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The health systems perspective

Biomarkers, Health Technology Assessment and sustainability of healthcare systems

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September 2018

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Cancer Drug Development Forum

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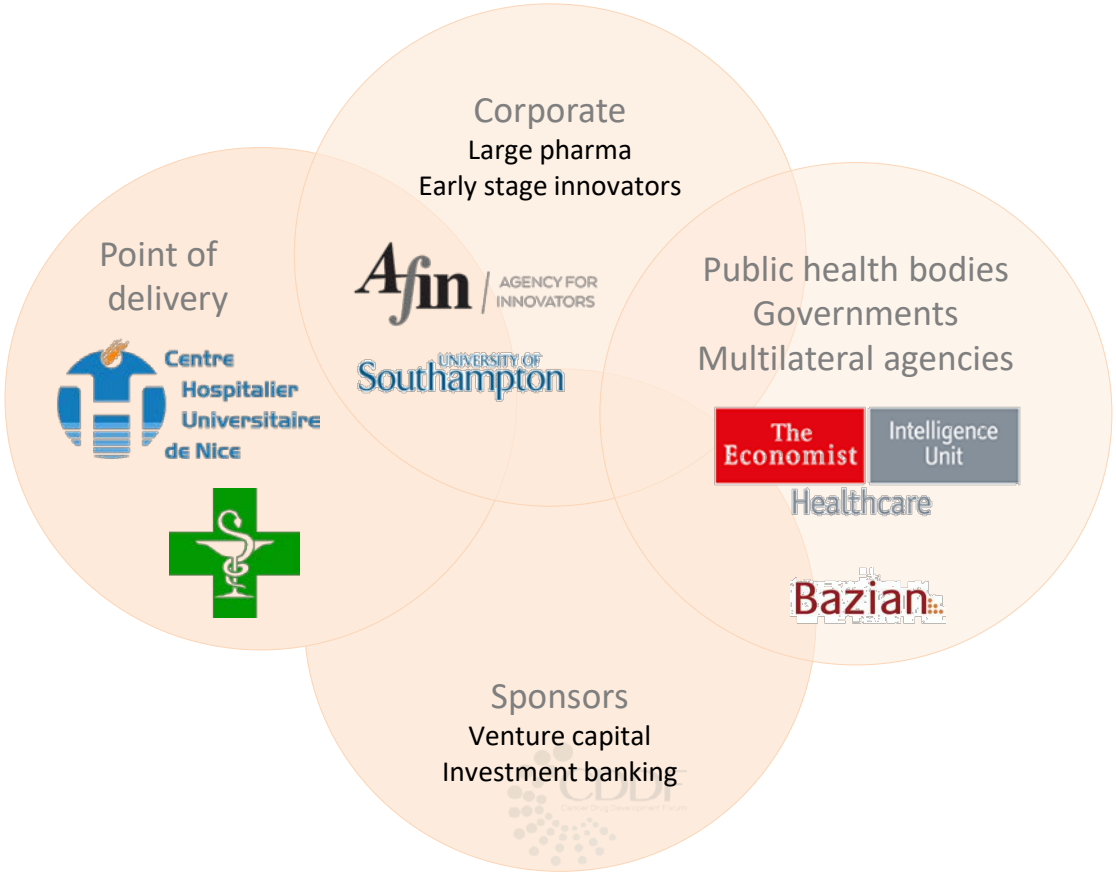
Annie Pannelay

Hands-on experience across the health ecosystem, with a focus on evidence based medicine and value-based healthcare



Agenda

- Growth of healthcare budgets is faster than economic growth
- Areas of focus include hospital and the cost of medicines
- Research on biomarkers has increased in the past 20 years
- Challenges to reconcile for HTA pathways to be suited to biomarkers
  - Geographical alignment challenges
  - Views on robust clinical evidence
  - Apprehension about costs
- Thoughts for the future: How to make sure industry is coming up with the right products

