Briefing

European Parliament

ENVIRONMENT, PUBLIC HEALTH AND FOOD SAFETY (ENVI)

Personalised Medicine - Current Status

KEY FINDINGS

Personalised Medicine has the potential to significantly contribute to a better and more sustainable health care. However, the implementation of the concept within the EU health systems is subject to ***challenges***:

- *Developing Awareness and Empowerment*
- *Integrating Big Data and ICT Solutions*
- *Translating Basic to Clinical Research and Beyond*
- *Bringing Innovation to the Market*
- *Shaping Sustainable Healthcare*

Associated ***EU policies are in an exploratory phase***, currently centred on research activities. Certain ***risk factors*** (complexity of the effort, Member States role and training of health care professionals) are not addressed yet in an appropriate manner. These risk factors ***might delay considerably*** the generalisation of Personalised Medicine. This could also contribute to a ***significant alteration of the implementation pathway***.

1. BACKGROUND

Personalised Medicine (PM - sometimes also termed as precision or stratified medicine) refers to the grouping of patients based on risk of disease, or response to therapy, using advanced diagnostic tests or techniques. This approach provides an opportunity for patients and healthcare providers to benefit from more targeted and effective treatments, potentially delivering more healthcare gain and improved efficiency for the healthcare system, while offering industry an expanded market for specialised treatments and the opportunity to benefit from the incremental value delivered by more effective products. The term 'P4' encompasses this personalised approach within a broader frame which also recognises the increasingly predictive, preventive and participatory nature of modern medicine. However, while such approaches have been under development for several years and are increasingly reaching the bedside, progress has been slower than anticipated; in particular, despite rapid advances in the research underpinning PM, barriers to its implementation in healthcare settings remain.

2. RESEARCH BASE

The advent of PM was made possible by research developments in the genetic and molecular basis of diseases brought on by the sequencing of the human genome (project completed in 2003), as well as the follow-up global R&D effort (largely supported also by the EU RTD Framework Programmes). These contributed to a much better molecular understanding of diseases and of the impact of environmental factors, down to the individual "personal" level,

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thus creating the possibility to differentiate much better diagnosis and treatment (i.e. more precisely). Recent tools developed for detection, diagnosis and treatment of diseases include '-omics' technologies (genomics, glycomics, lipidomics, metabolomics, pharmacogenomics, epigenomics, proteomics, transcriptomics and metagenomics), biomarkers, and biobanking[1].

3. EU POLICY INITIATIVES

PM was included as an area of interest in EU policy making already in 2008[2] and in view of providing a thorough coverage of the impact of "-omics" technologies onto healthcare.

The complexity of the tools supporting the implementation of PM into day-to-day practice indicated also the possible difficulties associated. Therefore, in 2011 the European Commission organised a conference on the perspectives of PM[3] with the objective to identify the challenges that will need to be addressed in order to make personalised medicine a reality. The conference established that the process towards truly PM only started and a long-term coordinated and holistic approach to innovation is required to bring PM into clinical practice. These challenges will need to be addressed at European, national, regional and local levels.

The conference also identified *fields of action* necessary to implement PM (increase the effectiveness of existing and future treatments, fine-tuning of medical care, unprecedented degree of collaboration amongst all of the players in the medical innovation cycle - researchers, companies, regulators, health technology assessors, reimbursement authorities, healthcare professionals) and *challenges* (standardization of tissue collection, biobank management, collection and analysis of clinical trials as well as associated regulation).

Further on, the European Commission issued a review of the impact of "-omics" technologies in a report[4] which focused on:

- the potential and issues with the use of -omics technologies in the research and development of personalised medicine and current EU research funding in the area;
- recent developments in EU legislation for placing medicinal products and medical devices on the market;
- factors affecting the uptake of personalised medicine in health care systems.

The Commission established that these technologies offer new opportunities for the treatment of patients and through this approach, *health care providers may be able to offer better targeted treatment, avoid medical errors and reduce adverse reactions to medicinal products.* The Commission considered that the pharmaceutical legislation is flexible enough to address current needs in PM and envisaged to act for the support of advancement in PM by using tools of Horizon 2020 and ongoing revisions of certain legislations (of the medical devices and of clinical trials directive). Moreover, a Health Technology Assessment (HTA) taking into account the new technologies would provide a methodology for addressing the uptake of PM.

