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Integrating China in the International Consortium for Personalized Medicine: A Position Paper on Personalized Medicine in Sustainable Healthcare

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Abstract

Introduction: Over the last decade, the emergence and spread of personalized medicine (PM) have defined a substantial revolution in healthcare. In principle, healthcare system sustainability is challenged by the investments required for research and development, as well as the adoption of PM techniques in routine clinical care. The "Integrating China in the International Consortium for Personalized Medicine" (IC2PerMed) EU-funded project aims to integrate China into the "International Consortium for Personalized Medicine" (ICPerMed). IC2PerMed aims to align the EU and China's research agendas in this field to enable a swift development of approaches in the EU and China with strong leverage upon EU-Chinese collaborations. ***Methods:*** Within this project, we first mapped relevant policies on PM in both the EU and China, and then we involved European and Chinese experts in PM in workshops and Delphi surveys in order to identify relevant priorities for the implementation of PM in sustainable healthcare. ***Results:*** As a result of this process, we identified nine overarching priorities, each addressing specific aspects of the sustainability of healthcare systems and PM implementation, with the main goal of supporting policymakers in integrating PM approaches in the EU and China. ***Discussion/conclusion:*** The implementation of PM in health systems is appealing in terms of improved accuracy in diagnostics, treatment, and prevention of disease, as well as reduction of the side effects resulting from inefficient use of drugs. Research, development, and implementation of needed techniques require time and resources that can slow the adoption of PM in healthcare systems. The nine priorities we identified address some of the most critical points, trying to lay the foundations for a comprehensive approach.

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Introduction

Personalized medicine (PM) is defined 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" [1]. Despite its appealing prospects and increasing applications in healthcare [2], the implementation of PM faces numerous barriers that slow its adoption, not least the management of the innovative but often expensive techniques in the context of healthcare systems' sustainability [3]. PM techniques are increasingly contributing to evidence-based medicine in the decision-making process of disposition of health system resources [4]. Targeted therapies and companion diagnostics can improve the effectiveness and reduce the harms and costs of treating patients who do not respond to or are adversely affected by therapy by better selecting patients and treatments. In doing so, targeted therapies are expected to save costs and resources, working toward healthcare sustainability [5]. However, concerns about the cost of implementing PM tools have been raised. For instance, identifying markers or genetic variations does not guarantee susceptibility to targeted therapies, with the risk that investments in this sense do not translate into relevant health outcomes [6]. In addition, the risk related to implementing tools that increasingly stratify the population targeted for health interventions is that, at some point, the PM technology's population of interest will not be large enough for the intervention to be cost-effective for the investment [7].

As defined by the World Health Organization (WHO), a sustainable healthcare system is a system that "improves, maintains, or restores health while minimizing negative impacts on the environment and leveraging opportunities to restore and enhance it, to the benefit of the health and well-being of current and future generations" [8]. When defining an intervention's value, it should be kept in mind that value in healthcare is measured as the improvement in a person's health outcomes for the cost of its achievement [9]. Ensuring that implemented interventions are value-based is crucial for healthcare sustainability, properly addressing available resources where they can make the highest impact on health needs.

Because of the complexity of tailoring diagnostics and therapeutics to everyone's needs while also addressing research and health system operability cost-effectively and sustainably, global efforts are needed to maximize gains. At European Union (EU) level, the different countries have adopted different national regulations, plans, or strategies, despite pursuing common objectives: for example, Italy has implemented dedicated national plans focusing on public health genomics and omics sciences; the UK has emphasized genomics, personalized prevention, and citizens' engagement; Estonia has pioneered PM implementation through biobanking and innovation strategies engaging private companies and startups with other Nordic countries like Sweden, Denmark, and Finland following a similar model, focused on genomics, biobanking, second use of data, and eHealth integration. For this reason, EU institutions have issued documents addressing the resulting heterogeneity toward a common path to achieve shared goals [10].

The European Commission initiated the International Consortium on Personalized Medicine (ICPerMed) [11] in 2016 to provide a platform for communication and exchange on PM research, funding, and implementation. As a part of its Strategic Research and Innovation Agenda, ICPerMed identified Shaping Sustainable Healthcare as one of the five challenges in PM [12], incorporating many core topics like quality improvement, process and systems design, and workforce planning issues across an integrated healthcare system [13].

