COMPONENT NETWORK META-ANALYSIS

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OUTLINE

- What is component network meta-analysis
- Additive vs Interaction Models
- Assumption check
- Strengths and Weaknesses
- Conclusion

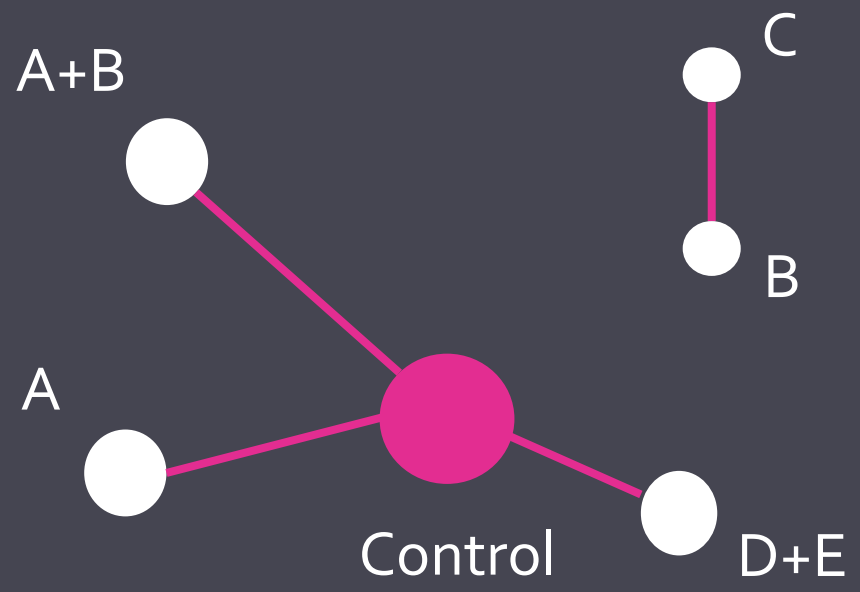
WHAT IS CNMA

Network meta-analysis

- Compare multiple interventions (direct- indirect evidence)
- Estimating (whole) intervention effect

Component network meta-analysis

- Complex intervention (multiple active parts)
- Estimating (each) component effect



Want to know

Effect of B alone?
Effect of C to control?
Effect of A+C?

MODELS

Additive and Interaction models

1) Additive model

No interaction

Sum of component AB = effect A + effect B

2) Interaction model

Sum of component AB = effect A + effect B + interaction AB (d_{AB})

Synergistic: $d_{AB} > 0$

Antagonistic: $d_{AB} < 0$

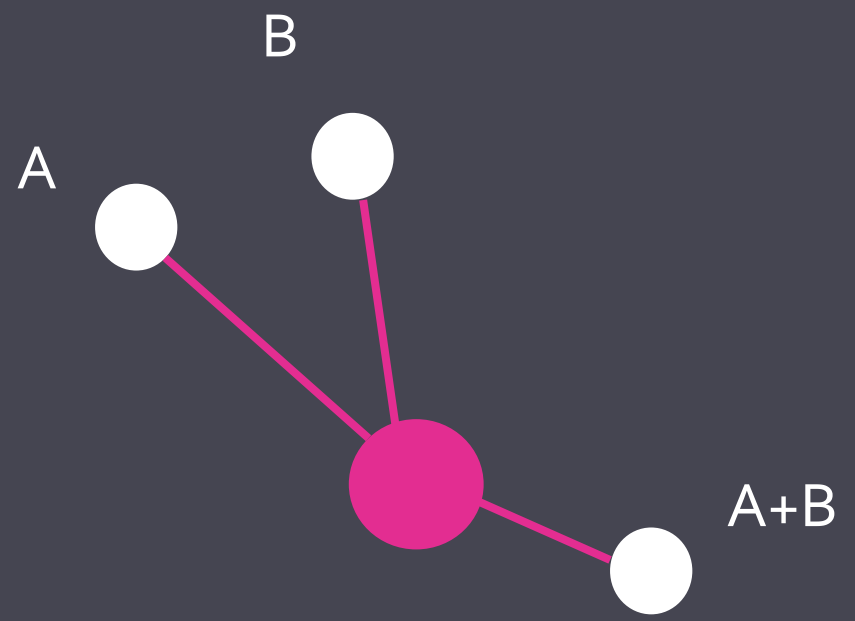
ASSUMPTION CHECKING

1. **Additivity Test**

- Compare the **Additive CNMA model** (assumes no interactions) vs **Standard NMA model**
  → No difference = additive model

- Cochran's Q statistic (variance explained by a model vs the residual variance unexplained)

- $p < 0.05$ → the additive model is *not* sufficient and significant interactions (synergy or antagonism) are likely present.



