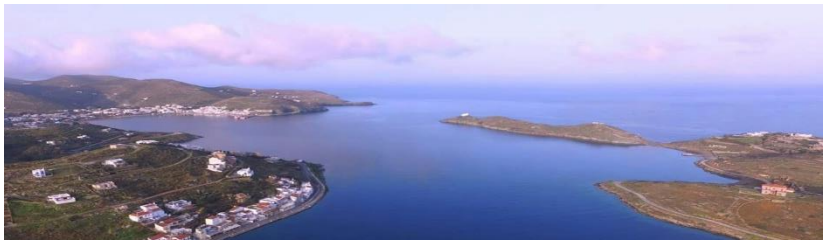


Writing network meta-analysis 2

Collecting data and reporting on analyses and results

Anna Chaimani

Network meta-analysis
A project-based course using R
Kea island, April 2018

What to keep in mind when deciding which interventions to include

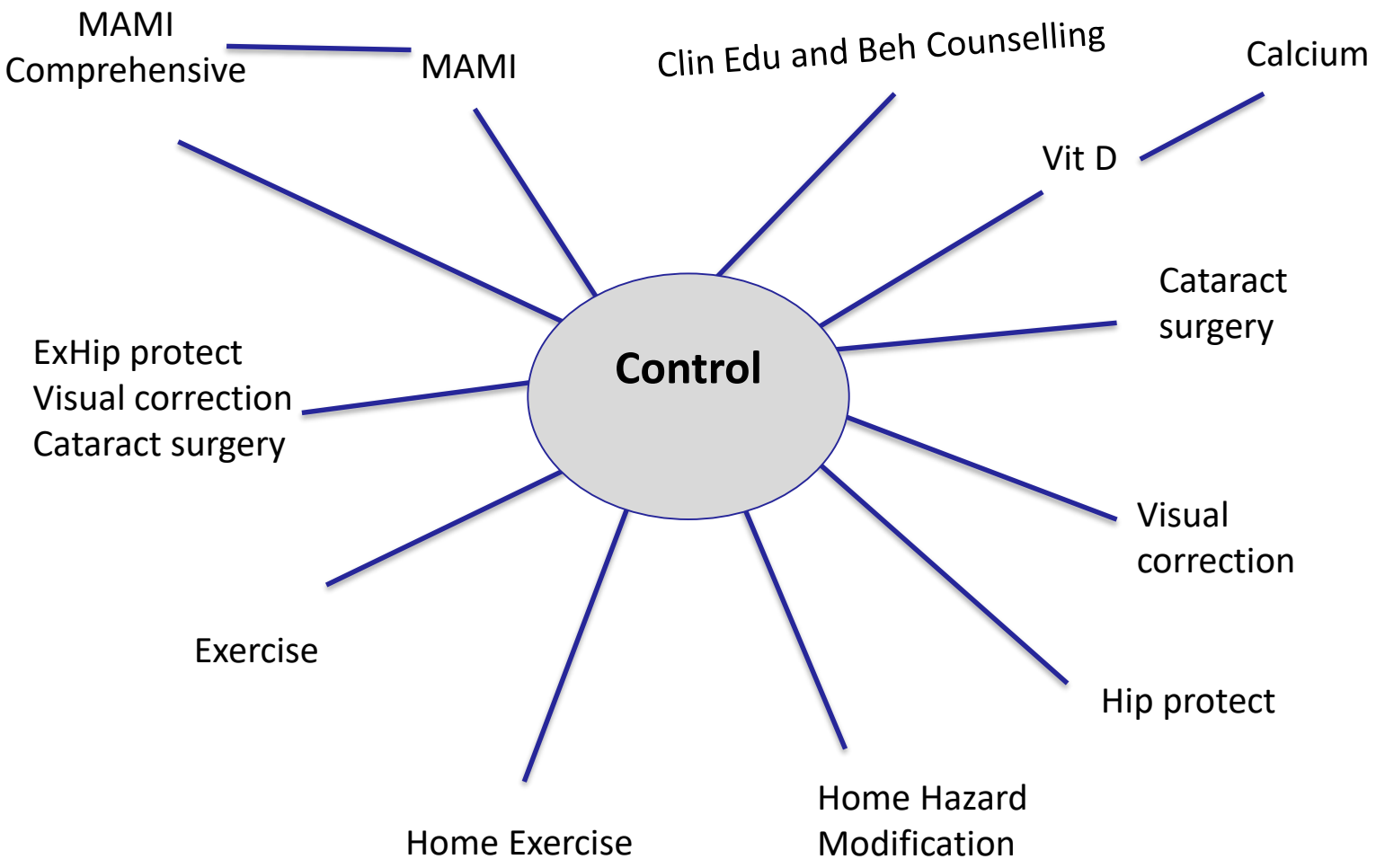
- Restricting your review to compare few interventions
  - limits its usefulness and applicability
  - you must justify your choice
  - risk to have unconnected networks
  - few data, low power (depends on the setting)

- Expanding the database too much to include many treatments
  - Jeopardizes the transitivity assumptions (or at least makes its defense challenging)
  - Renders review process long and data management difficult

- **Watch out for:** old and new treatments, ad-on treatments, intransitive legacy treatments

Example

Intervention to reduce falls in elderly



Outcome measures

- Define the outcomes of interest
- Define the outcomes that will be used to estimate the relative ranking of treatments
  - if it is included in the objectives of the review

Searching for studies

Search strategy should consider any study comparing at least two of the eligible interventions

- i.e. all available direct comparisons between the eligible interventions should be included