PM is a key element of the policy agenda in China as well, which in 2016 integrated PM into the 13th National 5-Year Plan as a part of the "Special Plan on Health and Health Technology Innovation." This document serves the purpose of tracing guidelines for promoting the innovation and industrialization of key sectors within the Chinese economy; for PM, the development of the biological industry and accelerating the development of new PM models are goals to be achieved by strengthening applied basic research, promoting cutting-edge technology innovation, enhancing disease prevention and control, protecting the health of key populations, developing pharmaceutical and health products, developing new health service technologies, strengthening health risk factor control, promoting the popularization of science and technology, advancing the modernization of Chinese medicine, strengthening innovation base platforms and capacity building, promoting the transfer and transformation of results, and building international cooperation networks [14].

The EU and China share common interests in several areas of PM. These include prioritizing the role of individuals in the care process, emphasizing tailored approaches to prevention, diagnosis, and treatment, utilizing health data collection and analysis, and promoting standardized technical requirements to ensure seamless collaboration and exchange across borders. Both sides

view this convergence as crucial for their healthcare systems, working together to adopt a personalized approach that offers customized treatment strategies for specific patient subgroups, with a greater emphasis on disease prevention as a response to rising healthcare costs. The concept of personalization in medicine emerged on both sides in the early 2000s, with the EU introducing personalized health system concepts for patients and citizens in 2004 [15], and China discussing precision surgery in 2006 [16]. The terms "PM" and "precision medicine" were, respectively, defined in the EU [1] and China [17] in 2015–2016, leading to the development of programs that implement omics technologies and precision/personalized prevention and treatment. Although there is currently no shared definition of PM, these terms are often used interchangeably.

In spite of these similarities, collaboration opportunities can benefit from reciprocal expertise in different fields and areas of PM, leading joint research projects and initiatives that combine resources, infrastructures, and expertise, also allowing studies with larger cohorts that involve diverse populations and provide a broader and more representative sample for research and understanding of peculiarities in each ethnic group. In addition, this can facilitate market access and commercial opportunities on both sides, with positive economic returns (e.g., facilitating the implementation of digital health interventions) [18], laying the foundations for cross-country collaborations on transnational and global public health issues. In turn, this approach will need to keep in mind the existing social and cultural differences, educating and engaging the public with educational programs and awareness campaigns to promote informed decision-making and fostering trust in PM practices, encouraging active participation of individuals and communities in their healthcare.

Despite sharing some priorities, the two sides have long developed their respective health systems differently. The most striking example is Chinese traditional medicine, a term that encompasses a range of practices widely adopted in China and beyond, both alone and in combination with conventional Western medicine, even in cancer therapy [19], but not as much in the Western countries. Identifying adopted approaches, and addressing differences to develop common techniques when needed, is relevant to ensure collaboration opportunities are not flawed by diverging standards and measures.

Among the projects promoted by the ICPerMed Consortium, the "Integrating China in the International Consortium for Personalized Medicine" (IC2PerMed) project aims to align the EU and China's research agendas in this field to enable a swift development of approaches in the EU and China with strong leverage upon EU-Chinese collaborations. The IC2PerMed project received funding from the Horizon 2020 (H2020) EU funding program [20, 21] and from the Chinese MOST Intergovernmental Project of National Key R&D program, and it involves ten partners, seven from the EU and three from China, with strong expertise in the field of PM. A relevant goal of IC2PerMed is to identify a set of priorities in PM directed to policy-makers, scientists, and industry members, aiming to build bridges between the EU and China in the field of PM. In order to reach this goal, a mapping exercise of PM policies and research and funding schemes in the EU and in China has been conducted from IC2PerMed [22–24].

The objective of our study, which is developed within the IC2PerMed project, was to arrive at a list of priorities regarding the main actions to be taken to promote the sustainable integration of PM approaches in healthcare systems. In order to achieve this goal, we made use of the results of the above-mentioned mapping activity, which were presented within a dedicated workshop. These results formed the basis for the experts' identification of priorities. A characterizing element of our work is to want to take into account a shared perspective at both the Chinese and European levels on the issue.