No diff between
Standard NMA & CNMA model

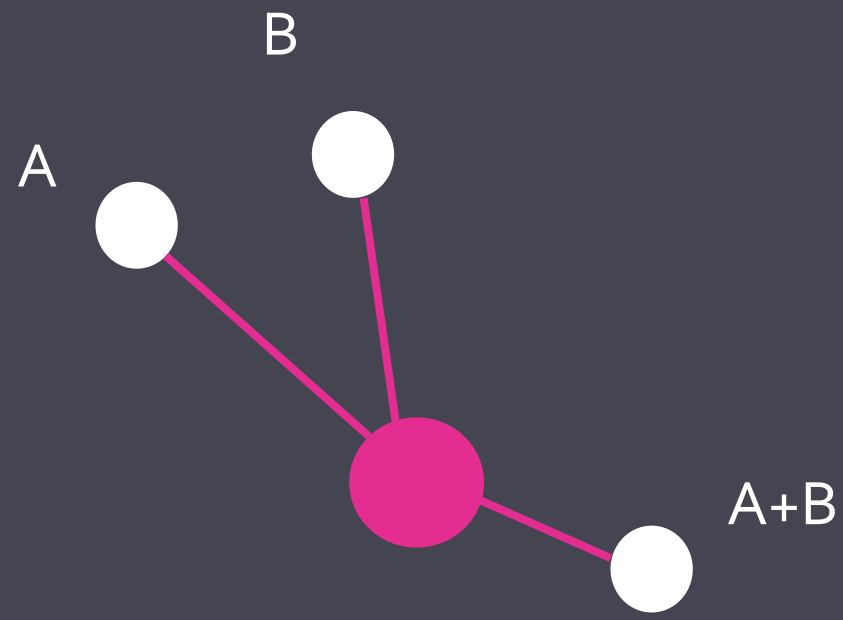
→ Additive model accepted

Model	Model statistics		Difference with Standard NMA			Difference with Additive model			Difference with previous nested model with lowest Q-statistic		
	Q-statistic	df	Q_{diff}	df_{diff}	p-$value_{diff}$*	Q_{diff}	df_{diff}	p-$value_{diff}$*	Q_{diff}	df_{diff}	p-$value_{diff}$*
Standard NMA	144.20	100									
Additive cNMA model	147.72	103	3.52	3	0.3182						
First-order interaction models											
1) exe*nut	144.69	102	0.49	2	0.7841	-3.03	1	0.0816			
2) exe*psy	147.64	102	3.44	2	0.1795	-0.08	1	0.7711			
3) exe*nut*psy	147.43	102	3.23	2	0.2931	-0.29	1	0.5882			
Second-order interaction models											
4) exe*nut + exe*psy	144.69	101	0.49	1	0.4839	-3.03	2	0.2193	0	1	1.0000
5) exe*nut + exe*nut*psy	144.24	101	0.04	1	0.8415	-3.48	2	0.1755	-0.45	1	0.5023
6) exe*psy + exe*nut*psy	147.41	101	3.21	1	0.0732	-0.31	2	0.8547	-0.02	1	0.8875
7) exe*nut + exe*psy + exe*nut*psy (i.e., full interaction model)	144.20	100	0	0	1.0000	-3.52	3	0.3182			

* Significance cut-offs: 1 df: p = 0.1573; 2 df: p = 0.1353; 3 df: p = 0.1116
df = degrees of freedom; diff = difference; NMA = network meta-analysis; Q = Cochrane's Q statistic
exe = exercise; nut = nutrition; psy = psychosocial

2. Interaction Model Selection

- Additive CNMA model + interaction term
- E_A+E_B + E_{AB} → Q_{diff} from additive CNMA
- Select model with $p < 0.05$ (lower Q statistic)



