Identifying Effective Components of Complex Interventions: Component Network Meta-Analysis (I)

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Cochrane Webinar, 22nd April 2020

Outline

- Two-part talk: (I) concepts and (II) methods
- Concepts:
  - What are complex interventions?
  - Complexity and evidence synthesis
  - Intervention level network meta-analysis
  - What are components and why focus on them?

Outline

- Two-part talk: (I) concepts and (II) methods
- Methods:
  - Component Network Meta-Analysis Models
    - Common effect ("lumped" MA)
    - Additive component effects
    - Two-way interaction models
    - Full interaction models ("split" NMA)
  - Illustrative examples

What are complex interventions?

- Cochrane handbook (Ch17) refers to “intervention complexity”, rather than “complex intervention”
  i. the number of components in the intervention;
  ii. interactions between intervention components and/or interactions between the intervention and its context; and
  iii. the wider system within which the intervention is introduced.

MRC definition of complexity (interventions)

- A number of interacting components within the experimental and control interventions,
- A number and difficulty of behaviours required by those delivering or receiving the intervention,
- A number of groups or organisational levels targeted by the intervention,
- A number and variability of outcomes,
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Craig et al 2008, BMJ; 337 doi: https://doi.org/10.1136/bmj.a1655

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Intervention complexity and evidence synthesis

- Systematic review of well-conducted RCTs provides *highest quality* evidence for evaluating intervention effectiveness
- Three (main) options for synthesis are
  i. non-quantitative synthesis (tabulation, narrative, graphical approaches)
  ii. standard meta-analysis methods (pairwise, fixed, random effects with meta-regression)
  iii. complex synthesis methods (NMA, MPES, MVMA)

Higgins et al 2019, *BMJ Global Health* 2019;**4:**e000858

Case study: An illustrative dataset

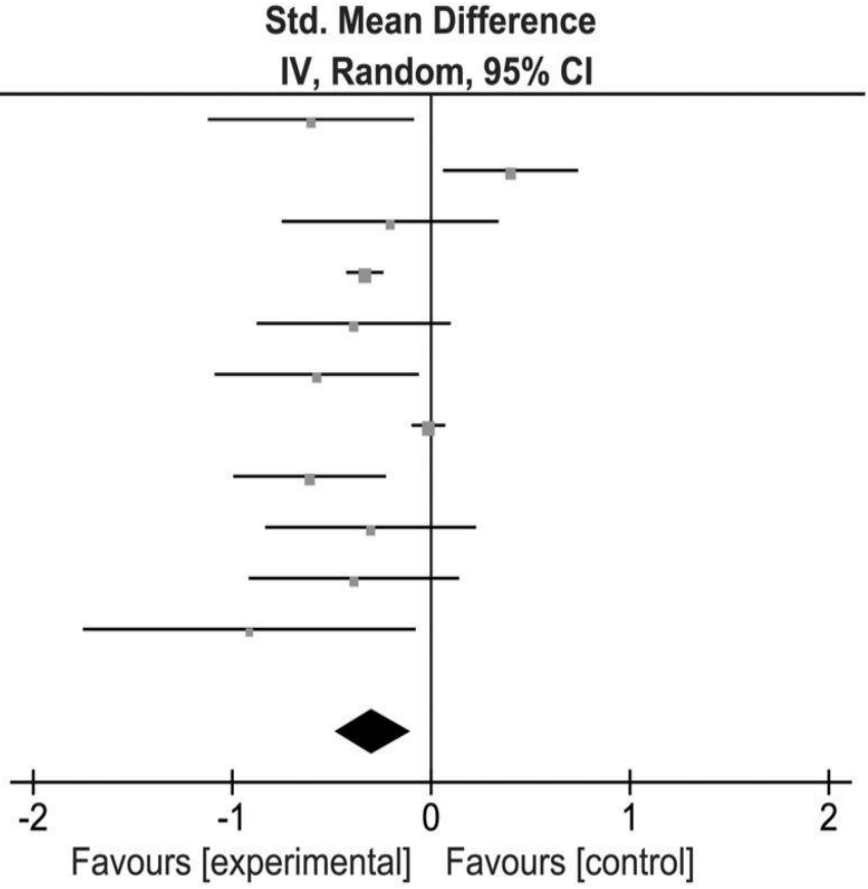
- Subset of studies from a 2004 Cochrane review examining psychological therapies for reducing depressive symptoms post-coronary heart disease.
  - inclusion criteria parallel group RCT, at least 6-months follow-up, and report at least one of the following outcomes: all cause mortality, cardiac mortality, non-fatal MI, total cholesterol, systolic or diastolic blood pressure, depression or anxiety
- Psychological intervention vs control (TAU)
- Depression symptoms, 11 studies

