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An overview of Personalized Medicine landscape and policies in the European Union

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Background: The spread of Personalized Medicine (PM) over the last decade defined a revolution in healthcare systems. PM is among the priorities of the European Commission's research agenda, which funded the IC2PerMed international project aiming to integrate China into the International Consortium of PM (ICPerMed). In the context of this project, we mapped the existing policies related to PM in the European Union (EU) and at the EU Member States (EU-MS) level. **Methods:** PubMed, Google Scholar, Google, Microsoft and national and international institutions' official repositories were searched in order to identify documents on PM-related policies, programmes and action plans at the EU and EU-MS level, published up to December 2020. **Results:** We identified 28 policies in the EU aimed at improving public health promoting and fostering PM implementation, through some actions including the standardization of good medical practice, use of big data and digital innovation, data sharing and cross-border interoperability, healthcare sustainability, disease prevention and patients'/citizens' engagement. We identified 23 policies at EU-MS level which, notwithstanding national differences, have a common focus, such as patient-tailored treatment and targeted prevention, education of healthcare workers, research and innovation, big data harmonization and healthcare system sustainability. **Conclusions:** The definition of an integrated regulatory framework is essential to turn PM into an opportunity for citizens and patients with the involvement of all the stakeholders. This work can provide a valuable tool for decision-makers to define common approaches, priorities for research, development and increase international collaboration, which could overcome the fragmented European scenario and align the future direction on PM.

Introduction

The enormous increase in innovative technologies and scientific breakthroughs in recent years, alongside with the substantial rise in healthcare expenditure, are putting strain on the sustainability of European healthcare systems.[1] The so-called 4P model 'Predictive, preventive, personalised and participatory medicine' promises to sharply reverse the ever-escalating costs of healthcare, improve patient outcomes and empower both the patient and the physician.[2] In this context, Personalized Medicine (PM) has become one of the models attempting to tackle the complexities of healthcare systems by implementing targeted prevention, diagnosis and treatment strategies for the right person at the right time.[3]

Given the implications of PM either on population's health outcomes and on health systems, different countries, and in particular the European Commission (EC), have been dedicating policies and a large amount of funds,[4] for the PM appropriate implementation into clinical practice and research. However, there is a wide variability among the existing regulations and strategies towards PM across European countries and worldwide.[5]

Several initiatives were established in recent years, such as the International Consortium for Personalised Medicine (ICPerMed), to facilitate and align the vision of different stakeholders in the field, to define common research and development approaches and to scale up international collaborations.[6] ICPerMed has played an important role in supporting the research and implementation of PM in Europe and beyond, funding several Coordination and Support Actions (CSAs), including IC2PerMed, 'Integrating China in the International Consortium for Personalised Medicine' (available from https://www.ic2permed.eu/).[7] IC2PerMed aims to provide key solutions for enabling the convergence towards a common approach of PM research, innovation, development and implementation between the European Union (EU) and China. The present work, embedded within the broader context of the project, is in line with the ICPerMed's vision to address some crucial issues regarding policy-making process and creation of Sino-European programmes in PM.[7] Hereby, we provide a comprehensive overview of the existing policies related to PM in the EU and at the EU Member States (EU-MS) level.

Methods

The methods of this work are reported in detail in the IC2PerMed first Deliverable (D1.1), entitled 'Scoping paper: Review on health research and innovation priorities in Europe and China', available at the IC2PerMed website.[7] We collected information about policy measures, programmes and action plans related to PM through a three-step methodological approach:

(1) In the first phase, in December 2020, a scientific literature search was performed on the PubMed database to retrieve any record in

English, reporting information on national laws or legislations at the EU level and EU-MS, with no other restrictions applied.

(2) In the second phase, two researchers conducted an extensive search in grey literature, using Google Scholar, Google and Microsoft Academic search engines, using a broad set of search terms, including 'policy, strategy, programme, personalised medicine, and Europe'. The search was conducted in English language and then adapted to other languages known by the authors, such as German, Spanish, French, Italian and Portuguese.

(3) In the third step, two researchers explored national and international official repositories, such as the EU Commission and Council, ICPerMed, EU-MS' Health Ministries and additional institutions related to public health, for eligible publicly available documents or reports.

For the purpose of this work, we referred to the definitions of 'policy', 'policy cycle', 'policy agency' and 'policy stakeholder' available in the Supplementary material.

Data extraction and synthesis

Data extraction has been conducted from January to March 2020 by two independent researchers, who created a list with the identified documents in Excel. The retrieved documents were carefully read and, from the ones who deemed pertinent, the following data were extracted: name of the policy, publication year, institution, country, language, topic and link.

A descriptive synthesis was then provided, grouping the results in two categories, according to whether the documents were issued from EU Institutional bodies or at the EU-MS level.

