



## Bayesian dose-response network meta-analysis

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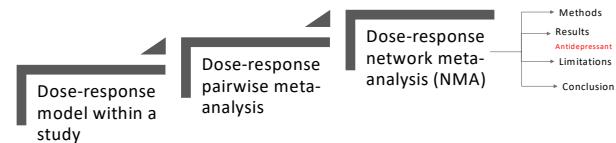
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### Outline



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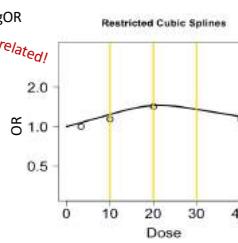
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### Dose-response model within a study

Restricted cubic spline fitted in each non-referral logOR  
 $\text{logOR}_j = \beta_1 \times \text{dose}_j + \beta_2 \times f(\text{dose}_j) + e_j$

dose	OR	logOR	se(logOR)
0	1.00	0.00	NA
3.35	1.00	$\text{logOR}_1 = 0.00$	0.47
10.05	1.14	$\text{logOR}_2 = 0.13$	0.45
20.1	1.43	$\text{logOR}_3 = 0.36$	0.42
40.2	1.14	$\text{logOR}_4 = 0.13$	0.45



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### Dose-response pairwise meta-analysis

#### single hierarchical model

Level 1: within each study

Dose-response

Level 2: across studies

Meta-analysis

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### Dose-response network meta-analysis

Three approaches used so far

1. Lumped NMA  
Drug A in dose 50mg is the same treatment as Drug A in dose 200mg

2. Splitted NMA  
Drug A in dose 50mg is a different treatment from Drug A in dose 200mg

3. Mawdsley et. al 2016 approach  

- Allow dose-response modelling within NMA (Bayesian)
- Emax model and linear model as a dose-response relationship
- MBNMAdose package

Our contribution:

- Extension to Mawdsley et. al 2016
- Restricted cubic spline as a dose-response relationship
- Network meta-regression
- Shiny App

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### Methods – standard NMA model

Steps 1-3

In a study  $i$  with dose  $j$  in treatment  $k$ ,

- Binomial likelihood:** for the observed events  $r_{ijk}$  with probability  $p_{ijk}$  and total number of observations  $n_{ijk}$

$$r_{ijk} \sim \text{Bin}(n_{ijk}, p_{ijk})$$

2. **Logistic transformation**

$$\text{logit}(p_{ijk}) = \begin{cases} u_i & \text{if } k = b \\ u_i + \delta_{ik} & \text{if } k \neq b \end{cases}$$

