Cross-design and cross-data format synthesis using network meta-analysis

Presented by: Tasnim Hamza

Authors: Tasnim Hamza , Fabio Pellegrini, Jens Kuhle, Pascal Benkert, Suvitha Subramaniam, Sabine Schaedelin, Cynthia Iglesias, Andrea Manca, Konstantina Chalkou, Georgia Salanti

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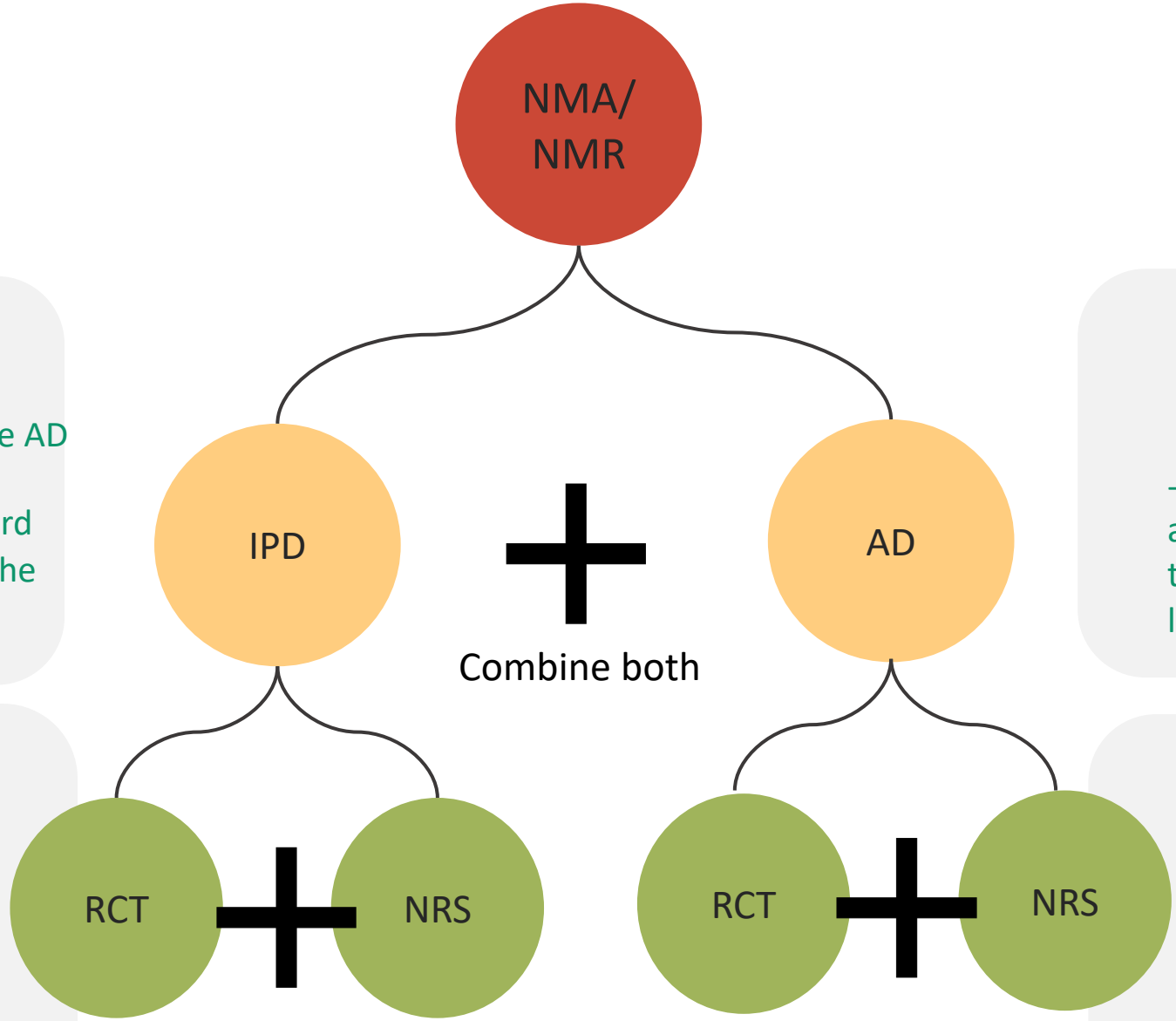


- Lengthy process, increased costs
- Inability to include IPD from all trials

- Overcome the AD shortcomings
- a gold standard
- Standardize the analysis

- Idealized settings
- Restricted inclusion criteria
- Limit generalizability

- 'Low' Bias
- Most reliable

- Data is accessible in the published literature

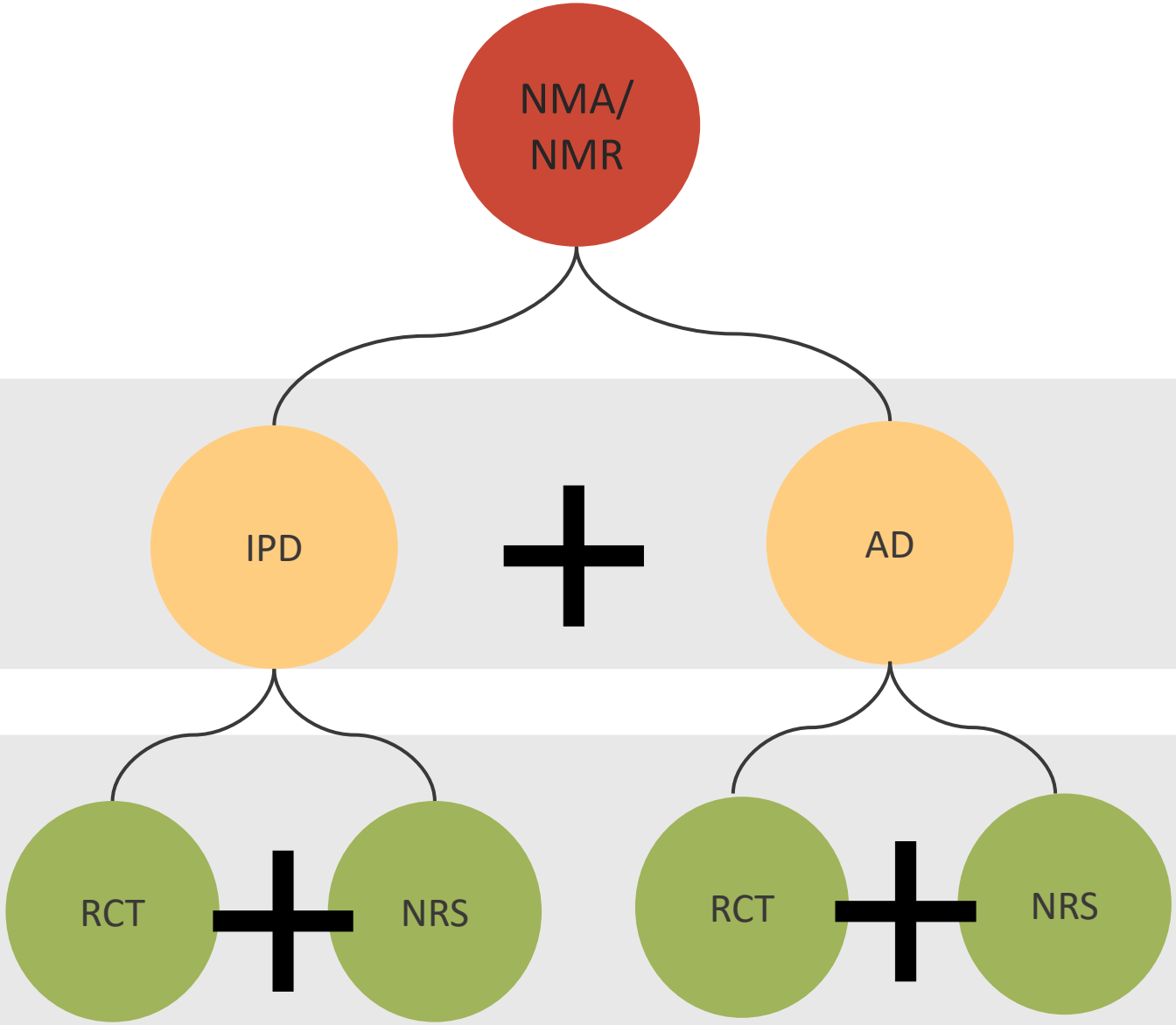
- Heterogeneity across trials
- meta-regression on aggregate information
- Ecological bias