Sig diff between
Standard NMA & CNMA model

→ Additive model unlikely

Model	Model statistics		Difference with Standard NMA			Difference with Additive model			Difference with previous nested model with lowest Q		
	Q-value	df	Q_{diff}	df_{diff}	p-$value_{diff}$*	Q_{diff}	df_{diff}	p-$value_{diff}$*	Q_{diff}	df_{diff}	p-$value_{diff}$*
Standard NMA	670.64	112									
Additive cNMA model	685.21	115	14.56	3	0.0022						
First-order interaction models											
1) exe*nut	684.61	114	13.97	2	0.0009	-0.595	1	0.4403			
2) exe*psy	683.80	114	13.16	2	0.0014	-1.410	1	0.2350			
3) exe*nut*psy	679.01	114	8.37	2	0.0153	-6.203	1	0.0128			
Second-order interaction models											
4) exe*nut + exe*psy	683.80	113	13.16	1	0.0003	-1.410	2	0.4940	0	1	1.0000
5) exe*nut + exe*nut*psy	672.13	113	1.49	1	0.2222	-13.08	2	0.0014	-6.88	1	0.0087
6) exe*psy + exe*nut*psy	677.61	113	6.97	1	0.0083	-7.59	2	0.0224	-1.40	1	0.2367
7) exe*nut + exe*psy + exe*nut*psy (i.e., full interaction model)	670.64	112	0	0	1.0000	-14.56	3	0.0022			

* Significance cut-offs: 1 df: p = 0.1573; 2 df: p = 0.1353; 3 df: p = 0.1116
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Model selection

IF THE ADDITIVE ASSUMPTION MET

1) Subtraction rule

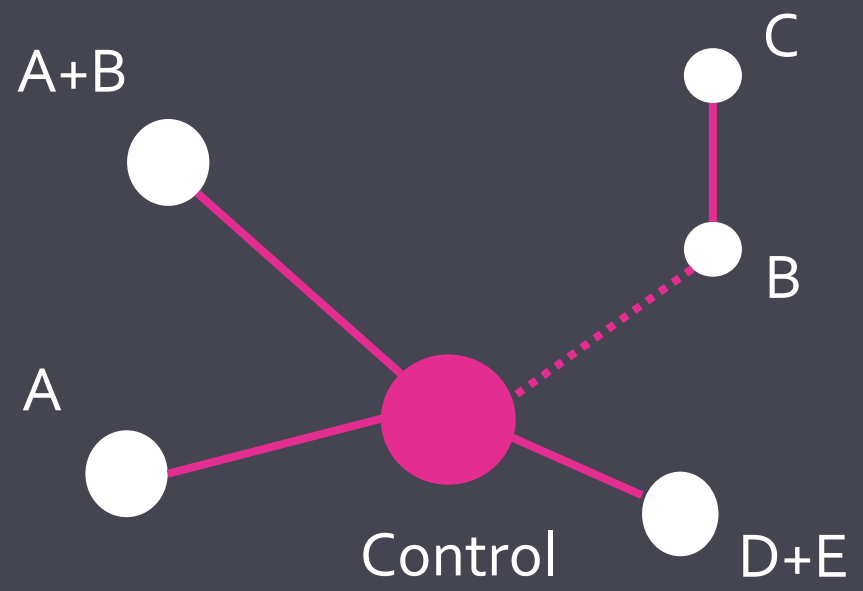
   want to know E_B: $E_B = E_{A+B} - E_A$

