For reprint orders, please contact: reprints@futuremedicine.com

Personalized medicine in Austria: expectations and limitations

Mirjam Pot^{*,1} , Marc Brehme² , Amin El-Heliebi^{3,4}, Brigitte Gschmeidler⁵, Philipp Hofer⁶, Thomas Kroneis^{3,4} , Michael Schirmer⁷, Simone Schumann⁵ & Barbara Prainsack^{1,8}

¹Department of Political Science, University of Vienna, Vienna 1010, Austria

²Ribbon Biolabs GmbH, Vienna 1030, Austria

³Medical University of Graz, Gottfried Schatz Research Center, Division of Cell Biology, Histology and Embryology, Graz 8036, Austria

⁴Center for Biomarker Research in Medicine, Graz 8010, Austria

⁵Open Science - Life Sciences in Dialogue, Vienna 1030, Austria

⁶Medical University of Vienna, Department of Pathology, Vienna 1090, Austria

⁷Department of Internal Medicine, Medical University of Innsbruck, Clinic II, Innsbruck 6020, Austria

⁸Department of Global Health & Social Medicine, King's College London, Strand, London WC2R 2LS, United Kingdom

*Author for correspondence: mirjam.pot@univie.ac.at

First draft submitted: 30 April 2020; Accepted for publication: 24 July 2020; Published online: 7 October 2020

Keywords: ethical issues • legal issues • policy issues

In this short article, we provide a summary and commentary on the discussion on expectations and limitations of personalized medicine (PM) that took place at the annual conference of the Austrian Platform for Personalized Medicine (ÖPPM) in October 2019. With this, we aim to provide insights into the questions and topics currently discussed in the context of PM in Austria.

The Austrian Federal Ministry of Education, Science and Research sees PM as one of the most significant societal challenges of our time. To support the coordination and the collaboration of stakeholders such as physicians, medical researchers (clinical, basic and translational), social scientists, science communication experts, patient advocates and representatives of the pharmaceutical industry in Austria and beyond, the Ministry made funding available for the establishment of the Platform in 2017. Founded by the three Austrian medical universities in Vienna, Graz and Innsbruck as well as the Research Center for Molecular Medicine of the Austrian Academy of Sciences, ÖPPM has been active as a non-profit association since then. To date, it has 140 individual and 16 institutional members; the latter include non-profit organizations such as universities, extramural research institutions, patient advocacy groups, scientific associations and the association of the Austrian pharmaceutical industry.

The Platform aims not only to foster collaboration across different organizations and disciplines, but also to raise awareness about PM and to contribute to health literacy within the Austrian general public. One of the means by which ÖPPM works toward these objectives is an annually held conference. One day of the 2019 conference was dedicated to the exploration of expectations and limitations of PM. This article provides an overview of the main issues as discussed at the conference, providing a picture of the status quo of cross-disciplinary debate in this field. Three topics featured most prominently: first, different definitions of PM and what implications these different definitions have for policy and practice; second, the benefits of PM for individual and population health as well as for the healthcare system; and third, the challenges that PM and the digitization of healthcare pose regarding equal access to care, patients' trust and the regulation of data use. Positive expectations seem to prevail when it comes to how PM influences individual and population health. Two important concerns articulated at the conference, however, were the emergence of new cleavages in access to healthcare and diminished patient trust – if PM is narrowly understood as data-driven decision-making that can easily be automated.

Different definitions of PM

About two decades after the end of the Human Genome Project, the question of how to define PM and how to separate it from other approaches is still a much-debated issue. Schwarz [1] has shown that Austrian experts

and citizens consider PM a somewhat inconsistent and ambivalent concept. Some experts find the term unduly vague – for them, it is little more than a buzzword that is strategically used to attract research funding. Others argue that PM is a well-established concept, but has yet to be filled with more specific practical meaning. Experts also expressed the concern that the term PM might wrongly create expectations about holistic ways of practicing medicine, including, for example, psychosocial care. Citizens, indeed, perceive exactly this extensive understanding of the term as positive, but also stress its vague and confusing character [1].

ÖPPM has adopted the definition of PM of the European Council that is also used by the International Consortium for Personalized Medicine. In this understanding “personalized medicine refers to a medical model using characterization of individuals’ phenotypes and genotypes (e.g., molecular profiling, medical imaging and 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” [2]. Among the members of the Platform, however, questions remain about what the term ideally should include. Narrow approaches that equate PM with genomic medicine are easier to measure and operationalize and allow for setting more specific goals defined by a limited number of stakeholders. At the same time, however, narrow definitions sometimes neglect important aspects of health and healthcare and miss out on the opportunity of achieving a more extensive impact that might come with broader approaches to personalization. Such a more expansive approach could foster the formal inclusion of patient preferences as well as information about patients’ social and cultural characteristics into healthcare provision. Furthermore, combining PM with the principles of person-centered care could yield benefits for prevention, diagnosis and treatment as well as the evaluation of new treatment options. In this context, the previously mentioned perceptions regarding the term PM expressed by Austrian citizens [1] are not so far off, and adopting a broader view would meet these expectations.

