Panel 2
Towards innovative methodologies & practices (continuation)

Moderation
Ri De Ridder, Belgium National Health Insurance System
Presentation

Panos Kanavos,
LSE Health and Social care,
London School of Economics
and Political Science
Overview of the Advance-HTA project
Advance-HTA Consortium

PARTNERS

1. London School of Economics and Political Science, UK (Coordinator);
2. London School of Hygiene and Tropical Medicine, UK;
3. University Castilla- La Mancha, Faculty of Health Science, Spain;
4. Institute for Economic Research, Slovenia;
5. Technische Universität Berlin, Germany;
6. Andalusian School of Public Health, Spain;
7. Istituto Superiore di Sanita, Rome, Italy
8. Pan-American Health Organisation, USA;
9. European Brain Council, Belgium;
10. University Paris Est Créteil, France;
11. NICE International, UK;
12. Health Technology Assessment Agency, Poland;
13. Dental and Pharmaceutical Benefits Board, Sweden

Scientific Advisory Board

- Professor David Taylor, Professor Emeritus, School of Pharmacy, University of London (Chair)
- Karen Facey, Independent Health Policy Consultant
- Professor Lise Rochaix, Paris School of Economics
- Professor Finn Borlum-Kristensen, EUNETHTA
- Dr Kees de Joncheere, Dep. of Essential Medicines, WHO Europe
- Dr Paolo Siviero, AIFA
- Professor Leszek Czupryniak, University of Lodz Medical School, Poland
- Professor Guillem Lopez-Cassasnovas, Pompeu Fabra University
- Professor Göran Hermeren, Lund University
- Dr Mary Baker, European Brain Council
- Dr Josep Figueras, European Observatory on Health Systems and Policies
- Hanne Bak Pedersen, Health Technologies and Pharmaceuticals, WHO Euro
WP1 Value for Money
WP2 Value assessment
WP3 Rare Diseases & Orphan Drugs
WP4 Quality of Life
WP5 Medical Devices
WP6 Emerging Settings
WP7 Potential implications: lessons learnt, policy recommendations and advances in HTA

WP8 Dissemination of objectives and results
Workshops with regional decision-makers:
Warsaw - Poland, September 2014
Mexico City – Mexico, November 2014

WP9 Coordination and Management

Rethinking the future of Health Technology Assessment

=> to contribute to advancing the methods for HTA in European and other settings by involving the wider stakeholder community in areas actively and heavily debated given their implications for decision-making and resource allocation
Work Package 2 – Value Assessment
Motivation and objectives

Motivation

• Economic evaluation (EE) does not adequately capture a number of value dimensions
• Increasing evidence that Decision Makers (DMs) are reluctant to base decisions on EE alone, seeking broader assessment
• Different stakeholders attach different value judgements to the criteria considered
• What additional benefits to incorporate, how to establish their relative importance, whose preferences to consider & how to elicit such preferences?

Objectives

• To understand the parameters of value in HTA appraisals from an international perspective;
• To explore how factors such as disease severity, burden of disease, distinguishing between levels of innovation, and the quality of the available evidence can be incorporated more explicitly – and in a quantifiable way, in the HTA process;
• To develop and explore how alternative analytical frameworks, such as MCDA can be used to elicit value;
• To conduct case studies in specific disease areas by using alternative analytical tools.
Retrospective versus prospective

Eliciting value and the multiple facets of value

• By developing methodological approaches:

  **Retrospective**
  • To identify and capture the taxonomy of criteria used in assessing value;

  **Prospective**
  • To account for these in an explicit and comprehensive manner.
Retrospective analysis: Methodological framework

A mixed methods study

- 3 stage decision-process
- Taxonomy of criteria
- Influence of criteria on final decision
- Reasons for differences
- Agency-specific preferences & agreement levels (quantitative analysis)
- Differences may be a consequence of weaknesses in the application of HTA

Interviews of competent authorities => insights about findings & reasons for differences
Source: Nicod & Kanavos, under review 2015.
### Classification of criteria

- **Study countries**: England, Scotland, Sweden and France

- **Evidence is often imperfect or incomplete**: Value judgments are made about the acceptability of uncertainty and additional considerations

=> Correspond to the decision-making criteria that we identified by applying this framework

<table>
<thead>
<tr>
<th>HTA body</th>
<th>Scientific assessment</th>
<th>Social or societal preferences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>National Health Service (NHS) and Personal Social Services (PSS) perspective</td>
</tr>
<tr>
<td><strong>Scotland</strong></td>
<td>Scottish Medicines Consortium - SMC</td>
<td>Clinical cost-effectiveness (ICER)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>National Health Service (NHS) and Personal Social Services (PSS) perspective</td>
</tr>
<tr>
<td><strong>Sweden</strong></td>
<td>Dental and Pharmaceutical Benefits Board - TLV</td>
<td>Human value, need and solidarity principle, and cost-effectiveness (ICER)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Societal perspective</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>Haute Autorité de Santé - HAS</td>
<td>Clinical benefit (SMR) and relative improvement in clinical benefit (ASMR)</td>
</tr>
</tbody>
</table>

### Notes

- **Source**: Nicod, Kanavos (2015, under review)

