

# DSEN ABSTRACT

## Evaluating Additive Treatment Effects in Network Meta-Analysis

### Summary

- The objective of this study was to evaluate the comparative statistical performance of the conventional NMA model and the additive effects NMA model in NMA scenarios where additivity holds true is mildly violated, or is strongly violated. For each scenario, 500 NMA data sets were simulated and the conventional and additive effects NMA models were fit in a Bayesian framework.

### Key messages

- Under true additivity, the additive effects model is superior. Under mildly violated additivity, the additive model generally yields more overestimates or underestimates, but comparable coverage and greater power. Under strongly violated additivity, the proportion of overestimates or underestimates and coverage is considerably worse with the additive effects model.

**Authors:** Edward Mills, Kristian Thorlund and John Ioannidis.

For more information, please contact Kristian Thorlund [thorluk@univmail.cis.mcmaster.ca](mailto:thorluk@univmail.cis.mcmaster.ca)

### What is the issue?

- Many medical interventions are administered in the form of treatment combinations involving two or more individual drugs (e.g., drug A + drug B).
- When the individual drugs and drug combinations have been compared in a number of randomized clinical trials, it is possible to quantify the comparative effectiveness of all drugs simultaneously in a network meta-analysis (NMA).
- However, current NMA models ignore the dependence between drug combinations (e.g., A + B) and the individual drugs that are part of the combination. In particular, current models ignore the possibility that drug effects may be additive, i.e., the property that the effect of A and B combined is equal to the sum of the individual effects of A and B.
- Current NMA models may thus be suboptimal for analyzing data including drug combinations when their effects are additive or approximately additive.
- However, the extent to which the additivity assumption can be violated before the conventional model becomes the more optimal approach is unknown.

### What was the aim of the study?

- The objective of this study was to evaluate the comparative statistical performance of the conventional NMA model and the additive effects NMA model in NMA scenarios where additivity holds true is mildly violated, or is strongly violated.

### How was the study conducted?

- We simulated NMA scenarios in which additivity held true was mildly violated, or was strongly violated. For each scenario, 500 NMA data sets were simulated and the conventional and additive effects NMA models were fit in a Bayesian framework. Under each scenario, we estimated the proportion of treatment effect estimates that were 20% larger than 'the truth' (i.e., % of overestimates), the proportion that was 20% smaller than 'the truth' (i.e., % of underestimates), the coverage of the 95% credible intervals, and the statistical power. This was performed for all the comparisons under both models.

### What did the study find?

- Under true additivity, the additive effects model is superior to the conventional model. Under mildly violated additivity, the additive model generally yields more overestimates or underestimates for a subset of treatment comparisons, but comparable coverage and greater power. Under strongly violated additivity, the proportion of overestimates or underestimates and coverage is considerably worse with the additive effects model.

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Link to publications: [Mills et al, 2012](#); [Thorlund et al, 2012](#)