Planning a Cochrane review to compare multiple interventions -
the role of network meta-analysis

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Conflict of interest disclosure

- Funding:
  Current: Grant UG1EY020522 (PI: Tianjing Li), the National Eye Institute, National Institutes of Health (NIH), USA.

  Past: PCORI, AHRQ, FDA, NIH, Cochrane, Johns Hopkins University

- Served as an Associate Editor and an author on several chapters of the new Handbook.

What is network meta-analysis (NMA)?

NMA is a technique for comparing three or more interventions simultaneously in a single analysis by combining both direct and indirect evidence across a network of studies.

Four interventions for heavy menstrual bleeding
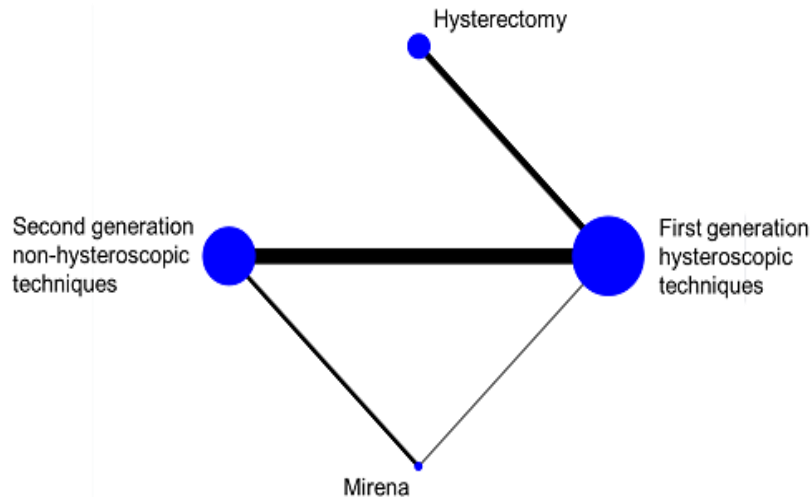
Pair-wise meta-analysis			
Hysterectomy	–	–	0.38 (0.22 to 0.65)
0.45 (0.24 to 0.82)	**Second generation non-hysteroscopic techniques**	1.35 (0.45 to 4.08)	0.82 (0.60 to 1.12)
0.43 (0.18 to 1.06)	0.96 (0.48 to 1.91)	**Mirena**	2.84 (0.51 to 15.87)
0.38 (0.23 to 0.65)	0.85 (0.63 to 1.15)	0.88 (0.43 to 1.84)	**First generation hysteroscopic techniques**
Network meta-analysis			

Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Chapter 11: Undertaking network meta-analyses.

Type of research questions addressed by NMA

Examples of NMA in *The ~~Cochrane~~ Library* (110 reviews and 51 protocols with NMA in the title as of Feb 4, 202~~1~~

- "Intervention~~s~~
  mental illnes~~s~~
- "Intervention~~s~~
  and network
- "Risk-reducin~~g~~
- "Immunomo~~dulatory~~
  a network me~~ta~~

Multiple competing interventions available
- What is the comparative effectiveness of any two interventions?
- What is the best intervention for…?

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Define and pre-specify the interventions (nodes) in NMA

- **P**opulations and **I**nterventions often need to be considered together given the potential for intransitivity

- A driving principle is that participants should be eligible for randomization to any included intervention

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Example of a network comparing four chemotherapy regimens, where transitivity is violated due to incomparability between the interventions