When evidence is incomplete or imperfect

=> Scientific judgment

When evidence does not capture certain (non-quantifiable) aspects of living with a disease

=> Social value judgment
Study drugs & HTA recommendations

- 31 drug-indication pairs: 10 orphan, 13 cancer, 8 CNS
- 61% (19/31) different HTA recommendations
- ASMR V considered as a negative recommendation (no added benefit)
- ASMR in France:
  - II-V orphan drugs
  - III-IV cancer drugs
  - III-V CNS drugs
  - Some cases with negative recommendation (DNL)

=> Why such differences?
Primary evidence appraised, common for all

- Similar primary evidence => comparable
- But different way of reporting outcomes from the same trials
- Preference for phase III
- But lower level of evidence for orphan drugs (smaller trials, subgroups, phase II trials due to early marketing authorisation)
- Greater number of direct comparisons for cancer and CNS compared to orphan indications

<table>
<thead>
<tr>
<th></th>
<th>ORPHAN</th>
<th></th>
<th></th>
<th></th>
<th>CANCER</th>
<th></th>
<th></th>
<th></th>
<th>CNS</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Primary trials</td>
<td>NICE N 10</td>
<td>SMC N 10</td>
<td>TLV N 5</td>
<td>HAS N 10</td>
<td>NICE N 13</td>
<td>SMC N 13</td>
<td>TLV N 6</td>
<td>HAS N 13</td>
<td>NICE N 8</td>
<td>SMC N 8</td>
<td>TLV N 8</td>
</tr>
<tr>
<td>Trial type (#)</td>
<td>13</td>
<td>13</td>
<td>6</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>6</td>
<td>13</td>
<td>19</td>
<td>18</td>
<td>13</td>
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<tr>
<td>Phase III (%)</td>
<td>85%</td>
<td>85%</td>
<td>83%</td>
<td>85%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>89%</td>
<td>94%</td>
<td>92%</td>
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<tr>
<td>Phase II (%)</td>
<td>15%</td>
<td>15%</td>
<td>0%</td>
<td>15%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>11%</td>
<td>6%</td>
<td>0%</td>
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<td>Indirect comparison (%)</td>
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<td>17%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>8%</td>
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<tr>
<td>Comparators (#)</td>
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<td>13</td>
<td>6</td>
<td>13</td>
<td>13</td>
<td>13</td>
<td>6</td>
<td>13</td>
<td>19</td>
<td>18</td>
<td>14</td>
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<td>Alternative treatment (%)</td>
<td>0%</td>
<td>0%</td>
<td>17%</td>
<td>0%</td>
<td>46%</td>
<td>46%</td>
<td>50%</td>
<td>46%</td>
<td>32%</td>
<td>28%</td>
<td>43%</td>
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<tr>
<td>Standard care (%)</td>
<td>69%</td>
<td>69%</td>
<td>83%</td>
<td>69%</td>
<td>23%</td>
<td>23%</td>
<td>0%</td>
<td>23%</td>
<td>0%</td>
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<tr>
<td>Placebo (%)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>31%</td>
<td>31%</td>
<td>50%</td>
<td>31%</td>
<td>68%</td>
<td>72%</td>
<td>57%</td>
</tr>
<tr>
<td>None (%)</td>
<td>8%</td>
<td>8%</td>
<td>0%</td>
<td>8%</td>
<td>0%</td>
<td>0%</td>
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</table>
Differences in the evidence appraised: the case of orphan drugs

### Differences in the evidence appraised:
- Levels of reporting endpoints
- Selecting the appropriate endpoints
- Using non-primary evidence
- Different economic models and comparators
  - What constitutes the appropriate endpoint meaningful to patients?
  - How do agencies deal with surrogates: e.g. progression-free survival versus overall survival?
  - To what extent is registry data and other forms of evidence accepted, for what type of data?
  - Why was quality of life data reported in some countries and not in others?
  - Economic models: Some agencies only accept CUA whereas others prefer CMA when non-inferiority proven => how does this impact on the assessments?

#### Differences in the evidence appraised:

<table>
<thead>
<tr>
<th>Main reasons</th>
<th>Eltrombopag</th>
<th>Mifamurtide</th>
<th>Trabectedin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eltimbopag</strong></td>
<td>Idiopathic thrombocytopenic purpura</td>
<td>Osteosarcoma</td>
<td>Soft tissue sarcoma</td>
</tr>
<tr>
<td><strong>Non-primary endpoint</strong></td>
<td>X Severe bleeding events (WHO 3-4) (NICE)</td>
<td><strong>Appropriate endpoint</strong></td>
<td><strong>Non-primary evidence</strong></td>
</tr>
<tr>
<td><strong>Quality of life data</strong></td>
<td>X Lack of QOL data (HAS) Not included for HAS, TLV</td>
<td>✓ Progression-free survival = primary endpoint (SMC, TLV HAS)</td>
<td>✓ Use of registry data as historical controls (NICE)</td>
</tr>
<tr>
<td><strong>Economic models</strong></td>
<td>X CUA-Standard care (NICE) ✓ CMA-romiplostim (SMC) ✓ CMA-romiplostim (TLV)</td>
<td>✓ Overall survival = primary endpoint (NICE)</td>
<td></td>
</tr>
</tbody>
</table>

