Series 2, Module 5:

Regulations and reimbursement of personalised healthcare solutions

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Agenda

1. Precision medicine – the role of medical devices and pharmaceuticals
2. Regulatory, access and reimbursement pathways
3. The role of stakeholders and major hurdles to realize the benefits of precision medicine

Precision Medicine: What is it?

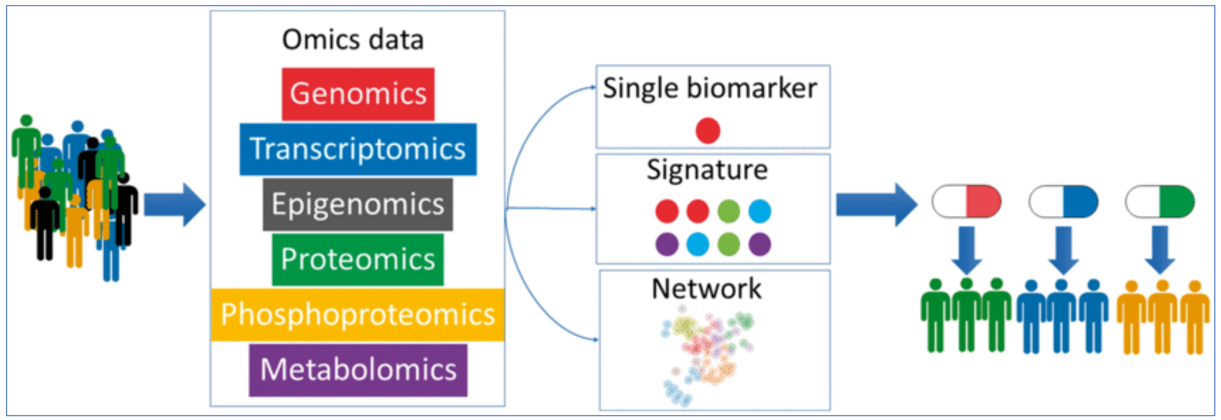
There is not a single definition of precision medicine.

“Precision medicine is a dynamic area adopting multiple approaches that allow the targeting of new
medicines, screening programs or preventive healthcare strategies, which include the use of biologic markers or complex tests driven by algorithms also potentially taking account of patient preferences.” Value Health 2020.

Tailored approach started to emerge in the last decades, to contrast this one-size-fits all approach and deliver preventative and therapeutic strategies which account for differences in genetic, environment and lifestyle factors.

Precision Medicine: What is it?

Precision Medicine promises to deliver tailored therapeutic and/or preventive interventions to patients.
This goal depends on understanding differences in health and diseases on a more granular level and should take into consideration environmental, genetic factors, etc.



Examples

1. Earlier detection
2. Diagnostic/prognostic applications
3. Better understanding of treatment response

Source (image): 1) Proteomics and phosphoproteomics in precision medicine: Applications and challenges

Precision Medicine: A few examples

Oncology

The ability to test for a specific mutation in a tumour and the use of specific treatments for it.

A particularly ripe field for precision medicine is certainly oncology due to availability of biomarkers and targeted therapies

Example

Herceptin (breast cancer): Human epidermal growth factor receptor-2 (HER-2) protein on the surface of breast cancer cells is over expressed in approximately 25–30% of breast cancer patients

The ability of identifying which patients overexpress HER-2 in order to prescribe Herceptin was a major milestone

Precision Medicine: A few examples

Neurology	Example
In neurological disorders, clinical scales have limitations, appointments are infrequent, and it might be difficult to understand the individual disease journey and take tailored treatment interventions.	Clinical outcome measures captured via sensors (wearables, applications) might help to capture subtle changes in diseases and tailor therapeutic interventions.

