Review

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Personalized Medicine

# Ethical, legal and social implications of incorporating personalized medicine into healthcare

As research focused on personalized medicine has developed over the past decade, bioethics scholars have contemplated the ethical, legal and social implications of this type of research. In the next decade, there will be a need to broaden the focus of this work as personalized medicine moves into clinical settings. We consider two broad issues that will grow in importance and urgency. First, we analyze the consequences of the significant increase in health information that will be brought about by personalized medicine. Second, we raise concerns about the potential of personalized medicine to exacerbate existing disparities in healthcare.

**Keywords:** discrimination • ELSI issues • ethical, legal and social implication issues • health disparities • personalized medicine • privacy

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In the last 10 years, as the technology and evidence base of personalized medicine were developing, bioethics scholars began contemplating the ethical, legal and social implications of the initial applications of this approach to medicine, forming the field of investigation known as 'ELSI' scholarship. Some of the foundational issues considered were safety and efficacy, informed consent, access and reimbursement. In recent years, technologies such as next-generation sequencers and gene expression assays have become less expensive and more suitable for clinical application, and as a result, personalized medicine has become established in a growing number of clinical areas. With these clinical applications, however, the implications of personalized medicine have expanded in scope and complexity. This trend is likely to continue in the coming years, with wider adoption throughout the healthcare system creating a need to broaden the focus of work in this area. This article considers two broad issues that will grow in importance: the consequences of the significantly increased amount of health information associated with personalized medicine (privacy, discrimination, physician–patient relationships and liability); and concerns about the potential of personalized medicine to exacerbate disparities in healthcare (the input–output problem, cost and access to healthcare and access to information technologies).

## Increased amount of health information

Personalized medicine is information intensive. High-dimensionality data created using genomics and other 'omics' technologies are central to many of the predictive, diagnostic and therapeutic applications of personalized medicine [1]. However, the substantial increase in individual health information this approach requires is also one of the main sources of ethical, legal and social concerns regarding personalized medicine. The capability to utilize genomic information in the clinic depends heavily on health information technologies. Electronic health records (EHRs) and EHR networks are being widely adopted in the developed world. Health information, traditionally in the sole possession of healthcare providers, increasingly is also in the possession of individuals (in the form of personal health records) and third parties (obtained pursuant to patient-signed

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authorizations). In this section, we explore four categories of concerns raised by generating, aggregating, analyzing, storing and using health information for personalized medicine.

## Privacy

Privacy and related terms are often used imprecisely and therefore it is valuable to begin with some definitions. Privacy is a condition of limited access to an individual or information regarding an individual [2]. In this article, we focus on informational health privacy, although there are several other types of privacy, including physical, decisional, proprietary and relational or associational privacy [3]. The related concept of confidentiality is a condition under which information obtained or disclosed within a confidential relationship is not redisclosed without the permission of the individual [2]. The paradigmatic example of confidentiality is a physician's duty not to disclose patient health information unless authorized by the patient or required by law. Security refers to the physical and electronic measures granting access to personal health information to persons or entities authorized to receive it and denying access to others [2].

In much of Europe, the term 'data protection' takes on a similar meaning to informational privacy in the USA [4]. In any jurisdiction, there are three main reasons why the protection of informational health privacy is so important. First, individuals may suffer from embarrassment, stigma, discrimination and other harms to their dignity if sensitive information is inappropriately disclosed. Second, the quality of healthcare may be compromised if individuals who fear improper disclosure of their sensitive information forego timely treatment for stigmatizing conditions or engage in defensive practices, such as withholding certain information from their healthcare providers [5]. Third, public health harms may occur if individuals with infectious diseases, mental illness, substance abuse or other sensitive conditions delay or decline treatment because they fear a loss of privacy [6].

The development of EHRs and EHR networks in much of the industrialized world increases the privacy risk because EHRs are typically comprehensive (containing records of clinical encounters with essentially all of an individual's healthcare providers), longitudinal (containing health records over an extended period of time) and instantaneously distributed to multiple parties. One consequence is that even decades-old, sensitive information remains a part of an individual's record and can be viewed by anyone with access to the EHR. Technologies and policies to give patients greater control of the contents of their health records and to limit third-party access to them, including data segmentation, are being widely considered in several countries. These measures are quite controversial, however, because they can result in certain healthcare providers having incomplete access to patient information [6]. In any event, data segmentation has not yet been adopted to any significant extent.

