

Patients' and Consumers' Interests and Perspectives in Personalized Healthcare

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I. INTRODUCTION

“Progress in [personalized medicine] will characterize medicine in the 21st century and extend life span much like the use of antibiotics did in the 20th century.”

-- Gerald Levey¹, Provost and Dean, University of California, Los Angeles School of Medicine, *FasterCures* Board member

The 20th century witnessed the greatest expansion of life expectancy in the history of humankind. The challenge for the 21st century is to not only extend the length, but to also improve the quality of life by preventing and defeating deadly and debilitating diseases. Across the spectrum - from basic science to clinical research to health services research - the impressive advances of recent decades in the biomedical, physical, computational, and behavioral and social sciences present unprecedented opportunities to improve human health and quality of life. Capitalizing on this reality will usher in an era of personalized medicine and solidify its place at the frontier of medical science.

The ultimate value of personalized medicine will be to improve treatment options for patients and prevent the onset of disease in the first place. But to realize these important gains, we need to transform our current research and healthcare systems from the outdated model of the last century to an integrated, information-based, high-quality, health-sustaining model that will extend life expectancy and improve the quality of life for generations to come.

To achieve this transformation the new system must focus on patients. How personal is personalized healthcare and what do consumers think about the advent of this era?

Embedded within each patient is the information – family history, medical records, lifestyle, biological samples, etc. – that is crucial to understanding, treating, and preventing disease. Patients need to be empowered by accurate information and armed with a clear understanding of the opportunities to:

- participate in research and clinical trials;
- donate biological material such as tissue and blood samples; and
- advocate to have interoperable electronic health records (EHRs) to aid care and research.

As a contribution to U.S. Department of Health and Human Services Secretary Michael O. Leavitt's Personalized Healthcare Initiative, *FasterCures* submits this white paper summarizing the perspective of patients and consumers, the prime constituency in the discovery of personalized medicine advances and the ultimate beneficiaries.

¹ Levey G, “Personalized Genetic Medicine: In Theory and In Practice,” *FasterCures* Essays for Change, <http://www.fastercures.org/voice/essays>.

To paint a complete picture and accurately represent the numerous patient perspectives on personalized healthcare, *FasterCures* conducted a qualitative research survey of disease research organizations, patient advocates, and patients to gauge understanding, awareness, and expectations of personalized healthcare and elucidate the issues that affect millions of Americans.

II. The Path to Personalized Medicine: Patient Involvement

“Success is when everyone can learn which methods and treatments work, and which don’t, in days instead of decades.”

-- Carol Diamond and Clay Shirky²

In 1799, explorers unearthed in Egypt a stone slab – the Rosetta Stone – bearing parallel inscriptions in Greek, Egyptian hieroglyphic, and demotic characters, which made it possible to decipher the written language of the ancient Egyptians and the stories that it told about the people and their culture. Each of us is, in a sense, a Rosetta Stone, for within us is the information necessary to unlock the relationship of genetics, proteomics, behavior, nutrition, and environment to the emergence and, ultimately, the management of disease.

The three "languages" of our Rosetta Stone are medical records; biological material such as tissue, blood, and DNA; and our biology as observed in clinical research. By participating in clinical research – trials to test potential new therapies as well as epidemiological, observational, or natural history studies – and by providing tissue samples, blood, or medical histories, patients can provide critical information and resources, without which the search for cures and advancements in personalized medicine could slow to a halt.

Many respondents to our survey felt that the greatest payoff to personalized healthcare will come from leveraging the patient’s role in these critical areas:

- ***Biological specimens.*** It is important that patients understand the key role that biospecimens play in medical research, and how critical they are to future research discoveries. To understand the connections between genes, proteins, and the environment, sophisticated comparisons must be conducted. These comparisons cannot be done by hand or by eye, or patient by patient.

It is interesting to note that the importance of tissue sample collection was generally not mentioned by our survey respondents. Some pointed out that patients can be uncomfortable with the notion of donating their tissue, and the time to educate patients about tissue donations for research is not at the moment a consent form is

² Diamond C, Shirky C, “Health Information Technology: A Few Years of Magical Thinking?” *Health Affairs*, September/October 2008; 27(5): w383-w390.

being signed for diagnosis or clinical care. Patients and patient groups must be brought into the process as partners in helping to ensure that the patient community understands how biobanks work, and the role they play in the clinical research infrastructure. *FasterCures* has a website devoted to this topic www.biobankcentral.org.

- **Clinical trials.** Clinical trials are the only way of evaluating whether new diagnostics, drugs, experimental medical devices, and surgical techniques actually work. These trials are dependent upon patient involvement. The *FasterCures* Patients Helping Doctors (PHD) Program facilitates the understanding of the critical role patients play in research, with the ultimate goal of increasing patient participation in this process. We have found that there are many reasons for the lack of patient participation including:
 - patients not having enough information about clinical research,
 - physicians not having enough information and not informing their patients about the possibility of enrolling in a clinical trial, and
 - patients and doctors having misconceptions about clinical trials.³

Respondents to our survey outlined how highly motivated their patients are to participate in clinical trials. For example, in the National Institutes of Health (NIH)-sponsored Alzheimer's Disease Neuroimaging Initiative (ADNI) trial, the enrollment has exceeded the study program director's expectations despite some of the painful medical procedures trial participants are undergoing.⁴

Overall, patients who enter trials see it as part of their larger role of advancing science. One respondent said, "Within the cancer community, there is a profound altruistic feeling. They want to help by participating in trials, and the data shows that when they do, they feel positively about the experience." Survey respondents did feel we need to incentivize more participation in clinical trials; otherwise, it will be hard to move personalized medicine forward.

