A Review of the Use of Network Meta-Analysis in NICE Single Technology Appraisals

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Overview

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Overview

- Background
  - NICE Single Technology Appraisal process
  - Network meta-analysis

- Methods

- Results
  - Systematic review
  - Statistical aspects
The Single Technology Appraisal (STA) process is used to evaluate a single product, device or technology for a single indication.

Key participants
- The manufacturer
- The Evidence Review Group (ERG)
- The NICE appraisal committee
NICE STA Process

- Appraisal Scope Agreed
- Manufacturer submits report to ERG
- ERG sends Letter of Clarification to the manufacturer
- Manufacturer responds to Letter for Clarification
- ERG produces report
- Appraisal committee assesses the evidence
Network meta-analysis

Diagram:

- Top left: A - B
- Top right: A - B - C
- Bottom left: A - B - C
- Bottom right: A - B - C - D - E - F
NICE guidance on NMAs

In cases where there is no evidence from head-to-head trials, manufacturers may use a NMA.

- Guide to the methods of technology appraisal
- Specification for company submission of evidence
- Decision Support Unit Technical Support Documents (TSDs) on evidence synthesis
  - TSD2: A general framework for MA and NMA
  - TSD3: Heterogeneity
  - TSD4: Inconsistency
  - TSD7: Reviewer’s checklist
Methods

- STAs published between 1 May 2015 and 30 April 2016 were eligible
  - Rapid reviews and terminated appraisals were excluded

- Documents for review
  - Manufacturer’s submission
  - Request for clarification
  - Manufacturer’s response to the request for clarification
  - ERG report (including the erratum)
  - Final appraisal determination
Methods

Data extracted

- Basic characteristics of the STA
- Was a NMA conducted?
- If a NMA was conducted
  - Systematic review
  - Network meta-analysis
- ERG feedback
Results

46 STAs published between 1 May 2015 and 30 April 2016

- Terminated appraisals (n=6)
- Rapid review (n=1)

39 eligible STAs

- 14 did not include indirect comparisons
- 25 included indirect comparisons
Results

46 STAs published between 1 May 2015 and 30 April 2016

Terminated appraisals (n=6)
Rapid review (n=1)

39 eligible STAs

14 did not include indirect comparisons
25 included indirect comparisons
Results: Identifying Trials

Searches

The search conducted for the primary intervention was intentionally broad enough to capture studies relevant to the NMA.

Additional searches were conducted to inform the NMA.

Study selection

The selection criteria for the NMA were either the same or more detailed than the selection criteria used for the primary intervention.
Of the 18 NMAs that carried out similarity assessment, they considered the following domains:

- Baseline characteristics
- Study design
- Outcome definition
- Analysis population
- Quality

Potential sources of heterogeneity should be considered.
Results: Risk of Bias

For each eligible study, the risk of bias should be evaluated.

- Of the 12 NMAs that assessed risk of bias, only one explored the impact of bias in the NMA.
Results: NMAs

Number of outcomes
Results: NMAs

Number of treatments

Number of studies
Results: NMAs

Number of treatments

Number of studies

Source: TA343

Source: TA388
Results: NMA methods

Statistical modelling approaches

- 5 STAs also used network meta-regression to adjust for differences between trials in key characteristics
Results: NMA methods

Statistical models for standard NMAs:

The choice between fixed effect or random effects models should be justified. TSD2 suggests that the Deviance Information Criterion (DIC) and the residual deviance should be used to compare fixed effect and random effects models.
Results: NMA assumptions

Heterogeneity:

Where possible, estimates of heterogeneity should be provided, e.g. $I^2$ statistics.
Results: NMA assumptions

Inconsistency:

Where possible, inconsistency should be evaluated.

– STAs used a variety of methods to check inconsistency including the Bucher method, inconsistency models and node-splitting.
Results: ERG feedback

- Poor justification of key decisions
  - e.g. why were specific trials included/excluded

- Lack of transparency
  - e.g. study selection process, input datasets for each network
  - **NMAs should be reproducible**

- Insufficient reporting
  - e.g. insufficient detail about studies included in the NMA
  - e.g. for Bayesian NMAs ERGs requested initial values, burn-in, number of iterations, DIC, residual deviance
Limitations

- Available information
  - Redaction
  - Appendices not always available

- Snapshot of one year:
  - May 2015 – April 2016

- Single data extraction
Conclusions

- NMAs are often included in STAs, however they do not always conform to the NICE guidelines

- Advice to manufacturers:
  - Use the checklist in the NICE DSU TSD 7 to review the NMA
  - Ensure that key assumptions/decisions are clearly justified
  - Ensure that the NMA methods are transparent and reproducible
References

Back-up slides
Network meta-analysis
Network meta-analysis

Homogeneity

Favours A

Consistency

Favours B