Although people are justifiably outraged by unauthorized hacking into sensitive information, including health records, unnecessarily broad, authorized access to health records is more common [7] and thus constitutes a greater problem. As described in more detail below, there are two main ways in which excessive, authorized disclosures may come about. First, a healthcare provider, especially a physician, with a legitimate need to use only part of an individual's health record ordinarily gets unlimited ('role-based') access, and this is a source of concern for some patients. For example, a physician in an emergency department treating a woman for a sprained ankle is unlikely to need access to the woman's reproductive health history or genetic information. As a practical matter, busy physicians do not have the time or inclination to troll through health records in search of sensitive information. Nevertheless, many patients are likely to prefer that potentially stigmatizing genetic test results, such as those indicating a risk for developing Alzheimer's disease, not be disclosed to every physician whom they encounter in the healthcare system. Second, many third parties with an interest in an individual's health and economic leverage over the individual can make signing an authorization to disclose health information a condition of, for example, applying for a life insurance policy. These 'compelled disclosures' increasingly include genetic and other information associated with personalized medicine. Thus, the ability of an individual or healthcare provider to keep the information confidential is seriously called into question [8].

## Discrimination

Discrimination is another widely used term with different meanings. One type of discrimination refers to drawing a legally or socially unacceptable distinction among individuals [9]. This type of discrimination often relies on questionable stereotypes rather than assessment of individual merit, eligibility or ability; it results in the impermissible stratification of society and the denial of essential opportunities to members of a disfavored segment of the population.

The other main type of discrimination simply refers to drawing distinctions in ways that, in the context, are considered rational or socially acceptable. This type of discrimination is best characterized by actuarial decision-making in the insurance industry. On this account, it is acceptable (and even imperative to

the industry) to treat individuals differently according to their risk so long as there is a sound actuarial basis for doing so. It should be noted, however, that some forms of irrational discrimination are at least tolerated by society and some forms of rational discrimination are not. For example, in the USA, it is lawful for an employer to hire employees on the basis of their zodiac sign (irrational) [9], but it is unlawful for an employer to refuse to hire a pregnant woman who will soon take maternity leave (rational) [9]. Public policy is based on more than rationality.

Depending on the context, genetic discrimination might be rational or irrational, legal or illegal. The possibility of genotype-based discrimination was one of the first concerns raised by scholars examining the ethical, legal and social implications of the Human Genome Project. An assumption of many genetics researchers and public officials was that individuals would be reluctant to undergo genetic testing, despite the clinical appropriateness of doing so, if it could result in discrimination in employment, insurance, mortgages or other important activities.

Personalized medicine, with its potential to draw ever-finer distinctions among individuals, could play a part in 'genetic discrimination', because even small genomic differences can have significant economic implications. For example, genomic information could indicate not only that an individual is more likely to develop a certain illness in the future, but also that the individual would not be responsive to standard medications and therefore represented an increased morbidity and mortality risk.

Legislation attempting to prevent genetic discrimination in life insurance and other transactions has been enacted in many countries [10,11]. Most of these laws treat genetic information separately from other health information, another policy that is potentially irrational since it is based on 'genetic exceptionalism' [12]. Many of these laws attempt to prevent genetic discrimination by limiting the information that can be used to assess an individual's likely future health. Beyond privacy concerns, the fundamental issue of genetic discrimination is risk allocation. For example, in the USA, as of 2014, private health insurance companies are not permitted to use an individual's health status (including genetic information) in deciding whether to issue an insurance policy [13]. Although predictive health information is highly relevant from an actuarial standpoint, the new law expresses the public policy in favor of unrestricted access to commercial health insurance that justifies spreading risk across all individuals with insurance. Similar policy questions animate discussions about underwriting for life insurance and other insurance products.

## Physician–patient relationships

Personalized medicine is likely to have major effects on the physician–patient relationship. In the pregenomic era, the diagnosis and treatment of genetic disorders was the exclusive province of clinical geneticists, pediatricians, neurologists, oncologists and a few other specialists. In the era of personalized medicine, the focus is shifting from rare monogenic disorders to common chronic diseases, and the responsibility for treating patients with asthma, hypertension, diabetes and similar disorders belongs to primary care physicians and a wide range of specialists. The first issue is whether these physicians have adequate training to provide the essential services of personalized medicine, such as the interpretation of whole-genome sequencing results, formulating prevention and treatment strategies based on genomic information and applying pharmacogenomic principles and products in prescribing.

Besides a lack of training on the part of physicians [14], another problem is the lack of time. Because personalized medicine will often involve the use of genome sequencing or other complex laboratory tests, this is likely to increase the time needed for a number of clinical tasks. For example, because a genetic test is performed, pretest genetic counseling is necessary to determine whether the patient understands the implications of the test on his or her healthcare, as well as the possible social implications of test results. After receiving the test results, the physician must interpret the information and apply genomic insights in designing a treatment plan. Widely varying health literacy among patients means that some patients will need much more time for explanations. All of these steps are time consuming, yet the trend in healthcare is not to increase, but to decrease the amount of time for clinical encounters.