3. **Exchangeable relative treatment effects**

$$\delta_{ibk} \sim N(d_{ibk}, \tau^2)$$

Steps 4-5

4. **Consistency equation**

$$d_{ibk} = d_{ik} - d_{ib}$$

$$d_{bb} = 0$$

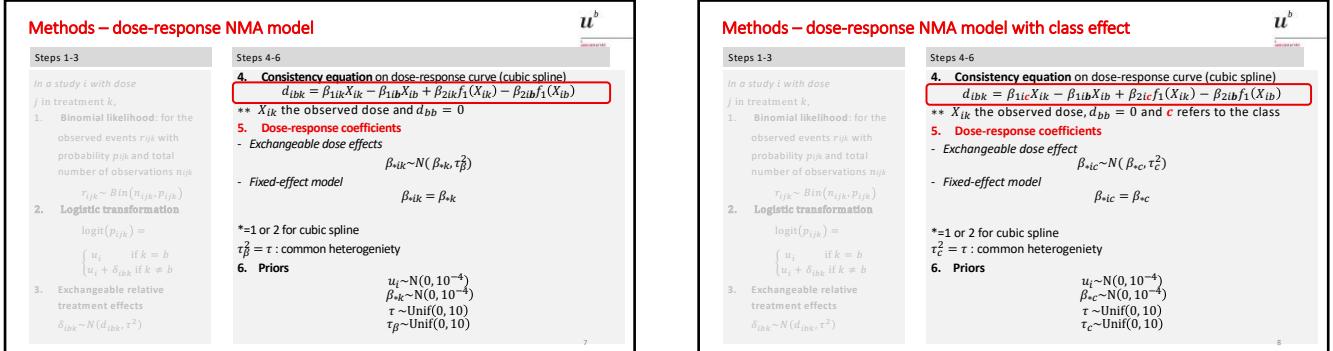
5. **Priors**

$$u_i \sim N(0, 10^{-4})$$

$$d_k \sim N(0, 10^{-4})$$

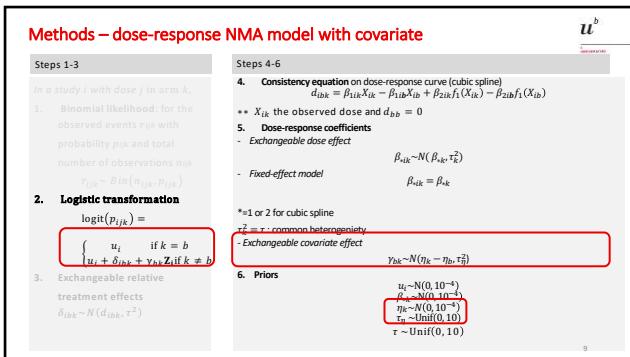
$$\tau \sim \text{Unif}(0, 10)$$

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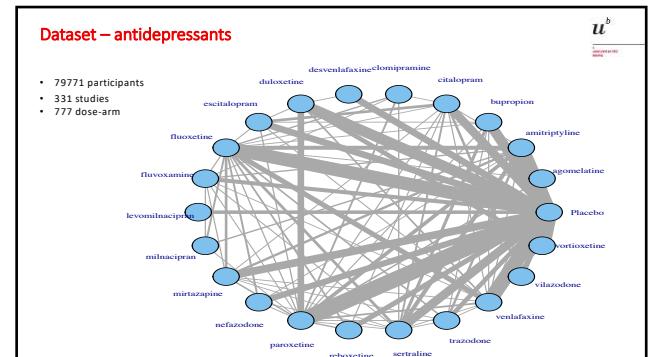