Results

PM policies issued from the EU institutions

The review process identified 28 policies issued by the institutions of the EU from 1998 to 2020, addressing PM approaches and themes (table 1). In the last two decades, Europe rapidly became a global leader in PM, thanks to centralized policies, programmes and major funding, such as the '7th EU Research Framework Program (2007-2013)', the 'Horizon 2020 Program (2014-2020)' and the recently launched 'Horizon Europe Program (2021-2027)'.[8]

At the EU level, policy measures range from legally binding instruments, such as directives, regulations and treaties, to legally non-binding ones.[9] Among legally binding instruments, directives set compulsory goals for the EU-MS to be implemented in their national law, whereas regulations are legislative acts that are applied in its entirety across the EU. At the highest level stand the constitutional treaties of the EU, such as the Treaty on the Functioning of the European Union, formerly known as the Treaty of Rome. Legally non-binding policy measures, including opinions, recommendations, conclusions and resolutions, convey important strategic positions and promote broad discussions on different topics and issues. Such classification might be helpful to understand the extent of applicability of the policy presented hereinafter.

The identified policies revolved around actions to ensure public health protection, promote and foster PM, covering topics, such as the standardization of good medical practice, big data and Information and Communication Technology (ICT), data sharing and cross-border interoperability, eHealth, innovation, healthcare sustainability, disease prevention and patients'/citizens' engagement.

Towards PM definition, the EC's efforts have been geared since 2008 in the report on safe, innovative and accessible medicines, acknowledging the emergence of new technologies, pharmacogenomics and patient-specific modelling and disease simulators.[10]

PM was defined in 2015, based on three legally binding policies on: (i) *in vitro* diagnostic medical devices;[11] (ii) processing and free movement of personal data;[12] and (iii) clinical trials on medicinal products for human,[13,14–17] as 'a medical model using characterization of individuals' phenotypes and genotypes (e.g. 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.[17,18]

Whilst the definition and formalization of the concept of PM only arrived in 2015, it is equally certain that its history and development started much earlier. In fact, the several policies available mainly in the field of genomics and genetics, of the late 1990s–early 2000s, were the precursors and key pillars in shaping the subsequent directives and initiatives in this regard.

According to the Article 168 of the Treaty on the Functioning of the European Union, issued in 2008, the high level of human health protection shall be ensured in the definition and implementation of all EU policies and activities.[14] In the same year, in PM landscape, the focus of EC recommendations shifted towards digital health and cross-border interoperability of data, aiming to define guidelines for interoperable Electronic Health Record (EHR), and create an integrated network for EU healthcare professionals and patients, in conformity with the fundamental rights to privacy and data protection.[15]

In 2009, the Council Recommendation on rare diseases encouraged the development of strategies that address healthcare systems' sustainability, empowerment of patient organizations and literacy of healthcare professionals.[19,20]

In 2010, a series of workshops boosted reflections on PM and led in 2011 to the conference report 'Perspectives in Personalised Medicine', which identified key challenges requiring action at the European level and emphasized the necessity of a long-term coordinated and holistic approach.[17]

Afterwards, several policies were issued in 2011 to address the interoperability of data, patients' rights, innovation and sustainability of healthcare systems, aiming to create a new, efficient, effective and financially sustainable health system.[18–20]

For the first time, EC addressed in 2013 the exploitation of '-omics' technologies, concluding that PM development using '-omics' technologies offer new treatment opportunities for the patients in the EU.[21] In the same year, healthcare accessibility and sustainability, throughout the integration of health information systems, were additionally addressed in Council conclusions, stating the importance for EU-MS to cooperate for the establishment of a sustainable and integrated EU health information system, exploring the potential of a comprehensive European health information research infrastructure consortium as a tool.[22]

Resilience, effectiveness and accessibility of health systems were addressed in the EC communication in 2014, acknowledging the increasing health needs of the population and the obligation for EU-MS to have a healthcare system that does not exclude parts of the population from receiving healthcare services.[23] Furthermore, through dedicated documents on clinical trials, the EC and Council steered the equitable access and transformation of healthcare systems by granting coordination and cohesion in the way that clinical trials are conducted in the EU and by establishing a united portal for all the EU-MS.[24]

Following the report Shaping Europe's Vision for PM,[25] in 2015, the 'PerMed' project (available from: www.permed2020.eu) an EU-funded CSA, was funded to step up coordination efforts between key European stakeholders, and to provide recommendations on fostering the implementation of PM in transnational research and health systems. ICPerMed was initiated during several workshops organized by the EC throughout 2016, and inherited PerMed's legacy.

Data exploitation led in 2016 to the Regulation of the European Parliament and of the Council on the protection of personal data processing and free movement, whereas from 2017 onwards, policies focused on sustaining the digital transformation of healthcare systems, with particular attention to EHR, data infrastructure and citizen engagement.[26] Accordingly, in 2017, the Communication on a

Table 1 Personalized Medicine policies' overview from 1998 to 2020 issued from the institutions of European Union

