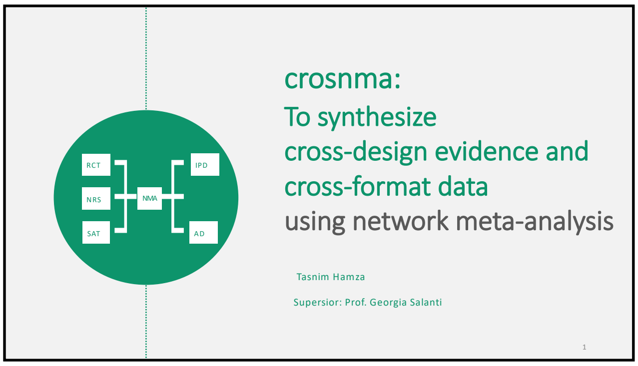
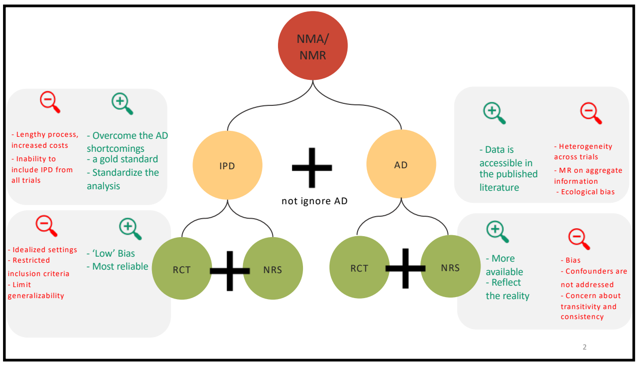
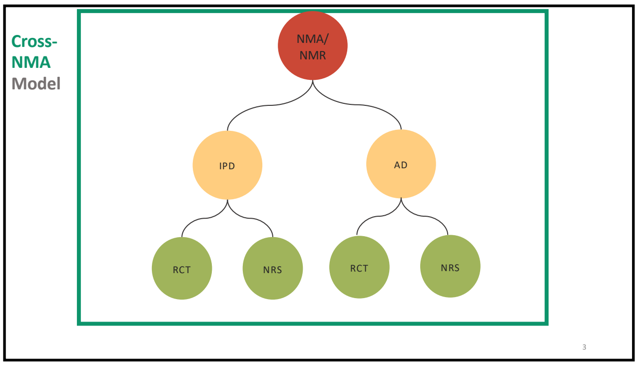

crosnma:
To synthesize
cross-design evidence and
cross-format data
using network meta-analysis
Tasnim Hamza
Supersior: Prof. Georgia Salanti
RCT
NRS
SAT
NMA
IPD
AD
1

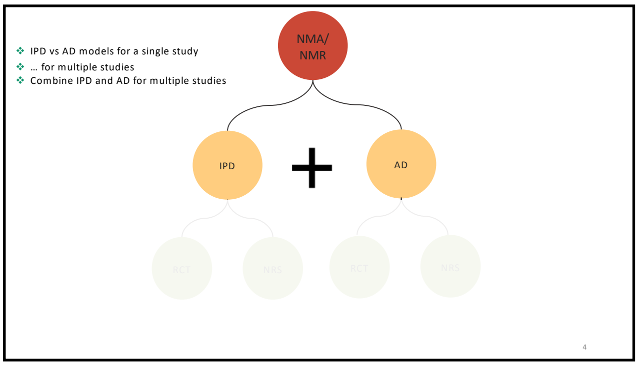
1


NMA/
NMR
IPD
AD
not ignore AD
RCT
NRS
RCT
NRS
- 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
- MR on aggregate information
- Ecological bias
- More available
- Reflect the reality
- Bias
- Confounders are not addressed
- Concern about transitivity and consistency
2

