Flexible generic framework for evidence synthesis in health technology assessment using network meta-analysis

Presented by: Tasnim Hamza

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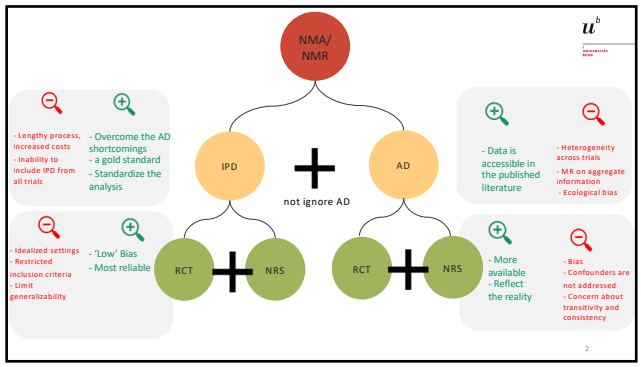

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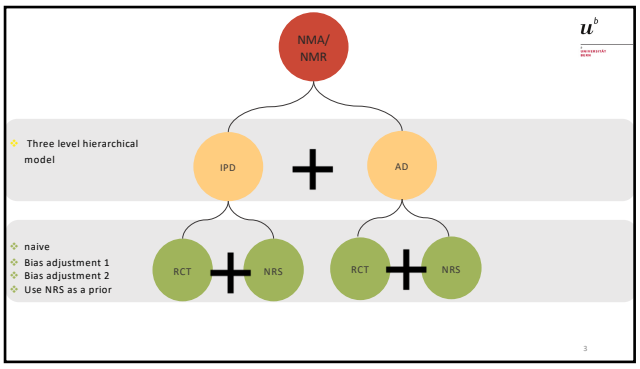

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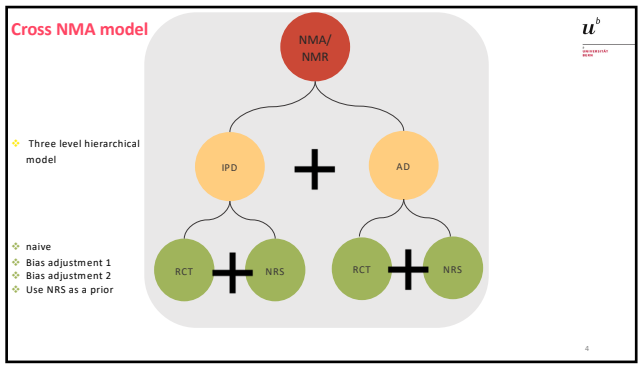

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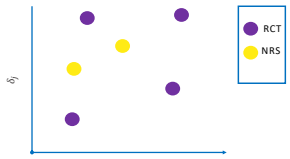
Cross NMR model naive

Treatment effect in study j: δ_j



AD RCT and NRS

For j study with k treatment

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

IPD RCT and NRS

For i individual in j study with k treatment

$$y_{ijk} \sim Bernoulli(p_{ijk})$$
$$\text{logit}(p_{ijk}) = u_{jb} + \beta_{1j} x_{ij} + \beta^W_{2,bk}(x_{ij} - x_j) + \beta^B_{2,bk} x_j + \delta_{jbk}$$

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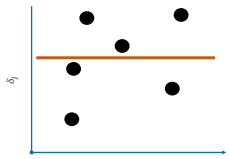
Cross NMR model naive

Treatment effect in study j: δ_j



Combine AD and IPD

$$\delta_{jbk} \sim N(d_{Ak} - d_{Ab}, \tau^2),$$
$$\beta^B_{2,bk} \sim N(B^B_{Ak} - B^B_{Ab}, \sigma^2_B),$$
$$\beta^W_{2,bk} \sim N(B^W_{Ak} - B^W_{Ab}, \sigma^2_W),$$
$$u_{jb}, \beta_{1j} \sim N(0, 10^2)$$

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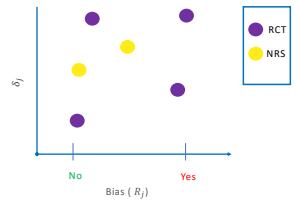
Cross NMR model adjust1

$\delta_j + \gamma_j R_j$



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Cross NMR model adjust1

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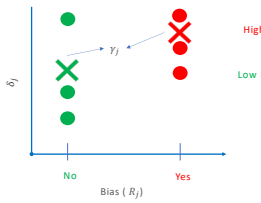

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$$y_{ijk} \sim Bernoulli(p_{ijk})$$
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Cross NMR model adjust1

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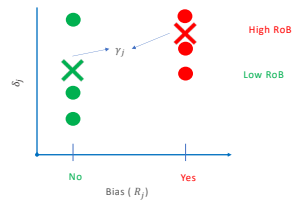