Pairwise, random-effects meta-analysis

Study or Subgroup	Std. Mean Difference IV, Random, 95% CI
Black	-0.60 [-1.12, -0.09]
Burgess	0.40 [0.06, 0.74]
Elderen	-0.21 [-0.75, 0.34]
ENRICHD	-0.33 [-0.43, -0.24]
HofmanBang	-0.39 [-0.88, 0.10]
Johnston	-0.57 [-1.09, -0.06]
Jones	-0.01 [-0.10, 0.07]
Lewin	-0.61 [-0.99, -0.23]
Stern	-0.30 [-0.83, 0.23]
Thompson	-0.39 [-0.92, 0.14]
Toobert	-0.91 [-1.75, -0.08]
Total (95% CI)	**-0.29 [-0.48, -0.10]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 50.32$, df = 10 ($P < 0.00001$); $I^2 = 80\%$

Test for overall effect: Z = 2.98 (P = 0.003)



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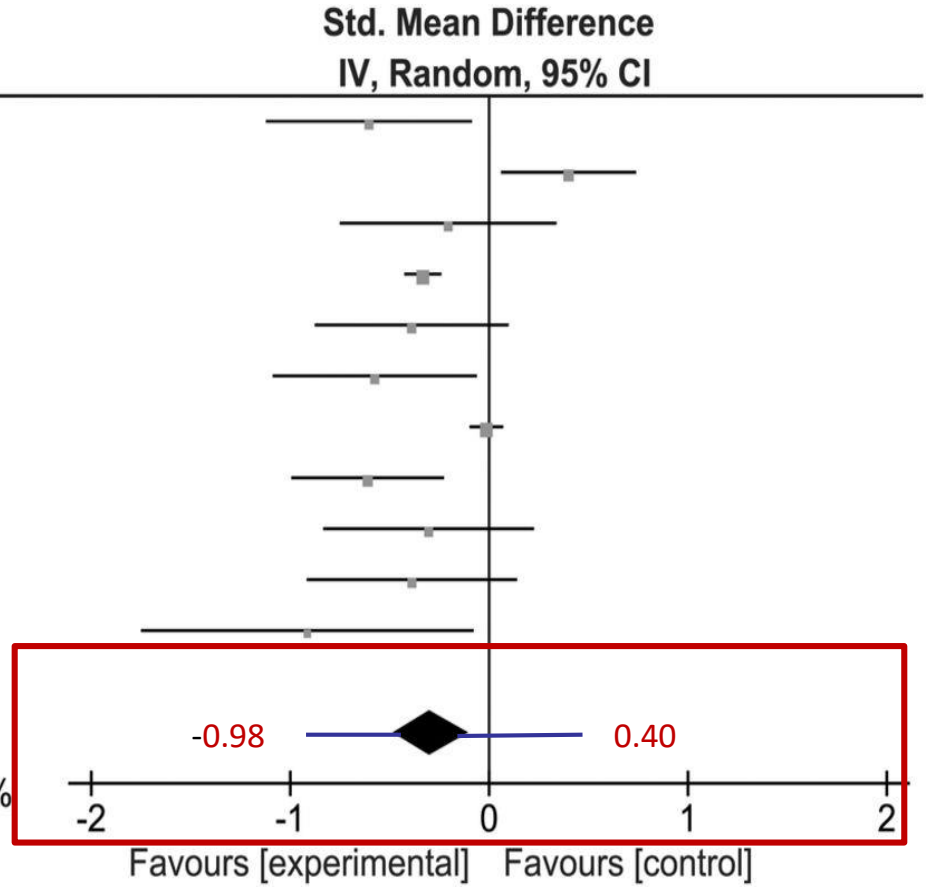
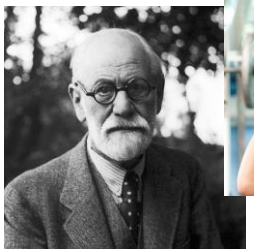
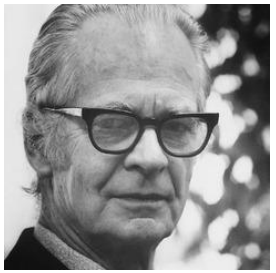
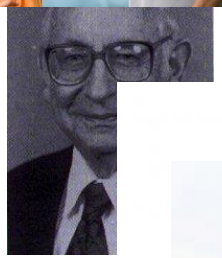
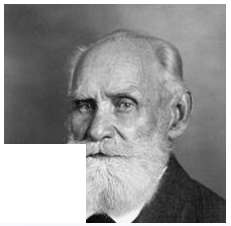
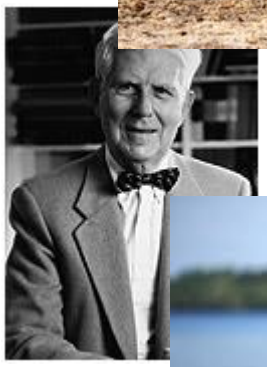


