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A novel method for modelling interactions between the components of complex interventions in networks of randomised trials

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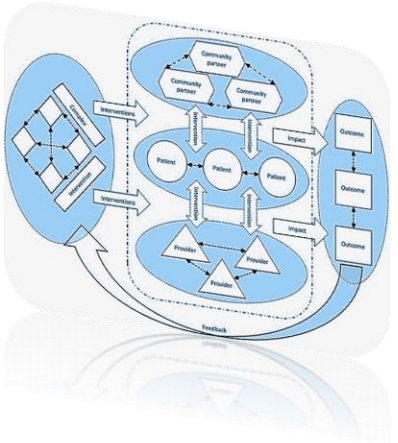
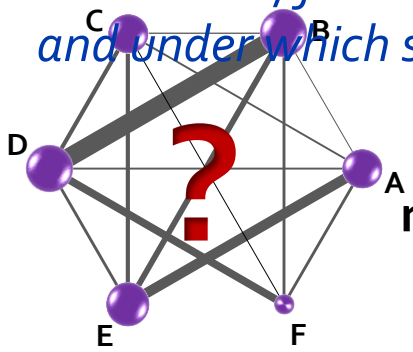
"I have no actual or potential conflict of interest in relation to this presentation"



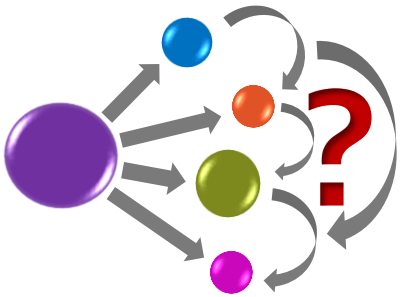
Background

"which are the most appropriate treatments, for which population and under which setting"

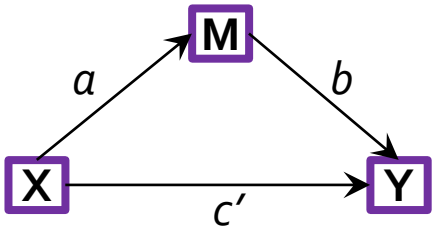


Network meta-analysis

Complex interventions



Mediation analysis



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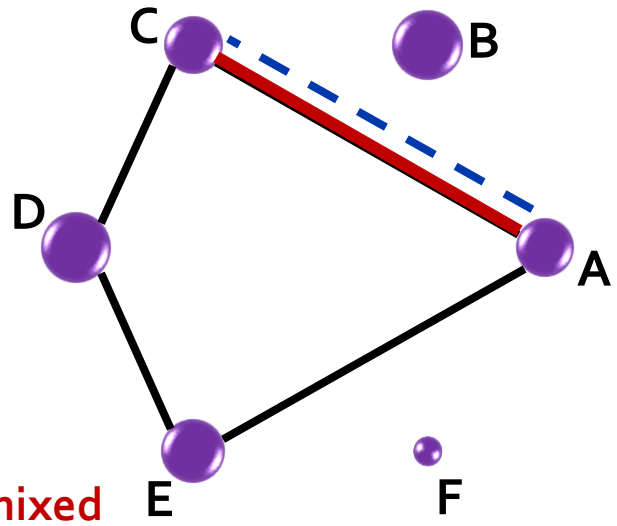

direct evidence + **indirect evidence** → **mixed evidence**

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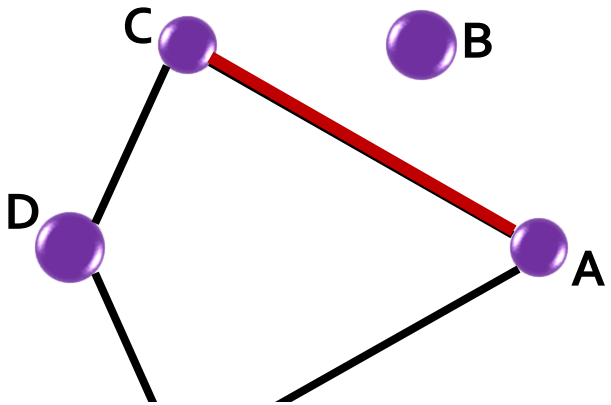