Regardless of what definition is employed, PM is crossing disciplines, medical specialties and contexts of practice. With the adoption of a broader definition, however, the intersections of professional fields will grow further. While it may seem that the continuing and partly iterative discussions about the definition of PM, as well as the question about the relevant stakeholders, are slowing down the implementation of PM, the opposite might be the case. Bensaude Vincent [3] has shown that PM is a buzzword open for interpretation but still stable enough to be recognized and adapted to the logic of different fields and research agendas. The primary function of buzzwords is to bring together a variety of actors with the common aim to achieve something – such as desirable societal futures but also more practical issues such as gaining funding or building research networks – even if their particular stakes and concerns differ. The reason why the discussion about the definition of PM remains, however, is that definitions are not only about semantics but also have real-world consequences. Whether we see PM as being more or less synonymous with genomic medicine or whether we consider patient-centeredness as a necessary feature of PM influences where research funding goes, what infrastructure spending is focused on and what expectations are raised among patients. This means that, whatever definition is used, PM is performative; it ‘has politics’, as Bensaude Vincent [3] argued.

Benefits for the few or the many?

The question of whether PM will primarily yield benefits for a small share of patients or whether it can contribute to better healthcare provision and health for the majority remains another much-debated issue. Furthermore, many issues around implementation are still unresolved. While these debates are not limited to Austria, we give a brief overview of the most pertinent issues discussed within ÖPPM.

For patients with rare diseases, faster and more accurate diagnoses and treatments are considered the prime benefit of PM. Site-specific studies on rare cancer entities, for example, suffer from extremely low incidence, and thus lack explanatory power. In this context, a promising feature of PM is its potential for cancer site-agnostic study designs providing multiple advantages over pathology- or symptom-driven approaches [4]. Cancer site-agnostic approaches allow for biomarker-based study designs across cancer entities, thereby increasing the number of cases, which will likely lead to a much better understanding of rare diseases. Recently, the FDA in the USA approved pembrolizumab, a PD-1 inhibitor, for the treatment of unresectable or metastatic solid tumors, regardless of tumor site or histology [5].

Some, however, argue that PM may provide not only benefits for individual patients but also the healthcare system and society as a whole [6]. Benefits include better possibilities for the timely diagnosis of disease, which could also reduce healthcare spending, and improvements in public health. The early identification of familial hypercholesterolemia through genetic testing, for example, has been proven to be highly cost-effective [7]. While the

focus currently still is on the diagnosis, PM could eventually also contribute to disease prevention. Furthermore, PM could also help to reduce healthcare spending via tailored therapeutics. For example, additional investments of 1.7 million Euros into EGFR genetic testing could save health insurers 69 million Euros through identifying lung cancer patients with this particular mutation [8]. Therefore, from an economic perspective, benefits for society may result from cost-savings in some parts of the healthcare system and the redirection of resources to underfunded areas. From a public health point of view, a large number of patients could also benefit from the adoption of a 'precision public health' approach [9]. In pharmacogenomics, for example, once variants that adversely react to therapeutics such as statins are identified, therapy decisions can be rather easily adapted [10]. The question of whether precision population health will yield more significant benefits than conventional public health approaches, however, remains [11]. Furthermore, Vogt *et al.* [12], have recently pointed out that the widespread use of PM and screening with big data might also increase overdiagnosis, which would mean a negative impact on population health.

Besides the promising opportunities of PM, such as improving patient outcomes and reducing costs, several limitations apply, especially when it comes to the translation of lab technologies into routine clinical care. This includes approaches such as multigene panel or liquid biopsy analysis [13]. Wild and Grössmann [14] recently evaluated such a translation attempt of a next-generation sequencing approach and assessed a multigene panel investigating a few hundred genetic alterations in cancer for their clinical utility to prolong overall survival and improve quality of life. Although studies indicate that 54–96% of solid tumors showed multiple genetic alterations by the multigene panel assay, for only a small number of investigated alterations, approved drugs were available that target these alterations. This is primarily due to the relatively low number of (only 31) approved cancer companion diagnostic tests approved by the EMA [14]. Therefore, to improve PM approaches, drugs at very early stages of development (e.g., research stages), which can be used for companion testing, are the most promising candidates to achieve the high expectation of PM. Genomics, moreover, is only one first step in PM, and more detailed molecular characterization of tumor heterogeneity, the immune system or metabolic states will further enhance PM approaches [15].