- More available
- Reflect the reality

- Bias
- Confounders are not addressed
- Concern about transitivity and consistency

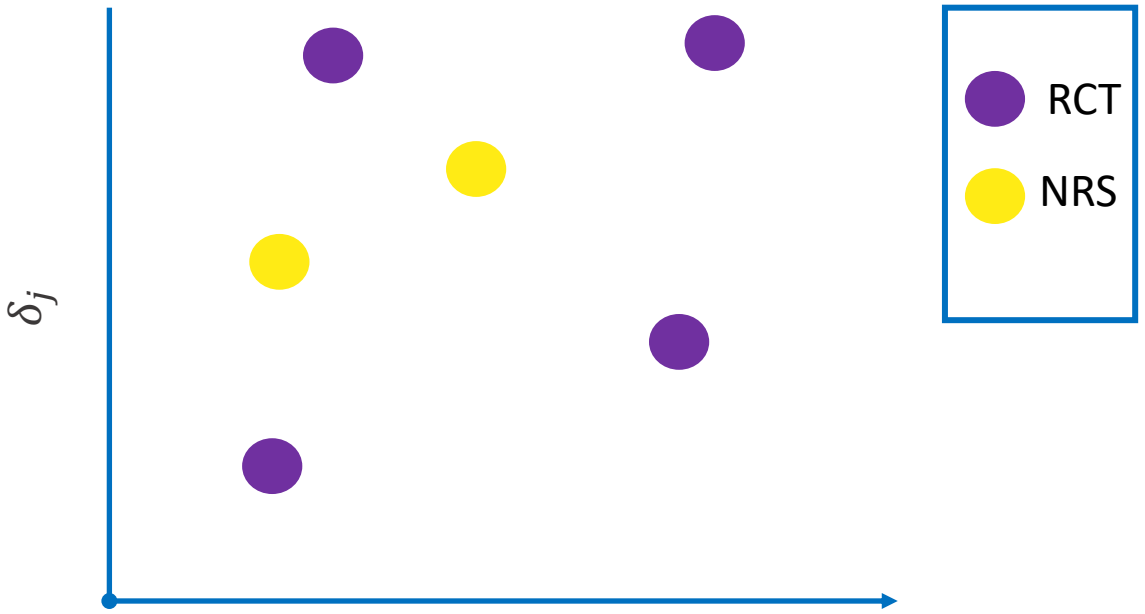
- Three level hierarchical model

1. naive
2. Bias adjustment 1
3. Bias adjustment 2
4. Use NRS as a prior



1. Cross NMR model naive

Treatment effect in study j: δ_j



AD RCT and NRS

For j study with k treatment

$$r_{jk} \sim Bin(p_{jk}, n_{jk})$$
$$\text{logit}\,(p_{jk}) = u_{jb} + \beta^{B}_{2,bk}\bar{x_j} + \delta_{jbk}$$

IPD RCT and NRS

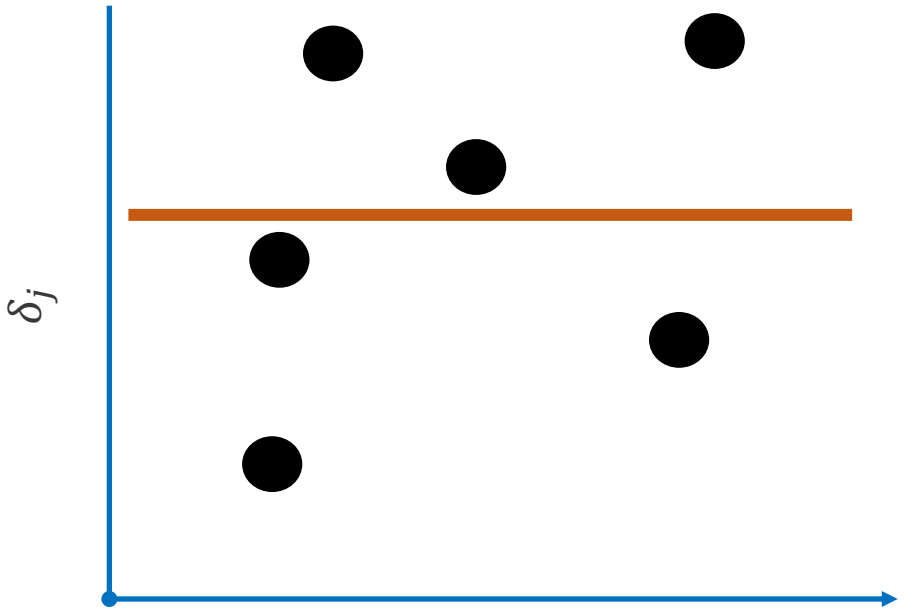
For i individual in j study with k treatment

$$y_{ijk} \sim Bernoulli(p_{ijk})$$
$$\text{logit}(p_{ijk}) = u_{jb} + \beta_{1j}x_{ij} + \beta^{W}_{2,bk}(x_{ij} - \bar{x}_j) + \beta^{B}_{2,bk}\bar{x_j} + \delta_{jbk}$$

1. Cross NMR model naive

Combine AD and IPD

Treatment effect in study j: δ_j



$$\delta_{jbk} \sim N(d_{Ak} - d_{Ab}, \tau^2),$$

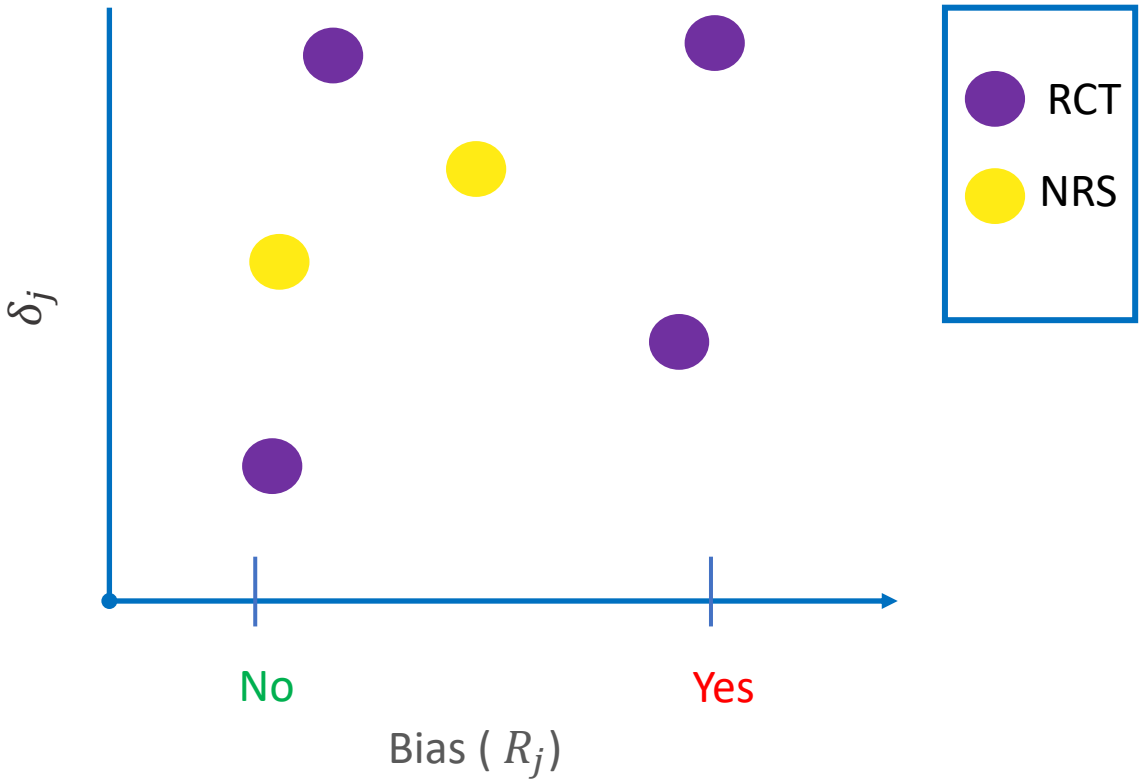
$$\beta^B_{2,bk} \sim N(B^B_{Ak} - B^B_{Ab}, \sigma^2_B),$$