2) Network bridge

   want to know E_C: E_B as a bridge

3) Fused component

   Can't separate E_D vs E_E



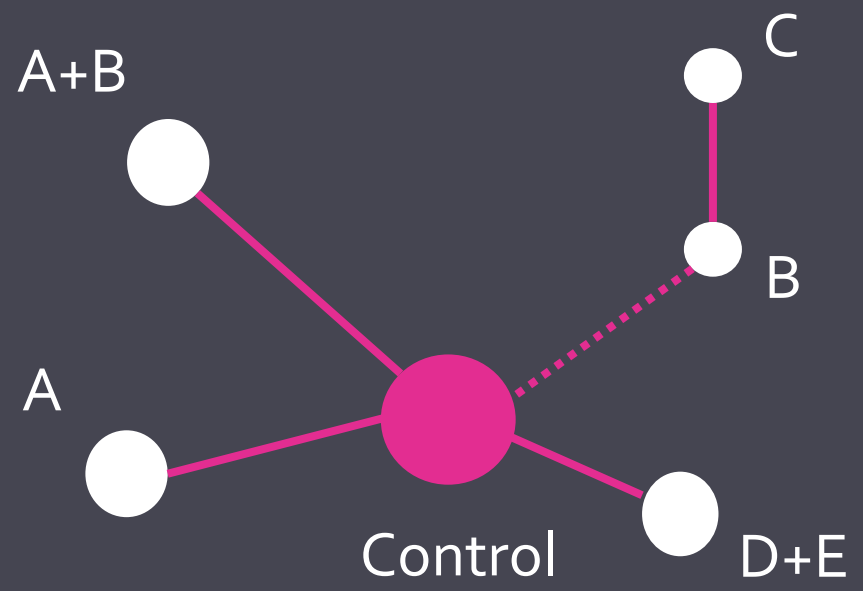
WHAT IS IT LOOKED LIKE

Results of the additive CNMA analysis suggest that exercise and nutrition components may reduce the odds of post-operative complications, while psychosocial components may increase the odds of complications.

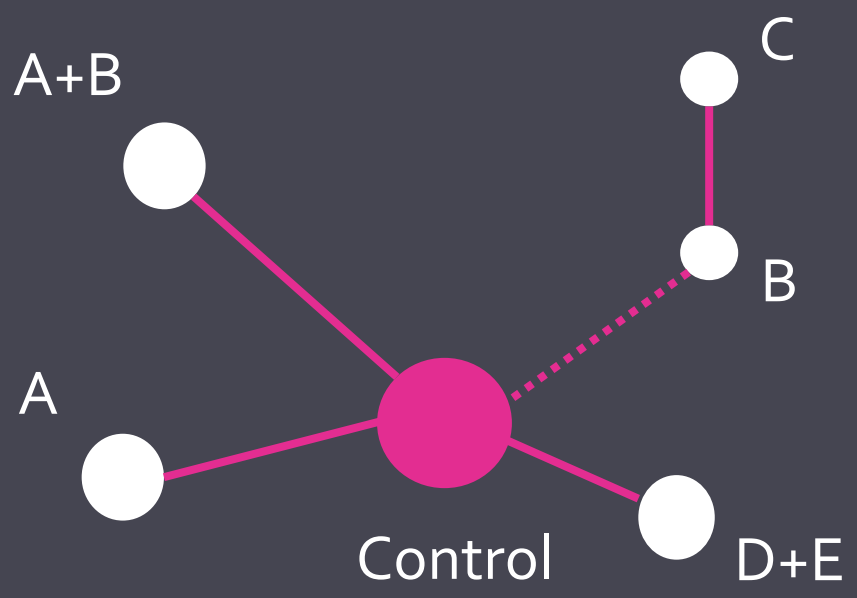
Component	OR (95% CI)
Exercise	0.53 (0.42 to 0.66)
Nutrition	0.66 (0.54 to 0.81)
Psychosocial	1.75 (1.17 to 2.61)
Cognitive	0.91 (0.43 to 1.92)

IF ADDITIVE ASSUMPTION IS NOT MET?

- Add interaction term
- $E_{A+B} = E_A + E_B + E_{A*B}$
- More complex model to analyze



STRENGTH VS WEAKNESS



Strength	Weakness
Deconstruct component effect	Need additive assumption
Network bridge → able to compare disconnected network	Definition of component: exercise, why not aerobic vs stretching
New possible combination	Heterogeneity of intervention: exercise from study 1 ≠ study 2

CONCLUSION

Reporting Item	Standard NMA	Component NMA (CNMA)
Intervention Description	Describe the "Nodes" (e.g., "Drug A + B").	Define the individual "Components"
Network Geometry	Network plot showing treatment combinations	Individual & combination treatment
Assumptions	Transitivity and Inconsistency	Additivity and model selection
Primary Results	Relative effects	Component Effects
Rankings	SUCRA	Rankings for components