Key issues in the health economics of stratified medicine

Adrian Towse
Director of the Office of Health Economics
Visiting Professor London School of Economics

Academy of Medical Sciences Forum:
Health economics for stratified medicine
5th October 2016
Agenda: Three big issues

• New elements of value come into play
  • The value of knowing and related elements

• Paying for value
  • Fair shares for diagnostics, drugs, payers and patients – the dynamic perspective

• Standards of evidence have to be different
  • Not that different – clinical utility evidence
The Economics of Personalized Medicine: A Model of Incentives for Value Creation and Capture

Personalized medicine is a concept promoted as a new paradigm for health care delivery, with particular emphasis on more tightly linking genomics-based diagnostics and therapeutics. Previous analyses focused on the pharmaceutical market; this analysis also addresses the incentives to develop linked genomics-based diagnostics and the broader public policy implications. Using a standard economic framework of an insurer-payer negotiating reimbursement with manufacturers of an innovative, targeted diagnostic and a companion patented therapeutic, several illustrative hypothetical scenarios are developed. The relative importance of the key economic factors is examined, including whether the reimbursement system is value or cost based, whether the therapeutic is already marketed, the strength of diagnostic intellectual property, and a current year versus longer time frame. The results suggest that health systems reforms that promote value-based, flexible reimbursement for innovative, patent-protected diagnostic and therapeutic products are critical to create stronger economic incentives for the development of personalized medicine.
<table>
<thead>
<tr>
<th><strong>Base Case: Tx with no Dx</strong></th>
<th><strong>Tx with perfect Dx</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>100 patients receive Tx</td>
<td>100 patients are tested</td>
</tr>
<tr>
<td>20% respond</td>
<td>20 receive Tx</td>
</tr>
<tr>
<td>Willingness to pay (WTP):</td>
<td>Willingness to pay (WTP):</td>
</tr>
<tr>
<td>$1000 per patient</td>
<td>$6000 per patient</td>
</tr>
<tr>
<td>Total value generated:</td>
<td>Total value generated:</td>
</tr>
<tr>
<td>• (100 x $1000)</td>
<td>• (100 x .2 x $6000)</td>
</tr>
<tr>
<td>=$100,000</td>
<td>=$120,000</td>
</tr>
</tbody>
</table>

Therefore, a Dx test has the potential to generate an **additional** $20,000.
Sources of value from PGx

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

Can and Should Value Based Pricing Be Applied to Molecular Diagnostics?

Martina Garau, Adrian Towse, Louis Garrison, Laura Housman and Diego Ossio

April 2012

Research Paper 12/03
The Value of Knowing and Knowing the Value: Improving the Health Technology Assessment of Complementary Diagnostics

Phase I: Complementary Diagnostics: A Literature Review on the Value of Knowing

Phase II: Landscape Review of Complementary Diagnostics in Europe
Agenda: Three big issues

- New elements of value come into play
  - The value of knowing and related elements
- Paying for value
  - Fair shares for diagnostics, drugs, payers and patients – the dynamic perspective
- Standards of evidence have to be different
  - Not that different – clinical utility evidence
Flexible, value-based pricing and reimbursement

**Recommendation 14**

To incentivise the development of stratified medicine products appropriately, we recommend that a pricing and reimbursement system is developed that (a) enables prices to be adjusted over time to reflect increases and decreases in value, and (b) can manage two diagnostic scenarios: companion tests of one biomarker and large platform tests of multiple biomarkers. This system should consider the impact on projected cost per quality-adjusted life years gained, the cost-offsets compared with existing practice, the value of greater certainty of response and the value of improved adherence and uptake in the population.
A possible way to split the value between Rx and Dx

**Recommendation 15**

To incentivise stratification, at least in the short term, we recommend that health technology assessment bodies develop a model to separate the value between the drug and companion diagnostic. The medicine should be considered as the primary source of the health gain in responders. The diagnostic should be valued in terms of the cost savings and improvements in quality and length of life from reduced adverse drug reactions in non-responders, and in terms of increased certainty of response. Better patient adherence and greater overall appropriate use may also result, and this value could be divided similarly.
Agenda: Three big issues

• New elements of value come into play
  • The value of knowing and related elements

• Paying for value
  • Fair shares for diagnostics, drugs, payers and patients – the dynamic perspective

• Standards of evidence have to be different
  • Not that different – clinical utility evidence
### Table 1: Companion diagnostic testing in PM