It is not clear what effects personalized medicine will have on time-pressured clinical encounters. One possibility is that providers will make trade-offs, spending less time on some patient complaints or conditions in order to spend more time on others. This might lead to an unsatisfactory physician–patient relationship, as well as the possibility that subtle sentinel events will be overlooked until they develop into more persistent medical problems. Another possibility is that nurses or other allied healthcare providers will be given greater responsibility in counseling or follow-up, despite a similar lack of training. Still another possibility is that patients will need to assume a larger role in their own health management. In any event, it is quite likely that personalized medicine will lead to changes in the physician–patient relationship.

### Liability

In the USA, and undoubtedly other countries, the development of personalized medicine will almost certainly increase personal injury litigation. Every new medical technology, from transplants to sophisticated imaging, has increased the complexity of medical interventions. With greater complexity comes an increased risk that an error by a healthcare provider will cause harm to the patient, thereby creating the potential for liability. There is a long list of parties that might be sued, including manufacturers of genome sequencers, testing laboratories, pharmaceutical companies, medical device manufacturers, pharmacists and hospitals. At the top of the list are physicians, who are responsible for a patient's overall diagnosis and treatment. As has been well documented [14], many physicians lack formal training and experience in the fast-moving field of personalized medicine, thereby raising concerns regarding their ability to meet a changing and more demanding standard of care.

Numerous possibilities exist for medical malpractice and related claims based on personalized medicine, including tumor genome sequencing, cancer predisposition screening, prenatal testing (including noninvasive prenatal testing), newborn screening and pharmacogenomic testing and prescribing [15]. A discussion of the legal issues is beyond the scope of this article, but it should be noted that the increased amount of genomic information associated with personalized medicine gives rise to additional professional responsibilities. The nature of these responsibilities remains uncertain, however. The possible duty of clinicians – and even researchers – to report incidental findings to patients revealed by whole-exome or whole-genome sequencing remains unsettled [16,17]. In addition, the responsibility to respect or override patient preferences on secondary genomic findings is hotly contested, as demonstrated by the recent modification by the American College of Medical Genetics and Genomics (ACMG) of its own recommendations on this issue [18,19]. Personalized medicine, to a currently unknown degree, raises the possibility of legal liability stemming from access to and use of an increased amount of sensitive health information.

## Exacerbation of existing disparities in healthcare

In addition to the goals already mentioned, leaders in this field have hoped that personalized medicine will contribute to the elimination of health disparities [20]. One proposed mechanism for attaining this goal is that the over-representation of particular phenotypes in certain racial or ethnic groups may serve as an indicator of underlying genotype–phenotype associations, which might then allow for the development of targeted therapies [21]. Similarly, there is hope that pharmacogenomics researchers may identify the genetic variants that contribute to recognized differences in drug responses among racial and ethnic groups [22].

This account of the potential for personalized medicine to address health disparities has raised controversy. In particular, a number of critics have argued that work to explain race-based health disparities within the framework of genomics has tended to reinforce the mistaken belief that racial categories can be mapped directly onto biological realities [23]. Others have argued that by highlighting genetics as an important avenue for addressing health disparities, we may obscure the importance of social, cultural and economic factors in perpetuating disparities [24].

Even though disagreement remains, the debate on these issues at least makes it clear that the elimination of health disparities is 'on the radar' within the personalized medicine movement. This is fortunate, since efforts to apply personalized medicine in routine clinical care have the potential not only to alleviate health disparities, but also to exacerbate them. In fact, the challenge of translating personalized medicine insights in a way that does not worsen health disparities should be a top priority of leaders in this area. In this section, we explore three dimensions of personalized medicine that could contribute to the problem of health disparities: the input–output problem, cost and access to healthcare and access to information technologies.

### The input–output problem

The clinical utility of personalized medicine depends on earlier scientific work focused on identifying genotype–phenotype associations within population groups. However, racial and ethnic minorities have been significantly under-represented in the studies that serve as the 'inputs' for translational efforts [25–27]. In a 2011 study of publications included in the National Human Genome Research Institute (NHGRI) Catalog of Genome-Wide Association Studies, nearly 75% of studies involved only populations of European descent. Fewer than 10% focused exclusively on non-European populations, and these primarily focused on populations from China, Japan and other Asian countries [28]. The proportion of genome-wide association studies conducted with members of racial and ethnic groups that have suffered from health disparities in the USA remains vanishingly small [27]. The causes of this disparity are complex [27], but an important contributing factor is suspicion of the research enterprise among potential research participants [26].

