Assessing added value of diagnostic tests in the concept of personalised healthcare

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Health Systems’ Goals / WHO

1. Improve the health of the population

2. Respond to people's legitimate expectations / responsiveness (quality of care, waiting times etc)

3. Provide financial protection against the costs of ill-health / fair financing
# Health Systems’ Goals / Increasing Quality & Value

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Less invasive treatment methods</th>
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<tbody>
<tr>
<td>Early detection</td>
<td>Faster recovery</td>
</tr>
<tr>
<td>Right diagnosis</td>
<td>More complete recovery</td>
</tr>
<tr>
<td>Early treatment</td>
<td>Less disability</td>
</tr>
<tr>
<td>Right treatment</td>
<td>Fewer relapses or acute episodes</td>
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<tr>
<td>Treatment earlier in causal chain of disease</td>
<td>Slower disease progression</td>
</tr>
<tr>
<td>Fewer delays in the care delivery process</td>
<td>Less need for long-term care</td>
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Functions of diagnostic tests

Screening

• Assess the likelihood of the presence of a disease or condition in apparently healthy or asymptomatic individuals who are at sufficient risk for a condition to benefit from further investigation or preventive action.

Diagnosis

• Determine the presence or absence of a specific disease or condition in symptomatic individuals. Diagnostic tests also may be used for prognosis, enabling selection of clinical care alternatives and treatments, and for monitoring treatment effectiveness and guiding treatment modifications.
Safety and effectiveness may vary from one individual to the next.

### Value of diagnostic tests in evidence based medicine

<table>
<thead>
<tr>
<th>Purpose</th>
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<tbody>
<tr>
<td>Screen for disease</td>
</tr>
<tr>
<td>Screen to determine risk for developing disease</td>
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<tr>
<td><strong>Rule in / Rule out of a therapeutic scheme</strong></td>
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<tr>
<td>Assess efficacy of an intervention</td>
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<tr>
<td>Assess compliance with an intervention</td>
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<tr>
<td>Assess prognosis</td>
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It is estimated that the results of diagnostic tests are immensely influential affecting around 60–70 % of all clinical decisions, although they still amount for only 4–5 % of healthcare costs.

Personalised healthcare

- Diagnostic Test
  - Prognosis: Responder for drug A
    - Patient gets drug A
  - Prognosis: Non-Responder for drug A
    - Patient gets drug B
  - Prognosis: Severe side-effects
    - Patient gets drug C

Personalised medicine is an evolving field of medicine in which treatments are tailored to the individual patient (characteristics, needs, preferences) through the use of genetic or other biomarker information.

Improvement of safety, effectiveness and health outcomes of patients via:
- Efficiency-targeted patient stratification
- Prevention
- Tailored medication
- Tailored treatment-management approaches
Companion diagnostic tests: fitting the treatment to the patients

- Companion diagnostics are medical devices that help doctors decide which treatments to offer patients and which dosage to give, tailored specifically to the patient.

- The companion diagnostic test is used to identify who would benefit from the treatment and sometimes to determine if there are patients who not only would not benefit, but could be harmed by use of a certain drug for treatment of their disease.

- Diagnostics tests used in personalised medicine are generally intended to identify the presence, absence, or amount of a biomarker or to assess physiological or anatomical patient characteristics.

- Today, close to 50% of the early-stage pipeline assets and 30% of late-stage molecular entities of the pharmaceutical companies involve the use of specific biomarkers.

Biomarkers – What do they stand for?

