Four Governance Challenges for Personalized Health: A Systematic Review

Authors[1]

Philipp Trein

Joël Wagner

Abstract

Policy points: To improve the governance and policymaking regarding personalized health, we suggest that policymakers should focus on the following action points:

- Harmonize research infrastructures to augment the possibilities for collaborative research.
- Build trust among citizens to utilize personalized health services.
- Create regulatory frameworks that organize collaboration and protect individuals against discrimination.
- Integrate the results of genomic research in health systems to provide better health care and prevention.

[1] Philipp Trein (philipp.trein@unil.ch) and Joël Wagner (joel.wagner@unil.ch) are with the Department of Actuarial Science, University of Lausanne, Faculty HEC, Extranef, 1015 Lausanne, Switzerland. Joël Wagner is also with the Swiss Finance Institute, Lausanne, Switzerland. Both authors acknowledge financial support from the Swiss National Science Foundation (SNSF, grant no. CRSII5 180350). Both are grateful to the colleagues from the SNSF Sinergia project “Development of Personalized Health in Switzerland: Social Sciences Perspectives" who made invaluable suggestions to improve the paper and for specific publications to be included in the review.

Context: In recent years, research on personalized health (PH) has advanced and promises many new possibilities for the treatment and the prevention of diseases; these innovations could change health systems profoundly. Against this background, it is crucial for researchers and policymakers to know about the governance- and policy challenges related to PH.

Methods: This paper presents the results of a systematic literature review on governance- and policy challenges related to PH. In using a PRISMA protocol search, we analyze publications dealing with governance and policy making in the field of PH. We conducted two search iterations in Web of Science. The first one consists of 47 publications that constitute the main corpus of papers for this review, which we examine in detail. Through a second search, we add 98 additional papers that complement the main corpus.

Results: Our analysis demonstrates that research regarding governance and policymaking of PH deals with four topics. Firstly, the establishment, steering, and harmonization of research infrastructure; secondly, the inclusion of citizens to create trust in the personalized approach to health; thirdly, the regulation of data production to avoid discrimination and to organize international collaboration; fourth, the inclusion of personalized health and medicine in existing health policies to improve the cure and prevention of diseases.

Conclusions: Our research contributes to the literature in mapping challenges for transferring technological innovations in personalized health into health policy. This literature review suggests that public policies for personalized health should integrate the four governance challenges into existing health systems.

Keywords personalized health; research infrastructure; trust; regulation; health system

Introduction

In the wake of the Human Genome Project and the development of new digital technologies, a whole range of novel possibilities has appeared in the area of public health and health care. In referring to labels such as personalized health (PH), personalized medicine, stratified health, or 4P (predictive, preventive, personalized and participatory) medicine (Chataway et al., 2012; Flores et al., 2013; Andreu-Perez et al., 2015; Heart, Ben-Assuli and Shabtai, 2017), researchers have explored how these technological innovations for preventing and treating diseases can be translated into health practice (Zeggini et al., 2019).

Against the background of these innovations in medical and health science, scholars have also discussed how to govern these technological advances in PH, notably how to translate them into health policies. For example, innovations regarding the personalized prevention and cure of diseases need to be integrated into existing systems of health care provision (Stark et al., 2019). Such efforts should be complemented by a regulatory framework to protect patients and citizens at large against discrimination based on their genetic profiles (Green, Lautenbach and McGuire, 2015), and should create incentives for providers and payers to develop products for medical markets (Phillips et al., 2014; Kukk, Moors and Hekkert, 2016).

In this article, we conduct a systematic review of the literature dealing with the governance of PH in a wider sense. In other words, the goal of this paper is to synthesize the vast literature that deals with the coordination of public and private actors (Kickbusch and Gleicher, 2012) at a national as well as at a global level (Frenk and Moon, 2013), aiming at making policies related to PH. Our review focuses on the challenges for policymakers – defined in a wide sense including private and public actors – that emerge against the background of technological developments to implement a more personalized approach in prevention and health care, for example policies regulating, financing and providing genetic tests. In using the results from a systematic literature review based on a PRISMA (Preferred Reporting Items for Systematic

Reviews and Meta-Analyses) protocol, we map four related challenges decisionmakers face when putting re- search on personalized health into practice.

According to our analysis, actors have to deal the following four interrelated policy problems. Firstly, there is a need to harmonize research infrastructure, for example biobanks. Secondly, policymakers need to cultivate trust into the new technologies for personalized health and medicine, in the population. Thirdly, there is a need to create appropriate regulations regarding standards for data protection and sharing concerning personalized health. Finally, policymakers face the problem of integrating these new technologies into existing health systems. The findings of our review contribute to our understanding of the challenges that policymakers face when transferring new technologies into practice, in general, and in the field of health specifically. Moreover, our literature review supports and reiterates expert recommendations regarding the implementation of personalized health into practice (Florin and Escher, 2017).

Review strategy and method

We conduct a review of the literature using the PRISMA protocol procedures (Moher et al., 2015). Usually, researchers use this review protocol in medical sciences (Booth et al., 2011) but more recently scholars have also applied it to problems beyond medical research, such as in public policy analysis. An example of such a study can be found in Biesbroek et al. (2018). To carry out our search, we use the Web of Science Core Collection database (cf. webofknowledge.com). We include all years (1900–2019), document types (journal articles, books, chapters, conference proceedings, etc.), as well as all Web of Science categories, i.e., subject areas.

Given that our review focuses on a (latent) theoretical concept, i.e., governance, we search the literature in two iterations (see Figure 1). The first step focuses on PH and different related search terms combined with “governance” while in the second step we replace the term governance with “policy”. The alike research terms to “personalized health” that we use are

"personalized health care", "precision medicine", "individualized medicine", "personalized medicine", "stratified medicine", "genetic medicine" and "genomic medicine". We also include all combinations of alternative spellings (personalized/ personalised, individualized/ individualised, health care/healthcare).[2] We choose the additional term policy, as governance essentially relates to the efforts of stakeholders to coordinate their activity to solve policy challenges through public policies (Goetz, 2008; Trein, Thomann and Maggetti, 2019). We have also tested the search term "public policy" but that search did not return meaningful results. This approach ensures that we do not miss articles that are substantially interesting to us but do not use the term governance.

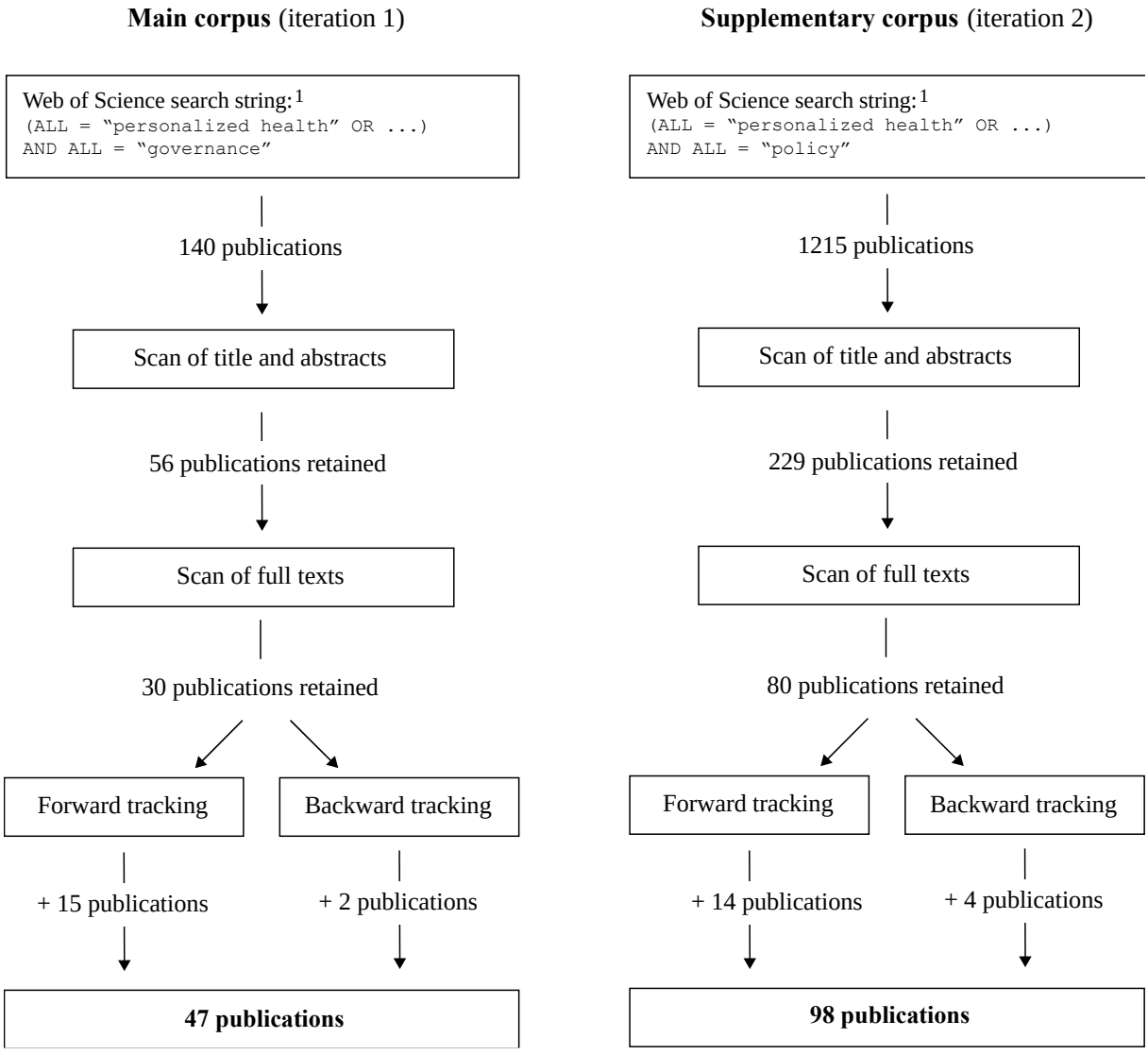
To conduct the literature review, we followed a five-step process (Figure 1). Firstly, we carried out the search in the Web of Science database using the above-mentioned keywords. Secondly, we read the title and abstract of the publications to verify if they are interesting for our topic and excluded those that do not fit. Thirdly, we scanned the full-text of the publications and retained those that corresponded to the criteria we are interested in. Fourth, we pursued a forward tracking search of the articles, i.e., we skimmed the titles of the publications that cite the selected works in Google Scholar (cf. scholar.google.com). Finally, we embarked in backward tracking, which entailed scanning the bibliography of the selected publications.