- **Electronic Health Records (EHRs).** The promise for personalized medicine offered by integrated EHRs is immense. EHRs will go a long way to solving the information gap that often exists as patients travel from one provider's office to another. EHRs will also provide much-needed ways to aggregate data about treatment and outcomes for research and offer unprecedented opportunities to speed up the quest for cures. As patients wait for better therapies and eventual cures however, EHRs will help to manage some of the chaos created by complex individual co-morbid conditions.

³ See the *FasterCures*' white paper, *Clinical Trials Recruitment and Retention: Best Practices and Promising Approaches*, September 2006, http://www.fastercures.org/objects/pdfs/meetings/FC_ClinicalTrials_report_art_spg.pdf.

⁴ Laurie Ryan, Program Director, Alzheimer's Disease Clinical Trials, National Institute on Aging, NIH, Presentation Comments, Institute of Medicine Forum on Drug Discovery, Development, and Translation workshop "Breakthrough Business Models: Drug Development for Rare and Neglected Diseases and Individualized Therapies," June 23, 2008, Washington, DC.

Enabling research use of information collected in the patient care process could significantly accelerate medical research. EHRs and clinical databases and warehouses can make the work of specialists in one discipline widely accessible to specialists in many disciplines. EHR systems could speed data acquisition and searching, allow mass computing and sampling, and provide the research community access to a broader and more diverse patient population. Improvements made in EHR systems in response to research needs will ultimately serve clinical care needs as well.

III. The Personalized Medicine Landscape: What Do Patients and Consumers Think?

“We must remember that the true foundation of this progress is public trust. It is not enough merely to develop the knowledge and information that will make personalized healthcare possible. In addition to developing the information, we must use it correctly.”

-- Michael O. Leavitt, Secretary of U.S. Department of Health and Human Services⁵

It would be inaccurate to say there is only *one* patient community. There are hundreds, perhaps thousands of them, each defined by different experiences as their members manage disease from diagnosis through treatment and possibly cure. Patient awareness and understanding of personalized medicine and healthcare has begun, but it will be an ongoing process that will vary and evolve based on the disease.

The national discussion about personalized medicine has mostly occurred at the 30,000 foot level and has yet to comprehensively engage and permeate the broad array of patient communities with its myriad concerns.

Methodology

In order to understand the key role of patients in driving the adoption of personalized healthcare approaches, *FasterCures* conducted a qualitative research survey of disease research organizations, patient advocates, and patients to determine understanding, awareness, and expectations of personalized healthcare. For the survey, we reached out to senior executives of 10 groups in the *FasterCures* Redstone Acceleration & Innovation Network (TRAIN). We also identified an additional five national organizations that are not in TRAIN that represent the issues related to diseases that affect millions of Americans.

TRAIN is a group of unique nonprofit foundations that fund medical research across a spectrum of diseases, from breast cancer to Parkinson’s disease.⁶ In many cases

⁵ See the Department of Health and Human Services report, *Personalized Health Care: Opportunities, Pathways, Resources*, September 2007, www.dhhs.gov/myhealthcare/news/phc-report.pdf.

TRAIN's member foundations have been created by patients and their families who are frustrated by the slow pace of change in the traditional medical research system. They represent the kind of organizations that are fast becoming the engine behind innovation in disease research – collaborative, mission-driven, strategic in their allocation of resources, and results-oriented. They are organizations that have a singular focus on, and a significant stake in, getting promising therapies from the laboratory bench to the patient's bedside as rapidly as possible.

Figure 1 – *FasterCures*' TRAIN Program



TRAIN has come together under the auspices of *FasterCures* – a nonprofit “action tank” whose mission is to save lives by saving time in the research, discovery and development of new medical solutions for deadly and debilitating diseases. The TRAIN network helps its members to more easily and effectively support each other’s efforts to produce better and faster results, and to bring their sense of the urgency about conducting more and better bench-to-bedside translational research to the medical research community as well as to the public at large.

FasterCures surveyed groups using email and telephone-based methods and attempted to reach representatives from a variety of diseases ranging from preventable to incurable. Specifically, representatives from the following groups were interviewed:

⁶ See www.fastercures.org for more information on *FasterCures*' TRAIN program.

Table I. <i>FasterCures</i>' Personalized Healthcare Qualitative Survey Respondents			
Organization	Organization Overview	Contact, Title/Role	Outreach Mechanism
Accelerated Cure Project for Multiple Sclerosis	Organizes the research process for multiple sclerosis and encourages collaboration between research organizations and clinicians.	Art Mellor, President & CEO, Co-Founder, Director	E-mail Correspondence
Alpha-1 Foundation	Identifies those affected by Alpha-1 Antitrypsin Deficiency (Alpha-1) and improves the quality of their lives through support, education, advocacy, and to encourage participation in research. The Association has over 70 volunteer-led support groups around the U.S	John Walsh, President	Phone Interview
Alzheimer's Association	Mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health. The organization's achievements and progress in the field have given thousands of people a better quality of life and brought hope for millions more.	Jennifer Zeitzer, Associate Director, Federal Policy	Phone Interview
American Heart Association	Nation's oldest and largest voluntary health organization dedicated to building healthier lives, free of heart disease and stroke. In fiscal year 2006–07 the association invested more than \$554 million in research, professional and public education, advocacy and community service programs to help all Americans live longer, healthier lives.	Derek Scholes, Government Relations Manager	Phone Interview
Autism Speaks	Focuses on increasing awareness of autism spectrum disorders, to funding research into the causes, prevention, treatments and cure for autism, and to advocating for the needs of affected families.	Nancy Jones, Program Director	Phone Interview
COPD Foundation	Mission is to develop and support programs which improve the quality of life through research, education, early diagnosis, and enhanced therapy for persons whose lives are impacted by Chronic Obstructive Pulmonary Disease.	John Walsh, President	Phone Interview
Epilepsy Therapy Development Project	Mission is to advance new therapies for people living with epilepsy; supports the commercialization of new therapies through direct grants and investments in promising academic and commercial projects.	Joyce Cramer, President	Phone Interview
Friends of Cancer Research	Raises awareness and provides public education on cancer research in order to accelerate the nation's progress toward better tools for the prevention, detection, and treatment of all cancers.	Jeff Allen, Executive Director	Phone Interview
Hydrocephalus Association	Provides support, education and advocacy for people whose lives have been touched by hydrocephalus and the professionals who work with them; advocates for increased research and funding to advance understanding, improve diagnosis and treatment, and find a cure.	Dory Kranz, Executive Director	E-mail Correspondence
Lance Armstrong Foundation	Focuses on cancer prevention, access to screening and care, research and quality of life for cancer survivors. LAF has raised more than \$260 million for the fight against cancer.	Adam Michael Clark, Director of Health Policy	Phone Interview
Michael J. Fox Foundation for Parkinson's Research	Mission is to ensure the development of a cure for Parkinson's disease within the decade through an aggressively funded research agenda. The Foundation has funded over \$126 million in research to date.	Debi Brooks, Co-Founder	Phone Interview

