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NIHR CRSU

Complex Reviews Support Unit

Network Meta-Analysis

CRSU & Cochrane Workshop

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Suzanne Freeman & Alex Sutton

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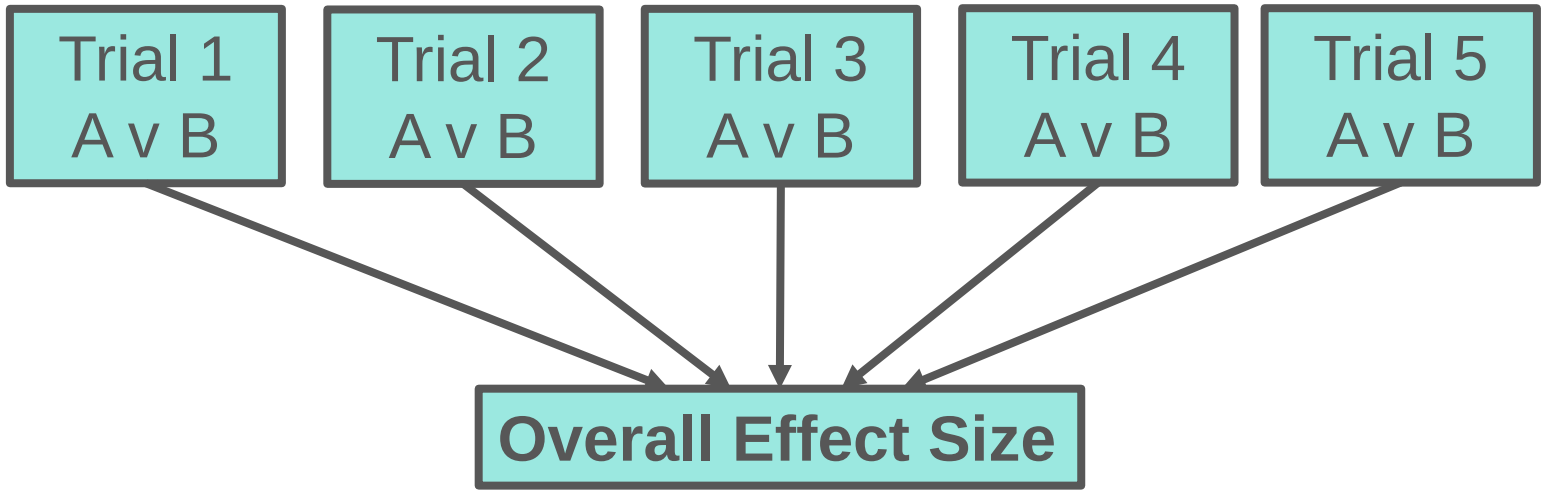
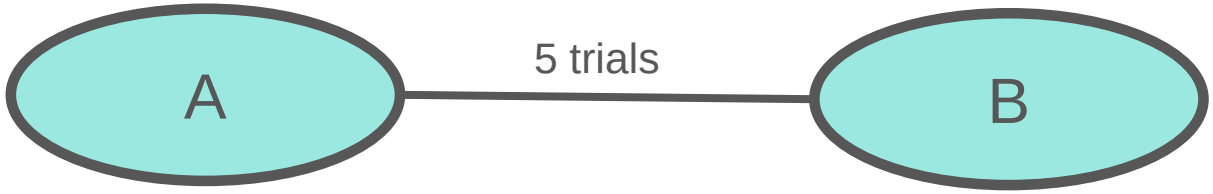
Outline

- Introduction to network meta-analysis
- Two examples
    1) Evaluation of the effectiveness of strategies for preventing fire related injuries in children within the home
    2) Evaluation of the effectiveness of complex interventions considering psychological preparation and postoperative outcomes for adults undergoing surgery
- Implementation barriers to network meta-analysis

Pairwise Meta-Analysis

- Meta-analysis combines estimates of treatment effect from several trials all comparing the same two treatments and reporting the same outcome
- This gives an overall estimate of the treatment effect