$$\beta^W_{2,bk} \sim N(B^W_{Ak} - B^W_{Ab}, \sigma^2_W),$$

$$u_{jb}, \beta_{1j} \sim N(0, 10^2)$$

2. Cross NMR model adjust1

$$\delta_j + \gamma_j R_j$$



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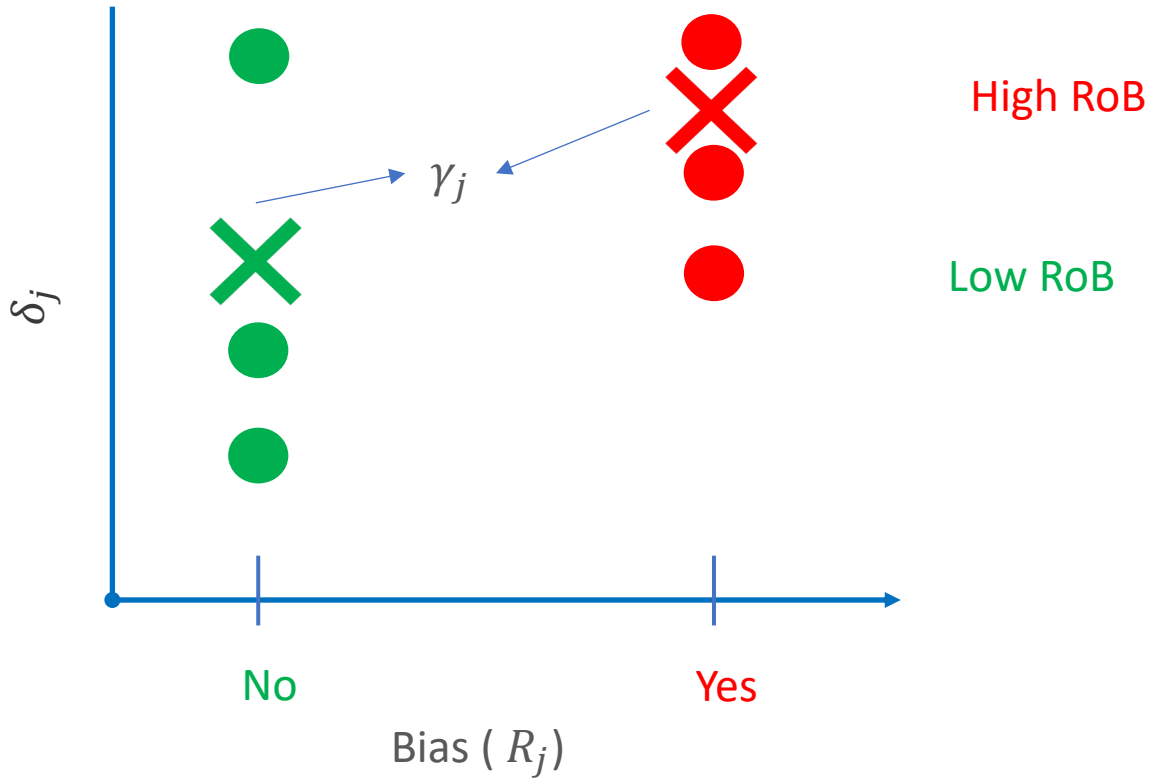

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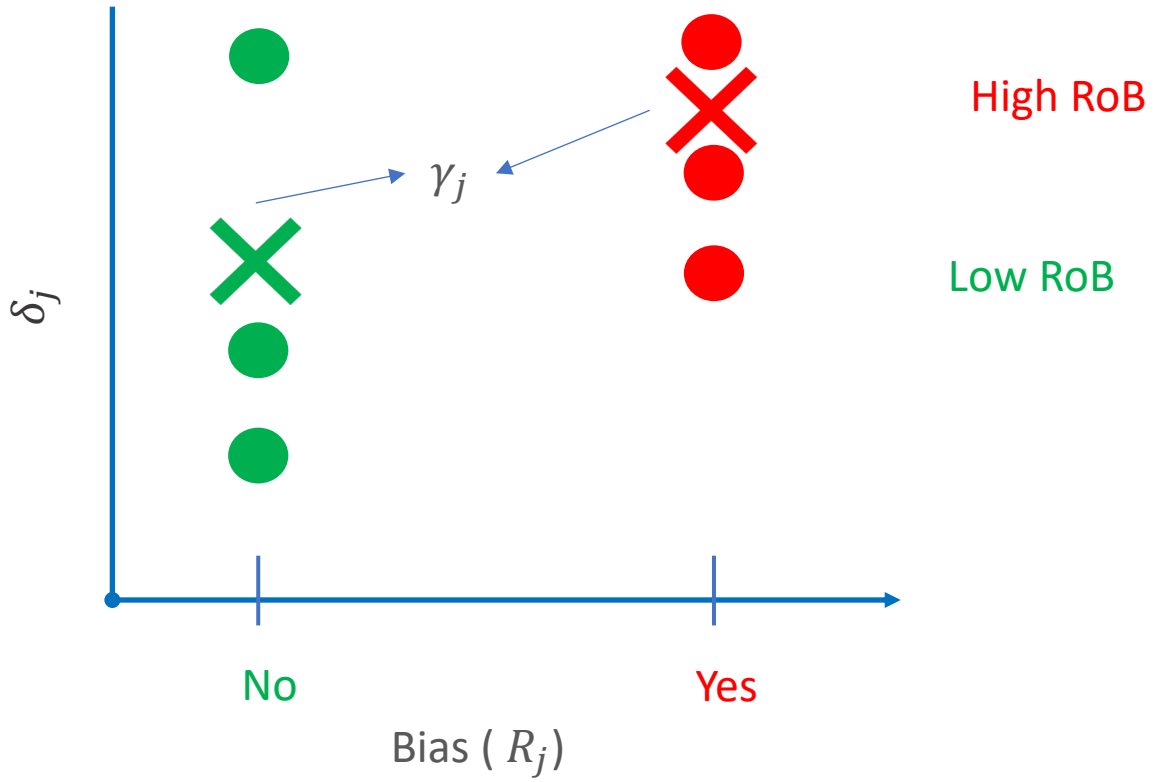


High RoB

Low RoB

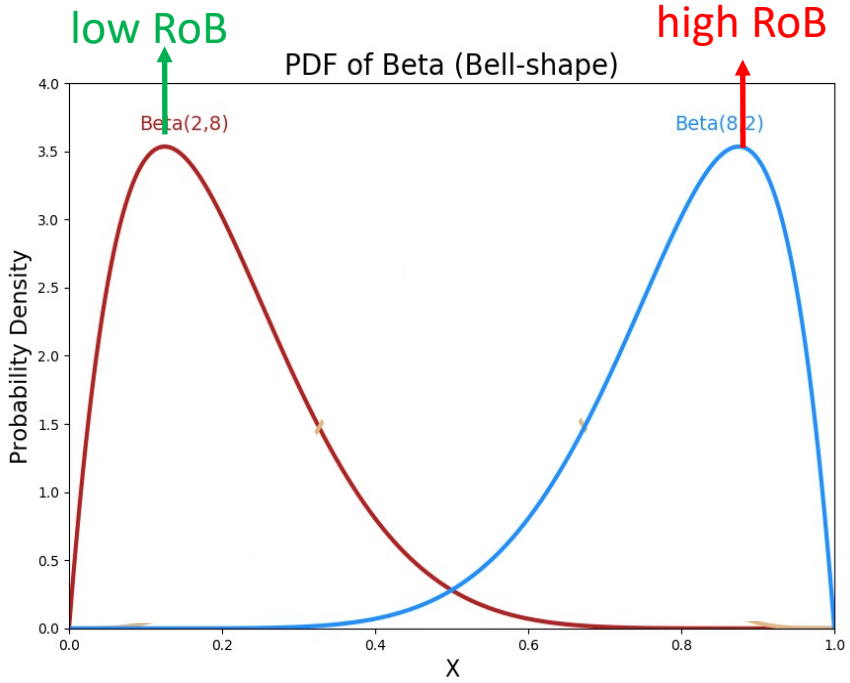
Bias assumptions

1. Bias effect: $\gamma_j \sim N(\Gamma, \sigma_\Gamma^2)$, $\gamma_j = \Gamma$
2. Bias indicator R_j:

We use the data from RoB tool
Either directly (high=Yes ($R_j = 1$), low=No ($R_j = 0$))
→ RoB is subjective, uncertainty

