How do you assess the value of co-dependent technologies?

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Issue panel

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Presentation 1
Assessment of co-dependent technologies

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Acknowledgements

The authors of

Definition of co-dependent technologies

- “Technologies that are dependent on another technology either to achieve their intended effect or to enhance their intended effect” (www.health.gov.au)

- In particular, a diagnostic tests (Dx) can be used to identify patients most likely:
  - to respond or to fail to respond to a drug treatment (Tx) (personalised medicine)
  - to exhibit adverse events
  But also
  - to monitor responses to drugs
  - to determine the risk of developing a disease

The issue of attribution of value of co-dependent technologies

- The value created is a “joint product” and there are no rules for the attribution of the value to one or the other

- Garrison and Austin (2007) pointed out that how value is allocated across patients, payers, Dx manufactures and Tx manufacturers depends on the institutional context
  - E.g. whether the Tx was priced before the Dx was available, the relative strength of intellectual property protection for Dx and Tx

- This will have consequences in terms of incentives for evidence generation and subsequent innovation
Framework to assess value of co-dependent technologies

1. Reducing drug adverse effects
2. Reducing time delays in selecting optimal Tx
3. Increasing adherence or willingness to start Tx
4. Enabling Tx effective in a small fraction to be made available
5. Reducing uncertainty about value

1. Reducing or avoiding drug adverse effects

Availability of Dx can improve average benefit-risk ratio so, depending on the severity of side effects,

- Tx obtains marketing authorisation, or
- Use of a licensed Tx in clinical practice increases

Example

- HLA-B*5701 is an allele associated with hypersensitivity to abacavir for HIV-1
- Identification of the marker has increased prescribing of abacavir, which now is recommended for HLA-B*5701-negative patients in European and US guidelines
2. Reducing time delays in selecting optimal Tx

Identifying non-responders and switching them to an alternative treatment regime/care can

- improve survival and/or quality of life (particularly in diseases at advanced stages)
- avoid or reduce the cost of treating non-responders
- avoids or reduces inconvenience to patients

Example

- BCR-ABL test identify chronic myelogenous leukemia (CML) patients who are receiving treatment but not responding to it.
- It can prevent the disease to progress to blast crisis and death and enables to stop first-line treatment when no longer effective

3. Increasing adherence or willingness to undertake Tx or other interventions

- Patients are more motivated if they know (ex-ante) the intervention is likely to work
- Issue of non-responders who might experience disutility (they can feel ‘left-behind’)

Example

- PreDx Diabetes Risk test estimates the patient risk for developing Type 2 diabetes over the next five years
- This can further encourage patients to follow a healthy lifestyle and take other preventive measures.
4. Enabling Tx effective in a small fraction to be made available

A biomarker or other genetic characteristic allowing for patient stratification can

a) “Rescue” Tx that may otherwise either not have been licensed or withdrawn
b) Increase the chance of a Tx meeting reimbursement criteria (if targeting responders improves cost-effectiveness)
c) Accelerate R&D process of Tx (if stratification ascertained at an early development stage)

4. Enabling Tx effective in a small fraction to be made available - Examples

a) Gefitinib for non-small-cell lung cancer (NSCLC) initially licensed but then withdrawn when Phase III failed to show a survival benefit. With the identification of EGFR mutations and its association with response rate to TKIs, gefitinib was approved in the EU and other markets in combination with the EGFR mutation test.

b) NICE recommended trastuzumab for advanced and early-stage breast cancer in HER2/neu positive patients identified with HER2/neu test. The Dx-Tx cost per QALY was found below the standard threshold.

c) Crizotinib targets a small subset of NSCLC patients with an ALK-positive molecular abnormality. The development of the ALK FISH test has accelerated the development process and increased the likelihood of crizotinib delivering health benefits and commercial value.
5. Reducing uncertainty about value

a) Uncertainty around expected health effects and costs. It influences the risk of poor value for money for payers

b) Value of information to patients as to their medical condition independent of the health outcomes
   • Effect of reassurance, reduction in patients’ anxiety (measured in EQ-5D?)
   • Dx results can also enable lifestyle choices and planning

Example

• Oncotype DX® and MammaPrint ® are multi-gene assays estimating the risk of recurrence in breast cancer patients following surgery
• They can guide intervention decisions and reduce the risk of dispensing unnecessary chemotherapy (reduce resource costs to the healthcare system and adverse effect for the patient)

Other factors affecting value of combined use of Dx-Tx

• Low accuracy of Dx will decrease potential net gains to patients and healthcare system
  • False positive and false negative patients will miss the opportunity to receive a clinical decision they can benefit from
  • Impact of misdiagnosis varies depending on the position in the treatment pathway (1st line, 2nd, last line) and the effectiveness of the alternative intervention/s

• If the Tx is licenced also for un-tested populations, Tx can be more cost effective when used on its own:
  • When Dx does not provide binary response, if the size of the subset for which the Dx does not provide clear-cut result is large relatively to the other two subsets and the Dx cost is high compared to the Tx cost
  • When Dx has low accuracy
**Proposed institutional processes for co-dependent technologies**

- A joint Dx-Tx review of “at launch” technologies, to be done by a drug committee to exploit synergies across Dx and Tx
  - However, there is a need to address the lack of expertise of most drug committees in the Dx area

- A separate Dx committee to develop Dx-specific expertise and to assess multiple tests with similar clinical use
  - However, there may be a trade-off if there are not enough decisions to justify a distinct committee

- A comprehensive and consistent approach to assessing value of both Dx and Tx

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**International experience. The case of Australia**