Legend: WHO bleeding events categorise these events by level of severity, WHO 3-4 corresponds to the more severe type of events; QOL : health-related quality of life; CUA: cost-utility analysis; CMA: cost-minimisation analysis
Differences seen in interpreting the evidence and dealing with uncertainty: the case of orphan drugs

- 14.5% of all concerns (N=114) about the same evidence were commonly raised across all four HTA bodies
- Double coding: main reason for final decision, how it compared across countries, provided through experts
- Different types of concerns (raised by some and not by others): trial duration, resource use, safety, quality of life improvement
- Different ways to deal with the same concerns: stakeholder input, orphan status, investigational nature, other study or other considerations

- Different risk preferences
- Subject to value judgments, as part of the deliberative process
- Cross-national differences in dealing with the same issues
- Do the different ways of dealing with uncertainty reflect contextual differences or could they be minimized and/or reflect weaknesses in the application of HTA?

<table>
<thead>
<tr>
<th>Main reasons</th>
<th>Eltrombopag</th>
<th>Imatinib</th>
<th>Mannitol dry</th>
<th>Mifamurtide</th>
<th>Trabectedin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Idiopathic thrombocytopenic purpura</td>
<td>GIST (adj, unresectable and/or metastatic)</td>
<td>Cystic fibrosis</td>
<td>Osteosarcoma</td>
<td>Soft tissue sarcoma</td>
</tr>
<tr>
<td>Same evidence applied</td>
<td>Short trial duration</td>
<td>X NICE, SMC</td>
<td>Not raised by HAS</td>
<td>No reduction in hospital days and use of antibiotics</td>
<td>X HAS</td>
</tr>
<tr>
<td>Same uncertainties raised addressed differently</td>
<td>Short trial duration</td>
<td>X NICE (experts), SMC, TLV</td>
<td>Overall survival not significantly improved</td>
<td>Risk of bronchospasms</td>
<td>Risk of interaction between treatments</td>
</tr>
<tr>
<td></td>
<td>X NICE (experts)</td>
<td>HAS (same length as comparator)</td>
<td>X NICE</td>
<td>Has (expert opinion)</td>
<td>X HAS</td>
</tr>
<tr>
<td></td>
<td>✓ HAS (orphan)</td>
<td>✓ HAS (ongoing trial)</td>
<td>Not raised by SMC</td>
<td>QOL not improved</td>
<td>NICE (expert opinion)</td>
</tr>
<tr>
<td></td>
<td>✓ NICE, SMC</td>
<td>X HAS</td>
<td>Not raised by SMC</td>
<td>X HAS</td>
<td>X HAS (other study)</td>
</tr>
</tbody>
</table>
### Other Considerations Accounted for, by Type of Information

#### Value Judgments
- Identification using the framework
- Differentiation of elicited versus non-elicited
- Double coding: main reason for final decision, how it compared across countries, provided through experts

#### Most Common Value Judgments Made as Part of the Deliberative Process:
- Unmet need
- Severity
- Innovation
  - Accountability for reasonableness
  - Defining social values based on retrospective cases
  - Eliciting societal preferences for those non-elicited value judgments
  - Consistency

#### Orphan Drugs: Proportion of Cases That Accounted for Other Considerations, by Cluster

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Unmet Need</th>
<th>Disease Nature Affecting the Patient</th>
<th>Rarity, Orphan Status, Small Patient...</th>
<th>Issues Around Current Treatment...</th>
<th>Complex Pathway, No Best Practices...</th>
<th>Clinical Benefit and Type of Benefit</th>
<th>Innovative Nature of the Treatment</th>
<th>Indirect Benefits from the Treatment</th>
<th>Adverse Events Manageable/Non...</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE</td>
<td></td>
<td></td>
<td></td>
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<td>SMC</td>
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<td>TLV</td>
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</tbody>
</table>

Panel 2 – Towards Innovative Methodologies & Practices

N = 10  N = 10  N = 4
Implications and recommendations – eliciting value based on a retrospective analysis

Contribution of this research

Methodological framework that captures the full taxonomy of criteria considered at each stage of the decision process, systematically and in a structured and comparable manner:

- Evidence
  - Primary trials: different levels of appraising the same trials
  - Non-primary trials: different acceptability
- Interpretation of the evidence (uncertainty, “other considerations”, stakeholder input)
  - Scientific and social value judgments: poor agreement in interpreting and dealing with the same evidence
  - Agency-specific risk and value preferences
- Influence on the final decision (double coding)
  - Main reasons for final decision: influence of criteria at each stage of the process on the final recommendation
  - How these compared across countries

Policy implications & Recommendations

- Extent of cross-national differences => differences matter (for patients)
- Reasons for cross-national differences: due to the application of HTA or contextual considerations => legitimacy of these differences
- Awareness about different ways in conducting HTA: dealing with uncertainty, levels of evidence, stakeholder input, other considerations, agency-specific risk and value judgments => cross-country learning (European collaboration)
- Value judgments => eliciting societal preferences, defining social values
- Accountability for reasonableness => criteria and its influence
- Consistency across decisions => retrospective identification
- Dealing with orphan drugs (e.g. lower levels of evidence, common issues related to small patient populations) => identification of specificities in dealing with orphan drugs and ways forward (cross-country learning)
Prospective analysis: MCDA methodological framework in the context of HTA

MCDA “is both an approach and a set of techniques, with the goal of providing an overall ordering of options” by looking at the extent to which a set of objectives are achieved.