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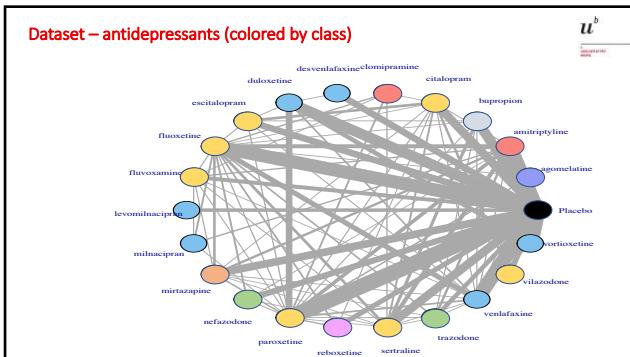
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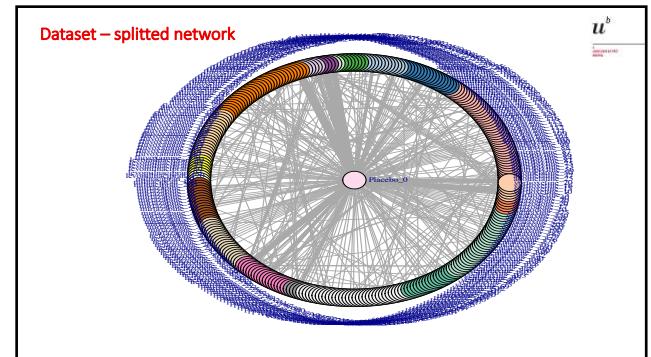
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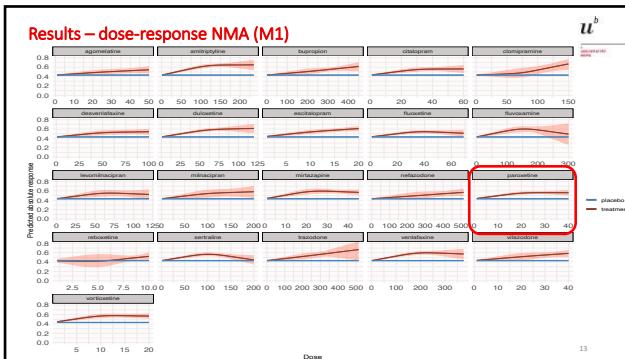
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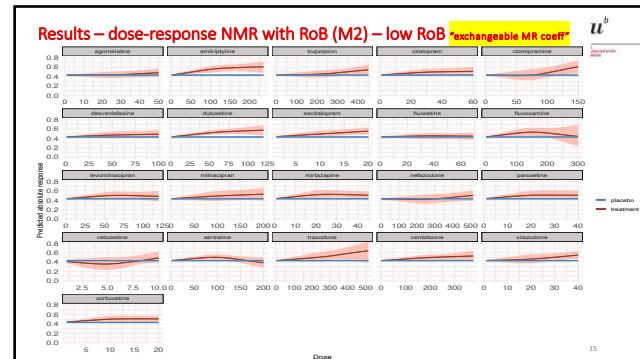
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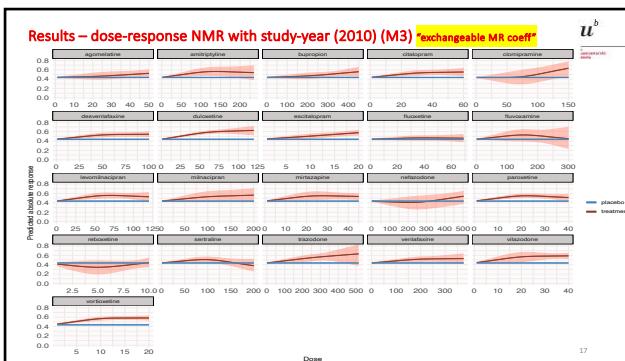
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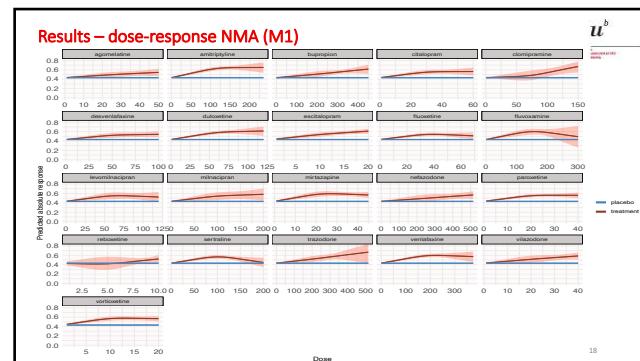
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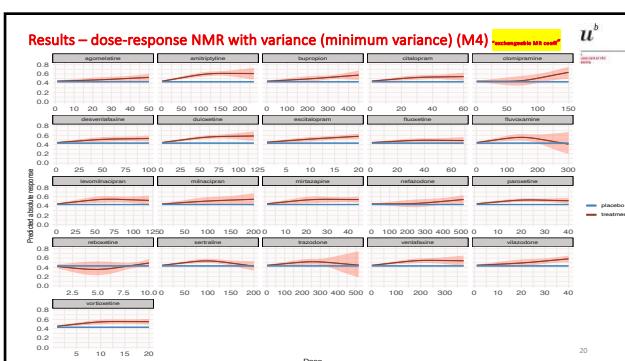
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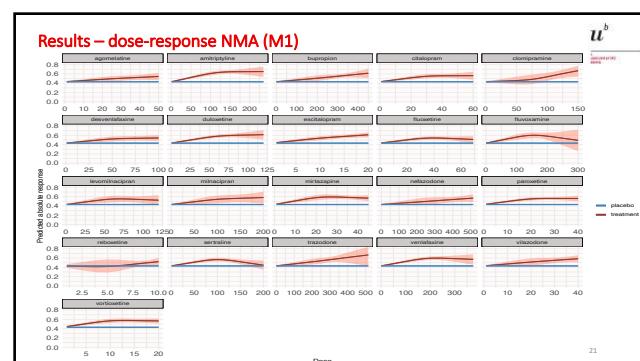