PM was taken on also on the agenda of the Luxembourg Presidency in 2015 that organised a high-level conference[5] aimed to:

- assess and address obstacles to the integration of PM into Europe's healthcare systems
- identify best practices and their added value
- outline the potential benefits of PM on public health and its impact on policymaking in the EU.

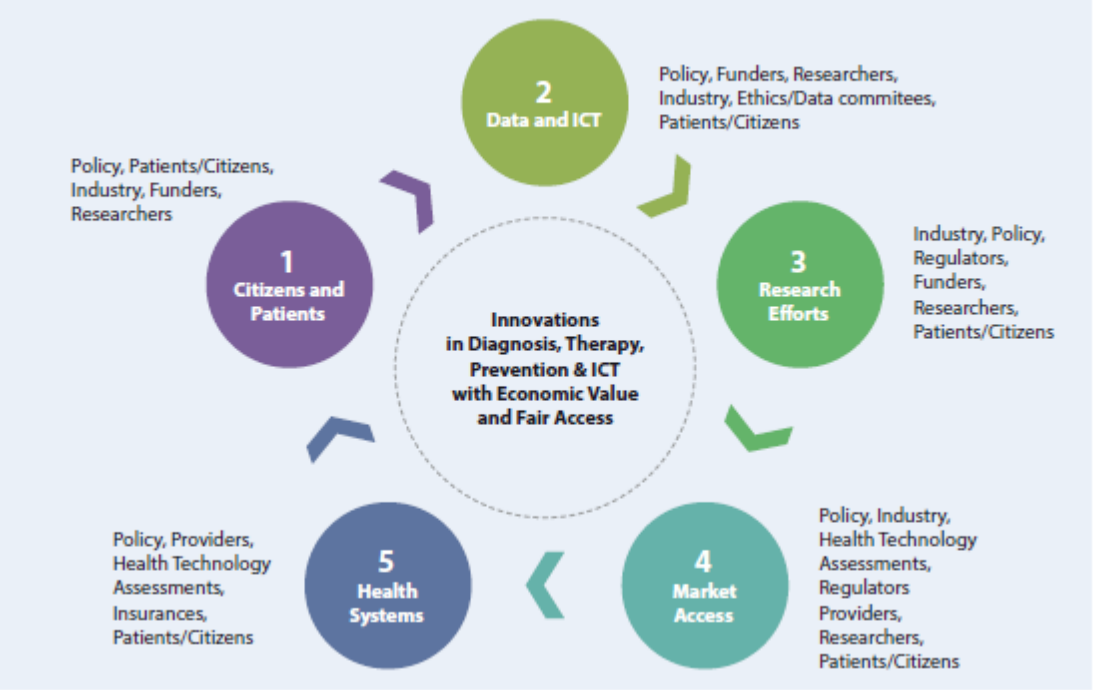
The conference provided input to the Employment, Social Policy, Health and Consumer Affairs Council of 7 December 2015 where ministers for health adopted the conclusions on the EU strategy on a number of health related issues, including PM, too[6]. In these the ministers invited the Member States to facilitate access to clinically effective and financially sustainable PM by developing patient-centred policies. However, Lydia Mutsch, the minister for health of Luxembourg stressed that the 'integration of PM into clinical practice and day-to-day care is

still difficult due to the many obstacles and challenges to timely access to targeted treatments'. In this context, she called on Member States to cooperate with a view to 'taking PM from a 'tailored' approach to a concept that is accessible to as many people as possible'.

Still in 2015 the Coordination and Support Action (CSA) PerMed[7] after having reviewed in a holistic manner all the fields associated with PM established[8] that the challenges for the further implementation of PM are:

- Challenge 1 – Developing Awareness and Empowerment
- Challenge 2 – Integrating Big Data and ICT Solutions
- Challenge 3 – Translating Basic to Clinical Research and Beyond
- Challenge 4 – Bringing Innovation to the Market
- Challenge 5 – Shaping Sustainable Healthcare

Figure 1:Circle of Challenges with important enablers and stakeholders.



Source: [7]

PerMed also presented a set of targeted achievements until 2020 and beyond - recommendations associated to each challenge (Annex 1):

- on biomedical, health-related ICT and health research
- on humanities and social sciences research
- to improve the framework for implementing PM (e.g. economic, organisational, regulatory, ethical, legal and social)

On 1-2 June 2016, the European Commission held a *second conference on personalised medicine*, around the five challenges already put forward by PerMed[9], in order to discuss a broader policy objective. This was to create a new ecosystem in the EU that would bring together research institutions, patients, healthcare practitioners and governments to use today's vast data resources to foster the well-being of its citizens by preventing disease, or when disease does strike, to manage it better.