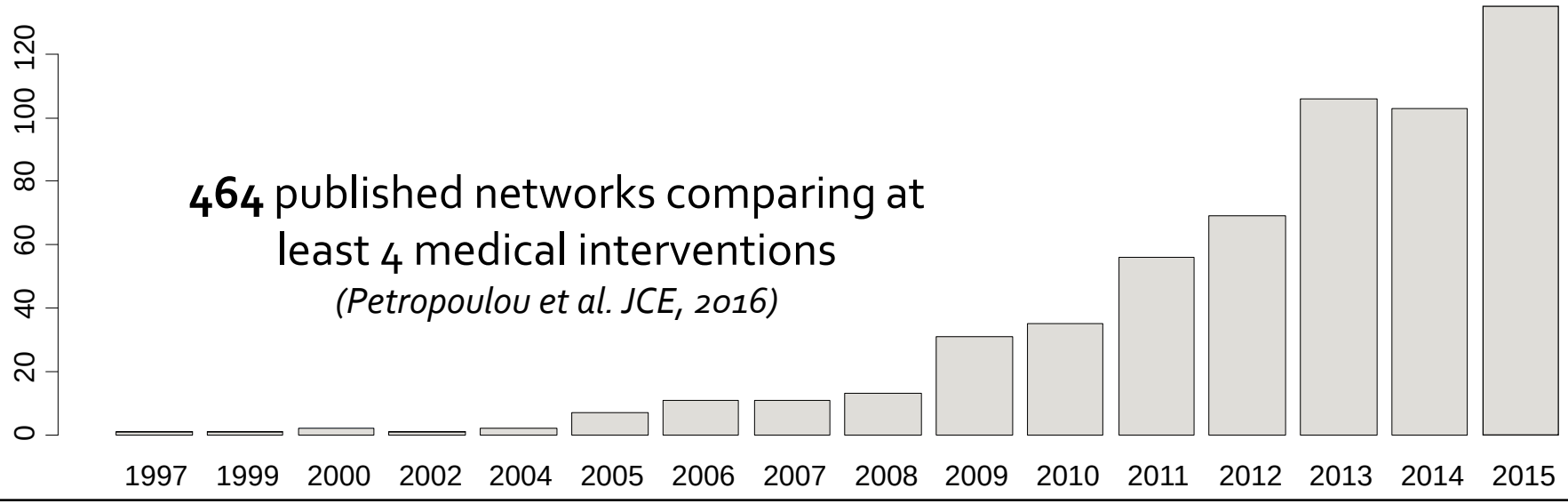

464 published networks comparing at least 4 medical interventions

(Petropoulou et al. JCE, 2016)

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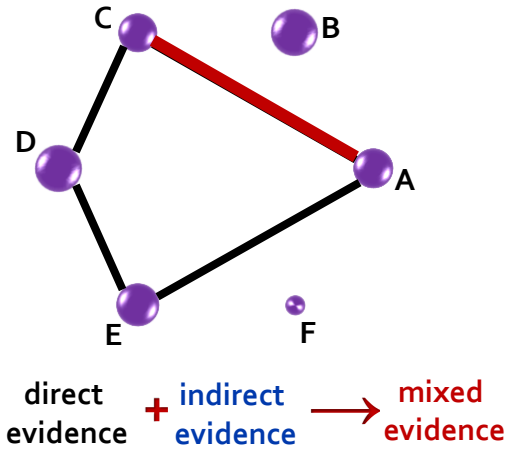
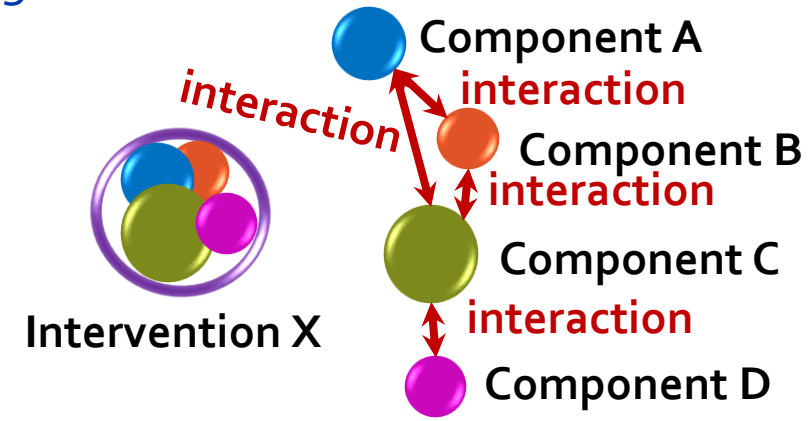


interventions consisting of multiple interactive components



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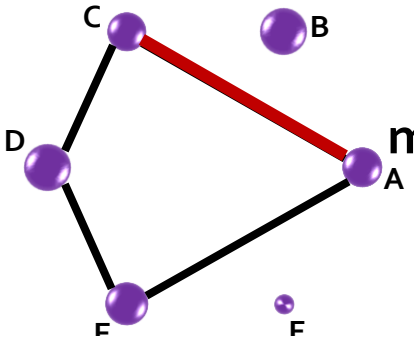