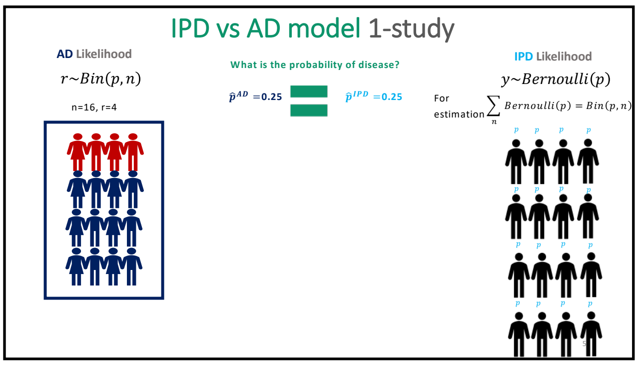
2


Cross-
NMA
Model
NMA/
NMR
IPD
AD
RCT
NRS
RCT
NRS
3

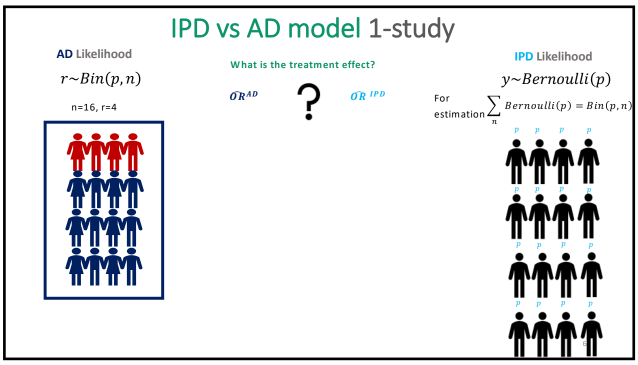
3


IPD vs AD models for a single study
… for multiple studies
Combine IPD and AD for multiple studies
NMA/
NMR
IPD
AD
4

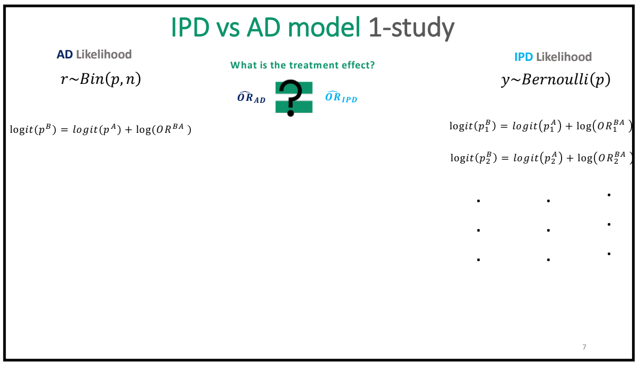
4


IPD vs AD model 1-study
AD Likelihood
$r \sim Bin(p,n)$
n=16, r=4
What is the probability of disease?
$\hat{p}^{AD}$ =0.25
$\hat{p}^{IPD}$ =0.25
IPD Likelihood
$y \sim Bernoulli(p)$
For estimation $\sum_n Bernoulli(p) = Bin(p,n)$

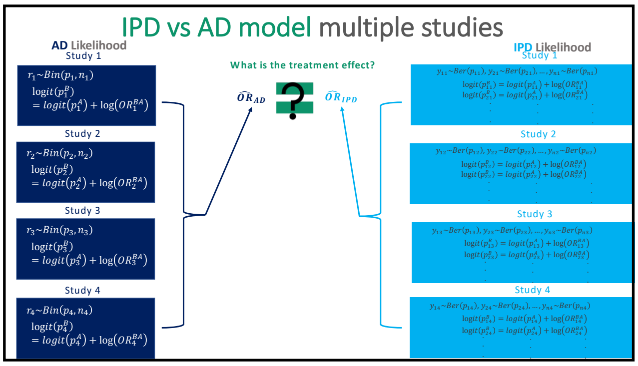
5


IPD vs AD model 1-study
AD Likelihood
$r \sim Bin(p,n)$
n=16, r=4
What is the treatment effect?
$\widehat{OR}^{AD}$
?
$\widehat{OR}^{IPD}$
IPD Likelihood
$y \sim Bernoulli(p)$
For estimation $\sum_n Bernoulli(p) = Bin(p,n)$