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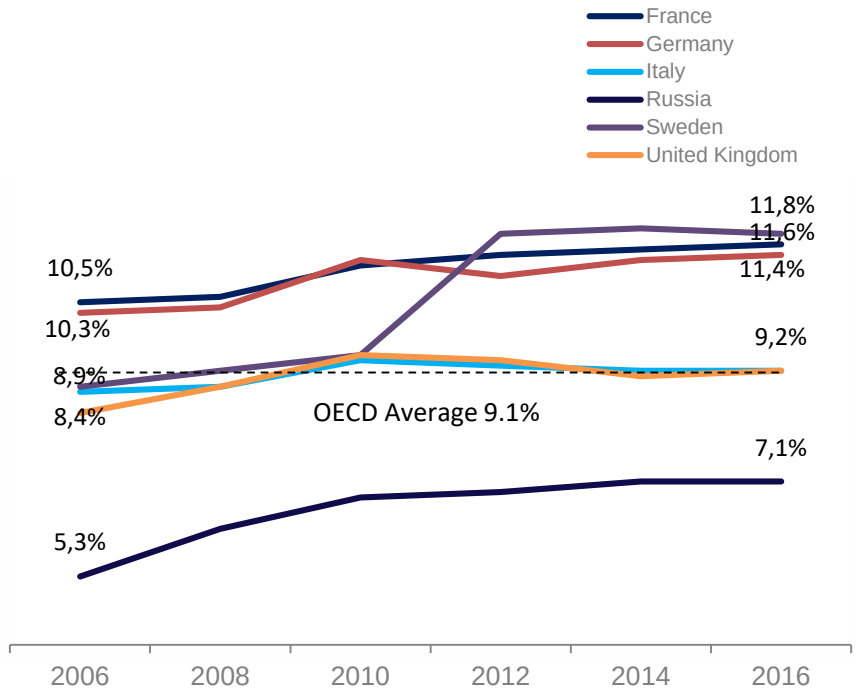
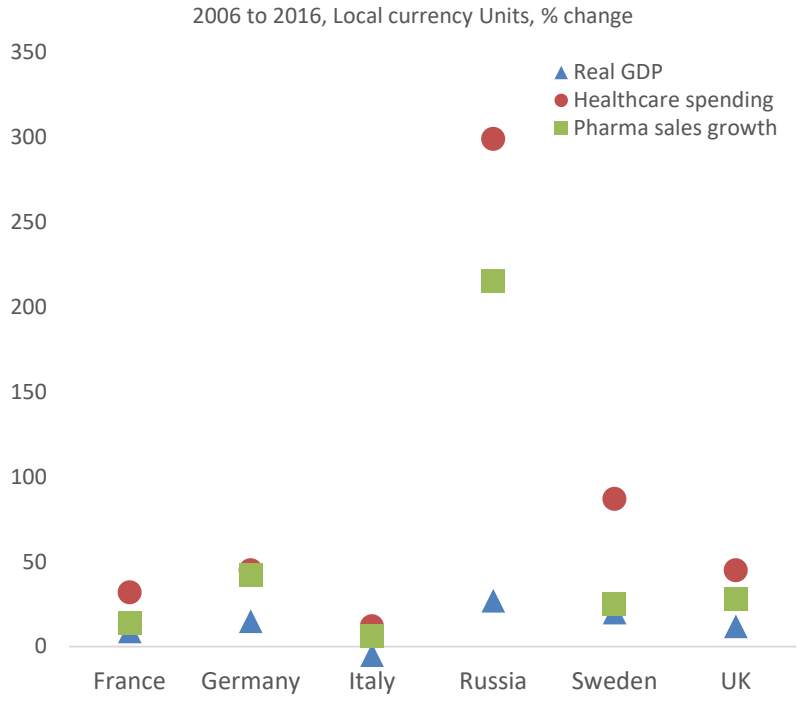
Healthcare budget growth outpace economic growth