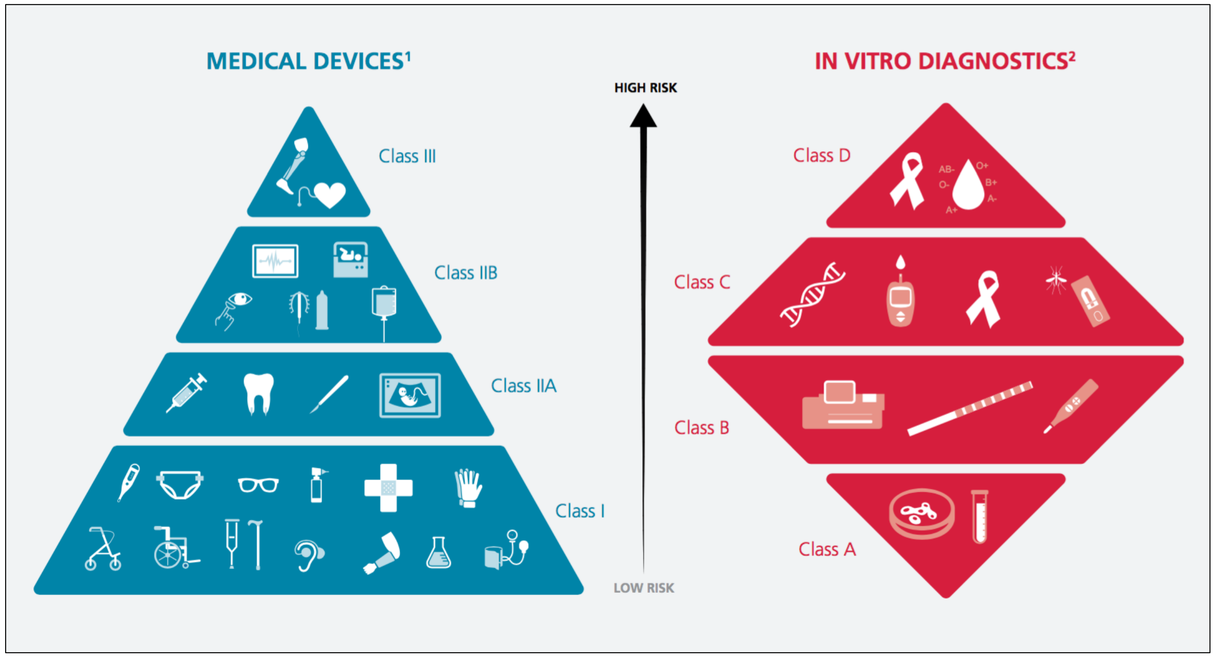
Precision medicine is a joint effort amongst pharmaceuticals and medtech

CD FUNCTION	THERAPEUTIC	CANCER TYPE	DIAGNOSTIC TARGET
Efficacy	Herceptin, Tykerb	Breast Cancer	Her2/neu
Efficacy	Tamoxifen, Arimidex, Aromasin, Femara	Breast Cancer	Estrogen/Progesterone Receptors
Efficacy	Tarceva, Iressa	Non-Small Cell Lung Cancer	EGFR
Efficacy	Erbitux	Colorectal Cancer	EGFR
Efficacy	Erbitux, Vectibix	Colorectal Cancer	K-ras

Sources: 1) https://www.ddw-online.com/overview-of-companion-diagnostics-in-the-pharmaceutical-industry-part-1-1766-201004/, 2) https://atm.amegroups.com/article/view/13043/13453

How is precision medicine regulated?

Europe



- For medical devices, responsibility falls within the “Notified Bodies” across Europe
- CE mark is issued by “Notified Bodies” that are accredited by a member country
- In 2017, the European Parliament adopted a **new Regulation on medical devices** and a Regulation on in vitro diagnostic medical devices.

Sources: 1) https://ec.europa.eu/health/sites/default/files/md_sector/docs/md_mdcg_2020_guidance_classification_ivd-md_en.pdf, 2) https://ec.europa.eu/docsroom/documents/10337/attachments/1/translations/en/renditions/pdf, 3) https://auradirect.be/category/mobile-medical-applications/

How is precision medicine regulated?

US

- In the USA, the evaluation and approval of medical devices is the responsibility of the Food and Drug Administration (FDA) through its Center for Devices and Radiological Health (CDRH).
- The manufacturer of the device receives marketing Clearance (510k) or Pre-Market Approval Letter (PMA), depending on device risk classification
- Different frameworks exist according to the product type:
  - Regulation for in-vitro diagnostics
  - Regulations for Software as a Medical Device (SaMD), relevant for digital health

Sources: 1) https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd , 2) https://ec.europa.eu/health/sites/default/files/md_sector/docs/md_mdcg_2020_guidance_classification_ivd-md_en.pdf

How is precision medicine regulated?