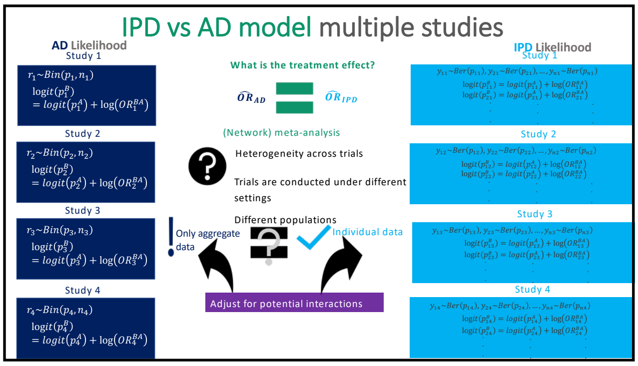
6


IPD vs AD model 1-study
AD Likelihood
r~Bin(p,n)
logit(p^B) = logit(p^A) + log(OR^BA)
What is the treatment effect?
OR_AD ? OR_IPD
IPD Likelihood
y~Bernoulli(p)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA)

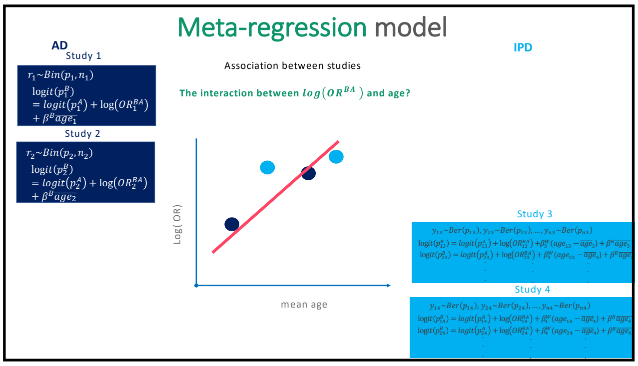
7


IPD vs AD model multiple studies
AD Likelihood
Study 1
r_1~Bin(p_1,n_1)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA)
Study 2
r_2~Bin(p_2,n_2)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA)
Study 3
r_3~Bin(p_3,n_3)
logit(p_3^B) = logit(p_3^A) + log(OR_3^BA)
Study 4
r_4~Bin(p_4,n_4)
logit(p_4^B) = logit(p_4^A) + log(OR_4^BA)
What is the treatment effect?
OR_AD ? OR_IPD
IPD Likelihood
Study 1
Study 2
Study 3
Study 4

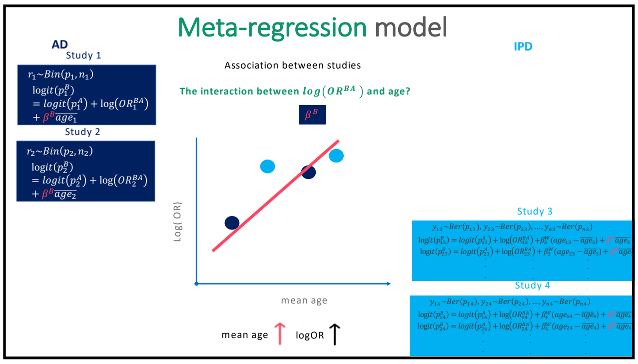
8


IPD vs AD model multiple studies
AD Likelihood
Study 1
r_1~Bin(p_1,n_1)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA)
Study 2
r_2~Bin(p_2,n_2)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA)
Study 3
r_3~Bin(p_3,n_3)
logit(p_3^B) = logit(p_3^A) + log(OR_3^BA)
Study 4
r_4~Bin(p_4,n_4)
logit(p_4^B) = logit(p_4^A) + log(OR_4^BA)
What is the treatment effect?
OR_AD = OR_IPD
(Network) meta-analysis
Heterogeneity across trials
Trials are conducted under different settings
Different populations
Only aggregate data
Individual data
Adjust for potential interactions
IPD Likelihood
Study 1
Study 2
Study 3
Study 4

