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

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1. Three-level hierarchical model
   - naive
   - Bias adjustment 1
   - Bias adjustment 2
   - Use IPD as a prior

2. Cross NMA model
   - naive
   - Use IPD and NRS
   - Combine AD and IPD

3. Cross NMR model naive
   - Treatment effect in study \(j\), \(i\):
     \[
     \delta_{ij} \sim N(\mu_{ij}, \tau^2) \\
     \mu_{ij} \sim N(p_{ij}, \sigma^2) \\
     \tau \sim N(\mu_{\tau}, \sigma_{\tau}^2)
     \]
   - For individual in study with k treatment:
     \[
     \gamma_{ijk} \sim \text{Bernoulli}(p_{ijk}) \\
     \logit(p_{ijk}) = u_{ijk} + \beta_1 x_{ij} + \delta_{ijk}
     \]

4. Cross NMR model
   - Treatment effect in study \(j\), \(i\):
     \[
     \delta_{ij} \sim N(d_{ijk} - d_{ijk}, \tau^2) \\
     \beta_{ijk} \sim N(\beta_{ijk}, \sigma_{\beta}^2) \\
     \mu_{ij} \sim \text{Normal}(0, 0.10^2)
     \]
Cross NMR model adjust1

\[ \delta_i = y_i R_i \]

Cross NMR model adjust2

\[ \delta_i = y_i R_i \]
1. Conduct MA/NMA only with NRS prior

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

Drug 1
Drug 2
Drug 3

\( d_k \sim \mathcal{N}(\mu_k, \sigma_k^2) \)

\( \mathcal{N} \)

\( \mathcal{N} \)

Cross NMR model prior

Cross NMR model prior

Cross NMR model prior

Cross NMR model prior

Case study

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of data</th>
<th>Treatment compared</th>
<th>Design/ROB</th>
<th>Probability of risk</th>
<th>Sample size</th>
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</thead>
<tbody>
<tr>
<td>DEFINE</td>
<td>IPD</td>
<td>Dimethyl fumarate  Placebo</td>
<td>RCT/high risk</td>
<td>Beta(3,1)</td>
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<td>CONFIRM</td>
<td>IPD</td>
<td>Dimethyl fumarate  Glatiramer acetate Placebo</td>
<td>RCT/high risk</td>
<td>Beta(3,1)</td>
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<td>IPD</td>
<td>Natalizumab        Placebo</td>
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<td>Beta(1,2)</td>
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<td>Glatiramer acetate Placebo</td>
<td>RCT/low risk</td>
<td>Beta(1,1)</td>
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<td>Johnson</td>
<td>IPD</td>
<td>Glatiramer acetate Placebo</td>
<td>RCT/unclear risk</td>
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</tbody>
</table>

Network diagram

\[ \text{Network diagram} \]

1 Introduction

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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

References