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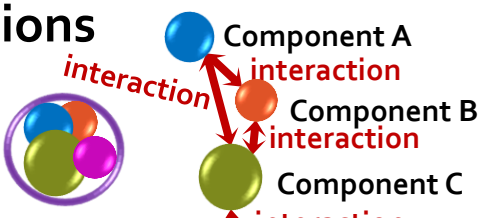
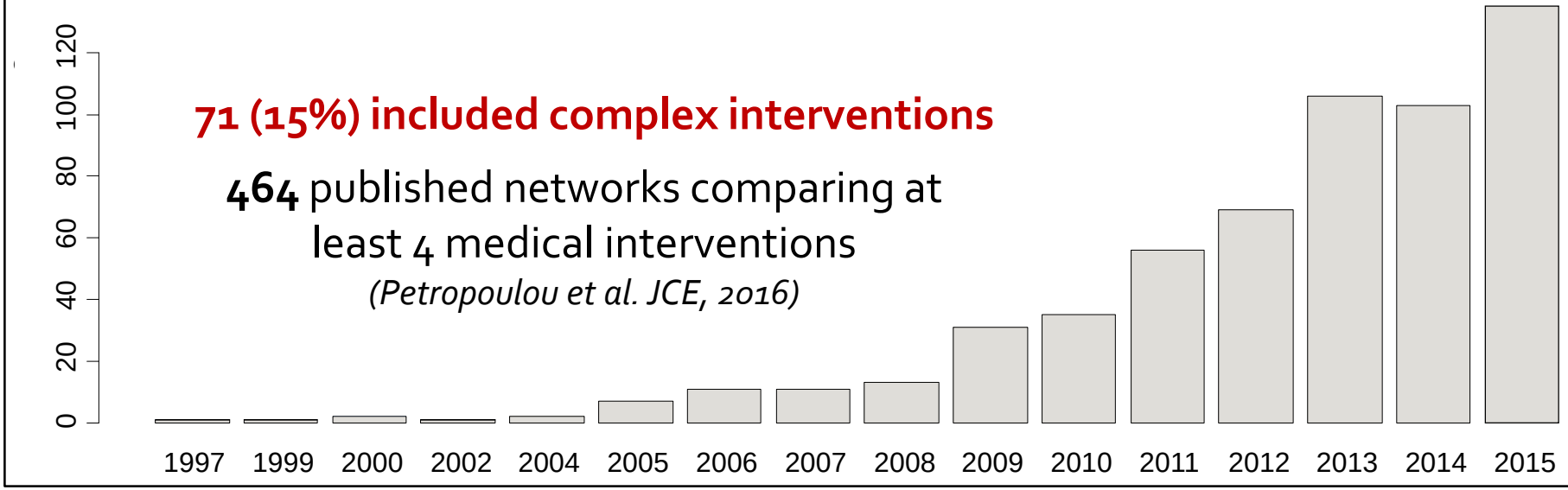
Complex interventions



71 (15%) included complex interventions

464 published networks comparing at least 4 medical interventions

(Petropoulou et al. JCE, 2016)



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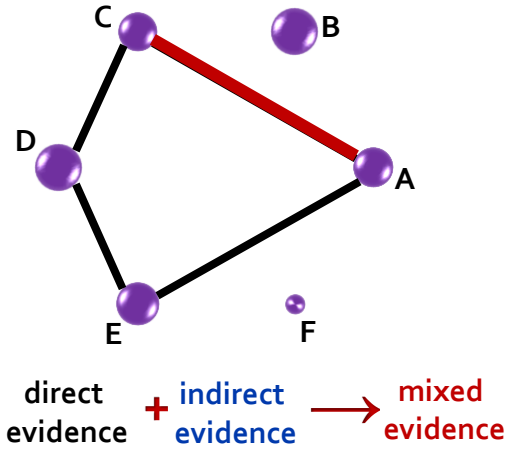
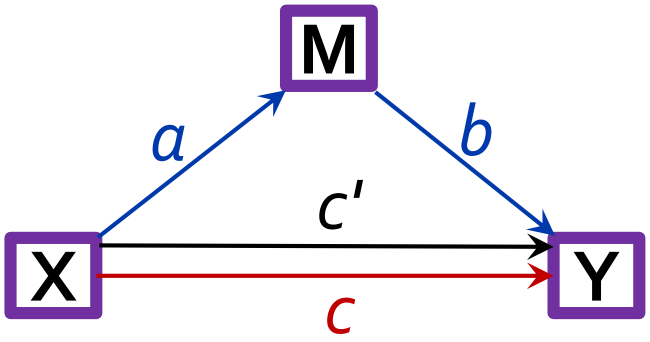
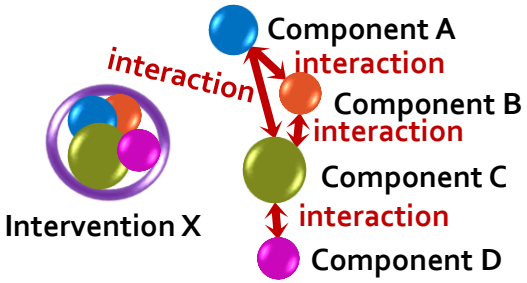




