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TITLE: A Bayesian longitudinal multilevel network meta-regression model for repeated outcomes

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ABSTRACT:

Indirect treatment comparisons is a methodological framework to compare data across randomized controlled trials in the absence of head-to-head evaluations. Multilevel network meta-regression (ML-NMR) extends this idea to population-adjusted comparisons when some trials provide individual participant data and others provide only aggregate data. In ML-NMR, the aggregate level likelihood is linked to the individual level model by integrating over the covariate distribution, rather than by simply inserting aggregate mean covariates into the regression model.

We extend this framework to longitudinal outcomes. The proposed Bayesian model synthesises repeated Gaussian outcomes from individual participant data and aggregate study-arm summaries within a common longitudinal framework. Time is modelled with a spline basis: a common smooth trajectory describes the response over time in the reference treatment group, while treatment-specific spline deviations allow relative effects to vary over follow-up. This allows studies to contribute at multiple reported visits, without requirement of consistent reported timepoints or follow-up time. As in standard ML-NMR, the linear predictor includes study baselines, treatment effects, prognostic variables, and treatment effect modifiers. Aggregate data contribute reported study-arm-time means and standard errors. Because repeated aggregate summaries from the same study arm may be correlated, we consider sensitivity analyses using independent and fixed working covariance structures within study-arm blocks.

The method is evaluated in simulations and applied to a real data example. The simulations assess recovery of time-varying treatment effects and covariate relationships when individual participant and aggregate data are combined. The real data analysis illustrates practical considerations for applying the model to an evidence network.

Although this work focuses on Gaussian outcomes with an identity link, we will discuss how the same multilevel structure could be extended to non-linear transformations and other likelihoods. Future work will evaluate non-Gaussian outcomes and examine when the longitudinal ML-NMR model begins to break down, for example with few time points, sparse networks, limited overlap in follow-up, weakly connected treatment classes, or limited aggregate covariate information.

PRESENTING AUTHOR BIO: Juan Pablo Diaz Martinez is a PhD candidate at the University of Toronto, with training in actuarial science and health research methodology. His doctoral work focuses on natural history modelling in health technology assessment, with interests in evidence synthesis, hidden Markov models, and statistical computing. He is currently a Senior Statistician at Broadstreet HEOR and previously worked as a biostatistician at University Health Network.