Research Briefing

A systematic literature review on the efficacy-effectiveness gap: comparison of randomized controlled trials and observational studies of glucose-lowering drugs


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Summary
Randomized controlled trials (RCTs) and observational studies investigating glucose-lowering drugs were compared. Neither efficacy effectiveness gap was found nor potential drivers of effectiveness.

Key points
- No clear differences in relative effect estimates from randomized, controlled trials and observational studies of oral glucose-lowering drugs suggest no efficacy-effectiveness gap
- Characteristics of patients in randomized, controlled trials and observational studies of oral glucose lowering drugs were similar and did not reveal potential drivers of effectiveness
- The quality of the observational studies was low which may have hidden a true efficacy-effectiveness gap

Introduction
The efficacy of a drug describes the optimal effect. The effectiveness of a drug describes the effect in routine clinical practice. A systematic literature review was conducted to determine a potential efficacy-effectiveness gap, and its drivers, with regards to glucose-lowering drugs, by comparison of RCTs and observational studies.

Methodology and findings
A total of 31 RCTs and 10 observational studies were included. The studies compared either GLP-1 with insulin or DPP-4i with sulfonylurea, and had change in HbA1C as outcome. Relative effect estimates and characteristics of the study populations (age, sex, BMI, time since diagnosis and HbA1c) were compared across study designs.

No clear differences in effect estimates across study designs were observed. Hence, no evidence of an efficacy-effectiveness gap was found. Furthermore, no potential drivers of effectiveness were identified.
Based on the available studies, it is however not possible to fully rule out the existence of an efficacy-effectiveness gap. There are two possible reasons why a true gap was hidden; it is a possibility that the observational studies were designed to mimic the RCTs. However this was not explicitly stated or could be deduced from inclusion criteria. Also, the quality of the observational studies was poor (e.g. no control for confounding). Therefore the effect may not be truly representative for effectiveness.

The investigated drivers of effectiveness were limited to information available in both RCTs and observational studies (age, sex, BMI, time since diagnosis, HbA1c, publication year, study duration or number of patients). Future studies, possible based on patient level data rather than a systematic review may investigate other potential drivers of effectiveness, e.g. comorbidity, comedication, delivery of care and adherence to treatment.

The literature review compared relative effect estimates across study designs, by identifying studies where glucose-lowering drugs were compared with each other. An alternative is to compare the absolute effect of a specific drug across study design. Such study would include studies not identified in the present review.