Mediation analysis

interventions consisting of multiple interactive components



factor X influences the intermediate factor M, which in turn influences the outcome Y

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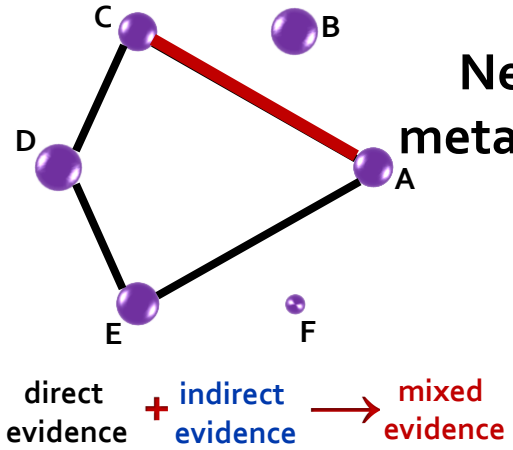
interventions consisting of multiple interactive components



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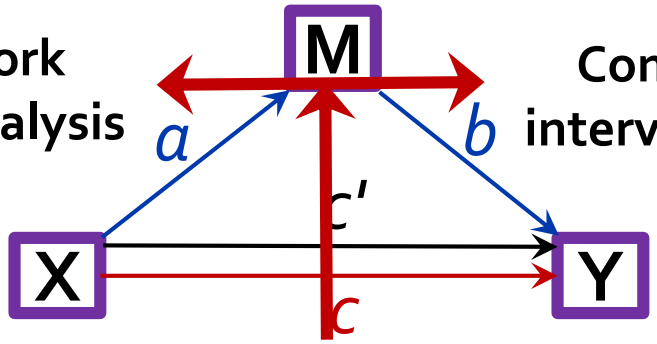
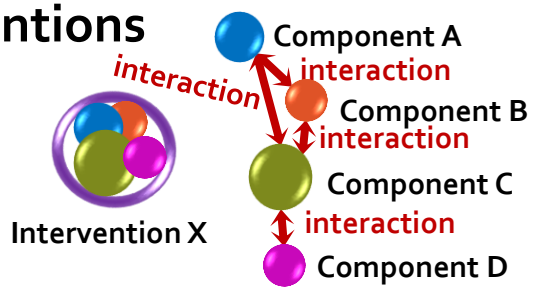


Mediation analysis

Complex interventions



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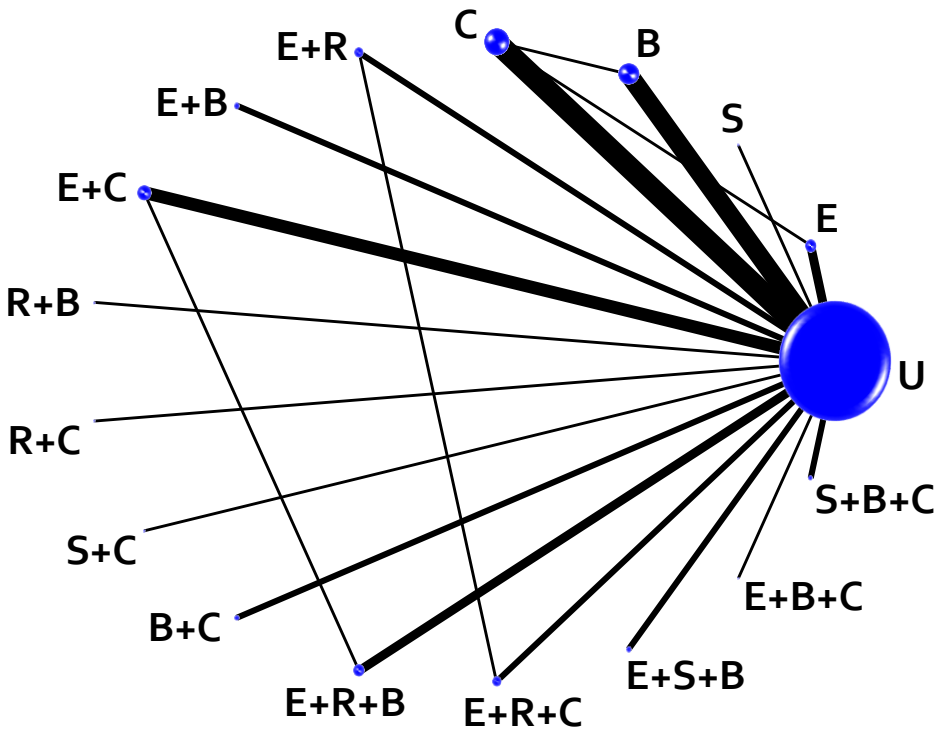
Example



