Modeling inconsistency as heterogeneity in network meta-analysis

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Abstract

Network meta-analysis enables the simultaneous synthesis of a network of clinical trials comparing any number of treatments. The key underlying assumption is that relative treatment effects are exchangeable across the entire network. In a pair-wise meta-analysis, violations of exchangeability manifest as heterogeneity within the treatment comparison. In a network meta-analysis, violations of exchangeability can additionally result in inconsistency between treatment comparisons.

A range of models to detect the presence of inconsistency have been proposed. These models typically attempt to draw a distinction between inconsistency and heterogeneity. However, in the presence of multi-arm trials such a distinction is necessarily arbitrary. This results in a range of different inconsistency models for a single network, potentially with very different results.

An approach that contrasts the estimates from individual studies with the estimates from evidence synthesis may be more insightful than separating inconsistency from heterogeneity. In essence, such an approach suggests that inconsistency and heterogeneity are the same. By using the decomposition of n-arm trials into $n(n-1)/2$ relative effects previously proposed by Gerta Rücker the contribution of multi-arm trials can be fairly represented and a model without any consistency constraints can be estimated even in networks with multi-arm trials. Then, simple extensions of the forest plot and I^2 statistic provide a unique and interpretable representation of inconsistency and heterogeneity in the network. In this representation, individual study results can be contrasted with unrelated pair-wise pooled estimates as well as consistent pooled estimates.