- Measurable characteristics (indicators) that reflect the presence or severity of some disease state – Can be chemical, physical or biological
- A biomarker indicates a change in expression or state of a protein that correlates with the risk or progression of a disease, or with the susceptibility of the disease to a given treatment – Characteristic biological properties that can be detected and measured in parts of the body like blood or tissue
- May indicate either normal or diseased processes in the body – Help in early diagnosis, disease prevention, drug target identification, drug response
- Can be specific cells, molecules, genes, gene products, enzymes, hormones

Improve patient safety

Efficacy biomarkers

Toxicity biomarkers

Patient biomarkers Personalised Healthcare

Disease biomarkers

More effective treatment
The role of biomarkers

From biomarkers to diagnostics: The road to success

**Eric Groves, M.D., Ph.D., Executive Global Strategic Drug Development Director, Quintiles**

**Table 1 Cancer biomarkers for which testing is mandated by the FDA prior to use of the drug**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Label</th>
<th>Indication</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal growth factor receptor (EGFR) expression</td>
<td>Patients enrolled in clinical studies were required to have immunohistochemical evidence of EGFR expression using the DakoCytomation EGFR pharmDX™ test</td>
<td>Colorectal cancer</td>
<td>Cetuximab (Erbitux®)</td>
</tr>
<tr>
<td>HER2/Neu over-expression</td>
<td>Detection of HER2 over-expression is necessary for selection of patients appropriate for Herceptin® therapy</td>
<td>Breast cancer</td>
<td>Trastuzumab (Herceptin®), Lapatinib (Tykerb®)</td>
</tr>
<tr>
<td>Philadelphia chromosome positivity</td>
<td>Dasatinib is effective for the treatment of adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ALL) with resistance or intolerance to prior therapy</td>
<td>Leukemia</td>
<td>Dasatinib (Sprycel®)</td>
</tr>
<tr>
<td>CD25 positivity</td>
<td>Ontak® is a CD25-directed cytotoxin indicated for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor.</td>
<td>Cutaneous T-cell lymphoma</td>
<td>Denileukin diftitox (Ontak®)</td>
</tr>
</tbody>
</table>
Advanced cancer: development of overall survival (progress in 2000-2010)


* average data, in months
Substantial difficulties in establishing direct causal links between ordering a test and changes in mortality, morbidity, quality of life, and other major patient health outcomes.

A diagnostic test is likely to be just one of many interventions and environmental and behavioral determinants of patient outcomes.
Defining value of diagnostic tests

- “Innovativeness” of DTs: high value from a commercial standpoint but also value to patients, physicians, or payers.
- CEA, CBA & CUA traditional methods to assess economic value of diagnostic tests.
- There is evidence that diagnostic tests have contributed to 30–50% reductions in direct hospital and outpatient charges.

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Condition</th>
<th>Economic Impact</th>
</tr>
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<tbody>
<tr>
<td>AdvanDx’s PNA FISH</td>
<td>Drug-resistant enterococcus faecium infections</td>
<td>42% reduction in mortality</td>
</tr>
<tr>
<td>EGFR</td>
<td>Metastatic colorectal cancer</td>
<td>Annual savings USD 604 million</td>
</tr>
<tr>
<td>Oncotype DX</td>
<td>Breast Cancer</td>
<td>44% change treatment</td>
</tr>
<tr>
<td>OraQuick ADVANCE</td>
<td>HIV</td>
<td>Transition from “laboratory-centered” to “user-centered” healthcare delivery</td>
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In total, 1703 tests were performed. Pooled FN rates were 11% for approved IVDs and 25% for laboratory-developed IVDs; FP rates were 0% and 5%, respectively.
Recurrences/progressions due to incorrect test results

- EBC:
  - Approved IVD: 150
  - Laboratory-developed IVD: 217
- MBC:
  - Approved IVD: 109
  - Laboratory-developed IVD: 109
Every $1 saved by laboratories by using cheaper reagents could potentially result in approximately $6 additional costs to the healthcare system.
Innovative diagnostic tests are becoming an essential part of disease management and therapy, helping physicians to stratify patient cohorts, choose more appropriate drug regimen, avoid adverse events, facilitate therapeutic monitoring, and define the predisposition to a disease.

Still frequently perceived as “additional costs”, as current systems consider drugs and diagnostics via separate evaluation and payment process.

No holistic approach to assessing personalized medicine.

Diagnostic tests impact directly on treatment decisions.

The accuracy of testing has economic, socioeconomic and clinical consequences.

Companion diagnostics, should be subject to in-depth regulatory scrutiny in order to ensure that all patients receive appropriate treatment.
Thank you!