Disentangling interactions between components in a network of complex health interventions

Silvia Metelli[1], Anna Chaimani[1]

[1] *Université Paris Cité, Inserm Research Center of Epidemiology and Statistics*

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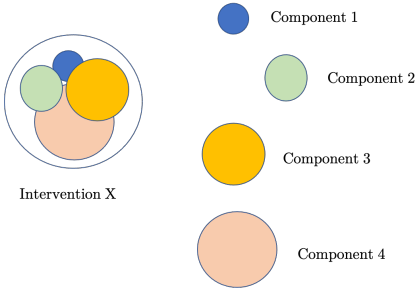
Overview

1. Defining complex health interventions
2. Networks of complex interventions ($\rightarrow$ network meta-analysis)
3. Related work & proposed approach
4. Some results
5. Conclusions

What is a Complex Intervention?

Intervention consisting of **multiple**, potentially **common** and **interactive** components



Example: *behavioural change or psychological interventions (e.g. smoking cessation). More recently, digital interventions...*

$\Rightarrow$ **need to disentangle the single effects to understand overall effectiveness**

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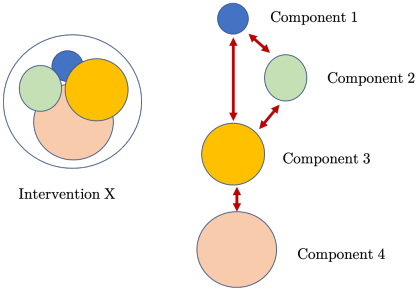

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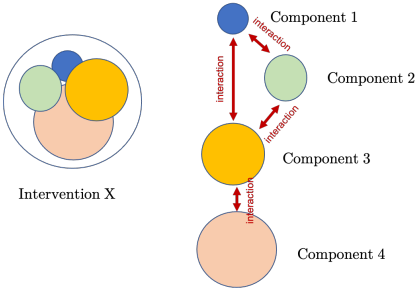

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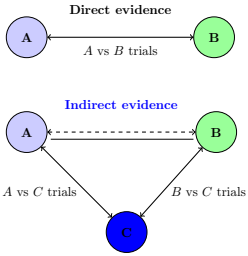
⇒ **need to disentangle the single effects to understand overall effectiveness**

Network meta-analysis (NMA)

NMA: pool evidence from multiple studies to simultaneously compare many treatments, by integrating direct with indirect evidence, forming a *network of interventions*

Research question: which intervention works best?



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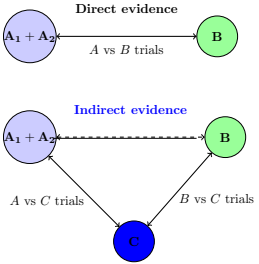


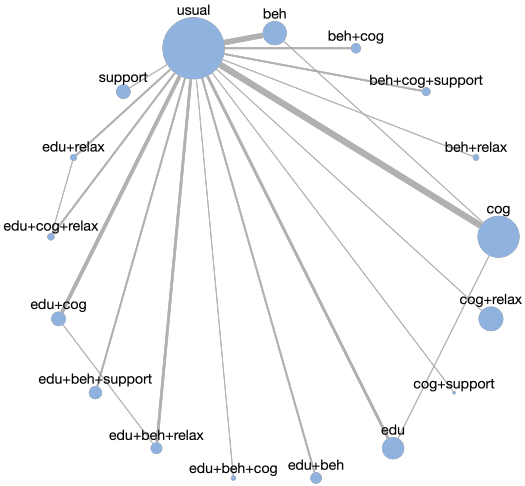
NMA of complex interventions

Research question: which components contribute the most to the effectiveness?

- so, may have complicated pathways
- there is typically larger heterogeneity

Motivating example: Coronary heart psychological interventions

Welton et al., 2009



Standard NMA model: (Bayesian) random effects model

N studies, T treatments

For each study i: $y_{i,XY}$ observed relative treatment effect (with se)

$$y_{i,XY} \sim N(\delta_{i,XY}, \sigma^2_{i,XY})$$
$$\delta_{i,XY} \sim N(\theta_{XY}, \tau^2_{XY})$$

- $\forall(X, Y)$ summary relative effect $\theta_{XY} = \theta_X - \theta_Y$ (basic parameters)
- common heterogeneity τ^2_{XY} across studies

▷ Bayesian inference: need to specify priors for parameters to estimate $\theta = (\theta_1, \ldots, \theta_{T-1})^T \sim P(\theta)$, $\tau \sim P(\tau)$

Standard NMA models for complex interventions

Study i comparing treatments X, Y where $X \ni \{c_1, c_2\}$ and $Y \ni \{c_3, c_4\}$:

Additive model:

$$
\begin{aligned}
y_i &\sim N(\delta_i, s_i^2) \\
\delta_{i,XY} &\sim N(\theta_X - \theta_Y, \tau^2) \\
\theta_X &= d_1 + d_2 \\
\theta_Y &= d_3 + d_4 \qquad \rightarrow \text{same effect as from sum of effects alone}
\end{aligned}
$$

Full interaction model:

$$
\begin{aligned}
y_i &\sim N(\delta_i, s_i^2) \\
\delta_{i,XY} &\sim N(\theta_X - \theta_Y, \tau^2) \\
\theta_X &= d_1 + d_2 + d_{1*2} \\
\theta_Y &= d_3 + d_4 + d_{3*4} \qquad \rightarrow \text{bigger/smaller than from sum of effects alone}
\end{aligned}
$$