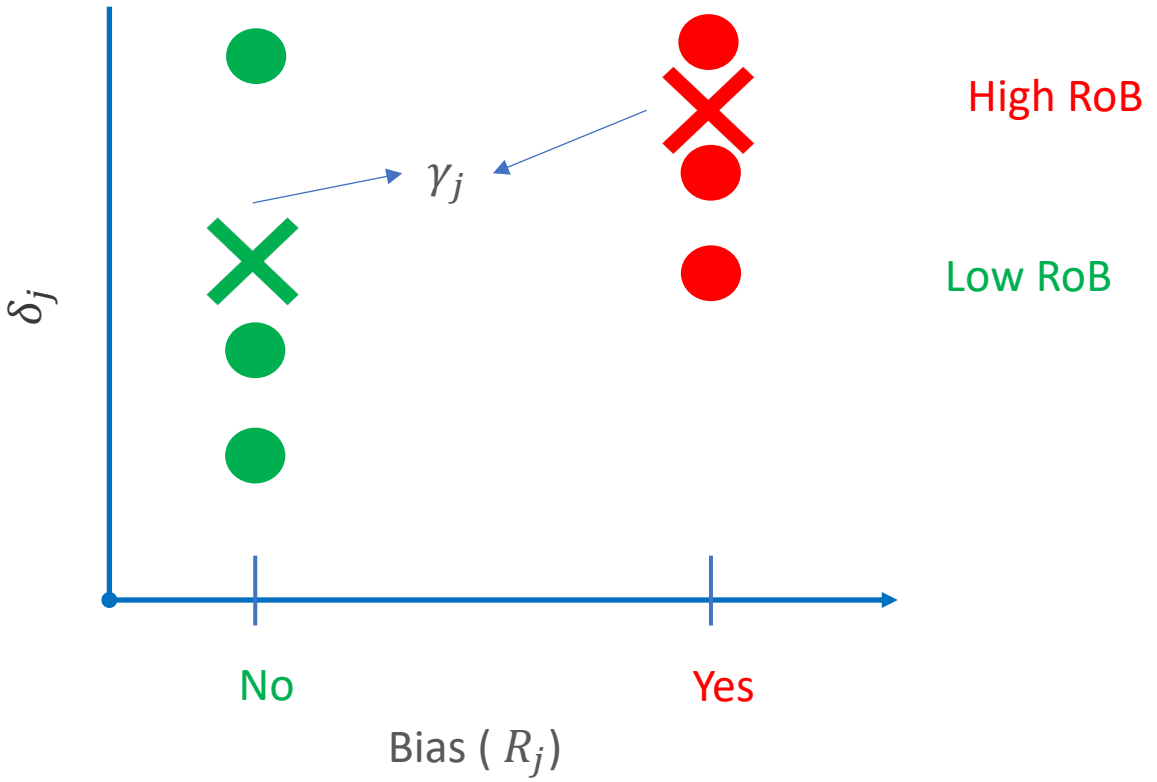
Give distributions

$$R_j \sim Bern(\pi_j), \pi_j \sim Beta(a, b)$$



2. Cross NMR model adjust1

$\delta_j + \gamma_j R_j$



Bias assumptions

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2. Bias indicator R_j:

We use the data from RoB tool
Either directly (high=Yes ($R_j = 1$), low=No ($R_j = 0$))
→ RoB is subjective, uncertainty

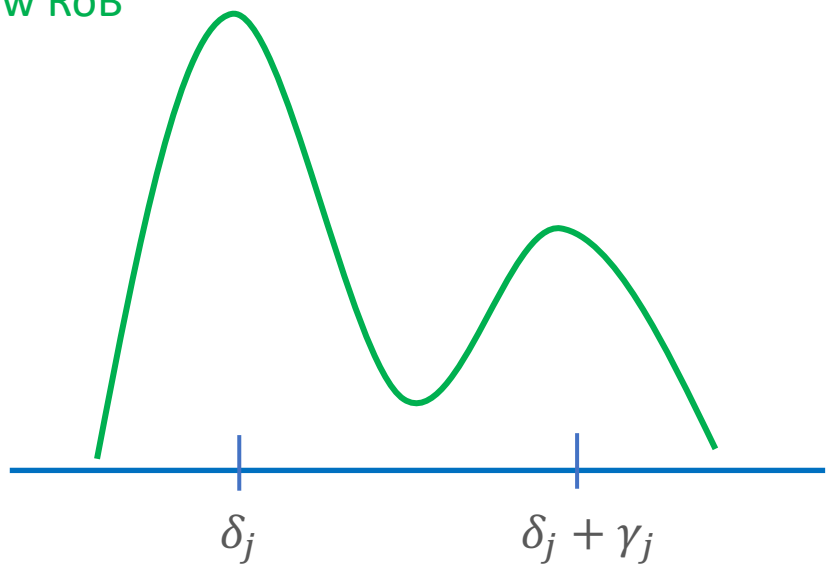
2. Use study characteristics'

$$logit(\pi_j) = a + b * z$$

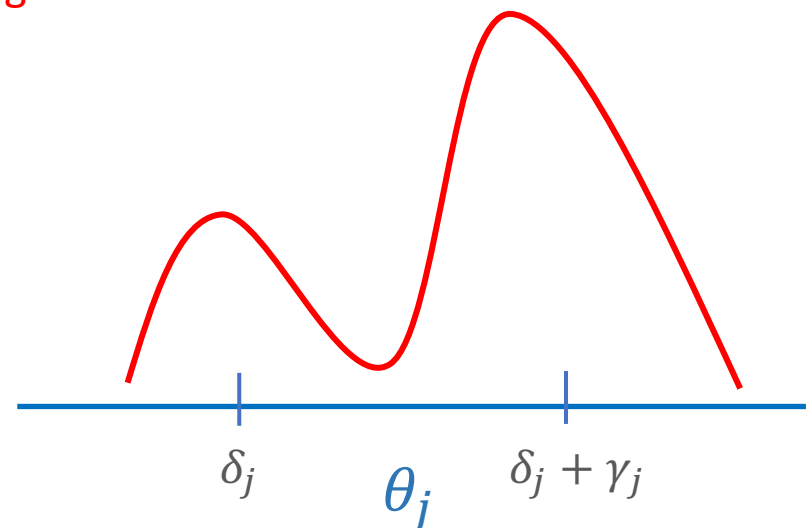
3. Cross NMR model adjust2

$$\theta_{jbk} \sim \pi_j N(\delta_{jbk}, \tau^2) + (1-\pi_j) N(\delta_{jbk} + \gamma_j, \tau^2 + \tau_I^2)$$

low RoB



high RoB



AD RCT and NRS

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$$\text{logit}\,(p_{jk}) = u_{jb} + \beta_{2,bk}^{B} \bar{x}_j + \theta_{jbk}$$

IPD RCT and NRS

For i individual in j study with k treatment

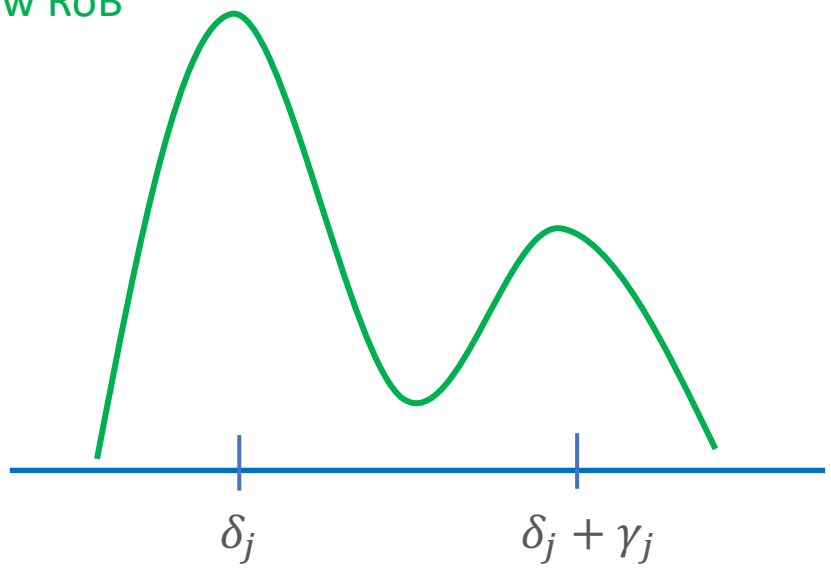
$$y_{ijk} \sim Bernoulli(p_{ijk})$$

$$\text{logit}(p_{ijk}) = u_{jb} + \beta_{1j} x_{ij} + \beta_{2,bk}^{W}(x_{ij} - \bar{x}_j) + \beta_{2,bk}^{B} \bar{x}_j + \delta_{jbk} + \theta_{jbk}$$