US

Some milestones:

- **2014**: The FDA issued "Guidance for Industry: In Vitro Companion Diagnostic Devices”
- **2016**: The FDA released the draft guidance, "Principles for Co-development of an In Vitro Companion Diagnostic Device with a Therapeutic Product”
- **2018-2020:** Release of the pilot programme within the Digital Health Innovation Action Plan, launch of the Digital Health Center of Excellence within CDRH

Sources: 1) https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd , 2) https://ec.europa.eu/health/sites/default/files/md_sector/docs/md_mdcg_2020_guidance_classification_ivd-md_en.pdf

How is precision medicine accessed?

- Generally, the process related to reimbursement of the test and of the drugs are separate even despite a potential joint co-development

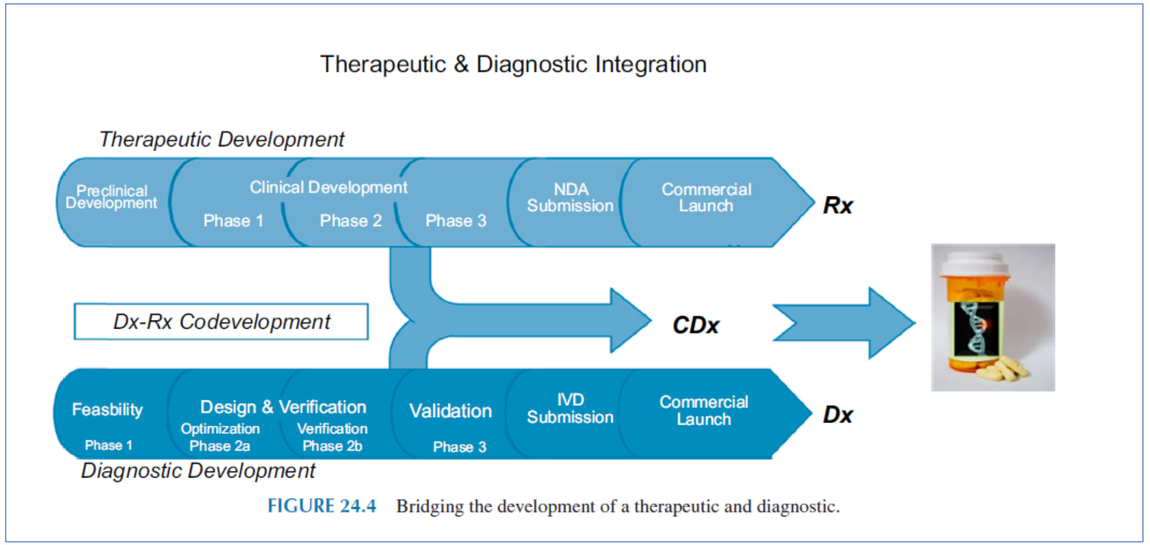


FIGURE 24.4 Bridging the development of a therapeutic and diagnostic.

Source (image): 1) Development and Commercialization of In Vitro Diagnostics: Applications for Companion Diagnostics (John F. Beeler, PhD, chapter 24)
https://www.sciencedirect.com/science/article/pii/B9780124047303000245

How is precision medicine accessed?

- Generally, the process related to reimbursement of the test and of the drugs are separate
- This can cause delays in timely access to the test and to the drug
- Delays between medicine approval by the European Medicines Agency (EMA) and inclusion in national or regional reimbursement lists can be significant
- Diverse laboratory infrastructure, capabilities can lead to slow integration of new biomarker tests into the standard of care for some diseases

Sources: 1) Unlocking the potential of precision medicine in Europe (LEK report, February 2021)

Precision Medicine: A multi stakeholder approach

- It is important to evaluate the incentives and the perspective of each stakeholder in order to adopt precision medicine and realize its full potential
- Key stakeholders include patients, physicians, payers, etc.