Analyse complex situations characterised by a mix of objectives:
- Disaggregate a complex problem into simpler components
- Measure the extent to which certain options achieve the objectives
- Weigh these objectives
- Re-assemble the components to show an overall picture

Five MCDA phases and distinct MCDA stages
- Criteria selection needs to adhere to key principles in order to lead to robust results
Decision problem: Which metastatic colorectal cancer (mCRC) treatment to cover?

Aim: To assess (and rank) the overall value of second-line biological treatments for mCRC following prior oxaliplatin-based (i.e. first line) chemotherapy

- Adopt NICE past TAs scope

Stakeholders: a group of experts, including health care professionals, methodology experts, patients, HTA/regulators

- Replicate NICE past committees
Three-stage process for criteria selection:

- Systematic review of the value assessment literature in the context of HTA
- Consultation with experts (Advance-HTA meetings, external experts)
- Dissemination activities (HTAi, ISPOR, Advance-HTA capacity building workshops)

- “Value focused thinking”: top-down approach, criteria selected prior to identifying the alternative options
- Five clusters capturing overall value: BoD, Therapeutic impact, Safety profile, Innovative potential, Socio-economic impact
mCRC-specific value tree outlining clusters of criteria and related attributes which capture the value of
the chosen treatments falling under the scope of the exercise

- “alternative focused thinking”: bottom-up approach, criteria emerged following the comparison of
  alternative treatment options
- …while ensuring criteria possess the right properties:
  - Essential, Understandable, Operational Non-redundant, Concise, Preference independent

- Alternatives options assessed:
  - Cetuximab \(\rightarrow\) included
  - Panitumumab \(\rightarrow\) included
  - Aflibercept + FOLFIRI \(\rightarrow\) included
  - Bevacizumab + non-oxaliplatin chemotherapy \(\rightarrow\) excluded, no evidence
  - Regorafenib monotherapy \(\rightarrow\) excluded, no evidence
Preferences & Decision Conferencing

• Stakeholder preferences used as the basis of value judgements
• Working together as a group, shared understanding of value
• Participant preferences elicited as part of a decision conference assuming that are representative
  ▪ Ideal number of 7-15 participants: preserve individuality while also allowing for group processes to emerge
  ▪ Composition of the group: based on the structure of the past NICE committees

Value Measurement Methods

A variety of MCDA techniques are available with regards to scoring, weighing and aggregating, mainly relating to the value judgement and preference elicitation processes

▪ Indirect techniques involve a series of questions aiming to uncover preferences by considering differences in the attribute scale and their relation to value scale
▪ MACBETH is an indirect approach to elicit value functions
Day of the workshop

Value tree presented and worked cluster by cluster

- Value tree validation: some criteria were excluded because they were irrelevant or non-fundamental
- Value functions were elicited for the different criteria
- Relative weights were assigned within the clusters and across clusters
- Overall value scores produced
Elicitation of value judgements: (a) within criteria & conversion into a value function (scoring) and (b) across criteria (weighting)

What is the difference in value between x and y: “very weak”, “weak”, “moderate”, “strong”, “very strong” or “extreme”?

“Of all the possible swings (changes) within these criteria ranges, which represents the biggest difference you care about?”

Swing weighting approach
Performance of different options and overall value scores

- OS + Grade 4 AEs = 50% of total weight
- THE 0.47; SAF 0.23; INNOV 0.29; SOCIO 0.12
- Cetuximab scored the highest overall value score

Technologies’ ranking based on their ICERs could be compared with their ranking based on their ICVRs
MCDA as a resource allocation mechanism

Summary

• An MCDA model has been developed
• An MCDA value based assessment was completed for a set of mCRC treatments
• A disease-specific value tree was developed reflecting all the critical value dimensions as criteria
• A decision conference was organised with the involvement of all key stakeholders
• Stakeholder preferences were elicited to assess the performance of the technologies and the relative importance of the criteria
• Technologies were ranked based on overall value and their costs

Policy implications

• MCDA can generate a more holistic metric of value
• Incorporation of costs can then produce a metric of efficiency, involving incremental cost per incremental MCDA value unit, that can be used to inform coverage decisions
• Overall, the MCDA approach provides improved comprehensiveness, flexibility, and transparency
• Attention should be paid to the theoretical foundations of DA so that the results are meaningful and decision recommendations robust
Invitation to the
Advance-HTA Conference
19th November 2015
The Law Society – Common Room
(113 Chancery Lane London WC2A 1PL, UK)

The London School of Economics and Political Science – LSE Health, have the pleasure to invite you to the final Advance-HTA Conference that will take place at The Law Society, in London - UK, on 19 November 2015.

