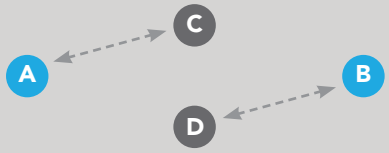
STC and MAIC

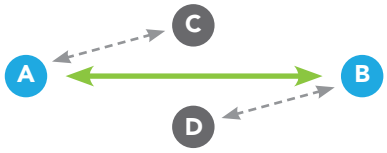
Targeted Approaches to Enhance Indirect Comparisons

Evidence on the relative effectiveness of treatments is rarely available from head-to-head studies, and as a result, published results from clinical trials must often be used for indirect comparisons via network meta-analysis (NMA). Although often very effective, NMA may be challenging if there is an incomplete or disjointed evidence network, or substantial heterogeneity between studies, or when key treatments to be compared are separated by multiple intermediate steps or linking comparisons within the network. Simulated Treatment Comparisons (STC) and Matching Adjusted Indirect Comparisons (MAIC) can often help to overcome these challenges, and may also provide additional depth and a different perspective when challenges do not exist. Submissions to health authorities have successfully employed these methods, and they may be required in the future.

STC / MAIC to Overcome Challenges with NMA



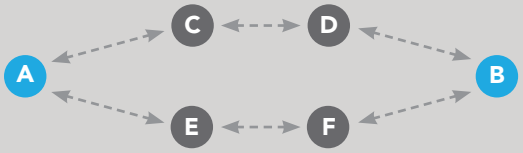
NMA with an incomplete network may not produce results for key comparisons of interest (e.g., A vs. B above).



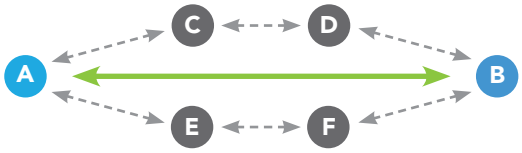
STC/MAIC can address this challenge because it does not rely on a common comparator; outcomes are compared directly after adjustment for potential confounding.

NMA with heterogeneity between studies may be unreliable due to important differences in study populations.

STC/MAIC can address this challenge by explicitly adjusting for differences between the trials.

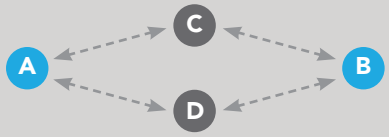


NMA with a multi-step comparison with traditional methods when the network is broad requires multiple intermediate steps to derive the main comparison of interest.

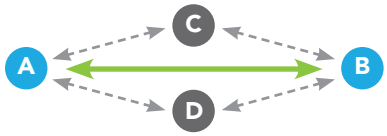


STC/MAIC can address this challenge since comparisons are targeted to treatments of interest (i.e., they are a single step comparison).

STC / MAIC to Provide Depth and a Different Perspective



NMA with a complete network produces an average comparison of treatments across a network of published evidence, e.g., A vs. C, A vs. D, B vs. C, B vs. D.



STC/MAIC can be complementary, providing a different perspective on the comparison of interest (e.g., A vs. B) reflecting how the treatments would have been compared if studied together in the same trial.

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	STC	MAIC
Approach to adjusting for population differences	• Uses predictive equations to model the relationship between outcomes and baseline characteristics • The equations are used to predict outcomes for the index treatment in the context of the comparator population • The resulting adjusted outcomes are comparable to the observed result in the comparator's trial	• Uses balancing weights to reweight patients in the index trial so that the mean of characteristics in the index population matches the means in the comparator's trial • The weights are applied to derive weighted outcomes for the index trial • The resulting adjusted outcomes are comparable to the observed result in the comparator's trial
When to consider…	• Reweighting index population leads to imbalanced distribution of weights (i.e., few patients driving results) • Limited/lack of overlap in some variables included in adjustment • Interested in multiple comparators and few outcomes	• Predictive equations from STC are weak or problematic • Working with time-to-event or other non-linear outcomes • Interested in multiple outcomes and few comparators

[Adapted from: Ishak KJ, Proskorovsky I, Benedict A. Simulation and Matching Based Approaches for Indirect Comparisons of Treatments. *Pharmacoeconomics.* 2015 Jun; 33(6):537-549]

Evidera Experience and Selected Publications

Evidera's team of statisticians and modelers are experts in innovative and alternative approaches to indirect comparison, with publications in this area for over five years. We have successfully supported National Institute for Health and Care Excellence (NICE) submissions[1,2] where targeted approaches have been applied for indirect comparisons. We are able to leverage expert health economics, modeling, and literature review teams for scientific and strategic support in assessing the need and suitability of targeted comparison, skillfully executing the analyses, clearly communicating the findings, and incorporating these into health economic assessments and agency submissions.

Ishak KJ, Proskorovsky I, Benedict A. Simulation and Matching-Based Approaches for Indirect Comparison of Treatments. Pharmacoeconomics. 2015 Jun;33(6):537-549.

Caro JJ, Ishak KJ. No Head-To-Head Trial? Simulate The Missing Arms. Pharmacoeconomics. 2010;28(10):957-967.

Ishak KJ, Caro JJ, Drayson MT, Dimopoulos M, Weber D, Augustson B, Child JA, Knight R, Iqbal G, Dunn J, Shearer A, Morgan G. Adjusting for Patient Crossover In Clinical Trials Using External Data: A Case Study of Lenalidomide for Advanced Multiple Myeloma. Value Health. 2011 Jul-Aug;14(5):672-678.

Ishak KJ, Phatak H, Masseria C. Making Sense of Novel Approaches for Indirect Comparison: Similarities and Differences of Simulation and Matching Based Approaches. Workshop Presented at ISPOR's European Meeting, 2015, Milan, Italy.

Ishak KJ, Proskorovsky I, Benedict A, Chen C. Overcoming Incomplete Evidence Networks and Heterogeneity Issues with Simulated Treatment Comparisons. Workshop Presented at ISPOR's European Meeting, 2013, Dublin, Ireland.

Ishak KJ, Eckert L, **Caro JJ**. Comparative Effectiveness Research using Simulated Treatment Comparison (STC). Workshop presented at ISPOR European Meeting 2011, Madrid, Spain.

1: Axitinib for Treating Advanced Renal Cell Carcinoma After Failure of Prior Systemic Treatment, February 2015, http://www.nice.org.uk/guidance/ta333

2: Lenalidomide for the Treatment of Multiple Myeloma In People Who Have Received at Least One Prior Therapy, January 2009, http://www.nice.org.uk/guidance/ta171