- Until now, Dx and associated Tx assessed via different committees (MSAC and PBAC)
  - no clear structure for consideration of the interactions and benefits from joint use

- New coordinated process and decision framework for “co-dependent technologies”.
  - “Integrated” applications combining information from Dx and Tx manufacturers
  - reimbursement decisions are made jointly by PBAC and MSAC to ensure optimal clinical use (Merlin et al., 2012)
  - Although it gives the option to provide different types evidence to demonstrate clinical benefits of test, the preferred option remains a patient randomisation to use the test (i.e. a double randomised trial)
International experience. The case of NICE in England and Wales

• **NICE has dedicated-process for stand-alone Dx which follows very closely that used for drugs**
  - Strong preference to measure health gains with the QALY
  - Value dimensions beyond health effects, such as value of information to patients and process-related benefits, are not explicitly factored in

• “At launch” combinations are appraised via the drug review programme (TAs)
  - there is no explicit consideration of test-related parameters (accuracy, costs)
  - Value dimensions beyond health effects are not explicitly factored in

Conclusions

• The use of Dx-Tx combinations can deliver health gains and cost savings within the healthcare systems but also generate broader benefits to patients and society

• To ensure efficient use of limited resources health decision makers should take account of the full value generated by health technologies

• Clear incentives needs to be set up to encourage evidence collection

• HTA and other decision makings systems need coordinated and consistent approach to assess value of Dx and Tx
References


How to Assess the Value of Co-dependent Technologies?
- An Industry Perspective -

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Agenda

• Impact of today’s reimbursement environment of Co-Dependent technologies
• How is the value of Co-dependent technologies currently assessed
• Improvement for the assessment of the value of Co-dependent technologies (Thoughts)
• Conclusions

Acknowledgements:
• Authors of the OHE Research Paper12/03 “Can and should value based pricing be applied to molecular diagnostics?”

Co-dependent technologies ⇒ CDx-Rx
• Focus on Dx as the ‘roadmap’ is less clear representing higher hurdles and challenges ahead
Reimbursement environment of Co-Dependent technologies:
Are we missing opportunities to improve Health Care Systems Efficiency & Patients’ Health?

P&R decisions are based mainly on the assessment of value from Drugs (Rx)

Reimbursement of diagnostics (Dx) based on ‘code-stacking’ rather than its impact on outcomes

Reimbursement for Rx and Dx sought independently with misperception of ‘double-charging’

Dx are usually funded by Rx-manufacturer before formal reimbursement

Poor industry incentives (Dx)
• Reduced Innovation
• Generation of clinical & economic evidence compromised

Increased uncertainty for decision-making processes

Lack of clarity on source of funding & guidance on implementation

ROI unclear deepening the gap in innovation & data generation

Are we capturing the full benefits brought to society by all the components of Co-dependent technologies: individually and as a package?

Yes

CDx-Rx launched simultaneously

No

Dx not linked to Rx

CDx linked to Rx

Do linked to Rx?

Single Dx launched separately

Multiple Dxs with same clinical use

National P&R process: CDx within Rx assessment
• Time-mandated
• Multi-criteria assessment: reimbursement, performance, inclusion into national catalogue (Rx)
• CDx characteristics (performance, pricing, etc.) usually not specified

Local/Regional Implementation:
• Rx manufacturer usually pays for CDx - Joint sales & marketing activities with Rx manufacturer become crucial
• Dx/Rx reimbursed according to procedures not its value
• Arguments to support decisions based on improved efficiencies

Impact
• Automatic concomitant use with Rx drug – lock-in of pharma partner
• Joint forces regarding product commercialization
• Reduced or no direct competition for CDx use
• CDx dependent on Rx drug commercialization success (as often exclusivity agreement)
• A negative opinion would lower probability of regional/local uptake
• Limitations regarding regional/local technology introduction (e.g. limit to certain centers, # of cases etc.)
Examples of Institutional Processes

The US System

- Formulary committees look into the value of new Rx but usually don’t assess the value of Dx
- Dx reimbursement based on code-stacking
- Elements of value can be recognised with the right evidence behind
- Oncotype Dx: value-based approach; cost-offsets vs. health gains; lengthy process to achieve adequate coverage

The UK System

- Assessment of the CDx in conjunction with Rx as part of the ‘Drug process’
- Incremental value of the 2 technologies is usually not clearly attributed
- HER2 testing for Trastuzumab in early-stage HER2-positive breast cancer
- Dx singularities are recognised -> Independent committee for ‘stand-alone Dx’

Moving towards a better assessment of the Value of Co-dependent technologies

- Institutional Processes
  - Characteristics of the Dx
    - Purpose: CDx vs. ‘stand-alone’; Timing of Launch; Other test available
  - Co-dependent technologies reviewed by 1 group in 1 package
    - Economies of scale
    - Common, comprehensive approach to assessing value for both Dx and Rx
  - Dx-specific expertise within the assessment group
- Value Assessment
  - Complete assessment of benefits brought by all the components of co-dependent technologies (aggregated and disaggregated)
- Guidance for Implementation
  - Clarity for decision-makers and payers facilitating reimbursement based on value (Dx)
  - Direction for Dx manufacturers regarding ROI increasing incentives for R&D & Evidence Generation
Conclusions

• A value-based approach can improve the current P&R environment for co-dependent technologies

  – Capture all benefits brought to society by all the components of Co-dependent technologies: individually and as a package
  – Provide a consistent approach to WTP for value that allows for clear P&R decision making
  – Presents clarity for manufacturers regarding ROI thus allowing for R&D investment.