A likelihood-augmented virtual inconsistency-adjusted analysis framework for assessing robustness in a star-shaped network meta-analysis

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BACKGROUND

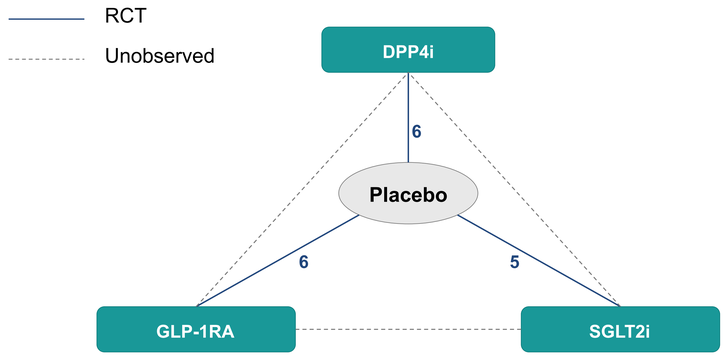
- In star-shaped network meta-analyses (NMA), active treatments are connected only through a common comparator.
- Relative effects among active treatments therefore rely entirely on indirect evidence.
- Inconsistency is unidentifiable and cannot be evaluated statistically.
- Original virtual-inconsistency-adjusted analysis (VIAA) used repeated multiple imputation (MI) and repeated Bayesian model fitting [1].

OBJECTIVE

- To develop a likelihood-augmented VIAA that incorporates virtual head-to-head evidence in a single Bayesian network meta-analysis model.
- To establish theoretical equivalence to multiple-imputation VIAA under a linear-Gaussian formulation.
- To evaluate computational efficiency and outcome-specific treatment ranking robustness in a published antihyperglycemic-agent network.

APPLICATION EXAMPLE

- Data: 17 placebo-controlled cardiovascular outcome trials in people with established cardiovascular disease [2].
- Treatments: DPP4i (n=6), GLP-1RA (n=6), and SGLT2i (n=5), each compared with placebo.
- Outcomes: cardiovascular (CV) mortality, fatal or nonfatal myocardial infarction (MI), and fatal or nonfatal stroke.
- Models: Bayesian random-effects network meta-analysis with log odds ratios and noninformative priors.



METHODS

I. Fit the observed star-shaped NMA: $y|d \sim N(Xd, V)$.
II. Define virtual head-to-head contrasts among non-reference treatments: $u = Ld$.
III. Specify a working distribution for the virtual head-to-head treatment effects: $u \sim N(\mu_\omega, \Sigma)$.
IV. Original MI-based VIAA repeatedly samples M virtual datasets and fits a Bayesian NMA to each completed network.
V. Likelihood-augmented VIAA replaces repeated imputation with pseudo-likelihood terms: $u_{obs}|d \sim N(Ld, \Sigma)$, with $u_{obs} = \mu_\omega$.
VI. Acceptable inconsistency is identified by comparing residual deviance under consistency and inconsistency models.

KEY FORMULATION

Observed evidence: $y \mid d \sim N(Xd, V)$

Virtual contrasts: $u = Ld, \quad u \sim N(\mu_\omega, \Sigma)$

Likelihood-augmentation: $u_{obs}|d \sim N(Ld, \Sigma)$, **with** $u_{obs} = \mu_\omega$

Under the linear-Gaussian formulation, the MI-based VIAA posterior mean converges to the likelihood-augmented VIAA posterior mean as $M \to \infty$.

WROKFLOW: MI-BASED VIAA vs. LIKELIHOOD AUGMENTATION

Original MI-based VIAA		Likelihood-augmented VIAA
Generate M virtual head-to-head datasets		Represent virtual evidence as pseudo-likelihood terms
Fit a Bayesian NMA to each completed network	Versus	Fit one augmented Bayesian NMA model
Pool posterior summaries with Rubin's rules		Obtain the same target posterior mean in one analysis
High computational burden: requires M repeated Bayesian fits for each scenario		Analytic marginalization replaces repeated imputation

One augmented model fit preserves MI-based inference while reducing runtime by >99.8%

RESULTS

Equivalent inference
The proposed augmented model yielded identical point estimates and 95% confidence interval to the original iterative approach.

~99.8% reduction in runtime
Computation time was reduced by more than 99.8% across model types.

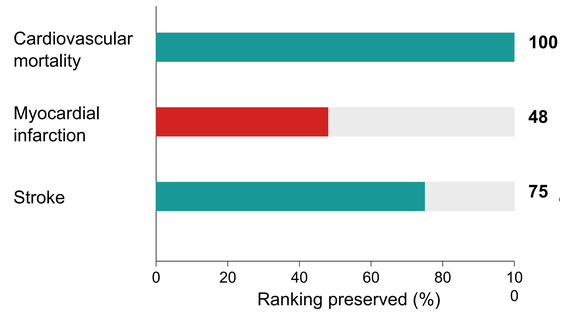
Ranking robustness
Agreement between the baseline NMA ranking and the VIAA ranking was quantified for each outcome.

RUNTIME COMPARISON (MEAN ACROSS 10 RUNS)

Model	MI-based VIAA (min)	Likelihood-augmented VIAA (min)	Time saved (%)
Consistency	54.55	0.04	99.93
Inconsistency	48.05	0.06	99.88

- Across both model types, likelihood augmentation reduced runtime by more than 99.8%.

AGREEMENT WITH BASELINE NMA RANKING (%)



Interpretation
CV mortality rankings were unchanged across the acceptable inconsistency scenarios. Stroke rankings showed moderate robust. MI rankings were sensitive to smaller inconsistency perturbations.

Why it matters
The method identifies which treatment decisions remain stable to plausible inconsistency and which require more cautious interpretation.

CONCLUSIONS

- The likelihood-augmented VIAA efficiently assesses robustness in star-shaped NMAs where consistency cannot be directly tested.
- It preserves MI-based VIAA inference while markedly improving computational feasibility.
- In the application, rankings were robust for CV mortality and stroke, but sensitive for MI.

References
1. Yoon J-H, Dias S, Hahn S. BMC Med Res Methodol. 2021.
2. Takaoka Y, et al. Cochrane Database Syst Rev. 2021.
3. Dias S, et al. Med Decis Making. 2013.

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Conflict of interest
- No relevant relationships to disclose.