How to use HTA for decision making?
Stakeholder involvement

EUnetHTA Training Course for Stakeholders
Rome, 29 Oct 2014

Anna Nachtnebel LBI-HTA, Austria
Tove Ringerike, NOKC, Norway
## Session outline

### 1. How to use HTA for decision making:
**Learning outcome:** Understand how HTA assessments (EUnetHTA pilots) can be used for decision making, its usefulness and its limits.

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00</td>
<td>Presentations</td>
</tr>
<tr>
<td></td>
<td>• Introduction to Rapid Assessments of other technologies</td>
</tr>
<tr>
<td></td>
<td>• Renal Denervation Assessment - Case Example</td>
</tr>
<tr>
<td></td>
<td>• Different forms of usage of pilots</td>
</tr>
<tr>
<td>14:30</td>
<td>Group work</td>
</tr>
</tbody>
</table>

### 2. Stakeholder involvement
**Learning outcome:** Provide patients and providers with tools and knowledge to facilitate participation in the HTA process

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:00</td>
<td>Presentation</td>
</tr>
<tr>
<td></td>
<td>• Overview on current stakeholder involvement in Strand B</td>
</tr>
<tr>
<td>16:10</td>
<td>Plenary</td>
</tr>
</tbody>
</table>
How to use HTA for decision-making
Work Package 5 - Objectives

To test the **capacity** of national/local HTA bodies to **collaboratively produce pilot rapid assessments**

To test the application (transportation) of those collaboratively produced assessments in the **national/local context**

Adaptation of the “HTA Core Model for Rapid Relative Effectiveness”
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

Strand A: pharmaceuticals

10 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
WP5 Members

- **Associated partners – AP (27 partners)**
  - ZIN (Netherlands); LP
  - LBI-HTA (Austria); Co-LP
  - HVB (Austria); active, Strand A + B
  - BIOQ/GÖG (Austria); less active, Strand A + B
  - KCE (Belgium); less active, Strand B
  - MoH (Cyprus); less active, Strand A
  - MoH (Czech Republic); less active, Strand A + B
  - AAZ (Croatia); active, Strand A + B
  - CR.DK (Denmark); active, Strand B
  - FIMEA (Finland); active, Strand A
  - THL (Finland); active, Strand B
  - HAS (France); active, Strand A + B
  - IQWIG (Germany); less active Strand A + B
  - GYEMSZI (Hungary); less active, Strand A + B
  - HIOA (Ireland); active, Strand B
  - Agenas (Italy); active, Strand B
  - Regione Veneto (Italy); active, Strand A + B
  - AIFA (Italy); active, Strand A
  - NHS (Latvia); less active, Strand A + B
  - VASPVT (Lithuania); active, Strand A + B
  - MFH (Malta); less active, Strand A + B
  - NOKC (Norway); active, Strand A + B
  - AHTAPol (Poland); less active, Strand A + B
  - INFARMED (Portugal); active, Strand A
  - Ministry of Health of the Slovak Republic (Slovakia); active, Strand A + B
  - NIPH (Slovenia); less active, Strand B
  - ISCIII (Spain); active, Strand B

- **Collaborating partners – CP (24 partners)**
  - Donau Universität Krems (Austria); less active, Strand B
  - RIZIV (Belgium); less active, Strand A + B
  - Medical University of Sofia (Bulgaria); active, Strand A + B
  - KORA (Denmark); less active, Strand A
  - Interdisciplinary Centre for Health Technology Assessment (HTA) and Public Health, University of Erlangen-Nuremberg, National BMBF-Cluster of Excellence „Medical Technologies - Medical Valley EMN“ (Germany); active, Strand B
  - NCPE (Ireland); less active, Strand A
  - CMSS Luxembourg
  - Laziosanità (Italy); active, Strand B
  - University Hospital “A. Gemelli” (Italy); active, Strand A + B
  - NCHTA (Russia); less active, Strand A + B
  - Healthcare Improvement Scotland (Scotland); less active, Strand A + B
  - AETSA (Spain); less active, Strand A
  - DGCF MSSSI (Spain); less active, Strand A
  - Basque Office for HTA (Spain); less active, Strand B
  - CAHIAQ (Spain); less active, Strand A
  - Avalia-t (Spain); active, Strand B
  - Swiss Federal Office for Public Health (Switzerland); Strand A + B
  - SAGEM HTA (Turkey)
  - KDTD (Turkey); less active
  - CHIF (Croatia); active, Strand A
  - SMCA (Lithuania); less active
  - SAGEM (Turkey); less active, Strand A + B
  - CMSS (Luxembourg); less active
  - NCPRMP (Romania); less active
  - SESCO (Spain)
  - Tubitak (Turkey)
Strand B

