GRADE: adaptation of GRADE evidence profiles to different evidence types – a case study of NICE motor neurone disease – non-invasive ventilation guideline

GIN 2010

Toni PY Tan
Faisal Siddiqui

Background

• GRADE and GRADE evidence profiles are becoming widely used in guideline development
• But GRADE and GRADE evidence profiles are only designed for intervention studies
• Clinical guidelines often cover clinical areas that required evidence from different study designs
• Consequently, inconsistency emerged within a guideline:
  – GRADE evidence profiles (intervention studies)
  – Traditional narrative summary (diagnostic accuracy and qualitative studies)
Purpose

- To improve consistency of a guideline
- Pilot different adaptations of GRADE evidence profiles to present evidence from diagnostic and qualitative studies
  - Diagnosis of respiratory impairment (diagnostic)
  - Clinical effectiveness of NIV (intervention)
  - Information and support needs (qualitative)

Methods 1

Diagnostic accuracy evidence

  - Study design
  - Limitations (risk of bias)
  - Indirectness
    - Outcomes
    - Patient populations, diagnostic test, comparison test, and indirect comparisons
  - Important inconsistency in study results
  - Imprecise evidence
### Results 1

**Example: evidence profiles (diagnostic)**

<table>
<thead>
<tr>
<th>Outcome (reference standard): Hypercapnia [defined as pCO₂ &gt; 45 mmHg]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of studies (study design)</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Quality</td>
</tr>
</tbody>
</table>

**Index test**: FVC (cut-off: 80% predicted) (n=199)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Prevalence (%)</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66.7 (45–84)</td>
<td>98.3 (59–73)</td>
<td>21.3 (14–32)</td>
<td>94.6 (89–97)</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Index test**: PImax (cut-off: 60% predicted) (n=199)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Prevalence (%)</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.1 (66–100)</td>
<td>82.9 (20–34)</td>
<td>19.8 (11–22)</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Index test**: PEmax (cut-off: 60% predicted) (n=199)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Prevalence (%)</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.1 (53–90)</td>
<td>26.9 (44–59)</td>
<td>15.8 (12–26)</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Index test**: Mouth occlusion pressure at 100ms (P₀.1) (n=199)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Prevalence (%)</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.1 (26–67)</td>
<td>62.9 (49–64)</td>
<td>12.5 (7–21)</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Index test**: Phrenic nerve motor response amplitude (PNmax) (n=199)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Prevalence (%)</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>PPV (%) (95% CI)</th>
<th>NPV (%) (95% CI)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.1 (53–90)</td>
<td>52.5 (55–70)</td>
<td>21.7 (14–32)</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

Mean study duration of disease at study entry = 17.2 months (15.6) (range: 1–72)

Methods 2

**Qualitative evidence**

- Adopted the concept of ‘evidence profiles’ based on outcomes
- Developed factors/criteria – based on NICE qualitative studies checklist (NICE Guideline Manual 2009) and GRADE criteria
Methods 2

Data synthesis (Miles & Huberman 1994):

- Thematic analysis with ‘clustering method’.
- ‘Thematic-Conceptual Meta Matrix’ was adopted and modified to resemble the GRADE profiles.
- Present the higher-level themes identified as a number of outcomes.

Methods 2

Developed factors/criteria (NICE checklist & GRADE):

- Adopted three quality criteria from GRADE, and modified based on the NICE qualitative studies checklist, summarised as:
  - **Study limitations**: including assessments on theoretical approach, study design, data collection, and validity.
  - **Indirectness**: including transferability (synonyms to ‘generalisability’ in quantitative research).
  - **Other considerations**: including analysis and synthesis methods, and any other limitations that may be subjected to bias.
Results 2

From the synthesis, 7 outcomes (or higher level themes) were identified:

- **Outcome 1**: Timing, level of information and ways of communication
- **Outcome 2**: Information needs for patients and carers
- **Outcome 3**: Support needs (or assistance required) for patients and carers
- **Outcome 4**: Carer specific information needs
- **Outcome 5**: Carer specific support needs
- **Outcome 6**: Decision making and end of life care (advance directives)
- **Outcome 7**: Knowledge and communication among healthcare professionals

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### Example of 2 outcomes: evidence profiles (qualitative)

<table>
<thead>
<tr>
<th>No. of studies and study design</th>
<th>Study sample in the studies</th>
<th>Themes emerged</th>
<th>Clarification</th>
<th>Rating</th>
<th>Study limitations</th>
<th>Indirectness</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome: Information needs (patients and carers)</strong></td>
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<tr>
<td>4 x interviews [HT] [BH] [Cu] [H] 2 x structured questionnaires [B]</td>
<td>P&amp;C = 204, Pr = 97, Total = 277</td>
<td>Information on causes and symptoms of MND, the natural progression of the disease and what to expect in the future, particularly the impact on mobility (arms and legs), respiratory function, speech, swallowing.</td>
<td>Mixed quality as:</td>
<td></td>
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<tr>
<td></td>
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<td>Some studies subjected to self-assessment bias or lack of details in methodology. Transferability: not all studies were UK/European studies.</td>
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<tr>
<td><strong>Outcome: Support needs (or assistance required) (patients and carers)</strong></td>
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<tr>
<td>1 x interview [HT]</td>
<td>P&amp;C = 20, Pr = 8, Total = 28</td>
<td>Support needs or assistance required to manage daily living:</td>
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<td></td>
<td></td>
<td>- Care support, including domestic assistance and night-time assistance</td>
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<td></td>
<td></td>
<td>- Physical/mobility assistance</td>
<td></td>
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<td></td>
<td></td>
<td>- Use of different equipments, including ventilator support</td>
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<tr>
<td></td>
<td></td>
<td>- Use of different activities to improve ability</td>
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<tr>
<td></td>
<td></td>
<td>- Use of emergency call alarm</td>
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</tbody>
</table>
Discussion

• The adaptations of evidence profiles (both diagnostic and qualitative) were well received by the GDG.
  – Better structure
  – Easy to follow
  – Better flow of discussion

• This has also enabled a consistent presentation of evidence throughout the whole guideline.

Limitations:

• GRADE for diagnostic evidence: ongoing development of the GRADE Working Group, awaiting further guidance

•Methods used in adapting the qualitative evidence profiles need further validation across different guidelines

• Ongoing project

Thank you

Contact: Toni Tan (toni.tan@nice.org.uk)
Faisal Siddiqui (faisal.siddqui@nice.org.uk)