Year	Title	Institutional body	Topics
1998	Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices	European Parliament, Council of the EU	Harmonization of national legislation, setting standards for medical devices, safety for patients
1999	Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products	European Parliament, Council of the EU	Treatment of rare diseases by orphan medicinal products
2001	Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use	European Parliament, Council of the EU	Good clinical practise, clinical trials for medicinal products
2001	Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use	European Parliament, Council of the EU	Drug safety, market authorization of medicinal products, key definition of terms
2004	Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004	European Parliament, Council of the EU	Establishing EMA as an independent entity, science over politics, transparency
2006	Council Conclusions on common values and principles in European Union Health Systems (2006/C 146/01)	Council of the EU	Setting common standards for health systems, patient-centred health
2007	Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products	European Parliament, Council of the EU	Advanced therapy medicinal products, combining medical devices and medicinal products, gene therapy, cell therapy, cell tissue production
2008	Article 168 of the Treaty on the Functioning of the European Union (2008)	European Commission	Stating the importance of public health, balancing responsibilities MS-EU
2008	Commission Recommendation of 2 July 2008 on cross-border interoperability of electronic health record systems (notified under document number C (2008) 3282)	European Commission	Interoperability of EHS, standardization, global outreach
2009	Council recommendation of 8 June 2009 on an action in the field of rare diseases 2009/C 151/02	Council of the EU	Putting focus to rare diseases, recognizing their importance, coordination of research
2011	Directive 2011/24/EU on the application of patients' rights in cross-border healthcare	Council of the EU	Promotion of cross-border healthcare
2011	Council conclusions on innovation in the medical device sector 2011/C 202/03	European Parliament, Council of the EU	Patient-centred innovation, importance of infrastructure and ICT
2011	Council conclusions: towards modern, responsive and sustainable health systems 2011/C 202/04	Council of the EU	Creation of modern, responsive, efficient, effective and financially sustainable health systems
2013	Council conclusions on the 'Reflection process on modern, responsive and sustainable health systems' of 10 December 2013	Council of the EU	Sustainability of health systems, accessibility of healthcare, integrations EU health information system
2014	Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use (not yet in application)	European Commission	Creation of single EU portal and database, setting standards for authorization within EU
2014	Council conclusions on innovation for the benefit of patients 2014/C 438/06	European Parliament, Council of the EU	Innovative products, services and treatments
2014	Communication from the Commission on effective, accessible and resilient health systems COM/2014/0215 final	Council of the EU	Strengthening the effectiveness of healthcare, increasing accessibility of health systems, improving resilience
2015	Council conclusions on personalised medicine for patients 2015/C 421/03	Council of the EU	Information and awareness, patient-centred approaches, stakeholders' networks, health professionals' literacy
2016	Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)	European Parliament, Council of the EU	Specifies detailed when health data is permitted for processing, strengthens privacy rights of patients
2017	Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on the implementation of the Digital Single Market Strategy A Connected Digital Single Market for All COM/2017/0228 final	European Parliament, Council of the EU	Supporting data infrastructure, to advance research, disease prevention and personalised health and care, EHR accessibility
2017	Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions European Interoperability Framework—Implementation Strategy COM/2017/0134 final	European Parliament, Council of the EU	Domain-specific interoperability framework, EHRs, digital health

(continued)

Table 1 Continued

Year	Title	Institutional body	Topics
2017	Council conclusions on Health in the Digital Society—making progress in data-driven innovation in the field of health (2017/C 440/05)	Council of the EU	New opportunities are arising from big data and improved data analytics capabilities, as well as from PM, mobile application, citizen empowerment, sustainability of health systems, health data governance frameworks
2018	Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society COM/2018/233 final (2018)	European Parliament, Council of the EU	Interoperability of EHS, standardization, accessibility of EHRs, citizen empowerment
2019 (Updated)	Council Conclusions on the EPC-Commission Joint Report on health care and long-term care in the EU	Council of the EU	Recommendations based on 2016 EPC EC joint report, promotion of integrated care; promotion integrated care
2019	Commission Recommendation (EU) 2019/243 of 6 February 2019 on a European Electronic Health Record exchange format (Text with EEA relevance.)	Council of the EU	Accessibility of EHRs, digital solutions
2019	Regulation (EU) 2019/881 of the European Parliament and of the Council of 17 April 2019 on ENISA and on information and communications technology cybersecurity certification	European Parliament, Council of the EU	Stating cybersecurity concerning ICT in health, cybersecurity certification framework
2020	Council conclusions on shaping Europe's digital future 2020/C 202 I/01	European Commission	Workflow optimizations in healthcare, epidemiological surveillance systems, sustainability of health systems

European Interoperability Framework, which could be used for the alignment of existing, or the creation of new, domain-specific interoperability frameworks, was issued.[31] Additionally, the Communication on a 'Connected Digital Single Market for All' and the Council conclusions on Health in the Digital Society, aimed to ensure a fair, open, and secure digital environment.[27,28] In 2018, the Communication on enabling the digital transformation of healthcare in the Digital Single Market highlighted the configuration of new care models, multidisciplinary and literacy of healthcare professionals and use of digital solutions for citizen empowerment and person-centred care, to advance research, disease prevention and personalized healthcare.[29]

Issued in 2016 and updated in 2019, the Council Conclusion on the EPC-EC joint report on healthcare and long-term care in the EU promoted, as a key element for good coverage, access and quality of care, the sustainability of financing and expenditure; strengthening of structural efficiency, competition and transparency; and improvement of the governance of the systems.[30]

In 2019, Commission Recommendation on a European EHR exchange format stressed the importance of digital solutions combined with a system that allows citizens secure access to their own health data.[31] Furthermore, the regulation on ICT cybersecurity was issued, aiming to establish a European cybersecurity certification framework for the improvement of the internal market functioning and to set up a mechanism to establish certification schemes that confirm ICT products, services and processes.[32]

