Apply(ing) the HTA Core Model for Rapid Assessment for national adaptation and reporting

Sime Warren, National Health Care Institute of the Netherlands, Diemen, the Netherlands
Anna Nachtnebel, Ludwig Boltzmann Institute for HTA, Vienna, Austria

WP5 - Applying the HTA Core Model for Rapid Assessment for national adaptation and reporting

Third WP2 Face to Face Training Course for EUnetHTA stakeholders, Brussels, 23rd of April 2015
WP5 Partners Overview

**Lead Partner:** ZIN, the Netherlands

**Co-Lead Partner:** LBI for HTA, Austria

**27 Associated Partners:**
Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain

**24 Collaborating Partners:**
Austria, Belgium, Bulgaria, Denmark, Germany, Italy, Ireland, Luxembourg, Russia, Romania, Scotland, Spain, Switzerland, Turkey
**Objective**

- Test the capacity of national HTA bodies to produce structured core HTA information (full core/rapid HTAs) together
- Apply the produced information in national context

**Products**

**Strand A: Pharmaceuticals**

- Development of procedure
- 7 pilot rapid assessments
- Update of HTA Core Model for Rapid REA of pharmaceuticals

**Strand B: Other Technologies***

- Development of procedure
- ≥ 4 pilot rapid assessments
- Adaptation of HTA Core Model for Rapid REA for other technologies

**± 30 national assessments**

<table>
<thead>
<tr>
<th>Month</th>
<th>1-12</th>
<th>Oct '13</th>
<th>13-24</th>
<th>Oct '14</th>
<th>25-36</th>
<th>Oct '15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct '12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct '13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct '14</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct '15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*such as medical devices, diagnostics and medical interventions*
Table of contents

SUMMARY OF RELATIVE EFFECTIVENESS OF THE DUODENAL-JEJUNAL BYPASS SLEEVE (DJBS) ................................................................. 6
  SCOPE ........................................................................................................ 6
  INTRODUCTION ..................................................................................... 7
  METHODS ............................................................................................... 8
  RESULTS .................................................................................................. 9
  DISCUSSION .......................................................................................... 13
  CONCLUSION .......................................................................................... 14

LIST OF ABBREVIATIONS ....................................................................... 15

1. SCOPE ................................................................................................... 16

2. HEALTH PROBLEM AND CURRENT USE OF THE TECHNOLOGY .......... 18
   METHODS .............................................................................................. 18
   MAIN RESULTS .................................................................................... 20
   DISCUSSION ........................................................................................ 29

3. DESCRIPTION AND TECHNICAL CHARACTERISTICS OF TECHNOLOGY ....... 30
   METHODS .............................................................................................. 30
   MAIN RESULTS .................................................................................... 31
   DISCUSSION ........................................................................................ 33

4. SAFETY ..................................................................................................... 34
   METHODS .............................................................................................. 34
   MAIN RESULTS .................................................................................... 35
   DISCUSSION ........................................................................................ 35

5. CLINICAL EFFECTIVENESS ................................................................. 36
   METHODS .............................................................................................. 36
   MAIN RESULTS .................................................................................... 38
   DISCUSSION ........................................................................................ 39

6. REFERENCES ............................................................................................ 41

No recommendations!
Work Package 5 Strand A

Rapid relative effectiveness assessment of pharmaceuticals
Topic Selection

- Technology under evaluation by Committee for Medicinal Products for Human Use (CHMP)
  → Expression of interest by WP5 SA members based on the CHMP list

- Expression of interest to participate by the Market Authorization Holder (by letter)
Tools for Strand A

- Model for rapid REA
  - HPCU
  - DTC
  - Clinical effectiveness
  - Safety

- Guidelines that provide methodological guidance

- Procedure manual that describes Strand A process

- Assessment template that provides guidance for reporting

- Submission file template that is submitted by manufacturer

Guidelines on Methodological Issues:
- Comparators and comparisons
- - Choice of choice of most appropriate comparator(s)
- - Method of comparator
- and control

Outcomes:
- - Clinical endpoints
- - Surrogate endpoints
- - Health-related quality of life
- - Safety

Level of evidence:
- - Internal validity
- - Applicability

*+ checklist for ethical, organisational, social and legal issues
Strand A - Processes for Rapid Assessments

author
Agency A

co-author
Agency B

pool of dedicated reviewers
agency C  agency D  agency E  agency F  agency G

MAH (Strand A)/ WP5 members review

1st version of REA

Editorial version of REA

Final of REA
Figure 2: Schematic overview of the Scoping Phase

It should be noted that these graphs represent the ideal picture; however, divergence is very possible for specific joint RFA's.

