AN EMPIRICAL INVESTIGATION OF THE IMPACT OF DIFFERENT METHODS FOR SYNTHESISING EVIDENCE IN A NETWORK META-ANALYSIS

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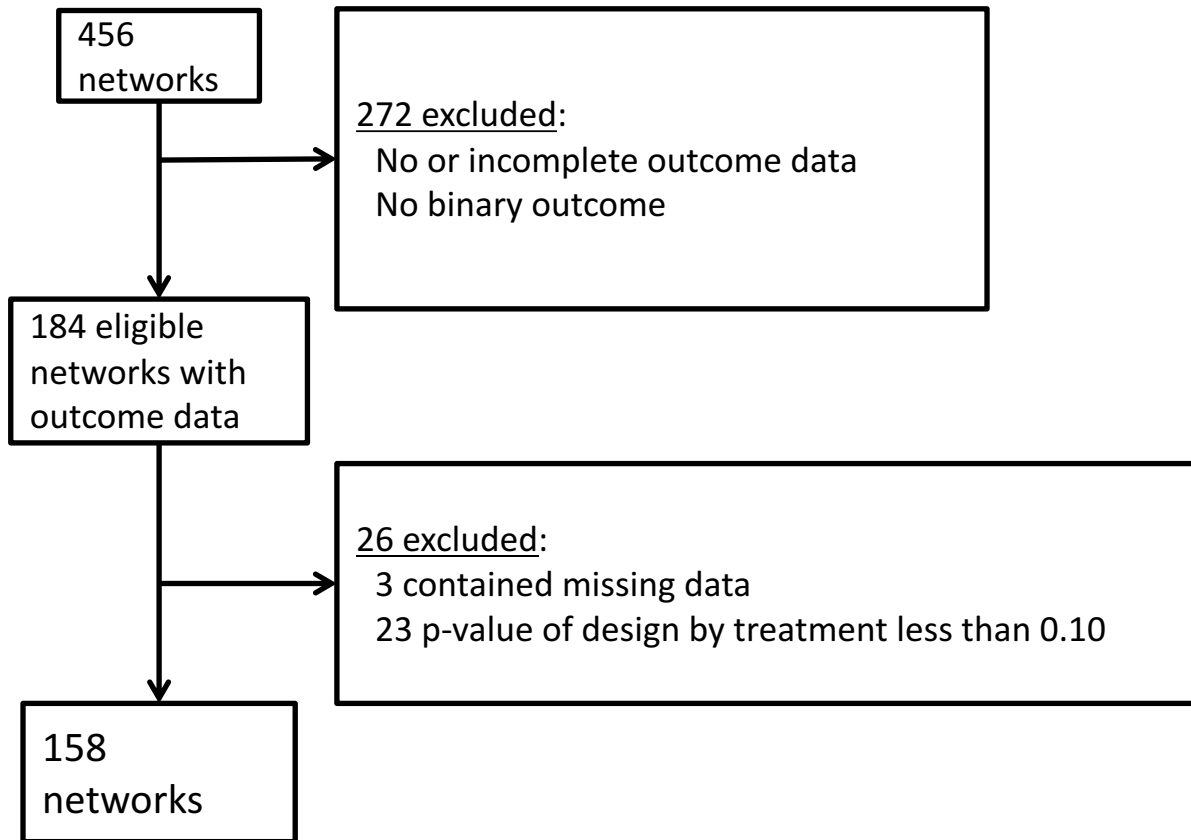
Aim/methods

- Assess impact of re-analysing published NMAs with binary outcomes using contrast-synthesis and arm-synthesis models
- Investigate results w.r.t. characteristics of the NMA (not presented here)
  - # treatments: # studies
  - # treaments: # comparisons
  - # studies : # treatments
  - proportion of arms with <10 events/outcomes

Eligibility criteria

- We included a subset of networks from a database of networks of randomised trials (Petropolou et al 2016)

- Our subset included networks meeting the following criteria:

  – Primary outcome was binary

  – No evidence of inconsistency

  – Outcome data available
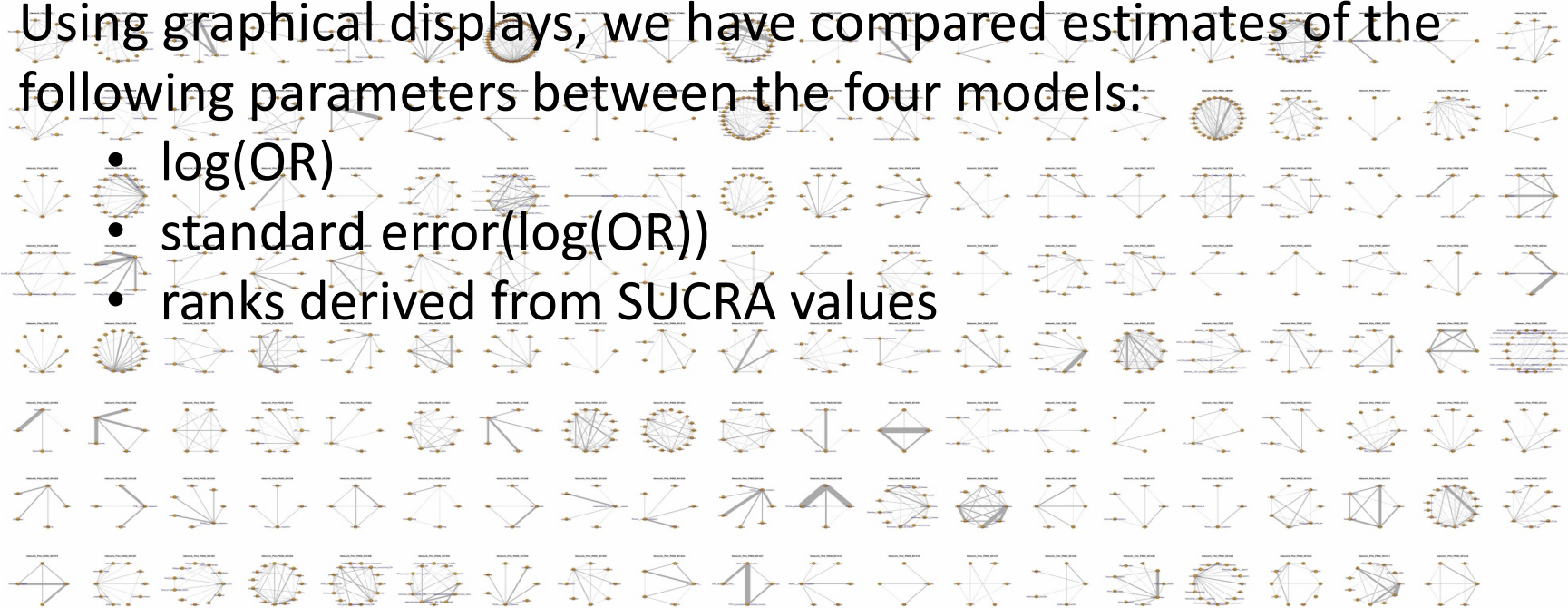
Flowchart of networks included in analysis

456 networks

272 excluded:
  No or incomplete outcome data
  No binary outcome

184 eligible networks with outcome data

26 excluded:
  3 contained missing data
  23 p-value of design by treatment less than 0.10