In 2020, Council conclusions 'Shaping Europe's digital future' underlined that the development of a European Health Data Space holds the potential to facilitate the development of effective prevention, diagnosis, treatments and care, and to ensure more cost-effectiveness and workflow optimizations in healthcare.[33]

Policies at the EU Member States level

Our mapping showed that starting from 2001, at the national level few EU-MS have developed national policies, plans, strategies, and programmes in the field of PM. We identified 23 policies at the EU-MS level, which although differing in the implementation process according to the national health systems, have a common focus, aiming at:

- providing patient-tailored treatment and targeted prevention;
- increasing public understanding of PM and the education of healthcare workers;
- growing patients' involvement in all phases of research and development;
- supporting healthcare delivery and enforce big data harmonization fostered by ICT infrastructures; and
- attracting investments in PM by the healthcare industry.

Hereby, we describe the landscape in EU-MS, which is extensively summarized in table 2.

Estonia. Estonia was the first country to address PM within the 'Human Genes Research Act' in 2001, regulating the role of genomics in clinical practice and biobanks. Then, in 2015, was issued a 5-year plan to boost health data infrastructure, research, development and innovation for the Estonian health system. Afterwards, the 2020 strategic development Plan focused on eHealth, based on specific choices and activities to be realized in the next 5 years.

Sweden. Sweden evaluated in 2003 the biobank involvement in care and how human biological material is to be collected, stored and used, whereas the 2019 national strategy took into account the integration of R&I into care delivery; the exploitation of health data; and the responsible, secure and ethical policy development.

United Kingdom. The United Kingdom pioneered the clinical translation of -omics discovery. In 2003, the policy paper 'Building on the best' set the basis for personalization of care and anticipated digital solutions for health data. In 2015, the 'NHS England: Improving Outcomes through Personalised Medicine' outlined four overarching principles: (i) prediction and prevention of disease; (ii) more precise

Table 2 Policies' overview at the EU-MS level

Year	Country	Name	Topics	Source
2001	Estonia	Estonia: Human Genes Research Act	Genomics, biobanks	Human Genes Research Act—Riigi Teataja [Internet]. (cited 20 October 2021). Available from: https://www.riigiteataja.ee/en/eli/531102013003/consolide
2003	Sweden	Swedish Biobanks in Medical Care Act (SFS 2002:297)	Biobanks	Biobanks in Medical Care Act. 2002 [Internet]. Available from: https://biobanksverige.se/wp-content/uploads/Biobanks-in-medical-care-act-2002-297.pdf
2003	UK	Building on the Best	Personalization of care, health data	Building on the Best | Choice, Responsiveness and Equity in the NHS. 2003 (cited 19 October 2021). Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/587438/dh_4068400.pdf
2013	Finland	Finnish Biobank Act	Biobanks	Biobank Act 688/2012. 2012 (cited 20 October 2021). Available from: https://www.finlex.fi/fi/laki/kaannokset/2012/en20120688.pdf
2013	Italy	Italian National Plan for Public Health Genomics	Genomics education, HTA and translation	• Documento tecnico di indirizzo per ridurre il carico di malattia del cancro per il 2011-2013 [Internet]. (cited 20 October 2021). Available from: https://www.salute.gov.it/portale/documentazione/p6_2_2_1.jsp? lingua=italiano&id=1440 • Piano Nazionale della Prevenzione 2010-2012 (National Prevention Plan 2010-2012) [Internet]. (cited 20 October 2021). Available from: https://www.mindbank.info/item/3711
2014	Finland	Finnish Gene Technology Act	Gene technology	Gene Technology Act 377/1995. Gene Technology Act Issued in Helsinki on [Internet]. 1995 (cited 20 October 2021); 377. Available from: https://www.finlex.fi/en/laki/kaannokset/1995/en19950377.pdf
2015	Estonia	Research, Development, and Innovation Strategy for the Estonian Health System 2015-2020	Health data infrastructure, research and innovation	RESEARCH AND INNOVATION FOR HEALTH Research, Development and Innovation Strategy for the Estonian Health System 2015–2020 [Internet]. (cited 20 October 2021). Available from: https://www.sm.ee/sites/default/files/content-editors/eesmargid_ja_tegevused/Tervis/strategy_research_and_innovation_for_health.pdf
2015	Finland	Finland's National Genome Strategy	Genomics literacy, ELSI of genomics	Finland's Genome Strategy—Ministry of Social Affairs and Health [Internet]. (cited 20 October 2021). Available from: https://issuu.com/sitrafund/docs/finland_genomestrategy
2016	Denmark	Denmark National Strategy for Personalised Medicine 2017–2020	Genomics, research ethics, sustainability, citizens' engagement	New national strategy for personalized medicine. Healthcare DENMARK [Internet]. (cited 20 October 2021). Available from: https://www.healthcaredenmark.dk/news/new-national-strategy-for-personalized-medicine.aspx
2015	UK	NHS England: Improving Outcomes through Personalised Medicine	Genomics, prevention, citizens' engagement	IIMMIMPROVING OUTCOMES THROUGH PERSONALISED MEDICINE Working at the cutting edge of science to improve patients' lives. (cited 20 October 2021). Available from: http://moz-extension://f695759d-d783-b344-9232-4565ce0b8fc8/enhanced-reader.html?openApp&pdf=https%3A%2F%2Fwww.england.nhs.uk%2Fwp-content%2Fuploads%2F2016%2F09%2Fimproving-outcomes-personalised-medicine.pdf
2016	Finland	Finland: Health Sector Growth Strategy for R&I Activities Roadmap for 2016–2018	Genomics, biobanks	Innovating together | Health Sector Growth Strategy for Research and Innovation Activities Roadmap for 2016–2018. (cited 20 October 2021). Available from: https://julkaisut.valtioneuvosto.fi/bitstream/handle/10024/75145/MEE_guidelines_8_2016_Health_sector_growth_strategy_17062016_web.pdf
2016	Norway	Norwegian Strategy for PM in healthcare (2017-2021)	Personalized medicine, healthcare	Norwegian Strategy for Personalised Medicine in Healthcare. 2017 (cited 20 October 2021). Available from: https://www.helsedirektoratet.no/rapporter/strategi-for-persontilpasset-medisin-i-helsetjenesten/Summary%20of%20the%20Norwegian%20Strategy%20for%20Personalised%20Medicine%20in%20Health%20Care.pdf/_/attachment/inline/5a6c511c-b245-4546-8dfa-daa057f275dc:f0a88b9e56dddd83901639bea4de5c04919bf407/Summary%20of%20the%20Norwegian%20Strategy%20for%20Personalised%20Medicine%20in%20Health%20Care.pdf
2016	UK	A national clinical strategy for Scotland	Healthcare sustainability	"A National Clinical Strategy for Scotland." www.gov.scot, www.gov.scot/publications/national-clinical-strategy-scotland/documents/ (31 January 2022, date last accessed)
2017	Italy	Italian National Plan for Innovation of the Health System based on -omics sciences	Omics	• Sanità CONFERENZA STATO-REGIONI DEL 13.03.2013: Intesa tra il Governo, le Regioni e le Province autonome di Trento e di Bolzano sul documento recante: "Linee di indirizzo su la genomica in sanità pubblica". [Internet]. (cited 20 October 2021). Available from: http://www.regioni.it/sanita/2013/03/25/conferenza-stato-regioni-del-13-03-2013-intesa-tra-il-governo-le-regioni-e-le-province-autonome-di-trento-e-di-bolzano-sul-documento-recante-linee-di-indirizzo-su-la-genomica-in-sanita-pub-290494/ • PIANO PER L'INNOVAZIONE DE L SISTEMA SANITARIO BASATA SULLE SCIENZE OMICHE. (cited 20 October 2021); Available from: https://www.salute.gov.it/imgs/C_17_notizie_3270_listaFile_itemName_0_file.pdf
2019	France	French National Health Strategy 2018-2022	Healthcare standards, innovation	National Health Strategy 2018-2022. 2018 (cited 20 October 2021). Available from: https://www.gouvernement.fr/sites/default/files/locale/piece-jointe/2018/10/france-national-health-strategy-2018-2022.pdf