The workshop is delivered by a consortium of 13 partner institutions, led the LSE, working together on Advance-HTA, a 3-year research project funded by the European Commission. The project aims to advance methods on and practices for HTA by involving the wider stakeholder community in areas actively and heavily debated, given their implications for decision-making and resource allocation.
Advance-HTA Final Conference Agenda

11:15-12:15 Session 1: New tools and approaches in the assessment of value of medical technologies

1. Multiple Criteria Decision Analysis in the context of HTA, Dr Panos Karavasilis and Angy Anagnostopoulou (London School of Economics)
   11:15-11:30

2. HTA of medical devices: how to group them, how to evaluate them - current status and perspectives, Professor Peter Auranen, Technische Universität Berlin (TUB)
   11:30-11:45

3. Stakeholder Perspectives:
   - Amelie Belslev, Health Policy Analyst Organisation for Economic Co-operation & Development (OECD), Paris, France
   - Hanae Bok-Pedersen, Research Manager for Health Technologies & Pharmaceutical, World Health Organisation, Copenhagen, Denmark
   - Theodore O’Connor, Head of Global Health Innovation, University of Pennsylvania (UPenn), Philadelphia, USA

4. GBA session moderated by the chair
   11:45-12:15

12:15-13:30 Session 2: Preference Estimation and Quality of Life

5. Whose preferences should we use in decision making in health care?, Valentine White (Institute of Economics Research, Lodz, Poland)
   12:15-12:30

6. Assessing the Societal Value in Rare Diseases by Decision Makers and Patients, Dr Ada Lagos-Rodrigue (University of London, London, UK)
   12:30-12:45

7. Stakeholder Perspectives:
   - Dr Peter Foy, Evidence Based Health Policy Consultant
   - Dr Insa Pietsch, Head, European Observatory on Health Systems and Policies

8. GBA session moderated by the chair
   12:45-13:15

13:45-15:15 Session 3: Strengthening and Implementing HTA in Emerging Settings

9. HTA in Emerging Settings - Mapping Exercise and ToolBox, Prof Jonine Ehrlich, Dirección General de Salud Pública, Grenada, Spain (EUR)
   13:45-14:30

10. The Importance of HTA in Emerging Settings - The REDWEST Experience, 14:10-14:45
    Dr Alexander Lempard, Pan-American Health Organisation (PAHO)

11. Stakeholder Perspectives:
    - Guillermo Del Valle, World Health Organization Europe, Copenhagen, Denmark
    - B. GBA session moderated by the chair
   14:45-15:15

2:15-2:30 Coffee break

15:00-16:30 Session 4: HTA and the future: Stakeholders Reflections (Chair: Dr Panos Karavasilis)

12. Anna Zawidzka, Head of Division of Health Care Programmes, Agency for Healthcare Assessment and Technology System, Poland
   15:00-15:45

   15:00-15:45

14. Frances Viterbo, MEIE International, UK
   15:45-16:30

15. Prof. Philippe Fournier, Chairman, Executive Committee of the European Network for Health Technology Assessment (EUnetHTA)
   15:45-16:30

   15:55-16:05

17. Prof. Daniel Henthorn, University College London (UCLi), London
   16:05-16:15

18. GBA
   16:15-16:40

16:40-18:10 Session 5: Lessons Learnt: and Future Directions

19. Dr Panos Karavasilis, LSE
   16:40-17:10

Conference End
Discussion

Keith Abrams, University of Leicester
Andrea Rappagliosi, European Federation of Pharmaceutical Industries and Associations
In collaboration with
General discussion

Keith Abrams, University of Leicester
Pascale Brasseur, Eucomed
Karen Facey, Scottish Health Technologies Group
Panos Kanavos, LSE Health and Social care, London School of Economics and Political Science
Andrea Rappagliosi, European Federation of Pharmaceutical Industries and Associations
Rosanna Tarricone & Aleksandra Torbica, CERGAS, Department of Policy Analysis and Public Management, Bocconi University
10 years | Forum HAS Health Technology Assessment sans frontières 30 October 2015 PARIS

In collaboration with
Panel 3
Way forward in implementing novel approaches in HTA and inform decision making

Moderation
Alric Rüther, IQWiG
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Aim of AdHopHTA - EU

“To produce information, knowledge and tools to aid managerial decisions regarding health care technologies using HTA”
For whom?

Hospital decision-makers
Why?

Increase in Spending and number of HTs

There are more than 500,000:
- Imaging equipment
- Medical devices
- E-health
- In-vitro diagnostics

1.5%** of pharmaceutical spending for in-patient care in the EU

Hospitals as main entry point

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

*The MEDTECH Industry
**EFPIA, 2012
What Hospital based-HTA (HB-HTA) is?

Hospital-based HTA means organising and performing HTA activities at hospital level.