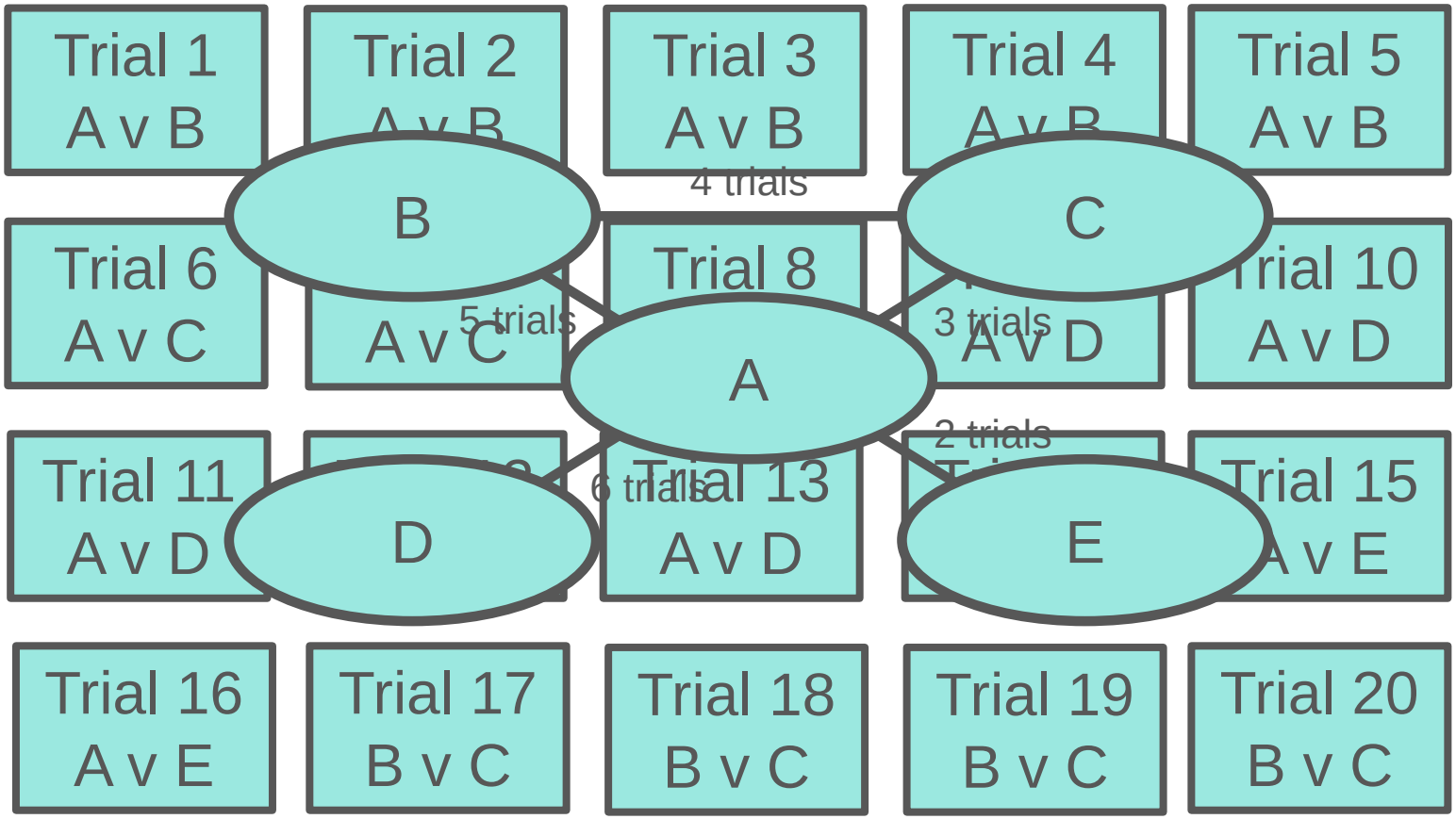
Network Meta-analysis

- Network meta-analysis combines evidence on a number of treatments from clinical trials comparing at least two treatments for a specific disease area

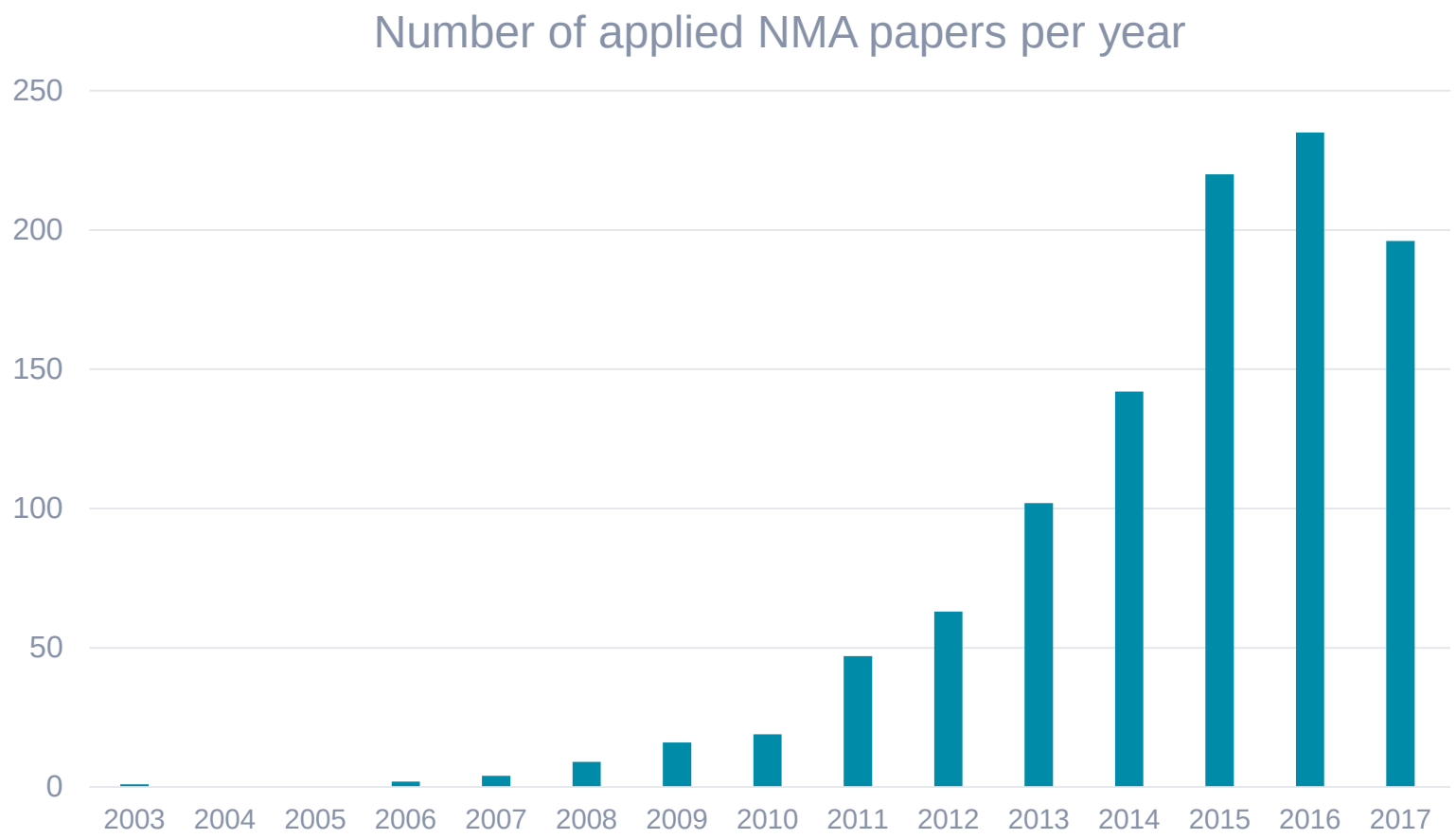
- We compare all the treatments in the network to each other to identify the most effective treatment for a specific disease area

- Treatments can be ranked in terms of efficacy

Network Meta-Analysis



NMA in recent years



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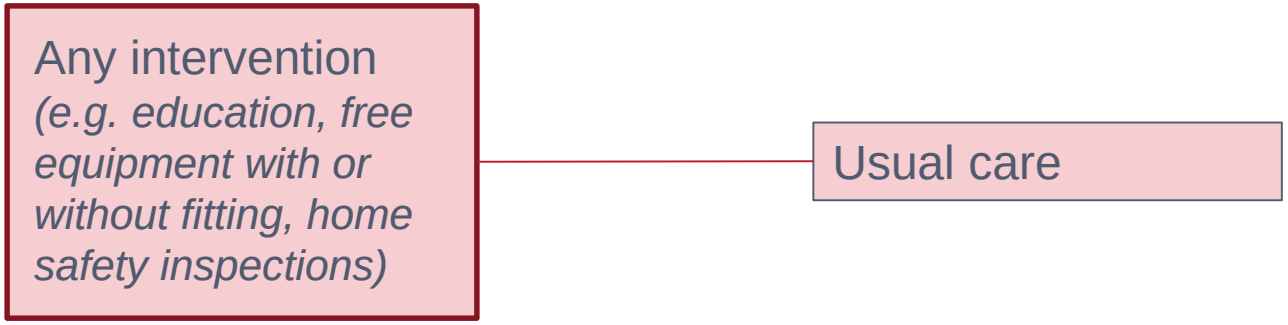
Example 1: (Pre-CRSU)
Home safety education and provision of safety equipment for injury prevention

