Precision Medicine.
A Health Economic perspective

Lieven Annemans
Ghent University
Lieven.annemans@ugent.be
Exponential technology ➔ exponential cost?

http://medicalfuturist.com
The conflicting goals of healthcare policy
no blind investments

“We need to make available only those innovative technologies that offer an added value to patients and/or society at an acceptable cost (i.e. are cost-effective), and fill unmet medical needs”

NOTE: ‘technology’ = devices, medicines, diagnostics, prevention programmes,…

- Report of the Belgian EU Presidency, adopted by the EU Council of Ministers of Health in Dec 2010
- European Commission – Investing in Health February 2013
Public pricing of medicines: two options

• “cost+” price → price justified by costing structure.
  ☻ acceptable mark-up as compensation for costs of R&D
  ☹ what is the true cost of R&D (what about failures?)
  ☹ wrong incentives (‘spend a lot on R&D’)  
  ☹ added value not sufficiently recognized

• Value based pricing → more value = higher price
  ☻ incentives recognizing better added value
  ☹ profits may not be in reasonable proportion to cost structure
  ☹ evidence may not be sufficiently convincing
Cost-effectiveness explained

Cost - effectiveness explained

Health effect (QALYs)

Current care

“intervention”

Not C-EFF

Threshold

C-EFF

dominant

Annemans L. HEALTH ECONOMICS FOR NON-ECONOMISTS. Principles, methods and pitfalls of health economic evaluations. 2nd Edition. Pelckmans. Upcoming May 2018
PROBLEM: where is the threshold?

- HISTORICAL BENCHMARK $\pm 50,000\text{€ per QALY}$:
  = cost effectiveness of caring for a dialysis patient
  ($\pm 4$ QALYs gained for an investment of $\pm 200,000\text{€}$)
- WHO: $<1$ GDP per capita (e.g. Belgium $= \pm 37000\text{€}$)
  (exceptionally up to 3x GDP per capita)
- At the discretion of the decision maker (e.g. England $30,000 \text{ £ per QALY}$)
## Some examples: “league table”

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost per QALY gained (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac rehabilitation and prevention program</td>
<td>dominant</td>
</tr>
<tr>
<td>Helpline for suicide prevention</td>
<td>dominant</td>
</tr>
<tr>
<td>New anticoagulants for stroke prevention in atrial fibrillation</td>
<td>5,000</td>
</tr>
<tr>
<td>Intensive secondary prevention after a heart attack</td>
<td>12,000</td>
</tr>
<tr>
<td>Total Hip Replacement</td>
<td>14,000</td>
</tr>
<tr>
<td>New generation drugs in MS</td>
<td>35,000</td>
</tr>
<tr>
<td>Low dose Bevacuzumab in 1st line advanced ovarian cancer</td>
<td>70,000</td>
</tr>
<tr>
<td>Biannual screening for prostate cancer in all men 40-80 yrs</td>
<td>500,000</td>
</tr>
<tr>
<td>Annual CT in former heavy smokers to detect lung cancer</td>
<td>1,000,000</td>
</tr>
</tbody>
</table>
The Belgian solution for medicines

→ Class I: if the company believes its medicine offers added therapeutical value, and it claims a price premium, then the medicine will be assessed according to the following criteria:

1. Added therapeutical value
2. Medical therapeutical need
3. Cost-effectiveness
4. Impact on the Budget
PROBLEM: Uncertainty

“Give us more evidence that your medicine is value for money”

“Allow us first to the market (reimburse the medicine) and then we will be able to show real life evidence”
Example ipilimumab

Solution? Outcomes based entry agreements!
Or: PRECISION MEDICINE? Or BOTH
Outcomes based agreements

1. Coverage upon evidence development
   - *Temporary approval, then final decision*

2. Performance Linked Reimbursement (outcomes guarantee)
   - *Not as good as promised → industry pays back*
Types of agreements (Toumi et al 2016; n = 143)

- Financial agreements: 39%
- Coverage upon evidence development: 24%
- Outcomes guarantee/P4P: 37%

Appl Health Econ Health Policy. 2016 Aug 31
And what about precision medicine?
On first sight, precision medicine is better for all

- **Patients**
  - Reduced uncertainty, improved care and less exposure to ineffective treatments

- **Physicians**
  - More effective options and outcomes for their patients

- **Industry**
  - Innovative products that offer a clear improvement for patients

- **Payers & policy makers**
  - More cost-effective use of our healthcare Euros
But despite the new paradigm, the same questions need to be addressed:

- Standard of care A
- New Drug B
- Disease X
- No test
- Test(s)
- Disease X

Before

Now

- A?
- B?
- No treatment?
- A!
- B!
- No treatment!

