TOOLS AND METHODS FOR CROSS-BORDER COLLABORATION IN HTA

ISPOR 13th Annual European Congress, Prague
Educational Symposium, Introduction
7 November 2010
Finn Barlum Kristensen, EUnetHTA Secretariat, Denmark

Symposium

HTA Core Model Online - Structure and Storage for HTA Information
Iris Pasternack MD, Medical Officer
National Institute for Health and Welfare (THL), Finnish Office for HTA (FinOHTA), Helsinki, Finland

Relative Effectiveness Assessment of Pharmaceuticals
Anne d’Andon MD, Head of Medicine Assessment
Haute Autorite de Santé (HAS), Paris, France

Tools for Collaboration on New Technologies
Speaker: Francois Meyer MD, Director, HTA Division
Haute Autorite de Santé (HAS), Paris, France

Q&A

Redundancies in HTA: can we work together?

– Yes if
  • we know what the others do
  • the timing is right
  • we trust each other
  • we use same template
  • we use same language

Adaptation of information from other HTAs: enabling factors

• Relevance
• Acceptable quality standards
• Structured format > elementary structure
• English language
• Transparent reporting

The HTA Core Model

ONTOLOGY
Questions that an HTA should answer

METHODOLOGICAL GUIDANCE
How to answer the questions

REPORTING STRUCTURE
How to present the answers
### Domains
1. Health problem and current use of the technology
2. Description and technical characteristics
3. Safety
4. Clinical effectiveness
5. Costs and economic evaluation
6. Ethical analysis
7. Organisational aspects
8. Social aspects
9. Legal aspects

### Clinical effectiveness:
- **Topics**
  - Mortality
  - Morbidity
  - Function
  - HRQL
  - Patient satisfaction
  - Change-in-management

### Domain: Clinical effectiveness:

#### Topic: Mortality

**Issues:**
- What is the effect of the intervention on overall mortality?
- What is the effect of the intervention on the mortality caused by the target disease?
- What is the effect of the intervention on the mortality due to other causes than the target disease?

**etc**

### Domain: Clinical effectiveness

#### Topic: Morbidity

**Issues:**
- How does the intervention modify the progression of disease?
- How does the intervention modify the severity and frequency of symptoms and findings?
- How does the technology modify the effectiveness of subsequent interventions?

**etc**

### Domain: Social aspects

#### Topic: Major life areas

**Issues:**
- What kinds of changes does the use of the technology generate in the patient's role in the major life areas?
- Who are the important others that the use of the technology may affect in addition to the patient?
- What kind of support and resources are needed or might be released as the technology is put to use?

**etc**

### Core HTA Structure

**Pool of structured HTA information**

**CORE HTA**
- A multidisciplinary assessment protocol using HTA Core Model
- All-care elements
- Summary of key findings
- No recommendation on technology use

**LOCAL HTA**
- A health technology assessment for local use
- Information from Core HTA
- State of HTA information
- Takes into account local information and views

**Shortcut possible**
Work Package 5 - Relative Effectiveness of Pharmaceuticals

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Anne d’Andon, HAS, France

The main objectives of WP5

- Development of HTA tools and methods for Relative Effectiveness Assessments
- Application and field testing of developed tools and methods

Basics
- Using existing expertise and knowledge
- Should be based on national practice
- Must be applicable in daily practice in the EU

WP5 Objectives’ implementation

- Sub Group 1
  - Perform an overview of the processes, the scientific methods used for REA of pharmaceuticals in European countries / US / Canada / Australia & New Zealand

- Sub Groups 2 and 3
  - Develop Models for Rapid and Full REA of Pharmaceuticals
    - Rapid: one drug, just after market authorization, assessed within the transparency directive delay
    - Full: groups of pharmaceuticals aiming the same indication, a longer period after market authorisation, assessed during a longer timeframe
  - Perform pilot assessments
    - Rapid
    - Full

- Sub Group 4:
  - Set up guidelines on methodological issues for REA

The WP5 Partners

- 1 Lead
- 1 Co-lead
- 17 Associated Partners
- 12 Collaborative Partners

WP5 Objectives' implementation
SG1 (CVZ)
Overview

- Literature search on country overviews and methodologies referred to by organisations
- Data abstraction per country based on a standardised data abstraction form
  - Data abstraction performed by 7 organisations: NICE, AHTAPol, REGLOM, IRF, AETSA, ESKI, HAS
- Missing items are discussed with the countries
- Content of the questionnaire (38 questions)
  - Health care system
  - General information about reimbursement of pharmaceuticals
  - REA of pharmaceuticals as part of rapid/single technology assessment
  - REA of pharmaceuticals as part of full/multiple technology assessment
- Report and publication of the results and conclusions

SG1 (CVZ)
Preliminary results of the overview

- 18/34 countries
- Relative efficacy or effectiveness performed by all for reimbursement purpose
- All perform relative efficacy assessment
- A majority performs always relative effectiveness assessment
- One third perform always benefit/risk assessment
- One half perform always cost-effectiveness analysis

For more results look at poster on: RELATIVE EFFECTIVENESS ASSESSMENT OF PHARMACEUTICALS

SG2&3 (CVZ)
Rapid and full REA models

- Three phases during the construction of the Rapid and the Full REA model:
  - Phase 1: Develop 1st version of Rapid and Full model
  - Phase 2: Pilot test
  - Phase 3: Develop final version of Rapid and Full model
- Rapid model
  - For countries that assess directly after market authorisation
  - Use selected domains/topics from the core model
- Full model
  - For countries that assess groups of pharmaceuticals a longer period after market authorisation (indication-based)
  - Use most domains/topics from the core model