While acknowledging that there is no universally accepted definition of PM (as there are other ways to describe patient-centric healthcare, such as stratified medicine and precision medicine), the Commission has elected to use the term PM. The definition, which was selected to be the basis for the *International Consortium for Personalised Medicine* or IC PerMed (IC PerMed) is the same as that used in the European Council Conclusions on PM for patients (2015/C 421/03) and the Horizon 2020 work programme for Societal Challenge 1: Health, demographic change and well-being. According to this, *PM "…refers to a medical model using characterisation of individuals' phenotypes and genotypes (eg molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention."*

The conference concluded that the goal of PM is to put the patient at the centre of healthcare, but how this will happen in practice is still open for discussion. Nevertheless, it advanced these discussions for example by showing how integrated healthcare models are working in specific places – Scotland and Estonia – and how business models for PM can involve patients more directly in their healthcare.

Recommendations from the conference report, together with conclusions from the conference, formed the basis of a new initiative to be called IC PerMed which would work to:

- Establish Europe as a global leader in PM research;
- Support the PM science base through a coordinated approach to research;
- Provide evidence to demonstrate the benefit of PM to citizens and healthcare systems; and
- Pave the way for PM approaches for citizens.

A number of actionable points and comments that can inform the continued work on IC PerMed were also identified.

ICPermed's central aim is to align and encourage joint efforts in PM research and implementation and it developed its activities in five working groups, covering the previously identified PM challenges with topics covering all aspects along the value chain and beyond, culminating in an Action Plan[10] intended to be the blueprint for establishing research activities within the entire range of PM either at national, European or international level. This Action Plan will feed into national and European strategic discussion of research funders shaping their future programmes including both single actions and joint efforts. One of the latter will be the European Research Area Network for PM (ERA-PerMed), which is in preparation and should begin work by end of 2017 with Joint Transnational Calls (JTCs) on PM as a core element. The main elements of the Action Plan, grouped in two parts (Part A which concerns data - A1-8, technologies, methods and process - A9-18, people - A19-21, cross cutting - A22, and Part B concerning structures - B1-2, methods and processes - B3-6, people - B7-8) are summarized in Annex 2.

4. CONCLUDING REMARKS

Implementation of PM proves to be an *extremely ambitious enterprise* at the EU level. According to the challenges identified the *key enablers*, actually stake-holders in its implementation cover all organisations/institutions involved in the value chain of health care at European and national level, including industry (EC, societies and patient organisations; ministries of health, finance, research and justice, economics; institutions for public health and health insurance, medical and scientific societies, foundations, healthcare providers and hospital associations; patient involvement via EFPIA/IMI; European research infrastructures, large consortia/cluster projects, standardisation authorities and organisations; national computing centres, ethics and data committees, universities, academia, public research bodies including systems biology/medicine, research technology organisations; ICT and telecommunication, healthcare industry, eHealth and mHealth, European research centres, national research centres, ethics committees, registries, agencies responsible for biobanks and data-banks; pharmaceutical, biotech, medical technologies, diagnostic and IT industry, EMA, IMI, national regulation authorities including notified bodies, HTA, regulatory authorities).

The ICPerMed Action Plan provides also an insight on the implementation timeframe for PM, which ultimately it is considered to be on the long run.

Until now, however, *risk factors* that might influence the implementation of PM where not identified and handled. The *main risk factor lies in the complexity of the effort*, as it needs action on all levels, with the involvement of all stake-holders.

Another risk factor originates in the legal basis (Article 168, paragraph 7 of the Treaty on the Functioning of the European Union) of EU level actions in health care (particularly in public health). These shall respect the responsibilities of the Member States for the definition of their health policies and for the organisation and delivery of health services and medical care. Although the responsibilities of national and reimbursement authorities are taken into consideration, the new health care delivery structure which PM is based on, will require *considerable change effort* from the national health systems (primarily financial investment).

Finally, a key element in the implementation of PM are the ultimate health care delivery professionals. PM would require a significantly changed approach in the delivery of training of these professionals, both of the new entrants in the system, as well as of those already being part of it, which is a major risk factor, too. In this respect the expected time frame might not be sufficient. It is also problematic as the current policies concerning PM still do not make a link to EU level education and training policies (ERASMUS, the Bologna process[11]). Further on, changes in training of physicians proves to be very difficult (in certain Member States the introduction of the three cycle system in this training has no chance to be accomplished for the moment; medical training has also experimented with a number of other methodological approaches, which finally did not proved to be more efficient as the traditional ones, e.g. Problem Based Learning, thus failing to generalize new methodologies).