Our search results in two corpora of publications (Figure 1). The main corpus contains those publications that have emerged from the selection procedure of the first iteration and contain the term governance. The publications emerging from the second iteration, using the search term policy, form the corpus of supplementary publications. The sizes of both corpora differ, which is due to the two different populations from which we started our search but also as

[2] The exact search string for the first iteration is (ALL="personalized health" OR ALL="personalised health" OR ALL="personalized healthcare" OR ALL="personalised healthcare" OR ALL="personalized health care" OR ALL="personalised health care" OR ALL="precision medicine" OR ALL="individualized medicine" OR ALL="individualised medicine" OR ALL="personalized medicine" OR ALL="personalised medicine" OR ALL="stratified medicine" OR ALL="genetic medicine" OR ALL="genomic medicine") AND ALL="governance". For the second iteration, the chain of keywords is the same while at then end of the search string "governance" is replaced by "policy".

authors use the term policy much more frequently than governance, even when it does not refer to public policies.

Figure 1: Review protocol



The scanning of titles, abstracts, full-texts, backward and forward tracking, as well as the subsequent reading applied themes related to governance (Ansell and Torfing, 2016), public policy (Knoepfel et al., 2011), health policy (Blank, Burau and Kuhlmann, 2017) and health governance research (Böhm et al., 2013). More precisely, retained papers needed to deal with the following themes:

- Regulations, e.g., laws, guidelines and voluntary codes, regarding PH and individualized medicine provision, for example regarding quality standards for precision medicine. This includes but is not restricted to regulations on financing and providing preventative and curative interventions as well as on research and data-related infrastructure.
- Public and private actors involved in (public) policymaking regarding PH and individualized medicine, such as administrations, governments, health insurers, doctors, pharmaceutical agencies, patient organizations, and the relations between them, including conflicts and coordination between these actors.

The first author selected the papers. The second author re-selected some of the papers as a validity test. In addition, to this systematic literature review, we include publications suggested by colleagues from the interdisciplinary research project "Development of Personalized Health in Switzerland: Social Sciences Perspectives" which we mention in the acknowledgments of the paper.

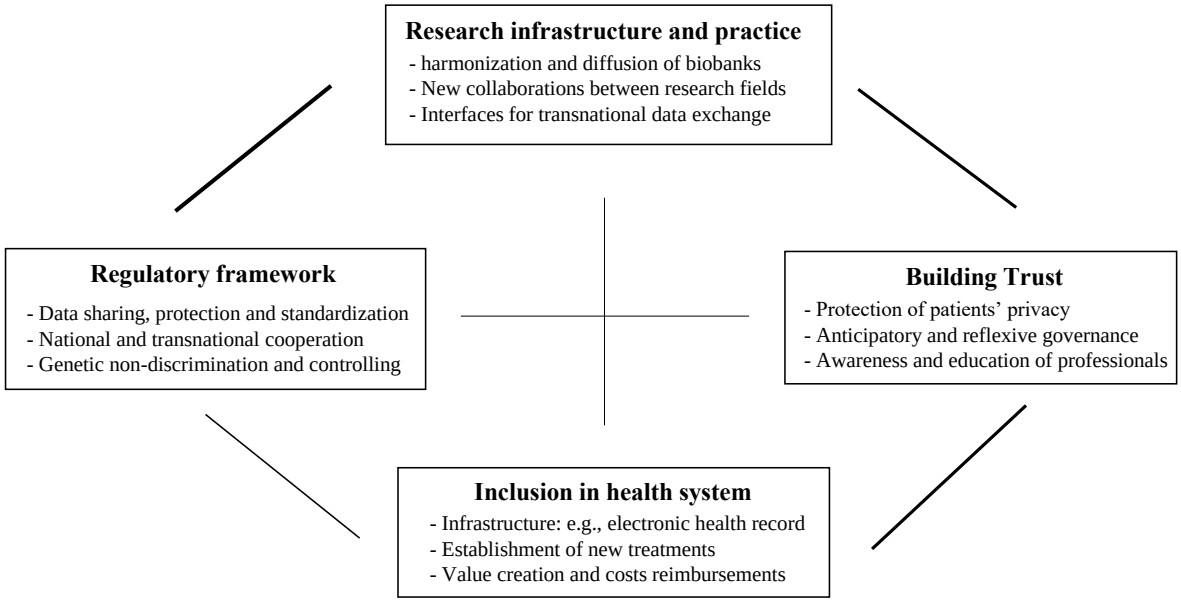
For the substantial analysis of the publications, we focus on the main corpus of publications. For each of the 47 publications we record the region, the methodology, the key contents and main results, as well as to which of the main governance challenges discussed in the sequel it relates to (see the synopsis of the reviewed papers provided in the Appendix). These governance challenges are derived from our readings of the main text corpus. Further, we use the publications from the supplementary corpus to complement our reading and illustrate the four governance challenges that emerge from the literature.

Four governance challenges

We summarize the results from our reading of the selected publications in both main and supplementary corpora in the format of four governance challenges. The first governance challenge entails to create a research infrastructure and practices that correspond to the new

advances in genetic research but also to the new possibilities of data sharing and analysis that emerge from digitalization. The second challenge deals with the building of trust, notably among patients but also among citizens in general. The third governance challenge concerns regulation, for ex- ample regarding data storage and protection as well as non-discrimination of individuals based on their genetic profiles. Finally, the fourth governance challenge deals with the inclusion of PH into health systems, for example through the admission and reimbursement of new medications and treatments. We report the four governance challenges in Figure 2.

Figure 2: Four governance challenges



Our literature review reveals that the four identified governance challenges relate to one another, in terms of how they co-appear in the different publications. The thicker the line between the different challenges, the more both governance challenges are discussed together within a publication (see Figure 2 and Appendix). Concerning the links between the different challenges, we find that authors analyze most frequently the link between the governance of the research infrastructure and the regulatory framework. Further, studies examine the relation

between trust building and inclusion in health systems on the one hand, and between trust building and research governance on the other hand. Researchers make only weak connections between research infrastructure and the inclusion of PH in health systems as well as between trust building and the regulatory framework.