psychological interventions in coronary heart disease

- ✓ 36 studies
- ✓ 17 different active interventions compared with usual care (U)
- ✓ Outcome: all-cause mortality
- ✓ Components:
  1. Educational (E)
  2. Relaxation (R)
  3. Support (S)
  4. Behavioural (B)
  5. Cognitive (C)

Welton et al. Mixed treatment comparison meta-analysis of complex interventions: psychological interventions in coronary heart disease, AJE 2009

Conceptual model

Key assumption

In studies combining two or more components there is a pathway leading from one component to the outcome via the other components

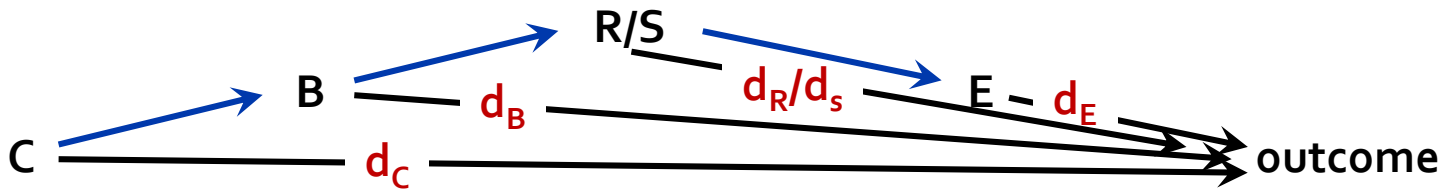
Control arm

All studies have usual care (U) as the control intervention

U ⟶ outcome

Active arms

Effect of 'stronger' components is mediated from the incorporation of 'weaker' components:



Conceptual model

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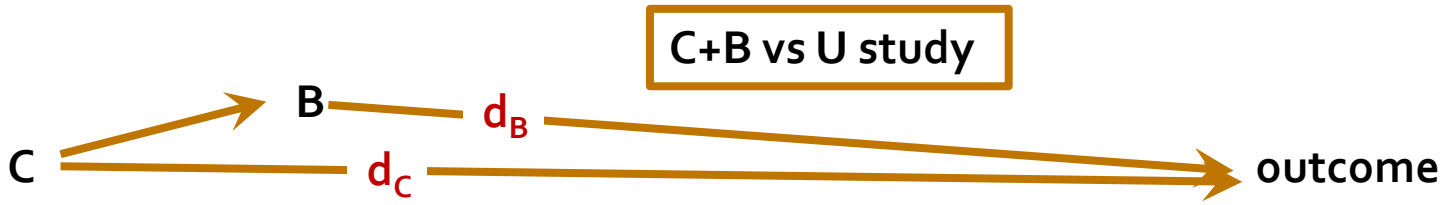
$$d_{C+B} = d_C + \beta_1 * d'_{C+B}$$
$$d'_{C+B} = d_B + \beta_2 * d_C$$