Materials and Methods

Expert Selection

European and Chinese experts in PM were identified in late 2020 using a bottom-up and top-down approach that eventually involved 57 experts from the EU and 10 from China. Specifically, the bottom-up approach refers to an open call for expert interest on the IC2PerMed website, while the top-down approach refers to the identification of experts through review of the latest reports, scientific publications, conference programs, partners and coordinators of EU-funded projects, and the IC2PerMed partner network [25]. All the experts identified were asked to volunteer to participate in three thematic online workshops, of which one was about PM in sustainable healthcare. Two coordinators were identified among IC2-PerMed partners, one European and one from China, to support expert discussion in each workshop development. The workshop dedicated to PM in sustainable healthcare was held on June 22, 2021, and was participated by 16 experts (10 from the EU and 6 from China). In preparation for the workshop, a list of guiding issues has been reported to foster the discussion, based on a mapping exercise of European and Chinese policies in PM [10, 22, 26–28].

Delphi Survey Design

Immediately after the workshop, a Delphi survey was conducted using a 3-round scheme to validate a potential set of priorities that emerged during the discussion until consensus was reached [23, 29]. Experts were invited to review the content of the priorities and rate each in terms of validity and relevance by indicating a value from 1 to 5 on a Likert scale, where 1 = strongly disagree and 5 = strongly agree. Experts could propose additional priorities based on their experience or comment on the presented priorities. After each round, the questionnaire was modified, integrating feedback from all participants, and sent again to the panel for the following round of consultation until consensus was achieved.

Statistical Analysis

According to the Delphi methodology, we calculated the Content Validity Index (CVI), the ratio between the number of experts that rate a singular item with 4 and 5 and the total number of experts involved. CVI ranges from 0 to 1, or from 0% to 100%. A CVI greater than 79% was deemed to be suggestive of the item's inclusion in the position paper, a rate between 70 and 79% was considered indicative of the item's revision, and a rate lower than 70% was deemed to be suggestive of removing the item [23]. The Delphi survey was implemented between July 2021 and December 2021.

Results

The discussion of experts during the workshop identified 20 main potential priorities. After implementing the Delphi process, nine overarching priorities were identified with 10 experts completing all the rounds (Fig. 1).

Five Chinese and five European experts filled out the survey. Four experts came from Chinese workplaces, while six experts had European affiliations. One Chinese expert reported working in Belgium at the time of the survey. European countries represented were Switzerland, Italy, Estonia, Bulgaria, and the UK. Four experts were from research institutions (academic sector), three worked in a hospital, and 3 worked for a patient organization, government, and pharmaceutical industry, respectively. The nine priorities are listed in Table 1, along with the main elements of the discussion reported within each priority below.

Priority 1: Increase Efforts to Allocate Resources to PM to Foster Healthcare Systems' Sustainability

Investments in PM require significant amounts of funding for research and development (R&D) of new technologies and techniques. Yet, the frequent scarcity of resources makes it imperative to choose carefully where these resources are allocated. The recommended measures include standardization and economic regulation of Health Technology Assessment (HTA) agencies among different countries; facilitation of the assessment processes; promotion of partnerships between academic and pharmaceutical sectors; complementation of individual project grants with limited core grants by public funding bodies; close monitoring of this financial support, ensuring the excellence and the usefulness of the recipient organization; avoiding the duplication of existing research infrastructures.

Priority 2: Adopt a System of Continuous Evaluation of Disruptive Innovation

The ongoing innovative approaches brought by the implementation of PM require that HTA bodies perform a continuous evaluation of new technologies and processes. Traditional methods adopted in assessing new drugs and technologies, such as randomized controlled trials (RCTs), are often unfeasible for PM. Classic view in the management of RCTs involves a drug-centered approach, in which study participants, sharing elements such as histologic or tumor site characteristics, are given the same type of drug treatment, but this is not an approach compatible with interventions that can be called personalized. Next-generation clinical trials must move toward a patient-centered approach, which matches therapeutic agents to patients according to a large number of variables, such as biomarkers, tumor genomic profiles, individual pharmacogenomic data, and other variables that make therapy highly personalized [30]. This change of perspective in trial management might however result in lowering the availability of patients with the same characteristics; for this reason, this area would benefit from renewed data provision, facilitating secondary use of health data for research purposes and real-world data from personal health data repositories to complement data from RCT [31]. In contradiction with this need, current data privacy provisions protect the secondary use of health data, particularly genomics data, making it very difficult to perform research in this field [32].

