

An Automated Feasibility Assessment Tool for Indirect Treatment Comparisons Across Multiple Analytical Methods

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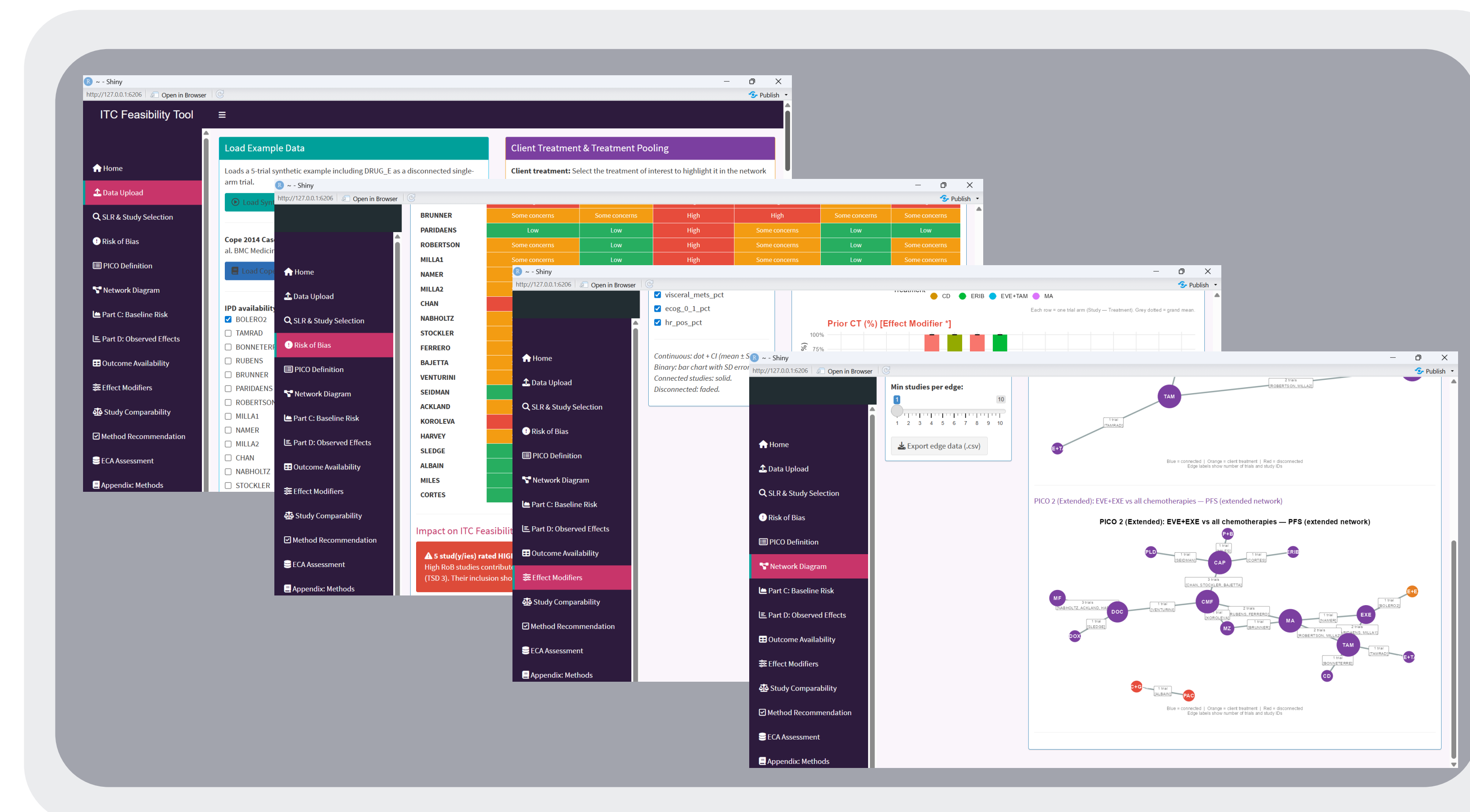
INTRODUCTION