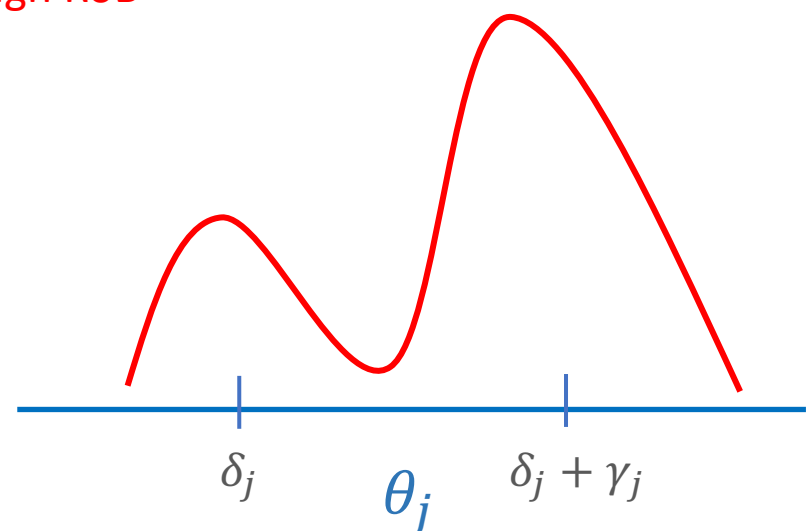
3. Cross NMR model adjust2

$$\theta_{jbk} \sim \pi_j N(\delta_{jbk}, \tau^2) + (1-\pi_j) N(\delta_{jbk} + \gamma_j, \tau^2 + \tau_\Gamma^2)$$

low RoB



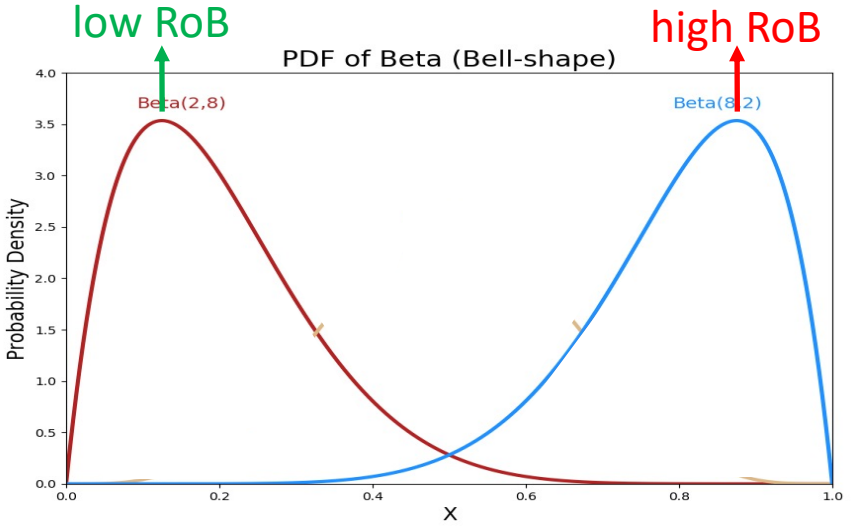
high RoB



How do we find the weight of each peak, π_j?