(continued)

Table 2 Continued

Year	Country	Name	Topics	Source
2019	Finland	Finland Act on secondary use of social and health data	Accessibility of EHRs, health data infrastructure, research	Secondary use of health and social data—Ministry of Social Affairs and Health [Internet]. (cited 20 October 2021). Available from: https://stm.fi/en/secondary-use-of-health-and-social-data
2019	Sweden	Sweden's National Life Science Strategy	Research and innovation, ELSI, stakeholders' networks	Sweden's national life sciences strategy.
2020	Finland	Finland: Health Sector Growth Strategy 2021-2023 (Draft)	Healthcare	National Health Sector Growth Strategy [Internet]. (cited 20 October 2021). Available from: https://www.healthcampusturku.fi/research-parties/national-health-sector-growth-strategy/
2020	UK	GENOME UK: 2020 national genomic healthcare strategy	Citizens' engagement, research translation, targeted PM treatment and prevention, innovation, ELSI, accessibility of EHRs	Genome UK: the future of healthcare—GOV.UK [Internet]. (cited 20 October 2021). Available from: https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare
2020	Estonia	Estonian eHealth Strategic Development Plan 2020	Health data infrastructure, eHealth	Estonian eHealth Strategic Development Plan 2020 [Internet]. (cited 20 October 2021). Available from: https://www.sm.ee/sites/default/files/content-editors/sisekomm/e-tervise_strateegia_2020_15_en1.pdf
2020	Finland	The Finnish National eHealth and eSocial Strategy 2020	eHealth, citizens' engagement	eHealth and eSocial Strategy 2020 - Finland [Internet]. (cited 20 October 2021). Available from: https://julkaisut.valtioneuvosto.fi/handle/10024/74459
2020	Luxembourg	National Research Priorities for Luxembourg in 2020 and beyond	Sustainability, eHealth	NATIONAL RESEARCH AND INNOVATION STRATEGY FOR LUXEMBOURG. (cited 20 October 2021). Available from: http://www.mesr.public.lu/presse/communiques/2020/FEVRIER-2020/Presentation-de-la-strategie-nationale-de-la-recherche-et-de-l_innovation1/09711_MESR_SnRI_Broch_en_WEB-_002_.pdf
2020	Spain	Spanish Strategy for Personalised Medicine 2020	Big-Data, genomics, training in Precision Medicine	Ministerio. "Detalle de Publicación." Ciencia.gob.es, 2021, www.ciencia.gob.es/InfoGeneralPortal/detalle-publicacion/MCIN/EECTI-Estrategia-Espanola-de-Ciencia-Tecnologia-e-Innovacion-2021-2027.html (31 January 2022, date last accessed)