- Indirect treatment comparisons (ITCs) are used to inform comparative efficacy and effectiveness when head-to-head trials are unavailable.
- Health Technology Assessment (HTA) guidance as well as methodological literature including the Cope framework, emphasize that appropriate ITC method selection depends on evidence connectivity, alignment of treatments and populations, and assumptions of exchangeability.¹⁻⁹
- Some feasibility considerations can be assessed before data extraction (e.g., comparator availability, network structure), while others require post-extraction evaluation based on outcome data and covariate behavior.
- Joint Clinical Assessments (JCAs) have increased the need for rapid, transparent, and efficiently repeatable feasibility assessment across ITC methods, making automation particularly valuable while retaining expert judgment.

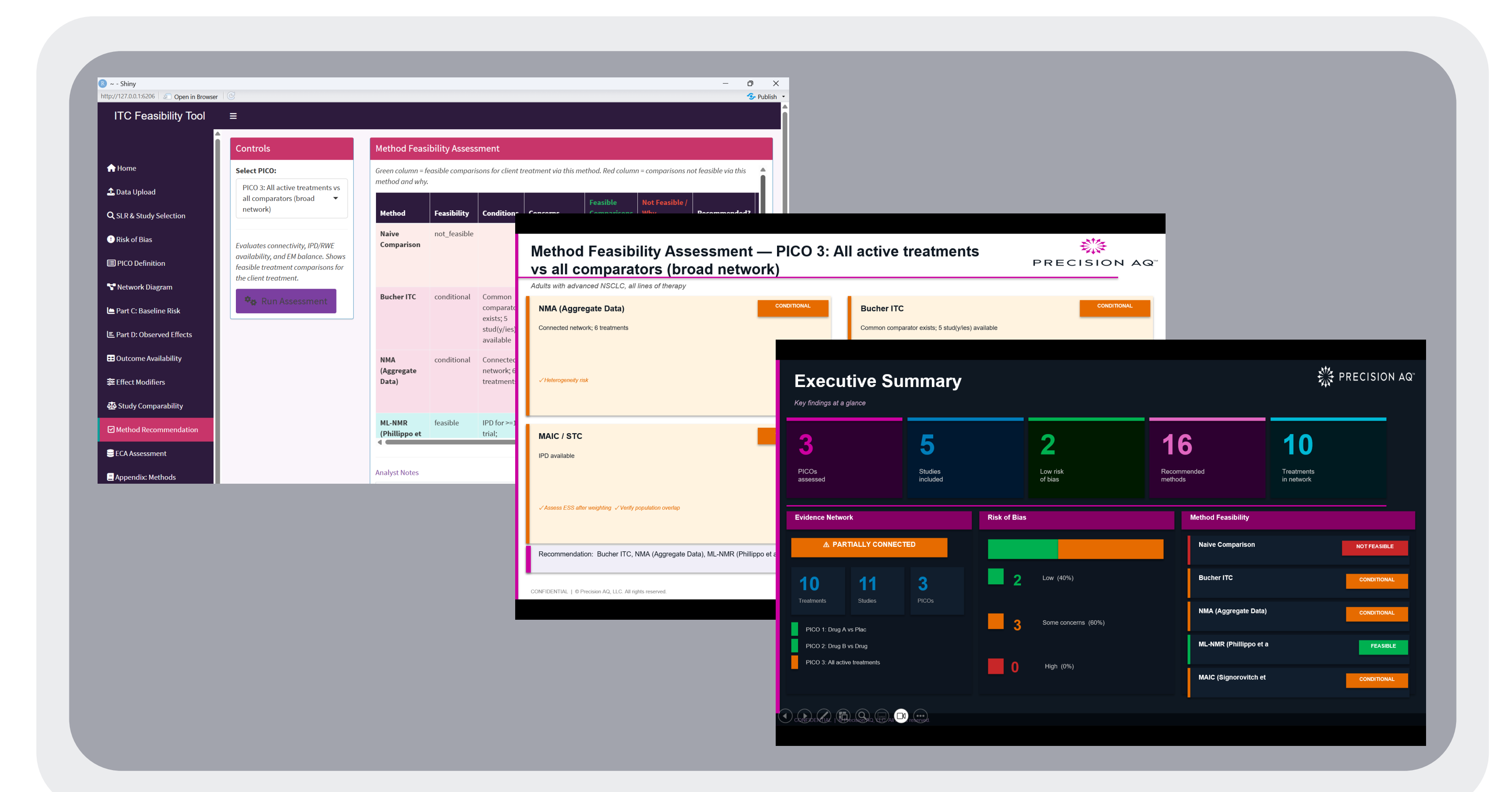
METHODS

- A rule-based automated feasibility tool to support ITC method selection was developed in R, with a web-based interface programmed using the *shiny* R package.
- Feasibility was assessed for network meta-analysis (NMA), meta-regression, multilevel network meta-regression (ML-NMR), population-adjusted indirect comparisons, and external control arm analyses.
- Structured review outputs were used to evaluate evidence connectivity, treatment and population alignment, and method-specific data requirements.
- The tool was tested using hypothetical inputs and a network of evidence based on a published breast cancer case study⁹, with AI-assisted comparison of trial inclusion and exclusion criteria and automated trial summaries, and expert review to inform analytical strategy and clinical plausibility.

RESULTS



- The tool identified feasible ITC methods for both hypothetical structured inputs and the breast cancer case-study dataset.
- Following appropriate formatting of structured systematic literature review (SLR) and data extraction input sheets, setup and execution time was under one minute.
- The automated assessment characterized network connectivity, trial eligibility comparability, and availability of key effect modifiers and prognostic factors, and flagged design considerations requiring user input (e.g., treatment or dosing pooling).
- Outputs were delivered via an interactive dashboard and automatically generated slide deck, with configurable formatting to meet different template requirements; the platform also supports embedded functionality based on large language models (LLMs) for enhanced trial comparison and summarization.



