Component Network Meta-Analysis

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COMPLEX REVIEWS SUPPORT UNIT

Recap: Pairwise Meta-Analysis & Network Meta-Analysis

Pairwise Meta-Analysis	Network Meta-Analysis
Two treatment options (i.e. Is 'treatment B' better than 'treatment A'?)	Can consider three or more treatment options for a condition (i.e. which treatment is 'best'?)
Can result in large between-study heterogeneity estimates if there is heterogeneity in treatment effects	Could reduce between-study heterogeneity if it is explained by heterogeneity in treatment effects
Can be performed with few studies	Requires at least as many studies as the number of treatments in the network
Requires 'Lumping' of treatments if there are more than two treatment options e.g. does any form of intervention reduce the outcome of interest?	Allows 'Splitting' of treatments if there are more than two treatment options e.g. which intervention reduces the outcome of interest?
	Requires a connected network

Example – Psychological Preparation

- Meta-analysis published in the Cochrane Database of Systematic Reviews identifying better postoperative outcomes (e.g. reduced length of stay in hospital, lower pain, reducing negative emotion) for patients who received any psychological preparation (strategies designed to influence thoughts, feelings or actions) compared to usual care

Cochrane Library

Cochrane Database of Systematic Reviews

Psychological preparation and postoperative outcomes for adults undergoing surgery under general anaesthesia (Review)

Powell R, Scott NW, Manyande A, Bruce J, Vögele C, Byrne-Davis LMT, Unsworth M, Osmer C, Johnston M

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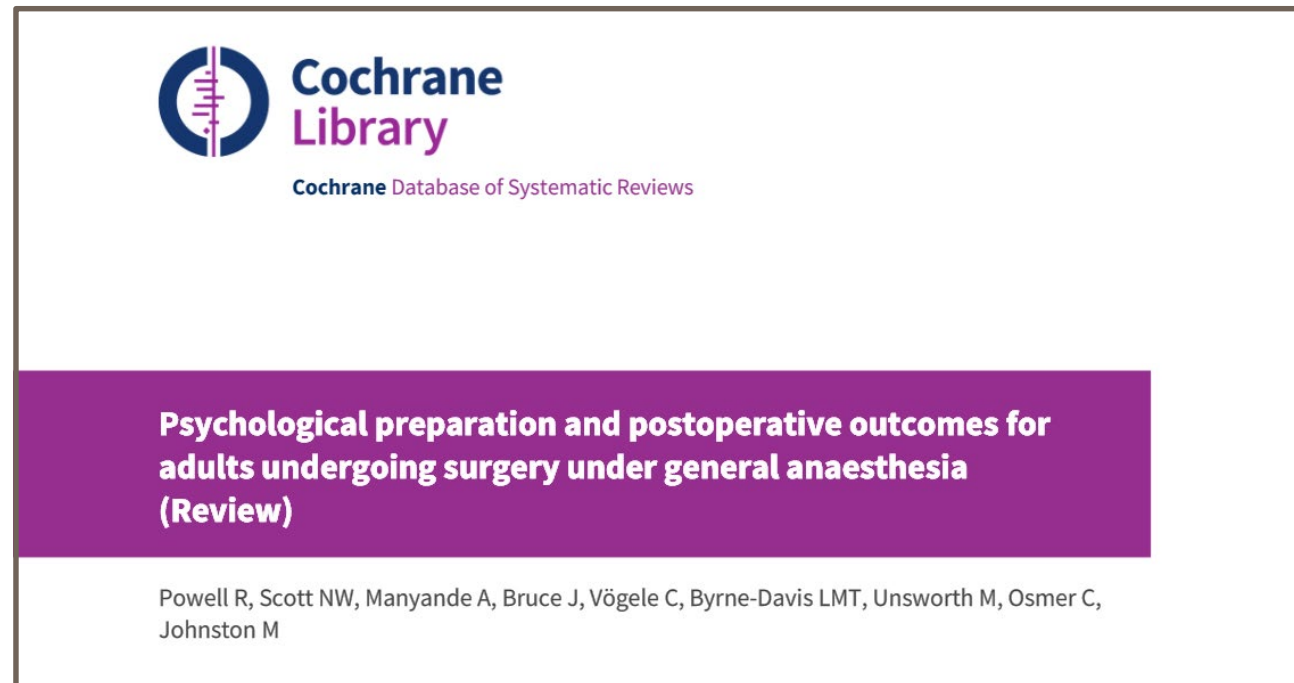
What is Psychological Preparation?