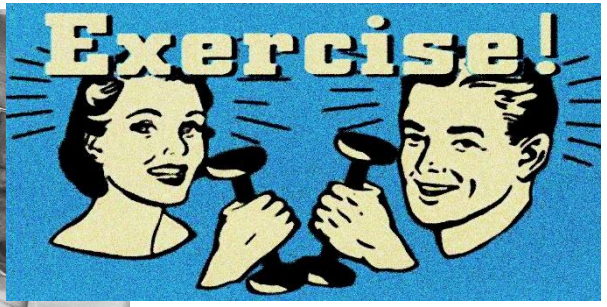





PSY

TAU


Complex interventions: lumping or splitting

- 'Lumping' of interventions can mask heterogeneity,
- 'In principle' research question such as "Do psychological therapies (as a whole), reduce depression after coronary heart disease?"
- What is the purpose of the review?
  - If is to investigate which type of psychological intervention is effective, or which intervention characteristics are effective, then 'splitting' may be the more appropriate approach

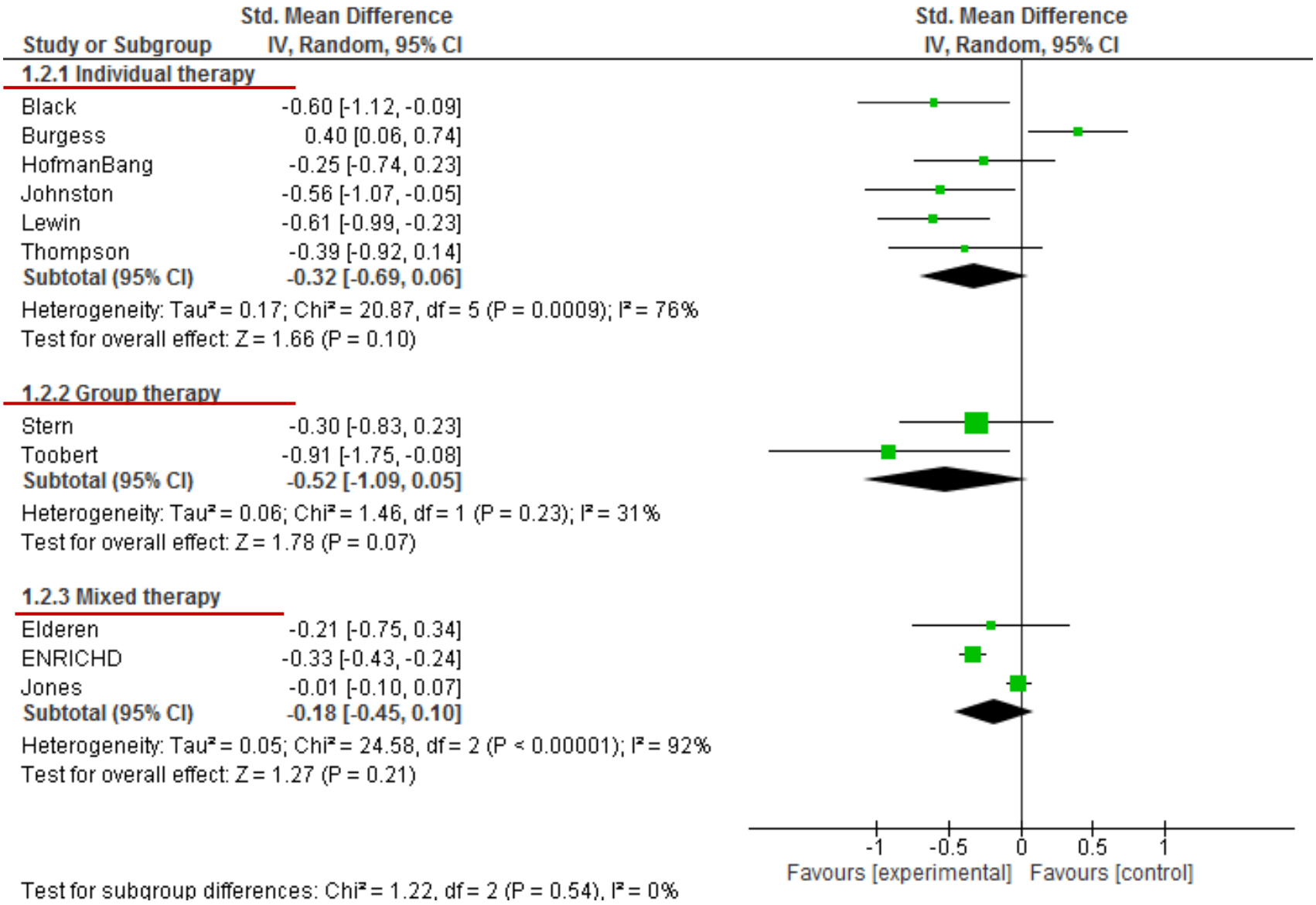
Subgroup analyses for exploring complexity

- Guise et al (2014) ways of grouping studies :
  - Key characteristics of interventions (e.g. group therapy, individual therapy, self-help)
  - Compare subclasses of intervention (mutually exclusive subgroups such as type of therapy – CBT, BT, counselling)
- Melendez-Torres (2015) “Clinically meaningful units”
  - by modality or similar theory of change