Spending on healthcare as % GDP



Economic growth, health spending and pharma trends



Source: OECD

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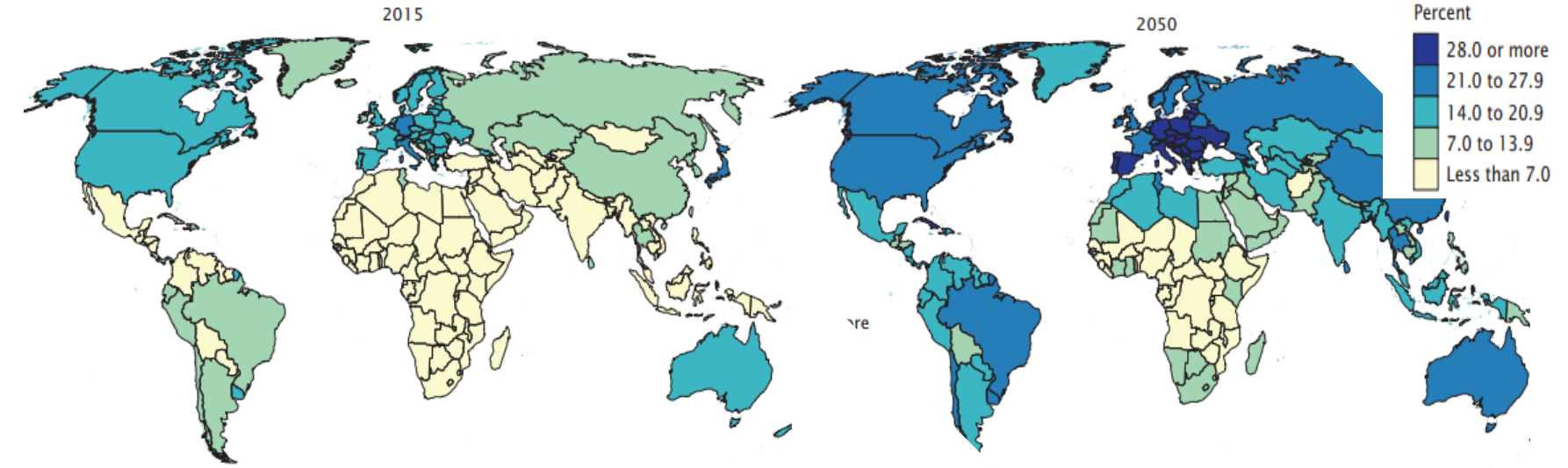
This is driven by population ageing – but not only

Ageing population: forecast

% 65 and Over: 2015

% 65 and Over: 2050



The population of people older than 65 years represented ~ 7% in 2015 . By 2050, this proportion of the population will more than double, reaching 15.6%.

Sources: U.S. Census Bureau, 2013, 2014; International Data Base, U.S. population projects

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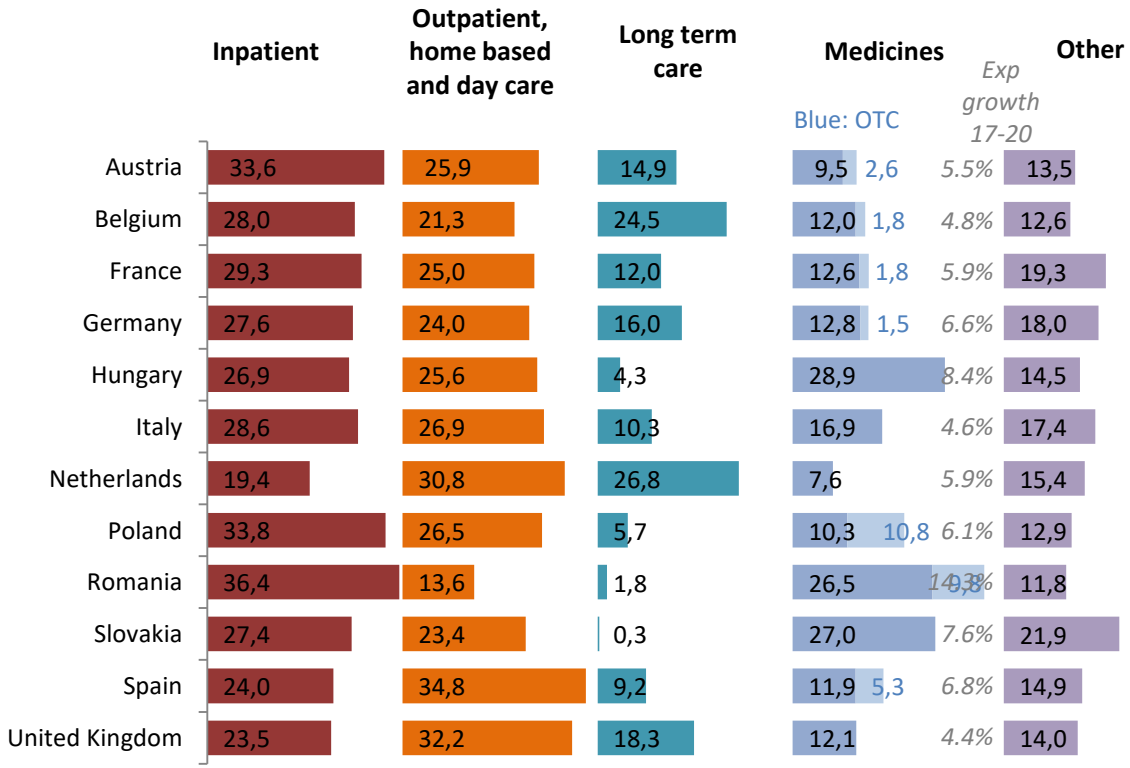
Payers focus is on high contributors to health spending