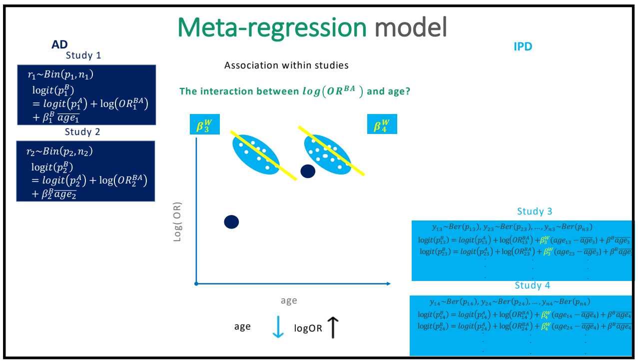
9


Meta-regression model
AD
Study 1
r_1~Bin(p_1,n_1)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA) + β^B age_1
Study 2
r_2~Bin(p_2,n_2)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA) + β^B age_2
IPD
Association between studies
The interaction between log(OR^BA) and age?
Log( OR)
mean age
Study 3
Study 4

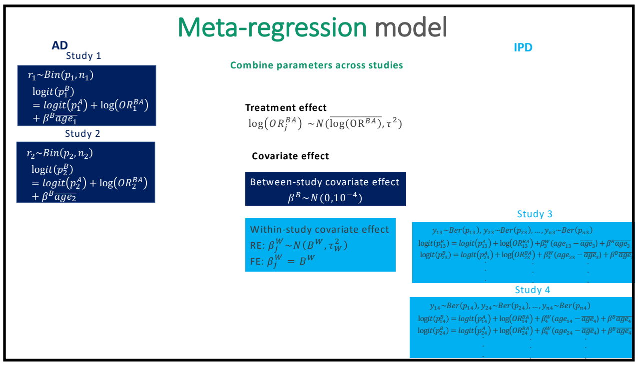
10


Meta-regression model
AD
Study 1
r_1~Bin(p_1,n_1)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA) + β^B age_1
Study 2
r_2~Bin(p_2,n_2)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA) + β^B age_2
IPD
Association between studies
The interaction between log(OR^BA) and age?
β^B
Log( OR)
mean age
mean age
logOR
Study 3
Study 4

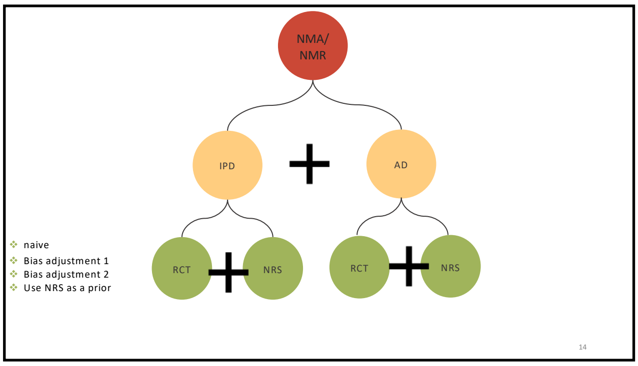
11


Meta-regression model
AD
Study 1
r_1~Bin(p_1,n_1)
logit(p_1^B) = logit(p_1^A) + log(OR_1^BA) + β_1^B age_1
Study 2
r_2~Bin(p_2,n_2)
logit(p_2^B) = logit(p_2^A) + log(OR_2^BA) + β_2^B age_2
IPD
Association within studies
The interaction between log(OR^BA) and age?
β_3^W
β_4^W
Log( OR)
age
age
logOR
Study 3
Study 4