Original Cochrane review

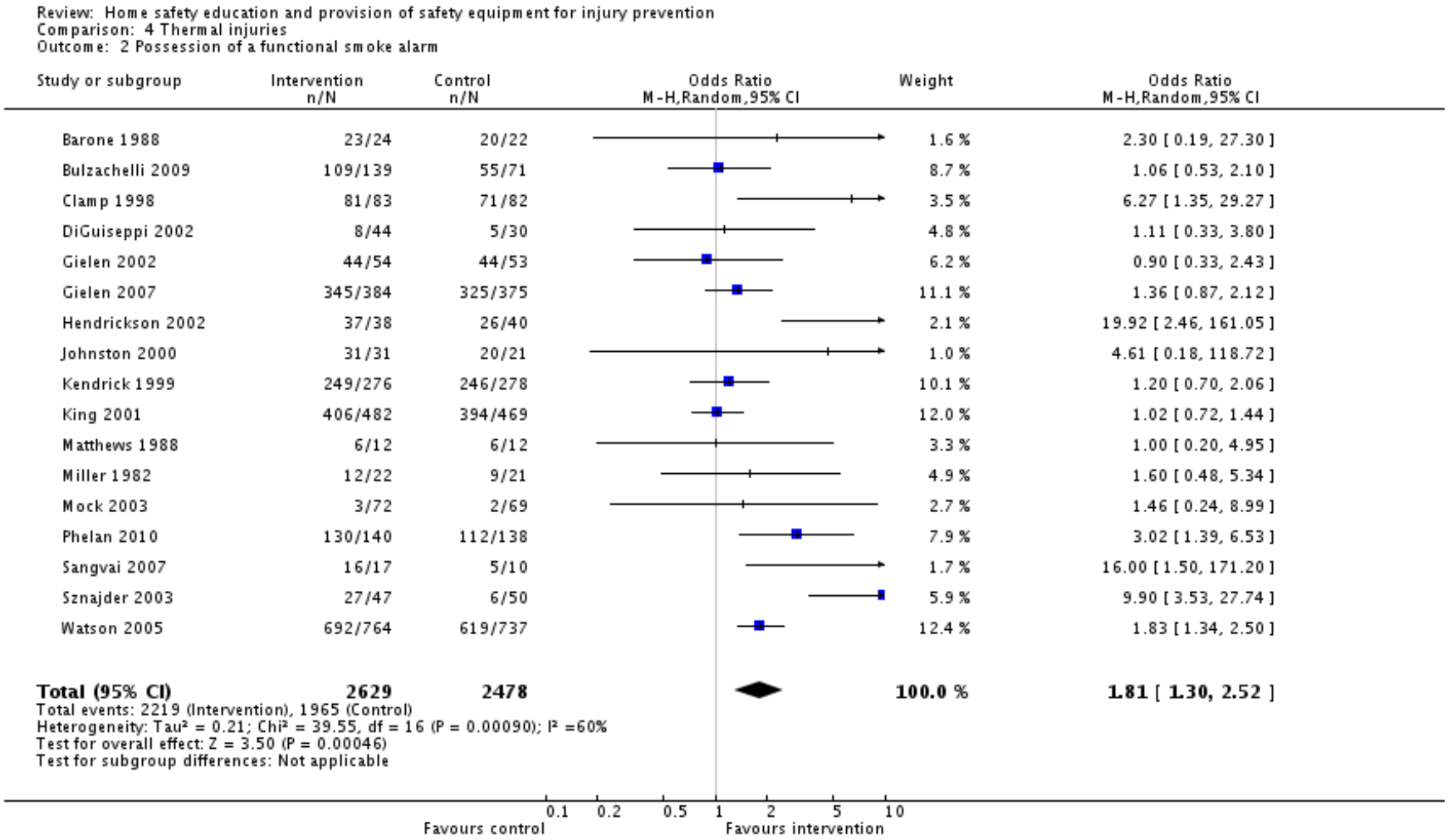
"To identify whether strategies for increasing the ownership of safety equipment in households *(e.g. smoke alarms, fire extinguishers, fire guards, safe storage of matches/lighters)* is more effective than usual care"

Interventions for increasing ownership of *functioning smoke alarms* – Pairwise MA



(Kendrick et al. Cochrane Review 2012)

Possession of a *functional smoke alarm*

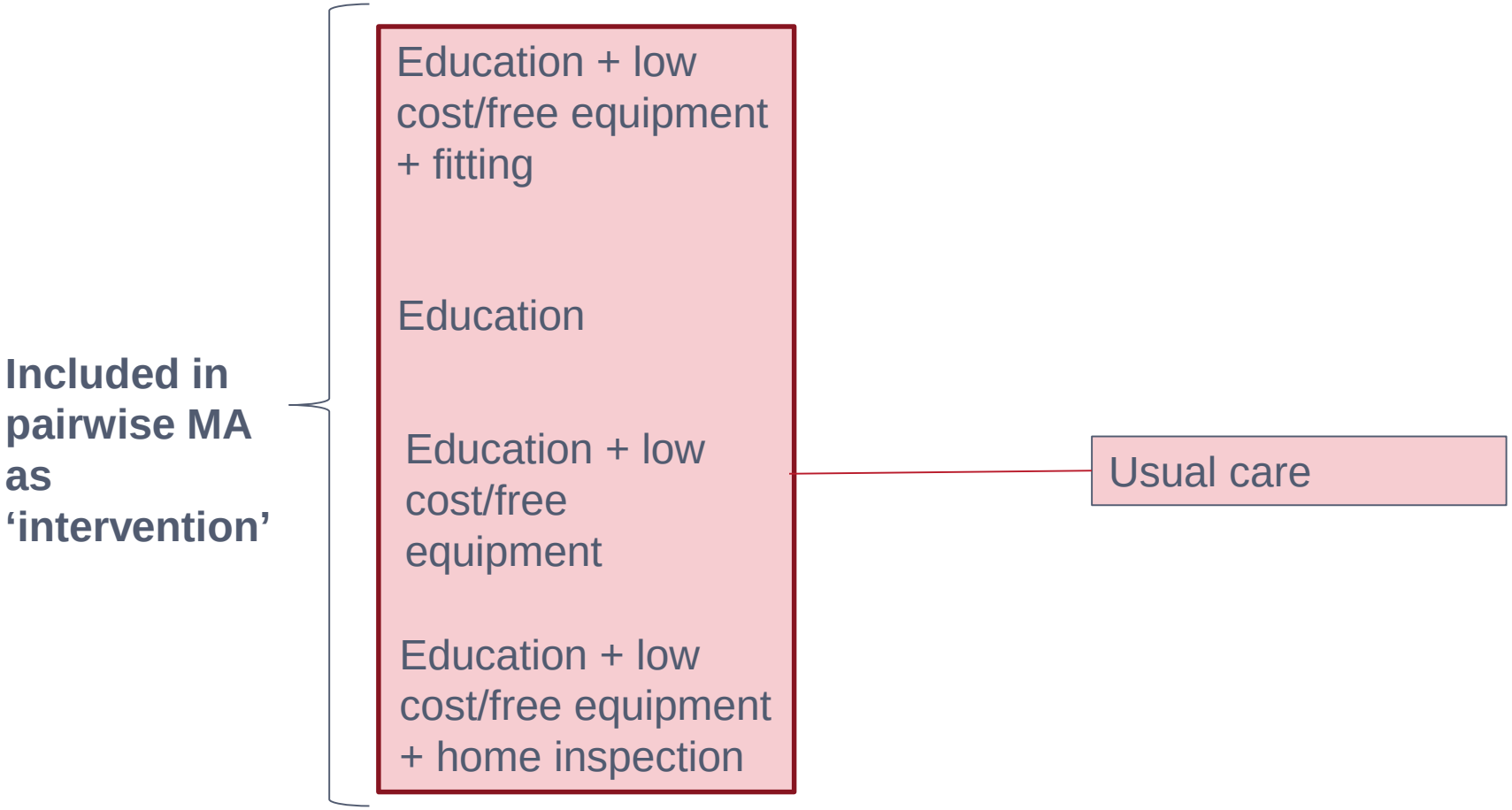


- Households who received an intervention more likely to possess a functional smoke alarm

