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:

<table>
<thead>
<tr>
<th>Search location</th>
<th>Search strategy</th>
</tr>
</thead>
</table>
| 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):

<table>
<thead>
<tr>
<th>Excluded Trials</th>
<th>Key Issues</th>
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| 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