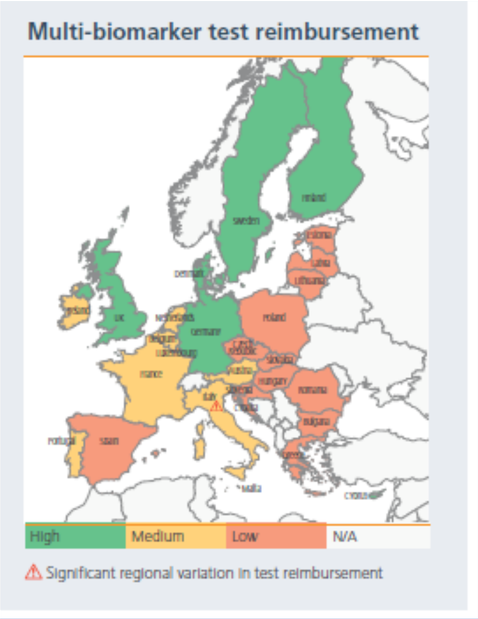
Precision Medicine: A multi stakeholder approach

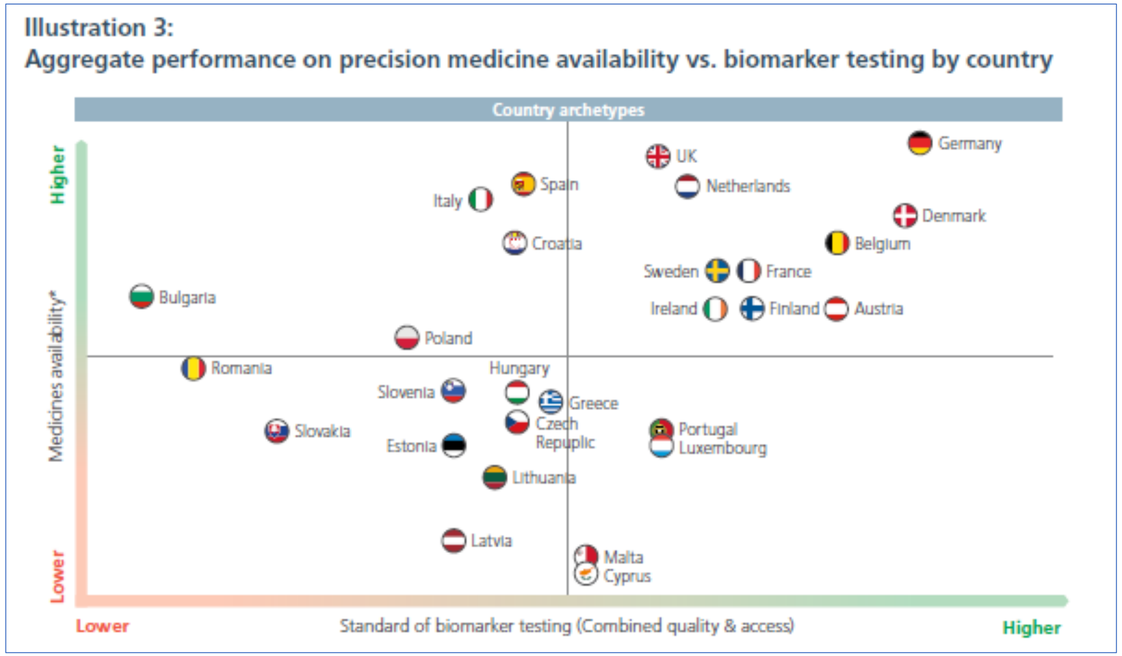
Sources: 1) Executive Insights Research

- A clear, agreed definition of personalized medicine is required
- The value of companion diagnostics must be demonstrated (payer and HTA point of view)
- Education for policymakers is required
- Reimbursement frameworks shall be in place to incentivize adoption

A recent report revealed major challenges (oncology biomarkers, EU)

- Limited access / reimbursement
- Limited infrastructure in place
- Limited education / awareness





Sources: 1) Unlocking the potential of precision medicine in Europe (LEK report, February 2021)

Challenges to realize the full potential

1. **For regulators**, the scope of precision medicine and its components is still not fully clear
2. **For payers**, evaluations of benefits are complex as there are many groups involved and there is broad heterogeneity of evidence supporting diagnostic tests in general
3. **For society**, despite its potential precision medicine might further exacerbate differences in access and reduce equity
4. **For health systems and for providers**, there is uncertainty in availability and accessibility of new tests, and the interpretation and benefits of tests shall be proven