The development of a tool for the critical appraisal of studies reporting moderators of treatment effect

R van Hoorn*; W Kievit; GJ van der Wilt; M Tummers on behalf of INTEGRATE-HTA

*PhD student, Radboud Institute for Health Sciences

This project is co-funded by the European Union under the Seventh Framework Programme (Grant Agreement No. 306141)
INTEGRATE-HTA

INTEGRATE-HTA aims to adapt and develop concepts and methods for HTA to enable an integrated assessment of issues of complex technologies.

- Complex technologies
  - Heterogeneity of patients
  - Interacting factors
  - Multiple outcomes

http://integrate-hta.eu
Moderators of treatment outcome

Factors that influence treatment effects

• To determine which treatments work best for whom
• Making medicine more personalised
• Better valuation of research outcomes
Definitions
Definitions
Moderator/predictor analysis

- Usually secondary analysis (subgroup or regression analysis)
  - Common in Randomized Controlled Trials
- Often part of a larger collection of hypothesised factors
- Despite accessible guidance, quality of analyses is variable

“While it is generally recognised that subgroup analyses can produce spurious results, the extent of the problem is almost certainly underestimated” (Brookes et al., 2001)

Deciding on analysis after looking at the data is “dangerous, useful, and often done” (I.J. Good 1983)
Aim

- Critical appraisal is needed
- Current appraisal tools aim to appraise main effects
- Appraisal of moderators is important
  - Post hoc versus a priori

Critical appraisal is the process of carefully and systematically examining research to judge its trustworthiness, and its value and relevance in a particular context (A Burls, 2009)
Methods

• Literature search
  • Theoretical pieces, guidelines
  • Existing critical appraisal tools
  • Identification of relevant researchers

• Delphi panel
  • RAND/UCLA appropriateness method
  • Relevant participants
  • Two rounds

• Testing of the tool: palliative care case study
• Revision
  • Third Delphi panel round
• Finalisation
Design choices

- Considerations on tool design based on existing tools
  - Checklist
  - Multiple choice (Yes, Partially, No, Not (clearly) described, Don’t know)
  - No summarising score
  - No overall study design appraisal
First results

• 48 items retrieved from literature → 31 items included in test version
  • Study design (4)
  • Population selection and measurements (4)
  • Analysis (3)
  • (presentation of) results (9)
  • Meta-analysis (8)
  • Body of evidence (3)

Study design
1. Was the selection of moderators to consider based on expert knowledge and/or theoretical considerations?
   - Yes
   - Partially
   - Not (clearly) described
   - No
   - Don’t know

2. Is there (in)direct evidence that supports the hypothesized interaction (e.g. biological rationale)?

3. In the case of hypothesis-testing, are moderator hypotheses and their analyses defined a priori?

4. In the case of hypothesis-testing, was the selection of moderators to consider pre-specifed?
First results

• Strong points
  • Added value over existing checklists
  • Helps systematically appraising studies
  • Common problems in literature (e.g. power analysis)

• Problems
  • [Identification of moderator versus appraisal]
  • Reporting bias
  • Items discerning hypothesis testing and generating
  • Non-randomised studies
  • Non-intervention studies
What is next?

• Revision of the checklist
• Final adjustments using
  • Delphi panel
  • External expert panel
• Finalisation
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