Evaluating the validity of network meta-analyses: locating inconsistency and visualizing the flow of evidence

Network meta-analysis is a new methodological development in the field of meta-analyses that connects evidence of all randomized clinical trials on a defined set of competing treatments. The resulting trial network allows estimating the relative effects of all pairs of treatments taking indirect evidence into account. While the validity of the results depends on a consistent network of treatment effects, there might be some direct comparisons that lead to inconsistency.

We investigate how such direct comparisons can be identified in the context of fixed-effects meta-analysis, using the inverse variance weighting method. The analysis can be performed in two stages: initially summarizing evidence of studies with the same treatment arms, and secondly fitting a linear model to the aggregated treatment effects. We propose to explore a set of models that results from successively relaxing the assumption of consistency by adding new parameters to the model. The change in inconsistency can then be assessed by chi-square statistics. Based on this, we provide a graphical tool to highlight hot spots of inconsistency between specific direct evidence. Since one deviating direct comparison may have side effects on the network estimates of others, the plot comprises also the contribution of each direct estimate to network estimates resulting from regression diagnostics. This enables to render transparent which direct comparison might have introduced the inconsistency in the network. On the other hand, consistent results from different information sources emphasize the external validity.

In this presentation, I will illustrate the approaches for some network analysis examples and will discuss the flow of evidence and the possibility to track down inconsistency to only one or at least a few direct comparisons.