Network Meta-Analysis
including
Individual Participant Data
When do benefits arise?

Thomas Debray
Julius Center for Health Sciences and Primary Care,
University Medical Center Utrecht, Utrecht, The Netherlands

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies’ in kind contribution.

www.imi.europa.eu
Background

- Network meta-analysis (NMA) often based on aggregate data (AD)
- Concerns regarding validity of indirect comparisons
- About 1/8 of AD-NMA suffer from network inconsistency
- Heterogeneity may also degrade usefulness of NMA
- NMA framework used for inclusion non-randomized studies

What can we gain by obtaining Individual Participant Data (IPD)?
Case study

- 18 anti-depressant trials
- Comparison of 3 treatments
- Evaluation of Hamilton Depression score (HAMD)

Available response data

- Placebo
- TCA
- TeCA

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies’ in kind contribution.

www.imi.europa.eu
Scenario 1: no access to IPD

• Possible types of aggregate data
  – All trials: complete case analysis (CCA)
  – All trials: last observation carried forward (LOCF)
  – All trials: multivariate regression (MVR)

• Common methods
  – Pairwise meta-analysis
  – Network meta-analysis
  – Network meta-regression

We investigate the relative change in HAMD score between TeCA and TCA after 6 weeks
Scenario 1: meta-analysis using published aggregate data
Scenario 1: meta-analysis using published aggregate data

- **Heterogeneity (τ)**
  - Pairwise MA
  - Network MA
  - Network meta-regression

- **Network inconsistency**
  - Pairwise MA
  - Network MA
  - Network meta-regression

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies’ in kind contribution.

www.imi.europa.eu
Scenario 2: IPD are available for all trials

- Extensions of AD-NMA methods
  - Adjust for confounders & prognostic factors (NMA-PF)
  - Adjust for effect modifiers (NMA-TX)
  - Use information from trials with limited follow-up (MNMA)

- Questions
  - Can we improve precision?
  - Can we reduce/explain heterogeneity and network inconsistency?
Scenario 2: Meta-analysis using IPD

Effect size

Standard error of effect size

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies in kind contribution. www.imi.europa.eu
Scenario 2: Meta-analysis using IPD

Heterogeneity ($\tau$)

<table>
<thead>
<tr>
<th>Method</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMA</td>
<td>1.6</td>
</tr>
<tr>
<td>NMA</td>
<td>1.4</td>
</tr>
<tr>
<td>NMA-PF</td>
<td>1.8</td>
</tr>
<tr>
<td>NMA-TX</td>
<td>0.6</td>
</tr>
<tr>
<td>MNMA</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Network inconsistency

<table>
<thead>
<tr>
<th>Method</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMA</td>
<td>1.2</td>
</tr>
<tr>
<td>NMA</td>
<td>1.0</td>
</tr>
<tr>
<td>NMA-PF</td>
<td>0.8</td>
</tr>
<tr>
<td>NMA-TX</td>
<td>0.6</td>
</tr>
<tr>
<td>MNMA</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Recommendations

Prioritization of IPD retrieval

- Presence of network inconsistency
- Presence of heterogeneity
- Publications with inappropriate summary statistics
An overview of methods for network meta-analysis using individual participant data: when do benefits arise?

Thomas PA Debray,1,2 Ewoud Schuit,1,2,3 Orestis Efthimiou,4,5 Johannes B Reitsma,1,2 John PA Ioannidis,3 Georgia Salanti,4,5,6 and Karel GM Moons1,2 on behalf of GetReal Workpackage4
Background

The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement no [115303], resources of which are composed of financial contribution from the European Union’s Seventh Framework Programme (FP7/2007-2013) and EFPIA companies’ in kind contribution.

www.imi.europa.eu