Priority 3: Integrate End Users' Perceptions in the Entire Innovation Process

For PM implementation in healthcare systems to be complete and sustainable, the process needs to consider the end users of these technologies, i.e., patients and healthcare professionals. People diagnosed with a new condition must learn a range of notions about their disease, integrate it with their social and cultural background, and measure it against their expectations; on the

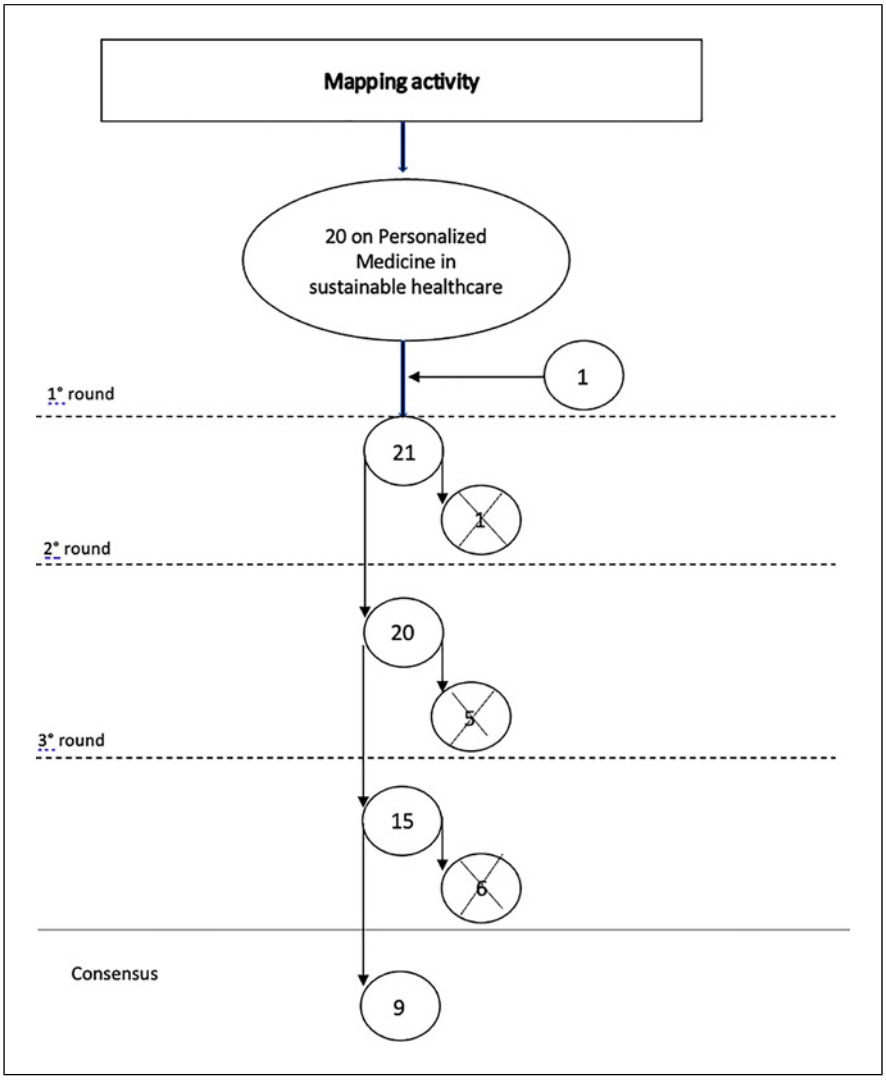

Fig. 1. Flowchart of the Delphi survey process. The vertical flow indicates the number of priorities stemming before and after each Delphi survey round. The circles containing an X mark the number of priorities eliminated after each Delphi survey round. Horizontal arrows refer to priorities that were included following experts' suggestions or any significant inputs from the workshops.