National Health Council	Represents 119 national health-related organizations working to bring quality health care to all people. Its core membership includes some 50 of the nation's leading voluntary health agencies representing about 100 million people with chronic diseases and/or disabilities. Other Council members include professional and membership associations, nonprofit organizations with an interest in health, and major pharmaceutical and biotechnology companies.	Myrl Weinberg, President	Phone Interview
Parkinson's Action Network	Serves as the voice of Parkinson's on numerous public policy issues affecting the Parkinson's community.	Mary McGuire Richards, Deputy Chief Executive Officer	Phone Interview
Prostate Cancer Foundation	Provides funding for more than 1,400 research projects at nearly 150 institutions worldwide; advocates for greater awareness of prostate cancer and more government resources, resulting in a twenty-fold increase in government funding for prostate cancer.	Jonathan W. Simons, President & CEO	Phone Interview
Susan G. Komen for the Cure	Largest grassroots network of breast cancer survivors and activists fighting to save lives, empower people, ensure quality care for all and energize science to find the cures. Invested more than \$1 billion in the fight against breast cancer in the world.	Elizabeth Thompson, Managing Director, Public and Medical Affairs	Phone Interview

Additionally, *FasterCures* posted a description of the goals of this white paper along with several questions on *PatientsLikeMe*⁷ to solicit candid feedback from patients. We received responses from 32 patients. The responses we garnered from this process are woven throughout this white paper. More patients are turning turn to online tools like *PatientsLikeMe* where they interact to help improve their outcomes. The data they provide helps researchers learn how these diseases act in the real world.

Overall Perspectives About Personalized Healthcare

Respondents identified a wide spectrum of current applications of personalized medicine for specific diseases. Our survey found that patient awareness and understanding of personalized medicine has begun, but it will be an ongoing process and that educational process will vary based on the disease. Everyone interviewed had some understanding of what personalized healthcare was, and the potential benefits it will offer as we transition from a trial-and-error, one-size-fits all approach to treatment to one that is tailored to individuals. Respondents on *PatientsLikeMe* were aware of it in a general sense, but didn't necessarily know that it was called personalized healthcare.

⁷ PatientsLikeMe is the leading treatment, symptom and outcome sharing community for patients with life-changing conditions, and creates new knowledge by charting the real-world course of disease through the shared experiences of patients with ALS, Multiple Sclerosis, Parkinson's, HIV, and Mood conditions (including depression, bipolar, anxiety, OCD and PTSD). The company endeavors to create the largest repository of real-world disease information to help accelerate the discovery of new, more effective treatments. See www.patientslikeme.com.

There were some differences in whether people thought personalized healthcare was simply a way to understand the genetic and individual basis of disease or rather another way to segment patient populations and offer tailored therapies.

Even among groups who characterize themselves as less engaged on this issue, there was still widespread acknowledgment that this is the direction in which 21st century medicine is heading. There was however, a sense that the leadership of the patient community lacked a clear sense of what was, and was not personalized medicine, identifying the need for additional work on definitions and illustrative examples. A wide spectrum of current applications of personalized medicine to specific diseases was represented by respondents including warfarin testing and BRAC1 for breast cancer.

Citing the Need for Patient-Centered Care

Some of the issues raised by the interviews were not always specific to personalized healthcare but instead represented challenges that patients have faced for years. Specifically, respondents expressed widespread frustration with the inability of the healthcare system to address each patient's needs, and to efficiently and effectively coordinate care across providers and conditions. **Personalized healthcare will not be immune to these challenges, and as innovative treatments and diagnostics grow more complex, it is a reasonable concern that the insufficiencies within coordination of care will become exacerbated.**

The need for ***patient-focused care*** is increasingly more important as scientific discoveries bring us closer to personalized health care. "We need to address the medical and social goals of the whole person with multiple co-morbidities in the context of their individual life circumstances. We must try to get away from a purely medical model that offers only a disease-by-disease approach without consideration of personal desires such as living independently, remaining in the workforce or managing chronic pain," offered Myrl Weinberg, President of the National Health Council, which represents over 120 member organizations including patient advocacy organizations.

"People with chronic conditions will interact with the health sector for the rest of their lives. If patients are an afterthought and not engaged at the front end of the research process, our collective opportunity to address the complicated medical and social needs of the whole person may be lost, and the scientific advances of personalized medicine and the expected benefits will be diminished," said Weinberg.

Even more strongly, a patient said, "What I've experienced so far in most hospital environments is all but personalized... I felt more like cattle than a human being in general."

If patients are an afterthought and are not engaged at the front end of the research process, the scientific advances of personalized medicine and the expected benefits to patients will be hindered. If patients are to be involved in clinical research leading to

advancements in personalized healthcare, they need better information and a deeper understanding of it based on clear, concise, and accessible information.