The governance challenges relate to policy problems that the various actors face in the health systems. To understand the issues, it is important to be aware of the different actor constellations policymakers need to deal with (Kuhlmann, 2001; Ansell and Torfing, 2016). Scholars have identified the main stakeholders concerning PH as follows: "promoters", e.g., researchers, commercial and nonprofit developers, sponsors of research and development, lobbyists and other advocates, "monitors", e.g., editorial boards, regulatory bodies and curriculum committees, "providers", e.g., clinicians and hospitals, and "users", e.g., patient-based organizations (Juengst et al., 2012). These actors are similar to stakeholder constellations in other health policy issues (Lewis, 2006; Blank, Burau and Kuhlmann, 2017) and they will contribute in shaping policy responses to the governance challenges. At the same time, they will be affected by policies for PH. In the following sections, we discuss the four governance challenges in more detail.

Research infrastructure and practice

The first challenge for the governance of PH concerns the establishment of infrastructures and practices that assemble the necessary information for research on prevention and treatment. Genetic data stored in biobanks is key to the development of PH services. Research on the governance of biobanks is already well advanced. For example, a literature review dealing with the diffusion of biobank initiatives concerning PH holds: "Biobanking services must improve rapidly to serve the needs of personalized medicine and biospecimen research should be encouraged and supported at all levels from project funding to publication of results" (Hewitt, 2011, p. 112). A very important element for the establishment of biobanks is that "formal

governance structures are a common and necessary component of biobanks," such as a formal access or oversight (Olson et al., 2014, p. 51) and ethics approvals are a common element (Zika et al., 2011, p. 100).

The creation of biobanks has advanced all around the world, in recent years (Olson et al., 2014; Kohane, 2011; Zawati et al., 2018). To better understand these global dynamics, future research could analyze the global diffusion of biobanks to understand the economic, political and social factors determining their creation. Such research would not only improve our understanding of how biobanks are distributed but also the factors that determine their participation. Furthermore, research on PH offers new opportunities for scientific collaboration, such as in the Human Epigenome Consortium (Stunnenberg et al., 2016; Chiapperino and Panese, 2018), which in turn provides new governance challenges, since, for example, these initiatives require an adequate research infrastructure.

Another governance challenge for PH related to research is the harmonization of research infrastructures to allow data exchange (Stark et al., 2019) between different geographical areas. This is all the more important since the use of genomic data coincides with the technological revolution in health and medicine aiming to utilize big data (Vayena et al., 2018; Galetsi, Katsaliaki and Kumar, 2019). Related to global data sharing is the creation of interfaces between research and health care, notably between different technological systems operating within and between organizations (Kawamoto et al., 2009; Heart, Ben-Assuli and Shabtai, 2017). Particularly the establishment of compatible electronic health records (EHR) can create a database for research, linking genetic profiles and the history of health problems for patients (Kohane, 2011). EHR can become a "tool for genetic research, addressing concerns on accessibility, return of results and privacy and help in educate patients and healthcare providers" (Caenazzo, Tozzo and Borovecki, 2015, p. 4185). To develop research possibilities even further, linking EHR and genetic data with geo-spatial data could provide new insights into individualized medicine (Schinasi et al., 2018). At the same time, the personalization

approach requires to revise existing disease taxonomies to allow for more fine-grained analysis in the context of PH and medicine (Green, Carusi and Hoeyer, 2019).

Building trust

The second challenge for the governance of PH is to build trust of citizens and patients against the background of the new technical possibilities and insights, especially when it comes to the use of their genetic and personal data (Platt and Kardia, 2015). Research on the governance of PH has demonstrated the importance of trust regarding the storage of genetic data.

To build trust, researchers suggest to "(1) address the role of history and experience on trust, (2) engage concerns about potential group harm, (3) address cultural values and communication barriers, and (4) integrate patient values and expectations into oversight and governance structures" (Kraft et al., 2018, p. 3). Furthermore, researchers argue that there needs to be room for bottom-up developed rules and practices in the governance of biobanks, which includes citizens and patients and helps to increase trust and transparency (Meslin, 2010). Scholars use the terms reflexive and anticipatory governance to denote the particular governance challenges of PH. Reflexive governance means that decisionmakers include citizens' input in rule-making related to biobanks (Laurie, 2011). Anticipatory governance refers to the need to anticipate potential negative consequences of new technologies, such as loss of data in case of personalized medicine, when creating governance frameworks (Ozdemir, Faraj and Knoppers, 2011).

Trust-building and the inclusion of citizens are important because PH bears the risk of discrimination based on genetic profiles (Feldman, 2012). Research based on over 100 interviews with geneticists, clinicians, computer scientists, ethicists, regulators, policymakers, and program administrators in the United States (US) involved in the creation of biobanks suggests that the collection of genetic data bears the risk that this data will eventually be used to interpret and frame health disparities by conflating race, ethnicity, and nationality with

biological information (Lee, 2015a). Consequently, scholars call for a solidarity-based approach to implement PH and medicine (Prainsack, 2018). Thereby, one opportunity to create solidarity is to pursue data protection governance through community efforts (Wang et al., 2017).

At the individual level, building trust can be created by relying on health care professionals as intermediaries to build trust among citizens. In a research with focus groups, one participant reported, "I might trust my doctor to use my information more than some third, fourth, fifth party removed in some library [biobank, precision medicine research program] somewhere. I know my doctor [...]" (Persaud and Bonham, 2018, p. 26). This quote illustrates the importance of the trust relationship between providers of health care services and patients when it comes to the sharing of individual health data (Laurie, 2011). Survey data confirms this insight: patients trust particularly their health care providers when it comes to sharing their personal data (Bühler, Hermann and Lambertus, 2019). Against this background, the awareness and education of health care professionals concerning trust and PH is crucial (Caenazzo, Tozzo and Borovecki, 2015).

Regulatory framework(s)

The third PH challenge concerns the establishment of regulatory frameworks. Notably, regulations are required to ensure the technical compatibility between different databases, such as biobanks, to encourage researchers and providers to create new treatments, to protect citizens from discrimination, to generate equitable access to the promises of personalized medicine, and to organize collaborations at different levels.

Creating a regulatory infrastructure for PH entails regulating the exchange of data between different systems, for example of biobanks or EHR, to protect privacy concerns (Williams, Walker and Egede, 2016). This seems somewhat self-evident but it might be a challenge as it could slow down the innovation (Juengst et al., 2012). In fact, PH requires data sharing between

different stakeholders involved in healthcare, notably patients, medical practitioners, hospital operators, pharma- and clinical researchers, as well as health insurers. The literature has focused on the very technical aspects of these data applications (Palanisamy and Thirunavukarasu, 2017). In addition to sharing data within health systems (Muddyman et al., 2013), there is a necessity to exchange data between different countries. This problem poses a challenge not only for industrialized but also for developing countries. A review of the biobanks in low- and middle-income countries demonstrates that there is a lack of harmonized data sharing systems and that data formatting is often not standardized (Zawati et al., 2018). Common regulations and standards can help to solve this problem. This regulatory dimension has a large transnational component and requires to establish regulations beyond single countries to support innovation. For example, pharmacogenomics require the creation of a transnational regulatory regime that comprises a network including regulatory agencies, academic scientists and industry, and aim at creating a space for data sharing and to set standards that span across jurisdictional boundaries (Hogarth, 2012).

Another important theme for regulation of PH is to ensure genetic non-discrimination of individuals. For example, the US Congress passed the Genetic Information Nondiscrimination Act (GINA) in 2008 (Dressler and Terry, 2009; Feldman, 2012; Feldman and Darnell, 2013; Green, Lautenbach and McGuire, 2015; Rothstein, 2018). The legislation aims to rule out genetic discrimination regarding health insurance admission and employment. Feldman (2012, p. 743) states that "GINA prohibits insurers from using genetic information to adjust group or individual premiums, deny coverage, or impose preexisting condition exclusions, and makes it illegal for them to require or request genetic testing or intentionally obtain genetic information." The law received overwhelming support in the US Congress and has important implications for medical providers and health care organizations, which must familiarize themselves with the specificities of the act. Other countries, for example European Union (EU) member states, have also legislated to prevent discrimination on a genetic basis (Borry et al., 2012). Protection

against discrimination and diffusion of health care innovation is a transnational regulatory challenge, cf. the jurisdiction of European directives (Salas-Vega, Haimann and Mossialos, 2015). The EU's general data protection regulation and the Organization for Economic Co-operation and Development's recommendations for digital health governance are two cases that exemplify the transnational dimension (Vayena et al., 2018). Policymakers and scholars need to deal with regulatory compatibility between countries to ensure certainty for researchers and providers.