- Can be considered as the intervention received by patients prior to surgery to help prepare them for surgery and minimise length of stay, pain and negative affect

- Psychological preparation can consist of multiple components:
  - Procedural information (What, when and how events will occur)
  - Sensory information (What it will feel/smell like)
  - Behavioural instruction (Teaching patients actions to perform to enhance the experience)
  - Cognitive intervention (To change how an individual thinks)
  - Relaxation (including hypnosis)
  - Emotion-focused techniques (To help an individual manage their feelings)

What did they do in the Cochrane review?

- All components of psychological preparation were combined into one treatment arm and compared to control (despite most components being given in combination with other components)
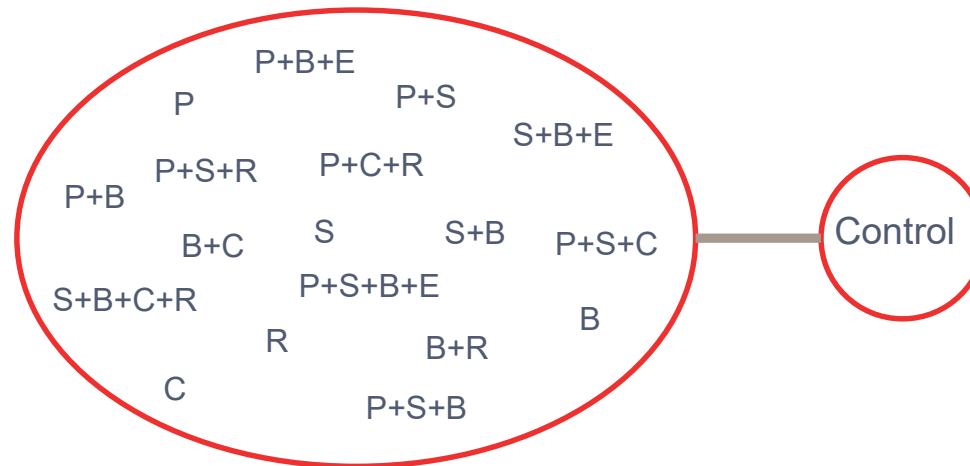
P = procedural information, S = sensory information, B = behavioural instruction, C = cognitive intervention, R = relaxation techniques, E = emotion-focused intervention

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Any Intervention ——————— No Intervention

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Assumptions in the Cochrane review

Wanted to answer the question:

"What is the effect of psychological preparation on postoperative outcomes in adults undergoing elective surgery under general anaesthetic?"

Any Intervention —— No Intervention

Assumptions:

- The effect of each component of intervention is the same

- The effect of a single component is the same as a combination of components

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Network Meta-Analysis

- Estimate effect size for all unique combinations of components

P=Procedural information, S=Sensory information, B=Behavioural instruction, C=Cognitive intervention, R=Relaxation, E=Emotion-focused techniques