Table 1. The nine IC2PerMed priorities on "PM in sustainable healthcare" in EU and China

1. Increase efforts to allocate resources on PM to foster healthcare systems' sustainability
2. Adopt a system of continuous evaluation of disruptive innovation
3. Integrate end users' perceptions in the entire innovation process
4. Include Ethical, Legal, and Social Implication (ELSI) aspects and the related costs in the process of PM policymaking, evaluation, and management of technological innovation
5. Foster PPPs for sustainable reimbursement systems that allow the PM implementation in the healthcare system
6. Identify new payment models for the public reimbursement of PM interventions (i.e., value-based bundled payments as opposed to fee-for-service)
7. Enhance multidisciplinary and intersectoral collaborations for sustainable PM-oriented healthcare systems
8. Create an international professionals' network, to share experiences, promote, and evaluate best practices and progress in PM
9. Define investment priorities for product and process innovation, considering the relationship between outcome over cost

other hand, healthcare professionals must learn to deal with every patient's unique health, social, and personal condition. These situations must be considered to address research correctly and efficiently in this field from a clinical but also a financial point of view, together with patients' background, knowledge gaps, and needs. A

better connection between data subjects and users should be built on trust, leading to improved collaboration, increased communication, and profound confrontation on critical issues.

Priority 4: Include Ethical, Legal, and Social Implication Aspects and the Related Costs in the Process of PM Policymaking, Evaluation, and Management of Technological Innovation

The complex process of PM policymaking should be as comprehensive as possible to ensure public trust and engagement. An integrated ethical, legal, and social framework should be included in the newly made policy to ensure equity and protect those whose interests may be at stake, considering the sensitivity of health and genomic data and the commercial interests of private companies. The need for a significant data flow between certified users does not lessen the importance of the requirement for peculiar ethical and privacy issues to be addressed in an appropriate legal framework, specifically for genomic data. This includes adequate arrangements for data protection and patient consent, so people may be encouraged to contribute with biological material and personal data for analysis. The policymaking process should consider that the stakeholders involved are many and can have conflicting interests, e.g., when private partners are involved. Ethical, legal, and social frameworks need to be considered in newly made policies to ensure equity and protect those whose interests may be at stake. In addition, the confrontation between different parts should also focus on these topics.

Priority 5: Foster Public-Private Partnerships for Sustainable Reimbursement Systems That Allow PM Implementation in the Healthcare System

Collaboration between public and private stakeholders is crucial for increasing resource allocation and targeting fundamental issues in implementing PM in healthcare systems. Public-private partnerships (PPPs) are a suitable model for driving forward PM research, bringing together experts and competencies from a range of stakeholders, and making the best use of the available resources in areas where disruptive innovation could yield better returns in terms of patient benefit, but requires a more significant effort in terms of the investment [33]. PPPs involve at least one public (nonprofit, academic, or government) unit and at least one private-for-profit partner, making it good opportunities to bring together different experiences and viewpoints with the aim of implementing PM approaches. A major area of application of these partnerships looks at innovative drug discovery and development. Such initiatives aim to leverage the collective expertise of stakeholders involved in order to reduce obstacles in the implementation phase of new drugs. Actions under this topic typically include accelerating the understanding of diseases, developing tools and platforms to share resources between public and private entities, and identifying gaps in drug development processes. Research in these areas, if properly guided by academic and institutional perspective, could open up PM to new medical as well as economic scenarios capable of justifying private sector investment. In addition to pharmaceutical development, other areas of application for PPPs are sharing of compounds, development of machine learning models, and sharing of intellectual data. All these fields find broad points of contact with PM, demonstrating that PPPs constitute potentially valuable models for fostering investment in the implementation of these approaches [34].

Priority 6: Identify New Payment Models for the Public Reimbursement of PM Interventions (i.e., Value-Based Bundled Payments as Opposed to Fee-For-Service)

Most advanced PM interventions, such as targeted therapies against specific cancer antigens, gravitate primarily around genetic testing, with over 74,000 diagnostic tests on thousands of genes [35]. The potential benefits of these methods range from patient disease outcomes to reducing costs associated with inappropriate, costly, and often harmful drug treatments [36]. Their cost-effectiveness depends on many factors, e.g., the prevalence of a particular allele in a population [37]. Because PM interventions are so complex and unique, traditional reimbursement models (e.g., fee-for-service models) are inadequate. In contrast, value-based bundled payments allow a more comprehensive evaluation of the set of interventions required for a given condition in a given patient. Nonetheless, these are far from adequate, too: new payment models should be identified for public reimbursement of PM interventions. Recently, value-based healthcare models have been proposed to measure the value of PM interventions and demonstrate their cost-effectiveness to inform policy decisions about reimbursement and investment in R&D, particularly in solidarity-based health systems [38]. The overall benefit-risk balance, cost-effectiveness of the tests, magnitude of the genomic effect, and the strength and conclusiveness of the evidence should guide the inclusion and positioning of PM information in medical practice [39].