If disparities in the scientific work that informs personalized medicine continue, any benefits that person-

alized medicine will be able to deliver are likely to be distributed unevenly among population groups. This is because the diagnostic and therapeutic approaches that inform personalized medicine practice are developed using data from this type of research. This research reveals, for example, which genetic variants are relevant to disease risk and what "effect size" each variant has on disease risk or response to therapies. The input–output problem arises because allele frequencies and environmental exposures tend to vary among population groups [26]. Because of this, the assumptions that inform personalized medicine practice in well-studied populations are not necessarily generalizable to poorly studied populations. Genetic test panels designed using data from one population group may not capture the genetic variants relevant to disease risk or treatment response in another group [29]. In addition, pharmacogenomic algorithms that guide drug dosing or selection may lead to suboptimal outcomes in patients whose 'background' genetic variants and environmental exposures are significantly different from well-studied populations. This is especially concerning because the groups that have been under-represented in genomic research are also the groups that are already receiving suboptimal benefits from existing healthcare services [30].

## Cost & access to healthcare

Another set of challenges that threaten to exacerbate health disparities in the coming decade are economic barriers that both limit access to healthcare and reduce the benefit patients are able to derive from that care. This characteristic is common to many new healthcare technologies: if patients are unable to access a new technology, then they are also unable to enjoy the benefits of that technology.

In the case of personalized medicine, the laboratory tests that inform personalization, such as next-generation sequencing, are likely to be quite expensive at first, despite optimism that the US$1000 genome has arrived [31]. Such milestones do not account for labor costs, analytical costs or commercial mark-up [31,32]. An additional source of increased cost will be the interventions that are recommended in light of these laboratory test results. For example, pharmacogenomic testing may have the potential to decrease overall costs at the level of the healthcare system. At the level of individual patients, however, many are still likely to end up taking medications with higher direct costs compared with the standard therapy [33,34].

The costs of personalized therapeutics and the tests that inform their use are unlikely to cause difficulty for patients who are already well served in the healthcare system. In countries with private insurance systems, patients with comprehensive health insurance coverage or the ability to cover such costs out-of-pocket will be able to undergo new tests and receive the benefits of individualized treatments despite their cost. Patients with no insurance, as well as patients with insurance designed to provide only urgent care, are unlikely to benefit from these advances.

Patients living in countries with nationalized health insurance systems are likely to fare somewhat better. Nevertheless, these systems generally limit coverage to treatments with established efficacy. Since studies related to clinical applications of personalized medicine could require larger study samples compared with conventional approaches, it may take longer for an evidence base to emerge for such applications [35,36]. If this is the case, nationalized health insurance systems may be slow to adopt personalized medicine approaches. If this occurs, even interventions that eventually prove efficacious might be available only on the private market for an extended period of time.

Regardless of the nature of the health insurance system, most patients in developed nations will eventually receive benefits from personalized medicine. In comparison, improvements in the care received by patients in developing nations are likely to be limited. The cost of new diagnostic tests and alternative treatments are likely to limit their availability in these parts of the world for the foreseeable future. Even more importantly, perhaps, the medical problems that cause the most morbidity and mortality in developing nations are comparatively rare in the developed world. If personalized medicine is to be efficacious for these patients, then research efforts focused on personalized medicine will need to expand to include work on the medical conditions endemic to these areas. Furthermore, since 'background' genetic variants and environmental exposures are so important to personalized treatments, this work will need to be performed with the populations of these developing nations, a group that has previously been under-represented in personalized medicine research [37].

In both developed and developing nations, the costs associated with health behavior changes are another source of disparity in the benefits personalized medicine will deliver. There is already ample evidence that medical problems influenced by health behaviors disproportionately affect patients in lower socioeconomic strata [38,39]. Among other insights, this disparity reflects the degree to which personal finances affect patient access to healthy foods, exercise facilities and other resources related to healthy behaviors. Many advocates for personalized medicine have argued that genomic tests might improve health by helping patients identify their health risks and

undertake health behavior changes that could help mitigate these risks [20,40–43]. However, the likelihood that risk information will help individual patients make meaningful changes in health behaviors will be influenced by a range of factors beyond the control of the healthcare system [44]; one of these will undoubtedly be the financial resources that patients have to support these changes.

### Access to information technologies

Information technologies that allow patients to access their own health records play a central role in many visions of personalized medicine. In part, this is due to the value of such technologies for addressing the challenge of information overload. However, the centrality of these technologies to personalized medicine also reflects growing interest in empowering patients to monitor their own health, perform research on their own health problems and make positive health behavior changes. In this way, personalized medicine reflects more general trends in healthcare to encourage patients to use information technologies in order to take responsibility for their own health needs [45,46].