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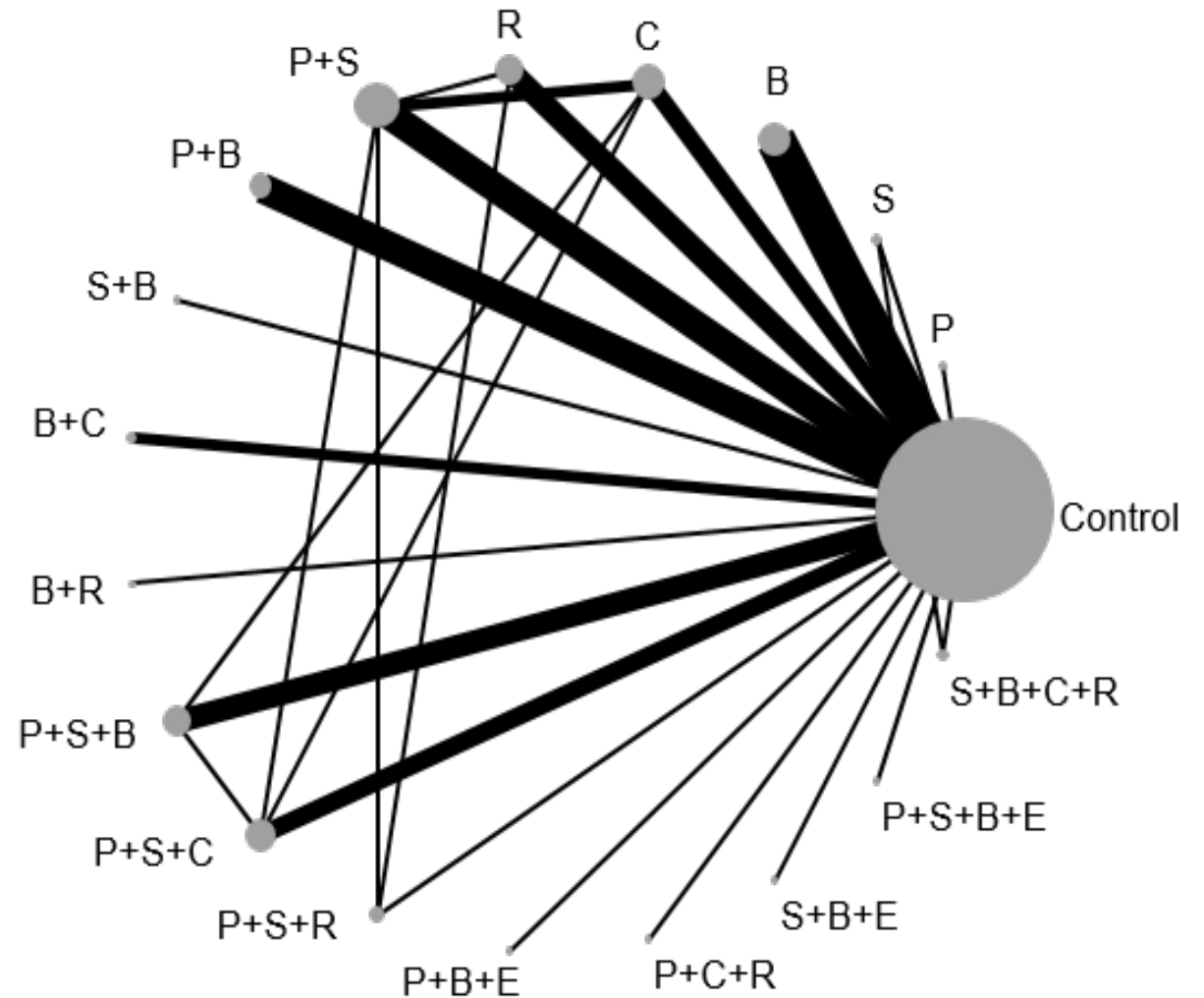
Component Network Meta-Analysis

"Which components of these multi-component interventions are most effective?"

or

"What would be the predicted effectiveness of a particular combination?"

Example: Which components of psychological preparation for adults undergoing surgery reduce length of stay in hospital?

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Component Network Meta-Analysis

Additive Effects – the effect of a combination of components is the sum of it's parts

