INDIRECT TREATMENT COMPARISONS: Guidance On Technical Aspects Of Conducting & Interpreting Network Meta-Analyses

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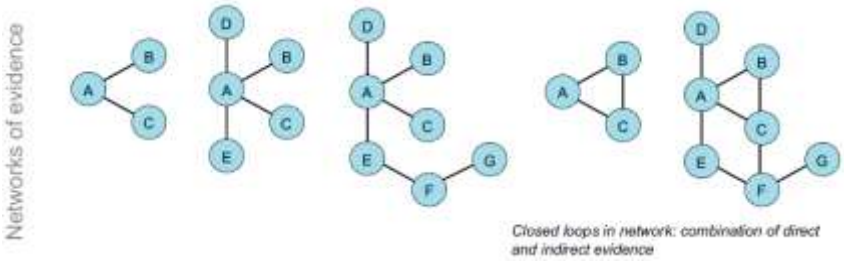
Workshop Objectives

- Provide conceptual overview of the rationale for conducting indirect treatment comparisons / mixed treatment comparisons (ITC/MTC)
- Discuss ISPOR's initiatives in the area of ITC/MTC
- Understand fundamental concepts and strengths & limitations of ITC/MTC
- Provide practical examples of ITC/MTC

What is ITC/MTC?

- A simple extension of meta-analysis to multiple comparators:
  - Indirect comparisons occur when treatments have not been studied head-to-head but have been studied against a common reference treatment (eg, placebo)
  - Mixed comparisons occur when treatments have been studied head-to-head AND against a common reference treatment



Closed loops in network: combination of direct and indirect evidence

QUINTILES

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Why do ITC/MTC?

- It is rare that all available treatments for a given condition would have been evaluated in the same study
- On the other hand, it is common for certain treatments to have been evaluated in multiple studies
- ITC/MTC is a scientifically rigorous approach to evidence synthesis that enables comparisons across all treatments included in a network of evidence
- In the era of comparative effectiveness research (CER), there is heightened interest in understanding how treatments compare—and ITC/MTC is an important tool for this

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ISPOR Initiatives in ITC/MTC

- ISPOR has initiated two different Task Forces for good research practices in ITC/MTC

- The first worked from 2010-2011 and generated a two-part report
- The second was a joint task force in conjunction with the Academy of Managed Care Pharmacy and National Pharmaceutical Council that worked from 2011-2013
- It generated a questionnaire to assess relevance and credibility of ITC/MTC studies to inform healthcare decision-making

QUINTILES

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2010-11 Task Force Report, Part 1

SCIENTIFIC REPORT

Interpreting Indirect Treatment Comparisons and Network Meta-Analysis for Health-Care Decision Making: Report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: Part 1

- Nicknamed the “consumer’s report”
- Provides guidance on interpretation & use of ITC/MTC studies by decision makers
- Areas of focus:
  - Evidence networks
  - Terminology & definitions
  - Frequentist vs Bayesian analytic approaches
  - What to look for in a study report
  - Trade-offs between & implications for timing of evidence accumulation & decision making

Jansen JP, Fleurence R, Devine B, et al. Interpreting indirect treatment comparisons & network meta-analysis for health care decision-making: Report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices—part 1. Value Health 2011;14:417-28.

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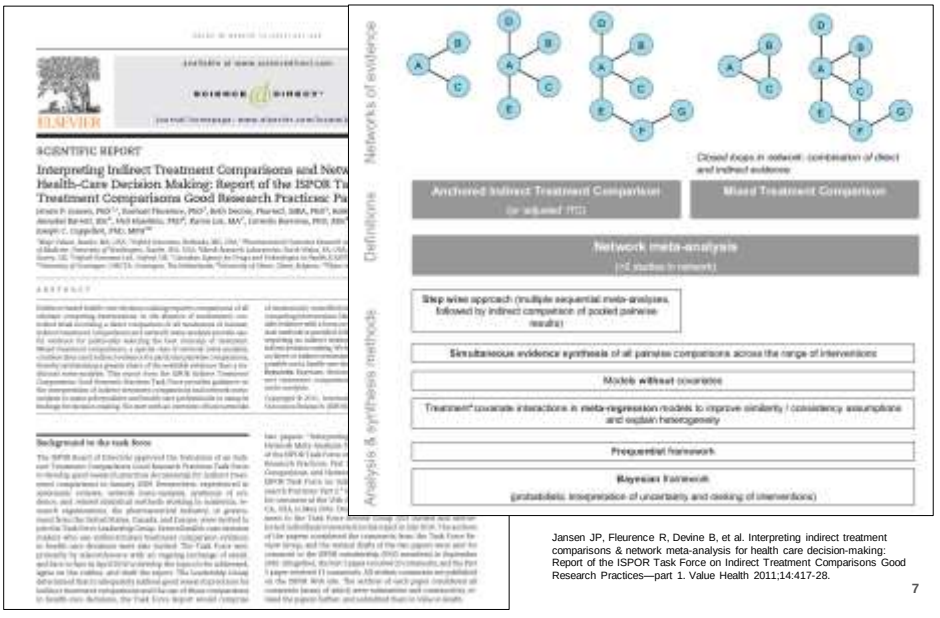
2010-11 Task Force Report, Part 1



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2010-11 Task Force Report, Part 2

- Nicknamed the “producer’s report”
- Provides guidance on conduct of ITC/MTC studies by researchers
- Areas of focus:
  - Building an evidence network
  - Similarity, consistency & other key assumptions of ITC/MTC
  - Technical aspects of frequentist vs Bayesian statistical approaches
  - Checklist for good research practice
  - Illustrative examples

Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect treatment comparisons and network meta-analysis studies: report of the ISPOR task force on indirect treatment comparisons good research practices—Part 2. Value Health 2011;14:429-37.