PM has the potential to improve the health outcomes of patients with both rare and common diseases. Outcome parameters, however, are still often difficult to define as they, besides mortality, also include life-quality, which is composed of physical, mental and social aspects [16]. In this context, digital health technologies provide new opportunities to improve the assessment of multiple outcome parameters, and therefore can also better reveal potential inequalities in current healthcare provision. It is expected that based on such comparative outcome data, we will gain evidence on important quality aspects, which can support preventive medicine. Most importantly, for PM, however, such data can guide the implementation of evidence-based approaches to lower costs through the stratification of patients according to the risk of certain side effects or reduced treatment responses.

Challenges posed by digital health technologies

In the context of digital data and technologies gaining more importance in healthcare, a concern raised at the meeting pertains to developments toward automated decision-making. Especially against the backdrop of healthcare systems facing budget cuts and austerity measures, we may see the emergence of a new cleavage emerging in healthcare, in particular, if PM is narrowly understood as the data-driven personalization of prevention, diagnosis and treatment. Artificial intelligence, more generally, and machine learning, in particular, have been suggested as solutions to deal with the problem that we are creating massive amounts of data that human beings do not have the training, resources or capacities to interpret [17]. Automating aspects of healthcare that are currently delivered by humans is not always a bad thing, because, for example, it could leave doctors with more time for communication with patients. In a context of budgetary restraints and already existing unequal access to healthcare, however, the employment of automation technologies may lead to a scenario where those who can afford it might have access to boutique medicine where human doctors provide high-tech and high-touch services. The others, in contrast, would have access to mostly automated medicine, where machines analyze increasing amounts of data, and patients' engagement with the healthcare system occurs evermore through digital technologies.

In this sense, the proliferation of digital technologies is not a problem in itself because such technologies can be helpful tools to deal with the ever-increasing amount of healthcare data. If such technologies, however, were used to replace human doctors to cut costs, they might exacerbate already existing inequalities in access to services. In Austria, for example, new personalized cancer therapies – like most healthcare interventions – are covered by the social insurance system. At the same time, we see a devaluation of high-touch services and the interactional

aspects of care more generally; for example, physicians receive relatively low remunerations for conversations with patients in comparison with conducting diagnostic tests. Furthermore, the Austrian healthcare system is ever more dependent on a growing private sector that covers an essential share of service provisions [18]. In this context, it might not so much be the access to therapies, but the relational aspects of healthcare that are based on human interaction and the interpretation of data by doctors that might become a luxury good [19]. Already now, private doctors have more time to spend with their patients than doctors in the public system. The advancement of PM and digital technologies could contribute to an aggravation of this cleavage, where everyone has access to diagnostic tests and tailored therapies. Still, only some enjoy the privilege of extensively discussing their results with doctors and weighting treatment options together. This means that in the age of PM, personal care may become a scarce resource.

This, in turn, also raises the question of how data-driven PM is affecting the doctor-patient relationship. On the one hand, technological support may lead to more accurate decision-making and thereby increase patients' trust. This is particularly the case for rare diseases where doctors often lack the specific expertise to make informed decisions. More generally, the employment of technologies to support the automated interpretation of variants could also increase patients' trust by creating more time for providers to spend on communication with patients and the interpersonal aspects of care. On the other hand, in his keynote lecture at the ÖPPM conference Shlomo Cohen identified three potential challenges to doctor-patient-trust in PM. Data-driven, automated analyses might decrease patients' trust due to the decline in relevance of doctors' experience and clinical competencies, less intimate communication between doctors and patients because of the 'intrusion of technology' into exam rooms, as well as new problems and patients' concern about data privacy and confidentiality [20]. A decline in patients' trust would likely have negative implications for individual health outcomes as well as for the performance of the healthcare system in general. While there are benefits to automation, the concerns regarding this issue call for a considered integration of digital data technologies into healthcare settings.

As to concerns that patients' trust might diminish due to a decrease in the relevance of doctors' experience and expertise in connection with PM, data-intensive medicine also brings with it the need for new clinical competencies necessary for the interpretation of data [17]. In this sense, it might as well be that PM leads to a diversification or change in doctors' competencies, rather than a general decrease of their relevance. At least if data technologies take a supportive function in clinical practice and not replace crucial aspects of patient-provider encounters based on human interaction. Ultimately, only a synergistic interplay of data-driven technologies, the professional interpretation of data, personal care by physicians and patients' involvement represents a meaningful approach to outcome-based medical care for the Austrian society.