e.g. Effect of P+S = Effect of P + Effect of S
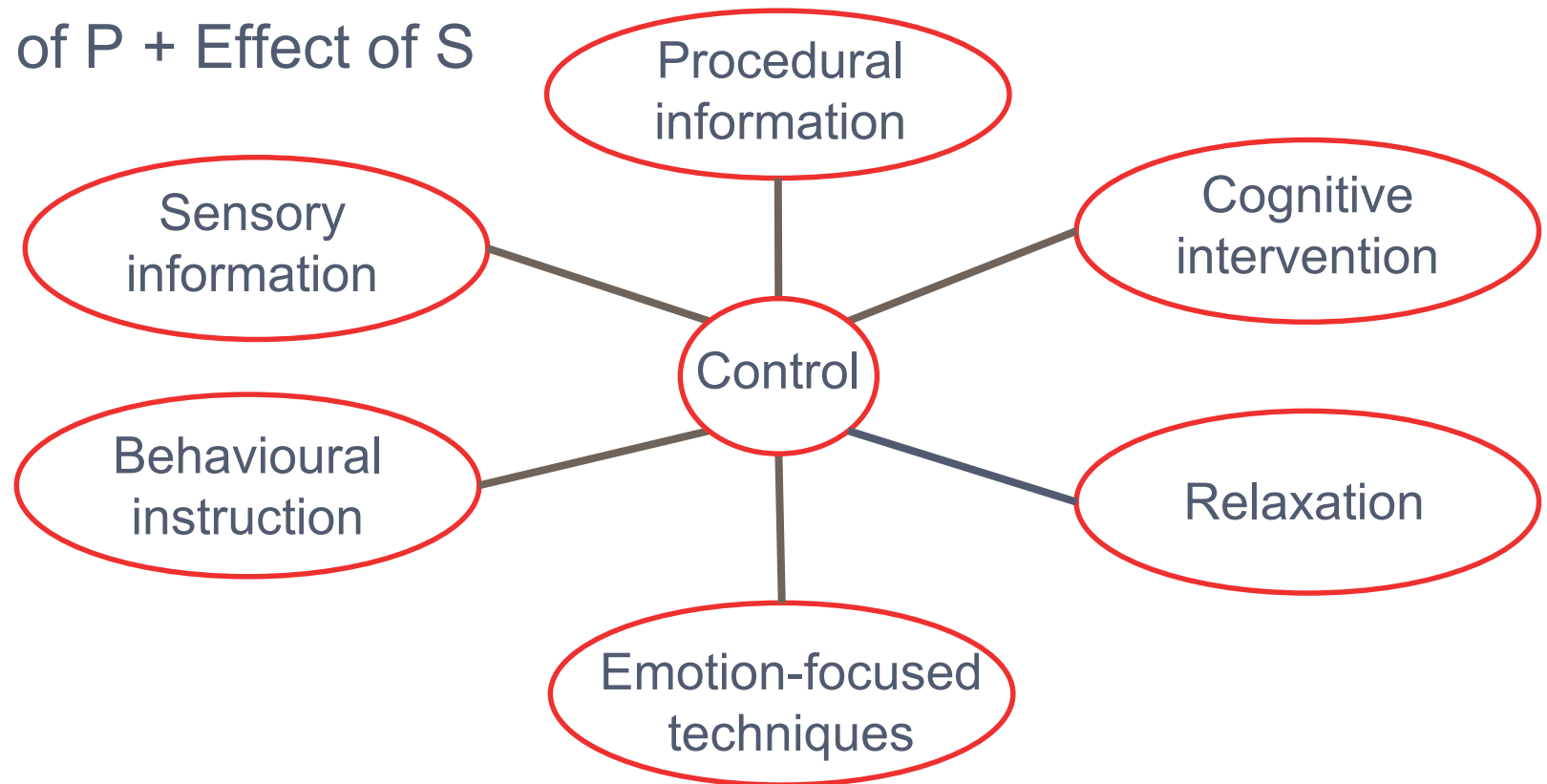
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Component Network Meta-Analysis

Interaction model - Interaction terms between pairs of components to allow for synergistic or antagonistic effects

Are components more effective when delivered on their own or in combination?