Annex 1: PM key challenges and targeted achievements until 2020 and beyond - recommendations

Challenge	Biomedical, health-related ICT and health research	Humanities and social sciences research	Improve the framework for implementing PM
Developing Awareness and Empowerment	Provide further evidence for the benefit delivered by PM to health systems	Understand how the changes relating to PM will impact public health and ensure that they translate directly to benefits for individual citizens and society	Incorporate patient participation in the healthcare system and increase the patient's role in all phases of research and development
	Develop and promote models for individual responsibility, ownership and sharing of personal health data	Improve communication and education strategies to increase patient health literacy	Develop common principles and legal frameworks that enable sharing of patient-level data for research in a way that is ethical and acceptable to patients and the public
	Develop mobile health applications to maximise engagement of patients with their treatment pathways and track the safety and effectiveness of these interventions		
Integrating Big Data and ICT Solutions	Promote strategies to make sense of 'big data'		Create a European 'big data' framework and adapt legislation
	Develop and encourage the fast uptake of technologies for data capture, storage, management and processing		
	Promote the development of high quality sustainable databases including clinical, health and wellbeing information		
	Support translational research infrastructures and enforce data harmonisation fostered by specific ICT infrastructures designed to the health data		
	Support analytical methods and modelling approaches to develop new disease models, e.g. 'Computerised Twins' or a 'Virtual Patient'		
	Develop new decision support tools and methodologies of ICT to analyse and interpret data in order to support physicians in their decision-making process		
Translating Basic to Clinical Research and Beyond Introduction	Develop methods to better integrate and evaluate the information provided by genomic, epigenetic, transcriptomic, proteomic, metabolomic and microbiome analyses		Develop suitable funding models to enable cross-sector working in PM research
	Support research in preclinical models to validate hypotheses resulting from molecular analyses of patient samples and treatment outcomes		

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	Instigate a European-wide biomarker evaluation and validation process		
	Promote longitudinal studies in the areas of PM		
	Support development of new clinical trial designs and promote integration with concomitant preclinical testing		
	Re-classify diseases at the molecular level		
Bringing Innovation to the Market	Formalise a risk-based approach for the evaluation of PM		Support research on an adequate regulatory and legal framework for PM
	Optimise individual drug therapies and poly-pharmacy especially in the case of multi-morbidity		Encourage a systematic early dialogue between innovators, patients and decision-makers throughout all regulatory steps to provide guidance and clarity
			Facilitate partnerships and innovation networks to encourage cross-disciplinary and cross-border collaboration in research and development using an 'Open Innovation' approach
			Provide support and guidance for companies to enter the market for PM with sustainable business cases
Shaping Sustainable Healthcare	Support health economics research of PM to support decision-makers	Develop prospective surveillance systems for personal health data that facilitate accurate and on-going assessment of highly dynamic health information across the life course	Encourage a citizen-driven framework for the adoption of electronic health records
		Develop training programmes on PM for health professionals	Promote engagement and close collaboration between patients, stakeholders and healthcare actors across sciences, sectors and borders
			Develop a framework for pricing and reimbursement for PM that ensures equitable access for all patients – regardless of economic or geographic status – and is sustainable for health systems
			Develop an optimised overall healthcare financing strategy

Annex 2: Summary table of actionable items indicating a reasonable time frame and scope

Part A

Action Item Number	Title	Time frame*	Scope**
A.1	Research projects to ensure the quality, completeness, validity and analysis of datasets	S	E
A.2	Support research on data harmonisation in the context of personalised medicine needs	M, L	E, I
A.3	Studies on data integration and interpretation of multifactorial diseases	S	R/N, E
A.4	Support research on enabling the extraction of structured data from unstructured sources	S, M	R/N, E, I
A.5	Pilot projects to assess the impact of sharing data for researchers and other parties	S, M	R/N, E, I
A.6	Research projects to optimise data security, privacy and ownership within personalised medicine approaches	S, M	R/N, E, I
A.7	Research projects to develop innovative decision support tools for healthcare providers	S, M	R/N, E, I
A.8	Support research to develop telehealth and telemedicine applications to support the implementation of personalised medicine	M, L	R/N, E
A.9	Development and implementation of high-throughput preclinical models	M	R/N, E
A.10	Implement translational programmes with shared access to, for example, genetically defined patient populations	S, M	E, I
A.11	Integrate actions aimed at supporting and developing research for clinical validation of pharmacogenomics. Global impact evaluations of these actions on health systems	M	R/N, E, I
A.12	Classification of diseases at the molecular level	L	R/N, E
A.13	Support research for clinical trials – a three-level process	S, M, L	R/N, E
A.14	Longitudinal cohort studies of disease outcomes	S, M, L	R/N, E, I
A.15	Research in adequate regulatory structures and pathways in personalised medicine	S, M	E
A.16	Support research in and development of health economics models and pharmaeconomic models for personalised medicine	M, L	E, I
A.17	Support research in post-marketing surveillance methodologies aimed at accessing patient outcomes	S, M	E, I