Governing data regulation is more than passing regulation, it also concerns the implementation of such regulations in practice. For example, scholars emphasize that there is a need for data controllers who are able to support researchers in dealing with legal challenges: "It cannot be the responsibility of the researcher who wants to access data to handle the legal intricacies of EU and national data protection legislations; this must be done by the data provider who acts as a data controller" (Kuchinke et al., 2016, p. 17). Such practices not only protect researchers from the legal challenges that come along with research dealing with PH but they also make research more transparent (Kaye et al., 2018), and therefore increase the trust in PH and medical innovation. Eventually, the general regulatory architecture for PH needs to include ethics regulation and a committee for genomic research to ensure "accessibility, return of results and privacy and help in educate patients and healthcare providers" (Caenazzo, Tozzo and Borovecki, 2015, p. 4185).

Inclusion in health systems

The fourth governance challenge is to include PH (Hedgecoe, 2004; Nwaru et al., 2017; Minari, Brothers and Morrison, 2018) in existing health systems, in other words, to integrate PH in the regulation, financing, and provision of public health and health care (Trein, 2018). In many countries, for example in Japan, Great Britain, and the US, policymakers have included precision medicine schemes in the context of national health systems (Minari, Brothers and

Morrison, 2018). According to the literature, the inclusion of PH and individualized medicine in national health systems should be assessed along six key themes: healthcare system, governance, access, awareness, implementation, and data. Concerning the governance dimension, this entails, a national strategy, a comprehensive legislation and guidelines, an ethical, social, and legal framework on the provision of personalized medicine and for genetic data. Further indicators are a national research center or large-scale research initiative, a consumer test legislation or code of conduct, as well as working groups with multiple stakeholders (Chong, Allotey and Chaiyakunapruk, 2018, p. 2 and Table 2). For example, the US created the national Precision Medicine Initiative (PMI). Its goal is to create more genetic research programs, which should ideally result in better health care programs (Sabatello and Appelbaum, 2017). Scholars have linked the PMI to the idea of a genetic citizenship, which entails the exchange of personal information in exchange for information from genetic research to make the best health-related choices for themselves. Put differently, this concept entails a new contract between citizens and the state, respectively health care providers, and entails risks, benefits, and responsibilities for each participant (Sabatello and Appelbaum, 2017).

More precisely, including PH in health systems requires to deal with the national regulations and specific financing issues. The first element is the application of EHR in the practice of health care and to include information beyond the clinical health data (Heart, Ben-Assuli and Shabtai, 2017; Lu et al., 2018). A second point concerns the assessment and certification of genetic tests' actual public health value. Nowadays, consumers can choose between a widening array of genetic tests but it is not clear to what extent these tests effectively contribute to improving individual and public health and should therefore be reimbursed by health insurance (Hall, Mathews and Morley, 2010; Caulfield and McGuire, 2012). The third element concerns the establishment of new treatments (Bertier et al., 2016), for example orphan drugs or personalized drugs (Garrison Jr et al., 2008) as well as new cancer therapies, such as precision immunotherapy for metastatic melanoma (Chin-Yee et al., 2018, p. 383). The fourth element

about integration is the reimbursement of new treatments and their inclusion in health care payers plans (Messner et al., 2016). New treatments and drugs tend to be expensive (Degtiar, 2017), which raises the question how to ensure equity in the access to new treatments (Williams, Walker and Egede, 2016). Finally, policymakers face the challenge whether PH will increase or reduce the disparities between medical health care and public health. On the one hand, genetic testing provides new possibilities for prevention, such as stillbirth prevention (Ker, 2018), but, on the other hand, the predictive qualities (Bourret, Keating and Cambrosio, 2011; Juengst et al., 2012) of precision medicine might re-enfore health inequalities rather than decreasing them and therefore aggravate the differences between individual health care and public health (Khoury and Galea, 2016; Chin-Yee et al., 2018). The last point is particularly relevant since it is very unlikely that there is a truly "personalized" medicine with individually designed plans for prevention and treatments becoming reality in the near future. We rather see stratified medicine that considers genetic variations between different groups emerging (Juengst et al., 2012; Tutton, 2012; Minari, Brothers and Morrison, 2018). This situation makes equity problems all the more relevant.

At an organizational level, these policy challenges need to be absorbed by the existing structure of the national health systems. For example, in Italy, "the State-Region conference approved and published the national plan of public health genomics. A further step has recently been made with the approval of a 'National Plan for Innovation of the Health System based on omics sciences.'" This plan includes measures to introduce the use of big data in the health system but it also aims to support economic growth through investment in PH (Boccia et al., 2017, p. e12782-2). Taking a comparative perspective, scholars have focused on the organizations that are responsible for managing genetic tests. In the US, the Centers for Medicare and Medicaid Services are responsible for the Clinical Laboratory Improvement Amendments program that controls laboratories responsible for genomic testing. In addition, several government agencies are involved in creating regulatory standards for integrating genomic testing in clinical practice.

The Secretary's Advisory Committee on Genetics, Health and Society and the National Human Genome Research Institute deal with the question on how genetic tests can be reimbursed for patients (Vozikis et al., 2016, p. 353). In the EU, genetic tests are regulated by the EU directive on medical device regulations which requires certification of the device to have a '*Conformité Européenne'* (CE) mark. Reimbursement of the tests is regulated differently in each EU country. For example, "in Germany, it is administered by *Der Gemeinsame Bundesausschuss* (GBA), in France by *La Haute Autorité de Santé* (HAS), in the UK by the *National Health Service* (NHS), in Italy by *Il Servizio Sanitario Nazionale* (SSN) and in Spain by *El Instituto Nacional de la Salud (INS)*" (Vozikis et al., 2016, p. 354). Nevertheless, a comprehensive analysis on how PH has been included in health governance is lacking for European countries.

Conclusions

In this paper, we conduct a systematic review of the literature dealing with the governance of PH. We outline which governance challenges policymakers and practitioners face to integrate PH in a holistic manner into society in general and into existing research environments, regulatory frameworks as well as health systems. With our literature review we have identified four main governance challenges, namely, creating and maintaining an infrastructure for research, building trust in PH amongst citizens in general and patients in particular, establishing regulatory frameworks to ensure cooperation and to avoid discrimination, and integrating PH into existing health systems. These four governance challenges are relevant for practitioners and researchers alike.

Further research on the governance and policymaking of PH should be directed on the link between trust building and regulatory frameworks on the one hand, as well as on the relationship between the research infrastructures and the question of health system integration on the other hand. In fact, these are topics that have currently been given less attention, in particular regarding research on the different governance issues discussed in this paper. Beyond this

research agenda, scholars should focus on researching how existing policies govern the four challenges that we outline. Such studies should indeed consider different countries to develop a holistic view of the various governance challenges. Researchers should explore why there are potentially differences and similarities in how various countries govern the four challenges now, or why in some countries and settings one of the discussed governance challenges is particularly difficult to deal with.

In addition, the four governance challenges are relevant for practitioners as they underline the practical steps that are necessary to translate technological innovation into new public policies. For example, a recently published roadmap for decisionmakers has outlined that the development of personalized health and medicine needs to create appropriate context conditions, should focus on incremental implementation, address the data issue and reform regulation and payment systems (Florin and Escher, 2017). Our literature review informs these practical steps, notably in pointing at the different topics – research, trust, and health system delivery – where we need to regulate and coordinate actors for integrating personalized health into existing policies.

References

Andreu-Perez, J., C. C. Y. Poon, R. D. Merrifield, S. T. C. Wong and G. Yang. 2015. "Big Data for Health." *IEEE Journal of Biomedical and Health Informatics* 19(4):1193–1208.

Ansell, Christopher and Jacob Torfing. 2016. *Handbook on theories of governance*. Cheltenham: Edward Elgar Publishing.

Bertier, Gabrielle, Jian Carrot-Zhang, Vassilis Ragoussis and Yann Joly. 2016. "Integrating precision cancer medicine into healthcare—policy, practice, and research challenges." *Genome medicine* 8(1):108.

Biesbroek, Robbert, Lea Berrang-Ford, James D Ford, Andrew Tanabe, Stephanie E Austin and Alexandra Lesnikowski. 2018. "Data, concepts and methods for large-n comparative climate change adaptation policy research: A systematic literature review." *Wiley Interdisciplinary Reviews: Climate Change* 9(6):e548.

Blank, Robert H., Viola Burau and Ellen Kuhlmann. 2017. *Comparative Health Policy*. 5 ed. Basingstoke: Palgrave Macmillan.