Guise et al, AHRQ; 2014. Report:14-EHC003-EF

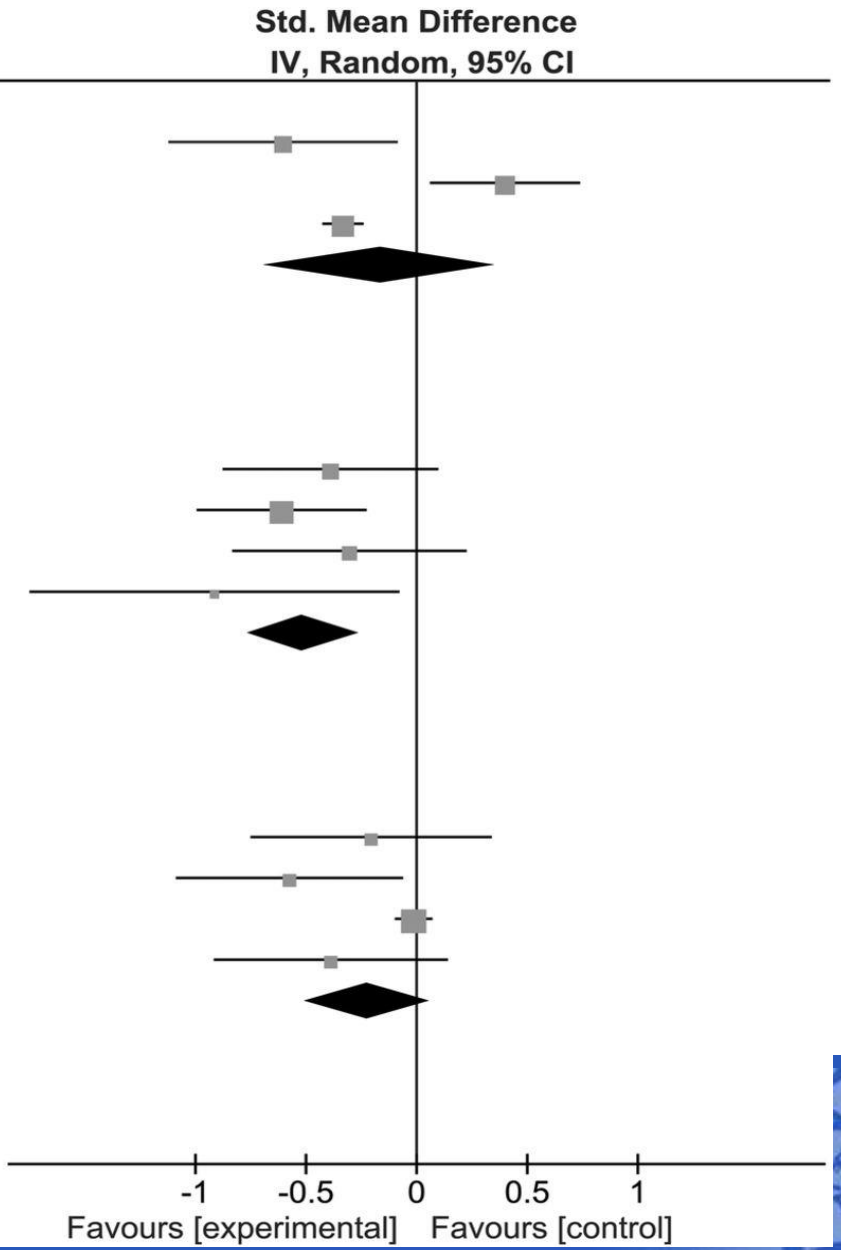
Melendez-Torres. 2015 *BMC Med Res Methodol* **15,** doi.org/10.1186/s12874-015-0040-z