- Across Europe, inpatient care represents the largest contributor to health spending
- In the sample, the expected growth for spending on medicines is over 5% from 2017-2020

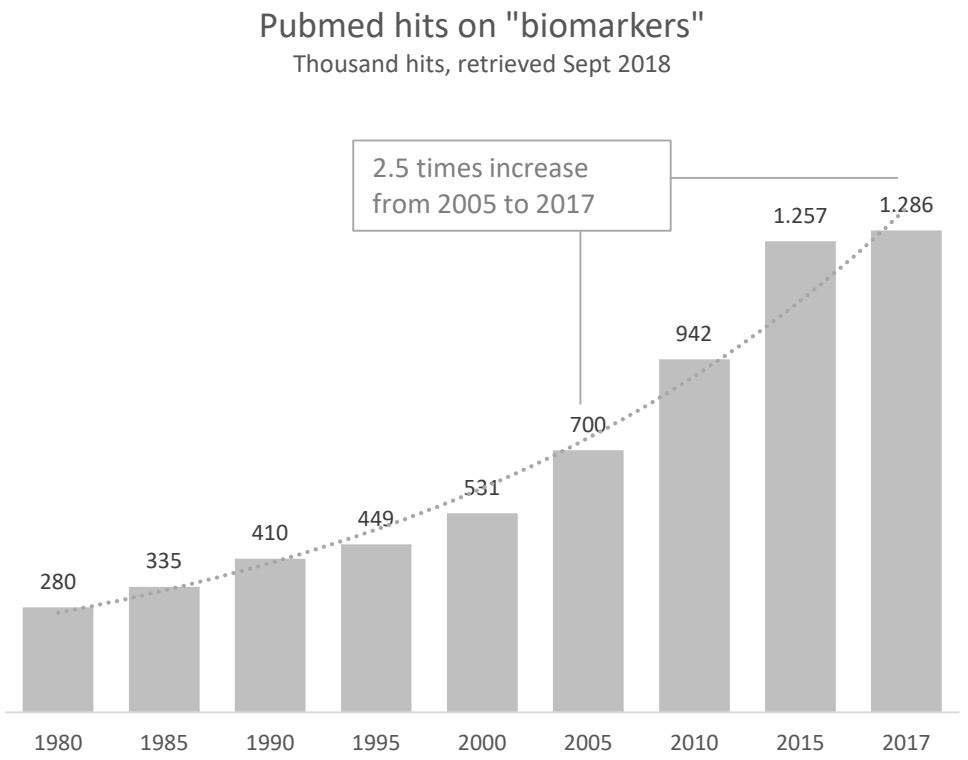


Source Eurostat, 2014

Research on biomarkers has grown – adoption remains low

- There is no separate framework for qualification of novel technologies unless medical device/medicine
- Pharmacoeconomics require whole of pathway approach
- There are no value-based pricing guidelines for innovative diagnostics in any of the EU member states
- The outcome of underdeveloped pricing system might limit access of patients to novel "therapy-test" products

What are the gaps to be filled to facilitate adoption of biomarkers?