Chaimani A, Caldwell DM, Li T, Higgins JPT, Salanti G. Chapter 11: Undertaking network meta-analyses.
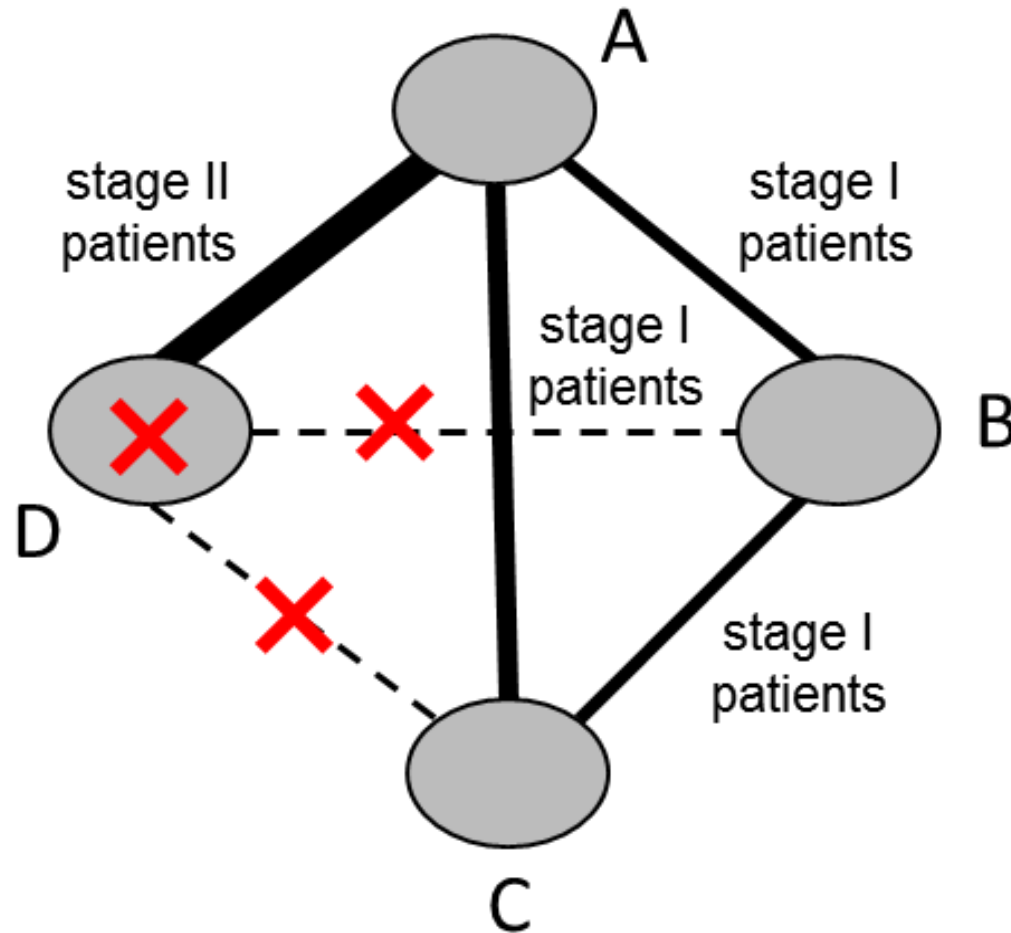
Decision sets and supplementary sets of interventions

- **Decision set:** interventions of direct interest

- **Supplementary set:** interventions, such as placebo, that are included in the network meta-analysis for the purpose of improving inference
  - More useful for spare network
  - Broadening the network challenges the transitivity assumption

