An evidence-based analysis to characterise the benefits of personalised medicines to patients, society and healthcare systems

July 2018
Purpose of this report

- The European Biopharmaceutical Enterprises (EBE), and the European Federation of Pharmaceutical Industries and Associations (EFPIA) has asked Charles River Associates (CRA) to conduct an evidence-based analysis of the value of personalised medicines (PM).

- In particular, the objectives are to:
  - Characterise and measure the benefit of PM to patients, society and healthcare systems
  - Identify the key enablers to the adoption of PM but also the main barriers that impede the development of PM in Europe from an economic and access perspective
  - Elaborate strategic recommendations for decision-makers to overcome these barriers and incentivise the development and adoption of PM in Europe
This considered a range of PM technologies

We define PM as any technology that aims to improve the prevention, diagnosis and treatment of diseases by using patients’ individual characteristics to identify the most appropriate care.

- Broadly classified into two categories:
  - **Targeted therapies**: These are therapies that act on specific molecular targets associated with a disease. These targets can arise from specific mutations associated with the disease or protein-expression targets within biological pathways.
  - **Individualised therapies**: This includes modified T-cell therapies and gene therapies, which are considered ATMPs. These technologies are specifically targeted at an individual patient.

- PM refers to a process by which genetic information is used to evaluate patients at risk of developing particular diseases, or who have mutations which can be targeted by specific medicines. This includes next generation sequencing (NGS), assays for specific mutations, and gene expression profiles which characterise sections of an individual’s genome.
Four tumour types were selected as cases studies to develop a fact-based landscape analysis

- CRA selected case studies in consultation with the EBE/EFPIA steering group

<table>
<thead>
<tr>
<th>Products / targets</th>
<th>Non-small cell lung cancer</th>
<th>Breast cancer</th>
<th>Ovarian cancer</th>
<th>Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multiple specific mutations (ALK+, ROS+, EGFR) plus protein-expression targets (PD1)</td>
<td>Germline and somatic mutation-targeted therapies</td>
<td>Introduction of PARP inhibitors</td>
<td>Introduction of BRAF inhibitors (and later BRAF / MEK inhibitors)</td>
</tr>
<tr>
<td></td>
<td>Companion and complementary diagnostics</td>
<td>Potential usage of advanced diagnostics (e.g. Oncotype) separate from treatments</td>
<td>Use of diagnostics in screening programs for BRCA mutations</td>
<td>Use of tumour mutation testing for treatment decision-making</td>
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- To investigate the environment for each case study we chose a subset of European markets to examine in detail

Countries were selected on the basis that they:
- represent different regions of Europe
- represent different reimbursement mechanism and approach to HTA
- have some level of policy activity and prioritisation for PM
- have sufficient treatment infrastructure to enable adoption of PM

- CRA conducted a set of interviews with external stakeholders to fill evidence gaps and gather different perspectives in each country (n=19)
The benefits of Personalised Medicines
The benefits of PM can be classified into three main categories

<table>
<thead>
<tr>
<th>Delivering better treatments for patients</th>
<th>Delivering benefits to healthcare systems and society</th>
<th>More efficient development of novel medicines</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Improved efficacy i.e. patient more likely to receive a medicine delivering a clinical benefit</td>
<td>- Prevention and prediction of disease</td>
<td>- More effective clinical trials</td>
</tr>
<tr>
<td>- Improvement in overall survival</td>
<td>- Improvement in patient management of diseases</td>
<td>- Efficient clinical trials and reduction in cost</td>
</tr>
<tr>
<td>- Reduced adverse events</td>
<td>- Prevention or delay of more expensive care costs and allowing scarce healthcare resources to be using most efficiently</td>
<td>- More ethical clinical trials</td>
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<tr>
<td></td>
<td>- Reduces hospitalisation</td>
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</table>
Targeted and personalised interventions have led to better patient outcomes and optimized regimens

- PM offers the opportunity to move away from ‘trial-and-error’ prescribing to initial prescription of optimal therapies and deliver better response by patient

- Progression-free survival and overall survival has increased in many cancers due to PM:
  - Alongside the introduction of immunotherapies (CTLA4 and PD1-targeting), the combination BRAF/MEK inhibitors are cited by oncologists as driving improvements in melanoma survival
  - There has been an overall reduction in EU mortality from breast cancer and an increase in ten-year survival to 78%

