Using network meta-analysis to identify effective components of complex mental health interventions

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Network Meta-Analysis

• Network meta-analysis (NMA) allows pooling evidence on multiple interventions from a set of studies
• A “network” is constructed by displaying the interventions compared in each study
• Comparison of multiple interventions for a health condition enables to address relevant questions for practitioners and policy makers
Pair-wise vs. network meta-analysis

• Corticosteroids in septic shock
  • Annane and colleagues (2015) published a Cochrane review comparing the efficacy of corticosteroids vs. placebo
  • Gibbison and colleagues (2017) reanalysed the data from the review and conducted a NMA to examine each corticosteroid separately

Fig. 2 Network plot (left) and network meta-analysis results (right) of mortality up to 28 days for the different interventions. ORs <1 favour the first intervention. DEXb Dexamethasone bolus, HYDb Hydrocortisone bolus, HYDi Hydrocortisone Infusion, MPREDb Methylprednisolone bolus, MPREDi Methylprednisolone infusion, PRED Prednisolone
Complex interventions for mental health

• Systematic reviews of interventions in mental health and other areas often deal with complex interventions which include several active ingredients or “components”

• If each combination of components is considered as a separate intervention, then NMA could be used to simultaneously compare the different interventions

• However, this could lead to a very large number of interventions (and possibly to disconnected networks)
Component-Level NMA

• Component-level network meta-analysis methods have been developed within a Bayesian framework (Welton et al., 2009)
• Component-level NMA may be used to examine
  • Role of each individual component
  • Interactions between multiple components
Example 1: CBT for adult depression

- Depression represents a substantial public health concern worldwide
- Cognitive-Behavioural Therapy (CBT) is an effective psychological intervention for depression
- CBT interventions are complex
  - Multiple content components
  - Delivered in different ways
Example 1: Systematic review

- Inclusion criteria:
  - Randomised controlled trials
  - Examining CBT interventions
  - In depressed adults
- Primary outcome: Change in depressive symptoms at short term
- Effect size index: standardised difference in mean change (sDIMC)
Example 1: Included studies

• 91 studies reported one or more relevant outcomes
• Primary outcome: 76 studies, 6973 patients
• Large variability in
  • Publication year
  • Study size
  • Country
Example 1: Definition of comparators

• Treatment as Usual (TAU): 38 interventions
• No treatment: 7 interventions
• Wait list: 33 interventions
• Psychological/attention placebo: 14 interventions
Example 1: defining components

- Cognitive Techniques
- Behavioural Activation
- Psychoeducation
- Homework
- Problem Solving
- Social Skills Training

- Relaxation
- Goal Setting
- Final Session
- Mindfulness
- Acceptance & Commitment Therapy
Example 1: delivery methods

• Face-to-Face (F2F) CBT: 100 interventions
• Hybrid CBT: 7 interventions
• Multimedia CBT: 33 interventions
Example 1: Network meta-analysis models

- Full Interaction Model
- Main Effects Model
- Therapy Effects Model
Example 1: Full Interaction Model

• Standard Bayesian NMA (Dias et al., 2013)
• Each delivery format and combination of components is a unique intervention
Example 1: Main Effects Model

For a continuous outcome, treatment effect $d_t$ is estimated from:

$$d_t = d_{CBT} + \beta_1 \text{Multi}_t + \beta_2 * \text{Cog}_t + \beta_3 * \text{BA}_t + \beta_4 * \text{PsEd}_t + \beta_5 * \text{Home}_t + \beta_6 * \text{Prob}_t + \beta_7 * \text{Soc}_t + \beta_8 * \text{Relax}_t + \beta_9 * \text{Goal}_t + \beta_{10} * \text{Final}_t$$
Example 1: Therapy Effects Model

• Standard Bayesian NMA (Dias et al., 2013)
• Treatments included
  • TAU
  • No treatment
  • Wait list
  • Psychological/Attention placebo
  • Face-to-face CBT
  • Hybrid CBT
  • Multimedia CBT
Example 1: Results for Full Interaction Model
Example 1: Results for Full Interaction Model

![Diagram showing the standardised difference in mean change compared to TAU for different interventions and their corresponding 95% CrI intervals. The interventions include a range of combinations such as Cog+BA+PsEd+Home+Goal+Final, Cog+BA+PsEd+Home+Goal, Cog+BA+PsEd+Final, etc., each with their respective difference in means and credible intervals.]
Example 1: Results for Main Effects Model

