HTA, innovation and value: what we need to do

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Two parallel events about dialogue

Last week in Rome, the archbishop of Canterbury called for clarity on the future of Catholic-Anglican dialogue.

This week in Paris, a DIA conference asked for clarity of definition of “relative effectiveness” but none was forthcoming, suggesting to me that the patient - regulator – payer - industry dialogue on pragmatic HTA has barely begun.
Two gaps in HTA that need real collaboration, rather than consultations or for - information papers

Gap 1: HTA view of dynamic efficiency and PGx

- Reduction in ADRs
- Targeting of best responders
- Improved compliance with Rx, lower ADRs
- Smaller clinical trials
- Lower hospital costs
- Better health outcomes
- Faster time to regulatory approval

Incentives to invest and dynamic efficiency:
1. Lower if Dx restricts Rx market size
2. Lower if Rx already on market AND there is no pricing flexibility
3. Lower if IP protection is confined to the biomarker
4. More likely if conditional approach includes ability to renegotiate Rx and Dx prices once clinical utility is established
5. Uncertain if both products are launched together with/without flexible pricing and with/without competition
6. Uncertain if regulatory authority sets unreasonably high standards of evidence (and higher costs of generating data) to inform drug labelling
Gap 2: HTA view of the costs of evidence

After Towse, 2009

PGx reimbursement is optimal when:

Price of PGx = expected net monetary benefit (ENMB) = (QALY gain) + non PGx cost offsets

ENMB (is this RE?)

Non PGx cost offsets

In what subgroup does patient belong?

What number of patients will be treated in each subgroup?

Utilization uncertainty

Response uncertainty

Health outcomes

Biomarker outcomes

Costs of obtaining diagnostic data, patient preferences, patient expected use of PGx, patient preferences for future health status and patient WTP

Costs of evidence collection when PGx requires GWA collections and biobanks to validate genotype-phenotype associations

Process for interpreting new evidence and conversion into a revised reimbursement and copays

HTA in the EU: regulation, innovation and value
EMEA new paradigm: CE benefits > costs?

**Current paradigm**
- Assessors
  - Quality, Safety, Efficacy (First 3 hurdles)
  - Benefit-Risk Profile
- Payers
  - Relative Efficacy / Effectiveness
  - Cost vs Health Benefit
  - Budget Impact
  - MA (Marketing Authorisation)

**Future paradigm?**
- Assessors
  - Quality, Safety, Efficacy (First 3 hurdles)
  - Benefit-Risk Profile
- Payers
  - Cost vs Health Benefit
  - Budget Impact
  - MA (Marketing Authorisation)

Enter CE assessment -> Sequential -> overlap

Source: EMEA

NICE diagnostics meeting 4 November 2009 missed opportunity on EVPI in HTA

- Key factors supporting EVPI in diagnostic HTA are
  - relevant health outcome indicators and
  - the economic value attributed to these outcomes

- Yet much discussion at NICE meeting was
  - who should fund further research and
  - what incentives should be provided to manufacturers.

- Conclusion: No fast tracking of EVPI when the key factors ignored in this form of “consultation”
Harmonisation in pan-EU HTA processes: two divides

<table>
<thead>
<tr>
<th>Driver</th>
<th>Entity</th>
<th>Core proposition</th>
<th>Reality test</th>
<th>Inevitable industry response</th>
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</thead>
<tbody>
<tr>
<td>EU joint action</td>
<td>EUnetHTA</td>
<td>Network to share information at the scientific level</td>
<td>Proposed “stakeholder consultation” is formal, limited</td>
<td>A seat at the table with active participation, NOT consultation or “for information”</td>
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<tr>
<td>EMEA</td>
<td>EMEA</td>
<td>1. EMEA to own “comparative effectiveness” 2. Local member differences do not matter for CE, only for economic evaluation</td>
<td>EMEA bound by legislation to focus on quality, efficacy and safety, but not on CE</td>
<td>1. EMEA does not yet have a demonstrated capability for CE assessment 2. How will CE flow back into economic evaluation?</td>
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Value proposition: HTA role in reducing information asymmetry

The value proposition from all sides

**Pharma**
- Drug discovery challenge better understood
- Drug development strategy more overt
- Drug pricing business model developed earlier (and shared?)
- Reimbursement and contracting expectations ready before product development (early stage CEA models)
- Conditional reimbursement and willingness to reduce risks post marketing approval

**Providers and payers**
- Value of appropriate use of diagnostics
- Value of patient “channelling”
- Patient WTP for “value”
- Value-based benefit design
- Value of new evidence assessed
- Value of conditional reimbursement

**Regulators**
- Potential value of new technology to society
- Value of new risk/benefit calculus with subgroups (channelling)
- Value of information to manufacturers, payers, patients and society
- Value of pragmatic clinical trials in regulatory approval

- How can PMS reveal unmeasured risks?
  - Are RCTs feasible in Phase III, in non-responders, or with theranostics (Berger, Temple 2009)?
The innovation piece in EU HTA

1. Is innovation already counted in benefits?
   - Not in German EF or NICE version of ICER/QALY
   - In reimbursement policy or industry R&D support?
   - With displacement cost calc?

2. Should innovation be counted in benefits?
   - New mechanisms of action
   - New disease targets
   - New preferences for delivery or site of care
   - Evidence of stratified impact of efficacy or CE (70% of target?)
   - Evidence of R-B ratio

3. What constitutes exceptional proof of innovation?
   - New mechanisms of action
   - New disease targets
   - New preferences for delivery or site of care
   - Evidence of stratified impact of efficacy or CE (70% of target?)
   - Evidence of R-B ratio

4. What evidence of CE is possible with PGx?
   - New mechanisms of action
   - New disease targets
   - New preferences for delivery or site of care
   - Evidence of stratified impact of efficacy or CE (70% of target?)
   - Evidence of R-B ratio

With what methods of economic appraisal in HTA or by increasingly sophisticated payers?

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HTA 2009: Bruegel the Elder warning 441 years ago

**FACT 1:** The six men have different types of blindness, they are all oblivious to warning signs, and once one falls, they all fall. EC, HTA agencies, payers, regulators, providers and patients beware.

**COROLLARY 1:** Any HTA process without new tools to measure innovation in healthcare is myopic, potentially hazardous to health status and impedes investment in R&D.

**COROLLARY 2:** Any HTA process that ignores health literacy, patient access and patient preferences in the race to pursue efficiency is dangerous to both governments and the governed.