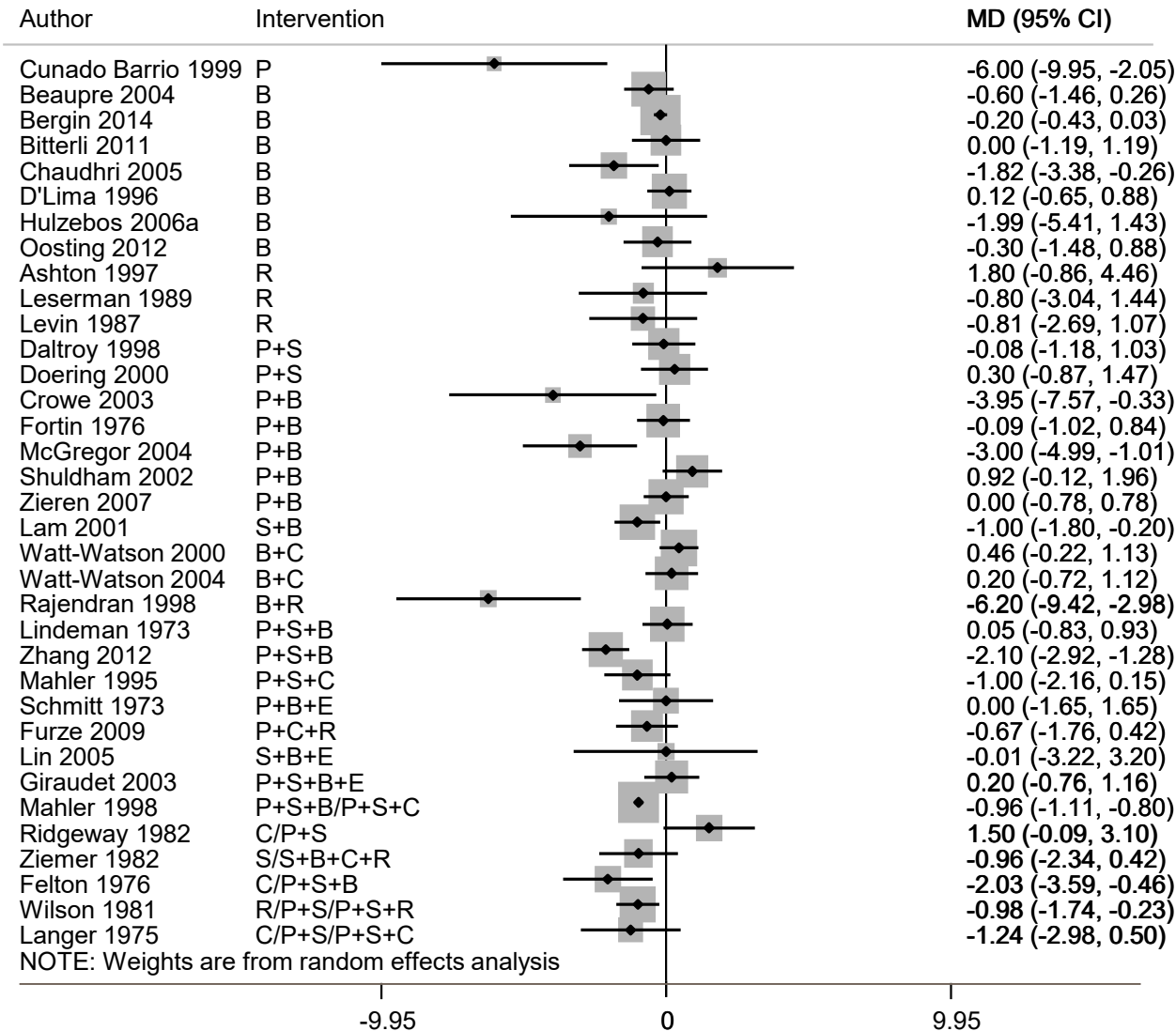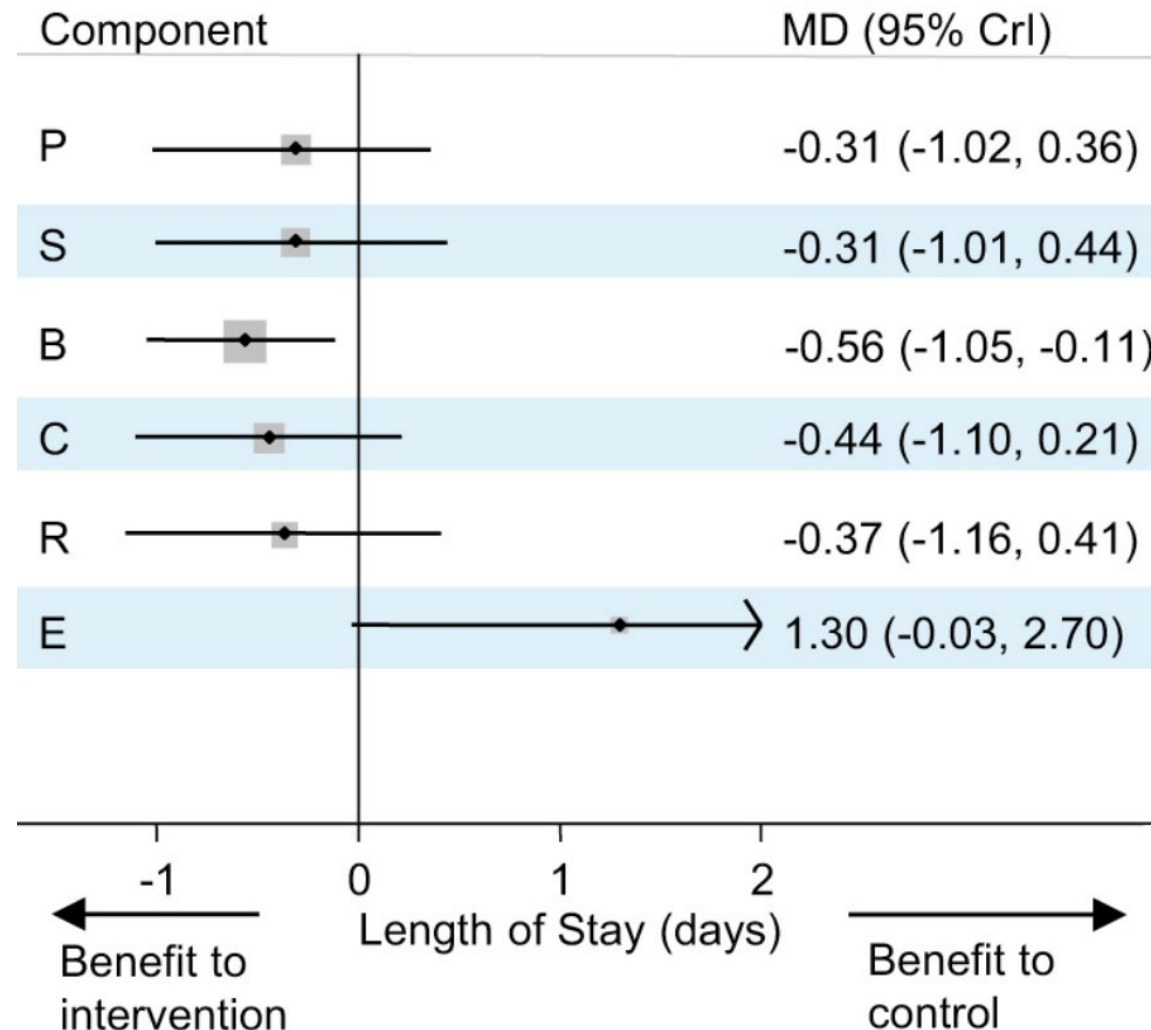- E.g. Effect of P + S = Effect of P + Effect of S + Interaction between P & S