- The introduction of PM has allowed targeting of the underlying genetic mutations in diseases, including chronic myeloid leukaemia (CML) and Cystic Fibrosis

- An analysis of 570 phase II clinical trials showed that oncology PM therapies had 4X the response rates compared to cytotoxic therapies

- Studies evaluating severe to life-threatening adverse events in advanced urothelial carcinoma, showed anti-PD-1 treatment reduced frequency adverse events from 49.4% with chemotherapy to 15.0%

PM offers many possible treatment options to facilitate earlier treatment or prevention protocols

- Molecular analysis can determine precisely which sub-phenotype of a disease a person has, or whether they are susceptible to medicine toxicities, to help guide treatment choices. This shifts the emphasis in treatment from reaction to prevention.

- This has the potential to lower overall healthcare costs through early-detection, prevention, accurate risk assessments and efficiencies in care delivery.

**Early identification of Familial Hypercholesterolemia (FH)** through genetic testing has led to significant savings in healthcare costs – in the UK estimated savings to the NHS are £6.9 million per year.¹

In France, INCa allocated an additional €1.7M to regional genetics centres across the country for EGFR testing. This resulted in substantial increase EGFR screening in patients²:

- INCa concluded that this **additional investment in EGFR testing** would save €69 million to the French health insurance by identifying patients who harboured the EGFR mutation.

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¹ Marks D (2002); ² Nowak, F. (2012)
Better patient management is associated with savings to healthcare systems and society

Case Study: NSCLC

- Treatment algorithms for NSCLC have changed dramatically over the last few years, following the approval of the first generation of targeted therapies
- PM is associated with more savings to society compared to standard chemotherapy in terms of increased productivity and decreased social benefits paid to patients who are able to work in France, Germany, Italy, and Spain
- Mean incremental savings to society per patient receiving bevacizumab plus chemotherapy treatment ranged from €2,277 in Italy to €4,461 in Germany

Source: Lister et al (2012)

\(^1\) Lister et al (2012)
PM allow scarce healthcare resources to be used more efficiently

<table>
<thead>
<tr>
<th>Type of impact</th>
<th>Supporting evidence collected</th>
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| Reduction in use of ineffective therapies for patients | **The estimated cost of lost productivity** in early-stage breast cancer was €602 lower for patients undergoing genetic testing prior to starting chemotherapy\(^1\)**  
**A 34% reduction in chemotherapy use** occurs if women with breast cancer receive a genetic test of their tumour prior to treatment\(^2\)**  
A systematic review identified 147 studies that demonstrated the economic benefit of Oncotype DX, illustrating an impact on effective use of health resources through the **avoidance of unnecessary chemotherapy in breast cancer care**\(^3\)**  
An estimated that **$604 million in annual health care cost savings** would be realised if patients with metastatic colorectal cancer receive a genetic test for the KRAS gene prior to treatment\(^4\)**  
INCa deduced that additional €1.7 million investment in EGFR testing would save €69 million to the French health insurance by **identifying patients with the mutation**, ensuring PM was only prescribed to patients who were more likely to respond\(^5\)** |
| Reduction in long-term cost of chronic diseases      | **Molecular testing before first- or second-line treatment initiation in NSCLC results in better survival with limited additional costs. In the scenario the ICER was €8,308 per life years saved (LYS) compared with standard care**\(^6\)**  
**Genetic testing to target dosing of blood thinner treatment could prevent 17,000 strokes and could avoid 43,000 hospital visits**\(^7\)** |
| Reduction in hospital stay                          | **Oncologists estimate that the mean hospital stay for PM is 3-4 days, whereas it is more than a week for chemotherapy regimens**\(^8\)**  
In France 293,628 people were hospitalised with chemotherapy in 2013. However, with the increasing use of PM therapies, there has been a decrease in overall number of stays (public + private) by 2.7% (260,390 stays in 2012 and 253,392 in 2013)\(^9\)** |

\(^1\) Katz et al (2015); \(^2\) US: Genomic Health, EU: Albanell (2016); \(^3\) Blok et al (2018); \(^4\) Akhmetov & Bubnov (2015); \(^5\) Nowak F (2012); \(^6\) Drezet et al (2016); \(^7\) McWilliam (2006); \(^8\) Dutch medical oncologist interview; \(^9\) Katz et al (2015)
Developments in PM directly impact clinical trial design and patient recruitment

