Introduction

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Abstract The transformative vision of a European Health Union, driven by digital innovation and personalized medicine, is based on the idea that health data, when shared responsibly, can enhance individual care and public welfare. This collected volume is situated within the EU's evolving legal and policy landscape and introduces key themes such as data altruism, cybersecurity, and AI governance in healthcare. The volume's structure is presented through three thematic sections: enabling personalized medicine, mapping stakeholder challenges, and addressing liability concerns. Each contribution offers interdisciplinary actionable insights for policymakers, researchers, and industry actors. Given the tension between visionary policy and practical implementation, there is a pressing need for sustainable, inclusive, and patient-centered healthcare systems. This volume calls for continued research to navigate the complexities of personalized medicine as a timely response to Europe's digital health transformation.

Europe has a vision: a society where our medical histories are easily accessible at the tip of a finger no matter where we are. Electronic health records and other data related to our health flow freely but in keeping with respect for European values such as the privacy of our most sensitive information. In this new world, advancements in e-health and telemedicine mean medical personnel can engage with us holistically, devising the most appropriate therapy for our specific needs and personal characteristics. Patients become the decision-makers, developing a partnership with practitioners[1] that transforms the traditional methods of delivering healthcare into a patient-centered process. The benefits are widespread, spilling over into human, social, economic, and planetary well-being.[2] And what we find at

[1] Edgman-Levitan and Schoenbaum (2021).

[2] World Health Organization European Region (2024).

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the end of this spectrum is that when data are not only used for the welfare of one individual but, rather, are safely shared with an "as open as possible, as closed as necessary" approach, the wealth of information shared can strongly support advancements in research, innovation and policymaking, such as developing new drugs and medical devices, optimizing how healthcare is provided, enhancing public policies, and boosting European competitiveness globally.[3]

This is a novel vision of society that counts on the progress of technologies as an accelerator of individual and public welfare. It is also steeped in the firm belief that sharing information is a crucial element for advancing science—one that emerges from the ashes of the global COVID pandemic in the early 2020s. Accelerated by this outbreak and the immeasurable harm it caused, the European Union has looked to strengthen many of the policies that previously underpinned fragility in the continent's numerous national health systems. Today, a new set of policies strategically addresses existing weaknesses, while driving modernization and innovation towards a more resilient Europe. This political priority, called the European Health Union is charged with a set of manifold actions, the expected benefits of which are not confined to broader equity in access to healthcare but also seek to improve the health status of European citizens at large. As such, the European Health Union is expected to have a wide impact on the complete functioning of Europe's societies and economies.[4]

One of the founding elements of the European Health Union is the security of medical supplies. Accordingly, the new policy framework includes updated legislation to govern the development and sale of medical devices. To this end, both the Medical Devices Regulation (MDR)[5] and the In Vitro Diagnostics Regulation (IVDR)[6] were drafted to better protect public health and address safety concerns. For instance, the new regulations increase transparency over the lifecycle of medical products and ensure better monitoring when they are put on the market.[7] Another key pillar of the legislation concerns creating more resilient, accessible, and inclusive health systems. Mindful of the extraordinary benefits that an open science approach brought to the fight against the pandemic (e.g., rapid vaccine development[8]), the EU has placed strong emphasis on digitalizing instruments and services across the healthcare sector as well as on e-health so as to enable broader access to

[3] Machado and Polónia (2022).

[4] European Commission (2024), p. 3.

[5] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

[6] Regulation (EU) 2022/112 of the European Parliament and of the Council of 25 January 2022 amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and the deferred application of conditions for in-house devices.

[7] European Commission (2024), p. 9.

