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TOOLS AND METHODS FOR CROSS-BORDER COLLABORATION IN HTA

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

Symposium

HTA Core Model Online - Structure and Storage for HTA Information
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Relative Effectiveness Assessment of Pharmaceuticals
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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

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HTA Core Model Online®

Structure and Storage for HTA Information

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Iris Pasternack, FINOHTA/THL

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**

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Adaptation of information from other HTAs: enabling factors

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

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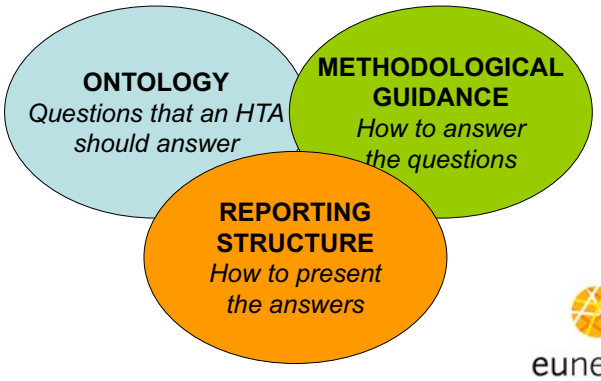
The HTA Core Model



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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***

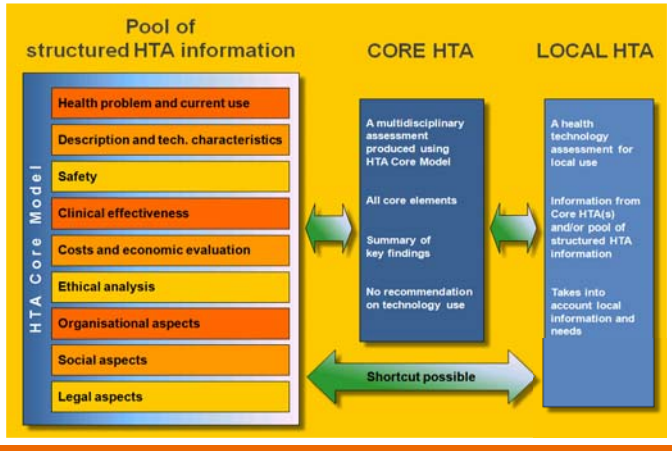
Domain: Social aspects

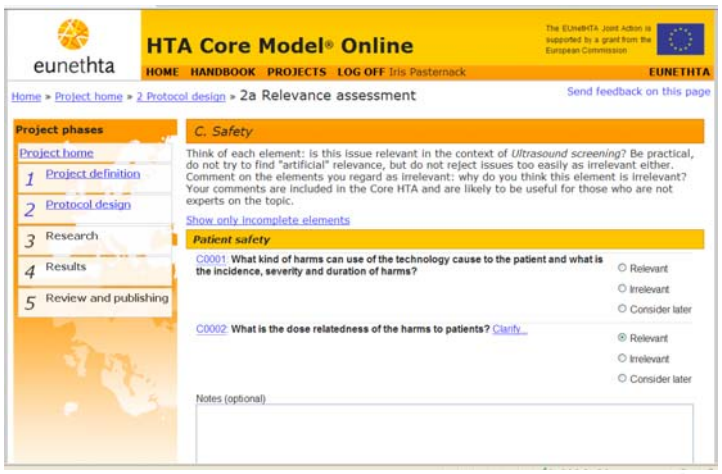
Topic: Major life areas

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





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Work Package 5 - Relative Effectiveness of Pharmaceuticals

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Anne d'Andon, HAS, France

EUnetHTA WP5 Relative effectiveness of pharmaceuticals

- **Integration of REA of pharmaceuticals in the scope of EUnetHTA JA**
- **Based on the definitions of the Pharmaceutical Forum**
  - **Relative effectiveness can be defined as the extent to which an intervention does more good than harm compared to one or more intervention alternatives for achieving the desired results when provided under the usual circumstances of health care practice**

The main objectives of WP5

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

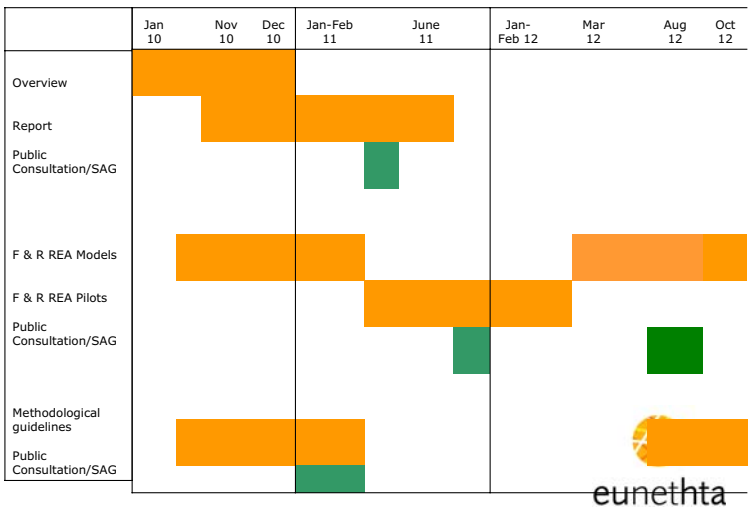
Basics
- Using existing expertise and knowledge
- Should be based on national practice
- Must be applicable in daily practice in the EU

The WP5 Partners

- **1 Lead** CVZ **1 Co-lead** HAS
- **17 Associated Partners**
- **12 Collaborative Partners**

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**



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

SG4 (HAS)
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

SG4 (HAS)
Example of first concept guideline 'Clinical outcomes'

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- 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.**

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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

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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

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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

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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)**

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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

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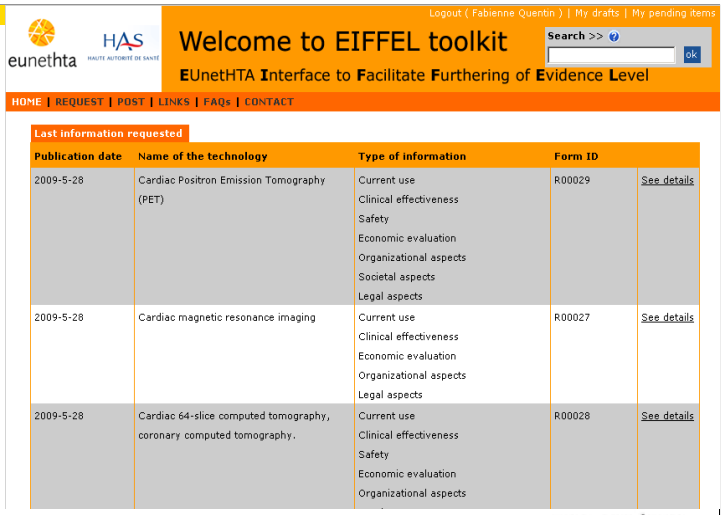
Practical deliverables

- **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



E.g. for each new technology

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

Thank you !

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EDUCATIONAL SYMPOSIUM