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Personalized Health Care Five Years Later

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The year was 2010. It was seven years since the completion of the Human Genome Project in 2003, and the excitement and anticipation of the promise of genomics was palpable. Our hope was that genomics would finally allow the ability to more precisely predict disease risk, customize therapies, and prevent disease—the concept of which is commonly referred to as "personalized health care." But in 2010, we rarely used genomic technologies in clinical practice. Why was it taking so long for us to see the fruits of this project?

When I entered the field of personalized health care, the charge I was given by our visionary leader and chief executive officer Toby Cosgrove, MD, was to integrate genomics into mainstream clinical practice. The timing was ideal, I thought, as President Obama had just brought to national attention the crisis of health care spending in the United States. We were spending more than any other developed country on health care[1] and yet scoring the worst in measures of access, quality, equity, and efficiency of care.[2] As a general internist, I knew this was true. We were ordering too many unnecessary tests, we allowed care to be delivered haphazardly by specialists who were only focused on one piece of the puzzle, and we were incentivized to do more—particularly more procedures. My hope was that by leading this charge at Cleveland Clinic, a national model for coordinated care, I might be able to help shift the curve of health care spending, allowing us to deliver more precise care—the right care for the right patient—that might result in targeted interventions and screening, higher quality, and lower cost.

Table 1. Examples of Clinical Indications for Cancer Genomics

Disease	Indicator	Therapy	References
Non-small cell lung cancer	EGF-R over-expression	Gefitinib/erlotinib	5, 6
Chronic myeloid leukemia	BCR-ABL Philadelphia chromosome +	Imatinib	7
Breast cancer	BRCA1 mutation	Parp inhibitors	8

Table 2. Examples of Clinically Relevant Pharmacogenomics Tests from CPIC Website

Drug	Test	Clinical relevance	FDA warning exists
abacavir	HLA-B*5701 positive	High risk for hypersensitivity	Yes
allopurinol	HLA-B*58:01 positive	High risk for severe cutaneous adverse reactions (SCAR)	No
carbamazepine	HLA-B*1502 positive	High risk for severe cutaneous reactions (SJS/TEN)	Yes
warfarin	CYP2D6/VKORC1	Result may guide initial dosing	Yes
clopidogrel	CYP2C19*17 allele	High risk for bleeding	Yes

I am a primary care general internal medicine physician, trained in the 1990s when genomics was a very very small piece of the medical school curriculum. First on my list was to read up on genomics to separate hype from fact. In my mind, personalized genomic health care served two purposes: predicting risk and customizing therapies. What I found from scouring the medical literature was that there were very few genomic tests that could predict risk for disease accurately because most of the diseases we see as internists are multi-factorial. Even if we carry a gene or group of genes that are associated with a specific disease, we usually need some sort of environmental or other exposure to actually change phenotype and trigger expression of the disease. While scientists continued to search for the right combination of genes that would enable accurate prediction of disease risk (and offer potential drug or vaccine targets to prevent disease), it was clear from the medical literature that the best predictor of disease risk continued to be family health history (FHH). FHH is often overlooked, and while crude, it encompasses a combination of both genetic and environmental risk factors. Yes, it's true! FHH, a portion of the history that we clinicians often spend less than 2.5 minutes collecting and that the literature indicates we do not routinely discuss with patients,[3] has been proven repeatedly to be a better predictor of risk than genomic testing for many condi-

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tions we see in clinical practice—breast cancer, colon cancer, diabetes, and AAA, to name a few.[4]

In contrast, when it came to predicting response to therapies, there were many evidence-based successes in the realm of cancer genomics (Table 1) with broad acceptance and implementation of these already taking place in major medical centers such as mine. I also found a large body of scientific literature in the field of pharmacogenomics (i.e. genes that predict drug response and adverse events) and rising national interest in the use of pharmacogenomics in standard medical practice. One such national group is the Clinical Pharmacogenomics Implementation Consortium (CPIC), a branch of PharmGKB that has since published 34 peer-reviewed recommendations on the use of pharmacogenomics in clinical practice.[9] A few examples of clinically relevant pharmacogenomic tests are outlined in Table 2. CPIC's recommendation statements provide useful guidance on how to change clinical management based on a pharmacogenomic test, but we still do not have clear consensus on when these tests should be ordered.

What was clear from my investigation was that we were very early in the process of integrating genomics into mainstream clinical practice and that the opportunities for implementation fit two categories: 1) the consistent collection and systematic use of FHH for disease risk prediction and 2) laying a framework and structure for the integration of pharmacogenomics into clinical practice. These became our initial projects, and along with a team of talented and dedicated individuals, we built a FHH collection and risk assessment tool with clinical decision support (MyFamily) and an alert-based pharmacogenomics program (Personalized Medication Program) that are both still in use today. The importance of these programs is not only in their current use but also in the foundation they provide for future incorporation of genomic information into clinical practice. At the same time, we recognized that many clinicians, myself included, who were trained before 2000 had limited knowledge of genomics and understanding of when genomic tests are clinically helpful or how to interpret them. As such, we dedicated large amounts of time and effort providing education around topics of FHH, pharmacogenomics, and basic principles of genetics and genomics. I am incredibly grateful to my personalized health care team members; to my mentor David Bronson, MD; to the many clinicians who supported our efforts; and to the Personalized Medicine Coalition, an advocacy group under the direction of Ed Abrahams, MD, who provided us with education and advocacy opportunities and helped us to forge key strategic collaborations.

We made great strides in the integration of genomics into clinical practice, and I am incredibly proud of the work we did. We also learned some important lessons. This investment in the future of medical practice was costly and time consuming. We need to spend more effort on research—discovery, implementation science, and the randomized controlled trials that many want to see before changing clinical practice. We need to advocate for funding for such research. We need to continue the good work being done in personalized cancer care. And we need to increase our efforts to educate and keep all of our clinicians up to date on the latest that genomics has to offer, including developing an increased understanding of when these tests are useful. There is much to be done, and I continue to hope that genomics and a better understanding of FHH risk will allow patients to be healthier for longer periods of time. In the meantime, I urge clinicians to keep abreast of current research in this field and seek opportunities to learn how genomics may influence an individual's risk for disease and response to therapies. We should re-dedicate our efforts toward accurate FHH collection and use of FHH for risk prediction. As for me, it is clear that genomics and FHH are important ingredients, but they are just one portion of our overall ability to provide personalized care. Personalized health care will require a convergence of biology and science; community and individual health and wellness; patient engagement; and coordinated, team-based, accessible health care. Some call this population health; some call this value-based care. Regardless of the name, we need to move together as a team of clinicians, scientists, teachers, patient advocates, and innovators so that we can achieve the goal of better health for our patients and communities and the vision of the *right* care for the *right* patient.

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