Subgroup analysis (splitting - characteristic)

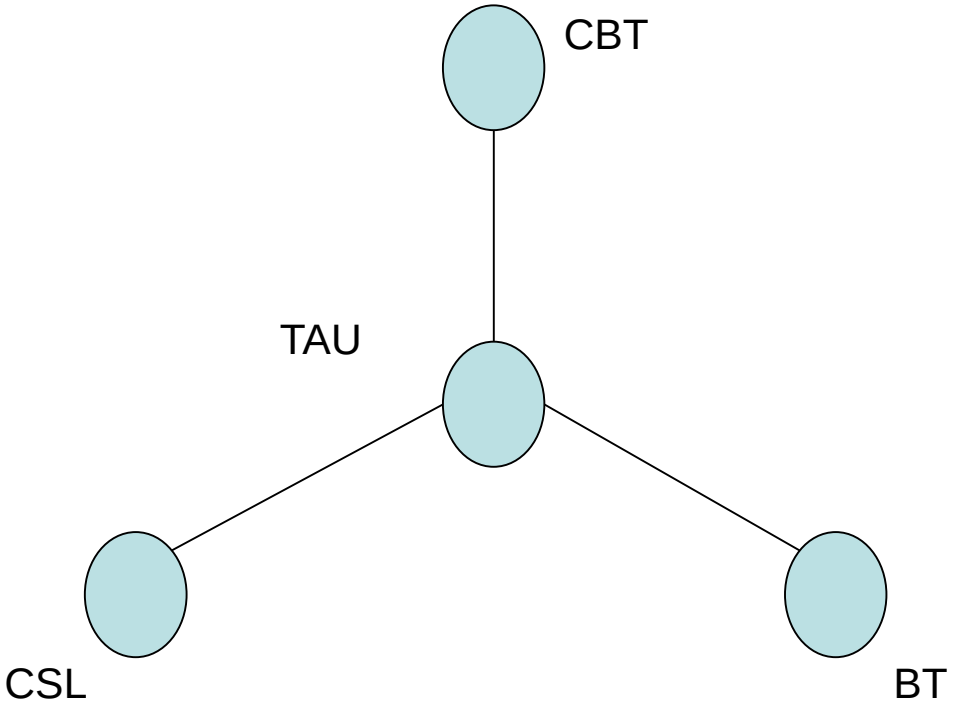


Subgroup analysis (intervention type)