Priority 7: Enhance Multidisciplinary and Intersectoral Collaborations for Sustainable PM-Oriented Healthcare Systems

PM is a multidisciplinary field and needs multidisciplinary collaboration that brings together multiple healthcare providers and liaises with healthcare professionals from different specialties. This is crucial to synergize on compatible competencies and fill each other's gaps. Multidisciplinary collaboration brings together healthcare providers and professionals from different specialties: professionals acquire new competencies and skills needed to promote health, considering not only the well-being of the citizen/patient but also the ethical, social, and economic constraints related to the use of health resources [40]. Healthcare professionals involved in implementing PM approaches are many. First, it is important to create effective engagement strategies with general practitioners, who must be able to propose PM tools in a weighed and targeted manner. To do this, of course, it is necessary to have the functional information to understand the potential of such tools; here emerges the central role of clinical geneticists and molecular biologists to support continuous updating of knowledge [41]. However, familiarity with the clinical potential of a tool is not sufficient to master it, so it is necessary to engage all professionals responsible for test use in a dialogue with citizen representatives and patients. Their views are essential in identifying the barriers and bottlenecks to be attended to in communicating the ethical and medical implications of these tools. Upstream of all this, for the purposes of integrating an approach within a health system, it is necessary to include analyses of resource use, expected ethical implications, and organizational feasibility, consequently requiring specific professional figures for each of these areas. If such collaboration is lacking, the wrong address of efforts by different stakeholders can slow down progress in the fields of research as well as in clinical care; hence, to prevent this, collaborations between different disciplines must be fostered and coordinated, bringing together healthcare providers and non-healthcare workers.

Priority 8: Create an International Professionals' Network to Share Experiences, Promote, and Evaluate Best Practices and Progress in PM

Creating a network of international partners involved in all the different PM areas would ensure a periodic confrontation aimed at identifying best practices and leading to a better implementation of PM on an international scale. International networks aimed at sharing best practices and projects in the field of PM could play a central role in promoting innovative approaches. The possibility of creating bridges among partners and ensuring a confrontation with peers from different environments is a precious opportunity that should be pursued. This kind of network should include professionals and experts in the field of PM, brought together in online meetings or using web portals to share updates of PM and foster real-time discussion on these issues. This international information exchange should expand the literacy of healthcare and workers, promoting advances in PM and, ultimately, reaching decision-makers and policymakers, leading to the update of existing healthcare policies and drafting of new ones.

Priority 9: Define Investment Priorities for Product and Process Innovation, Considering the Relationship between Outcome over Cost

Considering the limited availability of resources for innovation to be successfully implemented, appropriate investment priorities must be first set. The progress of biomedical research in the field of PM runs the risk that the inclusion of new tools in clinical practice may increase costs without correlating with actual positive effects on patient health [42]. In this sense, research aimed at developing economic tools to capture the value of individualized care by virtue of the cost-benefit ratio, both from the perspective of the patient and the health system, represents a focal point for defining investment priorities in the field of PM [43]. Priorities in terms of investment vary according to context, so each country or health system must channel its resources based on local analysis inclusive of several elements, such as the availability of funds, the capacity of the system to accommodate and exploit them, and much more. In this sense, it is clear that countries with less availability will have to make choices aimed at laying the ground and for the implantation of PM techniques, e.g., by promoting specific training programs or the creation of useful organizational tools (platforms, pathways and regulations for data sharing and use, etc.). These structures make it possible to prepare not only healthcare personnel but also the population to use the instruments and medical devices necessary for the implementation of PM, as well as to justify future major investments required in this area [44]. At the same time, it is worth remembering that, due to the multidisciplinary nature of PM, a wide set of opportunities derived from private and public investments are entering the market, each with a specific target, specific peculiarities, and requesting different levels of investment and commitment, thus validating the importance of setting financial priorities.

Discussion

Health systems worldwide face unprecedented pressure, with aging populations carrying an increasing disease burden. Meanwhile, exponential progress in technological improvements and scientific research have paved the way for new medical models in healthcare that are increasingly tailored to a single person's characteristics. PM implementation in health systems is appealing in terms of improved accuracy in diagnostics, treatment, and disease prevention, as well as reduced side effects resulting from inefficient use of drugs [45]. Both Europe and China have grasped the value of these innovations, promoting organized strategies to analyze their potential and promote their integration into their respective healthcare systems [14, 27]. However, researching, developing, and implementing the techniques needed to ensure a truly personalized approach to these relevant fields require dedicating time and resources to the purpose. These issues can slow PM adoption in healthcare systems if not faced systematically, constructively, and effectively. The nine priorities we identified address some of the most critical points, shared between Europe and China, trying to lay the foundations for a comprehensive approach.