Boccia, Stefania, Antonio Federici, Roberta Siliquini, Giovanna Elisa Calabro and Walter Ricciardi. 2017. "Implementation of genomic policies in Italy: the new National Plan for innovation of the Health System based on omics sciences." *Epidemiology, Biostatistics and Public Health* 14(4).

Boeckhout, Martin and Conor MW Douglas. 2015. "Governing the research-care divide in clinical biobanking: Dutch perspectives." *Life sciences, society and policy* 11(1):7.

Böhm, Katharina, Achim Schmid, Ralf Götze, Claudia Landwehr and Heinz Rothgang. 2013. "Five types of OECD healthcare systems: empirical results of a deductive classification." *Health Policy* 113(3):258–269.

Booth, Alison, Mike Clarke, Davina Ghersi, David Moher, Mark Petticrew and Lesley Stewart. 2011. "An international registry of systematic-review protocols." *The Lancet* 377(9760):108– 109.

Borry, Pascal, Rachel E Van Hellemondt, Dominique Sprumont, Camilla Fittipaldi Duarte Jales, Emmanuelle Rial-Sebbag, Tade Matthias Spranger, Liam Curren, Jane Kaye, Herman Nys and Heidi Howard. 2012. "Legislation on direct-to-consumer genetic testing in seven European countries." *European Journal of Human Genetics* 20(7):715.

Bourret, Pascale, Peter Keating and Alberto Cambrosio. 2011. "Regulating diagnosis in post-genomic medicine: Re-aligning clinical judgment?" *Social Science & Medicine* 73(6):816–824.

Bowman, Diana M, Neal Woodbury and Erik Fisher. 2016. "Decoupling knowledge and expertise in personalized medicine: who will fill the gap?" *Expert Review of Precision Medicine and Drug Development* 1(4):345–347.

Bühler, Gordon, Michael Hermann and Michael Lambertus. 2019. *Observatoire "Société numérique et solidarité" Opinion et comportement de la population Suisse 2019*. Zürich: Sotomo / Fondation Sanitas.

Caenazzo, Lucciana, Pamela Tozzo and A Borovecki. 2015. "Ethical governance in biobanks linked to electronic health records." *Eur Rev Med Pharmacol Sci* 19(21):4182–4186.

Caulfield, Timothy and Amy L McGuire. 2012. "Direct-to-consumer genetic testing: perceptions, problems, and policy responses." *Annual review of medicine* 63:23–33.

Chalmers, Don, Dianne Nicol, Jane Kaye, Jessica Bell, Alastair V Campbell, Calvin WL Ho, Kazuto Kato, Jusaku Minari, Chih-hsing Ho, Colin Mitchell et al. 2016. "Has the biobank bubble burst? Withstanding the challenges for sustainable biobanking in the digital era." *BMC Medical Ethics* 17(1):39.

Chan, Sarah and Sonja Erikainen. 2018. "What's in a name? The politics of 'precision medicine'." *The American Journal of Bioethics* 18(4):50–52.

Chataway, Joanna, Caroline Fry, Sonja Marjanovic and Ohid Yaqub. 2012. "Public–private collaborations and partnerships in stratified medicine: making sense of new interactions." *New biotechnology* 29(6):732–740.

Chiapperino, Luca and Francesco Panese. 2018. “Gendered imaginaries: situating knowledge of epigenetic programming of health.” *Sociology of health & illness* 40(7):1233–1249.

Chin-Yee, Benjamin, SV Subramanian, Amol A Verma, Andreas Laupacis and Fahad Razak. 2018. “Emerging Trends in Clinical Research With Implications for Population Health and Health Policy.” *The Milbank Quarterly* 96(2):369–401.

Chong, Huey Yi, Pascale A. Allotey and Nathorn Chaiyakunapruk. 2018. “Current landscape of personalized medicine adoption and implementation in Southeast Asia.” *BMC Medical Genomics* 11(1):94.

De Vries, Raymond G, Kerry A Ryan, Linda Gordon, Chris D Krenz, Tom Tomlinson, Scott Jewell and Scott YH Kim. 2019. “Biobanks and the Moral Concerns of Donors: A Democratic Deliberation.” *Qualitative health research* 29(13):1942–1953.

Degtiar, Irina. 2017. “A review of international coverage and pricing strategies for personalized medicine and orphan drugs.” *Health Policy* 121(12):1240–1248.

Doheny, Shane, Angus Clarke, Daniele Carrieri, Sandi Dheensa, Naomi Hawkins, Anneke Lucassen, Peter Turnpenny and Susan Kelly. 2018. “Dimensions of responsibility in medical genetics: exploring the complexity of the “duty to recontact”.” *New Genetics and Society* 37(3):187–206.

Dove, Edward S. 2015. “Biobanks, data sharing, and the drive for a global privacy governance framework.” *The Journal of Law, Medicine & Ethics* 43(4):675–689.

Dressler, LG and SF Terry. 2009. “How will GINA influence participation in pharmacogenomics research and clinical testing?” *Clinical Pharmacology & Therapeutics* 86(5):472–475.

Dry, Sarah M, Sarah B Garrett, Barbara A Koenig, Arleen F Brown, Michael M Burgess, Jen R Hult, Holly Longstaff, Elizabeth S Wilcox, Sigrid Karina Madrigal Contreras, Arturo Martinez et al. 2017. “Community recommendations on biobank governance: Results from a deliberative community engagement in California.” *PloS one* 12(2):e0172582.

Feldman, Eric A. 2012. “The Genetic Information Nondiscrimination Act (GINA): Public Policy and Medical Practice in the Age of Personalized Medicine.” *Journal of General Internal Medicine* 27(6):743–746.

Feldman, Eric A and Chelsea Darnell. 2013. Health insurance, employment, and the human genome: genetic discrimination and biobanks in the United States. In *Comparative Issues in the Governance of Research Biobanks*. Springer pp. 63–75.

Flores, Mauricio, Gustavo Glusman, Kristin Brogaard, Nathan D Price and Leroy Hood. 2013. “P4 medicine: how systems medicine will transform the healthcare sector and society.” *Personalized medicine* 10(6):565–576.

Florin, Marie-Valentin and Gérard Escher. 2017. *A roadmap for the development of precision medicine. Lausanne*. Lausanne: EPFL International Risk Governance Center (IRGC).

Frenk, Julio and Suerie Moon. 2013. “Governance challenges in global health.” *New England Journal of Medicine* 368(10):936–942.

Galetsi, P, K Katsaliaki and S Kumar. 2019. “Values, challenges and future directions of big data analytics in healthcare: A systematic review.” *Social Science & Medicine* p. 112533.

Garrison Jr, Louis P, Rick J Carlson, Josh J Carlson, Patricia C Kuszler, Lisa M Meckley and David L Veenstra. 2008. “A review of public policy issues in promoting the development and commercialization of pharmacogenomic applications: challenges and implications.” *Drug metabolism reviews* 40(2):377–401.

Geller, Gail, Rachel Dvoskin, Chloe L Thio, Priya Duggal, Michelle H Lewis, Theodore C Bailey, Andrea Sutherland, Daniel A Salmon and Jeffrey P Kahn. 2014. “Genomics and infectious disease: a call to identify the ethical, legal and social implications for public health and clinical practice.” *Genome medicine* 6(11):106.

Goetz, Klaus H. 2008. “Governance as a Path to Government.” *West European Politics* 31(1-2):258–279.

Gray, Ian D, Andrea R Kross, Melanie E Renfrew and Paul Wood. 2019. "Precision Medicine in Lifestyle Medicine: The Way of the Future?" *American Journal of Lifestyle Medicine* p. 1559827619834527.

Green, Robert C, Denise Lautenbach and Amy L McGuire. 2015. "GINA, genetic discrimination, and genomic medicine." *New England Journal of Medicine* 372(5):397–399.

Green, Sara, Annamaria Carusi and Klaus Hoeyer. 2019. "Plastic diagnostics: The remaking of disease and evidence in personalized medicine." *Social Science & Medicine*.

Hall, Wayne D, Rebecca Mathews and Katherine I Morley. 2010. "Being more realistic about the public health impact of genomic medicine." *PLoS medicine* 7(10):e1000347.

Hawkins, Alice K and Kieran C O'Doherty. 2011. "" Who owns your poop?": insights regarding the intersection of human microbiome research and the ELSI aspects of biobanking and related studies." *BMC Medical Genomics* 4(1):72.