A theme emerging from our analysis was that perspectives on personalized healthcare are directly shaped by the state of the science in a given disease area. All groups expressed knowledge of personalized healthcare and a majority had participated at some level in meetings and discussions on this topic. However, for diseases with a strong understanding of the mechanism causing the illness and associated targeted therapeutics, respondents offered an even more robust understanding and appreciation of personalized healthcare.

Many recognized the potential advances on the horizon for their disease area, but remarked that it still feels far enough away that it is difficult to reach and therefore difficult to plan for. “We are here and we are far away from personalized healthcare all at once,” mentioned one respondent. With some chronic diseases like heart disease it is difficult to project where the science will go, since its prevention and its treatment utilize both medical and public health approaches.

Co-morbidities are an increasing issue for many patient groups. For example, 65 percent of patients with chronic obstructive pulmonary disease (COPD) report six to ten co-morbidities, including conditions such as arthritis, diabetes, and cardiovascular disease.⁸ For example, in the case of Alzheimer’s disease, 96 percent of patients have other conditions and data shows that Medicare spends up to three times more for an Alzheimer’s patient with diabetes.⁹

“Personalized healthcare of the future clearly needs to address co-morbidities,” asserted John Walsh, of the COPD Foundation. It will be important to recognize the interaction among different diseases and that personalized healthcare for one individual might require coordinating multiple treatments. Moreover, pharmacogenomics will play a crucial role in understanding efficacy and toxicity of drugs given to patients with co-morbid diseases.

Benefits of Personalized Healthcare to Patients

All respondents clearly understood the benefits of personalized healthcare described by the Personalized Medicine Coalition as the “right treatment for the right person at the right time.”¹⁰ We found a consensus that it would be a significant advancement if the tools of personalized healthcare allow for earlier diagnosis and improved treatment success, including targeting drugs for use in people who will derive a benefit.

⁸ Personal communication with John Walsh, President of COPD Foundation, September 4, 2008.

⁹ Personal communication with Jennifer Zeitzer, Associate Director, Federal Policy, Alzheimer’s Association, September 10, 2008.

¹⁰ See the Personalized Medicine Coalition report, *The Case for Personalized Medicine 2006*, http://www.personalizedmedicinecoalition.org/communications/pmc_pub_11_06.php.

We found a dearth of understanding among respondents in the role personalized healthcare can play in avoiding drugs that will lead to adverse events. The removal of Vioxx from the market and the black box warning placed on other drugs attract big headlines in the media and patients are aware of these events. However, they do not always recognize that the identification of a drug causing severe side effects in a population subset is an advance in personalized healthcare. Some saw that future relabeling or warnings for medications could serve as teaching opportunities for the patient community about what personalized healthcare can offer.

Personalized healthcare has been defined as offering the promise of better care delivered more efficiently. In areas such as oncology, patients want better assurances that treatments will work for them. Particularly in cancer treatment, patients do not always have confidence that their treatment will be effective, thus they fear the side effects of a treatment that may not yield benefit. In the breast cancer community, survivors are focusing more on survivorship care plans that help them track the impact and potential for side effects of the treatments on their health down the road.¹¹

Impact of Personalized Healthcare on Costs

Many respondents felt it is difficult to completely predict how personalized healthcare will unfold in the next 10-15 years and its impact on escalating healthcare costs. If personalized healthcare can help reduce costs, everyone regarded this as a positive and important benefit. Most respondents mentioned that they saw costs going up before going down as a result of personalized healthcare.

Patient advocates believe that personalized healthcare will ultimately lower costs by:

- reducing the need for repeat visits,
- reducing the number of adverse events and some hospitalizations, and ultimately resulting in better health outcomes,
- saving patients and providers time, money, and wasted effort since most drugs are not working in some subset of certain patient populations, and
- providing tools that give providers information about which subpopulations are likely to respond to therapy.

Respondents thought the cost to develop targeted, personalized therapies could be higher than the costs of developing existing treatments and might be labeled for use in smaller market sizes which could increase drug pricing. Thus there is concern that as therapies become more tailored, they may also become more expensive, and that investment in drugs for lower incidence populations won't get pursued. Uncertainty about how payers will integrate targeted therapeutics into coverage and reimbursement decisions exists.

¹¹ Personal communication with Elizabeth Thompson, Managing Director, Public and Medical Affairs, Susan G. Komen for the Cure, September 18, 2008.

Concerns about Personalized Healthcare

Drug Development. Respondents acknowledged that the drug development models that currently exist will have to evolve to prepare for the personalized healthcare advances. There needs to be a process in place that considers the implications of the creation and characterization of subgroups of patients within a disease by both pharmaceutical and biotechnology companies and by the U.S. Food and Drug Administration (FDA). There are opportunities within FDA to make sure all the required policies are in place to promote the advancement of personalized healthcare practices. A robust post-marketing system needs to be in place to identify safety risks as these drugs are used by a more heterogeneous population. Also, the research building blocks with FDA drug safety efforts need to be aligned to learn more about how drugs are experienced in a large population.