NEW ELEMENTS
- Cost of test
- Performance of test
- False positives and false negatives
- ....
**Example lung cancer**

*Doblea et al.* Cost-effectiveness of precision medicine in the fourth-line treatment of metastatic lung adenocarcinoma: An early decision analytic model of *multiplex targeted sequencing* (MTS)

Lung Cancer - Volume 107, May 2017, Pages 22-35
### Results Doblea et al 2017

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Mean LYs/QALYs per patient</th>
<th>Mean costs per patient (AUD)</th>
<th>ICER (excluding dominated strategies)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSC</td>
<td>1.458</td>
<td>189,529</td>
<td>–</td>
</tr>
<tr>
<td>CHO</td>
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<tr>
<td>MTS</td>
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<tr>
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<td>193,832</td>
<td>489,338</td>
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</table>
POLICY PERSPECTIVES

Challenges in the Development and Reimbursement of Personalized Medicine—Payer and Manufacturer Perspectives and Implications for Health Economics and Outcomes Research: A Report of the ISPOR Personalized Medicine Special Interest Group

Eric Faulkner, MPH1,2,3,4,*, Lieven Annemans, PhD, MSc5, Lou Garrison, PhD6, Mark Helfand, MD, MPH7, Anke-Peggy Holtorf, PhD, MBA8, John Hornberger, MD, MS9,10, Dyfrig Hughes, PhD, MRPharms11, Tracy Li, PhD12, Daniel Malone, PhD13, Katherine Payne, PhD14, Uwe Siebert, MD, MPH, MSc, ScD15,16,17, Adrian Touse, MA18, David Veenstra, PhD, PharmD6, John Watkins, PharmD, MPH, BCPS19, for Personalized Medicine Development and Reimbursement Working Group
Pitfalls of personalized medicine

- Additional cost for true and false positive patients
- Expanded patient populations for drugs (e.g., by screening and prevention)
- Increased diagnostics budgets
- Enforcement of privacy safeguards
- Extended patent protection by secondary test-treat product

- **Consequences of false negatives**

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Faulkner et al, 2012, adapted
“If 100,000 cancer patients will all receive a personalized treatment at 50,000€ the budget impact will be 5 Bln €”
(J. De Grève – VUB)
in 2020 oncology PMx will represent 8.9 to 9.5% of the total pharmaceutical specialties budget, a raise from 1.6% in 2005.

Figure 14: Projection of the budget impact before savings of reimbursed PMx in Belgium from 2005 to 2020.
HIScreenDiag – Project

Building a Tool to Evaluate and Improve Health Investments in Screening and Diagnosis of Disease

Focus on biomarkers as companion to drugs

Lieven Annemans, Fernando Antoñanzas, Cornelis Boersma, Katharina Fischer, Dolores Ibarretat, Ian Jacob, Reiner Leidl, Daniele Paci, Katherine Payne, Maarten J. Postma, Roberto Rodriguez, Wolf Rogowski, William Sullivan, Dominique Vandijck
“surprising” finding: the current decision processes in the EU are not transparent, fragmented and highly different

• Enormous differences in
  – who triggers the health economic evaluation of tests
  – who participates in the assessment
  – the criteria for assessment
  – the way they are conducted

• “coverage decisions about biomarkers frequently appear to be made outside of the scope of national decision making bodies, presumably on a local decision making level”
Presenting solutions using the innovation cycle

The market usage challenge

Value deficit

The development challenge

Provide Value for money

Add value

The market access challenge
Ten Actions to Stimulate Patient Access to Personalised Medicine in Europe

1 June 2015

Jo De Cock¹, Lieven Annemans²

Introduction

The European Commission published a Report in 2013 on the "Use of '-omics' Technologies in the Development of Personalised Medicine"³ which highlights the potential of Personalised Medicine. Personalised Medicine (PM) is defined as "a medical model using molecular profiling for tailoring the
I. The Development Challenge

• Early economic evaluations for different diagnosis-treatment combinations in different indications

• Move away from the traditional RCT paradigm

• Early dialogues and joint advice

• Co-ordinate the regulatory processes of diagnostics and therapies
II. The Market Access Challenge

- Integrated health technology assessment processes and criteria for diagnostic tools and medicines/devices
- Risk sharing agreements recognising uncertainties of personalised medicine
- Horizon scanning required for better understanding of future health budget impact
III. The Market Use Challenge

• Organisational measures and financial incentives to allow the market penetration of truly innovative precision medicine, e.g. regional centres of excellence, quality assurance schemes

• Training and education about precision medicine

• Real life data collection
Some final thoughts

• Also for personalized medicine, cost-effectiveness must be demonstrated – it is not a ‘given’

• All personalized treatments together induce a large budget impact ➔ will affect our societal willingness to pay

• Current decision making processes are suboptimal

• Re-investing in health