

Hierarchical network meta-analysis models for the inclusion of randomised and observational comparative studies in evidence synthesis

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Background

There is an increasing interest in the inclusion of observational studies in network meta-analyses (NMAs) of randomised controlled trials (RCTs) due to potential benefits in expanding the evidence base, connecting disconnected networks or improving generalisability.

However, methods to combine these two sources of data need to account for the increased bias due to unmeasured confounding in observational studies. This study aims to explore a number of NMA models that adjust and account for the different study designs, by assessing their impact on effect estimates and uncertainty.

Methods

Models were applied to an illustrative example of a systematic review of RCT and observational data for two classes of glucose-lowering medications in type 2 diabetes; sodium-glucose co-transporter 2 inhibitors (SGLT-2is) and glucagon-like peptide-1 receptor agonists (GLP-1RAs).

Bayesian random-effects models were fitted accounting for differences in study designs (hierarchical analysis accounting for study design, class and treatment and bias adjustment for study design), and point estimates, precision and model fit compared to naïve pooling.

Results

Network plot for HbA1c (%) is shown in figure 1, with nodes representing treatments and edges representing direct comparison.

Across all methods, the estimated mean differences in HbA1c (%) after 24 weeks remained similar with the inclusion of observational data (Figure 2). However, the uncertainty around these effect estimates increased when fitting hierarchical models and bias adjusted models.

Hierarchical models and bias adjustment models all provided a better fit in comparison to the naïve-pooling method (Table 1).

Figure 1. Network plot

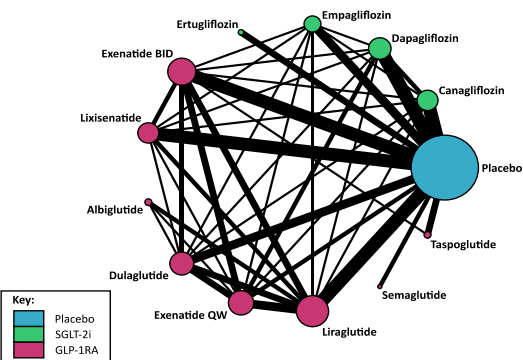


Figure 2. Forest plot

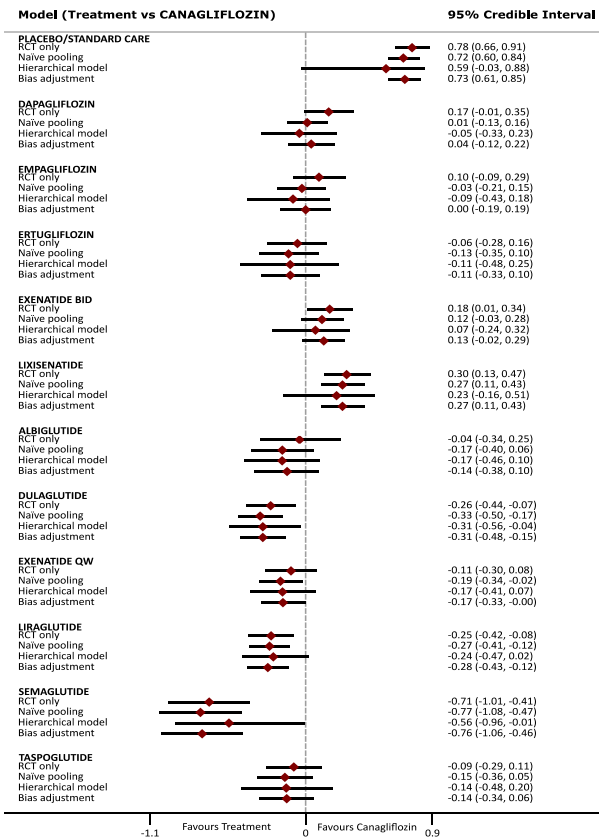


Table 1 DIC calculations for each model fitted

Model	Deviance Information Criterion (DIC)
Naïve pooling	-161.78
Hierarchical model	-173.81
Bias adjustment	-171.15

Smaller DIC calculations represent better fit of the model

Summary

Hierarchical and bias adjustment NMA models accounting for study design may be more appropriate when conducting NMA of RCTs including observational studies. Accounting for differences in the study designs allowed for more detailed and appropriate modelling, preventing overly optimistic conclusions.

Simulation studies are needed to be considered to assess the capabilities of the methods compared under a range of scenarios.