Furthermore, data-driven healthcare presses also for appropriate preventive legal and regulatory frameworks such as in the field of privacy protection. With the introduction of the General Data Protection Regulation (GDPR), the EU has improved the existing Data Protection Directive by further harmonizing and strengthening the rights of data subjects. This also includes the protection of their health-related personal data, as derived during medical examinations. While general mechanisms and aspects of the GDPR, such as privacy by design [21] or the prohibition of discriminatory profiling [22], are relevant and enforced for health data, additional more specific safeguards for personal health data have been implemented within the GDPR. While the GDPR recognized that clinical trials or innovations in mobile health require data protection safeguards to ensure peoples' trust and confidence, further and related privacy protection mechanisms ought to be developed and implemented. Different EU bodies have already started to act on issues such as patient data transfer and exchange in cross border healthcare [23]. Evidence-based PM is per definition data-intensive, and its success is dependent on high-quality computing technologies such as machine learning algorithms. Considering these technologies reliance on sensitive patient information, the European Commission evaluates the use of artificial intelligence in medicine as highly sensitive and is planning to create and implement tests and certifications before approval within the EU marketplace.

While we welcome these efforts overall, they also have some shortcomings. In the context of big data approaches and algorithmic analyses, the differentiation between sensitive health data and other kinds of less sensitive data have to be questioned. This is because self-learning algorithms can also detect correlations impacting health in data that is not health-related at first sight; for example, when social media data are analyzed to identify people with depression [24]. This means that all digital data are potentially sensitive. In this context, instead of differentiating data based on their degree of sensitivity, Prainsack [25] has suggested to distinguish between different forms of data use. Accordingly, the collection and use of data intended to create public value should be regulated more permissively than data uses mainly directed to the generation of private profits. This also points to the fact that

there is more at stake than only privacy protection when it comes to data regulation in connection with PM. Patients' and public trust in the use of data technologies will also depend on whether their use will contribute to the common good or not. In this sense, a crucial aspect of creating trust is a broader public debate about PM. Such a debate should be focused on the value and benefits of PM, but also include the discussion of hitherto unsolved social, ethical, legal and economic questions. Besides initiating a public debate about what kind of PM we want, governments and payers should incentivize patients' engagement and reward their cooperation and trust in PM.

Conclusion

In the Austrian discussion, the question of how to define PM, its benefits for individual and populations health as well as for the healthcare system and the challenges connected to the implementation of digital data technologies feature prominently. Although in Austria, PM is still very much focused on genomic medicine, more detailed molecular characterizations of patients, and different stakeholders' perceptions and interests shape the future direction of PM approaches. By many, PM is considered to create benefits for patients with rare diseases but also implies better treatment options and improved outcomes for patients with common diseases as well as the potential to optimize the use of healthcare resources. Research on the financial impact of PM on healthcare systems and optimal funding schemes, however, is ongoing, and different future scenarios seem possible (see, e.g., the project Health Economics for Personalized Medicine, HEcoPerMed). Importantly, to secure and further equitable access to high-quality healthcare, concerns about the aggravation of cleavages in connection with austerity measures and the automation of healthcare have to be taken seriously, and such developments have to be counteracted on time. More generally, we have to discuss which role we want digital technologies in connection with PM to play in healthcare settings and how we can implement them in ways that are beneficial for patients, providers and the healthcare system.

Acknowledgments

The authors thank Katharina Kieslich for her valuable comments.

Financial & competing interests disclosure

The Austrian Platform for Personalized Medicine (ÖPPM) is funded by the Austrian Ministry for Education, Science and Research (Grant number: BMWFW-360.086/0001-WF/V/5b/2017). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Open access

This work is licensed under the Attribution-NonCommercial-NoDerivatives 4.0 Unported License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>

