How network meta-analysis can aid decision making in guidelines with limited or poor quality evidence

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Introduction

- The National Institute for Health and Clinical Excellence (NICE) commissioned the National Clinical Guidelines Centre (NCGC) to produce a guideline on the management of bedwetting (nocturnal enuresis) in children.

- Started in October 2008

- Pre publication check currently on NICE website

- Will be published in October 2010

- This presentation will describe our experience of using a network meta-analysis to aid the formation of recommendations
Clinical issue

- What is the most effective intervention for treating nocturnal enuresis

- The answer will lead the Guideline Development Group (GDG) to make a decision and form recommendations
NICE methods used to review evidence

- Review the evidence for the management of bedwetting in children
- We conducted pairwise meta-analysis of the identified RCT evidence
- 51 pairwise comparisons of 25 interventions in 2 subgroups, many of which were from low quality data
- These 51 pairwise comparisons did not help answer the question of the most effective intervention
- A network meta-analysis was conducted
The Problem

- Pairwise comparisons did not help the GDG answer the question or make decisions and form recommendations

- Why not?
  - Multiple pairwise comparisons
  - No direct data for some
  - Low quality, limited data for all comparisons
  - No check for consistency between direct and indirect effect estimates

- The GDG found it difficult to conclude anything from all the evidence presented in this pairwise fashion
Example network

Population: Bed wetting only
Inclusion criteria: Treatment - 8 weeks for pharmacological treatments or 12 weeks for behavioural treatments, RCT evidence.
Network meta-analysis

- A synthesis of all the clinical evidence
- Network meta-analysis is being increasingly used by guideline developers to synthesise evidence when evaluating multiple comparisons

- Adapted from code found here: https://www.bris.ac.uk/cobm/research/mpes/mtc.html

Network meta-analysis

- Use network meta-analysis to simultaneously compare 25 interventions on the most important outcomes in two subgroup populations
  - Dryness
  - Relapse rates

- Fed results of network meta-analysis into the health economics model
<table>
<thead>
<tr>
<th>Interventions</th>
<th>Median relative risk (95% Credible Interval)</th>
<th>Probability intervention is most effective (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet desmopressin and alarm</td>
<td>8.519 (3.567 – 9.578)*</td>
<td>41.16</td>
</tr>
<tr>
<td>Dry bed training with alarm</td>
<td>8.116 (2.538 – 9.523)*</td>
<td>29.23</td>
</tr>
<tr>
<td>Tablet desmopressin and oxybutynin</td>
<td>7.640 (2.012 – 9.525)*</td>
<td>18.89</td>
</tr>
<tr>
<td>Tablet desmopressin</td>
<td>7.281 (3.727 – 9.109)*</td>
<td>3.22</td>
</tr>
<tr>
<td>Alarm</td>
<td>5.497 (2.633 – 8.079)*</td>
<td>0.11</td>
</tr>
<tr>
<td>Homotoxicological Remedy</td>
<td>4.969 (0.820 – 9.032)</td>
<td>2.7</td>
</tr>
<tr>
<td>Imipramine and oxybutynin</td>
<td>4.188 (0.561 – 8.737)</td>
<td>1.85</td>
</tr>
<tr>
<td>Retention control training with alarm</td>
<td>3.484 (0.224 – 9.031)</td>
<td>2.28</td>
</tr>
<tr>
<td>Nasal Desmopressin</td>
<td>2.785 (0.387 – 7.743)</td>
<td>0.35</td>
</tr>
<tr>
<td>Imipramine</td>
<td>2.259 (0.513 - 6.172)</td>
<td>0.01</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>1.696 (0.153 – 7.277)</td>
<td>0.23</td>
</tr>
</tbody>
</table>
Results of the network meta-analysis

- This information along with other considerations informed recommendations
How did it help?

- Brought together all the relevant RCT evidence
  - Produced estimates of effect for all possible comparisons
  - Generated ranking of all interventions in terms of effectiveness
- Provided a single set of relative risks for all interventions compared to placebo / no treatment
- Reflected the uncertainty in the overall evidence
- The GDG was able to see all the evidence in one place and make their recommendations considering all of it simultaneously
Lessons learned

- Takes time, ensure enough time is scheduled in to the work plan
- Ensure GDG understands the methods
- Low quality data combined with low quality data = low quality data
- Uncertainty in the results put into NMA = uncertainty in results from NMA
- Good way to see all results together
Final considerations

- Recommend using NMA in guidelines where there is lack of pairwise comparisons or sporadic pairwise comparisons as well as in other guidelines
- It helps to inform the health economics model
- Quality of results are only as good as the data you put in
- Still need to reflect uncertainty in recommendations
- Does help the GDG to concentrate their thoughts on the evidence and inform recommendations