**Title:** Treatment effectiveness in patients with multimorbidity: sharing information and shared trial data

**Author list:** L. J. Hannigan, S. Dias, N. J. Welton, < Neil, Claudia, others? > D. A. McAllister

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*Background.* Multimorbidity (where two or more conditions occur together) is common and increasing. Patients with multimorbidity are less likely to receive recommended drug treatments than those with a single disease. However, individual clinical trials usually have insufficient data to adequately estimate treatment-comorbidity interactions, and so it is unclear if they would benefit differentially from treatment. A major advantage of Bayesian methods is that they allow sharing of information across related groups. We aim to exploit this strength to address the high-dimensional problem of multimorbidity.

Here, we present the results of a set of simulation demonstrating the utility of Bayesian hierarchical models for estimating treatment-comorbidity interactions from clinical trial data. These models allow information from individual trials to be shared at the level of drugs, drug classes, and wider groupings of related classes.

Methods: Using the US clinical trials register (clinicaltrials.gov) we identified two distinct sets of phase 3 placebo-controlled trials with >= 300 participants upon which to base simulations. The first, comprising 161 trials including 210,046 participants, was a set of trials of non-insulin glucose lowering drugs for diabetes. This set included 24 separate drugs from 7 different ATC-5 level classes (e.g., DPP-4 inhibitors, SGLT-2 inhibitors). The second (162 trials including XXXX participants) was a set of trials of drugs for inflammatory conditions such as rheumatoid arthritis, psoriasis, and Crohn’s disease. Based on these data (and reported results for a continuous outcome) we simulated an overall covariate-treatment interaction of -0.1 standard deviations. We examined a range of scenarios with different assumptions about the between-trial, between-drug and between-class variation. For each scenario we simulated 1000 datasets, fitting a hierarchical generalized linear model using the R-INLA package to each. The resultant estimates were used as priors in a hypothetical scenario in which the same covariate-treatment interaction was being estimated for new drugs in a novel class (Figure).

Conclusion: Sharing information across trials from related drug-classes may provide useful prior information to inform estimates of comorbidity-treatment interactions.