Heart, Tsipi, Ofir Ben-Assuli and Itamar Shabtai. 2017. "A review of PHR, EMR and EHR integration: A more personalized healthcare and public health policy." *Health Policy and Technology* 6(1):20–25.

Hedgecoe, Adam. 2004. *The politics of personalised medicine: Pharmacogenetics in the clinic*. Cambridge University Press.

Heeney, Catherine and Shona M Kerr. 2017. "Balancing the local and the universal in maintaining ethical access to a genomics biobank." *BMC medical ethics* 18(1):80.

Hewitt, Robert E. 2011. "Biobanking: the foundation of personalized medicine." *Current Opinion in Oncology* 23(1):112.

Hogarth, Stuart. 2012. "Regulatory experiments and transnational networks: the governance of pharmacogenomics in Europe and the United States." *Innovation: The European Journal of Social Science Research* 25(4):441–460.

Ingrams, Alex. 2019. “Big Data and Dahl’s Challenge of Democratic Governance.” *Review of Policy Research* 36(3):357–377.

Juengst, Eric T, Richard A Settersten, Jennifer R Fishman and Michelle L McGowan. 2012. “After the revolution? Ethical and social challenges in ‘personalized genomic medicine’.” *Personalized medicine* 9(4):429–439.

Kawamoto, Kensaku, David F Lobach, Huntington F Willard and Geoffrey S Ginsburg. 2009. “A national clinical decision support infrastructure to enable the widespread and consistent practice of genomic and personalized medicine.” *BMC medical informatics and decision making* 9(1):17.

Kaye, Jane, Sharon F. Terry, Eric Juengst, Sarah Coy, Jennifer R. Harris, Don Chalmers, Edward S. Dove, Isabelle Budin-Ljøsne, Clement Adebamowo, Emilomo Ogbe, Louise Bezuiden- hout, Michael Morrison, Joel T. Minion, Madeleine J. Murtagh, Jusaku Minari, Harriet Teare, Rosario Isasi, Kazuto Kato, Emmanuelle Rial-Sebbag, Patricia Marshall, Barbara Koenig and Anne Cambon-Thomsen. 2018. “Including all voices in international data-sharing governance.” *Human Genomics* 12(1):13.

Ker, Chin-Ru. 2018. “A Comprehensive Update on Stillbirth Prevention: from Preconception to Postpartum, Individuals to Public Health Administrations.” *Current Obstetrics and Gynecology Reports* 7(4):172–178.

Khoury, Muin J and Sandro Galea. 2016. “Will precision medicine improve population health?” *Jama* 316(13):1357–1358.

Kickbusch, Ilona and David Eric Gleicher. 2012. Governance for health in the 21st century. Technical report WHO Regional Office for Europe.

Kirchhof, Gregor, Josef Franz Lindner, Stephan Achenbach, Klaus Berger, Stefan Blankenberg, Heiner Fangerau, Henner Gimpel, Ulrich M Gassner, Jens Kersten, Dorothea Magnus et al. 2018. “Stratified prevention: opportunities and limitations. Report on the 1st

interdisciplinary cardiovascular workshop in Augsburg." *Clinical Research in Cardiology* 107(3):193–200.

Knoepfel, Peter, Corinne Larrue, Michael Hill and Fr´ed´eric Varone. 2011. *Public policy analysis*. Bristol: Policy Press.

Kohane, Isaac S. 2011. "Using electronic health records to drive discovery in disease genomics." *Nature Reviews Genetics* 12(6):417–428.

Kraft, Stephanie A., Mildred K. Cho, Katherine Gillespie, Meghan Halley, Nina Varsava, Kelly E. Ormond, Harold S. Luft, Benjamin S. Wilfond and Sandra Soo-Jin Lee. 2018. "Beyond Consent: Building Trusting Relationships With Diverse Populations in Precision Medicine Research." *The American Journal of Bioethics* 18(4):3–20.

Kuchinke, Wolfgang, Christian Krauth, René Bergmann, T¨oresin Karakoyun, Astrid Woollard, Irene Schluender, Benjamin Braasch, Martin Eckert and Christian Ohmann. 2016. "Legal assessment tool (LAT): an interactive tool to address privacy and data protection issues for data sharing." *BMC Medical Informatics and Decision Making* 16(1):81.

Kuhlmann, Stefan. 2001. "Future governance of innovation policy in Europe—three scenarios." *Research policy* 30(6):953–976.

Kukk, Piret, Ellen HM Moors and Marko P Hekkert. 2016. "Institutional power play in innovation systems: The case of Herceptin*Q*R ." *Research Policy* 45(8):1558–1569.

Laurie, Graeme. 2011. "Reflexive governance in biobanking: on the value of policy led approaches and the need to recognize the limits of law." *Human Genetics* 130(3):347–356.

Lee, Sandra Soo-Jin. 2015*a*. "The Biobank as Political Artifact: The Struggle over Race in Categorizing Genetic Difference." *The ANNALS of the American Academy of Political and Social Science* 661(1):143–159.

Lee, Sandra Soo-Jin. 2015*b*. "The biobank as political artifact: The struggle over race in categorizing genetic difference." *The ANNALS of the American Academy of Political and Social Science* 661(1):143–159.

Lewis, Jenny M. 2006. "Being around and knowing the players: networks of influence in health policy." *Social Science & Medicine* 62(9):2125–2136.

Lu, Christine Y, Marc S Williams, Geoffrey S Ginsburg, Sengwee Toh, Jeff S Brown and Muin J Khoury. 2018. "A proposed approach to accelerate evidence generation for genomic-based technologies in the context of a learning health system." *Genetics in Medicine* 20(4):390.

Meslin, E.M. 2010. "The Value of Using Top-Down and Bottom-Up Approaches for Building Trust and Transparency in Biobanking." *Public Health Genomics* 13(4):207–214.

Messner, Donna A, Jennifer Al Naber, Pei Koay, Robert Cook-Deegan, Mary Majumder, Gail Javitt, Patricia Deverka, Rachel Dvoskin, Juli Bollinger, Margaret Curnutte et al. 2016. "Barriers to clinical adoption of next generation sequencing: Perspectives of a policy Delphi panel." *Applied & translational genomics* 10:19–24.

Minari, Jusaku, Kyle B. Brothers and Michael Morrison. 2018. "Tensions in ethics and policy created by National Precision Medicine Programs." *Human Genomics* 12(1):22.

Moher, David, Larissa Shamseer, Mike Clarke, Davina Ghersi, Alessandro Liberati, Mark Petticrew, Paul Shekelle and Lesley A Stewart. 2015. "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement." *Systematic Reviews* 4(1):1.

Muddyman, Dawn, Carol Smee, Heather Griffin and Jane Kaye. 2013. "Implementing a successful data-management framework: the UK10K managed access model." *Genome medicine* 5(11):100.

Nwaru, Bright I, Charles Friedman, John Halamka and Aziz Sheikh. 2017. "Can learning health systems help organisations deliver personalised care?" *BMC medicine* 15(1):177.

Olson, J. E., S. J. Bielinski, E. Ryu, E. M. Winkler, P. Y. Takahashi, J. Pathak and J. R. Cerhan. 2014. “Biobanks and personalized medicine.” *Clinical Genetics* 86(1):50–55.

Özdemir, Vural, Edward S Dove, Ulvi K Gürsoy, Semra Sardas, Arif Yıldırım, Senay Görücü Yılmaz, I Ömer Barlas, Kıvanc Güngör, Alper Mete and Sanjeeva Srivastava. 2017. “Personalized medicine beyond genomics: alternative futures in big data—proteomics, environtome and the social proteome.” *Journal of Neural Transmission* 124(1):25–32.

Özdemir, Vural, Samer A. Faraj and Bartha M. Knoppers. 2011. “Steering Vaccinomics Innovations with Anticipatory Governance and Participatory Foresight.” *OMICS: A Journal of Integrative Biology* 15(9):637–646.

Palanisamy, Venketesh and Ramkumar Thirunavukarasu. 2017. “Implications of big data analytics in developing healthcare frameworks–A review.” *Journal of King Saud University- Computer and Information Sciences* .

Persaud, Anitra and Vence L. Bonham. 2018. “The Role of the Health Care Provider in Building Trust Between Patients and Precision Medicine Research Programs.” *The American Journal of Bioethics* 18(4):26–28.

Phillips, Kathryn A, Julia R Trosman, Robin K Kelley, Mark J Pletcher, Michael P Douglas and Christine B Weldon. 2014. “Genomic sequencing: assessing the health care system, policy, and big-data implications.” *Health affairs* 33(7):1246–1253.