SG2&3 (CVZ)
Rapid and full REA models

- Authors and reviewers were sought for the different domains
- Difficulties to find authors and domain leads for some domains
- Solutions:
  - Cooperation with WP4 on some domains in order to decrease duplication;
  - Responsibilities for author- and reviewership are shared for smaller parts of the domain.
- First results from the domain teams are coming in now

SG4 (HAS)
Set up guidelines on methodological issues for REA

1. Comparator and comparisons
   - Criteria for choice of the best/most pertinent comparator(s)
   - Methods of comparison
   - Direct and indirect comparisons
2. Outcomes
   - Clinical outcomes
   - Surrogate markers
   - Composite end-points
   - Quality of life outcomes
   - Patient relevant outcomes
   - Safety
3. Level of evidence
   - Internal validity
   - External validity and Extrapolation from efficacy results to real life situation (effectiveness)
   - Grading confidence in experts and experience

SG4 (HAS)
Methodological issues

- For each subject a guideline is elaborated
- One or two agencies are elaborating one guideline
- Initial version based on literature review
- External experts perform a critical review
- Coherence and link between subjects will be ensured
- Guidelines will be used during the Rapid-REA and Full-REA pilots
Example of first concept guideline
‘Clinical outcomes’

- Prepared by HIQA (National Irish HTA agency)
- Expert involved is Prof A. de Boer (University of Utrecht, The Netherlands)
- Search Strategy
- Analysis and synthesis
- Conclusion
- Final recommendations: a set of 17 pragmatic recommendations

Clinical outcomes
C. Teljeur, P. Harrington, M. Flattery HIQA

Recommendations (1)

Clinical outcomes should be:
- comprehensively defined
- clinically relevant to the disease being treated
- presented to show both statistical and clinical significance
- expressed in natural units (e.g. post-operative infections prevented)

Clinical outcomes
C. Teljeur, P. Harrington, M. Flattery HIQA

Recommendations (2)

- The implications of the outcome should be easy to interpret.
- Clinical outcomes should be sensitive to treatment differences.
- Preference is for an objectively measured clinical outcome.
- Clinical outcomes should be long-term or final outcomes where possible although short-term outcomes are acceptable for acute conditions with no long-term consequences.

Clinical outcomes
C. Teljeur, P. Harrington, M. Flattery HIQA

Recommendations (3)

- All-cause mortality should be used where possible as it is the most unbiased outcome.
- Multiple outcomes can be presented, including adverse outcomes.
- Clinical outcomes should be measurable within a reasonable period of time for all or a high proportion of patients.
- A clinical outcome should be free from measurement or assessment error.

Clinical outcomes
C. Teljeur, P. Harrington, M. Flattery HIQA

Recommendations (4)

- A clinical outcome should be unbiased, especially with respect to detection bias (e.g. appropriately blinded).
- An outcome should be independent of jurisdiction or region to maximise comparability.
- Both relative and absolute measures should be presented.
- Where a continuous outcome is converted to dichotomous, there should be a clear justification for the choice of cut-point.
- Overall survival is the preferred clinical outcome in a survival analysis.
WP7- New Technologies

WP7a
Facilitating evidence generation

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François MEYER, HAS, France

What is it about?

- Sharing agreed relevant information on
  - additional evidence generation required for new technologies
  - planned primary research of relevance to policy

What is the situation?

- For some new technologies (drugs, others)
  - Evidence gaps are identified, common need for additional evidence
  - Data requirements not coordinated or harmonised
  - Multiple studies performed, not coordinated
- Lack of critical mass of robust data to reduce uncertainty
- Waste of money

What is the expected benefit?

- Updated information on new technologies and identified evidence gaps
- Updated information on data requirements in the countries where the technology was assessed
- Possible collaboration to harmonise data requirements
- Studies (multinational or not) with comparable outcomes
- Better information provided to decision makers at the time of the reassessment

Action Plan - Objectives

- Define criteria to select technologies for additional evidence generation
- Share information (database) on technologies
  - Evidence gaps, recommendations for additional data collection (research question, type of study), HTA guidance and coverage and reimbursement status
- Registry of planned clinical studies
  - Pico structure
  - Minimum dataset development (NETSCC and HAS)

Development process

- Review of published information on selection criteria
- Input from WP7 partners: surveys, meetings
- Synthesis of all collected information and proposal of first draft of deliverables by HAS and NETSCC
- Comments from stakeholders on preliminary versions of deliverables
- Public consultation
**Practical deliverables**

- **Criteria**
  - to select, among new technologies, the ones for which data collection will be useful and efficient

- **Interactive web-based tool**
  - User friendly IT functionalities
  - Visual structure with rapid information access

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**E.g. for each new technology**

<table>
<thead>
<tr>
<th>Country, partner organization</th>
<th>DE</th>
<th>IT</th>
<th>FR</th>
<th>PT</th>
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<tbody>
<tr>
<td>Name of New technology</td>
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<td>Type : device, drug, procedure</td>
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<td>Therapeutic domain</td>
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<td>HTA status (HTA report and e-link)</td>
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<td>Status of the technology (Reimbursement/Coverage)</td>
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<td>Rationale for additional evidence generation</td>
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<td>Research question</td>
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<td>Minimum dataset for each study</td>
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<td>Status of the study requested /funded</td>
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<td>Study results (when available) and decision taken</td>
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**Thank you!**

f.meyer@has-sante.fr
sh.leerobin@has-sante.fr