<table>
<thead>
<tr>
<th>Treatment</th>
<th>sDiMC [95% CrI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Treatment</td>
<td>0.08 [-1.04, 1.23]</td>
</tr>
<tr>
<td>Wait list</td>
<td>0.75 [0.09, 1.41]</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.53 [-1.41, 0.35]</td>
</tr>
<tr>
<td>CBT</td>
<td>-1.77 [-2.57, -1.01]</td>
</tr>
</tbody>
</table>

**EFFECT MODIFIERS**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>sDiMC [95% CrI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multimedia</td>
<td>0.36 [-0.24, 0.96]</td>
</tr>
<tr>
<td>Cognitive Techniques</td>
<td>0.38 [-0.21, 0.97]</td>
</tr>
<tr>
<td>Behavioural Activation</td>
<td>0.54 [-0.09, 1.16]</td>
</tr>
<tr>
<td>Psychoeducation</td>
<td>0.04 [-0.66, 0.75]</td>
</tr>
<tr>
<td>Homework</td>
<td>-0.21 [-0.90, 0.49]</td>
</tr>
<tr>
<td>Problem Solving</td>
<td>-0.04 [-0.67, 0.59]</td>
</tr>
<tr>
<td>Social Skills Training</td>
<td>0.55 [-0.37, 1.45]</td>
</tr>
<tr>
<td>Relaxation</td>
<td>0.03 [-0.81, 0.88]</td>
</tr>
<tr>
<td>Goal Setting</td>
<td>0.61 [-0.40, 1.62]</td>
</tr>
<tr>
<td>Final Session</td>
<td>-0.55 [-1.66, 0.54]</td>
</tr>
</tbody>
</table>
Example 1: Results for Therapy Effects Model

<table>
<thead>
<tr>
<th>Intervention</th>
<th>sDiMC [95% CrI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>0.20 [-0.91, 1.31]</td>
</tr>
<tr>
<td>Wait list</td>
<td>0.72 [0.09, 1.35]</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.34 [-1.21, 0.52]</td>
</tr>
<tr>
<td>F2F CBT</td>
<td>-1.11 [-1.62, -0.60]</td>
</tr>
<tr>
<td>Hybrid CBT</td>
<td>-1.06 [-2.05, -0.08]</td>
</tr>
<tr>
<td>Multimedia CBT</td>
<td>-0.59 [-1.20, 0.02]</td>
</tr>
</tbody>
</table>
Example 2: School-based interventions to prevent mental-ill-health in children and young people

• Aim: to identify the most effective and cost-effective intervention component(s), or combination of components for prevention of common mental health problems in children and young people

• Protocol available at http://www.crd.york.ac.uk/prospero/display_record.php?RecordID=48184&VersionID=75497
Example 2: School-based interventions to prevent mental-ill-health in children and young people

• Main outcomes
  • Self-reported anxiety
  • Self-reported depression
  • Conduct problems

• Effect size index: standardised difference in mean change (sDIMC)

• To be considered separately:
  • Population: universal, targeted (selective/indicated)
  • Context: primary, secondary, university
  • Time point
Example 2: results for therapy effects model

- Change in depression scores at mid term, universal, primary
**Example 2:** results for full interaction model

- Change in depression scores at mid term, universal, primary

<table>
<thead>
<tr>
<th>Intervention</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>WL</td>
<td>C</td>
</tr>
<tr>
<td>None</td>
<td>C</td>
</tr>
<tr>
<td>AtCnt</td>
<td>C</td>
</tr>
<tr>
<td>Cog Beh</td>
<td>C</td>
</tr>
<tr>
<td>Cog Beh Relax</td>
<td>C</td>
</tr>
<tr>
<td>PsEd Cog Beh</td>
<td>C</td>
</tr>
<tr>
<td>PsEd Cog Beh Relax</td>
<td>C</td>
</tr>
</tbody>
</table>

UC: Usual Curriculum; WL: Wait List; AtCnt: Attention Control; Cog: Cognitive; Beh: Behavioural; Relax: Relaxation; PsEd: Psychoeducation
Conclusions

• Component-level NMA is a promising approach with the potential to address relevant policy questions

• Adequate reporting of interventions is essential, as we rely on primary studies to characterize each intervention

• Further steps
  • Use Main Effects model to identify effective components
  • Simulation work to determine sample size required to obtain precise results
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