Platt, Jodyn and Sharon Kardia. 2015. “Public trust in health information sharing: implications for biobanking and electronic health record systems.” *Journal of personalized medicine* 5(1):3– 21.

Prainsack, Barbara. 2018. “The “We” in the “Me”: Solidarity and Health Care in the Era of Personalized Medicine.” *Science, Technology, & Human Values* 43(1):21–44.

Ricciardi, Walter and Stefania Boccia. 2017. “New challenges of public health: bringing the future of personalised healthcare into focus.” *European Journal of Public Health* 27 (suppl 4):36– 39.

Rose, Susannah L. 2013. “Patient advocacy organizations: institutional conflicts of interest, trust, and trustworthiness.” *The Journal of Law, Medicine & Ethics* 41(3):680–687.

Rothstein, Mark A. 2018. “GINA at ten and the future of genetic nondiscrimination law.” *Hastings Center Report* 48(3):5–7.

Sabatello, Maya and Paul S. Appelbaum. 2017. “The Precision Medicine Nation.” *Hastings Center Report* 47(4):19–29.

Salas-Vega, Sebastian, Adria Haimann and Elias Mossialos. 2015. “Big data and health care: challenges and opportunities for coordinated policy development in the EU.” *Health Systems & Reform* 1(4):285–300.

Sardas, Semra and Asligül Kendirci. 2019. “Panvigilance: Integrating biomarkers in clinical trials for systems pharmacovigilance.” *Omics: a journal of integrative biology* 23(3):134–137.

Schinasi, Leah H, Amy H Auchincloss, Christopher B Forrest and Ana V Diez Roux. 2018. “Using electronic health record data for environmental and place-based population health research: a systematic review.” *Annals of epidemiology* 28(7):493–502.

Song, Chie Hoon, Jeung-Whan Han, Byeongki Jeong and Janghyeok Yoon. 2017. “Mapping the patent landscape in the field of personalized medicine.” *Journal of Pharmaceutical Innovation* 12(3):238–248.

Stark, Zornitza, Lena Dolman, Teri A Manolio, Brad Ozenberger, Sue L Hill, Mark J Caulfied, Yves Levy, David Glazer, Julia Wilson, Mark Lawler et al. 2019. “Integrating genomics into healthcare: a global responsibility.” *The American Journal of Human Genetics* 104(1):13–20.

Stunnenberg, Hendrik G, Sergio Abrignani, David Adams, Melanie de Almeida, Lucia Altucci, Viren Amin, Ido Amit, Stylianos E Antonarakis, Samuel Aparicio, Takahiro Arima et al. 2016. “The International Human Epigenome Consortium: a blueprint for scientific collaboration and discovery.” *Cell* 167(5):1145–1149.

Trein, Philipp. 2018. *Healthy or Sick? Coevolution of Health Care and Public Health in a Comparative Perspective*. Cambridge: Cambridge University Press.

Trein, Philipp, Eva Thomann and Martino Maggetti. 2019. "Integration, functional differentiation and problem-solving in multilevel governance." *Public Administration* 97(2):339–354.

Tupasela, Aaro and Sandra Liede. 2016. State responsibility and accountability in managing big data in biobank research: Tensions and challenges in the right of access to data. In *The ethics of biomedical big data*. Springer pp. 257–275.

Tutton, Richard. 2012. "Personalizing medicine: Futures present and past." *Social Science & Medicine* 75(10):1721–1728.

Vayena, Effy, Tobias Haeusermann, Afua Adjekum and Alessandro Blasimme. 2018. "Digital health: meeting the ethical and policy challenges." *Swiss medical weekly* 148:w14571.

Vozikis, Athanassios, David N. Cooper, Christina Mitropoulou, Manousos E. Kambouris, Angela Brand, Vita Dolzan, Paolo Fortina, Federico Innocenti, Ming Ta Michael Lee, Lada Leyens, Milan Macek Jr, Fahd Al-Mulla, Barbara Prainsack, Alessio Squassina, Domenica Taruscio, Ron H. van Schaik, Effy Vayena, Marc S. Williams and George P. Patrinos. 2016. "Test Pricing and Reimbursement in Genomic Medicine: Towards a General Strategy." *Public Health Genomics* 19(6):352–363.

Wang, Shuang, Xiaoqian Jiang, Haixu Tang, Xiaofeng Wang, Diyue Bu, Knox Carey, Stephanie OM Dyke, Dov Fox, Chao Jiang, Kristin Lauter et al. 2017. "A community effort to protect genomic data sharing, collaboration and outsourcing." *NPJ genomic medicine* 2(1):33.

Williams, Joni Strom, Rebekah J Walker and Leonard E Egede. 2016. "Achieving equity in an evolving healthcare system: opportunities and challenges." *The American journal of the medical sciences* 351(1):33–43.

Woolley, J Patrick, Michelle L McGowan, Harriet JA Teare, Victoria Coathup, Jennifer R Fishman, Richard A Settersten, Sigrid Sterckx, Jane Kaye and Eric T Juengst. 2016. "Citizen science or scientific citizenship? Disentangling the uses of public engagement rhetoric in national research initiatives." *BMC medical ethics* 17(1):33.

Zawati, Ma'n H., Anne Marie Tasse, Maimuna Mendy, Elodie Caboux and Michael Lang. 2018. "Barriers and Opportunities in Consent and Access Procedures in Low- and Middle-Income Country Biobanks: Meeting Notes from the BCNet Training and General Assembly." *Biop- reservation and Biobanking* 16(3):171–178.

Zeggini, Eleftheria, Anna L Gloyn, Anne C Barton and Louise V Wain. 2019. "Translational genomics and precision medicine: Moving from the lab to the clinic." *Science* 365(6460):1409– 1413.

Zika, Eleni, Daniele Paci, Anette Braun, Sylvie Rijkers-Defrasne, Mylène Deschenes, Isabel Fortier, Jens Laage-Hellman, Christian A Scerri and D Ibarreta. 2011. "A European survey on biobanks: trends and issues." *Public health genomics* 14(2):96–103.

Synopsis of reviewed papers.

Reference	Region	Methodology	Key contents and main results	RP	TB	RF	HS
Dry et al. (2017)	US (California)	Deliberative community engagement (*N* = 51)	– Biobank governance and oversight recommendations – Educate the public, share samples broadly, monitor researcher behavior – Use informative consent procedures and involve community members	✓	✓	✓	
Caenazzo, Tozzo and Borovecki (2015)		Commentary	– Pairing disease biobanks with electronic health records (EHR) for research – Specific ethics committees for each biobank to improve governance – Committees to set up EHR utilization guidelines and to address concerns	✓	✓		
Hewitt (2011)		Literature review	– Description of advances in biobanking and biospecimen research – Quality management and professional organization of biobanks – Improvement of collection models and patient protection	✓	✓		
Meslin (2010)	US (Indiana)	Case reviews (*N* = 279 and 1000)	– Building trust and transparency in biobanks governance structures – Top-down steering to be complemented with bottom-up governance – Bottom-up strategies to include researchers and local communities	✓	✓		
Zawati et al. (2018)	Low/middle income countries	Literature review/ meeting notes	– Review of challenges and opportunities identified by biobank researchers – Informed consent, access policy and data sharing is critical – Biobanking should account for political and social conditions	✓	✓		
Chalmers et al. (2016)	AU, DE, JP, SG, TW, GB, US	Country review (7 countries)	– Operational, sustainability and funding challenges in biobanking – Resources, viability and usefulness of running biobanks – Technologies and strategies to minimize overly complex structures	✓		✓	
Kaye et al. (2018)		Commentary	– National governance hinders international exchange of research data – Need of public consultations on access and use data-sharing issues – Digital technologies to encourage accessibility, transparency, accountability	✓		✓	
Laurie (2011)	GB	Conceptual investigation	– Reflexive governance as approach without specific basis in law – High-level policy documents guide decisions and practice – Commitment among participants, researchers and society avoids regulation	✓		✓	