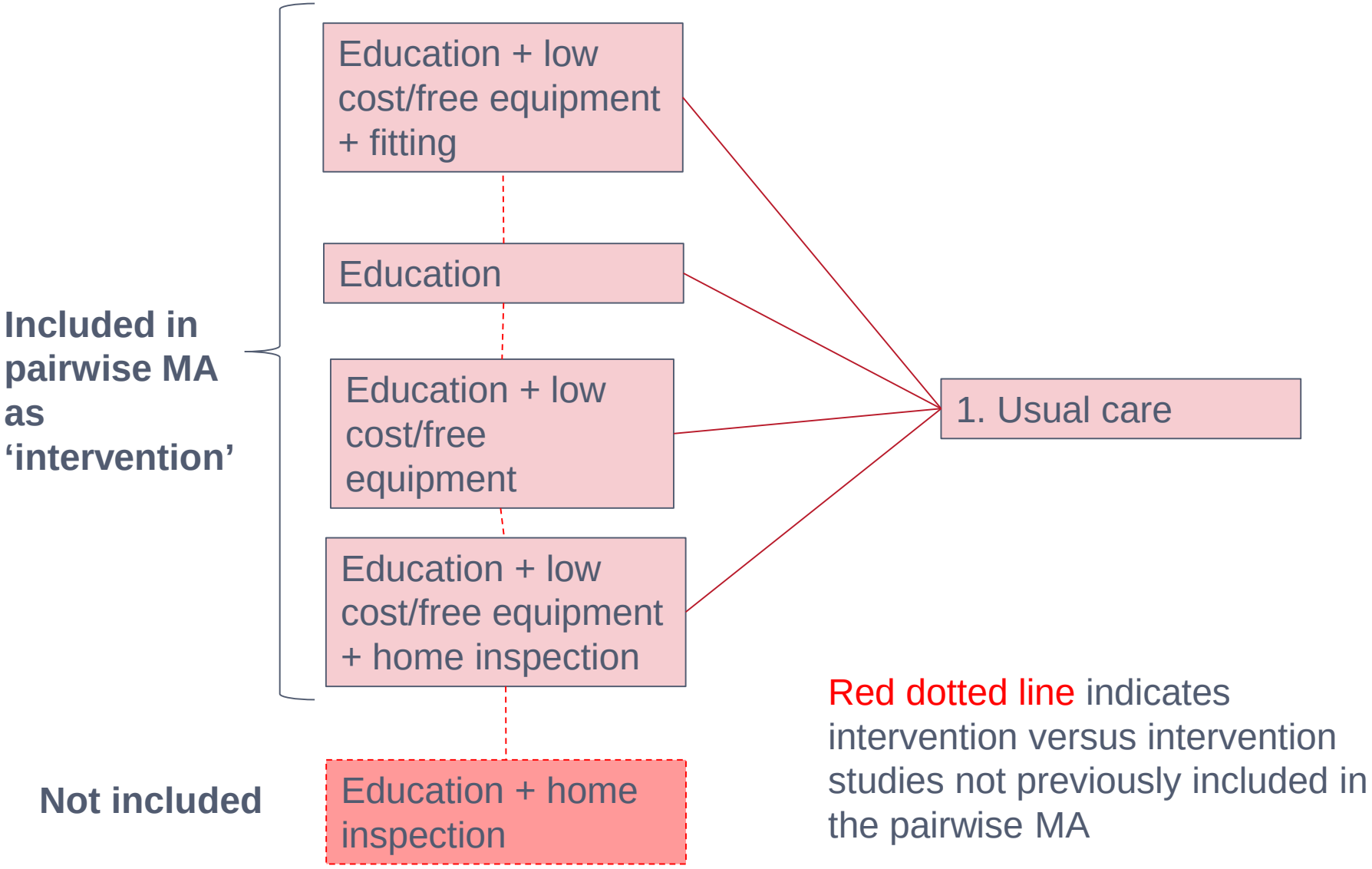
Additional Clinical question of relevance

"To identify the most effective (i.e. "best") strategy for increasing the ownership of safety equipment in households *(e.g. smoke alarms, fire extinguishers, fire guards, safe storage of matches/lighters)*"

Interventions for increasing ownership of *functioning smoke alarms* – Pairwise MA



Interventions for increasing ownership of *functioning smoke alarms* – Network MA



Pairwise MA Results – Odds Ratios

Results of separate pairwise MAs

	Usual care	Educ	Educ + Equip	Educ + Equip + HI	Educ + Equip + Fit	Educ + HI	Educ + Equip + Fit + HI
Usual Care							
Educ	1.34 (0.66, 2.65)						
Educ + Equip	3.25 (0.49, 22.95)	2.29 (0.23, 22.61)					
Educ + Equip + HI							
Educ + Equip + Fit	5.94 (0.96, 48.79)		0.82 (0.30, 2.22)				
Educ + HI	1.65 (0.30, 7.61)	9.90 (3.53, 27.74)			1.17 (0.34, 6.98)		
Educ + Equip + Fit + HI	5.24 (0.84, 26.41)				4.82 (3.88, 6.00)		