- The proportion of trials using selection biomarkers continues to increase across phases
- Trials that do use selection biomarkers have a higher probability of success thus making an R&D program more cost-effective
The environment for Personalised Medicine

Identifying barriers and enablers to PM
There are a mix of approaches to prioritising PM in terms of health care policy across EU markets

- The clear benefit of having PM strategies in addition to national cancer plans (NCPs), is to allow for a forward-looking perspective on the value of genomics to healthcare systems; to support the testing infrastructure towards the development of whole genome sequencing (WGS) and its applicability to other conditions outside oncology.

- Countries have adopted different approaches to implementation, however plans have common elements:
  - Denmark has implemented NCPs from an early stage relative to other European countries; the first plan was published in 2000. In 2017 Denmark opened a national genome centre for personalised medicine which will serve as a hub for integrating genomic data.
  - England was the first to launch a dedicated program to whole genome sequencing in Europe. NHS England is supporting the integration of genomics into its services though setting up a new national network of Genomic Laboratory Hubs (GLHs) by November 2018.
  - France initially invested centrally in molecular diagnostics and infrastructure as part of its NCP, with the development the French National Cancer Institute (INCa) in 2004. In 2016, France announced the “France Médecine Génomique 2025” program.

**Notes:**
- Green – High (dedicated national plan on PM)
- Amber – Medium (inclusion of PM in health strategies or national cancer plans)
- Red – Low (no policies on PM)
A coherent PM strategy should articulate the approach to disease profiling versus whole genome sequencing

- Countries have clearly taken account of the advances in genomic technologies and their application in clinical practise by making substantial investments in this space:
  - Per capita investments in genomics and increasing diagnostic capacity is a clear priority within the NHS Five Year Forward View
  - The French Genomics Plan aims to open 12 sequencing centres
  - Denmark has invested heavily in genomics in previous years, which is why its latest figures are lower as there is already more developed infrastructure

- There is a question as to whether to focus on particular diagnostics test, profiling or WGS. Most countries in Europe have prioritised whole genome sequencing (WGS), rather than increasing uptake of NGS technology for more genomic profiling of tumours within current clinical pathways

- **Clinical genomic profiling strategies should be better optimised to screen more patients**, using sufficiently broad targeted gene panels, rather than fewer patients with WGS. This will ensure that greater numbers of patients are more quickly identified and benefit from currently available treatments

![Per capita investment in genomics compared to other cancer initiatives](image_url)
Centralising and increasing coordination of care is important, but should not limit PM as it is incorporated into standard of care

- Countries have varying degrees of centralisation of cancer care:
  - **Centralisation by tumour type**
    In Denmark, national cancer patient pathways results in centralisation of treatment to specialised centres. Whereas in the Netherlands the degree of centralisation varies, e.g. EGFR+ NSCLC is not centralised, resulting in variation to treatment approach.
  - **‘Hub-and-spoke’ delivery of cancer care**
    In England, patients benefit from a cancer management strategy formulated by a multidisciplinary team (MDT) found across cancer units in general hospitals, with specialist MDTs located in larger specialised hospitals.
  - **Accredited hospital networks**
    INCa coordinates cancer institutions across regions to support consistency and multidisciplinary team have also been introduced in France. A similar model is being implemented in Poland.

- **Concentration of expertise and infrastructure investment** in specific centres support the availability of specialised testing units to identify patients. This is particularly important for rare cancers that require specialist diagnosis.

- There is evidence demonstrating that centralising rare cancer care to specialist centres of excellence improves outcomes for patients. Similarly, studies have also suggested that centralisation may be associated with increased cost effectiveness of PM.