158 networks

Statistical methods – using R

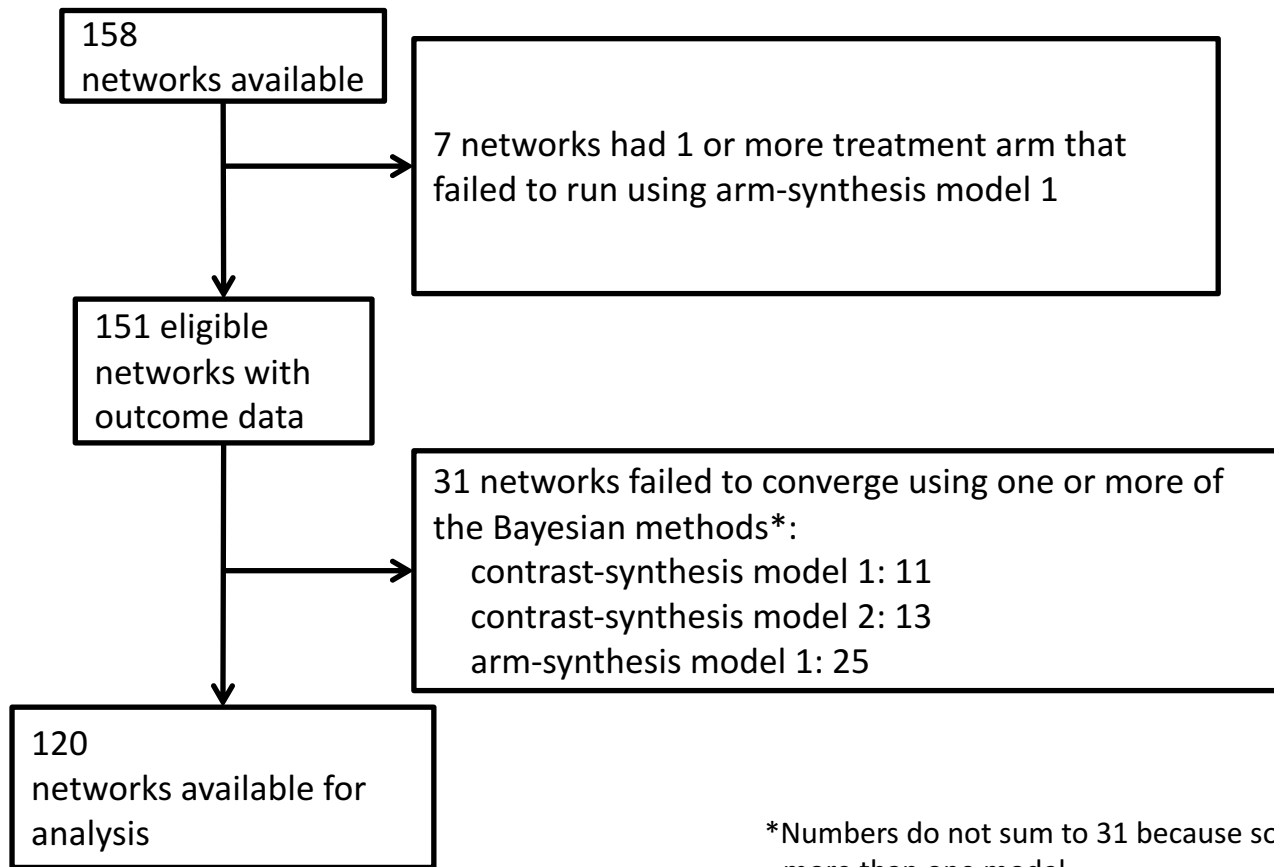| Method label	Package used in R	Contrast-level or arm-level input data	Frequentist or Bayesian framework	Likelihood and link functions	Heterogeneity	Prior distributions		
						Treatment specific fixed effects	**Mean effect of treatment k relative to baseline**	**Heterogeneity or random effects parameter**
Contrast-synthesis model 1	gemtc (version 0.8.1)	Arm-level	Bayesian	Binomial likelihood and logit link	Homogeneous/ common	N/A	$d_k \sim N(0, (15*5)^2)$	$\tau_{bk} \sim U(0,10)$
Contrast-synthesis model 2	gemtc (version 0.8.1)	Arm-level	Bayesian	Binomial likelihood and logit link	Homogeneous/ common	N/A	$d_k \sim N(0, (15*5)^2)$	Informative
Contrast-synthesis model 3	netmeta (version 0.9-2)	Contrast-level	Frequentist	N/A	Homogeneous/ common	N/A	N/A	N/A
Arm-synthesis model 1	pcnetmeta (version 2.4)	Arm-level	Bayesian	Binomial likelihood and probit link	Homogeneous/ common	$\mu_k \sim N(0, 1000)$	N/A	$\sigma_k \sim U(0,10)$
Arm-synthesis model 2	pcnetmeta (version 2.4)	Arm-level	Bayesian	Binomial likelihood and probit link	Heterogeneous	$\mu_k \sim N(0, 1000)$	N/A	$\sigma_k \sim U(0,10)$

Preliminary results

Using graphical displays, we have compared estimates of the following parameters between the four models:
- log(OR)
- standard error(log(OR))
- ranks derived from SUCRA values

Flowchart of networks analysed

158
networks available

7 networks had 1 or more treatment arm that failed to run using arm-synthesis model 1

151 eligible networks with outcome data

31 networks failed to converge using one or more of the Bayesian methods*:
    contrast-synthesis model 1: 11
    contrast-synthesis model 2: 13
    arm-synthesis model 1: 25

120
networks available for analysis

*Numbers do not sum to 31 because some networks failed to converge for more than one model

Time taken after excluding the networks that failed to converge (n = 120)

Model	Time taken (minutes*)				
	Average	**SD**	**Median**	**Minimum**	**Maximum**
Contrast-synthesis model 1	5.24	4.32	4.00	1.00	20.00
Contrast-synthesis model 2	5.26	4.40	4.37	0.00	19.66
Contrast-synthesis model 3	0.00	0.00	0.00	0.00	0.00
Arm-synthesis model 1	98.89	202.49	37.14	6.55	1262.66