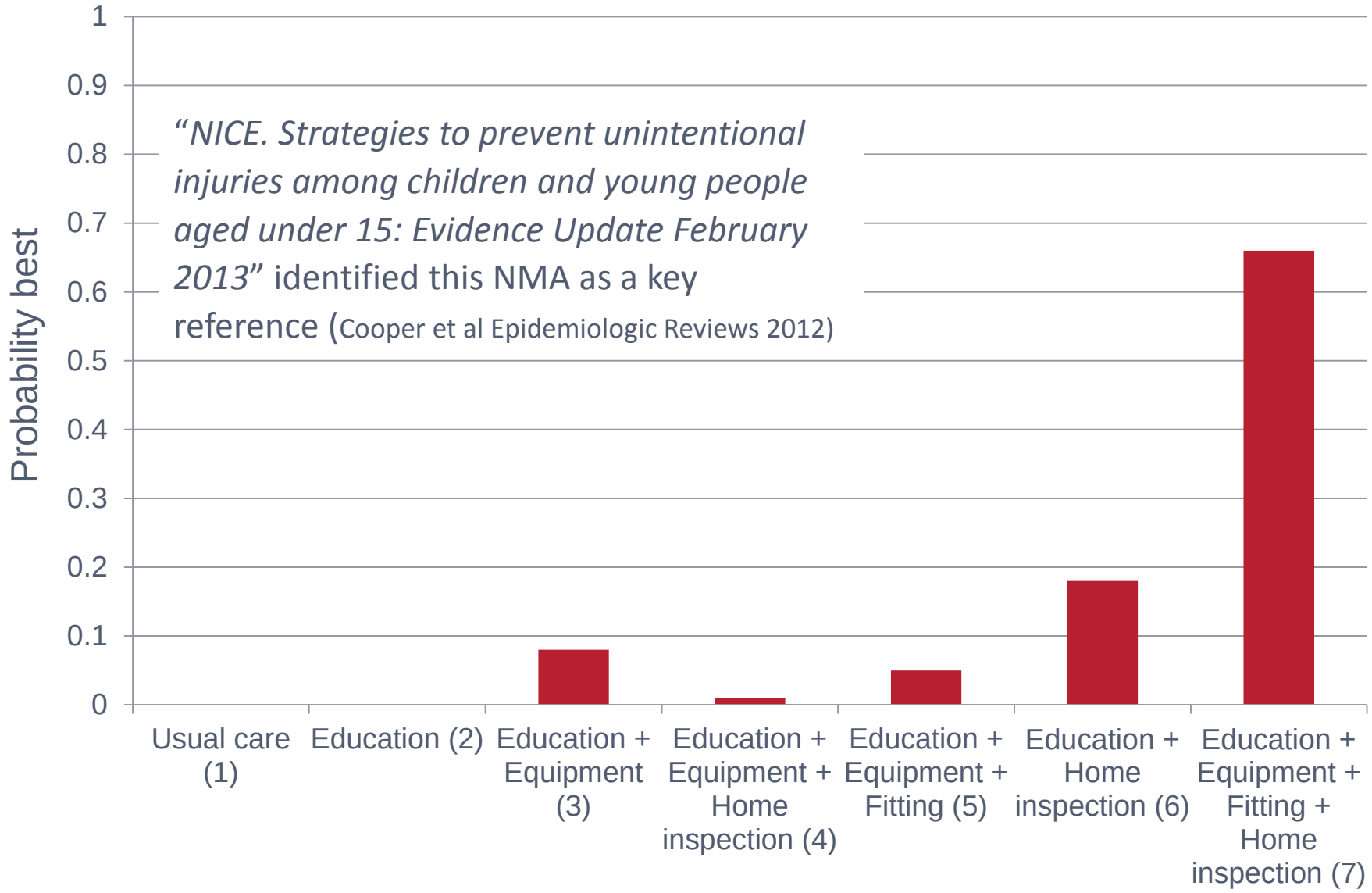
NMA Results – Odds Ratios

Results of Network MA

Results of separate pairwise MAs

	Usual care	Educ	Educ + Equip	Educ + Equip + HI	Educ + Equip + Fit	Educ + HI	Educ + Equip + Fit + HI
Usual Care		0.99 (0.39 , 2.33)	3.18 (0.98, 11.18)	2.82* (1.13 , 8.93)	2.71 (0.85 , 8.88)	3.48 (0.75 , 26.53)	7.15* (2.40 , 22.73)
Educ	1.34 (0.66, 2.65)		3.52 (0.84 , 14.46)	2.87 (0.84 , 13.19)	2.76 (0.80 , 10.27)	3.56 (0.64 , 34.50)	7.25* (1.87 , 30.33)
Educ + Equip	3.25 (0.49, 22.95)	2.29 (0.23, 22.61)		0.89 (0.24 , 3.57)	0.86 (0.16 , 4.51)	1.10 (0.19 , 9.00)	2.26 (0.46 , 10.55)
Educ + Equip + HI					0.98 (0.17 , 4.49)	1.24 (0.35 , 5.55)	2.59 (0.64 , 8.13)
Educ + Equip + Fit	5.94 (0.96, 48.79)		0.82 (0.30, 2.22)			1.27 (0.19 , 13.37)	2.61 (0.52 , 13.26)
Educ + HI	1.65 (0.30, 7.61)	9.90 (3.53, 27.74)			1.17 (0.34, 6.98)		2.09 (0.24 , 10.52)
Educ + Equip + Fit + HI	5.24 (0.84, 26.41)				4.82 (3.88, 6.00)		

NMA Results – Probability "Best"



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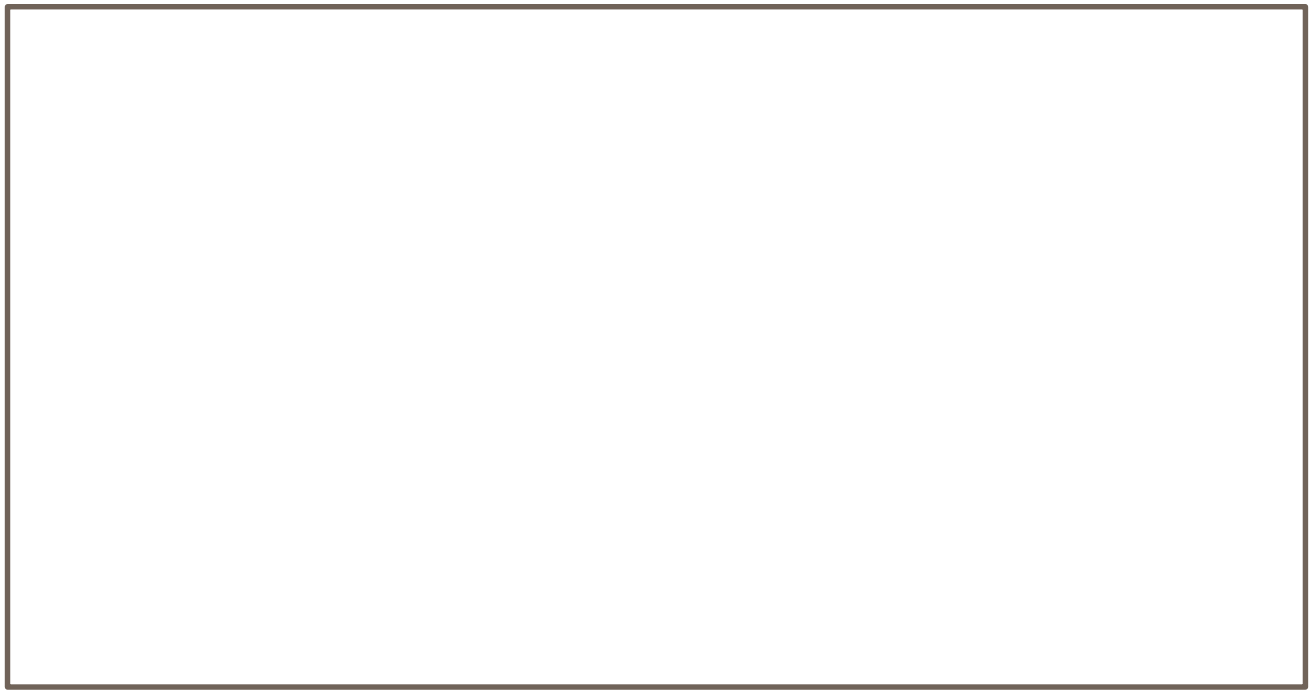
Example 2: Psychological Preparation & Postoperative Outcomes for Adults undergoing Surgery under General Anaesthesia