Data extraction

Describe you will extract data on

- **Outcomes:** study-level or arm-level preferable?
- **Potential effect modifiers: (**population and study characteristics that may act as effect modifiers selected based on bibliography and clinical understanding) required to evaluate statistically the transitivity assumption and clinical/methodological heterogeneity
- **Other data:** any additional information (e.g. risk of bias items) that will be extracted

Example

Effectiveness and safety of treatments for panic disorders

"From each included study we will extract data on the following study, interventions and population characteristics that may act as effect modifiers: Methods: study design, randomization (individual or cluster), total duration of study, number of study centres and location, study setting, withdrawals, and date of study.
Participants: number, setting, diagnostic criteria, presence or absence of medical and psychiatric comorbidities, presence or absence of elderly participants, percentage of patients with agoraphobia, percentage of patients with baseline depression, inclusion criteria, and exclusion criteria.
Interventions: medication dose, medication dose range, use of rescue medication.
Outcomes: primary and secondary outcomes specified and collected, and time points reported. Where possible we will extract data at the arm level, not summary effects.
Notes: sponsorship/funding for trial, and notable conflicts of interest of trial authors"

Guaiana et al. Cochrane Database Syst Rev 2015

Selecting effect measures for the analysis

Usual considerations in choose between OR/RR/RD or MD/SMD

- **Be aware that** different effect measures sometimes impacts the results
- More than one effect measures might be used
  - describe how any disagreements will be handled
- Report whether the same or different measures will be used in the analyses and the presentation of results

State which **measure will be used to rank the treatments**

- Avoid probability to be the best, use mean ranks/SUCRAs instead

Evaluating the assumption of transitivity

- Describe how you will evaluate the clinical and methodological comparability of studies (**heterogeneity**)
  - As in standard meta-analysis
- Describe how you will evaluate the plausibility of the **transitivity assumption**
  - the comparability/similarity of studies evaluating *different* comparisons
  - You can compare the distribution of effect modifiers across sets of studies grouped by comparison
  - In practice this is often difficult – be prepared and remember lack of evidence is not evidence of lack

Example

Efficacy and acceptability of psychological interventions for bipolar disorder

"To infer about the assumption of transitivity:
1. We will assess whether the included interventions are similar when they are evaluated in RCTs with different designs; for example, whether interventions are administered the same way in studies comparing active treatments to usual care (or no treatment) and in those comparing active treatments to other active treatments.
2. We will compare the distribution of the potential effect modifiers across the different pairwise comparisons (see 'Data extraction and management' for the list of potential effect modifiers). If the distributions are balanced across comparisons we will conclude against evidence of intransitivity."

not against intransitivity!

Cipriani et al. PROSPERO 2015:CRD42015016085

Describe the statistical analyses (1)

- **Two possible types of analyses**:
  - A series of independent pairwise meta-analyses (only as the first step of NMA)
  - Network meta-analysis
  - State whether both types of analyses will be performed
    - if the required assumptions are plausible

- Describe the **statistical model**
  - Bayesian or frequentist setting
  - fixed or random effects
  - common or different heterogeneity across the comparisons

- Report the **modelling details** (e.g whether NMA is fitted as meta-regression or hierarchical model, estimation method for heterogeneity)

Describe the statistical analyses (2)

- Explain how you will **handle variability in treatment definition** (e.g. different doses or modalities)
  - Analyze as separate treatment modes nodes
  - Model explicitly their variability
  - Additive/multiplicative models for complex interventions?

- Report the **software** of the analysis
  - e.g. STATA, R, WinBUGS
  - Give the WinBUGS code

- Give **additional details**, if analyses will be performed in a Bayesian framework
  - prior distributions, how convergence will be assessed, etc. (in an appendix)

Example

Effectiveness and safety of treatments for panic disorders

"Random-effects pairwise meta-analyses will be conducted for every treatment comparison with at least two studies, using Stata 2013. A random-effects model is considered preferable […]
A random-effects NMA, taking into account the correlations induced by multi-arm trials, will be conducted in a Bayesian framework and implemented using WinBUGS 1.4.3.
There are three possible models that could be fitted
1. A class (lumped) model.
2. An individual treatment (possibly dose specific) model.
3. A hierarchical model where we include both class and treatments.
We will investigate models depending on the available data. The goodness of fit of the model to the data will be measured by the posterior mean of the residual deviance. […]"

Guaiana et al. Cochrane Database Syst Rev 2015

In the manuscript…

Network geometry and transitivity

- Methods
  - Describe methods used to explore the geometry of the treatment network under study and potential biases related to it
  - How the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence
  - How transitivity was evaluated
- Results
  - A brief overview of characteristics of the treatment network.
  - Amount of data for the different interventions and pairwise comparisons in the network and gaps of evidence in the treatment network
  - Potential biases reflected by the network structure.
  - Risk for intransitivity

Summary measures

- Methods
  - State the principal summary measures (e.g., risk ratio, difference in means)
  - Additional summary measures, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values

Statistical analysis (1)

- Methods
  - Describe the methods of handling data and combining results of studies for each network meta-analysis.
  - Handling of multi-arm trials
  - Selection of variance structure
  - Selection of prior distributions in Bayesian analyses and assessment of model fit.

Statistical analysis (2)

- Results
  - Present results of each meta-analysis done, including confidence/credible intervals and the respective estimate of heterogeneity
  - In larger networks, authors may focus on comparisons versus a particular comparator (e.g., placebo or standard care), with full findings presented in an appendix.
  - League tables and forest plots may be considered to summarize pairwise comparisons.
  - If additional summary measures were explored (such as treatment rankings), these should also be presented.