1. Give distributions

$$\pi_j \sim Beta(a, b)$$

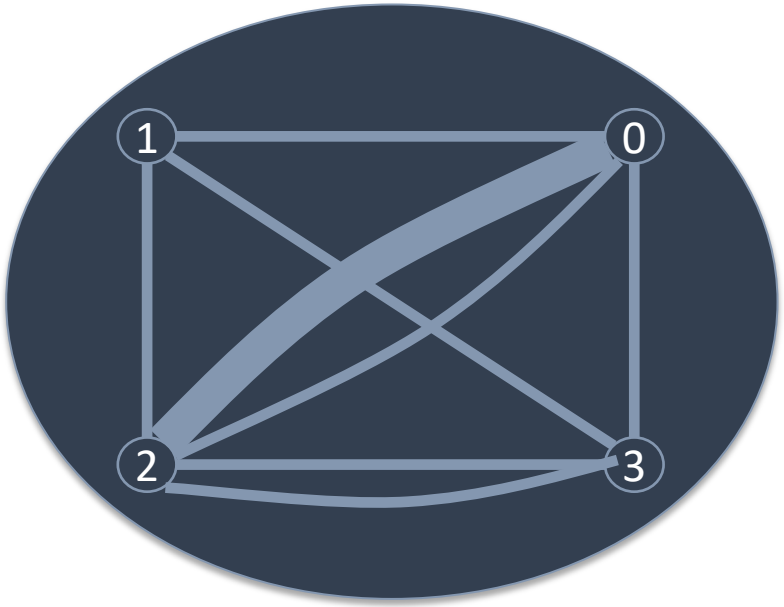


2. Use study characteristics'

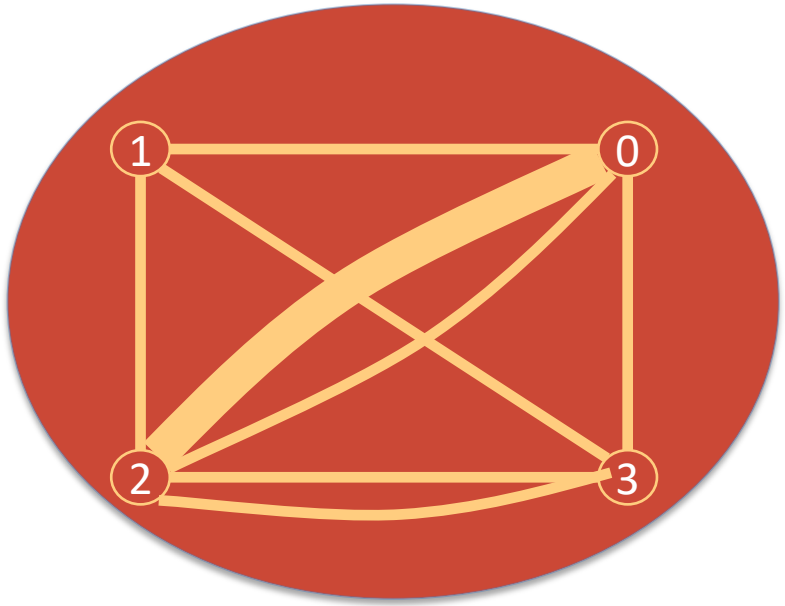
$$logit(\pi_j) = a + b * z$$

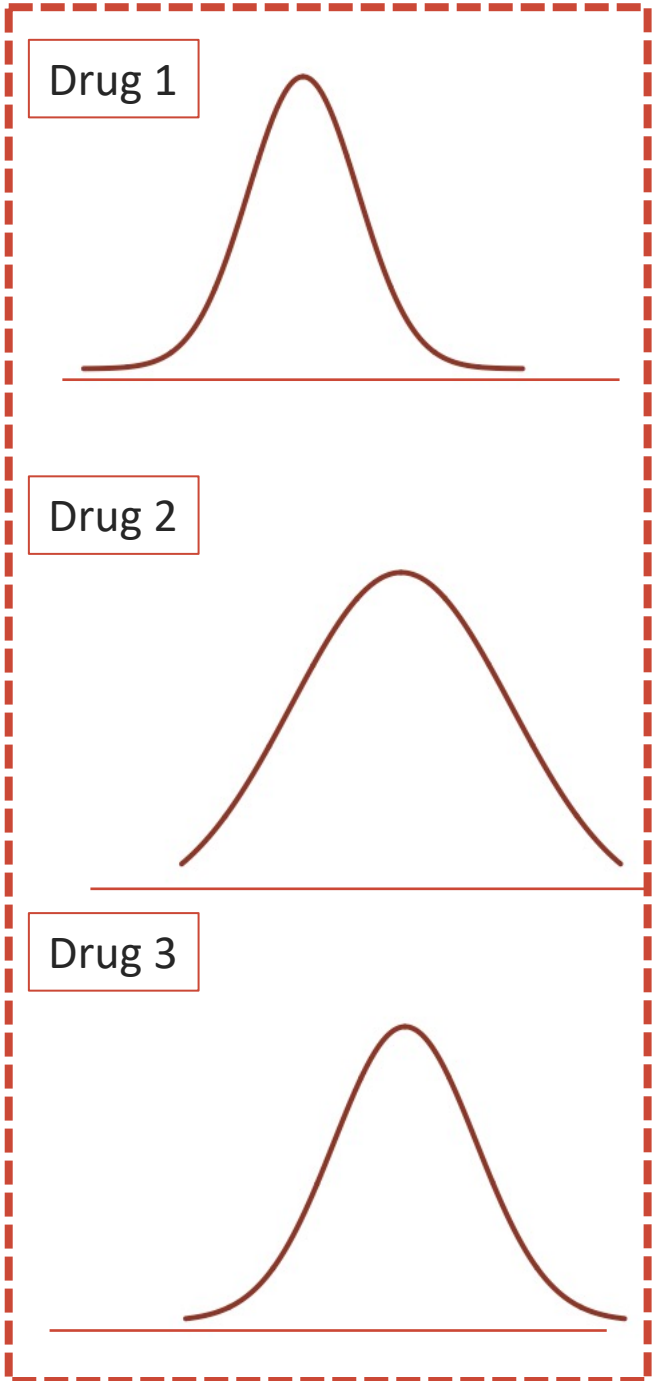
4. Cross NMR model prior

2. Conduct MA/NMA for RCTs with NRS as prior



1. Conduct MA/NMA only with NRS

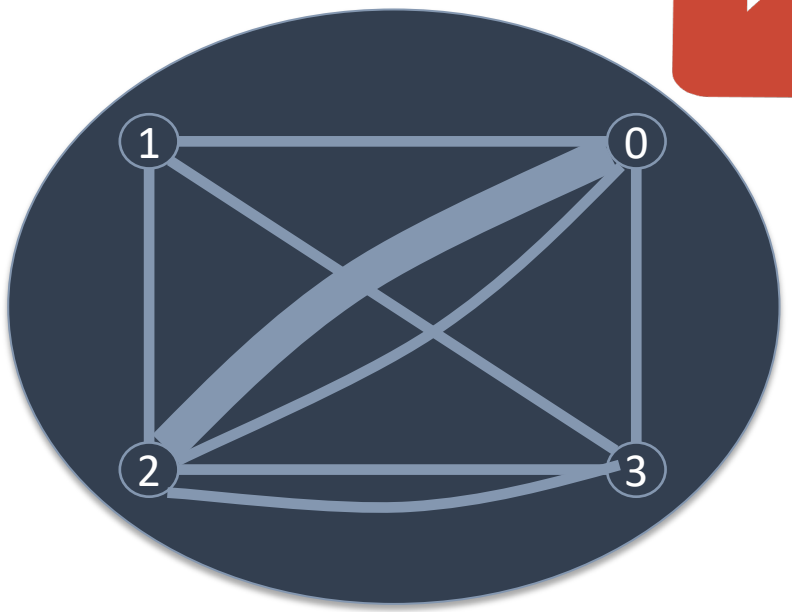


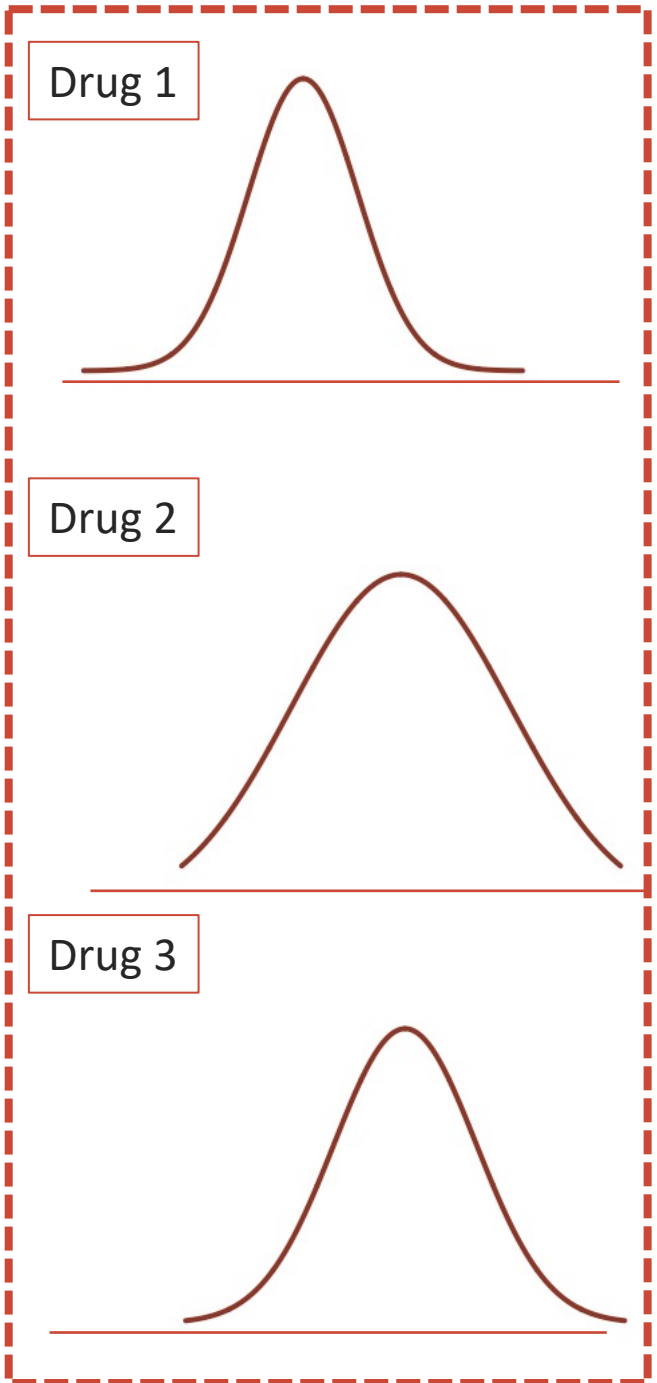


4. Cross NMR model prior

$$d_k \sim \mathrm{N}\left(d_k^{NRS}, V^{NRS}\right)$$

2. Conduct MA/NMA for RCTs with NRS as prior

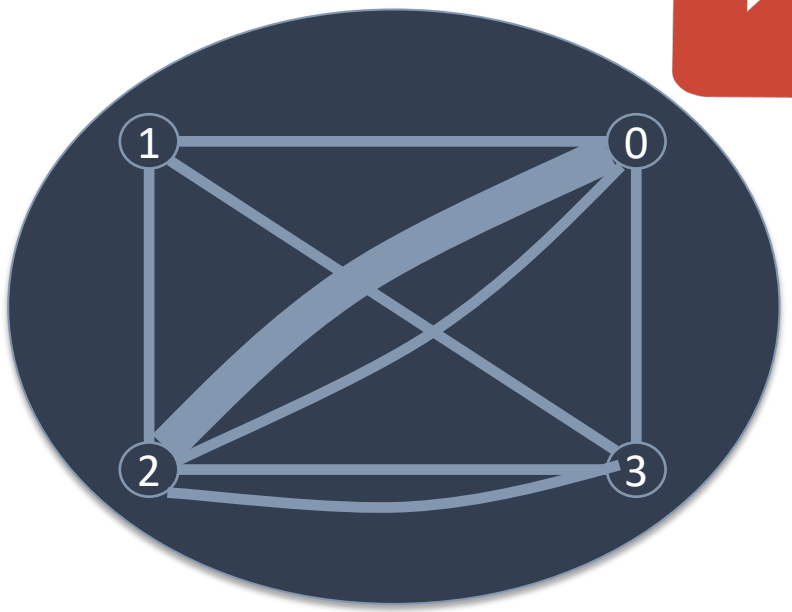