![Graph](image_url)

**Source:** CRA analysis of various sources

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The adoption of technologies by laboratories and the factors influencing this varies depending on the technology

- The lab’s decision to adopt a particular test may be dependent on the reimbursement regime for diagnostics locally. For example, if NGS panels are reimbursed and single gene tests are not, this will lead to greater use of NGS
  - While usage of NGS systems is increasing, this varies by country. Approximately 17% of MolDx labs in Europe have an NGS machine and, of those not currently running NGS, another 21% plan to acquire it in the next 5 years.
- Despite the importance of testing, there is currently no standard metric or central public data-set which shows usage of diagnostic tests in Europe with geographical breakdown, either in terms of biomarker testing performed by laboratories or in terms of the sales of commercial test kits and equipment.
- Additionally, the degree to which diagnostics are subject to a value assessment and the degree to which they are integrated with the assessment of associated therapies varies across Europe:
  - The evaluation of diagnostics (including the impact on costs) is integrated into the NICE appraisal of PM.

### Estimated uptake and access to diagnostic tests across case study markets

<table>
<thead>
<tr>
<th>Indication</th>
<th>Diagnostic test</th>
<th>DK</th>
<th>EN</th>
<th>FR</th>
<th>NL</th>
<th>PL</th>
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<tbody>
<tr>
<td>Breast cancer</td>
<td>HER2</td>
<td></td>
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<td></td>
<td>BRCA 1/2</td>
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<tr>
<td>Melanoma</td>
<td>BRAF V600 mutation</td>
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<td>PD-L1</td>
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<tr>
<td>NSCLC</td>
<td>EGFR *</td>
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<td></td>
<td>ALK</td>
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<td></td>
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<tr>
<td></td>
<td>PD-L1</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Ovarian cancer</td>
<td>BRCA 1/2</td>
<td></td>
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<td></td>
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<tr>
<td>Gene panel testing</td>
<td>NGS</td>
<td></td>
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</tr>
</tbody>
</table>

Notes: Green – High uptake / Full reimbursement; Amber– Medium uptake / Conditional reimbursement; Red – Limited uptake / limited reimbursement

* Includes both ctDNA testing by liquid biopsy and traditional tumour solid biopsy approaches

Source: CRA analysis
The funding model should take into account infrastructure investment and the need to encourage competition between diagnostic providers.

- There are wide variation in per capita expenditure on in vitro diagnostics (IVD) across selected countries in Europe.
- Disease-specific funding has enabled diagnostic services to be funded as part of broader efforts to improve oncology care, this has allowed for infrastructure investment and high levels of access.
- In France, there is good access to lab based testing services but appears to be limited access for specific diagnostic kits.
- In other markets, testing services are integrated into hospital budgets and are expected to be covered through a Diagnosis-related group (DRG)-type funding.
- HER2 breast cancer diagnostic testing in Poland is predominantly the responsibility of pathology laboratories in hospitals. This creates challenges for new tests.
- Until now, investment in CDx was linked to the value of an individual medicine. Therefore access to testing could be supported by the manufacturer. England has many examples of this.
  - As testing moves away from direct associations to particular products, and towards panel sequencing, individual manufacturer funding becomes no longer justified.

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### Per capita expenditure on In vitro diagnostics (IVD) (€)

<table>
<thead>
<tr>
<th>Country</th>
<th>Expenditure (€)</th>
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<tbody>
<tr>
<td>Switzerland</td>
<td>56,3</td>
</tr>
<tr>
<td>Germany</td>
<td>27,2</td>
</tr>
<tr>
<td>Denmark</td>
<td>26,2</td>
</tr>
<tr>
<td>Italy</td>
<td>26,3</td>
</tr>
<tr>
<td>Spain</td>
<td>21,4</td>
</tr>
<tr>
<td>France</td>
<td>21,3</td>
</tr>
<tr>
<td>Netherlands</td>
<td>16,3</td>
</tr>
<tr>
<td>UK</td>
<td>15,3</td>
</tr>
<tr>
<td>Poland</td>
<td>8,8</td>
</tr>
</tbody>
</table>

*Source: MedTech Europe*
Variation in Dx testing approaches and quality may create inconsistencies in testing services both within and across countries

- A number of countries in Europe have invested heavily in molecular testing laboratory infrastructure:
  - Both France and Denmark have setup a national program to support molecular testing with the establishment of regional molecular genetics centres – this has allowed for good access to newer, complex, Dx methods (e.g. NGS/ctDNA).

- In other countries, the access to Dx testing is limited by the testing environment or the coding of diagnostic tests that is required for reimbursement:
  - Poland has a significant gap between demand and provision for testing in some cancers (such as Lung cancer)
  - Until recently the approach to testing has been too fragmented leading to significant variation in access to diagnostics

- Various methods are being used across labs (e.g. ctDNA example data) resulting in variation in the quality of testing results

  Multiple factors may be influencing the quality of Dx testing resulting in inconsistent laboratory/test performance.