**Timeline (days):**
- **180 days before CHMP opinion:**
  - WPS members: WPS expression of interest on topic proposition
  - Dedicated reviewers: Selection of 1 author 1 co-author and 2-5 dedicated reviewers
  - Authors/Co-authors: Request for authorship (2 weeks)
  - Coordination Team: Request for draft submission file
  - Company applying for MAA: Expression of interest
  - Draft submission file

- **90 days before CHMP opinion:**
  - Pre-Scope: Scoping meeting
  - Scoping face-to-face meeting
  - Feedback on draft submission file (2 weeks)

- **0 days:**
  - Receive final submission file
  - Finalisation of project plan incl. timelines
  - Final submission file (4 weeks)

**EMA:** Ongoing EMA process (start of official MAA process = 210 days / 150 days until CHMP opinion)

Legend:
- External products
- EU net MTA products
- Meetings

* Based on the list of applications for new human medicines under evaluation by CHMP
1. Expression of interest regarding topic by:
   - Pharmaceuticals company
   - HTA organisation (WP5 members)
2. Selection of Author/Co-Author/Reviewers (WP5 internal process)
3. Receive draft submission file from MAH
4. Pre-Scoping E-Meeting
5. Scoping meeting with MAH (f-t-f)
6. Feedback from Authors on draft submission file
7. Receive final submission file
8. Finalisation of project plan including timelines
WP5 Strand A - Assessment Phase

Figure 3: Schematic overview of the Assessment Phase
It should be noted that these graphs represent the ideal picture; however, divergence is very possible for specific joint REA’s.
WP5 Strand A - Assessment Phase

1. Preparing the first draft of the assessment by the Author and Co-Author (35 days)

2. Review by dedicated reviewers (10 days)

3. Preparation of second draft of the assessment by authors (15 days)
WP5 Strand A - Assessment Phase

4. Editorial review and layouting (15 days)

5. Consultation phase of all WP5 members and market authorization holder (10 days)

6. Final version of the assessment (15 days)

7. Publication of final report and implementation into the national context
First Pilot: Zostavax

- Zostavax for the prevention of herpes zoster and post herpetic neuralgia
- Pilot team:
  - Author: CVZ (NL)
  - Co-Author: “A. Gemelli” Teaching Hospital (IT)
  - Dedicated reviewers: HAS (FR), GOG (A), MoH Czech Republic, DPA/MFH (M), RIZIV (B), MSSSI (S), Regio Veneto (IT)
- Duration: 04/2013- published on the EUnetHTA website on 08/2013
- Uptake or use in local/national reports: Austria (twice, 2013), Spain (2013), the Netherlands (2014), possible France (2014)

Second Pilot: Canagliflozin

- Canagliflozin for the treatment of type II diabetes mellitus

- Pilot team:
  - Authors: AAZ (Croatia), FIMEA (Finland), Regione Veneto (Italy)
  - Dedicated reviewers: HAS, HVB; CAHIAQ; Medical University of Sofia; MoH Czech Rep.

- Duration: 05/2013 - 02/2014
  - Delay mostly due to external factors (i.e. delayed decision of CHMP)

- Local reports → Finland, Croatia, the Netherlands
  - (Data still being updated)

Third Pilot: Sorafenib

- Sorafenib for the treatment of progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma refractory to radioactive iodine
- Pilot team:
  - Authors: AIFA (Italy), INFARMED (Portugal)
  - Dedicated reviewers: RIZIV (Belgium), FIMEA (Finland), GYEMSZI (Hungary), NCPE (Ireland), Slovakian MoH
- Duration: 07/2014 - 03/2015
- Local reports → Awaiting more information

Fourth Pilot: Ramucirumab

- Ramucirumab in combination with Paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma

- Pilot team:
  - Authors: NOKC (Norway), AAZ (Croatia),
  - Dedicated reviewers: Slovak Ministry of Health, FIMEA (Finland), GYMSZI (Hungary), A.Gemelli Teaching Hospital (Italy)