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Group variants of an intervention
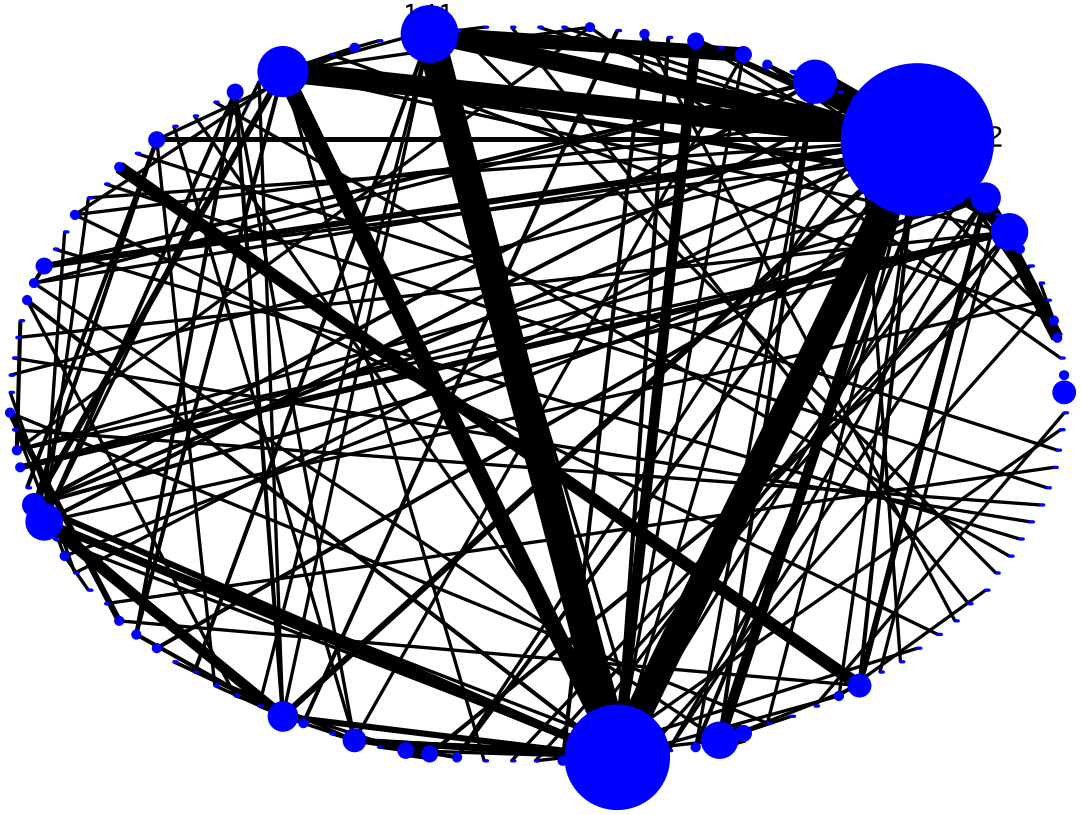
367 trials examining 136 unique drug-concentration combination for glaucoma