Idea: path-specific mediation

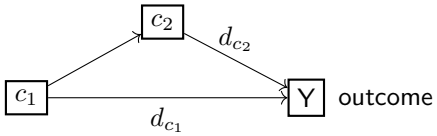
Key assumption: in studies combining two or more components there is a pathway leading from one component to the outcome via the other component(s)

Example: study comparing complex intervention $X \ni \{c_1, c_2\}$ vs placebo

$X = c_1 + c_2$: suppose that c_1 is a **strong** component and c_2 a **weak** component

$\downarrow$

effect of component c_1 is "mediated" by component c_2



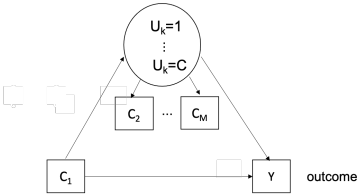
$$\theta_X = d_{c_1} + \beta_1 \theta'_X$$
$$\theta'_X = d_{c_2} + \beta_2 d_{c_1}$$

Latent class mediation

Idea: unobservable groups (latent classes) of components, sharing common characteristics

$$
\begin{aligned}
y_i &\sim N(\delta_i, s_i^2) \\
\delta_i &\sim N(\theta_Y - \theta_X, \tau^2) \\
d_k &\sim N(m_{D_C}, \tau_k^2)
\end{aligned}
$$

with component $k \in D_C$ with C classes to infer, and τ_k^2 within-class variance



Applications:

- ▷ Simulated networks of complex interventions
- ▷ Network of coronary heart psychological interventions

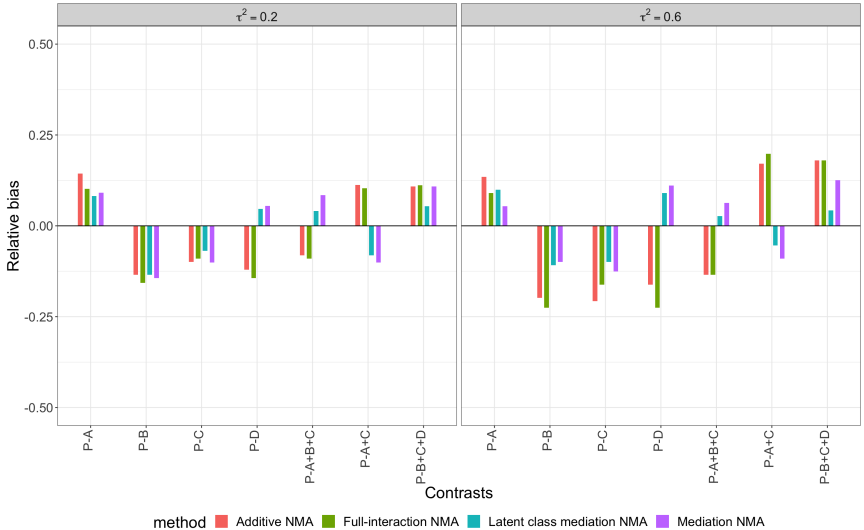
Small simulation study

Simulated data:

1. two-arm studies only, fairly connected networks
2. five interventions (A,B,C,D,P); three combinations (A+B+C, A+C, B+C+D)
3. $\tau^2 \in \{0.2, 0.6\}$
4. 1,000 data sets generated

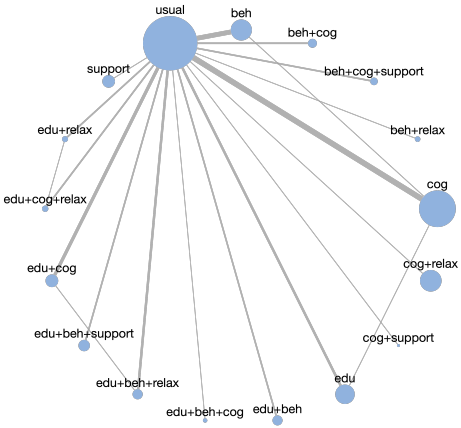
- models: mediation model, latent class mediation, additive, full interaction model
- Bayesian framework: non-informative priors, 50,000 iterations (10,000 burn-in)

Simulation results



Motivating example: Coronary heart psychological interventions

Welton et al. (2009)



- 36 studies
- 17 active interventions
- outcome: all-cause mortality

components:

edu – educational
relax – relaxation
support – support
beh – behavioural
cog – cognitive

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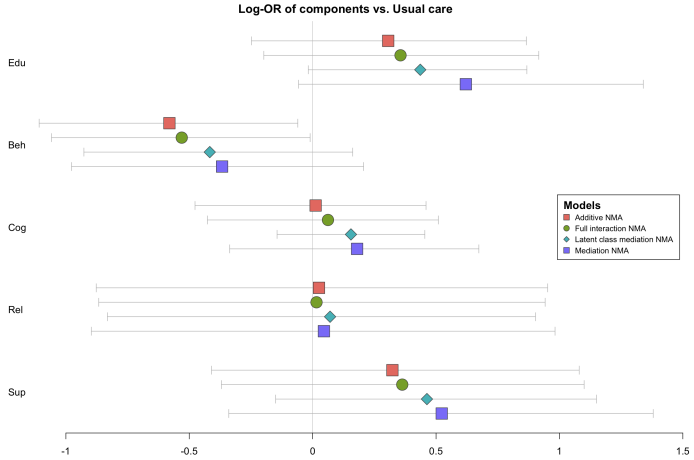

Final Remarks

Conclusions:

- complex interventions are hard to synthesise
- our approach tackles how components interact, accounting for heterogeneity
- results suggest pathway analysis seems suitable

Future directions:

- give structure in the priors for the relative effects of complex interventions
- IPD data would help to better explain heterogeneity

Some references

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