

Random-effects network meta-analysis of studies of binary outcomes: Comparison of frequentist, MCMC and INLA method with data on exacerbations in COPD patients

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The information on relative effectiveness of several treatment options can be summarized in a network and all treatment contrasts can be analysed in one model, including both direct and indirect evidence^[1]. We investigate a network of 5 inhalative double-blind treatments in patients with Chronic Obstructive Pulmonary Disease (COPD): Tiotropium (a long-acting anticholinergic), Salmeterol, Indacaterol, Formoterol (3 long-acting β_2 -agonists), and placebo. The selection of studies has been described recently^[2]. All trials lasted minimally 24 weeks and maximally 1 year. The binary endpoint is the occurrence of at least 1 exacerbation of the COPD during the trial.

We investigate random effects for study and treatment arm. The GLMM for the proportion π of patients with event on treatment i in study k and arm ik is $\text{Logit}(\pi_{ik}) = \tau_i + \mu_k + a_{ik}$ with μ_k fixed for all k , τ_i fixed for all i , $a_{ik} \sim N(0, \sigma^2)$ and $a_{1k} = 0$ (Placebo). [Correction 2014-12-09: study effects fixed, random arm effects added.]

Treatment contrasts would then be estimated through the common model for all 5 treatments.

We compare the classical frequentist method^[1], the MCMC method as implemented in WinBUGS^[3], and, as deterministic-numerical approximation to the distribution of treatment contrasts, the integrated nested Laplace approximation (INLA) method^[4]. Of particular interest here is the goodness of the approximation as well as practical means of result presentation^[5].

References:

1. Jones B, Roger J, Lane PW et al. Statistical approaches for conducting network meta-analysis in drug development. *Pharmaceutical Statistics* 2011; 10: 523-531
2. Buhl R, Vogelmeier C, Kögler H et al. Network Meta-analysis Comparing Tiotropium With Long-acting β_2 -agonists. Poster #G69, Abstract A4365, International Conference of the American Thoracic Society, Philadelphia/PA 2013
3. Woods BS, Hawkins N, Scott DA. Network meta-analysis on the log-hazard scale, combining count and hazard ratio statistics accounting for multi-arm trials: A tutorial. *BMC Medical Research Methodology* 2010; 10(54): 1-9
4. Rue H, Martino S, Chopin N. Approximate Bayesian inference for latent Gaussian models using integrated nested Laplace approximations (with discussion). *Journal of the Royal Statistical Society, Series B*, 2009; 71: 319-392
5. Salanti G, Ades AE, Ioannidis JPA. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: an overview and tutorial. *Journal of Clinical Epidemiology* 2011; 64: 163-171