[8] Watson (2022).

healthcare. In these ways, the new policies reflect evidence-based policy-making to future-proof Europe.[9]

Notably, distinct actions support this goal. For example, the European Parliament has passed financial and legislative instruments designed to boost research and innovation in both the public and private sectors. A European health data space has been created as part of a broader EU data strategy.[10] Based on the idea that "data should be available to all – whether public or private, big or small, start-up or giant",[11] the strategy envisions the free flow of personal and non-personal data across organizations, sectors and Member States. This principle is destined to promote competitive innovation, advance scientific research, and provide the necessary evidence for better decision-making. Another principle underpinning the policy framework is an "as open as possible, as closed as necessary" mindset. This brings sharing data into line with European values through a strong legal framework that is based on data protection, consumer protection, safety, cybersecurity, competition, and fundamental rights.[12] This is why the existing digital acquis is strengthened by regulations that strive to establish: diverse, trustworthy data governance mechanisms (via the Digital Governance Act);[13] the safe design and commercialization of artificial intelligence systems (with the AI Act);[14] and a harmonized level of cybersecurity for digital products (with the Cyber Resilience Act).[15]

Among the many objectives arising from this complex and visionary policy architecture, a key goal concerns realizing the full potential of personalized medicine, which is widely understood as a medical model based on the phenotypes and genotypes of individuals sourced from data like molecular profiles, medical imaging, and lifestyle information. It is felt that, with these data, practitioners should be able to: determine a person's predisposition toward a disease; deliver timely and targeted prevention; and/or tailor the right therapeutic strategy for the right person at the right time. Moreover, all these objectives should be achievable within a healthcare system that is "patient-centred" i.e., a system that is better geared to respond to the needs of patients than the status quo.[16] Recognizing the uniqueness

[9] See e.g., the EU4Health Program, European Commission (n.d.).

[10] Regulation (EU) 2025/327.

[11] European Commission (2020), p. 1.

[12] European Commission (2020), pp. 1 and 5.

[13] Regulation (EU) 2022/868 of the European Parliament and of The Council of 30 May 2022 on European data governance and amending Regulation (EU) 2018/1724 (Data Governance Act).

[14] Regulation (EU) 2024/1689 of the European Parliament and of The Council of 13 June 2024 laying down harmonized rules on artificial intelligence and amending Regulations (EC) No 300/2008, (EU) No 167/2013, (EU) No 168/2013, (EU) 2018/858, (EU) 2018/1139 and (EU) 2019/2144 and Directives 2014/90/EU, (EU) 2016/797 and (EU) 2020/1828 (Artificial Intelligence Act).

[15] Regulation (EU) 2024/2847 of the European Parliament and of The Council of 23 October 2024 on horizontal cybersecurity requirements for products with digital elements and amending Regulations (EU) No 168/2013 and (EU) 2019/1020 and Directive (EU) 2020/1828 (Cyber Resilience Act) (Text with EEA relevance).

[16] European Council (2015), p. 3.

of each human condition and the many factors that influence it, data-driven treatments and digital robotic devices are increasingly being developed to help patients and medical personnel benefit from accurate, personalized diagnoses and therapies. Further, the results are having a double-edged effect—at once improving the quality and safety of care for individuals while also bolstering the sustainability of entire healthcare systems.[17]

However, customizing healthcare requires there be synergies between healthcare systems, medical personnel, and patients, as well as cooperation with other branches of research and practice. Proactively including more patients in the system is one route to enhancing the efficacy of personalized medical interventions, but this is also an approach that must be evaluated for its sustainability. Further, the framework for developing new medical devices must account for the complex interplay of norms concerning personal and non-personal data, AI governance, cybersecurity, health law, and liability regimes without raising barriers to technological innovation, development and commercialization.

In the ever-evolving domain of medicine, where some of these new regulations have only recently been adopted, many stakeholders are facing challenges in navigating the new legal landscape. There appears to be a divide between the vision described and the reality of practice. For instance, access to health data for secondary uses is still limited, while legal provisions that protect certain kinds of data (such as personal data or information protected by intellectual property rights) are felt to be obstacles. The many questions that arise call for guidance so as to enable medical products and services that are "safe-by-design". Here, the most innovative research is taking an interdisciplinary approach that deliberately involves a range of different stakeholders from the healthcare economy. Many such collaborations are now being established at the very beginning of the research project and so reflect the concept of responsible data science, where ethical values are steering the reliable use of health data, particularly when the end product or service involves AI.

As an output of the "Biorobotics Research and Innovation Engineering Facilities"[18] and "SoBigData.it: Strengthening the Italian RI for Social Mining and Big Data Analytics"[19] PNRR projects, this volume represents a collection of theoretical, empirical, and case study-based contributions that span disciplinary boundaries to identify and critically dissect the most pressing issues arising from Europe's new policy architecture. Accordingly, most of the chapters suggest some course of action for particular stakeholders of the digital economy, including legislators, policymakers, and scientists. The contributions are organized into three thematic sections.