Improving resource allocation on PM is a problematic task: even talking about increasing resources in healthcare can be a tough hit. Currently, health systems in the EU and China share an approach focused on disease management, with spending inevitably becoming increasingly burdensome and difficult to sustain as the population ages. Prevention could play a key role in this perspective: if we think that at the European level only approximately 3% of health spending is dedicated to prevention we realize how increasing this amount is a priority [46]. The situation is similar in the Chinese context, where integration of prevention within health systems is an urgent need in favor of system sustainability [47]. In this context, the role of PM is identified not only as an element toward which to channel investments but also as a tool to optimize existing resources by defining increasingly targeted and effective prevention strategies with regard to the peculiarities of the individual, making it possible to intercept specific diseases in advance of their onset and consequently reducing the costs associated with treatments. This is the case, e.g., with the validation of polygenic risk scores for risk stratification and primary prevention of stroke, which is at an advanced stage of evaluation at both the European and Chinese levels [48, 49]. The example of polygenic risk scores effectively encapsulates all of the previously reported limitations in terms of implementing PM strategies. In the face of encouraging premises in terms of health potential and health system sustainability, there are many barriers that prevent their large-scale use in clinical practice: the need to promote the publication of further evidence, assess their ethical and legal impact on the population, study its cost-effectiveness in different settings. All this requires major investments, with a view to a potential improvement in terms of population health and savings for the system. Finding a way to foster R&D in PM is crucial; seeing the dividends, such an investment can give in the long run [50]. When academic, industrial, and corporate entities collaborate, public and private institutions can take the best out of each other, accelerating processes that would otherwise take much longer to be completed [51]: investing resources, correctly addressing policymaking approaches, and bringing academic institutions to collaborate with non-academic ones are all relevant points to implement PM in the health systems.

Nowadays, the classical process of diagnostics and treatment of a condition is based on the guidelines issued by governmental entities or medical societies [33]: when diagnosed with a condition, a patient receives treatment based on the information available, the physician's knowledge of the field, and the available scientific evidence on the issue. Nonetheless, this is hardly the last step of the process. Because the drug posology is mainly decided based on RCTs, this does not consider the individual's peculiar characteristics, which might result in treatment failure [33, 34]. Enabling physicians to access more information on their patients can be crucial to timely addressing emerging conditions that this kind of dynamic information can identify [35]. Here is where the prospect of using genomic-derived information to personalize drug therapy for patients meets with interest from the Chinese scientific community, with limitations also due to the need to thoroughly investigate the variations that exist among the different ethnic groups involved within the same population [52]. Also, the access to proteomic information by physicians is another suitable example: proteomics gives information on how proteins change their conformation over time, leading to increased or reduced susceptibility of the patient to disease or certain drugs [35, 53].

The emerged priorities lay the foundations also for future policymaking on a few PM-related issues. It is easy to imagine that data creation, storage, transfer, remodeling, and destruction, to name a few, will be broadly discussed, given how relevant they are for PM implementation. Medical devices, wearables, clinical examinations, and diagnostic exams will result in the quantity of medical data available spiking, opening up unprecedented paths for clinicians and researchers alike: as pointed out in the process of priority building; however, current data provisions are so restrictive toward secondary use of health

data that this process is not progressing as fast as it could [54]. Not less critical, the facilitation of data transfer between different platforms and infrastructures for the primary use of health data should be considered in light of all the existing restrictions and limitations of health structures, especially smaller ones, which could have an insufficient budget to comply with the technical requirements needed [55]. Besides the existing technical restrictions, ethical, legal, and social issues need to be addressed in the future, as emerging technologies and approaches to health and disease bring new challenges to light [56]. By considering the problem from the perspective of the patient and the relationships in the political, social, and economic fabric, there emerges the need to define and maintain, throughout the value chain, a set of principles and guidelines that declare the centrality of the patient, actor, and recipient of healthcare processes and services.