This movement towards increased patient responsibility for health is reflected not only in cultural trends, but also in public policy. In the USA in particular, a range of recent public policy changes are intended to encourage healthcare institutions to provide patients with direct electronic access to their health records. The 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act created financial incentives for institutions capable of demonstrating 'meaningful use' of an EHR. Patient portal functionality is one application that can help an institution prove it has attained meaningful use of an EHR [47]. Similarly, a recent amendment to regulations promulgated under the Clinical Laboratory Improvement Amendments of 1988 allows laboratories to give patients or their designated representative direct access to laboratory test reports; in the past, only healthcare providers were authorized to receive such results [48].

While efforts to empower patients are laudable, they raise significant challenges related to health disparities. A patient can only benefit from an electronic patient portal if he or she has access to internet services and an internet-capable device, as well as the necessary computer literacy to navigate to and within the portal website. Going further, the information presented on an electronic patient portal is only useful to those patients with adequate health literacy. This is especially problematic for 'omics'-based laboratory results, which can prove especially difficult to understand. In short, the patients who are most likely to have the resources needed to make productive use of a patient portal for personalized medicine are those patients who are already well served by the healthcare system [49].

Personalized medicine should account not only for the genetic individuality of patients, but also for individual environmental exposures and the unique social situations that influence patient abilities to utilize healthcare. In the current vision of personalized medicine, electronic patient portals are portrayed as one-size-fits-all tools for patient empowerment. If personalized medicine is to be successful, more targeted approaches will be required. Without such alternatives, it is possible that electronic patient portals may create an illusion that all patients have the resources they need to improve their health. Such an illusion could be counterproductive, since the more patients are perceived to have the power to improve their health, the more likely they are to be seen as responsible for their health outcomes [45,50,51].

## Conclusion & future perspective

As we enter the second decade following the Human Genome Project, we see a need to expand the scope of work on the ethical, legal and social challenges raised by personalized medicine to account for its growing clinical applications throughout the healthcare system. Fortunately, the fields of bioethics and clinical ethics have rich traditions of addressing issues such as health disparities, patient privacy and the physician–patient relationship. We believe it will be extraordinarily productive to expand the community of scholars working on the ethical, legal and social implications of genomic medicine to include new types of expertise. In particular, those who have worked on health policy and clinical ethics issues unrelated to genomics have much to contribute to ethical, legal and social implications scholarship. Collaborations with health economists, quality experts and implementation scientists could also be extraordinarily productive.

The issues this expanded community of ethical, legal and social implications scholars could be called upon to address are vast; the two issues we have identified are just a starting point. We anticipate, for example, that personal responsibility for health will be an increasingly important issue in healthcare in the coming years. As we observed earlier, the personalized medicine movement has demonstrated a strong interest in empowering patients to take responsibility for their health. We know, however, that the concept of individual responsibility for health is indelibly linked with debates in many countries over the best

approaches to funding healthcare [52]. This interplay between personalized medicine, individual responsibility and ideologies surrounding the funding of healthcare is just one topic of importance that is likely to benefit from interdisciplinary examination in the near future. In order to best address these issues and others, the next decade in personalized medicine should be a time of collaborative, proactive work to anticipate additional challenges and find collaborative ways to improve patient care that are responsive to ethical, legal and social concerns.

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## Executive summary

**Background**

- As personalized medicine becomes integrated into a growing number of clinical areas, its ethical, legal and social implications will expand in scope and complexity, incorporating existing issues raised by healthcare systems.
- We identify two broad issues that will grow in importance: the consequences of the significantly increased amount of health information associated with personalized medicine; and concerns regarding the potential of personalized medicine to exacerbate disparities in healthcare.

**Increased amount of health information**

- Genomic and other 'omics' technologies generate a large amount of data. For this reason, the application of these technologies in clinical settings will raise novel issues related to privacy and discrimination. The availability of these data is also likely to bring about changes in physician–patient relationships and increase personal injury litigation.

**Exacerbation of existing health disparities**

- Inequalities in research to collect medical evidence, as well as access to healthcare services and information technologies, are likely to increase existing disparities in healthcare. Work in this area will need to focus not only on disparities that exist within communities, but also those that affect fair access to healthcare globally.

**Future perspective**

- The next decade in personalized medicine should be a time of collaborative, proactive work to anticipate and address emerging challenges, including issues such as health disparities, patient privacy and the physician–patient relationship.

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