Main characteristics:

• Tailored to the hospital context
• Keeping a sharper focus on the HTs of specific interest for the hospital
• Timely adjustment
• In collaboration with the users of the HTs
3 + 1 reasons for adopting HB-HTA

1. HB-HTA leads to sound investment
   Decisions contributing to hospital efficiencies

2. HB-HTA provides with the information needed to make decisions

3. HB-HTA is used by hospital decision-makers

- **US$ 370K savings** from decrease in unnecessary lab tests
- **US$ 3M savings** from 16HB-HTA reports
- **100%** Satisfied by hospital decision-makers of a 5-year activity of an HB-HTA unit.
- **>90%** recommendations from HB-HTA reports adopted in 4 studied hospitals

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
## 3 + 1 reasons for adopting HB-HTA

### Answers informational requirements of hospital decision-makers

### Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

<table>
<thead>
<tr>
<th>DOMAINS</th>
<th>EUnetHTA</th>
<th>AdHopHTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1: Health problem and current use</td>
<td>* relevant</td>
<td>*** most important</td>
</tr>
<tr>
<td>D2: Description and technical characteristics</td>
<td>* relevant</td>
<td>* relevant</td>
</tr>
<tr>
<td>D3: Clinical effectiveness</td>
<td>* relevant</td>
<td>*** most important</td>
</tr>
<tr>
<td>D4: Safety aspects</td>
<td>* relevant</td>
<td>*** most important</td>
</tr>
<tr>
<td>D5: Costs and economic evaluation</td>
<td>* relevant</td>
<td>* relevant</td>
</tr>
<tr>
<td>D5.1 Societal point of view</td>
<td>*** most important</td>
<td>*** most important</td>
</tr>
<tr>
<td>D5.2 Hospital point of view</td>
<td></td>
<td>*** most important</td>
</tr>
<tr>
<td>D6: Ethical aspects</td>
<td>* relevant</td>
<td>* relevant</td>
</tr>
<tr>
<td>D7: Organizational aspects</td>
<td>* relevant</td>
<td>*** most important</td>
</tr>
<tr>
<td>D8: Social aspects</td>
<td>* relevant</td>
<td>* relevant</td>
</tr>
<tr>
<td>D9: Legal aspects</td>
<td>* relevant</td>
<td>* relevant</td>
</tr>
<tr>
<td>D10: Political and strategic aspects</td>
<td>* relevant</td>
<td>*** most important</td>
</tr>
<tr>
<td>D10.1 Political aspects</td>
<td></td>
<td>*** most important</td>
</tr>
<tr>
<td>D10.2 Strategic aspects</td>
<td></td>
<td>*** most important</td>
</tr>
</tbody>
</table>
In total **385** people from **20** countries have provided their input to the project.

**Brain storming sessions:**
AdHopHTA Partners

- **Large-scale survey:** 163 respondents
- **Delphi process:** 36 participants
- **Focus group:** 8 participants
- **Validation workshop:** 11 panellists

- **107** face-to-face interviews
- **6** Literature reviews
- **40** Case studies

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Handbook of HB-HTA
- knowledge base to improve the process of decision-making on health technologies in the hospital

Toolkit for HB-HTA
- guidance and tools for setting up and running an HB-HTA unit

Database of HB-HTA
- sharing of HB-HTA reports to make learning from each other easier
Information and Knowledge

- HB-HTA versus National/Regional HTA
- How hospitals are using HB-HTA
- Current Organisational models of HB-HTA
- Type and quality of HB-HTA reports and informational needs
- Collaborative experiences for HB-HTA with National/regional HTA Agencies
- **Guiding principles for Good Practices**
Guiding principles for Good Practice

HB-HTA:
- Organizing
- Performing
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Dimension 1
The assessment process

Excellent HB-HTA units design, manage, carry out, review and improve the assessment process to generate valuable, tailored information for hospital decision-makers. The assessment report should be relevant and reliable, carried out in an unbiased and transparent manner with involvement of stakeholders. Assessment results and recommendations should be properly communicated to hospital stakeholders.

Guiding principle 1
HB-HTA report: scope, hospital context and informational needs

The HB-HTA report clearly states its goal and scope, reflects the hospital context and takes into account the informational needs of hospital decision-makers.

TOOLS

**TOOL 2:** Official (submission) form requesting an HB-HTA assessment
**TOOL 3:** Example of scoping of an HB-HTA report (PICO, TICO questions)
**TOOL 4:** AdHopHTA mini-HTA template
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

<table>
<thead>
<tr>
<th>Description of potential problems</th>
<th>Proposed solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>The goal and scope of the HB-HTA report are unclear or represent a point of contention.</td>
</tr>
<tr>
<td>1.2</td>
<td>The new HT is not well defined. The intervention is adapted to the specific needs of the patient, and thus the content of the intervention will vary from patient to patient.</td>
</tr>
<tr>
<td>1.3</td>
<td>It is difficult to identify a comparator for the assessed HT, e.g., in the case</td>
</tr>
</tbody>
</table>
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Tools (example)

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

<table>
<thead>
<tr>
<th><strong>EPIDEMIOLOGICAL CALCULATORS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calculator for diagnostic test evaluation with results of:</strong></td>
</tr>
<tr>
<td>- Sensitivity.</td>
</tr>
<tr>
<td>- Specificity.</td>
</tr>
<tr>
<td>- Positive likelihood ratio.</td>
</tr>
<tr>
<td>- Negative likelihood ratio.</td>
</tr>
<tr>
<td>- Disease prevalence.</td>
</tr>
<tr>
<td>- Positive predictive value.</td>
</tr>
<tr>
<td>- Negative predictive value.</td>
</tr>
<tr>
<td>- Relative risk, 95% CI, z statistic and p value.</td>
</tr>
<tr>
<td>- Odds ratio, 95% CI, z statistic and p value.</td>
</tr>
<tr>
<td><strong>MedCalc easy-to-use statistical software</strong></td>
</tr>
<tr>
<td>[Click to Find out more]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Effect size type calculator:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Standardized Mean Difference (d).</td>
</tr>
<tr>
<td>- Correlation Coefficient (r).</td>
</tr>
<tr>
<td><strong>Odds-ratio (OR) and Risk Ratio (RR) calculator for:</strong></td>
</tr>
<tr>
<td>- 2 by 2 frequency table.</td>
</tr>
<tr>
<td>- Binary proportions.</td>
</tr>
<tr>
<td><strong>Practical Meta-Analysis Effect Size Calculator</strong></td>
</tr>
<tr>
<td>George Mason University, USA, The Campbell Collaboration</td>
</tr>
</tbody>
</table>
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