Bias assumptions

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

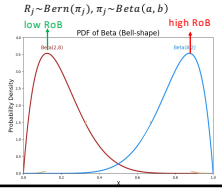
Either directly (high=Yes ($R_j = 1$), low=No ($R_j = 0$))

→ RoB is subjective, uncertainty

Give distributions

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

low RoB — high RoB



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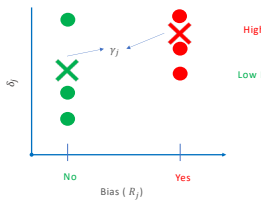
Cross NMR model adjust1

$\delta_j + \gamma_j R_j$



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

2. Use study characteristics'

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

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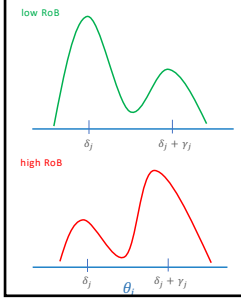
Cross NMR model adjust2

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



AD RCT and NRS

For j study with k treatment

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

IPD RCT and NRS

For i individual in j study with k treatment

$$y_{ijk} \sim Bernoulli(p_{ijk})$$
$$\text{logit}(p_{ijk}) = u_{jb} + \beta_{1j} x_{ij} + \beta^W_{2,bk}(x_{ij} - x_j) + \beta^B_{2,bk} x_j + \delta_{jbk} + \theta_{jbk}$$

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Cross NMR model adjust2

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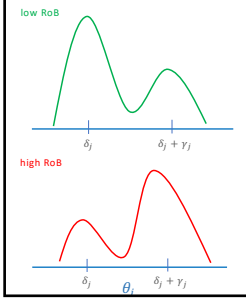
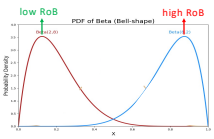


How do we find the weight of each peak, π_j?

1. Give distributions

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

low RoB — high RoB



2. Use study characteristics'

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

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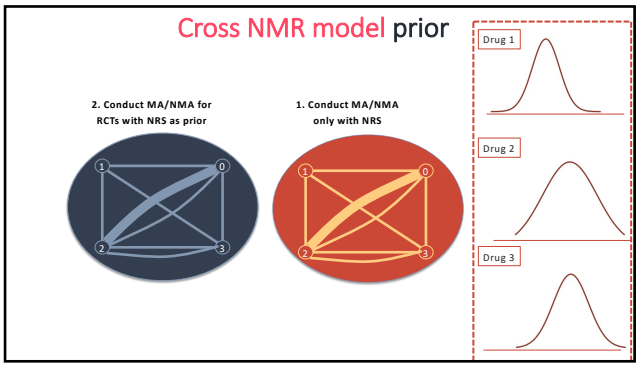
Cross NMR model prior



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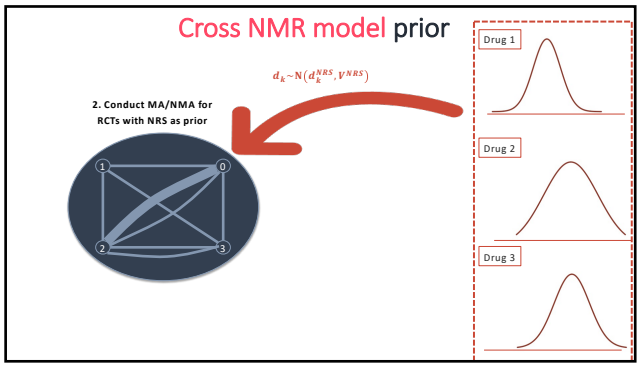
Cross NMR model prior



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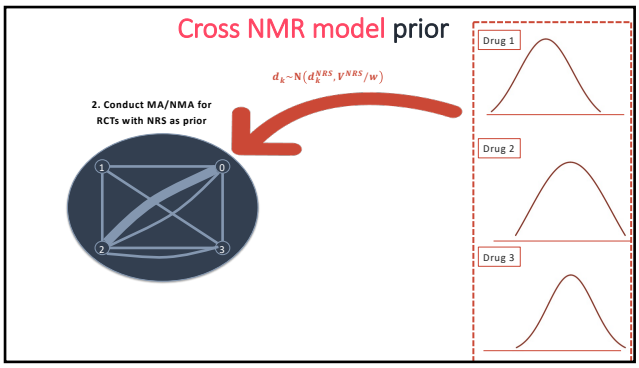
Cross NMR model prior



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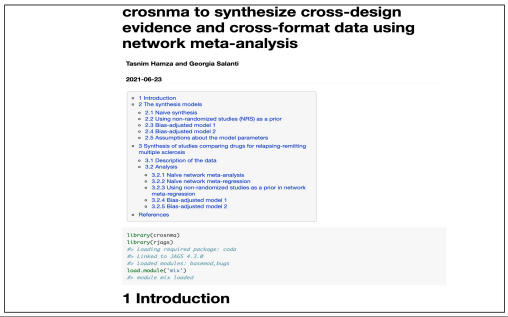
crosnma library