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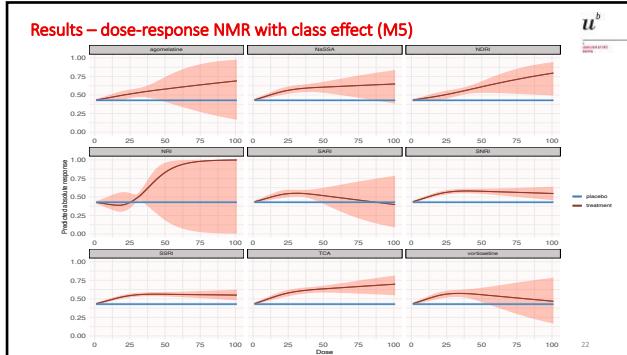
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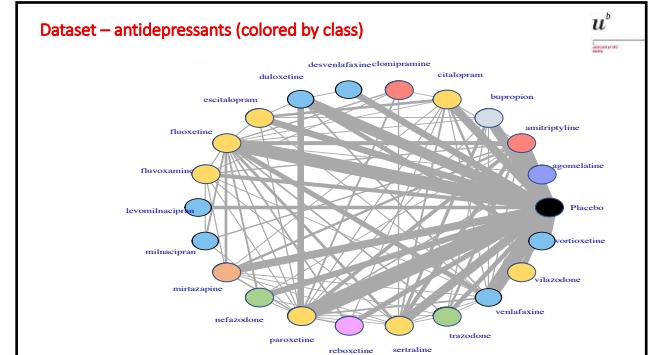
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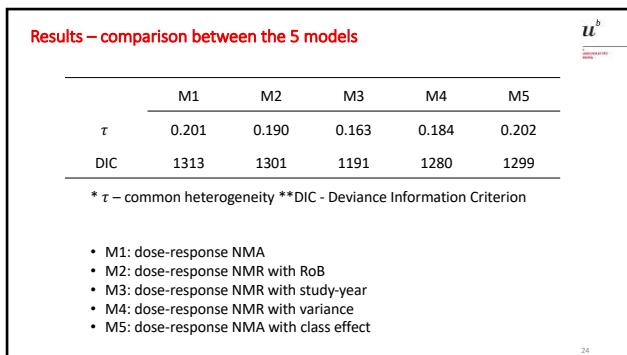
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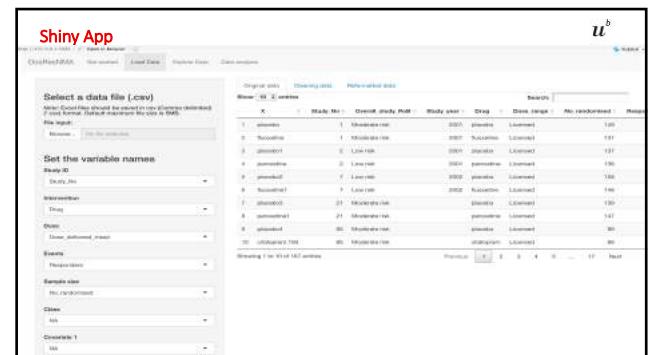
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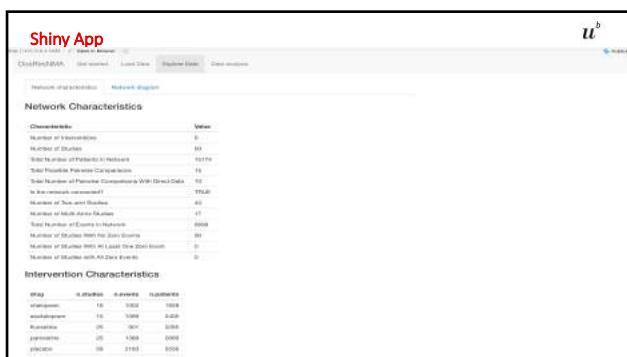
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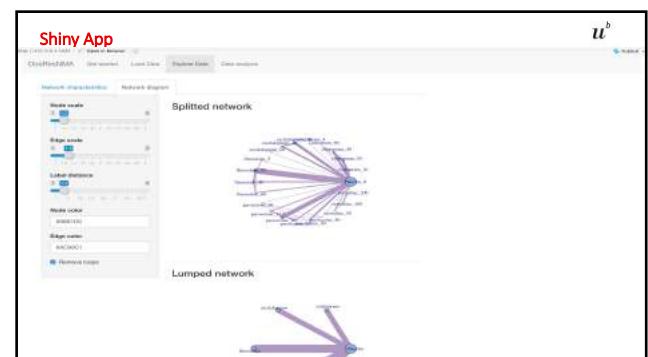
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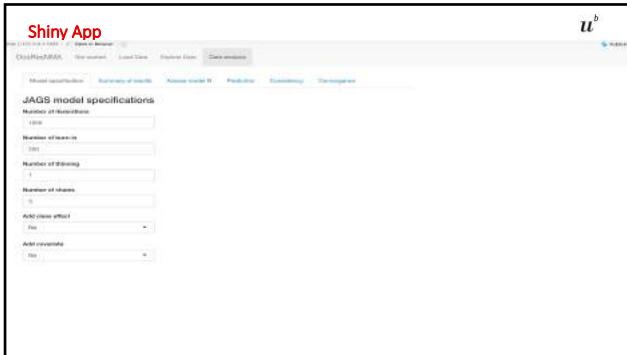
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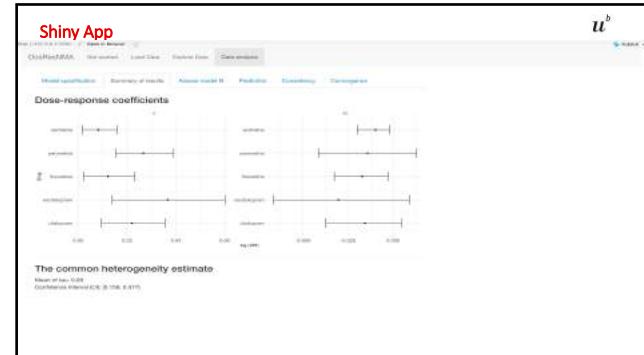