**Tools**

- **Model for Rapid REA**
  - Health Problem and Current Use
  - Description and technical characteristics
  - Clinical effectiveness
  - Safety
  - + other Core Model Applications

- **Guidelines on methodological issues**
  - Comparators and combinations
    - Criteria for choice of most appropriate comparator(s)
    - Methods of comparing clinical and clinical effectiveness
  - Outcomes
    - Clinical endpoints
    - Scoring analysis
    - Comparative effectiveness
    - Health-related quality of life
    - Safety
  - Level of evidence
    - Internal validity
    - Applicability

- **Assessment template that provides guidance for reporting**

- **Reliable, timely, transparent, transferable HTA information**

**Rapid assessments**

- **Model that provides framework through a set of research questions, but also other applications**
  - + checklist for ethical, organisational, social and legal issues

- **Guidelines that provide methodological guidance**

- **Assessment template that provides guidance for reporting**

- **Procedure manual that describes process of Strand B**

- **SUMMARY OF RELATIVE EFFECTIVENESS OF 2006**

### HTA Core Model for Rapid REA – assessment elements

<table>
<thead>
<tr>
<th>AE</th>
<th>Topic</th>
<th>Issue</th>
<th>Abbreviated clarification</th>
</tr>
</thead>
<tbody>
<tr>
<td>A0001</td>
<td>Utilisation</td>
<td>For which health conditions and populations, and for what purposes is the technology used?</td>
<td>List relevant conditions and populations (…); Point out e.g. if certain populations should be excluded from using the technology.</td>
</tr>
<tr>
<td>A0002</td>
<td>Target Condition</td>
<td>What is the disease or health condition in the scope of this assessment?</td>
<td>Target condition and ICD codes defined in the scope; details such as: description of anatomical site, disease aetiology and pathophysiology, types of disease or classification according to origin, severity, stages, or risk level, and different manifestations of the condition.</td>
</tr>
<tr>
<td>A0005</td>
<td>Target Condition</td>
<td>What is the burden of disease for the patient?</td>
<td>This element should describe the patient’s relevant symptoms before intervention with the technology, their severity and whether they are persistent, intermittent, or undulating.</td>
</tr>
<tr>
<td>A0007</td>
<td>Target Population</td>
<td>What is the target population in this assessment?</td>
<td>Subpopulation towards which the intervention is targeted (…) Use the target population defined in the scope of the project, and consider adding further details and description of who defined the selected subgroups and why.</td>
</tr>
<tr>
<td>B0001</td>
<td>Features of the technology</td>
<td>What is the technology and the comparator(s)?</td>
<td>Use the descriptions of the technology and comparator(s) defined in the scope and elaborate them here in more detail. Describe separately for the technology and the comparator the type of device, technique, procedure or therapy; its biological rationale and mechanism of action? etc</td>
</tr>
<tr>
<td>D001</td>
<td>Mortality</td>
<td>What is the expected beneficial effect of the intervention on overall mortality?</td>
<td>Mortality is the preferred, objective endpoint for assessments of life-threatening conditions. Overall mortality refers to all-cause mortality. It is expressed either as mortality rates (incidence in given population, at given time point and usually risk standardised), or survival (number of people alive for a given period after an intervention).</td>
</tr>
<tr>
<td>D0012</td>
<td>Health-related quality of life</td>
<td>What is the effect of the technology on generic health-related quality of life?</td>
<td>Report the results both in absolute terms and relative to the comparator. For further information see guideline Health-related quality of life and utility measures.</td>
</tr>
<tr>
<td>C0001</td>
<td>Patient safety</td>
<td>What kind of harms can use of the technology cause to the patient?</td>
<td>Here one should identify and describe the direct harms of the use and the administration of the technology. Comparative harms are described in C0008. etc</td>
</tr>
</tbody>
</table>
### Topic selection

1. **POP database**: overlaps in topics listed at POP?

<table>
<thead>
<tr>
<th>Intervention/Indication</th>
<th>Potential 1st Authors</th>
<th>Potentially collaborating agencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care programme for patients with chronic renal insufficiency</td>
<td>NOKC</td>
<td>HAS</td>
</tr>
<tr>
<td>Carpal tunnel syndrome</td>
<td>THL</td>
<td>HAS</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>NOKC</td>
<td>OSTEBA</td>
</tr>
<tr>
<td>Colorectal Cancer Screening Programs</td>
<td>THL</td>
<td>Reg Veneto</td>
</tr>
<tr>
<td>Early detection, prevention, risk prediction of breast cancer</td>
<td>HIQA</td>
<td>IQWIG</td>
</tr>
<tr>
<td>Endovascular treatment of abdominal aortic aneurysm</td>
<td>Agenas</td>
<td>LBI-HTA</td>
</tr>
<tr>
<td>HPV test screening for cervical cancer</td>
<td>HAS</td>
<td>MHEC-DPA</td>
</tr>
<tr>
<td>HPV vaccine</td>
<td>NOKC</td>
<td>AAZ</td>
</tr>
<tr>
<td>Internal radiation therapy of tumors of the gastrointestinal tract</td>
<td>Agenas</td>
<td>MHEC-DPA</td>
</tr>
</tbody>
</table>