*Note that all times measured in minutes

Comparison of the effect estimates and standard errors

Network_Plot_PMID_501192
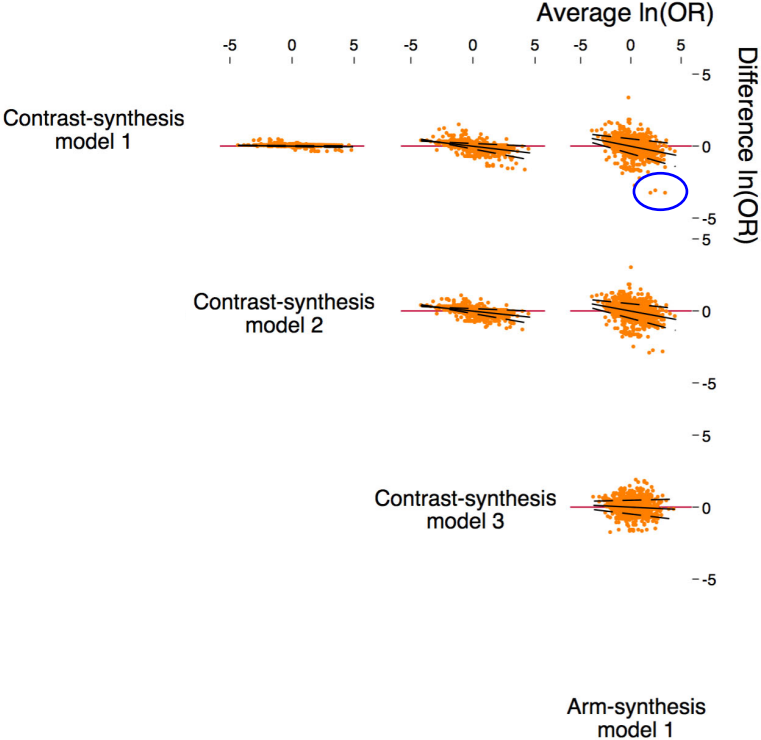
ln(OR)
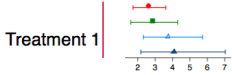
Treatment 1
Treatment 2
Treatment 3
Treatment 4
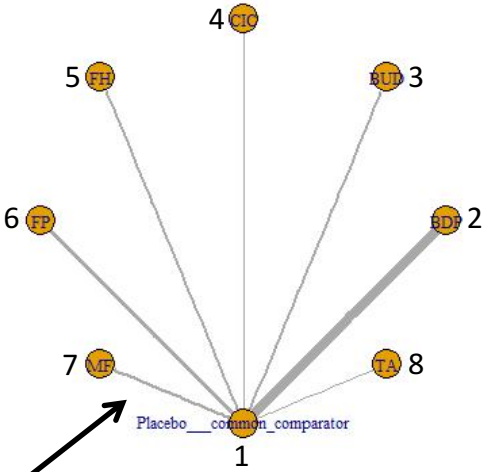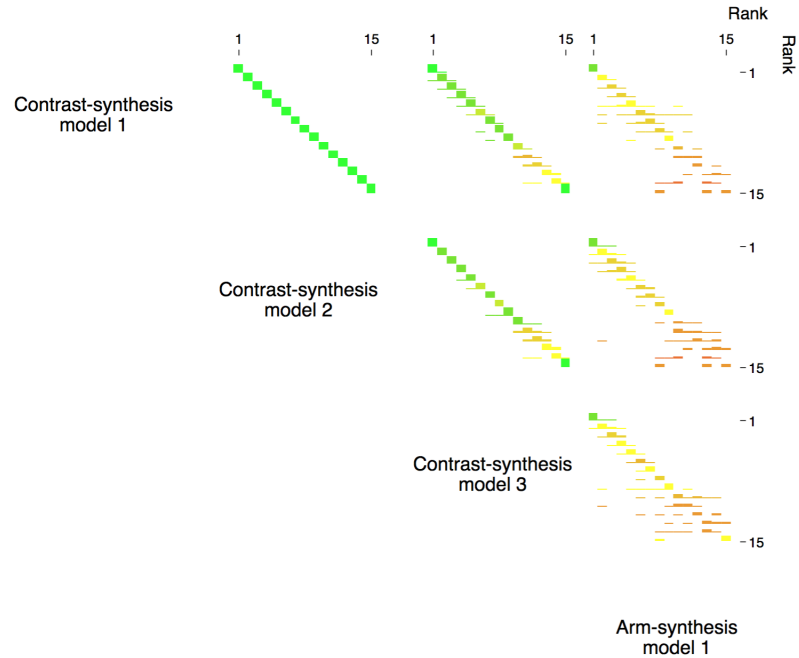Treatment 5
Treatment 6
Treatment 7
Treatment 8

2 studies
treatment 1: 2 events, 81 participants
treatment 7: 61 events, 172 participants

▲ Contrast-synthesis model 1   △ Contrast-synthesis model 2
■ Contrast-synthesis model 3   ● Arm-synthesis model 1

Comparison of the ranks and SUCRA values between methods

Summary

- From our preliminary results:
  - Good agreement between the contrast-synthesis methods in terms of effect estimates and treatment ranks
  - Differences are apparent in the effect estimates and ranks when comparing the arm-synthesis model to the contrast-synthesis models
  - Contrast-synthesis models have larger standard errors compared to the arm-synthesis models
  - More variability with respect to the standard errors for the arm-synthesis models compared to the other models
- Next steps:
  - Examine another arm-synthesis model
  - Fit multilevel models to estimate the differences between the methods and to explore the factors that might explain the differences