From Methods to Decisions: A Transparent Framework for Population-Adjusted Treatment Comparisons

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Hugo Pedder[1,2], Kate Ren[1,3], Tushar Srivastava[1]

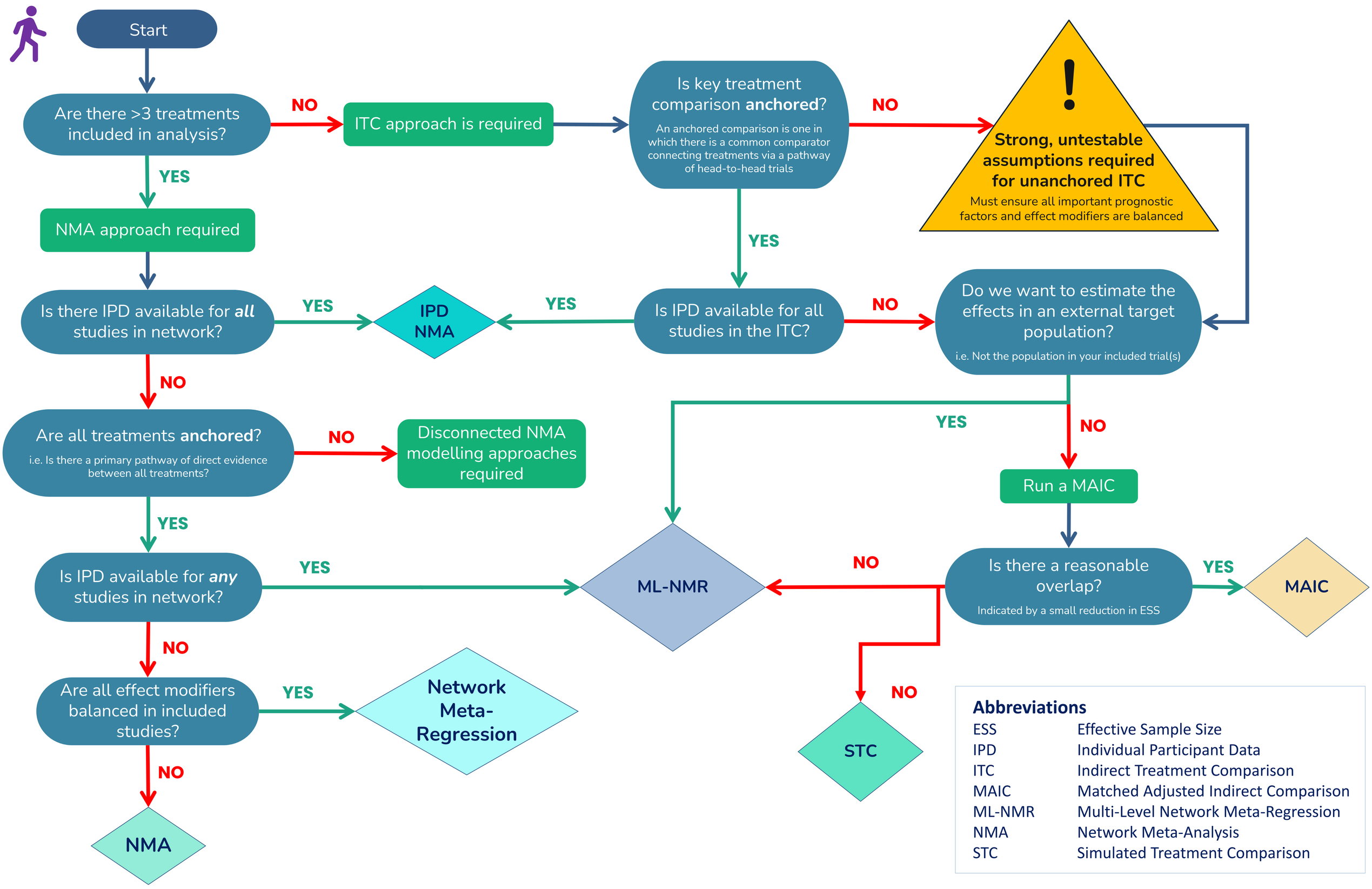
[1]ConnectHEOR, London, UK; [2]University of Bristol, Bristol, UK; [3]University of Sheffield, Sheffield, UK.
Email: hugo.pedder@connectheor.com

BACKGROUND

In the absence of head-to-head trials, indirect treatment comparisons (ITCs) are critical for assessing the comparative effectiveness of healthcare interventions. However, significant methodological developments in recent years, particularly with regards to population-adjustment, have led to a complex landscape of available methods. Considerable uncertainty persists among analysts and health technology assessment (HTA) bodies regarding the most appropriate ITC method for a given evidence scenario.

KEY FINDINGS

We propose a **decision framework** that offers a structured and transparent approach to navigating the complexities of modern ITC methods. By providing a clear **roadmap**, this work aims to reduce ambiguity in methods selection, improve the quality and consistency of HTA submissions, and ultimately **foster greater confidence** in the resulting comparative effectiveness evidence..



Abbreviations

ESS	Effective Sample Size
IPD	Individual Participant Data
ITC	Indirect Treatment Comparison
MAIC	Matched Adjusted Indirect Comparison
ML-NMR	Multi-Level Network Meta-Regression
NMA	Network Meta-Analysis
STC	Simulated Treatment Comparison

NMA[1] compares multiple interventions simultaneously by combining direct head-to-head evidence with indirect evidence through a common comparator to estimate all pairwise relative effects within a connected network of studies.

IPD NMA[2] is a network meta-analysis approach that uses individual participant data from each included study to compare multiple treatments, enabling consistent within-trial adjustment for prognostic factors and effect modifiers across the network to improve precision, ensure similarity/consistency, and provide subgroup- or population-specific relative effects.

Network Meta-Regression[1] is an extension of network meta-analysis that incorporates aggregate study- or patient-level covariates to balance effect modifiers, enabling adjusted comparisons and predictions for specific covariate values or target populations. When used with non-collapsible outcome measures this approach will induce aggregation bias.

MAIC[3] is a population-adjustment method that uses individual patient data from one trial to reweight participants, so their baseline characteristics match the aggregate characteristics reported in a comparator trial. This enables adjusted indirect estimates of relative treatment effects, typically in an anchored framework with a common comparator and, more cautiously, in unanchored settings when all prognostic and effect-modifying factors must be accounted for.

STC[4] is a population-adjustment method that fits an outcome regression model using individual participant data from one trial and then simulates what the outcomes in this trial would have been if patients has the same characteristics as the aggregate covariates in a comparator trial (by predicting using the regression model).

ML-NMR[5] is a unified framework that combines individual patient data and aggregate data within a single network meta-analysis model by integrating the individual-level likelihood over the aggregate studies' covariate distributions. Exploration of shared effect modifier assumptions allows balancing of effect modifiers and prognostic factors across trials and treatment comparisons with various degrees of individual participant data availability.

TELL US WHAT YOU THINK!

- **Do you agree with our proposed approach to selecting a method?**
- **Would you take a different path than the ones shown here?**
- **Is trying to simplify selection of a modelling approach in this way too prescriptive?**

FUTURE STEPS

- Join us for our ISPOR panel session "Navigating a maze of Indirect Treatment Comparisons" on **Tuesday 11th November 10:15-11:15**
- An open-source online decision-support tool, based on the diagram, is under development
- Propose an updated ISPOR Task Force on PAICs.

REFERENCES

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FINANCIAL DISCLOSURE

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