<table>
<thead>
<tr>
<th>Technology</th>
<th>Economic and testing features</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 testing for breast cancer</td>
<td>A low-cost immunohistochemistry (IHC) (approx. $100–$200) test for human epidermal growth factor receptor 2 (HER2)-positivity was used in the initial clinical trial program and was provided by diagnostic companies. Subsequently, a higher cost and more accurate test ($300–$500) was developed (called ‘FISH’) and is in use. Approximately 80% of initial testing is done with IHC, with FISH retesting for patient with equivocal results. The drug manufacturer receives nearly all of the economic value created by the combination from the drug trastuzumab (Herceptin®, Roche).</td>
</tr>
<tr>
<td>BCR-ABL testing for chronic myelogenous leukemia (CML)</td>
<td>An example of an <em>ex ante</em> test (breakpoint cluster region-Abelson (BCR-ABL) gene) closely tied to the development of the drug: large majority of value capture by the drug imatinib (Gleevec®, Novartis). A second, BCR-ABL test is used to monitor for resistance and assignment to second-line therapies.</td>
</tr>
<tr>
<td>Oncotype Dx (Genomic Health) for breast cancer recurrence</td>
<td>An example of a relatively high-cost, value-capturing test aimed at avoiding unproductive chemotherapy.</td>
</tr>
<tr>
<td>EGFR mutation testing in nonsmall-cell lung cancer (NSCLC)</td>
<td>An example where the stratifying mutation (epidermal growth factor receptor (EGFR)) was identified in trials that also included test-negative patients.</td>
</tr>
<tr>
<td>HLA-B*5701 allele testing for abacavir in HIV</td>
<td>Example of a test to identify patients who are more likely to suffer a severe adverse reaction to the HIV drug abacavir (Ziagen®, Viiv Healthcare).</td>
</tr>
<tr>
<td>KRAS testing in colorectal cancer</td>
<td>The KRAS mutation predicts which patients will not respond to two different monoclonal antibody treatments for colorectal cancer. The biomarker was identified after the products were on the market.</td>
</tr>
<tr>
<td>PreDx (Tethys Biosciences) diabetes risk test</td>
<td>This multimarker test identifies which prediabetic patients are at high risk of progressing to Type 2 diabetes: it indicates whether to begin prophylactic treatment with metformin.</td>
</tr>
<tr>
<td>ALK mutation testing in NSCLC</td>
<td>Example of the drug crizotinib (Xalkori®, Pfizer) that targets a small subset (approximately 4%) of patients in disease condition with significant unmet medical need. It offers substantial survival gains in the subset, but with high testing cost per identified responder that must be factored in.</td>
</tr>
</tbody>
</table>
Case studies: sources of evidence

Evidence from the 9 case-studies

- Predominant funders are the *drug developers* (as part of the Rx development) and *public research bodies*

- Less clear role from Dx manufacturer

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>n</th>
<th>Case studies</th>
<th>Main study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Developer</td>
<td>6</td>
<td>Her2-BCa; EGFR-NSCLC; KRAS-CRC; BCR-ABL-CML; HIV, and Hep-C</td>
<td>RCT</td>
</tr>
<tr>
<td>Public Research</td>
<td>5</td>
<td>GenProfiling-Bca; KRAS-CRC; CYP2C19; Hep-C, and PreDx DRS</td>
<td>RCT</td>
</tr>
<tr>
<td>Dx Developer</td>
<td>2</td>
<td>GenProfiling-Bca; CYP2C19, and PreDx DRS</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Payer</td>
<td>1</td>
<td>CYP2C19</td>
<td>Prospective observational</td>
</tr>
</tbody>
</table>
Reasonable evidence requirements for companion Dx

**Recommendation 16**

We recommend that health technology assessment bodies, payers and regulators adopt a flexible approach to the generation of clinical utility evidence required for diagnostic tests.

- A double randomisation model for the development of combination stratified medicine and diagnostic should not become a requirement.
- The delivery of a prototype diagnostic test for use in phase III development should not call for significant investment in advance of being in a position to recognise the efficacy or otherwise of the drug itself in phase II.
- Clinical utility of combination stratified medicine and diagnostic could be assessed in small randomised studies (if not built into phase III of drug development), which can lead to conditional reimbursement approval plus real-world data collection after launch.
Barriers to diagnostic innovation
Barriers to diagnostic innovation

Challenges:

- Lack of value-based pricing for diagnostics
- Difficulty of collecting evidence
- Limited ability to protect intellectual property
- Need for competition – first Dx is not necessarily the best
Consider intellectual property protection for companion Dx

**Recommendation 17**

We recommend that the problem of rewarding evidence generation for diagnostics used in combination with stratified medicines is addressed urgently. In determining the reward for a new stratifying diagnostic, pricing and reimbursement systems must consider the costs of evidence generation and not simply the costs of production. To incentivise the generation of evidence about analytical and clinical performance and clinical utility successfully, consideration should be given to promotion of commercially approved diagnostic tests unless an ‘in-house’ test has evidence of equivalent or improved quality.
Factors:
- Economies of scale in HTA review of Tx & Dx
- Economies of scope—evaluation expertise and disease area
- Complementary/tied products
- Consistency across health sector

Figure 2. Institutional processes for the assessment of value of new diagnostics

New Dx

Dx linked to a Tx (companion Dx, personalised medicine)
- Dx-Tx pair launched simultaneously

Dx not linked to a Tx
- Dx assessed via Diagnostic-dedicated process

Single Dx launched separately
- Dx assessed via Diagnostic-dedicated process
- Dx assessed via Diagnostic-dedicated process

Multiple Dxs with same clinical use
- Dx assessed via Diagnostic-dedicated process

Dx-Tx joint assessment via Drug process
References (i)

- Academy of Medical Sciences. (2013) Realizing the Potential of Stratified Medicine, London, UK.
References (ii)


THANK YOU FOR YOUR ATTENTION

Adrian Towse
The Office of Health Economics
Registered address Southside, 7th Floor, 105 Victoria Street, London SW1E 6QT
Website: www.ohe.org  Blog: http://news.ohe.org
Email: atowse@ohe.org