Length of Stay

- 35 trials including four three-arm trials and two four-arm trials

- 18 interventions

- Continuous outcome – number of days in hospital

- Cochrane review identified any intervention reduces length of stay by 0.52 days (95% CrI: -0.82, -0.22)

Length of Stay Forest Plot

Author	Intervention		MD (95% CI)
Cunado Barrio 1999	P		-6.00 (-9.95, -2.05)
Beaupre 2004	B		-0.60 (-1.46, 0.26)
Bergin 2014	B		-0.20 (-0.43, 0.03)
Bitterli 2011	B		0.00 (-1.19, 1.19)
Chaudhri 2005	B		-1.82 (-3.38, -0.26)
D'Lima 1996	B		0.12 (-0.65, 0.88)
Hulzebos 2006a	B		-1.99 (-5.41, 1.43)
Oosting 2012	B		-0.30 (-1.48, 0.88)
Ashton 1997	R		1.80 (-0.86, 4.46)
Leserman 1989	R		-0.80 (-3.04, 1.44)
Levin 1987	R		-0.81 (-2.69, 1.07)
Daltroy 1998	P+S		-0.08 (-1.18, 1.03)
Doering 2000	P+S		0.30 (-0.87, 1.47)
Crowe 2003	P+B		-3.95 (-7.57, -0.33)
Fortin 1976	P+B		-0.09 (-1.02, 0.84)
McGregor 2004	P+B		-3.00 (-4.99, -1.01)
Shuldham 2002	P+B		0.92 (-0.12, 1.96)
Zieren 2007	P+B		0.00 (-0.78, 0.78)
Lam 2001	S+B		-1.00 (-1.80, -0.20)
Watt-Watson 2000	B+C		0.46 (-0.22, 1.13)
Watt-Watson 2004	B+C		0.20 (-0.72, 1.12)
Rajendran 1998	B+R		-6.20 (-9.42, -2.98)
Lindeman 1973	P+S+B		0.05 (-0.83, 0.93)
Zhang 2012	P+S+B		-2.10 (-2.92, -1.28)
Mahler 1995	P+S+C		-1.00 (-2.16, 0.15)
Schmitt 1973	P+B+E		0.00 (-1.65, 1.65)
Furze 2009	P+C+R		-0.67 (-1.76, 0.42)
Lin 2005	S+B+E		-0.01 (-3.22, 3.20)
Giraudet 2003	P+S+B+E		0.20 (-0.76, 1.16)
Mahler 1998	P+S+B/P+S+C		-0.96 (-1.11, -0.80)
Ridgeway 1982	C/P+S		1.50 (-0.09, 3.10)
Ziemer 1982	S/S+B+C+R		-0.96 (-2.34, 0.42)
Felton 1976	C/P+S+B		-2.03 (-3.59, -0.46)
Wilson 1981	R/P+S/P+S+R		-0.98 (-1.74, -0.23)
Langer 1975	C/P+S/P+S+C		-1.24 (-2.98, 0.50)

NOTE: Weights are from random effects analysis

-9.95   0   9.95

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Length of Stay Results

P = procedural information, S = sensory information, B = behavioural instruction, C = cognitive intervention, R = relaxation techniques, E = emotion-focused intervention

Network Meta-Analysis or Component NMA?

Network Meta-Analysis	Component Network Meta-Analysis
Can be used if treatments consist of components but may not be 'optimal'	Only suitable if interventions consist of components
Disparate components across studies	Common components across studies
Which treatment is most effective at reducing the outcome of interest?	Which intervention component or combination of components is most effective at reducing the outcome of interest?
If evidence base consists of lots of unique interventions can result in a sparse network & large uncertainty around treatment effect estimates	Could reduce uncertainty around intervention effect estimates if the evidence base consists of lots of unique interventions
	Can predict optimal combinations of intervention components

Challenges & Practicalities

- Software
  - NMA & CNMA not possible within RevMan
  - Choice of Bayesian or Frequentist approach
  - Software options include R & WinBUGS
  - Be careful with coding of multi-arm trials & treatments/components

Resources

- Cochrane Learning Live webinar - Identifying effective component of complex interventions: Component network meta-analysis, https://training.cochrane.org/resource/identifying-effective-components-complex-interventions-component-network-meta-analysis

- WinBUGS code for Bayesian CNMA:
  - Binary outcomes: Welton *et al*. http://www.bristol.ac.uk/population-health-sciences/centres/cresyda/mpes/code/
  - Continuous outcomes, covariates: Freeman *et al*. https://doi.org/10.1016/j.jclinepi.2018.02.012

- Frequentist CNMA using R package netmeta: https://cran.r-project.org/web/packages/netmeta/netmeta.pdf

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