Study or Subgroup	Std. Mean Difference IV, Random, 95% CI
3.1.1 Cognitive behavioural therapy	
Black	-0.60 [-1.12, -0.09]
Burgess	0.40 [0.06, 0.74]
ENRICHD	-0.33 [-0.43, -0.24]
Subtotal (95% CI)	**-0.16 [-0.69, 0.36]**
Heterogeneity: Tau² = 0.18; Chi² = 18.06, df = 2 (P = 0.0001); I² = 89%	
Test for overall effect: Z = 0.62 (P = 0.54)	
3.1.2 Behavioural therapy	
HofmanBang	-0.39 [-0.88, 0.10]
Lewin	-0.61 [-0.99, -0.23]
Stern	-0.30 [-0.83, 0.23]
Toobert	-0.91 [-1.75, -0.08]
Subtotal (95% CI)	**-0.51 [-0.76, -0.26]**
Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 3 (P = 0.58); I² = 0%	
Test for overall effect: Z = 4.00 (P < 0.0001)	
3.1.3 Counselling	
Elderen	-0.21 [-0.75, 0.34]
Johnston	-0.57 [-1.09, -0.06]
Jones	-0.01 [-0.10, 0.07]
Thompson	-0.39 [-0.92, 0.14]
Subtotal (95% CI)	**-0.22 [-0.51, 0.07]**
Heterogeneity: Tau² = 0.05; Chi² = 6.55, df = 3 (P = 0.09); I² = 54%	
Test for overall effect: Z = 1.51 (P = 0.13)	



Intervention level network meta-analysis

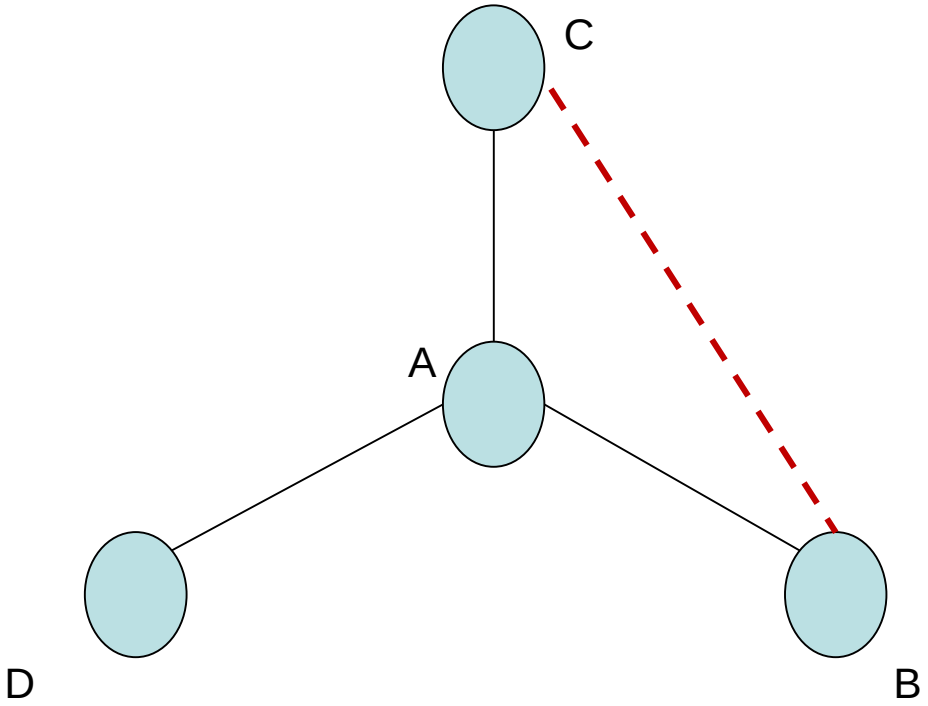


Allows more studies to be combined, as long as they connect to the network – evidence base is strengthened.