References

- Schwarz C. Personalisierte Medizin für und mit BürgerInnen: Bericht über die ExpertInnen-Dialoge, schriftlichen Stellungnahmen und BürgerInnen-Dialoge. Open Science, Vienna, Austria (2015). https://assets.openscience-files.or.at/_/38/11/38113459.pdf
- European Council. Council Conclusions on Personalised Medicine for Patients 2015/C421/03 (2015). [https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XG1217\(01\)](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XG1217(01))
- Bensaude Vincent B. The politics of buzzwords at the interface of technoscience, market and society: the case of 'public engagement in science'. *Public Underst. Sci.* 23(3), 238–253 (2014).
- Baretti M, Azad NS. Precision cancer trials with immunomodulatory agents: personalizing histology agnostic approaches. *Cancer J.* 25(4), 287–295 (2019).
- Marcus L, Lemery SJ, Keegan P, Pazdur R. FDA approval summary: pembrolizumab for the treatment of microsatellite instability-high solid tumors. *Clin. Cancer Res.* 25(13), 3753–3758 (2019).
- Wilsdon T, Barron A, Edwards G, Lawlor R. The benefits of personalized medicine to patients, society and healthcare systems: final report. Charles River Associates, London, UK (2018). <https://www.ebe-biopharma.eu/wp-content/uploads/2018/07/CRA-EBE-EFPIA-Benefits-of-PM-Final-Report-6-July-2018-STC.pdf>
- Pelczarska A, Jakubczyk M, Jakubiak-Lasocka J *et al.* The cost-effectiveness of screening strategies for familial hypercholesterolaemia in Poland. *Atherosclerosis* 270, 132–138 (2018).

8. Nowak F. Personalised medicine: a nationwide initiative for an equal access to cancer treatment in France. Presented at: *EuroBioForum*. Brussels, Belgium (18–19 April 2012).
9. Chowkwanyun M, Bayer R, Galea S. “Precision” public health: between novelty and hype. *N. Engl. J. Med.* 379(15), 1398 (2018).
10. Nagar SD, Moreno AM, Norris ET *et al.* Population pharmacogenomics for precision public health in Colombia. *Front. Genet.* 10, 241 (2019).
11. Khoury MJ, Galea S. Will precision medicine improve population health? *JAMA* 316(13), 1357–1358 (2016).
12. Vogt H, Green S, Ekström CT, Brodersen J. How precision medicine and screening with big data could increase overdiagnosis. *BMJ* 366, 15270 (2019).
13. Heitzer E, Haque IS, Roberts CE, Speicher MR. Current and future perspectives of liquid biopsies in genomics-driven oncology. *Nat. Rev. Genet.* 20(2), 71–88 (2019).
14. Wild C, Grössmann N. FoundationOne®CDx: Bestimmung von genetischen Profilen Solider Tumore. Rapid Assessment Nr. 14. Ludwig Boltzmann Institut für Health Technology Assessment, Vienna, Austria (2019). https://eprints.aihta.at/1215/1/Rapid_Assessment.014.pdf
15. Schütte M, Ogilvie LA, Rieke DT, Lange BMH, Yaspo ML, Lehrach H. Cancer precision medicine: why more is more and DNA is not enough. *Public Health Genomics* 20(2), 70–80 (2017).
16. World Health Organization (WHO). Constitution of the World Health Organization (2006). <https://www.who.int/governance/eb/who.constitution.en.pdf>
17. Fiske A, Prainsack B, Buyx A. Data work: meaning-making in the era of data-rich medicine. *J. Med. Internet Res.* 21(7), e11672 (2019).
18. Bachner F, Bobek J, Habimana K *et al.* Das österreichische Gesundheitssystem: Akteure, Daten, Analysen. *Gesundheitssysteme im Wandel* 20(3), 1–288 (2019).
19. Prainsack B. The advent of automated medicine? The values and meanings of precision. Submitted for inclusion in: *Can Precision Medicine be Personal; Can Personalized Medicine be Precise?* Barilan YM, Brusa M, Ciechanover A. (Eds). Oxford University Press, Oxford, UK.
20. Cohen S. Potential challenges to doctor-patient-trust in personalized medicine. Presented at: *3rd ÖPPM Annual Conference*. Vienna, Austria (14–15 October 2019).
21. O’Connor Y, Rowan W, Lynch L, Heavin C. Privacy by design: informed consent and internet of things for smart health. *Procedia Comput. Sci.* 113, 653–658 (2017).
22. Wachter S. Normative challenges of identification in the internet of things: privacy, profiling, discrimination, and the GDPR. *CLSR* 34(3), 436–449 (2018).
23. European Data Protection Board, European Data Protection Supervisor. Joint Opinion 1/2019 on the Processing of Patients’ Data and the Role of the European Commission within the eHealth Digital Service Infrastructure (eHDSI) (2019). https://edps.europa.eu/sites/edp/files/publication/19-07-15_edpb_edps-joint_opinion_ehealth_en.pdf
24. Nambisan P, Luo Z, Kapoor A, Patrick TB, Cisler RA. Social media, big data, and public health informatics: ruminating behavior of depression revealed through twitter. Presented at: *48th HICSS* Kauai, HI, USA (5–8 January 2015).
25. Prainsack B. Research for personalised medicine: time for solidarity. *Med. Law* 36(1), 87–89 (2017).