The first part ("Facilitating and protecting personalized medicine") provides an overview of some of the most pressing legal, ethical and practical challenges that need to be solved to enable health data sharing for commercial purposes or for the

[17] European Council (2015), p. 4.

[18] https://biorob-hub.eu/.

[19] https://www.sobigdata.it/.

public good. Research has been regulated in the digital strategy because various regulatory mechanisms can foster scientific advancements for tailored treatments. In this light, it is paramount to determine to what extent research endeavors are free from constraint when experimenting with new technological paradigms. In doing so, it becomes necessary to understand whether the research exemptions in recent law share similar meanings and scopes. This is a mission that Paseri undertakes by identifying different conceptualizations of the notion. Paseri also provides several criteria for action and governance mechanisms based on open science that could have a positive impact on realizing the full potential of personalized medicine. Notably, new legislative interventions also introduce concepts that put the individual at the center of transformative practices, essentially assigning them a new proactive role in contributing to science. The notion of data altruism introduced in the Data Governance Act (DGA) is key in this respect, where the greater availability of health data is meant to foster better diagnoses and treatments. Two authors examine this concept. First, Rossi explores the role of consent in the reuse of personal data for altruistic purposes, highlighting legal and technical challenges to its user-friendly implementation. In response to them, she provides practical recommendations, with a focus on personalizing the consent experience in a way that offers dynamic interoperable data controls. Complementary to this perspective, Spajic seeks to disentangle the overlaps and conflicts between the DGA as a cross-sectoral piece of legislation, the European Health Data Space (EHDS) Regulation as sector-specific legislation, and the General Data Protection Regulation (GDPR). She shows that existing misalignments, for example in terms of purpose limitation, can cause uncertainty and become practical hurdles to data altruism.

The EHDS Regulation sets forth stringent requirements that are meant to enable trustworthy and secure data sharing, with an important note that the data concerned are not just personal and non-personal health data but also socioeconomic and demographic data as well. In this context, health-related data are seen as a valuable asset and even a currency, and therefore access is tempting to both cybercriminals and data brokers alike. Today, anonymization is a key technique for ensuring the confidentiality of data but it is not foolproof. As a consequence, anonymized datasets may yet reveal personal information while not being tied to the stringent requirements that govern personal data. Gallese argues that we should overcome the blurred distinction between personal and non-personal data. Rather, our aim should be to increase protection over all kinds of data, and the very notion of anonymization should be redefined. Offering a complementary perspective on cyberthreats to health data, Casarosa focuses on wellness devices that have a medical-like function but are not medical devices, yet whose data may be used and/or reused for biomedical progress. She addresses the regulatory challenges and obligations that manufacturers face when security is compromised under the Cyber Resilience Act, the GDPR, the AI Act and the EHDS Regulation. As such, this chapter highlights the practical difficulties that arise from a piecemeal legal framework.

The second part (“Scoping challenges through the players of the personalized medicine ecosystem”) broadens this horizon, by seeking to recompose the views of the actors involved in the digital innovation of patient-centered care. After retracing

the history of personalized medicine, Emdin and Passino focus on empathy as the foundation between physician and patient, as it constitutes the necessary impetus for searching for the most appropriate therapy. While laying down the benefits of this welcome turn in healthcare, they also warn against several hurdles to the success of personalized medicine, such as sustainability risks, the poor representativity of data, the research efforts still required, the socioeconomic disadvantages that certain countries suffer from, and the ethical, legal, and social concerns that arise from targeted treatments. The chapter by Pappalardo, d'Ambrosio, and Calabrò underscores the robust contribution of Health Technology Assessment for ensuring that digital health technologies are developed and implemented in a cost-effective, equitable, and responsible manner throughout their whole lifecycle. While this assessment framework may work well with static medical diagnosis, it struggles when faced with the dynamic nature of emerging technologies. This is why the authors call for revisions to the methodology. Among other suggestions, they recommend that real-world data and real-world evidence, such as patient-reported outcomes, be embedded in the methodology to more reliably gauge the actual benefits and risks of the technologies being assessed. In this way, health technology assessments might ensure more patient-centered care.