2. **Call for collaboration**: authoring agency selects relevant topics out of its own work programme – notification/inquiry to Strand B members
2 Collaboration models for pilots so far…

Agency A: author of all domains

Agency B: co-author checks work of author

Agency C: 1-? domains

Agency D: 1-? domains

WP5 members:

Agency A:

Agency B:

Agency C:

Agency D:
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!
Assessments

- **2 Published:**
  - Duodenal-jejunal bypass sleeve for the treatment of obesity with or without Type II Diabetes mellitus: published August 2013
  - Renal denervation systems for treatment-resistant hypertension: published December 2013

- **3 Ongoing:**
  - Balloon Eustachian tuboplasty for the treatment of Eustachian tube dysfunction: external review, planned publication December 2014
  - Biodegradable stents for benign refractory esophageal stenosis: postponed – RCT in publication
  - Implantable devices for the treatment of mitral valve regurgitation (TBC)
EUnetHTA JA2 WP5 – Strand B: Renal Denervation Assessment Case Example

Tove Ringerike for the RDN pilot team
We could change the colors in my part of the presentation to “EunetHTA” colors, might look nicer. Do you know how to switch colors?

Author: 1/10/2014
Renal denervation systems for treatment-resistant hypertension

- Joint production by:
  - Public Health and Quality Improvement, Central Denmark Region (CFK), Denmark
  - Galician Health Technology Assessment (Avalia-t), Spain
  - Norwegian Knowledge Centre for the Health Services (NOKC), Norway
- Coordinating team WP5B: LBI-HTA, Austria

What is renal denervation?

Ablating Renal Sympathetic Nerves To Treat Resistant Hypertension

Three forms of energy are being studied for trans-catheter based renal denervation:

- Radiofrequency
- Ultrasound
- Chemical

Source: http://www.renaldenervationworld.org/
What do you need to know before making a decision?

In a HTA perspective, it is important that we choose the most relevant outcomes, especially patient centered outcomes.

Use methodological guidelines (http://www.eunethta.eu/eunethta-guidelines)

1. Clinical endpoints
2. Composite endpoints
3. Surrogate endpoints
4. Safety
5. Health-related quality of life
6. Criteria for the choice of the most appropriate comparator(s)
7. Direct and indirect comparison
8. Internal validity
9. Applicability of evidence in the context of a relative effectiveness assessment
### Scope

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with treatment-resistant arterial hypertension (defined as persistent hypertension despite administration of at least 3 antihypertensive drugs in adequate doses, including a diuretic) with blood pressure ≥ 140/90 mm Hg (Calhoun 2008, Mancia 2013) and without secondary cause of hypertension.</th>
</tr>
</thead>
</table>
| Intervention        | Renal nerve ablation and denervation systems  
This intervention entails the destruction of efferent sympathetic nerves and afferent nerves in the wall of the renal arteries to reduce sympathetic nerve traffic, thereby reducing blood pressure. |
| Comparator(s)       | Standard of care (which includes here: no treatment, additional pharmacological treatment, device-based therapy for hypertension and sham treatment)  
All patients continue treatment with at least 3 hypertensive drugs. Any additional intervention or comparator is administered as add-on therapy. |
| Outcome(s)          | **Primary outcomes:**  
Overall mortality  
Cardiovascular mortality  
Cardiovascular morbidity (stroke, myocardial infarction, heart failure)  
Blood pressure (changes in systolic and diastolic blood pressure)  
Complications during or after treatment  
**Secondary outcomes:**  
Left ventricular hypertrophy/systolic and diastolic cardiac function  
Kidney function  
Quality of life  
Effect on daily living |
| Study design        | Efficacy/effectiveness: Systematic reviews (SRs)/Health Technology Assessments (HTAs), randomised controlled trials (RCTs) and, if data from RCTs are lacking or insufficient, prospective, controlled studies  
Safety: Same as for efficacy and including all prospective studies |
| Languages           | English, Spanish, French, German, Swedish, Danish, Norwegian |
Process

Project plan
Final assessment

Feed-back and peer-review
- Dedicated reviewers
- Other WP5 members
- Public consultation /Stakeholders
- Medical editing
Why we chose to assess RDN

RDN suggested by NOKC, based on clinical interest/commission in Norway (winter 2012-2013)
The technology was in use in clinical trials, but not yet widely used in clinical practice

A perfect time for doing the assessment?
Delete? Depend on what you cover in your slide on topic selection/POP database.