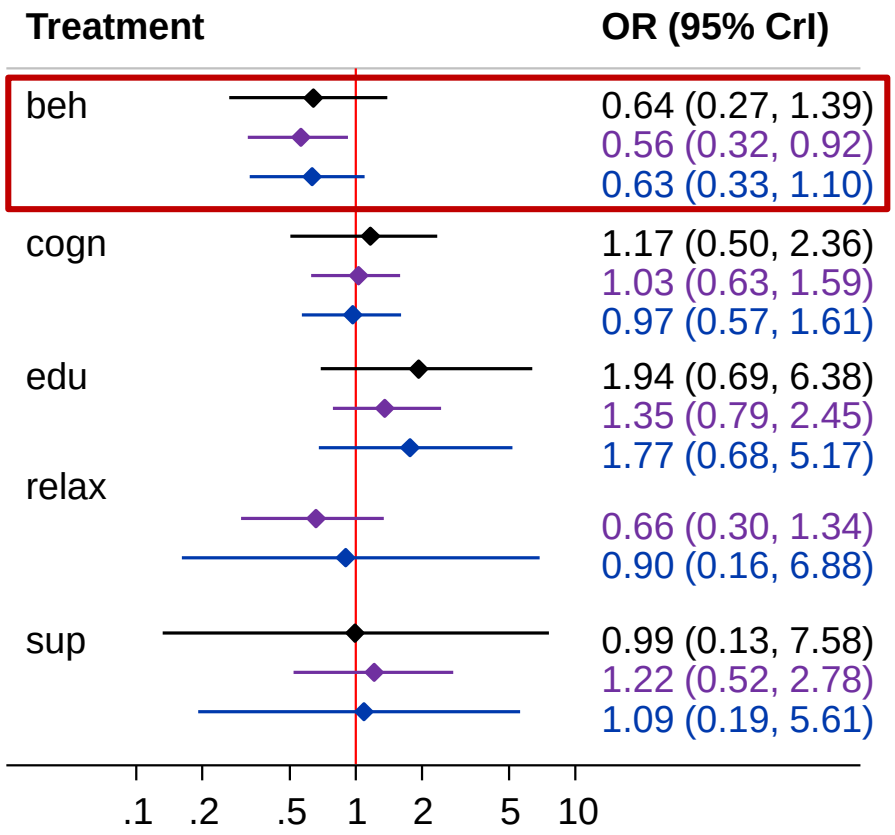
The additive model $d_{C+B} = d_C + d_B$ *is a special case of this model when* $\beta_1 = 1, \beta_2 = 0$

Effect of 'stronger' components is mediated from the incorporation of 'weaker' components:



Results

Active interventions against placebo



standard NMA model
additive NMA model
mediation NMA model

Results

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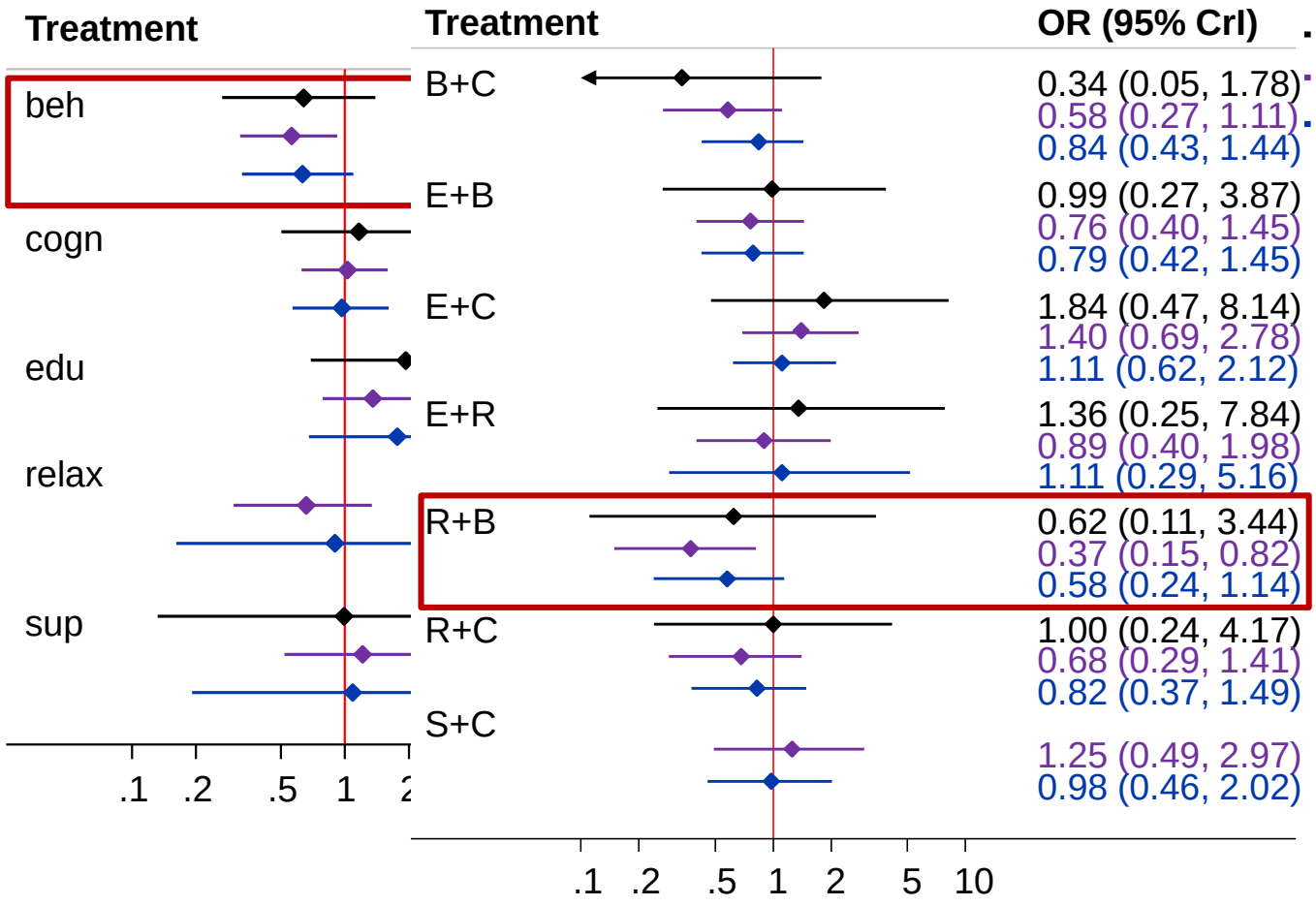