Health Technology Assessments are also at the core of the article by Trieste and Turchetti, who add an economic dimension to the evaluation process. Additionally, they lay down other challenges posed by personalized approaches to traditional evaluation methods. These authors also address the complexity and heterogeneity introduced by patient-tailored healthcare in terms of sustainability, recommending that evaluations also include the organizational and economic impacts of personalized medicine. This chapter offers concrete KPIs for a range of stakeholders, together with other tangible outcomes derived from performing Health Technology Assessments.

A stakeholder category that is too often ignored in the personalization processes, unless it is the subject of care, is that of patients. Grigolo, Barbon Galluppi, and Sirtori explore the progressive evolution of the role of expert patients as an indispensable agent within each phase of planning and executing personalized care. The proactive role they take on within the emerging medical framework completely replaces the traditional view of patients as passive receivers of care. Similarly, Christou assumes the role of an entrepreneur in the face of these newly introduced regulations, such as the Medical Device Regulation, to illustrate how medical device companies might struggle to comply with the host of new product safety requirements set in the legislation. He attributes many of these problems to traditional business models, a lack of resources, and a lack of capacity and knowledge.

Another empirical contribution is provided by Fagioli, Mazzarini, Gennari, and Crea, who delve into the cutting-edge bioengineering techniques that are adopted in the personalized control of active bio-robotic protheses. They argue that an integrated approach to responsible biomedical R&D requires ex-ante regulatory evaluation. As an example, they explore the applicability of the new AI Act's requirements and obligations as they pertain to robotic protheses. This section concludes with a multifaceted overview of the barriers to integrating robotics into rehabilitation,

drafted by Aprile, Germanotta, Mauro, and Fasano. The authors maintain that, to overcome these obstacles, it is imperative that we not only devise novel organizational models of treatment but that we also ensure they are evaluated for sustainability. Additionally, effectively training the medical personnel who administer these technologies is key, alongside robust regulatory frameworks that streamline reimbursement policies and ensure equitable access for all.

The third and last part ("The challenges of personalized medicine to liability") focuses on the ex-post issues posed by the adoption of highly specialized medical technology. Despite the effectiveness of medical devices and therapies, patients may suffer harm, which can be as personalized as the technology causing it. But how do the liability rules respond to such challenges in these cases? Parziale asks whether the newly introduced norms of the Product Liability Directive and the proposed AI Liability Directive may simply prompt medical device manufacturers to adopt countermeasures to address the new risks. They also suggest that the new rules do not offer sufficient guarantees to the "first victims" of unknown risks. Blatti and Tramacere illustrate another liability challenge posed by tomorrow's medicine by arguing that the medical predictions made by AI-based devices may be unrealistic and inappropriate when implemented in real-world conditions. Within such devices, design choices become paramount and should address transparency and accountability of various stakeholders, if the AI Act is to reduce all the likely risks to a patient's health. The chapter concludes with observations on a new standard of care that could emerge—one that may or may not draw from the obscurity of machine learning approaches in a similar way to the evidence-based frameworks already used in healthcare today. Lastly, Gennari analyzes ex-post liability under the new policy architecture as it applies to the software embedded in AI-based prosthetics. She highlights that the prescribed liabilities could positively influence market updates to these highly technical devices.

Thanks to these contributions that include both members of the BRIEF Law and Policy Hub (LaPoH) and fruitful collaborations with different institutions, this volume presents a suite of uniquely original analyses as well as a set of recommendations to be considered when assessing the EU's emerging digital strategy. The three sections of this book integrate pioneering theoretical and empirical knowledge about the cutting-edge technologies used in personalized medicine. The perspectives taken combine the various domains of law, medicine, computer science, bioengineering, and economics. In this ever-evolving area of knowledge, these observations and findings, which were first presented at the BRIEF conference held in Pisa on 14 October 2024 and now appear in these pages, only aim to provide preliminary answers to the many questions that the world of personalized medicine opens up. Further research is necessary to design a more equitable healthcare system where individual differences are valued.

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