diagnoses; (iii) targeted and personalized interventions; and (iv) more participatory role for patients. The strategy is interconnected with initiatives already shaping and informing the strategy for PM in the NHS, such as the '100,000 Genomes Project' (including its legacy and continued NHS transformation) and 'Re-procurement of the Regional Genetic Laboratories'.

In 2020, the 'GENOME UK: 2020 national genomic healthcare strategy' was issued as a broad plan addressing citizens' engagement, research translation, targeted PM treatment and prevention, innovation, accessibility of EHRs and Ethical, Legal and Social Implications (ELSI).

Finland. To regulate biobanks and genomics aspects of PM, Finland issued four important policies between 2013 and 2016: 'Finnish Biobank Act', 'Finnish Gene Technology Act', 'Finland's National Genome Strategy' and 'Finland: Health Sector Growth Strategy for R&I Activities Roadmap for 2016-2018'. Similarly, to what was happening at the European level, between 2019 and 2020, Finland explored and regulated digital health, health data infrastructure, accessibility of EHRs and citizens' engagement, thanks to the 'Finland Act on secondary use of social and health data'; 'Finland: Health Sector Growth Strategy 2021-2023' and the 'Finnish National eHealth and eSocial Strategy 2020'.

Italy. Italy also pioneered the implementation of Genomics in Public Health. Two policy documents set the fundaments of PM in this country: the '2010-2012 National Prevention Plan', published by the Ministry of Health and the regions, which defined the governance planning of predictive medicine, based on genomics; and the '2011–2013 Technical Document for the reduction of the burden of cancer diseases', which aimed at developing tools and processes to use genomic-based knowledge in decision-making. Afterwards, in 2013, the 'Italian National Plan for Public Health Genomics' was issued. This policy was based on three major pillars: (i) the systematic health technology assessment of genetic tests for complex diseases; (ii) the promotion of genomics education for healthcare professionals; and (iii) the promotion of basic genomic health literacy in the general population.

In the same vein, the 'Italian National Plan for Innovation of the Health System based on -omics sciences' was launched in 2017. It also addressed the genomic revolution and put in place a strategy of 'government of innovation' of genomics and related fields.

Denmark. 'Denmark National Strategy for Personalised Medicine 2017-2020', delivered in 2016, focused on patient-centred care, individual's right to self-determination, evidence-based and economically sustainable offer, data sharing for the benefit of future research and treatment, fair and adequate distribution of research funds, public sector's ownership of genome sequencing and data processing.

Norway. The development of a national strategy for PM was one of the key recommendations in a report published by the Regional Health Authorities in 2013–2014 in Norway. This led, in 2016, to the 'Norwegian Strategy for PM in healthcare (2017-2021)', a 5-year plan that aims to offer guidance to both citizens and healthcare professionals, contribute to research, development and innovation and implement the services accordingly.

France. In 2019, the French government issued the 'French National Health Strategy 2018-2022', outlining, as priorities, the health promotion and prevention; the equity in access to care; the quality and safety of care; and the innovative approaches to be applied to the healthcare systems.

Luxembourg. In Luxembourg, the 'National Research Priorities for Luxembourg in 2020 and beyond' addressed the emergence of data-driven healthcare and the importance of Preventive Medicine in PM.

Spain. In 2020, the 'Spanish Strategy for Personalised Medicine 2020' was launched, targeting the exploitation of genomics and big data in health, literacy and training in Precision Medicine alongside with the implementation of Predictive Medicine and Personalized Therapies.

Discussion

Our article, providing an overview of policies and regulatory actions on PM implemented at the EU and EU-MS level, emphasized the attention posed towards PM, as a driver for transforming healthcare. From 2008, the EC and the Council of EU addressed the challenges of PM through dedicated policies towards the definition of PM and the creation of the international consortium 'ICPerMed', to support further developments, collaborations and establish Europe as a global leader in PM. Annually, many initiatives arise from ICPerMed, with the objective of expanding relations between Europe and other countries, facilitating the international adoption and dissemination of PM.