Greater potential to explore heterogeneity

Coherent relative effect estimates based on more evidence, potentially more robust and precise

Intervention level network meta-analysis



$$SMD_{BC}^{Ind} = SMD_{AC}^{Dir} - SMD_{AB}^{Dir}$$

NMA of psychological interventions for CHD

Comparison	SMD	95% CrIs
BT vs TAU	-0.54	(-1.01 to -0.07)
CBT vs TAU	-0.17	(-0.66 to 0.32)
CSL vs TAU	-0.26	(-0.72 to 0.17)
CBT vs BT	0.37	(-0.33 to 1.06)
CSL vs BT	0.28	(-0.39 to 0.93)
CSL vs CBT	-0.09	(-0.78 to 0.56)

BT is ranked 1st (95% CrIs: 1st to 3rd)
CBT is ranked 2nd (95% CrIs: 1st to 4th)
Counselling is ranked 3rd (95% CrIs: 1st to 4th)

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- A number and variability of outcomes,
- A degree of flexibility or tailoring of the intervention permitted.

What are intervention components?

- Complex interventions often considered greater than the sum of their parts.
- Components are defined as the active ingredients, processes, intervention techniques or "*elements of an intervention that have the potential to causally influence outcomes*"
- "*Directly related to an intervention theory of change, which proposes the mechanisms by which an intervention works*"

Guise et al, AHRQ; 2014. Report:14-EHC003-EF.

Blase and Fixsen, US Department of Health and Human Services 2011

Why focus on intervention components in SRs?

- Can explain a source of ‘clinical’ heterogeneity
- To understand how an intervention works
- To identify core drivers of intervention effect
  - Which components are essential for effectiveness
- To allow decision makers to adapt interventions without compromising effectiveness
- To optimize interventions for future studies.

Framework for evaluating components in NMA

- A component-based NMA approach likened to a factorial trial
- Akin to treating the network of evidence as a set of 'dismantling trials' comparing different combinations of components against each other (Melendez-Torres 2015)
- Nicky will discuss the approaches to modelling

Melendez-Torres. 2015 *BMC Med Res Methodol* **15,** doi.org/10.1186/s12874-015-0040-z