A.18	Support health economics research and assessments of available as well as newly developed personalised medicine approaches.	S, M	R/N, E
A.19	Research and develop the tools and modus operandi of a knowledge network for enhancing health and digital literacy	S, M	I
A.20	Develop and share best practices of patient engagement approaches for the needs of a variety of European citizens	S, M	R/N, E, I
A.21	Research and develop the instruments for the evaluation of the effectiveness and impact of public engagement initiatives in PM	S, M	E, I
A.22	Support interdisciplinary research in challenges and drivers that influence bringing PM innovation to the market, from ethical, legal and societal perspectives	M, L	E, I

Part B

Action Item Number	Title	Time frame*	Scope**
B.1	Promote the development of high-quality sustainable databases for personalised medicine-relevant data	S, L	R/N, E, I
B.2	Development and maintenance of biobanks and population/disease cohorts	S, M, L	R/N, E, I
B.3	Establish a new collaborative funding organisation model with healthcare providers to facilitate investment in disease prevention research and therapy research	M	R/N, E
B.4	Develop common strategies in research to support comparative and effective research, and sustainable technology transfer capacities	M	R/N, E, I
B.5	Support strategies to identify financial and risk-sharing instrumentsto develop personalised medicine approaches	M	R/N, E, I
B.6	Support research to analyse, compare and optimise national and regional health systems in the light of personalised medicine implementation	S, M	R/N, E, I
B.7	Introduce curricula reforms to create new models of healthcare for patients and citizens and broaden the focus on basic and clinical sciences to include health systems sciences in the education of all healthcare professionals	S, M, L	R/N, E, I
B.8	Build sustainable resources for educating and training citizens, patients and patient advocates on involvement of patients and patient organisations across the entire research and development lifecycle of personalised medicine	S, M, L	R/N, E

* S: short term = 2-4 years
M: medium term = 5-7 years
L: long term = 8-12 years
The timeframe indicated here refers to the time for taking steps to address these actions (e.g. the initiation of a funding programme or a coordination action), not the time to reach results.

** R/N: regional/national
E: european
I: international
Scope indicates whether the respective action is regarded as suitable for implementation at a regional/national, European and/or international level-

[1] Scoltz, N. (2015) Personalised medicine-The right treatment for the right person at the right time, EPRS-European Parliamentary Research Service, October 2015
[2] COM(2008) 666 final Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, Brussels, 10.12.2008
[3] European Perspectives in Personalised Medicine, European Commission, conference report, 12-13 May 2011
[4] SWD(2013) 436 Commission Staff Working Document, Use of '-omics' technologies in the development of personalised medicine, Brussels, 25.10.2013
[5] The Government of the Grand Duchy of Luxembourg, Ministry of Health, High-level Conference "Making Access to Personalised Medicine a Reality for Patients" 8 July 2015, Luxembourg, Cercle Cité
[6] Council of the European Union Brussels, 26 November 2015 (OR. en) 14393/15 SAN 390 NOTE From: General Secretariat of the Council To: Permanent Representatives Committee/Council Subject: Employment, Social Policy, Health and Consumer Affairs Council meeting on 7 December 2015 Draft Council conclusions on Personalised medicine for patients - Adoption (Public debate in accordance with Article 8(2) of the Council's Rules of Procedure [proposed by the Presidency])
[7] http://www.permed2020.eu/
[8] PerMed (2015) Shaping Europe's Vision for Personalised Medicine Strategic Research and Innovation Agenda (SRIA)
[9] European Commission, Directorate-General for Research and Innovation, Personalised Medicine Conference 2016 Report
[10] The ICPerMed Action Plan (2017)
[11] http://ec.europa.eu/education/policy/higher-education/bologna-process_en

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