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

Tasnim Hamza and Georgia Salanti

2021-06-23

1 Introduction
2 The synthesis models
2.1 Naive synthesis
2.2 Using non-randomized studies (NRS) as a prior
2.3 Bias-adjusted model 1
2.4 Bias-adjusted model 2
2.5 Assumptions about the model parameters
3 Synthesis of studies comparing drugs for relapsing-remitting multiple sclerosis
3.1 Description of the data
3.2 Analysis
3.2.1 Naive network meta-analysis
3.2.2 Naive network meta-regression
3.2.3 Using non-randomized studies as a prior in network meta-regression
3.2.4 Bias-adjusted model 1
3.2.5 Bias-adjusted model 2
References


```
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

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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	Probability of risk	Sample size
DEFINE	IPD	Dimethyl fumarate Placebo	RCT/high risk	Beta(3,1)	1234
CONFIRM	IPD	Dimethyl fumarate Glatiramer acetate Placebo	RCT/high risk	Beta(3,1)	1417
AFFIRM	IPD	Natalizumab Placebo	RCT/low risk	Beta(1,20)	939
Bornstein	AD	Glatiramer acetate Placebo	RCT/high risk	Beta(3,1)	50
Johnson	AD	Glatiramer acetate Placebo	RCT/unclear risk	Beta(1,1)	251
Swiss cohort	IPD	All/placebo	NRS/high risk	Beta(30,1)	290

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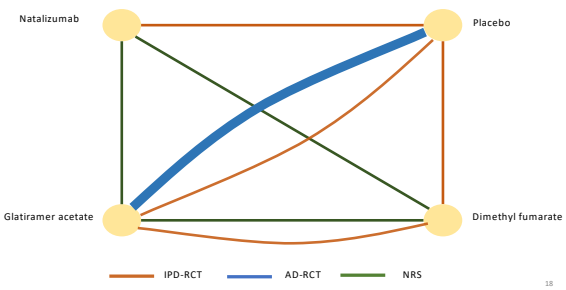
Network diagram



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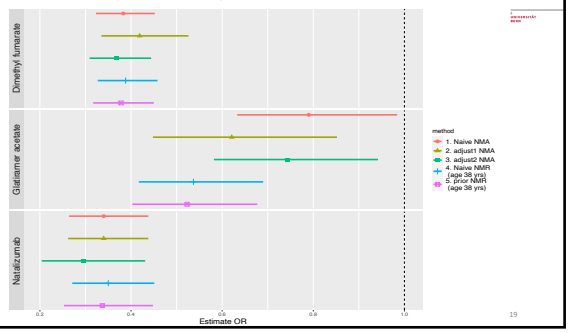
Results of RRMS analysis (active vs placebo)



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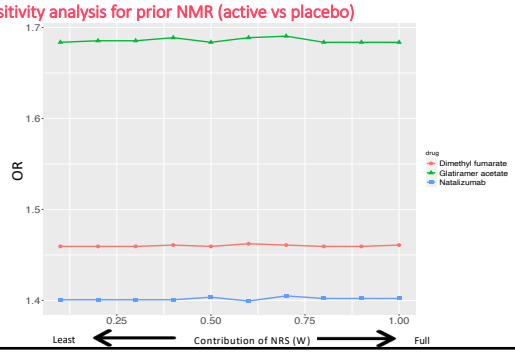
Sensitivity analysis for prior NMR (active vs placebo)



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Summary

- Introduce 4 cross NMA/NMR framework approaches
- All models are implemented in a new R package: crossnma
- 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 network

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References

- Dias, Sofia, N. J. Welton, V. C. C. Marinho, G. Salanti, J.P.T Higgins, and A. E. Ades. 2010. "Estimation and Adjustment of Bias in Randomized Evidence by Using Mixed Treatment Comparison Meta-Analysis." *Journal of the Royal Statistical Society* 173: 613–29.
- Verde, Pablo Emilio. 2020. "A Bias-Corrected Meta-Analysis Model for Combining, Studies of Different Types and Quality." *Biometrical Journal. Biometrische Zeitschrift*, September. https://doi.org/10.1002/bimj.201900376.
- Efthimiou O, Mavridis D, Debray TP, Samara M, Belger M, Siontis GC, Leucht S, Salanti G; GetReal Work Package 4. Combining randomized and non-randomized evidence in network meta-analysis. Stat Med. 2017 Apr 15;36(8):1210-1226. doi: 10.1002/sim.7223.

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For questions/comments, please contact me at
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