From the scientific perspective, data continues to come in on most diseases about the variability within the particular disease class. Scientists and advocates are increasingly discussing the possibility of different subtypes of their particular disease areas. For example, Parkinson's disease (PD) patients present to their doctors with their own personal mix of symptoms that roughly categorize them as PD patients. When treated, these patients often experience highly varied responses to medications. This known heterogeneity is still generally overlooked if not ignored as treatment protocols consider all these patients in a single category of disease. In fact, recent "failures" in clinical trials in PD might more appropriately be viewed as "inconclusive" findings with pockets of treatment success but insufficient (underpowered) evidence to propel the trial to its next stage of investment and/or investigation. The Michael J. Fox Foundation for Parkinson's Research (MJFF) is focused on attempting to better understand and characterize the "subtypes" of disease with the particular goal of improved patient selection for clinical trials in mind.¹²

Also, some respondents raised the question of what needs to be done to facilitate the process of subgroup analysis and how to study different populations that respond differently to treatments. It was also acknowledged that even in areas where there are some targeted therapies identified, more research is needed. The work is not over when the initial finding is made. For example, new analysis of the data shows that women taking Tamoxifen can metabolize the drug differently.¹³

"It is clear we need to find ways to do clinical trials that are faster and cheaper," asserted Debi Brooks, Co-Founder of MJFF. "One of our strategies is to fund creation of tools that can contribute to improved trial design in the first place." In addition to the continued work to identify subtypes of disease, MJFF has a collaborative project underway where the Parkinson's Institute and the company 23andMe are working to validate web-based surveys that could provide a proof-of-concept for tools to enable

¹² Personal communication with Debi Brooks, Co-Founder, Michael J. Fox Foundation for Parkinson's Research, September 4, 2008.

¹³ Personal communication with Elizabeth Thompson, Managing Director, Public and Medical Affairs, Susan G. Komen for the Cure, September 18, 2008.

more robust data collection in the clinical trials process. In smaller disease populations that have potential subpopulations of disease, improved and innovative clinical trial design to increase the power of smaller sample sizes will help researchers complete studies faster.

Additionally, until we have diagnostics that can identify who should receive which drug, patients want an improved adverse events reporting system that can contribute to research and development of such tests. One way to better understand extrinsic factors like drug-to-drug interactions, medical practice, diet, alcohol use and intrinsic factors like gender, genetics, and race is to establish systems that improve adverse event tracking. Currently the FDA is actively embarking on this task. In May 2008, FDA launched its Sentinel Initiative with the goal of creating and implementing a national, integrated, electronic system for monitoring product safety. This effort will strengthen FDA's ability to monitor the performance of a product throughout its life cycle and enable real-time reporting of potential safety signals for medical products currently on the market.

Some respondents are concerned about genetic testing companies and want assurance these tests are accurate and that support systems and providers are ready and waiting after patients take the tests. The regulatory framework for these testing companies is still being created; the FDA does not evaluate these tests for accuracy, though a federal panel recently recommended stepped-up oversight. Different states have different regulations about the ordering of tests and the involvement of medical professionals; several states have ordered direct-to-consumer testing companies to stop selling their tests to residents of their states until they prove they have met that state's quality standards (which several companies subsequently did and received licenses to operate). Two major associations for genetics professionals disagree about whether any genetic tests are appropriate for sale directly to consumers without a medical intermediary. While regulators and medical professionals deliberate, the popularity of genetic testing is undeniably increasing, helped along by "genetic social networking" Web sites and program launches at venues such as the Mayo Clinic, Canyon Ranch Institute, and the Cleveland Clinic, opening whole new frontiers in the consumer information revolution.

Gatekeepers. Many respondents identified their patients' need for a "medical home" to provide coordinated and targeted care. One patient said, "So, while providing more detailed tracking is helpful, one also needs a doctor who is receptive to that same tracking." Some saw how this approach may create a situation where the provider serving as a gatekeeper may instead block or slow access to care. As patients have more and more access to information, and as they have mobilized, they want access to providers that will discuss options and a gatekeeper may stand in the way of that. Similarly, as therapies start to become available for subgroups of patients, there is concern about how the payer community will react. One respondent said, "What if treatment is only available if it works for everyone with our disease?"

There has been a lot of discussion in the past couple of years about comparative effectiveness. This is the approach that many healthcare stakeholders are turning to as

a possible solution to curb healthcare spending. Comparative effectiveness research seeks to provide a cost-effective and efficient approach to identifying the best in drugs, devices, biologics, and medical procedures. However, as the drumbeat for comparative effectiveness intensifies, it is important to ensure that the law of averages does not steer decision-makers away from treatment that demonstrates true patient benefit. Comparative effectiveness needs to allow for new research findings, as well as allow for diseases that may ultimately encompass hundreds of genetic variations and subtypes.

Privacy. There is lingering concern about whether individual test results and large datasets with personal information will be used against people for employment or insurance purposes. One respondent said that the passage of the Genetic Information Nondiscrimination Act (GINA) hasn't assuaged those fears. (For more information about GINA, see page 18). However, a majority of the patient organization leaders we spoke with felt that privacy needed to be dealt with and closely monitored, but that it should not interfere with scientific and healthcare delivery advances. One respondent said, "We don't want the politics of fear of privacy breaches to get in the way of the needed advances."

Advances in 21st century healthcare will heavily depend on advances in genetic research and other medical solutions that fuel the search for new treatments and cures. The passage of the GINA allows patients to more confidently participate in studies that search for linkages between genes and disease, to enroll in clinical trials for new targeted drugs, or to provide samples for DNA analysis to optimize their own disease prevention and treatment.

Due to the lack of EHRs in many care systems, respondents noted that often patients' records were private, even to them. Some felt that the general consumer population was more concerned about privacy than patients, many of whom understand the value that pooled data can provide to the understanding of their disease. However, some still have concerns about posting their data onto some of the online personal health records systems. One patient said, "One of the risks that is going to emerge very quickly is the privacy status of medical records held by companies which function as control repositories."

The impact of the Health Insurance Portability and Accountability Act (HIPAA) and privacy were raised in the context of conducting research studies. In many disease areas, sample collection is becoming standard practice, and yet there is still confusion of what is and is not allowable under HIPAA. There was concern about the impact of restrictions on the speed at which research can be conducted, and the fact that patients continue to lose ground in battling their conditions with these delays.

Educating Patients

In order to be truly effective with optimal impact, patient-centric and proactive healthcare practices must be supported by comprehensive education and communications efforts. The general public needs to understand genetic medicine - what it can and cannot do -

and not be afraid of the power of this area of science. Healthcare providers need to be able to sift through the most recent advances in medicine and translate these into real-world scenarios, carefully putting the most promising developments into context for each patient. The doctor-patient relationship needs to be defined by clear and transparent lines of communication. It is vital that new developments brought about by personalized medicine approaches be managed and translated responsibly and effectively into tangible treatment protocols when appropriate.