Over the years, the stream of EU policies showed an increasing attention to the ethical, legal and social aspects of PM, in terms of accessibility and fair distribution of care. Patient-centred approaches became prominent from 2015 on, both in clinical practice and public health strategies, reflecting the shift in focus when addressing healthcare services. The engagement of patients and citizens highlights the value ascribed to prevention and has led to strive for higher standards of care.[24,33] Adopting patient-centred approaches, which enhance the quality of care and diagnostic and therapeutic pathways, ensures a long-term positive effect on the healthcare sustainability.[33] Sustainability has been often considered alongside innovation, given that in the last few years, digital health and ICT solutions created new opportunities for PM.[27,33] Nonetheless, the creation of domain-specific interoperability frameworks, EHRs and digital strategies, posed more challenges, for data privacy, standardization and accessibility, cross-border interoperability, infrastructure and cybersecurity.[34]

PM is addressed in national regulations, plans or strategies of the EU-MS, complying with the EC indications, differing from country to country. Italy, through dedicated national plans on public health genomics and omics sciences; the UK, through genomics, personalized prevention, and citizens' engagement; and Estonia, through innovation strategies and bio-banking, pioneered the PM implementation in healthcare. The model set by Estonia was instead followed by the Nordic countries, where Sweden, Denmark and Finland focused their national regulations on genomics, biobanking and second use of data, and converged, more recently, on eHealth. Nordic countries are excelling in aspects of integration of genomics and data from registries and biobanks, setting themselves as equals in comparison with more ambitious genome sequencing initiatives currently underway both, at the European level, and in major economies, such as the USA and China.[35]

The wide heterogeneity among different national policies and regulations has led to initiatives at the regional level, such as Region4PerMed (available from: https://www.regions4permed.eu/), a European project which aims to bring regional needs to the attention of European policymakers, by involving regional and national stakeholders.

The ICPerMed vision for 2030 offers a perspective for the policy direction, paving attention in healthcare professionals' capacity building and citizens' literacy, optimization of personalized care and healthcare system sustainability.[36] Our mapping, which is part of the activities from the project IC2PerMed, highlights these aspects and align to the Chinese efforts, ranking Europe and China among the global leaders in PM. In China, an announcement was made in 2016, establishing China Precision Medicine Initiative, a 15-year programme worth $9.2 billion, to radically shift the healthcare regime in the country and ensure that China remains a driver in PM.[37] Considering the differences among countries in regulating PM, a shared integrated regulatory framework at the international level may be needed in order to facilitate access, transferability and collaborations.

It is of utmost importance to consider that healthcare professionals and citizens alike will define the future of PM through the engagement, participation and interaction in policymaking. However, despite the growing number of education strategies, there is still the need to improve some aspects in terms of accessibility, target audiences or tools and methods used.

This study should be considered in the light of some limitations. We acknowledge that the publication bias might be present in this work, given that at the time of our mapping, some policies or regulation actions may have been in draft versions, or not yet been implemented, or even published in national languages that were not identified. However, to address this issue, we conducted extensive research on different sources and repositories and in several different languages—English, Italian, French, Spanish, Portuguese and German—which allowed us to retrieve data on actions implemented by a wide range of countries.

Our work represents the first attempt to summarize the existing policies in PM at EU and EU-MS, trying to bridge the literature gap on this topic. The policy landscape appears to be fragmented and coordinated efforts should be put in place to align the future direction on PM. Our work could be also a useful tool for policymakers for policy implementation and for international programmes and collaborations. In fact, exploring in detail the existing policies and their specific focus, it is possible to find fertile ground on which to base collaborations, identify facilitators, potential barriers and future directions. Therefore, bringing together policies on different aspects of PM could give new perspectives on how the relevant stakeholders should consider the weaknesses and strengths of PM-based healthcare transformation.

Supplementary data

Supplementary data are available at *EURPUB* online.

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Key points

- Personalized Medicine (PM) is one of the major priorities of the European Commission's research agenda.
- PM-related policies, programmes and action plans at the European Union (EU) and EU Member States level focus on patient-tailored treatment and targeted prevention, education of healthcare workers, research and innovation, big data harmonization and healthcare system sustainability.
- The policy landscape is fragmented and coordinated efforts should be put in place to align the future direction on PM.

References

1 Population Structure and Ageing—Statistics Explained. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_structure_and_ageing (19 October 2021, date last accessed).

2 Auffray C, Charron D, Hood L. Predictive, preventive, personalized and participatory medicine: back to the future. *Genome Med* 2010;2:57.

3 Nimmesgern E, Benediktsson I, Norstedt I. Personalized medicine in Europe. *Clin Transl Sci* 2017;10:61–3.

4 ICPerMed "Family"—Related Initiatives and ERA-Nets—ICPerMed. Available at: https://www.icpermed.eu/en/related-initiatives.php (19 October 2021, date last accessed).

5 Gaisser S, Vignola-Gagné E, Hüsing B, et al. EU policies in personalized medicine-related technologies. *Per Med* 2009;6:93–102.

6 ICPerMed. Available at: https://www.icpermed.eu/en/icpermed.php (19 October 2021, date last accessed).

7 IC2PerMed—Publications & Public Deliverables. Available at: https://www.ic2permed.eu/zh/publications-public-deliverables-2/#deliverables (7 December 2021, date last accessed).

8 Romagnuolo I, Mariut C, Mazzoni A, et al. Sino-European science and technology collaboration on personalized medicine: overview, trends and future perspectives. *Per Med* 2021;18:455–70.

9 EU Law | European Union. Available at: https://europa.eu/european-union/law_en (19 October 2021, date last accessed).

10 Safe, Innovative and Accessible Medicines: A Renewed Vision for the Pharmaceutical Sector. Available at: http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm (20 October 2021, date last accessed).