Background

- May 2016 - Meta-analysis published in the Cochrane Database of Systematic Reviews identifying better postoperative outcomes (e.g. reduced length of stay in hospital, lower pain) for patients who received any psychological preparation (strategies designed to influence thoughts, feelings or actions) compared to usual care

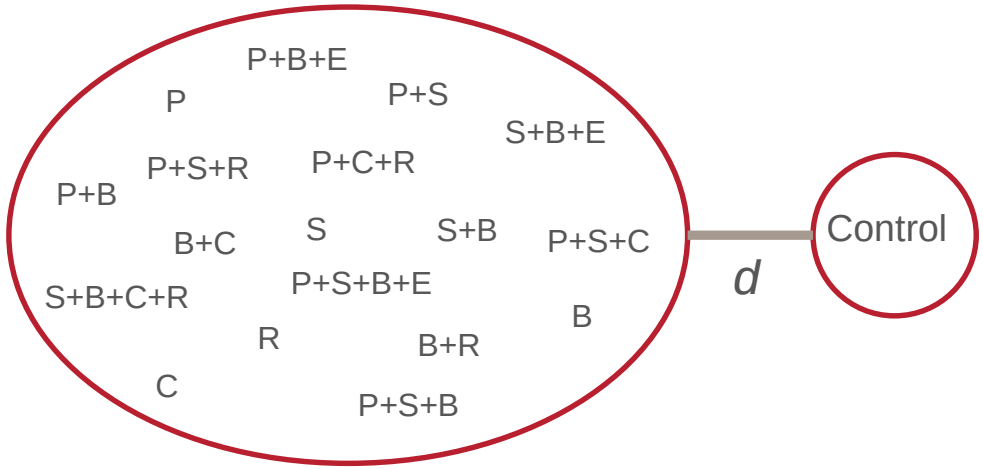


Background

- 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)

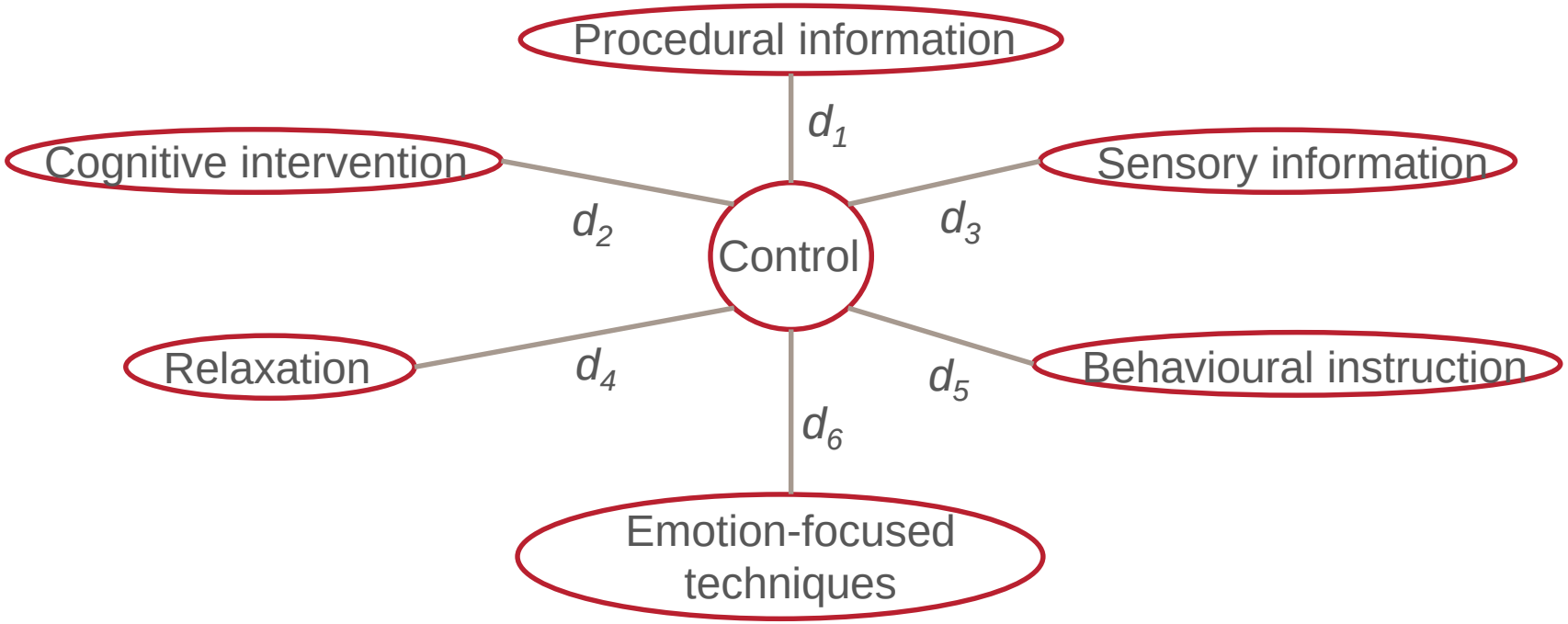
Cochrane Review - What did they do?

- 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)



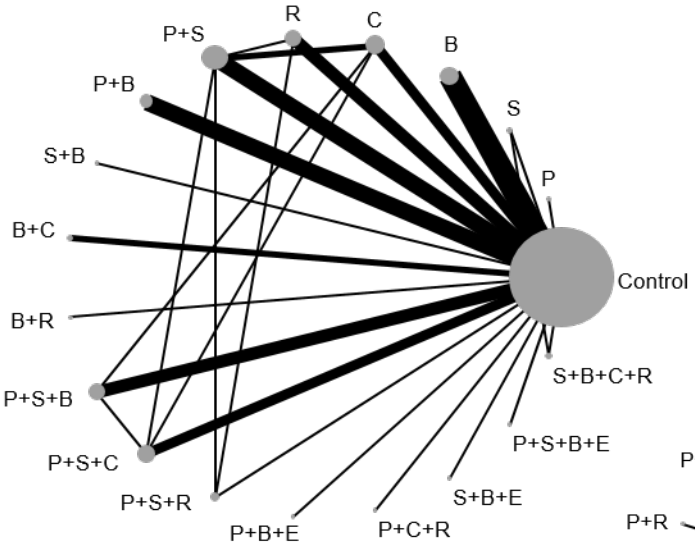
What did we do?