Most felt that it would not be difficult to educate patients about the advances that will come from personalized healthcare. Patients are hungry for information, and many survey respondents mentioned how self-motivated their constituencies are. Many respondents cited the high motivation their constituencies have to accelerate the research process in order to have better treatments available.

One respondent felt that trusted messengers (e.g., medical associations, advocacy groups, the U.S. Surgeon General) could lead national efforts to educate consumers. It was pointed out that a major risk relates to unrealistic expectations by the patient. This patient said, "Sometimes, even with the right diagnosis and treatment, I won't get better."

It was felt that all stakeholders involved need to carry the messages to patients about the potential benefits personalized healthcare offers. Providers ranging from primary care physicians to specialists and all other providers that intersect with the patient communities need to be given tools to help them communicate these messages.

There is still a lot to learn about how patients will respond to detailed genetic profiling as that becomes a reality. One person said, "The jury is still out about how this will really be rolled out over time and how patients will manage this new information."

Some groups talked about needing more documentation of successes in the area. "We need to have the demand for the science defined publicly so it is constituent driven." Another respondent spoke of the flat funding for NIH and the concerns that it raises for the future pace of scientific advances. **These comments speak to the need to engage fully with patients to be research advocates and suggests that the more motivated a patient is to get involved in a patient-oriented organization, the more likely they will be engaged in personalized healthcare.**

IV. Potential Impact of Personalized Healthcare in Healthcare Delivery

There are several areas of healthcare that will be significantly affected by the adoption of a personalized medicine approach. Most notably, personalized healthcare alters the traditional model of healthcare delivery, shifting some responsibility toward the consumer while simultaneously requiring healthcare providers to process even more information. It also raises questions about:

- when evidence is sufficient for use in health and disease management;
- how best to gather and assess evidence about effectiveness and efficacy; and
- how to appropriately regulate drugs used in personalized medicine.

Use of Genomics and Biomarkers to Predict Disease

An individual's genetic and molecular profile, if accurately assessed, has the potential to predict predisposition to certain chronic diseases – for example, prostate cancer, glaucoma, Alzheimer's disease, or heart disease – as well as guide disease prevention strategies and more effective use of therapies. Currently, many of these tests are predictive, rather than diagnostic, which means results are provided to otherwise healthy consumers as probabilities, or relative risks for an individual versus the general population. Most tests rely on SNP analysis or whole genome scans but others are based on non-DNA biomarkers associated with a particular pathological or physiological state.

As the technology for such testing – in particular genomic analysis – has advanced, the costs have decreased, which has spawned the growth of a new industry focused on personalized genomic services, frequently marketed directly to the consumer. Because in most cases the consumer can purchase the test and receive results without the direct involvement of a personal healthcare professional, several concerns have arisen.

- 1) Is the scientific evidence supporting the genomic-disease associated information sufficient for clinical use?¹⁴
- 2) Are consumers able to appropriately and effectively use such information in their own healthcare management?¹⁵ and
- 3) Are healthcare providers sufficiently proficient in the application of probabilistic genomic information to respond to patient queries and develop a healthcare management plan appropriate for individual patients?¹⁶

Those advocating for more consumer involvement in test decisions believe that the slow pace of provider uptake and professional education, combined with more focus on consumer education and autonomy warrants such an approach.¹⁷

¹⁴ Cecile A et al., "A Critical Appraisal of the Scientific Basis and Personalize Health Interventions," *The American Journal of Human Genetics*, 82:593-599, March 2008.

¹⁵ Gosline A, "Genome Scans Go Deep into Your DNA," *Los Angeles Times*, April 14, 2008, www.latimes.com/features/health/la-he-genome14apr14,0,2443364.story.

¹⁶ Harvey EK et al., "Providers' Knowledge of Genetics: A Survey of 5915 Individuals and Families with Genetic Conditions," *Genetic Medicine* 9(5): 259-267, 2007; Scheuner, et al., "Delivery of Genomic Medicine for Common Chronic Adult Diseases," *Journal of the American Medical Association* 299(11):1320-1334, 2008.

¹⁷ Wolfberg AJ, "Genes on the Web—Direct-to-Consumer Marketing of Genetic Testing," *New England Journal of Medicine*, 355(6):543-545, 2006.

Pharmacogenomics

A specific field in personal medicine is pharmacogenomics, sometimes called molecular medicine. Pharmacogenomics is based on identifying genetic factors that directly influence a person's response to a drug. It has the potential to enhance understanding of disease etiology and diagnosis as well as the determinants of drug effects so better prescribing decisions can be made. What makes pharmacogenomics both unique and a challenge is that it melds the worlds of diagnosis and treatment in new and different ways. It is an application of genetics and pharmacology that brings genetic testing into the purview of primary care, well beyond the more traditional bounds of rare diseases, where genetic testing has its historical roots.¹⁸

It is likely that in the future, drugs incorporating pharmacogenomic data will involve both a therapeutic agent and diagnostic test, wherein the diagnostic test will precede the prescription, which suggests a new model for healthcare delivery. Because pharmacogenomics can help physicians determine whether a proposed drug therapy is relevant to a given patient, this approach to clinical care has the potential to enhance preventative medicine and reduce the level of trial-and-error in patient management. As with the use of personalized genomics testing services, pharmacogenomics will increase the volume of information that will have to be processed and used by patients and their healthcare providers.

V. New Approaches and Opportunities to Transform the Drug Development Process

“...in the next 15 years the pharmacopoeia that we use for treating lots of disease will be very heavily influenced by the things we’re discovering right now about the molecular basis of disease. But that has the longest lead time, and so it won’t happen overnight for many conditions.”