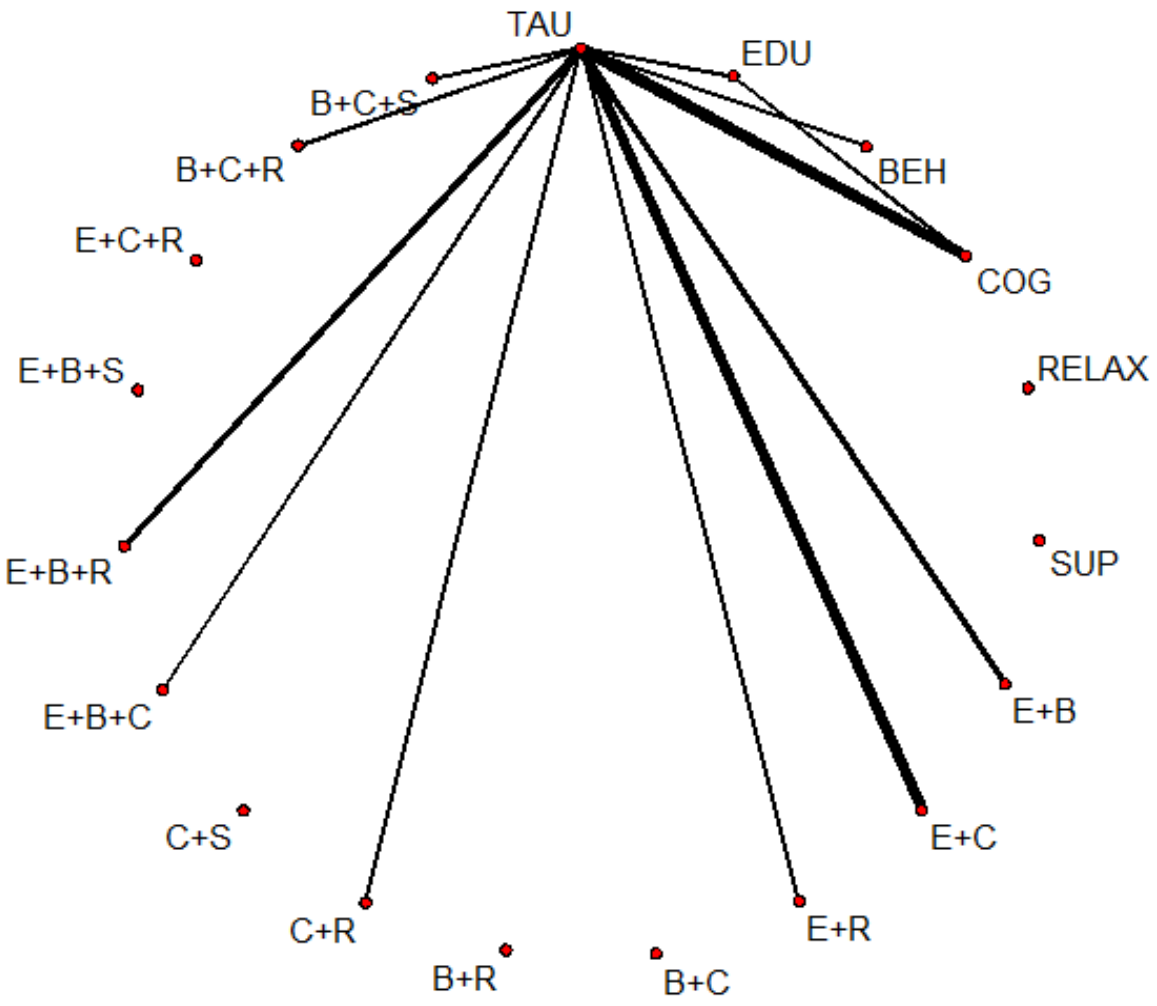
Approaches to component identification

1. Inductive & iterative classification; coding of published papers
   - Intervention component classification (Sutcliffe et al, 2015)
   - Constant comparative method (Hetrick et al, 2015)
2. Review of entire subject literature to develop a taxonomy, typically with Delphi consensus
   - E.g. Taxonomy of behaviour change interventions (Michie 2013)
3. Automated approaches: AI and machine learning to extract information from intervention evaluation reports (Michie 2017)
4. Author contact: de Bruijn (2020) contacted authors with a list of active and control components.
   - 35% of experimental and 26% of comparator BCTs could be identified from published materials.

Case study: Component classification

- Interventions were classified into 5 groups: educational, behavioral, cognitive, relaxation, and psychosocial support.
  - Educational (EDU): educating patients about cardiovascular health risks and basic anatomy
  - Behavioral (BEH): change in domains relevant to coronary heart disease e.g., smoking cessation courses, physical exercise training, food preparation classes, and nutritional counseling sessions.
  - Cognitive (COG): restructuring patients' beliefs and perceptions re. health and coronary disease
  - Relaxation (REL) focused on training patients in different relaxation techniques, such as yoga and breathing courses.
  - psychosocial support (SUP) interventions included attempts to bring patients together to encourage practical and/or emotional support.

Network plot: component combinations



TAU/T: treatment as usual
EDU/E: educational
BEH/B: behavioural
COG/C: cognitive
RELAX/R: relaxation
SUP/S, support.

+ indicates a combination of components, e.g. 'E+B' is educational and behavioural components.

Limitations of approach

- Networks may be sparse or not connected
  - Can only estimate effects between specific combinations that are connected in the network of evidence
  - Estimates of effect, may be imprecise
- Interventions are not only source of complexity
  - Interaction of intervention with setting should be considered.
- Methods of identifying and specifying components requires more research
  - Currently a balance between sufficiently specific for policy impact and sufficiently general for meaningful analysis
  - Reporting of complex interventions e.g. TiDier should improve field

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