<table>
<thead>
<tr>
<th>LITERATURE SEARCH</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Methodological guidance on search strategy</td>
</tr>
<tr>
<td>Systematized Research in Information Retrieval for HTA (StRiFT) on HTA Virtual platform. Source for search strategy development.</td>
</tr>
<tr>
<td>Peer Review of Electronic Search Strategies. Canadian Agency for Drugs and Technologies in Health (CADTH), 2008.</td>
</tr>
<tr>
<td>Grey Matters: a practical search tool for evidence-based medicine. Canadian Agency for Drugs and Technologies in Health (CADTH), 2014.</td>
</tr>
<tr>
<td>Development and Testing of Search Filters to Identify Economic Evaluations in MEDLINE and EMBASE. Canadian Agency for Drugs and Technologies in Health (CADTH), 2008.</td>
</tr>
<tr>
<td>B. Search strategy examples</td>
</tr>
<tr>
<td>PubMed Tutorial.</td>
</tr>
</tbody>
</table>
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Laura Sampietro-Colom is the Head of HB-HTA Unit Hospital Clinic and in her role she is assessing Health Technologies for hospital and industry
Coordinator

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Contact: Rabia Kahveci

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Contact: Jean-Blaise Wasserfallen

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Estonia
Contact: Raul – Allan Kiivet, Margus Ulst

Thank you!!
Discussion

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Ansgar Gerhardus, Institut für Public Health und Pflegeforschung, Bremem University
Roberto Grilli, Local Health Authority of Reggio Emilia
10 years

Forum HAS
Health Technology Assessment sans frontières
30 October 2015 PARIS

In collaboration with

European Commission
Presentation

INTEGRATE-HTA

Ansgar Gerhardus,
Institut für Public Health und Pflegeforschung, Bremem University
Novel approaches to inform decision making on complex technologies
The task

Meaningful assessments of complex technologies that inform decision-making

Lessons learnt:

• Make stakeholders part of the assessment – straight from the beginning of the process
• Map and consider complexity – do not “simplify complexity away”
• Offer an integrated assessment to decision-makers
Not complex: HTA on an antihypertensive drug

| Patient characteristics & preferences | Increased blood pressure (other conditions "ideally“ excluded) |
| Comparator | Another antihypertensive drug |
| Topics for assessment | (Cost-)effectiveness |
| Outcome | Well-defined, quantifiable primary outcome, e.g. reduction of strokes |
| Implementation | Of marginal relevance |
| Context | Of marginal relevance |
Traditional HTA (e.g. on an antihypertensive drug)

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
## Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

### Patient characteristics & preferences
- Early or late stage?
- In pain?
- In despair?
- Family around?

### Comparator
- Another complex technology?

### Topics for assessment
- (Cost-)effectiveness, social, cultural, legal impact?
- Impact on relatives?

### Outcome
- > 500 outcome parameter, e.g. quality of life, spiritual improvement, etc.

### Implementation
- By a nurse? A doctor? A relative?
- At home? In a hospice?

### Context
- Rural area? Degree of professionalization of services?
Traditional HTA

Effectiveness
Economic
Ethical
Social/Cultural
Legal

Patient characteristics
- Early or late stage
- Personal preferences

Implementation
- Professionals
- Relatives
- Non-related lay persons

Context
- Elaborated palliative care system at place?

Results
(evidence informed)
HTAs on complex technologies: Issues beyond cost-effectiveness gain importance

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
HTAs on complex technologies: Issues beyond cost-effectiveness gain importance

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Approach in INTEGRATE-HTA: 5 Steps

1. Involve stakeholders to elicit needs, topics, outcomes and likely scenarios
2. Model the complexity (including patient characteristics, context, and ways of implementation)
3. Assess the evidence regarding effectiveness, and economic, ethical, socio-cultural, and legal aspects
4. Integrate the evidence in a structured way to respond to the needs of the stakeholders
5. Structured process of decision-making (not part of the HTA in a narrow sense)
The INTEGRATE-HTA Model

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Step 1: Bring the generation of evidence into perspective

Input through Stakeholder Advisory Panels (SAPs) on: Topics, objectives, patients, context and implementation

• Example:
  135 individuals (professionals, voluntary workers, patients, and relatives) from 7 European countries

Common issues (selection):
  ▪ Availability & accessibility
  ▪ Effectiveness
  ▪ Ethical & legal concerns
Step 2: Identify patient characteristics, context, implementation to create a logic model

Identify patient-related moderators and preferences, context and implementation issues

- **Examples**
  - Patients and relatives with or without social support
  - Implemented by a relative or by a professional caregiver
  - Professional caregiving already established or not (context)

- **Create a logic model** covering patient characteristics, context and implementation issues
Step 3: Assess the available information/evidence

Assess information/evidence considering patient characteristics, context, implementation issues

- Systematic reviews
- Economic analyses
- Focus-group discussions
- Etc.

Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Step 4: Insert the evidence into the logic model

• Example - Patient characteristic as a modifier for the socio-cultural analysis:
  Socio-economic status is a moderator on the ability of relatives to take over home-based care
Step 5: Structured deliberative decision-making

Structured process of decision-making taking uncertainty, unanswered questions, and limitations into account
Lessons learnt (refined version)

Make stakeholders part of the assessment – a defined perspective is necessary for an integrated assessment

Identify and model relationships between the intervention, patient characteristics, implementation issues, and context

Offer an integrated assessment to decision-makers - integration needs to start from the beginning
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

This project is co-funded by the European Union under the Seventh Framework Programme (Grant Agreement No. 306141)
Please join us at the final conference of the INTEGRATE-HTA-Project at 12./13. November in Amsterdam

→ www.integrate-hta.eu
In collaboration with
Discussion

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10 years

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Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making

Presentation

Sabine Kirton,
Chairwoman, Regional Cancer Support Association M-V / S-H e.V.
Catch – Inform - Accompany

Structure:
Federal Cancer Support Association in Bonn
11 Regional Cancer Support Associations
345 Local Support Groups

In M-V/S-H:
28 Local Support Groups

We are:
Independent Non-ProfitOrganization

Take care of:
about 50,000 cancer patients (men and women)

Founded: 1976 in the West, 1991 in the East

Represent patients’ voices:
• Advisory board of the German Cancer Aid
• Forum of the German Medical Association
• Advisory Board of the German Society for Senology
• National Cancer Plan
• Joint Federal Committee
• Guideline development groups
• Certification Commissions of Oncology
• Certification Commissions of Breast Cancer Centers
• IQWiG
• Cooperation Network of Cancer Registries
Choosing “the right” health technologies can save lives

Example: Cancer

Improvements in prevention, early detection and treatments have led to a decreased cancer mortality*.

Minus 17%

Minus 11%

*Source: Zentrum für Krebsregisterdaten/Robert-Koch-Institut (www.krebsdaten.de) & Gesellschaft der epidemiologischen Krebsregister in Deutschland (www.gekid.de); age standardized data/ focus: last 10 years
Choosing “the right” health technologies can save lives

BUT:
How to decide whether a technology is “the right one”?
Choosing “the right” health technologies can save lives

“If you’re not failing every now and again, it’s a sign you’re not doing anything very innovative“.

Woody Allen
The amount of relevant data has grown immensely...

For example: Medical Articles

- Today (new articles in data bases) 10.000-25.000 per week !!!
- 1994-2001 MedLine Literature 25.000 per year
- 1978-1985 MedLine Literature 5.000 per year

Health Technology Assessment as a structured process can support sound decisions for “the best” health technology.

**Example for a structured approach: INTEGRATE-HTA**

HTA for complex technologies taking moderating factors into account

HTA for a complex technology such as Palliative Care

<table>
<thead>
<tr>
<th>Patient characteristics &amp; preferences</th>
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<td>Implementation</td>
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<td>Context</td>
<td>Rural area? Degree of professionalization of services?</td>
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</table>

Our share in the way forward:
What can we as “patient representatives” do to help move forward the assessment process to identify “the best” health technology?
Our contribution, our fears, our expectations

<table>
<thead>
<tr>
<th>Contribution</th>
<th>Fears</th>
<th>Expectations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Voicing patients’ needs/interests → Increased acceptance of decisions</td>
<td>• Assessment process too slow and past oriented</td>
<td>• Information sharing</td>
</tr>
<tr>
<td>• Feedback partner</td>
<td>• Decisions based on irrelevant factors</td>
<td>• Involvement in the process</td>
</tr>
<tr>
<td>• Broad network in area of expertise</td>
<td>• Varying process quality standards possibly lead to unreliable results</td>
<td>• Full implementation of existing policies and standards</td>
</tr>
<tr>
<td>• Support communication of decisions to patients as key stakeholders</td>
<td></td>
<td>• Shared decision-making</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Voting right as ‘‘experts by experience’’</td>
</tr>
</tbody>
</table>
Panel 3 – Way forward in implementing novel approaches in HTA and inform decision making
Never give up!

Thank you for your attention
Discussion

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General discussion

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Sabine Kirton, Women’s Cancer Support Association
Laura Sampietro-Colom, Research and Innovation Directorate, Hospital CLINIC de Barcelona
General discussion and concluding remarks

Jean-Luc Harousseau, HAS
Barbara Kerstiëns & Tapani Piha, European Commission
Each speaker declared his interest links with health industries related to the theme of the presentation (law of 4 March 2002)

Find these declarations on the HAS website, tab “Forum HAS”

www.has-sante.fr
The Haute Autorité de Santé thanks you for your participation in this session

www.has-sante.fr