12




13

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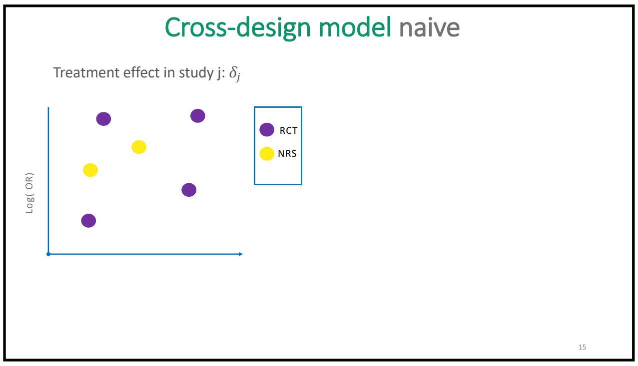


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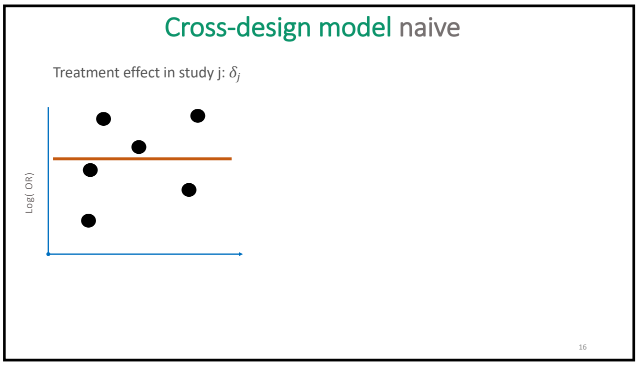


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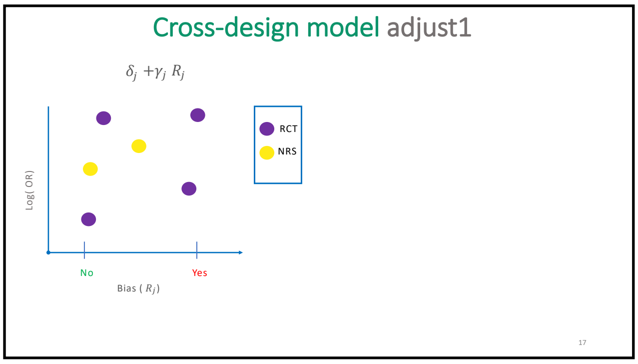


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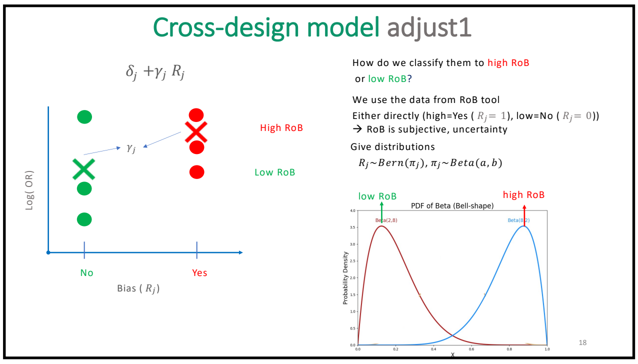


