NICE National Institute for Health and Care Excellence

Searching for evidence to inform HTA: View from NICE

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Outline

- Focus on technology appraisals and perspective of the people who support Committee
- Context setting: NICE methods guide and Committee decision making
- Evidence searching in the single (STA) and multiple (MTA) technology appraisal processes
- Case studies from STAs and MTAs
- Things that work well and less well
- How requirements might change in the future

NICE Methods guide

- Consideration of a comprehensive evidence base is fundamental to the appraisal process
- Evidence of various types and multiple sources may inform the appraisal
- Important that attempts are made to identify evidence that is not in the public domain
- Transparent identification of data for intervention(s), comparator(s), utilities and costs
- There are always likely to be deficiencies in the evidence base [….] despite such weaknesses […] decisions still have to be made about the use of technologies

Committee decision-making

- Committee takes account of cost effectiveness, as well as other criteria including: need, innovation, equalities, end of life criteria, non-health factors (with agreement from DH), certainty in evidence base and capture of HRQOL in health economic analysis
- Two Committee discussion slots are allocated per appraisal, approximately 4 hours for the initial Committee discussion, 2 hours for the second
- Committee discussion directed towards aspects of the evidence that influence the decision-making criteria

Single technology appraisal process

- Manufacturer provides an evidence submission
- Evidence Review Group (ERG) provides a critique of the evidence submission
- ERGs should clarify with manufacturer any issues that prevent them from replicating searches and identifying whether relevant evidence excluded
- In the report it is helpful to include:
  - Was the ERG able to replicate the searches?
  - Did the manufacturer exclude any relevant evidence?
  - What is the potential relevance of any excluded evidence to decision-making?

Case study TA271

In manufacturer submission:

Search location	Search strategy
PubMed *(Searched March 23 2012)*	#1: Fluocinolone acetonide
	#2: diabetic macular edema or diabetic macular oedema
	#3: (randomised OR randomized)
	#1 , #2 AND #3

In ERG report:

- The manufacturer's search strategy did not use MeSH terms
- It could have been run on EMBASE in addition to PubMed
- Despite this it did not miss any useful references that a more comprehensive search would have retrieved.

Case study TA271

- Helpful points in report:
  - ERG briefly describe some of the issues with the search
  - Language in report is accessible – not too technical
  - Report states that no useful references missed
- During Committee meeting:
  - Searches were not a focus because despite their weaknesses they were considered not to influence the decision making
  - Searches not discussed in final guidance documents

Case study TA108

- In manufacturer submission:
  - No systematic review of studies of intervention
- In ERG report:
  - States submission did not include a systematic review
  - Indicates that it was unclear on what basis the manufacturer had chosen the three trials they included, and what trials (if any) they omitted and why
  - Notes that few additional studies were found which added to the evidence base regarding efficacy, however their inclusion would have added to the safety data

Case study TA108

ERG report (continued):

Excluded Trials	Key Issues
Buzdar A U *et al*[26]	• Results were classed as interim • This trial is the only one that has an active comparator - the substitution of paclitaxel for 4 cycles of chemotherapy (FAC) • Disease free survival at 4 years was not significant
Citron M L *et al*[27]	• Did not compare paclitaxel to alternative treatments or placebo

Case study TA108

- Helpful points in report:
  - ERG highlight main issue with the review
  - Identify missing evidence
  - Describe the nature of the missing evidence to inform the Committee discussion
- During Committee discussion:
  - Committee discussed absence of systematic review
  - Heard advice from ERG that the results from other potentially relevant trials would be unlikely to affect the conclusion about the clinical effectiveness
  - Discussion reflected in guidance documents

Multiple Technology Appraisal process

- Assessment Group (AG) completes independent assessment of the literature
- NICE consults on the independent assessment before Committee meeting
- Stakeholders have to be able to:
  - Replicate searches
  - Understand how studies included and excluded
- AG provides the main source of evidence for Committee the report will be subject to scrutiny by stakeholders
- Tendency for stakeholders to focus on study selection rather than searches

Case study TA223

- During consultation on Assessment Report:
  - Concerns raised about transparency of trial selection
  - Exclusion of non-English language publications
- During Committee meeting:
  - AG responded to concerns: selection of trials followed a pre-planned protocol, a Cochrane review in subject area suggested no evidence of publication bias, language restrictions do not often influence the results of systematic reviews of conventional medicines
  - Discussion included in guidance document
  - Committee considered that whenever possible non-English language publications should be included.

Works well

- STA:
  - Statement of whether relevant evidence missed
  - Description of any relevant excluded evidence
  - Information about possible impact
  - Keep it succinct and non technical
- MTA:
  - Search strategies that can be replicated
  - Clear inclusion and exclusion criteria with justification
  - Justification of search limits applied
  - Be prepared to justify the process of identifying trials

Works less well

- STA
  - Technical discussion of search strategies - specialist terms tend not to be fully understood
  - Discussion of weaknesses in searches that do not lead to a conclusion about whether relevant evidence was missed or its possible impact
- MTA
  - Lack of justification for search limits and selection criteria
  - For some topics stringent restrictions by study design may not work well, RCTs alone may not be sufficient to provide a basis for decision making

Future information needs

- Within NICE
  - Pressure to provide guidance close to launch and to achieve this with greater efficiency – discussion focused on factors influencing decision making criteria
  - Revised draft submission template (STA) changes emphasis on requirement for systematic review of interventions
  - Value based assessment, the draft approach doesn't explicitly change information needs of Committee but not finalised
- Outside of NICE, but potentially affecting NICE
  - Adaptive licensing may change the nature of the evidence that ERG/AGs have to support the Committee to negotiate
  - Changes to access of trial reports could change the data available and may impact on how searches should be completed and most appropriate sources to search