- Duration: 11/2014 - 03/2015
  - Pilot met the agreed upon timelines

- Local reports → Awaiting more information

Future Pilot Planning

Work Package 5
Strand A

WP5-SA5
Assessment Phase

WP5-SA6
Scoping Phase

WP5-SA7
Topic selection
WP5 Strand B –
Joint Assessment on ‘other technologies’
- Test the capacity of national HTA bodies to produce structured core HTA information (full core/rapid HTAs) together
- Apply the produced information in national context

**Objective**

**Strand A: pharmaceuticals**
- 7 pilot rapid assessments
- Update of HTA Core Model for Rapid REA of pharmaceuticals

**Strand B: Other technologies**
- ≥ 4 pilot rapid assessments
- Adaptation of HTA Core Model for Rapid REA for other technologies
- ± 30 national assessments

*such as medical devices, diagnostics and medical interventions

<table>
<thead>
<tr>
<th>Month</th>
<th>1-12</th>
<th>Oct '12</th>
<th>13-24</th>
<th>Oct '14</th>
<th>25-36</th>
<th>Oct '15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oct '12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Tools for Strand B

Guidelines provide methodological guidance

Procedure manual that describes Strand B process

Assessment template provides guidance for reporting

Submission File template that is submitted by manufacturer(s)

Guidelines on Methodological Issues:
- Comparators and comparisons
- Criteria for choice of most appropriate comparator(s)
- Method of comparison
- Clinical comparativeness

Outcomes:
- Clinical outcomes
- Surrogate endpoints
- Cost-effectiveness
- Health-related quality of life
- Safety

Level of evidence:
- Internal validity
- Appropriateness

* + checklist for ethical, organisational, social and legal issues

+ consideration of other Core Model applications

Provides working framework through a set of research questions*
Team Building and Topic selection

Relevance of topic assessed will determine participation by other members AND uptake of assessment in local/national context,

**No technology specific assessments – class assessments**

2 options:

1. **Call for collaboration:** Authoring agency selects 2 topics out of their own work programme – WP5 members are asked to indicate their preference – choice of final topic

   Also members are asked if they want to contribute: co-authors, dedicated reviewers

2. **POP- Database:** overlap in topics indicate potential partners for collaboration and also relevance for other countries. Authors can approach agencies directly and ask if collaboration would be feasible
Team

1 authoring agency: responsible for the overall quality of the assessments, usually for Effectiveness and Safety Domain and for the Summary

1 – 3 co-authors: assist authoring agency in selection of relevant assessment elements of HTA Core Model for Rapid REA; quality of assurance of work of author; usually responsible for authoring 1 – 2 other domains

Dedicated reviewers: 3 – 6; read first draft of assessment – quality assurance

Coordination Team: LBI-HTA for managing contact with manufacturers/Stakeholder Forum(Stakeholder Advisory Group), overseeing communication/work-flow within pilot team
Modes of collaboration

Agency A: author of all domains

Agency B: co-author checks work of author

Agency C: 1-? domains

Agency D: 1-? domains

Authors and co-authors

Dedicated reviewers

WP5

Agency A: 1-? domains
Production of assessments

- **Pilot team:**
  - 1 – 3 (co)authors
  - 3 – 6 dedicated reviewing agencies
  - Coordination Team
  - EUnetHTA members

- **Stakeholders:**
  - Manufacturers: evidence, reimbursement status, project plan, assessment, submission file
  - Patient/Consumer representatives: project plan, assessment
  - Medical experts: project plan, assessment
  - Stakeholder Advisory Group/Stakeholder Forum: project plan
  - Public: project plan
Scoping Phase

Public

WP5 members

Dedicated reviewers

Co-authors

Authors

Coordination team

Manufacturer(s)

Selection of ≥ 1 co-author and ≥ 5 dedicated reviewers

Receive draft submission file

Writing first draft of Project Plan

Receive final submission

Draft Project Plan

Final project plan

Public consultation of final project plan

Identification of topics and call for collaboration

Request for draft submission file

Scoping e-meeting

Scoping face-to-face meeting

Submission of topics (optional)