-- Francis Collins, former Director of the National Human Genome Research Institute at the NIH¹⁹

New Approach to Clinical Trials

One of the challenges of personalized healthcare lies in assessing outcomes. First, because some of these interventions are being offered directly to the consumer it will be difficult to follow consumers to assess effectiveness and other outcomes. Thus, it will be critical that there be some publicly funded studies in these areas.

Second, because the very nature of clinical evidence will become more focused on individuals and subpopulations, personalized healthcare challenges the notion of randomized clinical trials as the gold standard for testing the safety and efficacy of new

¹⁸ Hanna KE, “Pharmacogenomics and the Evolving Regulatory Paradigm,” *Research Practitioner* 8 (6):210-216, November-December 2007.

¹⁹ Collins F, “Genomic Research and Personalized Medicine: An Expert Interview with Francis Collins, MD, PhD.” *Medscape Genomic Medicine*, May 8, 2008.

diagnostics and drugs. Simple reliance on biomarkers may be a poor method of predicting outcomes.

At least for some time it will be critical to evaluate large numbers of people before understanding the relative role of any given variant and its significance in personalized healthcare. Weak predictability combined with our lack of understanding of the causal relationship between genes and drug responses makes it difficult and costly to conduct appropriate validation studies. These studies are probably going to have to be large-scale, prospective studies that measure genetics and other biomarkers over time and follow up with patients for long-term outcomes.²⁰

As such, analyzing evidence emerging from personalized medicine will require a different set of skills than those used in traditional clinical trials, combining diagnostic evidence with safety and efficacy evidence. Research will be needed to develop the best methods for collecting and analyzing evidence and large numbers of subjects will be needed for clinical trials.

Seizing Proven Opportunities

While nearly 10 percent of the drugs approved by the FDA include pharmacogenomic information in their labeling, only four have a sufficient body of evidence to support a requirement for genetic testing before treating a patient.²¹ Many other drug labels reference validated biomarkers and associated diagnostic assays, but these are only ‘recommended’ to provide additional information—not because evidence has shown their impact on outcomes to be variable or unreliable, but because there is *no evidence regarding outcomes at all*. This highlights a fundamental imbalance in the progress of pharmacogenomic research: more and more studies are linking genotype to the mechanisms of drug metabolism and/or efficacy, but few are taking the critical next step of tying modified dosing or selective use of drugs based on genotype to improved patient outcomes. Stakeholders have identified the lack of clinical evidence base as a critical barrier to integration of personalized medicine into routine practice.²² Making this connection to outcomes is necessary to realize personalized medicine’s promise.

The stakes are even higher since many of the drugs for which pharmacogenetic factors have been identified are often dangerous to patients and adverse reactions can be lethal. The FDA’s list of drugs with genetic biomarkers includes chemotherapy agents, anticoagulants, and neurologic agents—drugs whose side effects would exclude them from use were it not for the lack of suitable therapeutic options for patients with grave conditions. With more than 770,000 injuries and deaths due to adverse drug reactions

²⁰ Garrison LP and Austin MJ, “Linking Pharmacogenetics-Based Diagnostics and Drugs for Personalized Medicine,” *Health Affairs* 25(5):1281-1290, 2006, p.1285.

²¹ See FDA’s *Table of Valid Genomic Biomarkers in the Context of Approved Drug Labels*, http://www.fda.gov/cder/genomics/genomic_biomarkers_table.htm.

²² Deverka PA et al., “Integrating Molecular Medicine in the US Healthcare System: Opportunities, Barriers and Policy Challenges,” *Clinical Pharmacology & Therapeutics*, 2007; 82(4): 427-34.

and medication errors each year²³, elucidating whether genetic information can improve outcomes and reduce some of these events is critical to ensuring the safety of patients who take these drugs.

A growing body of research reveals the great promise of using an individual's genetic information to guide his or her care; the next step for us is to seize that demonstrated opportunity by confirming whether this information can effect real change in short- and long-term patient outcomes. We can save patients' time by building the evidence base as soon as possible so that caregivers can act on the promise of personalized medicine. We can save patients' lives by defining how genetic tools can ensure a patient's treatment is not only timely and beneficial, but *safe*.

VI. Making Personalized Medicine a Reality: The Need to Address Privacy

“These are catch-all diseases (e.g., cardiovascular disease, Alzheimer’s disease, rheumatoid arthritis, and cancer) that look the same, but when you scratch below the surface, you begin to understand that the underlying physiology of similar phenotypes can be fundamentally different.”

-- John Sninsky, Vice President of Discovery Research at Celera²⁴

Precious patient resources are lost to medical research if individuals fear that genetic information, test results, or electronically stored health records might be used against them by insurers or employers. Public opinion has long reflected widespread anxiety about misuse of personal health information.

In a 2004 survey of 470 people with a family history of colorectal cancer, for example, about half said their concern about genetic discrimination was high, and that they would be significantly more likely to pay for genetic testing out of pocket, use an alias, or ask for test results to be excluded from their medical record.²⁵ Dr. Francis Collins, former Director of the National Human Genome Research Institute, has said that “at the NIH, fear of genetic discrimination is the most commonly cited reason that people decline to participate in research on potentially life-saving genetic testing for colon cancer and breast cancer. One-third of eligible participants have declined on this basis.”²⁶ People have been reluctant to know and act on genetic health risks, to their own detriment and society's as a whole.

²³ See Agency for Healthcare Research and Quality report, *Reducing and Preventing Adverse Drug Events to Decrease Hospital Costs. Research in Action, Issue 1*, March 2001, <http://www.ahrq.gov/qual/aderia/aderia.htm>.

²⁴ Mullin R, “Personalized Medicine,” *Chemical & Engineering News*, February 11, 2008.