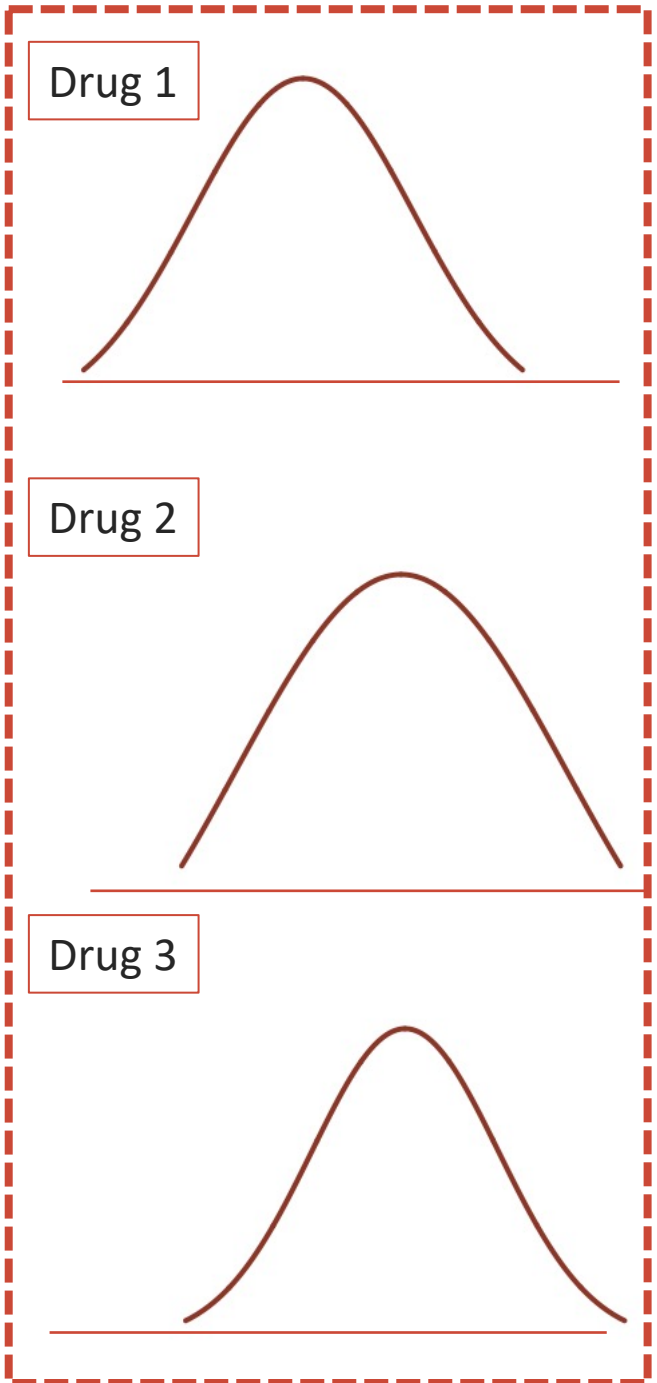


4. Cross NMR model prior

$$d_k \sim \mathrm{N}\left(d_k^{NRS}, V^{NRS}/w\right)$$

2. Conduct MA/NMA for RCTs with NRS as prior





crosnma library

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crosnma to synthesize cross-design evidence and cross-format data using network meta-analysis

Tasnim Hamza and Georgia Salanti

2021-06-23


```
library(crosnma)
library(rjags)
#> Loading required package: coda
#> Linked to JAGS 4.3.0
#> Loaded modules: basemod,bugs
load.module('mix')
#> module mix loaded
```