draft submission file

final submission file
Assessment Phase
## Published Joint Assessments

<table>
<thead>
<tr>
<th>Duration</th>
<th>Duodenal-jejunal bypass sleeve for the treatment of obesity with or without type II Diabetes mellitus</th>
<th>Renal denervation for treatment resistant hypertension</th>
<th>Balloon Eustachian Tuboplasty for the treatment of Eustachian tube dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>Duration</td>
<td>Duration</td>
<td></td>
</tr>
<tr>
<td>Pilot team agencies, n</td>
<td>8</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>(Co-)Authoring HTA bodies</td>
<td>LBI-HTA (Austria) AAZ (Croatia)</td>
<td>NOKC (Norway) Avalia-t (Spain) CFK (Denmark)</td>
<td>FinOHTA/THL HIQA (Ireland)</td>
</tr>
<tr>
<td>Dedicated reviewing HTA bodies</td>
<td>GYMEZSI (Hungary) HIQA (Ireland) HVB (Austria) ISCIll (Spain) NOKC (Norway) Charles University Prague (Czech Republic)</td>
<td>HIS (UK) FinOHTA/THL (Finland) AHTAPol (Poland) GYMEZSI (Hungary) IQWiG (Germany)</td>
<td>GYMEZSI (Hungary) HVB (Austria) AHTAPol (Poland)</td>
</tr>
</tbody>
</table>
## Ongoing Joint Assessment

<table>
<thead>
<tr>
<th>Duration</th>
<th>Biodegradable stents for benign refractory esophageal stenosis</th>
<th>Implantable devices for the treatment of mitral valve regurgitation</th>
<th>Mechanical thrombectomy in acute ischaemic stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2014 – August 2015</td>
<td></td>
<td>October 2014 – September 2015</td>
<td>April 2015 – December 2015 (TBC)</td>
</tr>
<tr>
<td>Pilot team agencies, n</td>
<td>5</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>(Co-)Authoring HTA bodies</td>
<td>ISCIII (Spain) SAGEM (Turkey)</td>
<td>Agenas (Italy) AAZ (Croatia) MoH (Slovakia)</td>
<td>HIQA (Ireland) Interdisciplinary Centre for HTA and Public Health University of Erlangen-Nürnberg (Germany)</td>
</tr>
<tr>
<td>Dedicated reviewing HTA bodies</td>
<td>VASPVT (Lithuania) Slovak Ministry of Health (Slovakia) LBI-HTA (Austria)</td>
<td>HAS (France) BIQG/GÖG (Austria) AETSA (Spain) AAZ (Croatia) HIQA (Ireland) HIS (Scotland)</td>
<td>CFK (Denmark) LBI-HTA (Austria) HAS (France) HIS (Scotland) A. Gemelli Hospital (Italy)</td>
</tr>
</tbody>
</table>
National adaptation...?
WP3 Survey results – Has your organisation used HTA information?

- CRC Screening (WP4): 20.00%
- Herpes zoster vaccine: 26.67%
- Canagliflozin (Invokana): 13.33%
- Duodenal-jejunal bypass site: 33.33%
- Renal denervation: 60.00%

Answered: 15  Skipped: 149
WP3 Survey results – Purpose of use

Duodenal-jejunal bypass sleeve (EndoBarrier®) (WP5 Pilot Strand B) n=5
- national report
- reimbursement decision
- Training purposes
- producing national report
- national report, is still not finished yet

Renal denervation systems (WP5 Pilot Strand B) n=10
- For updating and enhancing decision making
- the assessment had been planned but was withdrawn by applicant
- decision making
- disinvestment decision
- To compare with our own report on this topic and check coverage of evidence
- National report for hospital decision
- Local decision about implementation
- Decision making
- Directly for decision making
- To inform appropriate indications and funding at national level
WP3 Survey results – Have you planned to use HTA information
Examples for national adaptation of Assessments

LBI produced local report based on EUnetHTA Zostavax (November 2013) Assessment

- Translation to German
- Adaptation to LBI format
- Tables directly copied from English EUnetHTA assessment
- Shorter Version
- Adaptation with context specific Austrian data on e.g. epidemiology, costs
Examples of national adaptation

ISCIII produced local report based on EUnetHTA
EndobARRIER assessment
(September 2014)

• Translation to Spanish
• Adaptation to ISCIII format
• English summary
• Update of literature search
Group work

- Could you/would you use the assessment directly for deriving a decision? If so, why? If not, why not, which further information would you still need?

- Which decision would YOU derive based on the information provided in the assessment?
Thank you!

This presentation arises from the EUnetHTA Joint Action 2 which has received funding from the European Union, in the framework of the Health Programme