MSR89

A Novel Visualisation for Assessing the Consistency Assumption in Network Meta-Analysis

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Introduction

Network meta-analysis (NMA) is the established method to pool evidence from multiple clinical trials and make direct and indirect comparisons between different treatments. However, to ensure its validity, several assumptions need to be examined. Chief among these is the assumption that the different sources of information are consistent, which is to say that the direct and indirect effect estimates agree.

To do this, there are at least three components to check:

1. **The original effect sizes of the direct and indirect treatment effects**
2. **The difference between them and its associated uncertainty**
3. **The type of difference between them i.e., whether the direct and indirect estimates agree or disagree that a treatment is beneficial or harmful**

Current visualisation approaches typically use forest plots, but these are limited as at least one of the above aspects is usually absent to avoid introducing excessive complexity. Furthermore, as the number of treatments in the network increases, these visualisations can become difficult to read. Hence, a visualisation that combines the three aspects without being difficult to interpret would allow for a more thorough examination of the assumption.

Data Background

The data that we use to exemplify our proposed visualisation comes from the Senn2013 dataset from the *netmeta* R package. This dataset contains the results of several diabetes studies comparing the effect of different treatments on the HbA1c value, a blood glucose level measurement. This data was also used as an example in Senn et al. (2013)[1].

For convenience, we have used the following abbreviations for the treatment names: acar=Acarbose, benf=Benfluorex, metf=Metformin, migl=Miglitol, piog=Pioglitazone, plac=Placebo, rosi=Rosiglitazone, sita=Sitagliptin, sulf=Sulfonylurea, and vild=Vildagliptin.

[1]Senn S, Gavini F, Magrez D, Scheen A (2013): Issues in performing a network meta-analysis. *Statistical Methods in Medical Research*, **22**, 169–89

Method

Our proposed visualisation can be thought of as an integration of two plots: a scatter plot with the direct effects plotted against the indirect effects, and a forest plot showing the difference between those effects with its associated uncertainty. The scatter plot allows the first and third aspects to be examined, while the forest plot allows the second. Starting with the scatter plot, if we imagine the case of 'perfect consistency', where the direct and indirect effects agree exactly, then it follows that this hypothetical point would lie on the y = x line. The distance of a point from this line then gives an indication as to extent that the direct and indirect effects agree or disagree points closer to the line imply greater agreement, while points further from the line imply greater disagreement.

Now looking at the example forest plot in Figure 1, we can see that the y-coordinate is relatively arbitrary. However, here we've set this as the indirect effect estimate of each comparison to illustrate the idea of the proposed visualisation. By shifting each confidence interval to centre on the direct effect estimate, the line of interest transforms from the x = 0 line to the y = x line, thus providing a way to combine the advantages of both graphs in one visualisation (see Figure 2). The four quadrants in Figure 2 can now also indicate the type of difference between the direct and indirect effects.

To show that this transposition is valid mathematically, let $\delta = d - i$, where d is the direct effect estimate, i is the indirect effect estimate, and δ is the difference between these effects for a particular comparison. To centre the original confidence interval on the direct effect estimate, we simply need to shift it by i units to the right. The threshold of interest for each comparison then becomes x = i (as we're also shifting the original threshold of x = 0 by i units to the right), which drawn together is the y = x line, as a hypothetical perfect comparison would have the coordinates (d, i) = (i, i)

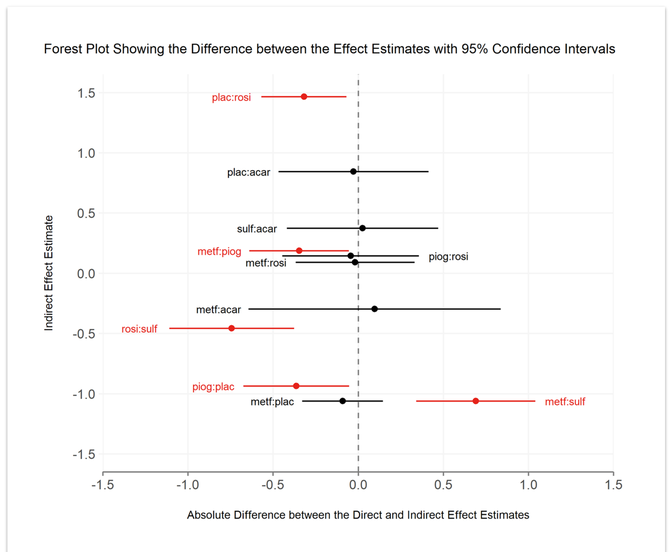

Figure 1 – Red confidence intervals indicate a significant difference between the effect estimates.

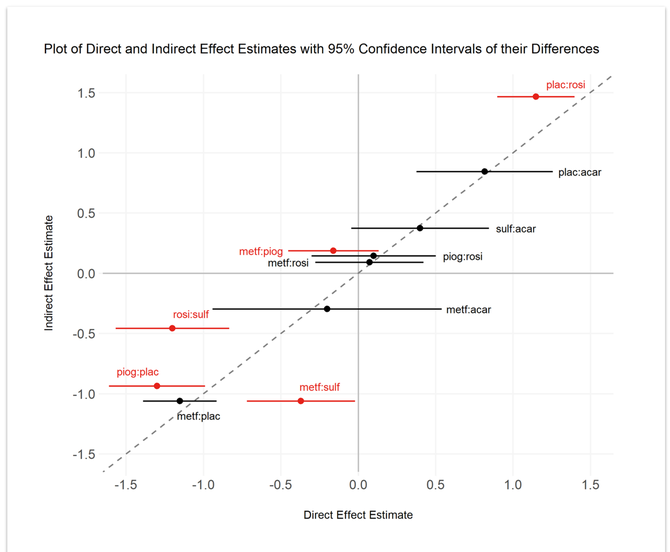

Figure 2 - Our proposed visualisation showing original effect sizes (direct and indirect), the difference, its uncertainty, as well as the type of difference.

Conclusion

The proposed visualisation intuitively combines the three aspects to examining the consistency assumption and is a potential alternative to current visualisation strategies.
Future research could aim at assessing its practicality and interpretability for clinicians.

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