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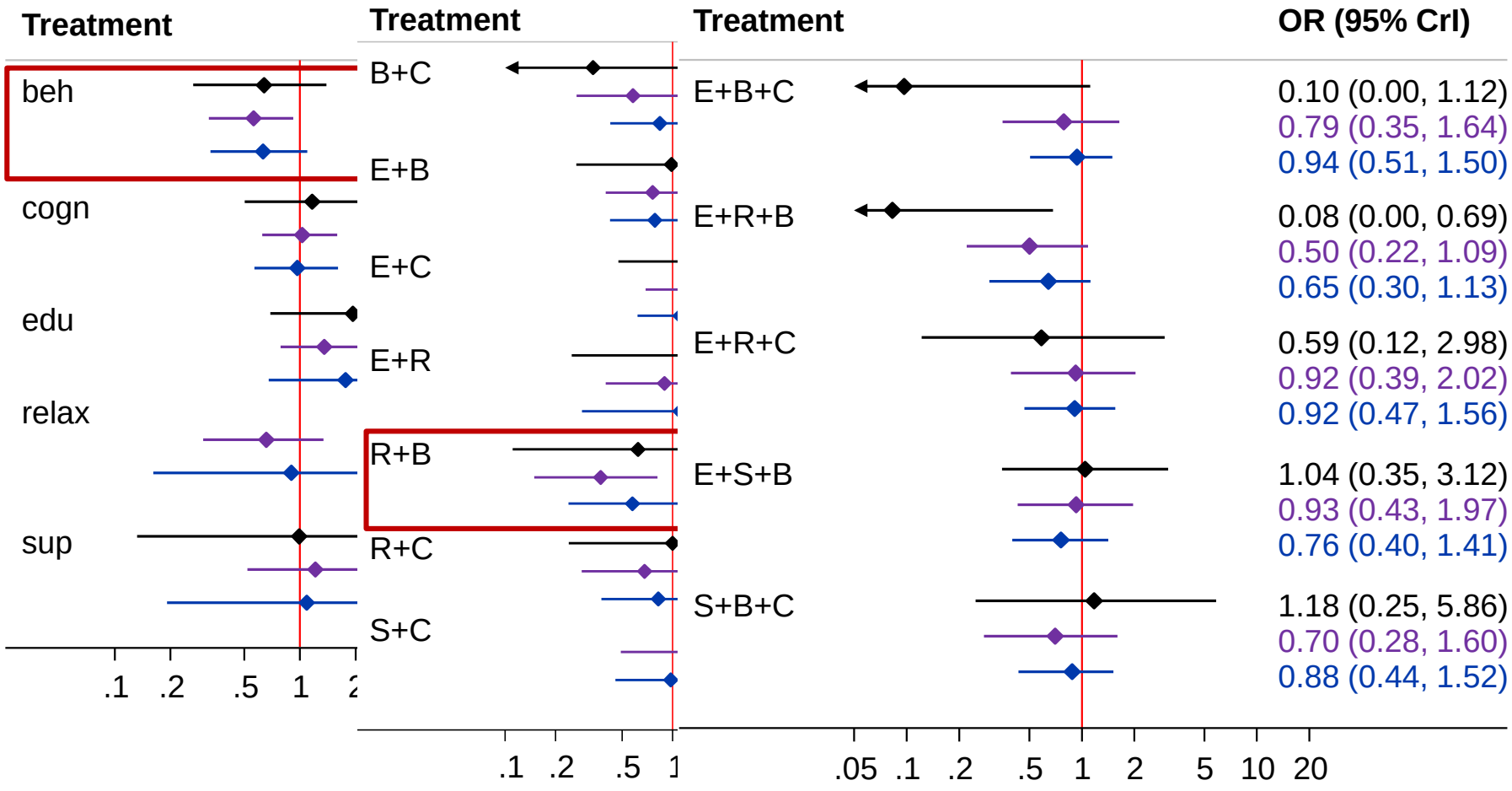