Li et al. *Ophthalmology.* 2016;123(1):129-40.
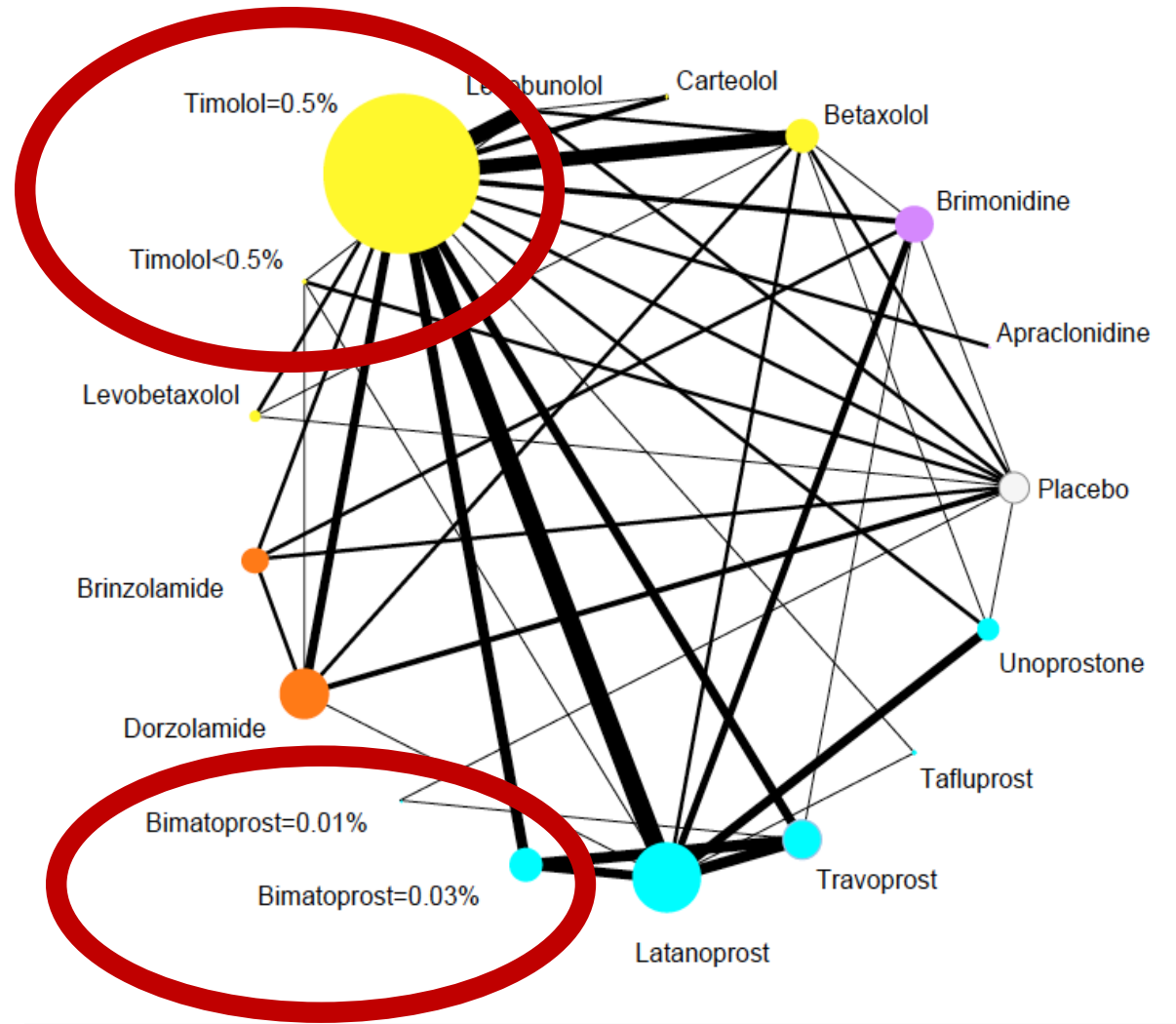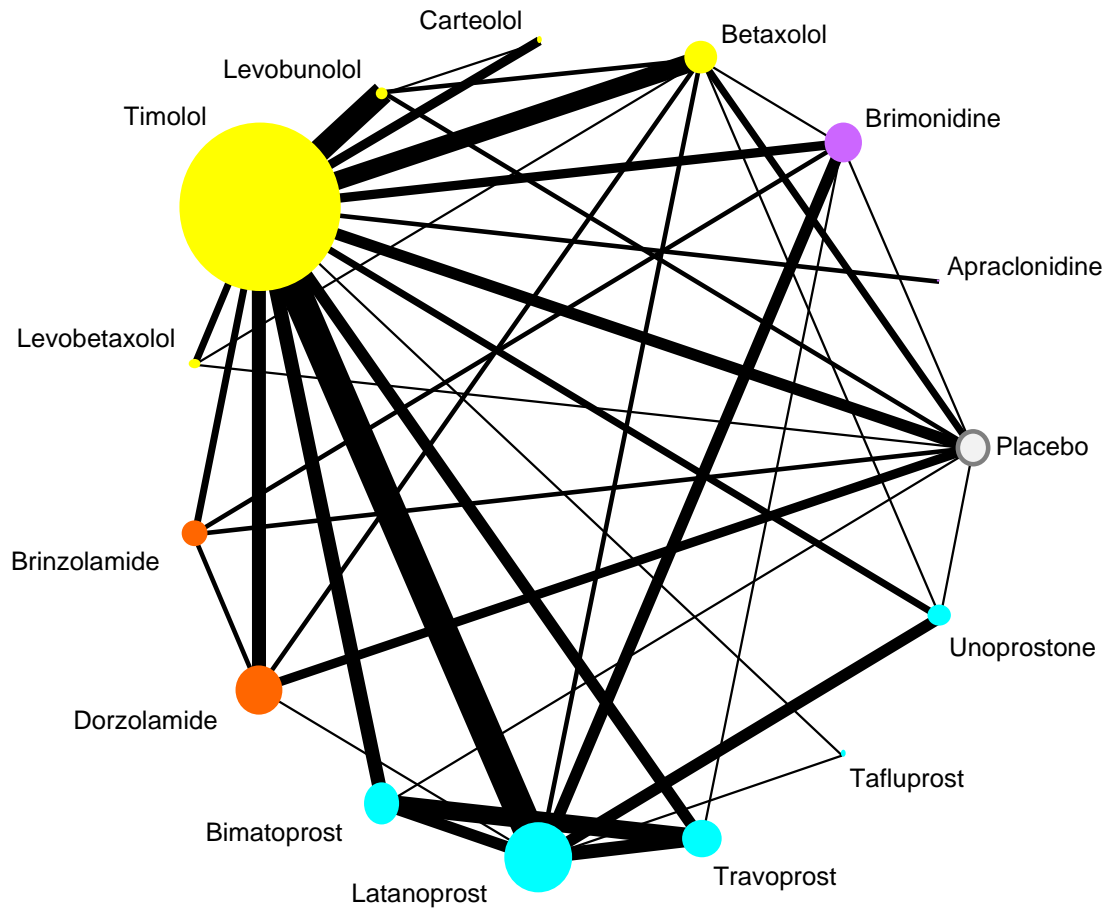
Pre-specify details of analysis