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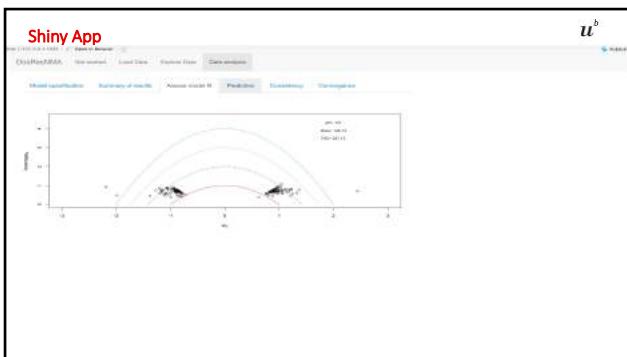
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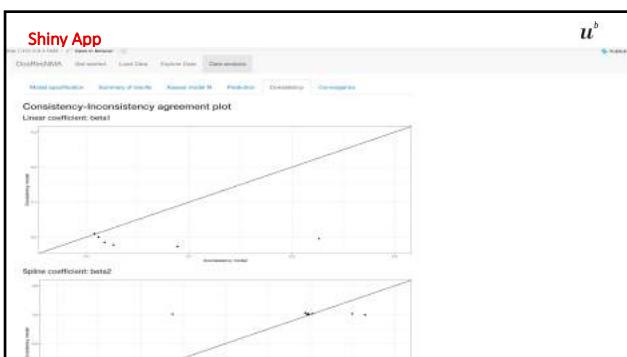
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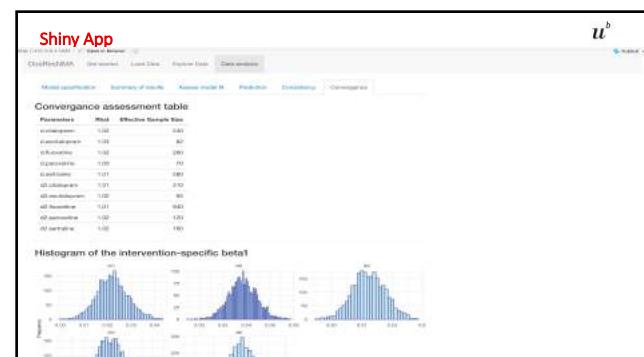
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**Limitations in the approach**

- Bayesian framework
  - Sensitivity to prior choice; sensitivity analysis
  - Time consuming
  - Ensure convergence
- Dose-response models
  - Categorization of the exposure
  - The dose-response shape
- Dose-response NMA model
  - Doses should be harmonized in class effect model

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