  There is little evidence base for recommendations on testing methods and how to improve testing quality.

  There is limited public information on lab performance or test usage. Applying External Quality Assessments (EQA) and collecting data to establish an evidence base for testing quality.
Access to PM is restricted when countries adopt more formal HTA

- Generally, the EU5, Scandinavian and Benelux markets grant greater access to innovative therapies, whereas Central and Eastern European markets such as Poland are more likely to restrict access to manage budget impact.

- In England, access to personalised cancer treatments has been problematic due to challenges in meeting required cost-effectiveness thresholds to achieve positive NICE recommendations. In these cases, patient access schemes and the Cancer Drugs Fund have been important programmes in facilitating access.

- Countries like the Netherlands which are more pragmatic about using available evidence, or facilitating the collection of RWE through registries have better access to novel treatments.

- Payer perceptions of products with CDx or specific biomarkers are generally more positive than of those without such biomarkers.

- Clinical guidelines play a different role in different EU markets; in England, guidelines are integrated into HTA, whereas in consensus driven markets such as Denmark, clinical guideline development is crucial for the introduction of novel therapies.
Delays to access and updating treatment guidelines to reflect innovative treatments are clearly a challenge for PM.

**ALK+ NSCLC: Xalkori (crizotinib)**

- In France, Xalkori benefited from an early access scheme – cohort ATU – allowing it be prescribed by oncology specialists for all patients.
- In Poland, access to PM in NSCLC has been delayed and underfunded in comparison to other European markets, with reimbursement taking 5 years.
- Timely updating of guidelines is also a clear barrier, with England and France yet to reflect Xalkori almost 5 years after the initial reimbursement decision.

**Ovarian Cancer: Lynparza (olaparib)**

- First-in-class PARP inhibitor Lynparza has seen variable access across Europe.
- NICE finally backed use of Lynparza in 2016 draft guidance, but in a later line of treatment and only after legal action from the manufacturer.
- As of March 2018, only Denmark has updated treatment guidelines to reflect Lynparza.
However, an important determinant of access is the introduction of early access schemes in several countries.

### REIMBURSEMENT DECISION

<table>
<thead>
<tr>
<th>Early access</th>
<th>Reimbursement decision</th>
<th>Inclusion in guidelines</th>
</tr>
</thead>
</table>

#### Melanoma: Zelboraf (vemurafenib)
- The Netherlands and Denmark (that exempted products from HTA) have faster access, providing access within 1 month following approval.
- All countries made a reimbursement decision within 1 year of approval. England and Poland took the longest, and there was a further 2 year delay to incorporate novel PM for Melanoma into treatment guidelines.
- The delay in updating treatment guidelines in Poland meant Zelboraf could only be available through compassionate use or clinical trial programs.

#### Melanoma: Keytruda (pembrolizumab)
- The use of Keytruda in melanoma was the first product to be launched through the UK’s Early Access to Medicines Scheme (EAMS), providing over 500 UK patients with early access. NICE have committed to start the HTA process in parallel with the MA review; earlier NICE assessment of EAMS-approved products is expected to shorten delays to reimbursement.
- Indeed draft NICE guidance for Keytruda within 5 weeks of EMA approval. Though NICE is yet to update melanoma treatment guidelines to reflect Keytruda.
Tackling delays to reimbursement of new treatments will ensure more systematic and equitable access

It is clear that access to PM depends on:

1. The **existence of early access mechanisms** that take into account unmet need and provide funding for early reimbursement.

2. The approach to HTA, with countries that have a more **pragmatic approach to use of clinical and economic evidence** (or requirements for additional data collection) to assess the relative benefit of a new personalised medicine exhibit faster access.

3. A fast process for **updating treatment guidelines and care pathways**. Although this varies depending on the role of clinical guidelines, this clearly has an important impact on enabling access in countries such as Denmark and Poland.