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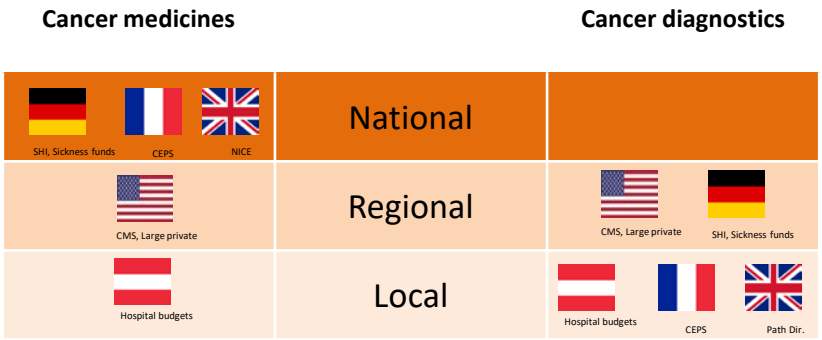
The HTA perspective

Global evidence, local decisions



- Coverage for Diagnostics is decided at local and regional level
- Innovators are often SMEs with low resources struggling to supply information to each organisation
- Harmonisation and design of good practice even more challenging than for medicines

Apprehension about costs and lack of clinical evidence

- Testing large @risk populations who may benefit might prove costly
- Tests for cancer diagnostic available for self pay market aren't supported by robust clinical evidence

Snapshot adapted from he Luzak study

Internet search on biomarkers available self pay in Germany	11	
No RCT identified for patient relevant outcomes	10	
RCT with the outcome of interest		1
RCT showing strong evidence of reduction of mortality		0

Adapted from Miller, I.; Ashton-Chess, J.; Spolders, H.; Fert, V.; Ferrara, J.; Kroll, W.; Askaa, J.; Larcier, P.; Terry, P.F.; Bruinvels, A.; *et al.* Market access challenges in the EU for high medical value diagnostic tests. *Pers. Med.* **2011**, *8*, 137–148.
Markus B.; Brüggenjürgen, B.; Stefan, W. Personalised Medicine in Europe—Enhancing Patient Access to Pharmaceutical Drug-Diagnostic Companion Products.

Luzak, Clinical effectiveness of cancer screening biomarker tests offered as self-pay health service: a systematic review, European Journal of Public Health 2016

What could support the development of HTA processes suited to biomarkers?

Early HTA definition

Early HTA includes all methods used to inform:

- **industry**
- **other stakeholders**

About the potential value of new medical products in development,

- **including methods to quantify and manage uncertainty**

Methods are varied

They include:

- Economic modelling – Markov models not always suited to complexity and effect of implementation of biomarkers on care pathways -> Systems modelling to address time dependent behaviors
- MCDA/stakeholders preferences (MCDA: Multi Criteria Decision Analysis)
- Headroom analysis – Applicable for industry only

Izjerman, 2017

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What could support the development of HTA processes suited to biomarkers? (2)

The EFLM TE-WG 14 item checklist

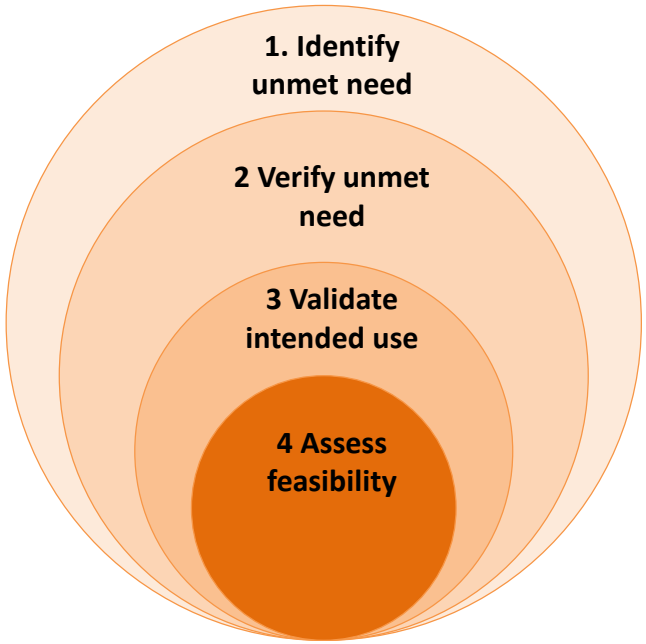
The European Federation of Clinical Chemistry and Laboratory Medicine

1 - What is the clinical management problem and desired outcome?

