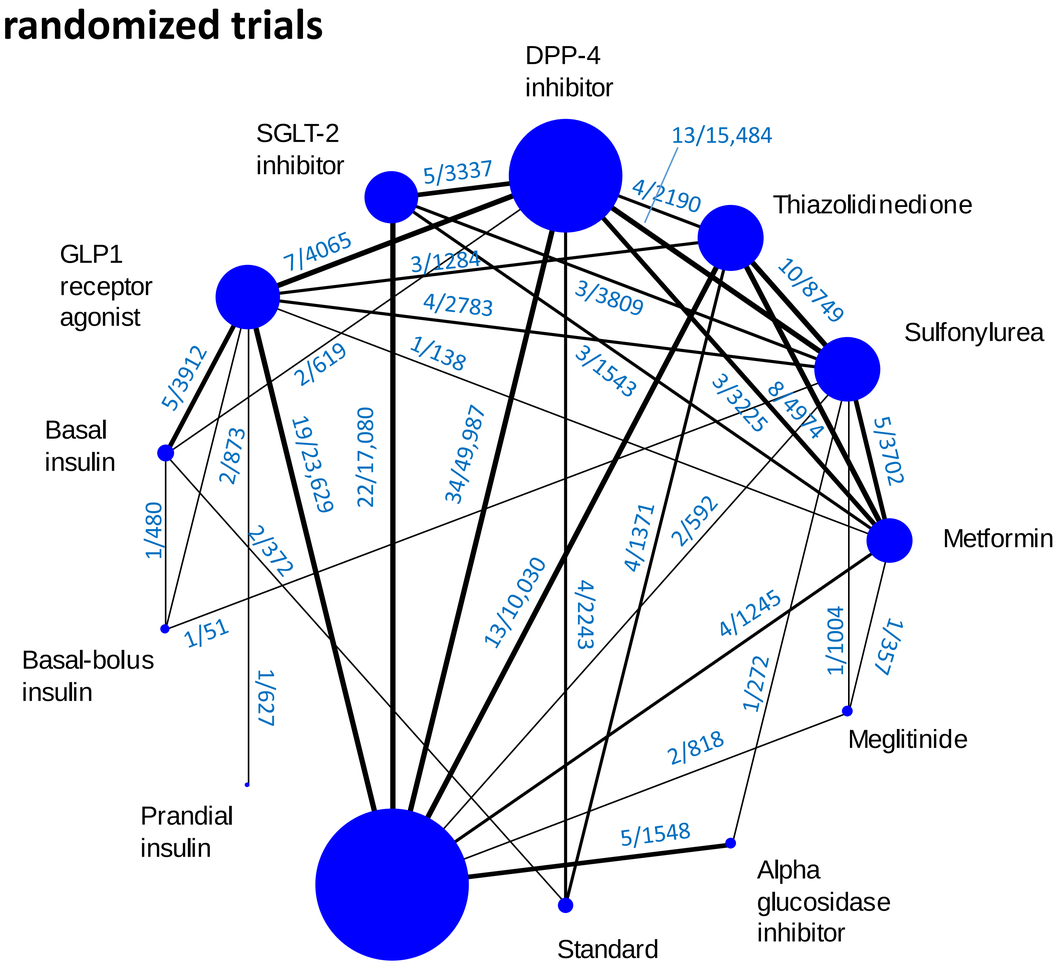
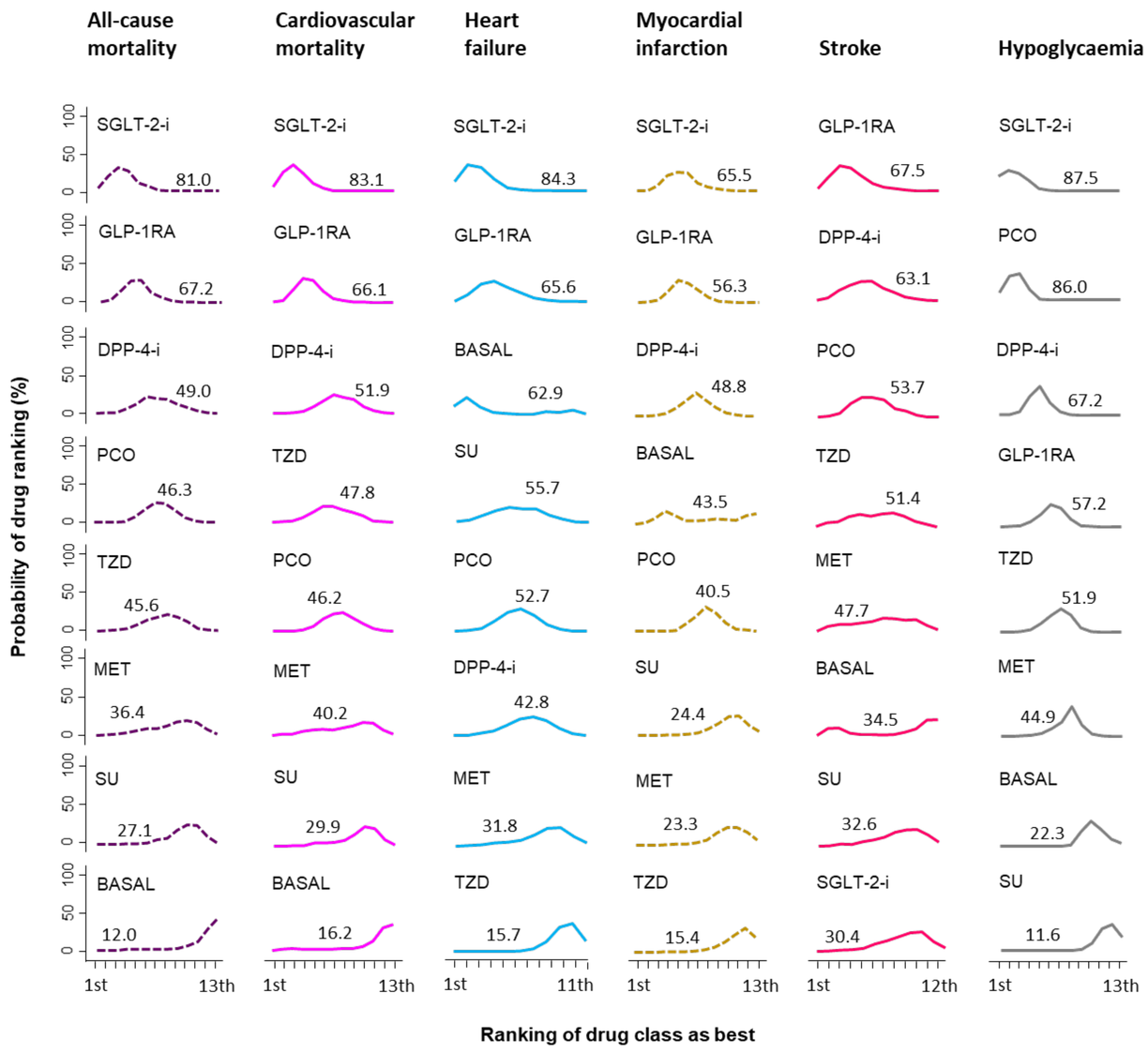


Figure 2. Rankograms for drug treatment effects (ranked best to worst). Showing probability of being ranked best (%).



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