11 Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in Vitro Diagnostic Medical Device. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31998L0079 (19 October 2021, date last accessed).

12 European Union, Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the Protection of Natural Persons With Regard to the Processing of Personal Data and on the Free Movement of Such Data, and Repealing Directive 95/46/EC (General Data Protection Regulation). Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679 (19 October 2021, date last accessed).

13 Council Conclusions on Personalised Medicine for Patients (2015/C 421/03). Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XG1217(01) (19 October 2021, date last accessed).

14 Consolidated Version of the Treaty on the Functioning of the European Union 2008/C 115/01. *Official Journal of the European Union*. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:C:2008:115:FULL&from=EN (19 October 2021, date last accessed).

15 Commission Recommendation of 2 July 2008 on Cross-Border Interoperability of Electronic Health Record Systems. 2008. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008H0594&from=EN (19 October 2021, date last accessed).

16 Council Recommendation of 8 June 2009 on an Action in the Field of Rare Diseases (2009/C 151/02). Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF (19 October 2021, date last accessed).

17 European Perspectives in Personalised Medicine—Publications Office of the EU. Available at: https://op.europa.eu/en/publication-detail/-/publication/3f8b5554-fe53-49bf-8df1-936c93f2f3f8 (20 October 2021, date last accessed).

18 Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the Application of Patients' Rights in Cross-Border Healthcare. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN (19 October 2021, date last accessed).

19 Council Conclusions on Innovation in the Medical Device Sector (2011/C 202/03). Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2011:202:0007:0009:EN:PDF (19 October 2021, date last accessed).

20 Council Conclusions: Towards Modern, Responsive and Sustainable Health Systems (2011/C 202/04). Available at: https://op.europa.eu/en/publication-detail/-/publication/a8e07317-dd76-4442-ae7c-f20cd77e5e6c/language-en (19 October 2021, date last accessed).

21 Commission Staff Working Document. Use of "-Omics" Technologies in the Development of Personalised Medicine. Available at: https://ec.europa.eu/transparency/documents-register/detail?ref=SWD(2013)436&lang=en (20 October 2021, date last accessed).

22 Council Conclusions on the "Reflection Process on Modern, Responsive and Sustainable Health Systems". Available at: https://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/lsa/140004.pdf (19 October 2021, date last accessed)

23 Communication from the Commission on Effective, Accessible and Resilient Health Systems. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52014DC0215&from=EN (20 October 2021, date last accessed).

24 Clinical Trials—Regulation EU No 536/2014 | Public Health. Available at: https://ec.europa.eu/health/human-use/clinical-trials/regulation_en (4 October 2021, date last accessed).

25 Shaping Europe's Vision for Personalised Medicine Strategic Research and Innovation Agenda (SRIA). Available at: http://www.permed2020.eu (19 October 2021, date last accessed).

26 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions Empty. Strengthening European Identity through Education and Culture, Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52017DC0673&from=EN (19 October 2021, date last accessed).

27 Council Conclusions on Health in the Digital Society—Making Progress in Data-Driven Innovation in the Field of Health (2017/C 440/05). Available at: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2017:440:0003:0009:EN:PDF (19 October 2021, date last accessed).

28 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. A Digital Single Market Strategy for Europe. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015DC0192&from=EN (19 October 2021, date last accessed).

29 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Enabling the Digital Transformation of Health and Care in the Digital Single Market; Empowering Citizens and Building a Healthier Society. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52018DC0233&from=EN (19 October 2021, date last accessed).

30 EPC—Commission Joint Report on Health Care and Long-Term Care in the EU. Available at: https://data.consilium.europa.eu/doc/document/ST-14182-2016-INIT/en/pdf (19 October 2021, date last accessed).

31 Commission Recommendation (EU) 2019/243 of 6 February 2019 on a European Electronic Health Record Exchange Format. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019H0243 (19 October 2021, date last accessed).

32 Regulation (EU) 2019/881 of the European Parliament and of the Council of 17 April 2019 on ENISA (the European Union Agency for Cybersecurity) and on Information and Communications Technology Cybersecurity Certification and Repealing Regulation (EU) No 526/2013 (Cybersecurity Act). 2019. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0881&from=EN (19 October 2021, date last accessed).

33 Council Conclusions on Shaping Europe's Digital Future (2020/C 202 I/01). Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52020XG0616%2801%29 (19 October 2021, date last accessed).

34 Joint Action Towards the European Health Data Space—TEHDAS—Tehdas. Available at: https://tehdas.eu/ (19 October 2021, date last accessed).

35 Personalised Medicine in the Nordic Countries NOS-M Report With Conclusions and Recommendations for Joint Actions in Personalised Medicine in the Nordic Countries. Available at: https://nos-m.org/news/nordic-common-strengths-and-future-potential-in-the-field-of-personalised-medicine (19 October 2021, date last accessed).

36 Vicente AM, Ballensiefen W, Jönsson J-I. How personalised medicine will transform healthcare by 2030: the ICPerMed vision. *J Transl Med* 2020;18:180.

37 Cyranoski D. China embraces precision medicine on a massive scale. *Nature* 2016;529:9–10.