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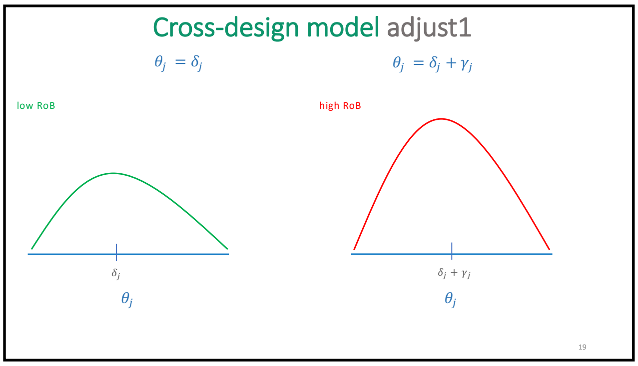
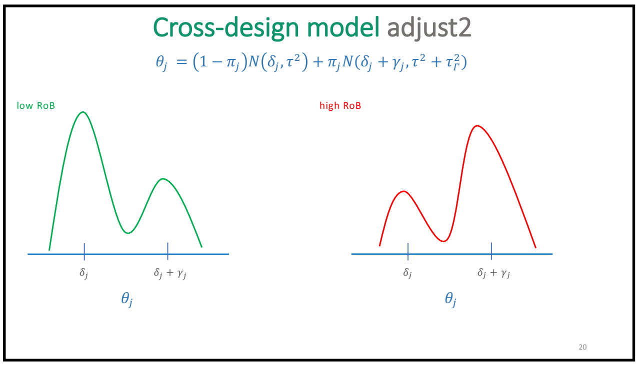



19

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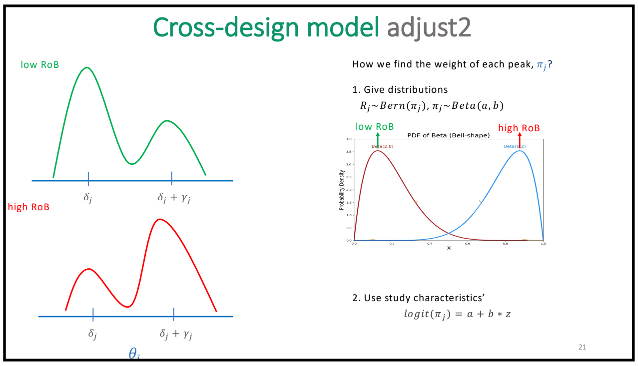


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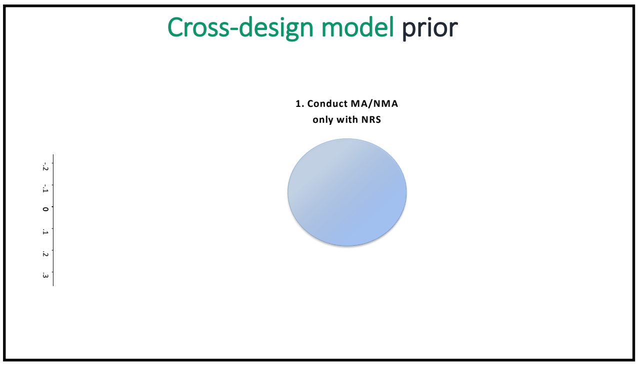
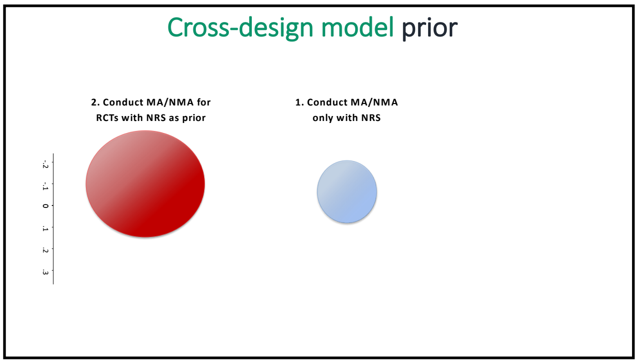
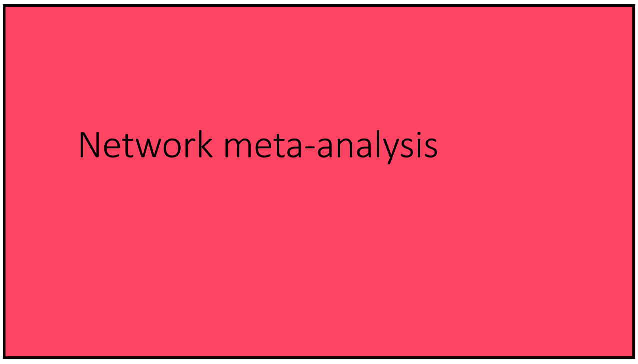