- What is the health condition and clinical management problem?
- What is the target group?
- What is current practice?
- What are the limitations of current practice?
- What are the desired outcomes?

3 -Would the biomarker contribute to the solution?

- How would the biomarker alter and improve current practice?
- What are the expected outcomes of test results?
- How do these outcomes compare to the desired outcomes defined in STEP 1



2 - Is there an existing solution?

- Could the problem be solved by optimising current practice?
- Could these solutions be effective?
- Could these solutions be cost effective?
- Are there any barriers for these solutions?

4 - Is the biomarker solution feasible in practice?

- Under what conditions would the new biomarkers be feasible?
- Commercially?
- Economically?
- Technically?
- Organisationally?
- Are there any other barriers?

Source: Practical guide for identifying unmet clinical needs for biomarkers Monaghan 2018 The Journal of the International Federation of Clinical Chemistry and laboratory medicines

Sources

Evaluation of Biomarkers: Application in Urological Cancers Thesis, Erasmus MC, University Medical Center Rotterdam	Moniek Martine Vedder	2016	
Market Access Advancements and Challenges in "Drug-Companion Diagnostic Test" Co-Development in Europe	Akhmetov	2015	Journal or personalized medicine
Methods of Early Health Technology Assessment in Precision Medicine	Janet Boutell	2018	Glasgow molecular pathology node, poster
Health Technology Assessment of Drugs With Companion Diagnostics at CADTH	CADTH	2017	Health Technology Assessment of Drugs With Companion Diagnostics at CADTH
Emerging Use of Early Health Technology Assessment in Medical Product Development: A Scoping Review of the Literature	IJzerma	2017	PharmacoEconomics
Procedural guidance for the systematic evaluation of biomarker tests		2014	Ludwig Boltzmann institute
Clinical effectiveness of cancer screening biomarker tests offered as self-pay health service: a systematic review	Luzak	2016	The European Journal of Public Health
Systematic review of frameworks for staged evaluation of predictive biomarkers	Malottki	2015	
Practical guide for identifying unmet clinical needs for biomarkers	Monaghan	2018	The Journal of the International Federation of Clinical Chemistry and laboratory medicines
Targeting biomarker development in response to unmet clinical needs	Monaghan	2014	for the Test Evaluation Working Group of the European Federation of Clinical Chemistry and Laboratory Medicine
Early Stage Health Technology Assessment for Precision Biomarkers in Oral Health and Systems Medicine	Steuten	2016	Journal of Integrative Biology
Precision Medicine in Oncology and Immuno-Oncology: Where We Stand and Where We're Headed	Scheuenpflug	2017	Biomed Hub 2017;2(suppl 1):18-18
Health Technology Assessment of Companion Diagnostic Biomarkers as Gatekeepers for Personalized Medicine Market Access	Spinner	2013	Value in Health
Attracting Investors: the value of HTA.	Tolley	2018	

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Annex: Categories of biomarkers

- **Susceptibility/Risk biomarker** - A biomarker that indicates the risk for developing a disease or sensitivity to an exposure in an individual without clinically apparent disease.
- **Diagnostic biomarker** - A biomarker used to identify individuals with the disease or condition of interest or to define a subset of the disease.
- **Monitoring biomarker** - A biomarker used to detect a change, over time, in the degree or extent of disease, safety indicator, or exposure.
- **Prognostic biomarker** - A biomarker used to identify likelihood of a clinical event, disease recurrence or progression.
- **Predictive biomarker** - A biomarker used to identify individuals who are likely to experience a favorable or unfavorable effect from a specific intervention or exposure.
- **Pharmacodynamic biomarker** - A biomarker used to show that a biological response has occurred in an individual who has received an intervention or exposure.
- **Safety biomarker** - A biomarker used to monitor toxicity.