- Two possible types of analyses, specify whether both types of analyses will be performed
  - a series of independent pairwise meta-analyses
  - NMA
- Specify the statistical model
  - e.g. fixed or random effects, common or different heterogeneity across the different comparisons
- Specify the modelling approach
  - e.g. as a multivariate meta-analysis or hierarchical model
- Specify the software
  - STATA, R, WinBUGS
- Provide additional details for analyses to be performed in a Bayesian framework
  - prior distributions, how convergence will be assessed, etc.
- Specify approaches to handling multi-arm studies
- Specify approaches to examining local and global incoherence

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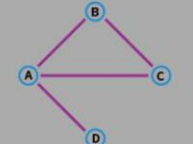# NMA training for review authors

Module 10: Network meta-analysis

⏱ *100 min*

Introduction to network meta-analysis (NMA) in the context of a systematic review of randomized trials. Read more

🔒 No access

Register here for access

Introduction to network meta-analysis (NMA)

What NMA is and when to consider it

What NMA can achieve

Assumptions required for NMA

Transitivity

Looking at transitivity using statistics

Planning, performing NMA and understanding the results

Planning a review to compare multiple interventions

Understanding the network structure and performing NMA

Understanding intervention effects and ranking

Evaluating confidence in the results of an NMA

Protocol and reporting considerations

What to include in your protocol and final review

Cochrane Training

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Network meta-analysis: Learning Live webinar series

Welcome to this series of five Cochrane Learning Live webinars, all dedicated to network meta-analysis. We are pleased to be joined throughout the series by leading experts in this field, and you can find out more about each of the five sessions and sign up to attend throught the links below.

Sign up for the series:

November 18, 2019
Question formulation and protocol development for systematic reviews with network meta-analysis
Anna Chaimani, co-convenor, Cochrane Statistical Methods Group & Cochrane Comparing Multiple Interventions Methods Group.
Dr. Tianjing Li, Associate Professor with tenure, Department of Ophthalmology, University of Colorado, Denver, USA.
[more info and sign up]

December 3, 2019
MetaInsight: The Complex Review Support Unit (CRSU) network meta-analysis (NMA) web-based app
Alex Sutton & Yiqiao Xin, members of the NIHR Complex Review Support Unit
[more info and sign up]

January 16, 2020
CINeMA – Confidence in network meta-analysis
Georgia Salanti, associate professor in Biostatistics and Epidemiology, University of Bern.
Theodore Papakonstantinou, postdoctoral researcher, University of Bern.
Adriani Nikolakopoulou, postdoctoral researcher, University of Bern.
Virginia Chiocchia, PhD student in Biostatistics, University of Bern.
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February 11, 2020
Presenting network meta-analysis results in Summary of Findings Tables
Holger Schünemann, professor, Department of Health Research Methods, Evidence & Impact and Department of Medicine, McMaster University
Dr. Romina Brignardello-Petersen, Assistant Professor, Department of Health Research Methods, Evidence, & Impact, McMaster University.
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March 17, 2020
Editorial considerations in reviews with network meta-analysis
Kerry Dwan, methods support unit lead and statistical editor, Cochrane Editorial and Methods Department.
Liz Bickerdike, Associate Editor, Acute & Emergency Care Network and the Abdomen & Endocrine Network.
[more info and sign up]

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