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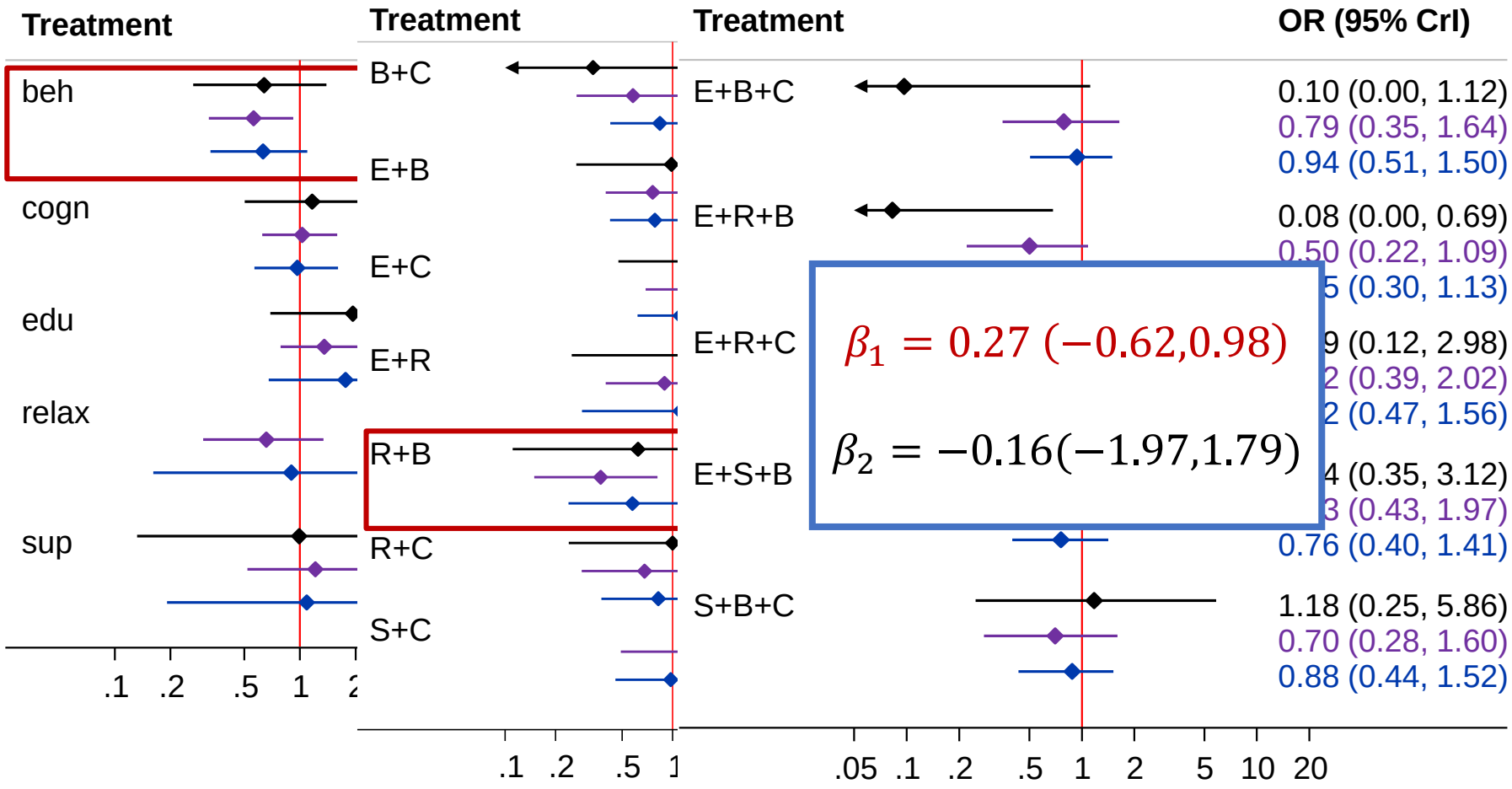

Discussion

- ✓ Applications of network meta-analysis surge in medical literature
- ✓ Complex interventions are frequently encountered in networks of randomised trials
- ✓ The suggested approach for disentangling the effects of components targets at two questions: a) which components work and b) how do they work
- ✓ Finding a reasonable pathway across components is often challenging
- ✓ Clinical input from experts in the field is always necessary