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The journey to market is designed for medicines

	Review of…	Flow of information	Biomarkers
Regulatory	• Safety • Manufacturing and clinical production standards	Is there a need? Is the product deemed safe in this indication?	• No separate framework for qualification of novel technologies unless medical device/medicine
Scientific advice	• Clinical performance	Should it be included in treatment guidelines?	• Evidence standards to be defined
Pharmaco-economics	• Correlation between clinical performance and potential price	Should we pay for this?	• Need whole of pathway approach – see next slide
Pricing and reimbursement	• Price negotiation with manufacturers	Any price adjustment?	• Unclear and challenging timelines for reimbursement frameworks
Purchasing and payment	• Medicines procured as efficiently as possible (tenders) and providers are reimbursed	Nominated tariffs and usage monitoring	• Effort needed to connect clinical diagnostic labs to where outcomes benefits can be seen

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Current trends in healthcare and challenges for biomarkers

Current trends	Biomarkers development
Outcomes	
• Focus on outcomes that matter to the patients: survival, degree of health	• Focused on surrogate endpoints/intermediary outcomes
Value demonstration	
• Need to demonstrate the impact and effectiveness	• Patients benefit from pathway improvement, not from the test
Data	
• Adoption of VBHC incentivises the harmonisation of data and processes	• Need for custom data domains – data managed separately in trials
Evidence standards	
• Strong need for evidence base and clinical utility measure	• Quicker discovery pace, lack of standards to qualify novel biomarkers

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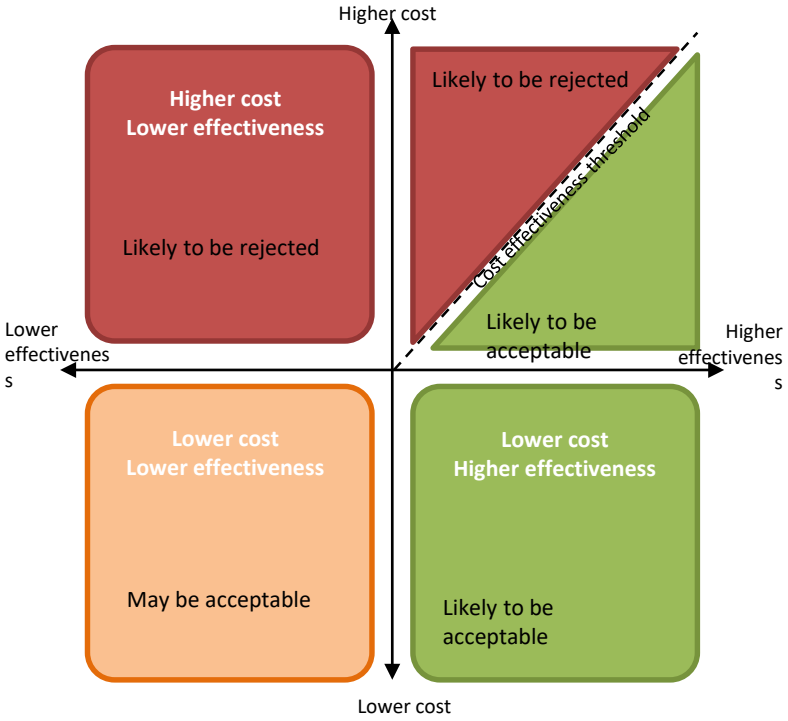
Demonstrating the value of tests: NICE approach

- META-Tool was developed as a light version of the NICE scientific advice suited to medtech companies
- Process includes a review of :
  - Product information
  - Regulatory and HTA requirements
  - Questions for economic evaluation
  - Value proposition
  - Clinical treatment pathway
  - PICO statement
  - Measuring clinical effectiveness
  - Economic data collection
  - Funding and commissioning
  - Adoption and impact

NICE Cost effectiveness framework



Adapted from NICE