- We utilised network meta-analysis to go beyond the Cochrane review to identify *which individual components are most effective*

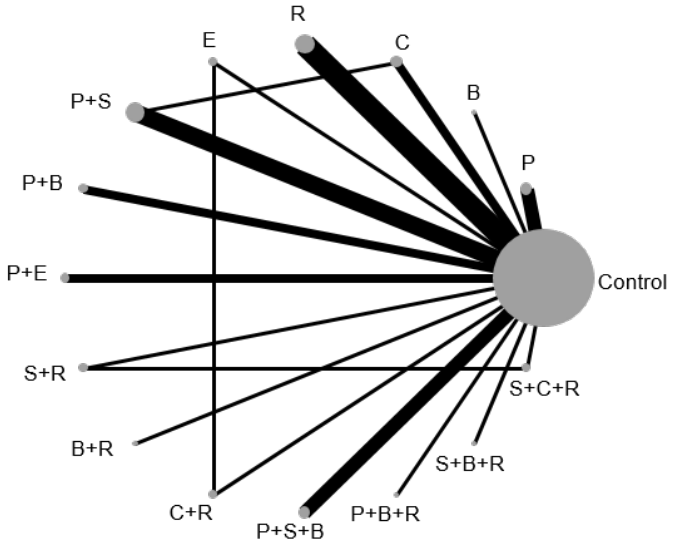


Freeman et al. Component network meta-analysis identifies the most effective components of psychological preparation for adults undergoing surgery under general anesthesia. Journal of Clinical Epidemiology 2018 https://doi.org/10.1016/j.jclinepi.2018.02.012