22




23

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## IPD + AD NMR model multiple treatments

**AD** Likelihood, logistic

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** Likelihood, logistic

For i individual in j study with k treatment

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

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

**Combine AD and IPD**

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

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## Cross NMR model naive

**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

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

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

**Combine AD and IPD**

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

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## Cross NMR model naive

This assumes NRS and RCTs of high risk bias contribute the same (according to their precision) with low risk of bias RCTs

We introduce $R_j$ which reflects the risk of bias in study j

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## Cross NMR model adjust 1

**AD** RCT and NRS

For j study with k treatment

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

$\text{logit}(p_{jk}) = u_{jb} + \beta^{B}_{2,bk} x_j + \delta_{jbk} + \gamma_j R_j$

**IPD** RCT and NRS

For i individual in j study with k treatment

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

$\text{logit}(p_{ijk}) = u_{jb} + \beta_{1j} x_{ij} + \beta^{W}_{2,bk}(x_{ij} - x_j) + \beta^{B}_{2,bk} x_j + \delta_{jbk} + \gamma_j R_j$

**Combine AD and IPD**

$\delta_{jbk} \sim N(d_{Ak} - d_{Ab}, \tau^2)$, $\beta^{B}_{2,bk} \sim N(B^{B}_{Ak}$ - $B^{B}_{Ab}, \sigma^2_B)$, $\beta^{W}_{2,bk} \sim N(B^{W}_{Ak}$ - $B^{W}_{Ab}, \sigma^2_W)$

**Bias assumptions**

$\gamma_j \sim N(\Gamma, \sigma^2_\Gamma)$, $R_j \sim Bern(\pi_j)$

$$\pi_j = \begin{cases} \pi_{low} \sim beta(1,20) \\ \pi_{unclear} \sim beta(1,1) \\ \pi_{high} \sim beta(20,1) \end{cases}$$

28

## Cross NMR model adjust 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

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

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

**Combine AD and IPD**

$\delta_{jbk} \sim N(d_{Ak} - d_{Ab}, \tau^2)$, $\beta^{B}_{2,bk} \sim N(B^{B}_{Ak}$ - $B^{B}_{Ab}, \sigma^2_B)$, $\beta^{W}_{2,bk} \sim N(B^{W}_{Ak}$ - $B^{W}_{Ab}, \sigma^2_W)$

**Bias assumptions**

$\theta_{jbk} \sim (1 - \pi_j) N(d_k, \tau^2) + \pi_j N(d_k + \Gamma, \tau^2 + \tau^2_\Gamma)$

$$\pi_j = \begin{cases} \pi_{low} \sim beta(1,20) \\ \pi_{unclear} \sim beta(1,1) \\ \pi_{high} \sim beta(20,1) \end{cases}$$

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

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## Cross NMR model prior

**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

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

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

**Combine AD and IPD**

$\delta_{jbk} \sim N(d_k - d_b, \tau^2) \beta^{B}_{2,k} \sim N(B^{B}_{k}$ - $B^{B}_{b}, \sigma^2_B)$ and $\beta^{W}_{2,k} \sim N(B^{W}_{k}$ - $B^{W}_{b}, \sigma^2_W)$

**Priors**

$u_j, B^W_k, B^B_k \sim N(0, 10^4), \tau, \sigma_B, \sigma_W \sim Unif(0, 10)$

First: NRS model: $d^{NRS}_k, V^{NRS}$ are data

Second: RCT model: $d_k \sim N(d^{NRS}_k, V^{NRS})$

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