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2010-11 Task Force Report, Part 2

Table 2 – Checklist of good research practices for conducting and reporting network-meta-analysis studies.

Checklist item	Recommendation(s)
Search strategies	• Follow conventional guidelines for systematic literature searches; be explicit about search terms, literature, and time frames, and avoid use of ad hoc data • Consider iterative search methods to identify higher-order indirect comparisons that do not come up in the initial search focusing on lower-order indirect comparisons
Data collection	• Set forth evidence network demonstrating direct and indirect linkages between treatments, based on identified study reports • Follow conventional guidelines for data collection; use a pre-specified protocol and data extraction form • Include sufficient study detail in data extraction to permit assessment of comparability and homogeneity (e.g., patient and study characteristics, comparators, and outcome measures)
Statistical analysis plan	• Prepare statistical analysis plan prior to data analysis, but permit modifications during data analysis, if necessary • Provide step-by-step descriptions of all analyses, including explicit statements of all assumptions and procedures for checking them • Describe analytic features specific to network meta-analysis, including comparability and homogeneity, synthesis, sensitivity analysis, subgroup analysis and meta-regression, and special types of outcomes
Data analysis	• Follow conventional guidelines for statistical model diagnostics • Evaluate violations of similarity or consistency assumption in evidence network • If similarity or consistency is a problem, consider use of meta-regression models with treatment × covariate interactions to reduce bias
Reporting	• Follow PRISMA statement for reporting of meta-analysis • Explicitly state the study research questions (e.g., in Introduction or Objectives section of report) • Provide graphical depiction of evidence network • Indicate software package used in the analysis and provide code (at least in an online appendix)

Hoaglin DC, Hawkins N, Jansen JP, et al. Conducting indirect treatment comparisons and network meta-analysis studies: report of the ISPOR task force on indirect treatment comparisons good research practices—Part 2. Value Health 2011;14:429-37.

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2011-2013 Joint ISPOR-AMCP-NPC Task Force Report

ELSEVIER

ScienceDirect

Indirect Treatment Comparison/Network Meta-Analysis Study Questionnaire to Assess Relevance and Credibility to Inform Health Care Decision Making: An ISPOR-AMCP-NPC Good Practice Task Force Report

- Part of ISPOR's comparative effectiveness research collaborative initiative (CER-CI) with AMCP and NPC
- Questionnaire has 26 items to guide users of an ITC/MTC:
  - 4 on relevance of study to decision maker
  - 22 on credibility of study, covering five areas:
    1) Evidence base
    2) Analysis methods
    3) Reporting quality & transparency
    4) Interpretation of findings
    5) Conflicts of interest

Jansen JP, Trikolinos T, Cappelleri JC, et al. Indirect treatment comparison/network meta-analysis study questionnaire to assess relevance and credibility to inform health care decision making: An ISPOR-AMCP-NPC Good Research Practices Task Force Report. Value Health 2014;17:157-73.

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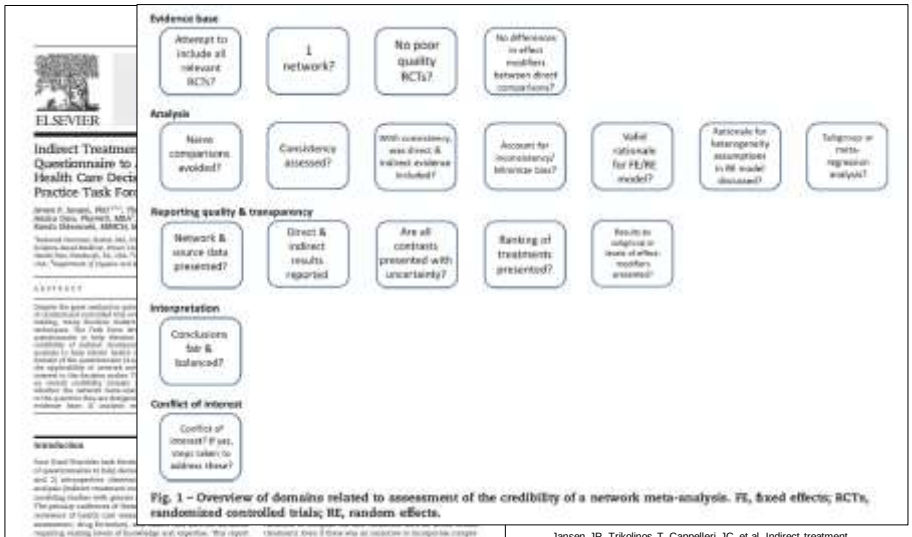

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