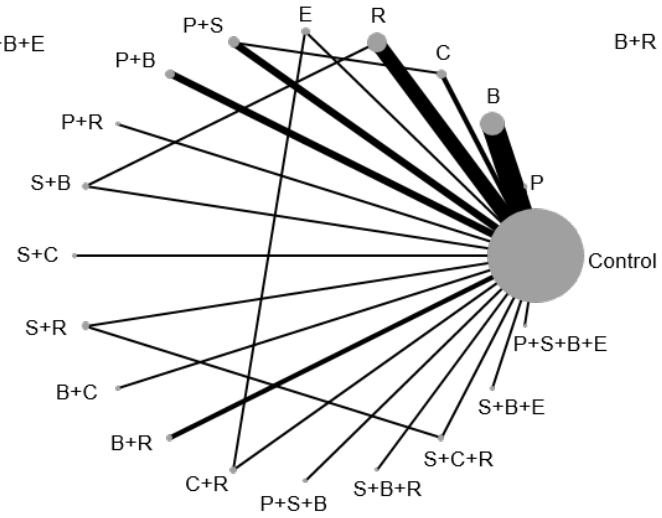
Network Diagrams



Length of stay



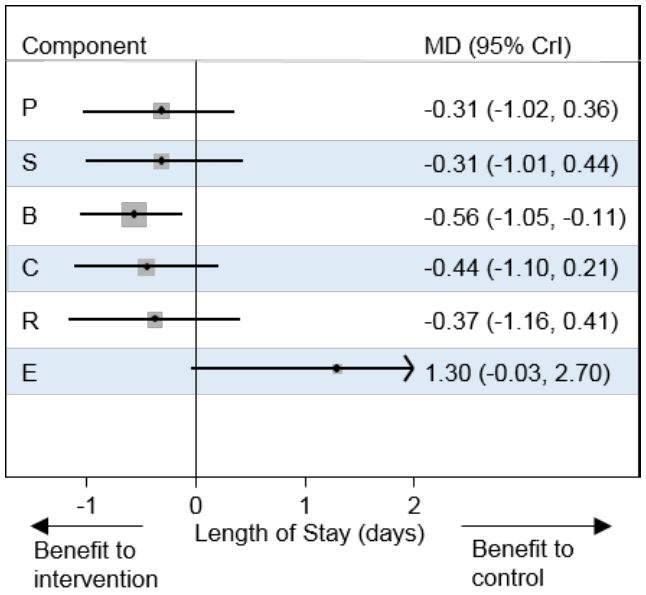
Negative affect

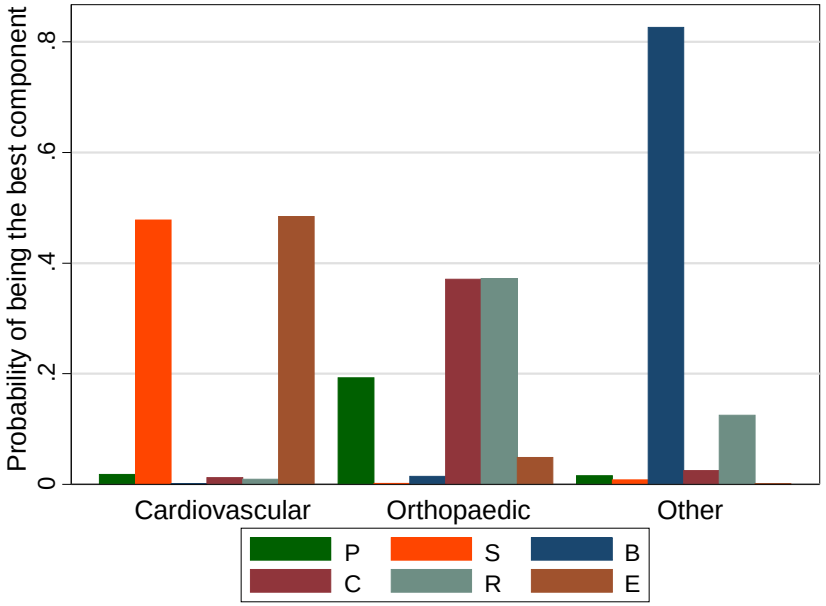


Pain

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

Results – Length of Stay



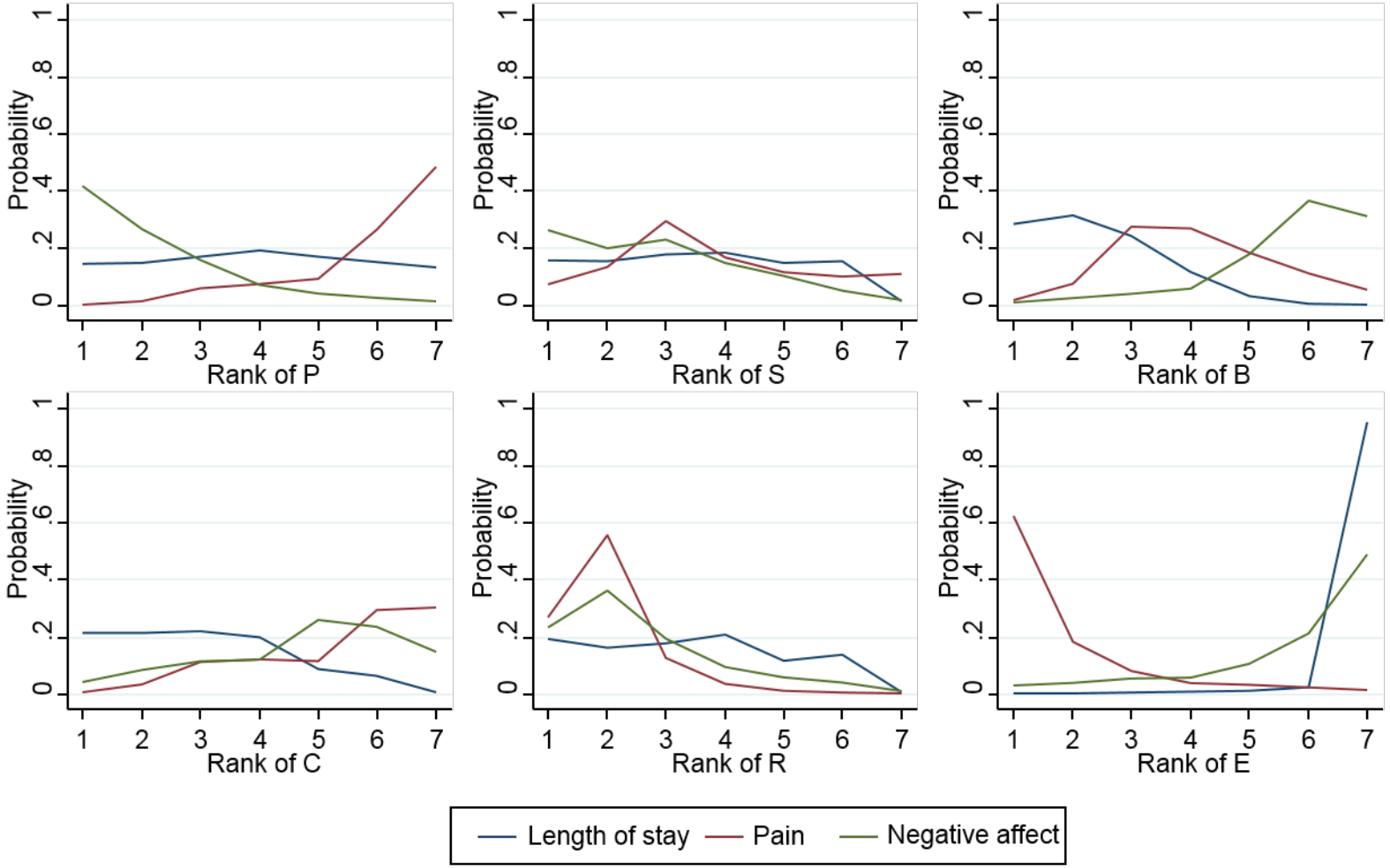


P = Procedural information, **S** = Sensory information, **B** = Behavioural instruction, **C** = Cognitive interventions, **R** = Relaxation, **E** = Emotion-focused techniques, MD = Mean difference, SMD = Standardised mean difference, CrI = Credible interval

- Combinations P+S+B and P+S+R reduced LOS by one day
- The longer the length of stay in the control group the greater the reduction in length of stay from receiving intervention
- Most effective component for length of stay dependent on type of surgery

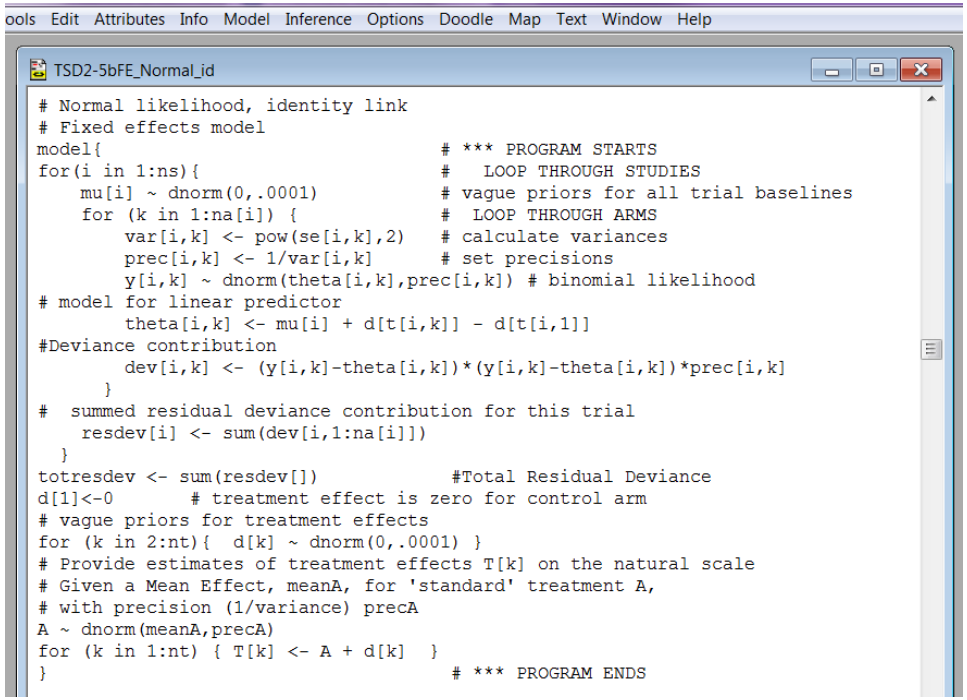
Simultaneous assessment across outcomes

- No one component can be identified as the most effective component across all three outcomes



Implementation

- WinBUGS:
  - code available from NICE Technical Support Documents available at http://nicedsu.org.uk/technical-support-documents/evidence-synthesis-tsd-series/



Implementation

- Stata:
  - network (White IR. Network meta-analysis. *Stata Journal* 2015;15:951)
- R:
  - netmeta (Rücker G et al. netmeta: Network meta-analysis using frequentist methods. R package version 0.9-8. Available: http://CRAN-R.project.org/package=netmeta)
  - GeMTC (vanValkenhoef G, Kuiper J. gemtc: Network meta-analysis using Bayesian methods. R package version 0.8-2. Available http://CRAN-R.project.org/package=gemtc)
  - pcnetmeta (Lin L et al. Performing arm-based network meta-analysis in R with the pcnetmeta package. *Journal of Statistical Software* 2017;80:1. Available http://CRAN-R.project.org/package=pcnetmeta)

The specialist knowledge required for using Stata, R and WinBUGS has been identified as a barrier to the uptake of network meta-analysis methods

MetaInsight

An interactive web-based tool for conducting network meta analysis

https://crsu.shinyapps.io/metainsightc/

Used by Cochrane Stroke in their analysis of comparisons of delays to mobilisation

'Very early mobilisation after stroke review' (currently under editorial review).