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### Average access timeline for personalised oncology medicines

<table>
<thead>
<tr>
<th>Country</th>
<th>Reimbursement</th>
<th>Inclusion in guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>4.2</td>
<td>10.8</td>
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<tr>
<td>England</td>
<td>9.6</td>
<td>34</td>
</tr>
<tr>
<td>France</td>
<td>7.6</td>
<td>23.2</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>8.2</td>
<td>19</td>
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<tr>
<td>Poland</td>
<td>30.3</td>
<td>10.5</td>
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**Notes:** Average access timeline from first-in-class PM in NSCLC, Melanoma and Ovarian Cancer (gefitinib; crizotinib; vemurafenib; pembrolizumab; olaparib)

**Source:** CRA analysis
There are important characteristics of a country’s landscape that facilitates more favourable access to PM

<table>
<thead>
<tr>
<th>Environment for Personalised Medicines</th>
<th>DK</th>
<th>EN</th>
<th>FR</th>
<th>NL</th>
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<tbody>
<tr>
<td>Policy prioritisation</td>
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<tr>
<td>Care environment</td>
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<tr>
<td>Diagnostic testing infrastructure</td>
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<td>Uptake of diagnostics</td>
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<td>Mechanism of value assessment</td>
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<td>Use of real-world evidence</td>
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<td>Speed of reimbursement</td>
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<td>Speed of updating guidelines</td>
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<tr>
<td>Funding and investment</td>
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Notes: Rating represents current state in the environment. England is trending green for future diagnostic testing infrastructure
Drawing on research and interviews we have identified key barriers and enablers to accessing PM

**Insufficient diagnostic testing capacity or poor quality labs limits use of novel tests**

**Delays or restricted reimbursement / access for novel personalised medicines**

**Lack of specific recognition of PM in value assessment guidelines**

**Delays to access and updating treatment guidelines to reflect innovative treatments**

**Limited level of physician exposure to current research and treatment trends**

**Lack of inclusion of mutation testing in clinical guidelines**

**Restrictions on funding for specific high-priority therapy areas (particularly oncology) limits applicability beyond oncology**

**Funding availability or lack of clarity leading to insufficient funding of testing services**

**Development of a specific plan or strategy on PM with dedicated investments in novel diagnostic technologies**

**Highly specialised and coordinated management of care (including testing infrastructure and expertise)**

**Availability of high quality testing platforms and technologies, supported by quality assessment protocols**

**Inclusion of PM in guidelines promotes usage and reflects the development of clinical consensus to support PM**

**Early access schemes that favour PM**

**Clear funding and value assessment mechanisms for diagnostic products, and the alignment into the assessment of medicines**

**Interim funding mechanisms (e.g. CDF in England)**

**Monitoring outcomes through population-based registries in order to facilitate managed entry agreements**
We have developed policy recommendations to improve equitable access to PM

- **National policy to ensure prioritisation of PM should work hand in hand with existing health strategic plans** (e.g. National Cancer Plans).
  - The level of resources and funding needs to be aligned to aspirations and the strategy should articulate the genomic profiling strategy.

- **Continued emphasis is needed on better management of care, consolidating expertise and resources to ensure the adequate ‘personalisation of care’**.
  - This can be achieved through a centralised approach (i.e. developing ‘centres of excellence’) or via cross-functional collaboration through healthcare networks.

- **National governments should continue investing and cooperating in next-generation testing infrastructure (such as molecular genetics labs) as well as developing dedicated funding pathways to ensure access to diagnostics.**
Conclusions and policy recommendations

The benefits of Personalised Medicines

Methodology

Introduction

Tackling delays to reimbursement of new treatments will ensure more systematic and equitable access. This can be improved by:

- Supporting better alignment of data requirements between regulators and health technology assessment (HTA) bodies – this would improve evidence development and facilitate the value assessment process
- Sharing best practices on HTA methodology for PM
- Developing a more flexible approach that incorporates new technologies (e.g. NGS)
- Being pragmatic in using the available evidence.
- Introducing Interim/early access programmes

Collecting data to track access to diagnostics (and making this public) as well as putting a greater emphasis on External Quality Assessments (EQA) of labs will help to ensure consistent testing quality throughout Europe and allow comparison between approaches.

- This means promoting international platforms for EQA of labs and research into quality (e.g. IQN Path) to improve diagnostics testing and make EQA participation mandatory for labs across the EU.
- This should also promote consequences for poor performance of labs, e.g. report to a supervisory authority.