Author: 1/10/2014
Plan A: Single technology assessment
Plan B: Multiple technology assessment

- The initial plan was to assess the Simplicity device from Medtronic
- However, feedback from other companies encouraged us to assess more than one device

One could ask if it was necessary to do a class review?
Identified systems

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>CE-marked</th>
<th>FDA review</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiofrequency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symplicity®</td>
<td>Medtronic</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Mariner®</td>
<td>Medtronic</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>EnlighHTN™</td>
<td>St. Jude Medical</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Vessix V2™</td>
<td>Boston Scientific</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>OneShot™</td>
<td>Covidien</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Iberis™</td>
<td>Terumo</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>ThermoCool®</td>
<td>Biosense Webster</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Ultrasound</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PARADISE™</td>
<td>ReCor Medical</td>
<td>Y</td>
<td>N</td>
</tr>
</tbody>
</table>

Y = yes; N = no
I will not draw any attention to the fact that we actually include information on devices without CE mark. But it is something we easily could have added as exclusion criteria. So much easier to know these things in hindsight.

Author: 1/10/2014
Selection of methods used:

Depend on:
- Maturity/developmental status of the technology
- Issues to be addressed in that domain
- Topic
- Resources

They may differ between projects and sections!
Description of the methods used is included in each domain.
Delete? Not relevant for the audience group?

Author: 1/10/2014
What we did

Search in electronic databases for published trials and in clinical trial registries for ongoing trials

For safety we included all prospective trials
For clinical effectiveness we only included prospective trials with a control group
What we found

Safety (3 RCT, 3 non-RCT, 16 case series) -> 13 studies reported procedure-related complications, mostly of mild to moderate nature.

Clinical effectiveness (3 RCT, 1 controlled trial) -> no/very limited data on hard endpoints or long-term effects. Limited data suggests decrease in blood pressure.

Several ongoing or planned studies
How to handle ongoing studies?

- We identified several ongoing studies.

It is important to assess the willingness to wait for additional data versus the need to make a decision?
Conclusion

The published data suggest that RDN is a safe procedure in the short to medium term. However, because safety was not considered the main endpoint, it can not be dismissed that some complications were not adequately reported.

In terms of clinical effectiveness, renal denervation using the Symplicity® system appears to decrease BP, whereas the effects of other systems on BP are uncertain, because they have only been examined in trials that included very few patients. The assessment of other outcomes, including mortality and cardiovascular morbidity, remains inconclusive.

So in plain language we did not find any alarming cause for concerns about safety, but are not quite sure if the technology will actually perform well on patient centered outcomes like mortality and cardiovascular events.
What has happened after publication of the pilot REA (dec 2013)

SYMPLICITY HTN-3, failed to meet its primary efficacy endpoint. The trial met its primary safety endpoint.

Covidien to Exit OneShot™ Renal Denervation Program This voluntary action is primarily in response to slower than expected development of the renal denervation market.
Questions?
Uptake of Assessments

National reports: Spain, Austria, Denmark …?

Directly used for decision making

Link on Homepages

Others: reusage in other WP5 pilot assessment, publication in peer reviewed journal
Group work

• Could you/would you use the assessment directly for deriving a decision? If so, why? If not, why not?

• Which decision would you derive based on the information provided in the assessment? Explain why.
Stakeholder involvement
Compilation of final project plan

- **Stakeholder Advisory Group & Stakeholder Forum**: informed about upcoming public consultation of project plan, inquiry to suggest external medical experts, patients representatives, identification of manufacturers

- **Manufacturer(s)**: informed about upcoming public consultation of project plan, to submit evidence/information on reimbursement status, submission file, scoping meeting(?)

- **Patients**: scoping - selection of relevant outcomes, comparators, draft project plan

- **Medical experts**: scoping - selection of relevant outcomes, comparators, draft project plan

- **Public**: draft project plan
Stakeholder involvement - Assessment Phase

Production of final assessment

Manufacturer(s), patients, medical experts: opportunity to comment on second draft of assessment, comments & answers publicly available

Further involvement
Update of HTA Core Model for Rapid REA
Plenary session

Where do you think stakeholder involvement is most relevant?

Could you think of other ways of stakeholder involvement?

Should there be criteria for selecting stakeholders?
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