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

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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)*

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Purpose

- To improve consistency of a guideline

- Pilot different adaptations of GRADE evidence profiles to present evidence from diagnostic and qualitative studies

- NICE Motor Neurone Disease – Non-invasive ventilation guideline (2010) (3 clinical questions):
  - *Diagnosis of respiratory impairment (diagnostic)*
  - *Clinical effectiveness of NIV (intervention)*
  - *Information and support needs (qualitative)*

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Methods 1

Diagnostic accuracy evidence

- Adopted factors from *Schunemann et al. (2008) Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ 336: 1106–10*
  - Study design
  - Limitations (risk of bias)
  - Indirectness
    - *Outcomes*
    - *Patient populations, diagnostic test, comparison test, and indirect comparisons*
  - Important inconsistency in study results
  - Imprecise evidence

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Results 1

Example: evidence profiles (diagnostic)

Outcome (reference standard): Hypercapnia [defined as $pCO_2 > 45$ mmHg]

No. of studies (study design)	Prevalence (%)	Sensitivity (%) [95%CI] (%)	Specificity (%) [95%CI] (%)	PPV (%) [95%CI] (%)	NPV (%) [95%CI] (%)	Other Analysis (%) [95%CI] (%)	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	Quality
Index test[a]: FVC (cut-off: 80% predicted) [n=199]												
1 Cohort [P]	12.1	66.7 (45—84)	66.3 (59—73)	21.3 (14—32)	93.6 (88—97)	AUC = 0.723	N	N	N	S (b)	N	Moderate
Index test[a]: PImax (cut-off: 60% predicted) [n=199]												
1 Cohort [P]	12.1	100 (86—100)	26.9 (20 —34)	15.8 (11—22)	100 (92—100)	AUC = 0.671	N	N	N	N	N	High
Index test[a]: PEmax (cut-off: 60% predicted) [n=199]												
1 Cohort [P]	12.1	75 (53—90)	52 (44—59)	17.7 (12—26)	93.8 (87—98)	AUC = 0.626	N	N	N	S (b)	N	Moderate
Index test[a]: Mouth occlusion pressure at 100ms (P0.1) [n=199]												
1 Cohort [P]	12.1	45.8 (26—67)	56.6 (49—64)	12.6 (7—21)	88.4 (81—94)	AUC = 0.546	N	N	N	S (b)	N	Moderate
Index test[a]: Phrenic nerve motor response amplitude (PNampl) [n=199]												
1 Cohort [P]	12.1	75 (53—90)	62.9 (55—70)	21.7 (14—32)	94.8 (89—98)	AUC = 0.772	N	N	N	N	N	High

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

[P] = Pinto et al. (2009)
MIP, MEP or PImax, PEmax = static inspiratory and expiratory mouth pressures
FVC = forced vital capacity
N = no serious limitation; S = serious limitation; VS = very serious limitation
[a] = cut-off values were based on normative limits commonly used in clinical practice.
[b] = wide confidence intervals for estimates of test accuracy.

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Methods 2

Qualitative evidence

- Adopted the concept of 'evidence profiles' based on outcomes

- Methods of data synthesis - based on Miles & Huberman (1994) Qualitative data analysis: an expanded sourcebook. 2nd edition. Sage Publications.

- Developed factors/criteria – based on NICE qualitative studies checklist (NICE Guideline Manual 2009) and GRADE criteria

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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.

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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.

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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)

No. of studies and study design	Study sample in the studies	Themes emerged *Clarification: not all participants reported in the study sample had contributed to the themes]*	Study limitations	Indirectness (Translatability)	Other considerations
Outcome: Information needs (patients and carers)					
4 x interviews [HT][H][BH][Co][J] 2 x structured questionnaires [S][C]	P&C = 304 Pr = 97 Total = 373	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, communication.	Overall comments: Mixed quality as: • Some studies subjected to self-assessment bias or lack of details in methodology. Transferability: not all studies were UK/European studies		
3 x interviews [HT][BH][W] 1 x structured questionnaire [S]	P&C = 119 Total = 119	Information on aids and equipments (eg. for mobility, eating, breathing, communication) and how to access it.	Overall comments: • Good quality interviews and structured questionnaire. • Transferability: not all studies were UK/European studies		
1 x interview [HT]	P&C = 46 Total = 46	Information on social and financial support ie. benefits	Overall comments: • Good quality. • Transferable to population addressed.		
Outcome: Support needs (or assistance required) (patients and carers)					
1 x interview [Co]	P&C = 20 Pr = 8 Total = 28	Support needs or assistance required to manage daily living: • Care support, including domestic assistance and night-time assistance • Physical/mobility assistance • Use of different equipments, including ventilator support. • Carry out activities to improve ability • Use of emergency call alarm	Overall comments: • Lack of details on synthesis methods. • Transferable to population addressed.		

[S] = Silverstein et al (1991), US study. Patients only.
[BH] = Bolmsjo & Hermeren (2003), Swedish study. Carers only.
[C] = Chio et al (2008), Italian study. Patients and carers.
[HT] = www.healthtalkonline.org (formerly DIPEX), UK study, regular updates. Patients and carers.
[H] = Hughes et al (2005), UK study. Patients, carers and professionals.
[J] = Johnston et al (1996), UK study. Patients only
[W] = Williams et al (1996), US study. Carers only.
[Co] = Cox (1992), UK study. Patients, carers and professionals.
P&C = patients and carers; Pr = professionals

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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

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Thank you

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