CONCLUSIONS

- Automated feasibility assessment provides a structured first draft for ITC planning, systematically evaluating key methodological components across multiple analytical approaches.
- The approach enables consistent and transparent identification of viable methods and key challenges, aligned with current HTA expectations for comparative effectiveness analyses.
- By making assumptions and limitations explicit, the tool supports informed exploration of complementary methods where appropriate, even in the presence of moderate data or design constraints.
- Final analytical decisions remain judgment-based, requiring expert interpretation to integrate clinical context, value considerations, and methodological nuance that cannot be fully resolved algorithmically.

[1] National Institute for Health and Care Excellence (2013). Guide to the Methods of Technology Appraisal. NICE, London; [2] Bucher, H.C., et al. (1997). The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *Journal of Clinical Epidemiology*, 50(6), 683–691; [3] Dias, S., et al. (2011). Evidence synthesis for decision making 2: A generalized linear modelling framework for pairwise and network meta-analysis of randomized controlled trials. *NICE Decision Support Unit Technical Support Document 2*; [4] Dias, S., et al. (2011). Evidence synthesis for decision making 3: Heterogeneity—Subgroups, meta-regression, bias, and bias-adjustment. *NICE Decision Support Unit Technical Support Document 3*; [5] Phillippo, D.M., et al. (2016). Methods for population-adjusted indirect comparisons in health technology appraisal. *NICE Decision Support Unit Technical Support Document 18*; [6] Signorovitch, J.E., et al. (2010). Comparing treatments using a matching-adjusted indirect comparison. *Pharmacoeconomics*, 28(6), 437–448; [7] Hoaglin, D.C., et al. (2011). Conducting indirect-treatment-comparison and network meta-analysis studies: Report of the ISPOR Task Force on indirect treatment comparisons good research practices. *Value in Health*, 14(4), 429–437; [8] Phillippo, D.M., et al. (2020). Multilevel network meta-regression for population-adjusted indirect comparisons. *Journal of the Royal Statistical Society: Series A*, 183(3), 1189–1210; [9] Cope, S., et al. (2014). A process for assessing the feasibility of a network meta-analysis: A case study of everolimus in combination with hormonal therapy versus chemotherapy for advanced breast cancer. *BMC Medicine*, 12, 93.