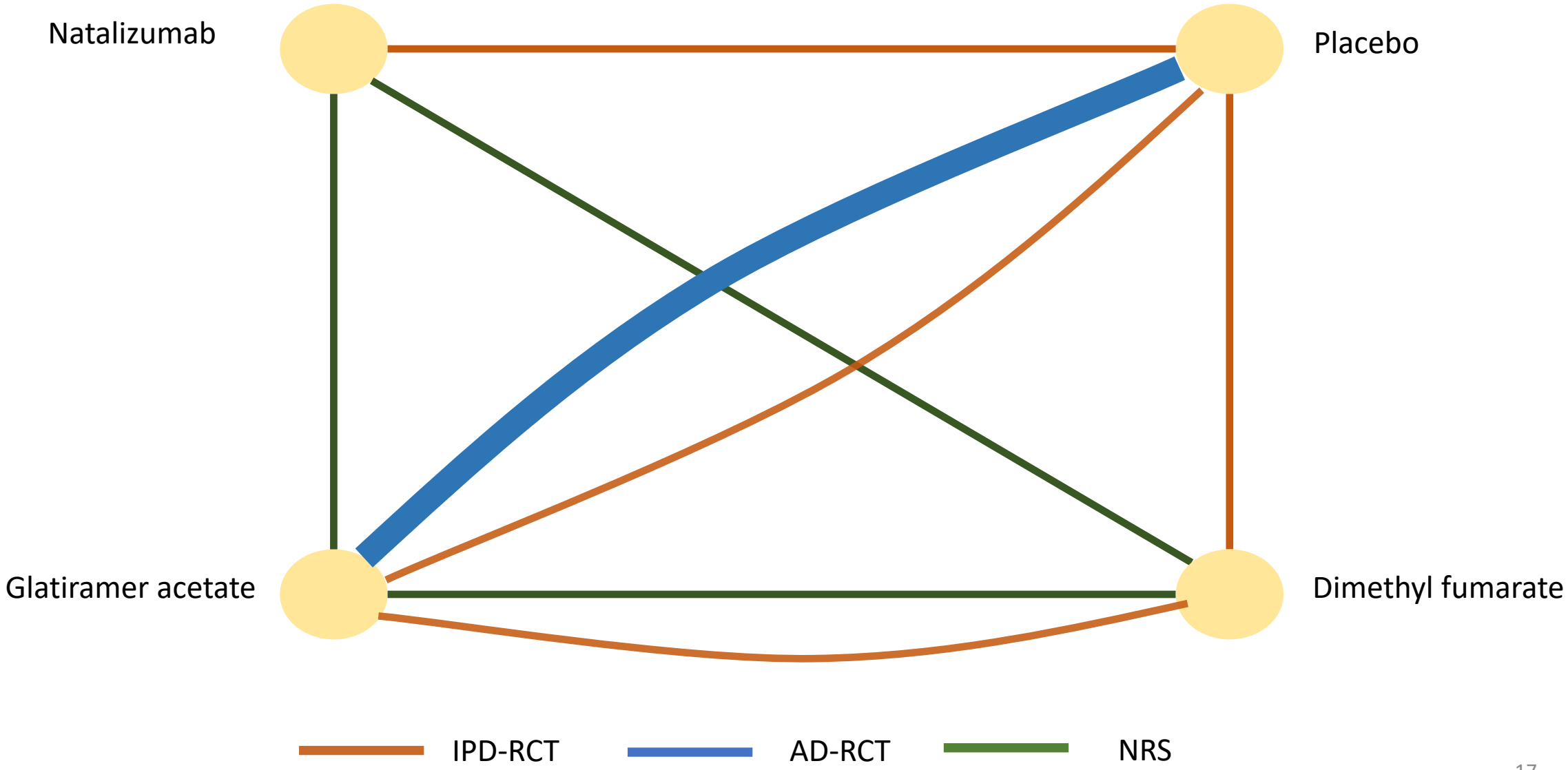
1 Introduction

Case study

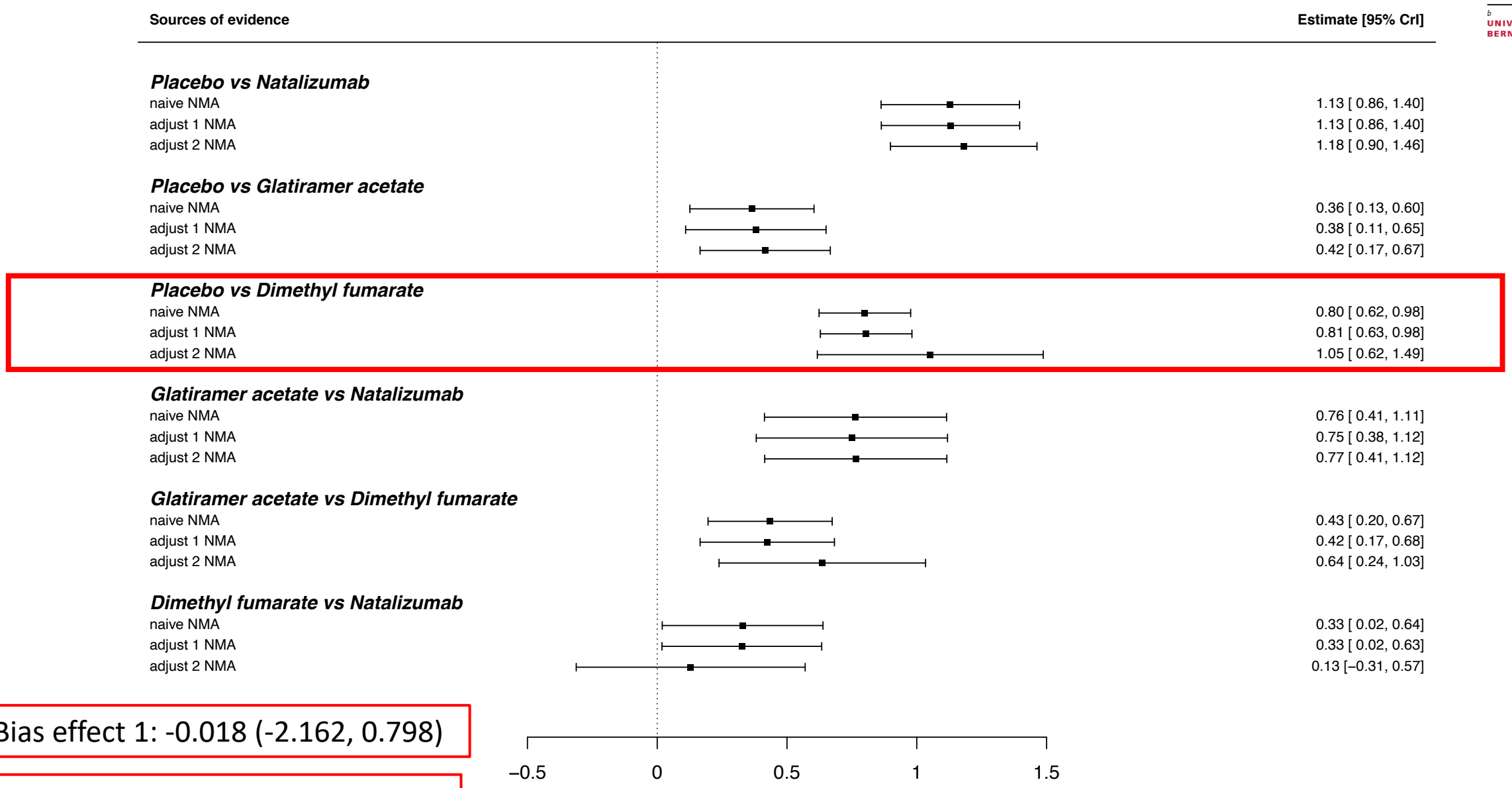
- Relapsing remitting multiple sclerosis (RRMS)
- Binary outcome: relapse in 2 years (0/1)
- Covariate: age

Study	Type of data	Treatment compared	Design/RoB	Sample size
DEFINE	IPD	Dimethyl fumarate Placebo	RCT/high risk	1234
CONFIRM	IPD	Dimethyl fumarate Glatiramer acetate Placebo	RCT/high risk	1417
AFFIRM	IPD	Natalizumab Placebo	RCT/low risk	939
Bornstein	AD	Glatiramer acetate Placebo	RCT/high risk	50
Johnson	AD	Glatiramer acetate Placebo	RCT/unclear risk	251
Swiss cohort	IPD	All/placebo	NRS/high risk	290

Network diagram



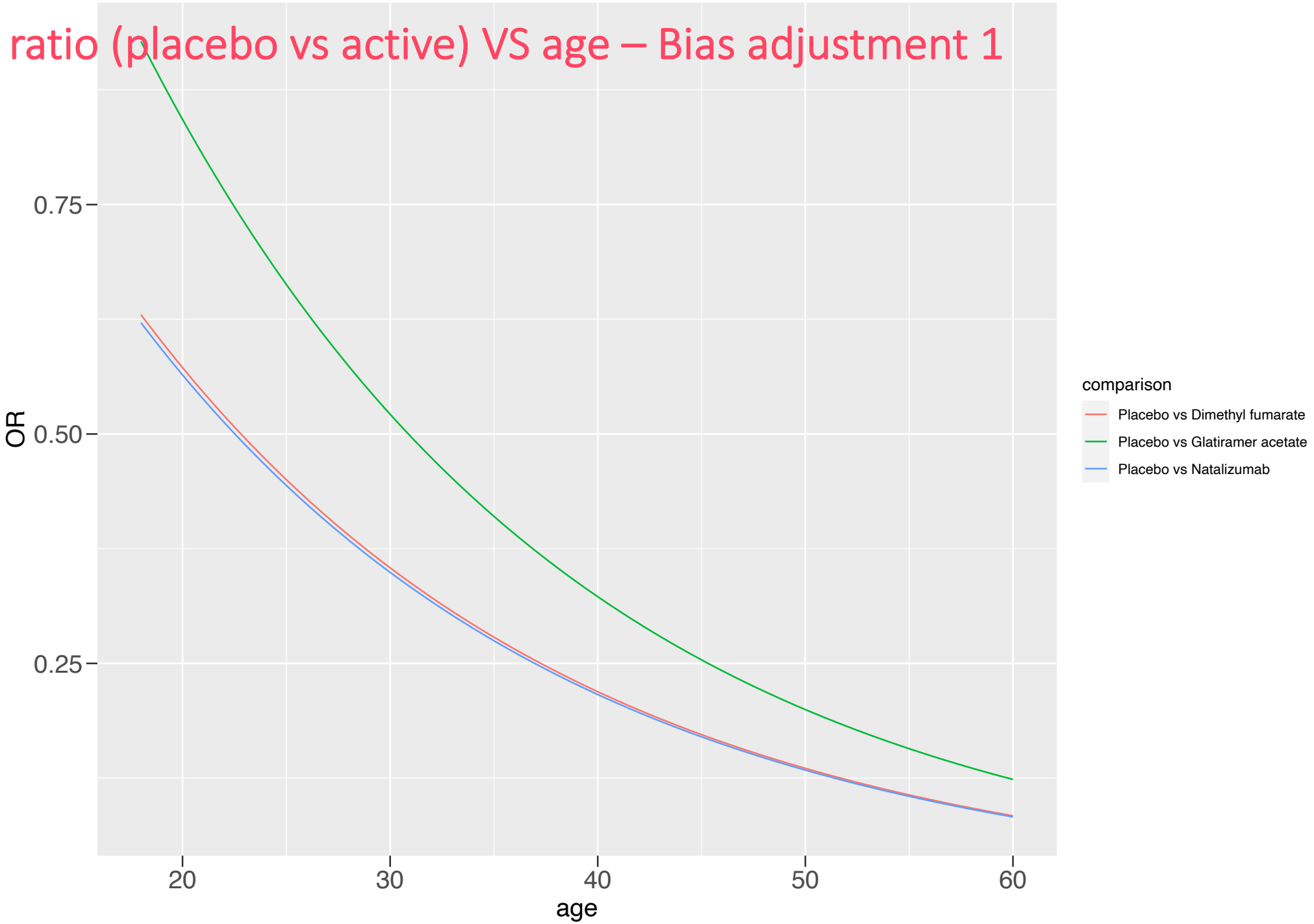
Results of RRMS analysis



Bias effect 1: -0.018 (-2.162, 0.798)

Bias effect 2: -0.231 (-0.594, 0.140)

Odds ratio (placebo vs active) VS age – Bias adjustment 1



Summary

- Introduce 4 cross NMA/NMR framework approaches
- All models are implemented in a new R package: crosnma
- Apply the models on a network of drugs about RRMS
- We have to acknowledge the differences between RCT and NRS
- The models need to be investigated further in larger networks

References

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