10 years of personalizing medicine: how the incorporation of genomic information is changing practice and policy

“...to effectively translate the advances that are now beginning to lead to the practice of personalized medicine will require systems-level innovations in order for personalized medicine to contribute substantially to patient care and health outcomes.”

Keywords: big data • bioinformatics • clinical decision support • economics • genome wide association studies (GWAS) • information technology • personalized genomic medicine • policy • regulatory • whole genome sequencing (WGS)

On this tenth anniversary of the founding of the journal Personalized Medicine, it is apropos to celebrate not only the founding of what has, over the past 10 years, grown into the premier journal for the field of personalized genomic medicine, but also the growth of the field itself. The field of personalized medicine has indeed grown by leaps and bounds over the last decade: from its tentative beginnings as a nom-de-plume for ‘pharmacogenomics’ to include a broader spectrum of genomic advances and technologies, including genome wide association studies (GWAS), exome sequencing, and next-generation sequencing (NGS) [1]. The personalized genomic medicine approach has now been applied to a number of disease areas including oncology, psychiatry and cardiovascular conditions [1–4]. Some of the most exciting personalized genomic medicine advances have occurred in oncology, including a number of diagnostic tests as a clinical prognostic factors (such as gene expression profiling assays for breast and colorectal cancer and the long-QT syndrome panel) and targeted therapeutics (e.g., trastuzumab and irinotecan).

Generally personalized genomic technologies have been applied towards three main purposes: to discern the contribution of polymorphisms to particular adverse drug events (ADEs) or sub- or supra-therapeutic drug responses; to identify potential biomarkers for specific diseases; and to assess clinical response with the use of targeted therapeutics. These applications have led to novel therapeutics, increased surveillance, monitoring and risk reduction measures in a number of diseases and conditions, including cancer, cardiovascular and cardiometabolic conditions (e.g., diabetes), and neurodegenerative disorders [1–4]. Since 2004, when the journal Personalized Medicine was launched, there have been major advances in the development and availability of commercially available genomic products, from the 21-gene recurrence score prognostic assay, Oncotype DX® for early-stage breast cancer, first marketed in 2004, and Gleevec used in the treatment of chronic myeloid leukemia patients who test positive for the Philadelphia chromosome to the use of VKORC1 and CYP2C9 testing to guide warfarin dosing. Indeed, there was more than a 10-fold increase in the number of commercially available products between 2004 and 2014, across different therapeutic areas. The US FDA now includes genomic information and associated recommendations for well over 100 approved drugs [5].

Enter the era of sequencing

In addition to these impressive advances, we have been making steady progress over the last few years in sequencing technologies, such as whole genome sequencing (WGS) and exome sequencing [1]. Indeed, exome sequencing is increasingly being used in clinical practice settings with some success [6]. The cost of sequencing genomic material is
Increasing (from a starting cost of about $300 million to roughly $3000 today), and is predicted to continue to drop, making it likely that we will begin to see more rapid developments in the use of sequencing technologies, and particularly WGS, on a more routine basis in clinical settings.

In addition to these scientific and clinical advances over the past decade, the field of personalized medicine has also led to both policy-relevant opportunities and challenges.

The policy landscape of personalized medicine
Economic & regulatory considerations
The value of various personalized genomic technologies has been investigated using health economic methods. The cost-effectiveness of different genomic diagnostics and targeted therapeutics has been studied, and in some cases found to be cost effective [7] and less so in others [8]. This area of research is still relatively young and economic analyses of the use of personalized medicine interventions in clinical settings are at this time not entirely conclusive [8]. Nevertheless, this pharmacoeconomic research is valuable for payers and other stakeholders for policy decisions.

“It is time to make a collaborative and global concerted effort to accelerate the adoption and effective implementation of personalized medicine within health systems.”

Internationally, regulatory agencies including the US FDA, EMA and Health Canada have made progress in regulatory statements and in some cases legislative actions, that have favored personalized medicine research and clinical developments. However, regulatory activity is still in a formative state throughout the world, even in countries where a lot of personalized medicine research and clinical developments have been made. Indeed, the need for appropriate regulatory guidance and international harmonization is an important emerging policy challenge that is necessary to foster innovation and the adoption of personalized medicine technologies into health systems.

Big data, information technology & personalized medicine policy
Continuing computational advances and information technology (IT) capabilities have spawned the new era of ‘big data’. Although there are varying definitions of the term ‘big data’, it is generally understood as voluminous amount of data that exceeds the capacity of readily available bioinformatic and computational tools. Although computational technologies, and particularly large databases and electronic medical records (EMR), have supported and underpinned many of the developments in personalized genomic medicine research, ongoing advances will depend on developing and implementing a stable and reliable infrastructure.

Going forward, what is needed for personalized medicine to become more fully incorporated into clinical settings and health systems is an infrastructure that allows for large multimodal data sets to accurately model biological complexity and integrate it with key clinical and patient-centered components such as phenotypic features, patient’s history and health status, as well as decision-support capacity, in order to derive effective decision algorithms that are necessary to allow more precise personalized and predictive outcomes for patients. This requires serious investment at national and international levels in IT infrastructure across health systems for reliable and accessible (to healthcare providers and patients) inpatient and ambulatory care that goes well beyond the mixed bag of EMR systems currently in place today, which, for the most part, do not allow for the decision support capabilities required to support and facilitate personalized medicine.

We [9,10] and others [11] have been investigating patient and provider decision-making related to personalized medicine over the past decade. However, this area of research is still in its infancy and clearly more work needs to be done to better understand patient and provider-decision-making and develop effective clinical decision support tools and strategies.

More recently, renewed interest in ‘patient-centered care’ [12] underscores the importance of understanding decisions surrounding personalized genomic medicine and personalized medicine applications. We need to continue to conduct research to better understand the role of patient and provider decisions surrounding personalized genomic medicine, probabilistic risk understanding and knowledge and the uncertainty that often underlies such decisions in order to better develop appropriate and effective decision aids and support tools that enable the delivery of information to facilitate good decision-making about personalized genomic medicine and to allow for positive health outcomes.

In addition to the issues discussed above, the policy landscape for personalized medicine has been inuanted with ethical, legal and social issues (ELSI), and progress has been made to recognize ELSI considerations from the earliest studies [13,14] to an increasingly broader array of research [15]. Some policy-relevant progress has been made such as the passage of the Genetic Information Non-Discrimination Act (GINA) in the USA in 2008, legislation designed to
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Editorial

In order to fully realize the adoption and implementation of clinical personalized genomic medicine in health systems globally, it is important to achieve an integration of basic molecular science, technological advances (including in bioinformatics and clinical decision support infrastructure), and clinical science and to develop appropriate and effective policies. In other words, to effectively translate the advances that are now beginning to lead to the practice of personalized medicine will require systems-level innovations in order for personalized medicine to contribute substantially to patient care and health outcomes. It is time to make a collaborative and global concerted effort to accelerate the adoption and effective implementation of personalized medicine within health systems.

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