Lee (2015*b*)		Ethnographic research	– Institutional practices of classifying and creating taxonomies – Biobanks as political artefacts framing health differences in populations – Avoid conflation of race, ethnicity and nationality with biological differences	✓		✓	
Sardas and Kendirci (2019)		Commentary	– Systems approach to pharmacovigilance and risk governance – Need for centers for panvigilance and global clinical trials – Harmonization of biomakers for product development and trials	✓		✓	
Chan and Erikainen (2018)	US	Commentary	– Term “precision medicine” is overly ambitious – Systems approaches relate to multiple ideas and aims – US genetic research is no public good due to the private health care providers	✓			✓
Kohane (2011)		Review article	– Use of electronic health records and related information for genetic research – Link genetic studies to clinical health care delivery – Such research can be conducted while maintaining patient privacy	✓			✓
Andreu-Perez et al. (2015)		Statistics (2007–2014), case reviews	– Development of big data in biomedical and health informatics – Big data will advance disease management (diagnosis, prevention, treatment) – Challenges in privacy, security, data ownership/stewardship, governance	✓			
Boeckhout and Douglas (2015)	NL	Case study	– Biobanking infrastructures positioned between healthcare and research – Changing relationship between care and research biobank governance – Medical responsibilities on both sides require new forms of governance	✓			
Hawkins and O’Doherty (2011)	CA	Semi-structured interviews	– Microbiome research adds to biobanking and data sharing complications – Revisit of privacy, consent, ownership, results, governance and benefit sharing – Minority views and facilitation to be considered in governance	✓			
Heeney and Kerr (2017)	GB (Scotland)	Literature review	– Standardization of data sharing and access in biobanking – Data access governance needs to be flexible and reflexive – Wider data sharing environment and local specificities need to be included	✓			
Olson et al. (2014)		Literature review	– Support of clinical genetics by carefully desinged biobanks – Setting up a biobank and linkage to electronic health records – Recruitment, investigations, re-use of data and sustainability	✓			

Özdemir et al. (2017)		Conceptual article	– Technology foresight analysis defining "environtome" and "social proteome" – Personalized health beyond genomics with big data technologies (proteomics) – Synergistic value of social and biological proteomes in psychology	✓			
Palanisamy and Thirunavukarasu (2017)		Literature review	– Success of big data healthcare applications depends on architecture and tools – Diversified data analytical capabilities for handling sources of data needed – Eco systems to include patients, doctors, hospitals, researchers and insurers	✓			
Ingrams (2019)		Conceptual article	– Application of Dahl's theory of democracy to health data governance – Recognition of the role of citizens in in policy making – Discussion of control and autonomy of citizens on health data		✓	✓	✓
Minari, Brothers and Morrison (2018)	JP, GB, US	Commentary	– Ethical dimensions in national strategies for precision medicine – Mitigate undesirable impact on privacy, commercialization and public trust – Approaches to consider equity, social justice, resources and politics		✓	✓	✓
Dove (2015)		Literature review	– Review of international disease and database consortia and projects – Coordination is critical in international governance of biobanking – Privacy laws need to be harmonized to allow for data sharing		✓	✓	
Persaud and Bonham (2018)		Commentary	– Crucial role of health care providers in creating trust of patients – Physicians to serve as agents and mediators in precision medicine programs – Patients tend to trust doctors the most with their genetic data	✓			✓
Sabatello and Appelbaum (2017)	US	Commentary	– Active, informed participation in research through "genomic citizenship" – Analysis of risks and benefits for participating in such initiatives – Individual empowerment as a result of genetic testing to remain doubtful	✓			✓
Woolley et al. (2016)	GB, US	Case studies	– Translational biomedical research requires large pools ("citizen science") – Initiatives to include an analysis of the role of citizenry – Terms "participation", "involvement" and "engagement" to be clarified	✓			✓
De Vries et al. (2019)	US (Michigan)	Democratic deliberations (*N* = 180)	– Moral concerns of donors in biobanking – Participants worry about ethical problems of consent – Public trust and (dis)trust in science to be addressed		✓		

Kraft et al. (2018)	US (Greater San Francisco Bay area)	Focus groups (*N* = 122)	– Build/maintain long-term, trust beyond consent with patient-participants – Address experience, concerns, cultural values, communication barriers – Integrate patient values to enhance trustworthiness		✓		
Platt and Kardia (2015)	US	Survey of citizens (*N* = 447)	– Public trust in health information sharing systems – Primary care provider and psychosocial factors positively influence trust – Privacy concerns and knowledge about sharing are negatively associated		✓		
Rose (2013)	US	Case study	– Trust in Patient Advocacy Organisations (PAO) – Limited industry funding to promote PAO trustworthiness – Separate fundraising and policymaking, increased transparency		✓		
Doheny et al. (2018)	GB (England, Wales)	Semi-structured interviews (*N* = 34)	– Patients to receive an updated interpretation of their genetic information – System responsibilities come with governance and legal issues – Interplay with professional obligations (duties, responsibilities, obligations)			✓	✓
Hedgecoe (2004)	UK, US	Semi-structured interviews	– Impact of pharmacogenetics technology on clinical practice – Industry and researchers have a simplified view compared to clinicians – Clinical context is widely resistant to the revolution from pharmacogenetics			✓	✓
Kirchhof et al. (2018)	DE	Case study	– Stratified prevention as a major change for health policy in Germany – Individual control and understanding of health information required – Updated governance and evidence-based development of taxonomies			✓	✓
Prainsack (2018)		Conceptual article	– Solidarity concepts to depart from the assumption of rational individuals – Relational understanding of personal and collective preferences – Policies and practices to focus on the overlap of the two			✓	✓
Kuchinke et al. (2016)		Legal analysis	– Development of a legal assessment tool for data access and sharing – Provides assessments and recommendations for researchers – Model develops usage scenarios and requirement clusters for data sharing			✓	
Hogarth (2012)	EU, US	Desk research, interviews	– Pharmacogenomics to transform drug discovery and development – Transnational regulatory regime encompassing national actors needed – Harmonization and standards setting across jurisdictional boundaries.			✓	

Muddyman et al. (2013)	UK	Case study	– Analysis of a data management system implementation (UK10K) – Reconciliation of data-sharing principles and system practicalities – Three key issues: study recruitment, data release and data access			✓	
Tupasela and Liede (2016)	Finland	Desk research, interviews	– Management of data in biobanks and sharing infrastructures – Practical implementation of the European Data Protection Directive – Governance to consider privacy concerns over individual data			✓	
Song et al. (2017)		Topic model	– Patent landscape dominated by therapeutic patents – Focus on areas of oncology and neurodegenerative and infectious diseases – Insights for future technology planning			✓	
Boccia et al. (2017)	IT	Commentary	– Integration of genomics into National Health Service – Areas of focus: prevention, diagnosis and care – Consider effectiveness (evidence-based) and sustainability (cost-effectiveness)				✓
Bowman, Woodbury and Fisher (2016)	US (Arizona)	Commentary	– Availability of health and blood tests in local pharmacies – Interpretation of health data shifts from professionals to consumers – Individuals circumventing physicians entails policy concerns and safety risks				✓
Chong, Allotey and Chaiyakunapruk (2018)	ID, MY, SG, TH	Scoping review, semi-structured interviews (N = 11)	– Adoption of personalized medicine in Southeast Asia's health systems – Governance, access, awareness, implementation and financing are reviewed – Balancing equity among populations and improving efficiency are critical				✓
Feldman (2012)	US	Commentary	– Genetic Information Nondiscrimination Act in health insurance/employment – Examination of fear and reality of genetic discrimination – Medical providers must be familiar with the terms of the law				✓
Geller et al. (2014)		Commentary	– Ethical, legal and social implications of genetic research on public health – Infectious disease management procedures in health care practice are affected – Balance health-related benefits/harms with impact of policy interventions				✓
Gray et al. (2019)		Literature review	– Precision medicine to add value in lifestyle medicine beyond genomics – Provide suitable types of support to people to adopt a healthy lifestyle – Holistic and person-centered approach to be chosen over a mere technological				✓

Ozdemir, Faraj and Knoppers (2011)		Conceptual article	– Anticipatory governance for vaccinomics and post-genomic technologies – Response to impredictability of consequences of a technology in early stages – Anticipation with participatory foresight to respond to inherent uncertainties				✓
Ricciardi and Boccia (2017)		Commentary	– Citizen engagement as prerequisite for policy change in public health – Governance, consent, trust, data-knowledge cycle to be improved – Adopt/adapt technology assessment while retaining humanity/community				✓
Vozikis et al. (2016)	EU (member states)	Conceptual article	– Pricing and reimbursement policies of genomic tests – Strategies to include universal access, cost monitoring and appropriate use – Develop research capacity and invest in human resources				✓

Note: **RP** = Research infrastructure and practice, **TB** = Trust building, **RF** = Regulatory framework, **HS** = Inclusion in health system.