Health systems should guarantee patients' examinations and diagnostic tests, removing any monetary obstacles, especially when these have a significant added value [57]. Furthermore, bringing patient care closer to people's homes and disadvantaged communities will be crucial to ensuring a more personalized approach to care [58]. Gaining people's trust and engaging them to have a more proactive approach to their health, anticipating the disease with examinations, when possible, is also crucial to this purpose [59].

Healthcare delivery reorganization is complex and will require adequate reimbursement models. Because complex patients are simultaneously affected by different conditions, they require multiple diagnostic tests and clinical examinations by various specialists, taking care of the person as a whole rather than just as a sum of different conditions [60]. Policymakers will need to address this when dealing with reimbursement forms, elaborating new schemes that keep this into account, building up a solid and personalized network revolving around each patient, fostering collaborations of medical and non-medical professionals toward common goals, crossing the borders of academic institutions and national countries, to access the largest amount of information and competencies available [61, 62].

Funding schemes and payment methods are essential to building compliance toward PM instruments. As previously pointed out, European as well as Chinese institutions have recently strongly promoted the development of PM and the study of its integration within healthcare systems. These initiatives have fostered a broad response from academic institutions and private companies, with the aim of enhancing technical capabilities to acquire and process data in this area [63]. However, the adoption of and compliance toward precision testing and medicine is still limited [28]. This is closely linked to the high cost and insufficient co-payment of PM technology. This aspect highlights how careful planning of sustainability and effective usability by end users is necessary during all steps of the implementation process. Economic evaluation and cost planning are of paramount importance in PM, as the adoption of new technologies often has a very high cost, and the benefits may not be immediately apparent.

Our work involved many participants and experts in the field, trying to address relevant issues using a well-defined and validated path to ensure an optimal approach. To our knowledge, our work is the most recent and advanced single piece of literature on the field of PM, trying to address specific issues and future perspectives, building on available evidence and increasing its completeness by adding experts' contributions, resorting to workshops and building up the basis of both discussions and questions to experts on the IC2PerMed project mapping and survey. Despite the strict methodology, this work should be considered in light of some limitations. The resulting priorities cover many topics, but more issues to be investigated might have been neglected, likely because of the inaccessibility of relevant documents on the web, or participants' and experts' own cultural and work background. In addition, bringing together European and Chinese perspectives could lack useful perspectives from participants elsewhere.

Conclusion

The path to implementing PM in health systems is challenging both in the EU and in China. During the IC2PerMed project, our group highlighted, discussed, and addressed several crucial issues for future challenges. In conclusion, a shared approach to addressing the highlighted priorities is crucial for the EU and China to successfully navigate their paths in PM and holds potential for scaling research efforts and maximizing returns. By collaborating closely, they can leverage their respective strengths, resources, and expertise to achieve breakthroughs at an accelerated pace. Through synchronous and coordinated efforts, they can pool their data, resources, knowledge, and infrastructure, enabling them to conduct larger scale studies, analyze diverse patient populations, and generate robust findings with broader applicability. This collaborative approach

would surpass the asynchronous efforts undertaken independently by each, leading to a cumulative impact that far exceeds what could be achieved individually. By combining their strengths, the EU and China can unlock the full potential of PM, revolutionizing healthcare and improving patient outcomes on a global scale. To facilitate this collaboration, the priorities listed in this position paper lay down the groundwork for this change to guide and stimulate future collaboration between the EU and China, strengthening their leadership in PM on a global level.

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Statement of Ethics

This study protocol was reviewed and approved by Ethics Committee of Fondazione Policlinico Universitario A. Gemelli (FPG), approval number 5249. Written informed consent was obtained from participants to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to report.

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Author Contributions

Francesco Andrea Causio and Flavia Beccia extracted the information from the pre-existing documents and drafted and revised the manuscript. Sara Farina, Tommaso Osti, Cosimo Savoia, Hui-Yao Huang, Lily Wang, and Wenya Wang contributed to drafting the manuscript. Stefania Boccia, Chiara Cadeddu, Ilda Hoxhaj, and Walter Ricciardi revised the manuscript. All authors read and accepted the final version of the manuscript.

Data Availability Statement

All the documents mentioned in the manuscript and the workshops' results are available for consultation at https://www.ic2permed.eu/zh/publications-publi. Further inquiries can be directed to the corresponding author.

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