²⁵ Apse KA, et al., “Perceptions of genetic discrimination among at-risk relatives of colorectal cancer patients,” *Genetics in Medicine*, 6:510-516, 2004.

²⁶ Kibak P, “After long wait, GINA becomes law,” *Clinical Laboratory News*, July 2008.

A patchwork of legislation at the state and national levels has tried to regulate the use and disclosure of personal health information, most prominently the 1996 HIPAA, which regulated the use and disclosure of such information by certain “covered entities.” Successfully navigating HIPAA and human research protections will be critical to advancing the science of personalized medicine.²⁷ And in 2008, after 13 years of effort, Congress passed and the President signed the GINA, which advocates have called the critical civil rights bill for the genome era.

To summarize, GINA:

- Prohibits use of an individual’s predictive genetic information in setting eligibility or premium or contribution amounts by group and individual health insurers;
- Prohibits health insurers from requesting or requiring an individual to take a genetic test;
- Prohibits use of an individual’s predictive genetic information by employers in employment decisions such as hiring, firing, job assignments, and promotions;
- Prohibits employers from requesting, requiring, or purchasing genetic information about an individual employee or family member.²⁸

The health insurance provisions of the bill will take effect in May 2009 and the employment provisions will take effect in November 2009. GINA does not apply to members of the U.S. military, or to other forms of insurance such as life, disability, or long-term care.

It is expected that passage of GINA will boost demand for genetic tests, leading to improvements in care and more participation in research that involves the collection of genetic information. But the passage of legislation is not enough. There has to be effective education of the public and providers about the protections that GINA confers. That includes compelling demonstration of the benefits genetic testing and personalized medicine will bring to them as individuals, as well assurance that new tests and personalized treatments will be paid for.

In addition, the application of GINA’s protections must be clear and consistent. Lessons must be learned from the experience with HIPAA, whose provisions regarding privacy have been misinterpreted and over interpreted in ways that have been detrimental to the conduct of medical research. In a 2007 survey published in the *Journal of the American Medical Association*, more than two-thirds of epidemiologists reported that the HIPAA Privacy Rule has made research more difficult, adding a great deal of cost and time to study completion without a countervailing positive influence on subjects’ privacy.²⁹

²⁷ Carhart S, “Coming Century to Witness Major Changes as Hospitals Adapt to Personalized Medicine,” *BNA’s Health Law Reporter*, 17(25): 1155, 2008.

²⁸ See Genetics and Public Policy Center, www.DNAPolicy.org

²⁹ Ness R, “Influence of the HIPAA privacy rule on health research,” *Journal of the American Medical Association*, 298(18):2164-2170, 2007.

And we need to continue to look beyond GINA at additional ways in which privacy concerns must be addressed in order to promote and facilitate the development of personalized healthcare. For instance, not addressed by GINA are all the security and privacy implications of the large databases of medical records tied to biological samples that will be required for the promise of personalized medicine to be realized.

VII. Genetic Literacy and the American Public

Patient-centered care requires that patients be informed, proactive partners with their physicians when facing health decisions. But a major hurdle for patient-centeredness in personalized medicine is a lack of ‘genetic literacy’ or a fundamental understanding of genetics and health in the general public. Informed patients are critical to patient-centered care, but as personalized medicine techniques become more sophisticated and information more complex, caregivers will face steeper challenges in communicating effectively with patients of all education levels and backgrounds. Improving the genetic literacy of the general public will be an important step in empowering patients to seek and understand personalized medicine.³⁰ As early as 1994, the National Research Council (NRC) was making calls for a "genetically literate public that understands basic biological research, understands elements of the personal and health implications of genetics, and participates effectively in public policy issues involving genetic information."³¹

Unfortunately, the past 14 years have not seen the NRC’s vision realized. A 2006 study on public attitudes about evolution showed that on an index of genetic literacy, American adults scored a median of 4 on a 0-10 scale, indicating that many adults are not well-informed of genetics principles.³² Some studies have shown that minority populations of diverse cultures, in particular, have limited genetic knowledge despite a desire to know more about genetics and health.³³

There are a number of programs aimed at addressing these deficits in genetic knowledge in the public: for example, March of Dimes has launched its Consumer Genetics Education Network (CGEN) Project, a five-year program to address genetic literacy in underserved populations and to increase access to culturally and linguistically appropriate genetics education programs and services.³⁴ The Health Resources and Services Administration funds the activities of the ‘Consumer Initiatives for Genetic Resources and Services’, a discretionary grant program through the Maternal and Child Health Bureau. Programs receiving grants provide education about genetics and

³⁰ Haga, SB, “Teaching resources for genetics,” *Nature Reviews Genetics*, 7, 223–229, 2006.

³¹ National Research Council report, *Assessing genetic risks: implications for health and social policy*, 1994, Washington, DC: National Academies Press.

³² Miller JD, et al., “Public Acceptance of Evolution,” *Science*, Vol. 313. no. 5788, pp. 765 – 766, August 11, 2006, Vol. 313. no. 5788, pp. 765 – 766.

³³ Catz DS, et al., “Attitudes about genetics in underserved, culturally diverse populations.” *Community Genetics*. 8(3):161-72, 2005.

³⁴ See March of Dimes CGEN Project Website

http://www.marchofdimes.com/professionals/15829_29466.asp

genetic testing to patients, usually in the context of specific screening tests or conditions.³⁵ Genetic Alliance is one of the recipients of MCHB grants to improve genetic literacy, and is also working with funding from Centers for Disease Control and Prevention to develop the Access to Credible Genetics (ATCG) Resources Network, a genetics information resource for patients with rare genetic diseases and their families and physicians.³⁶ The National Human Genome Research Institute (NHGRI) at the National Institutes of Health also has active grants awarded to projects addressing genetic literacy among underserved groups.³⁷

VIII. Personalized Healthcare: A Patient-Centered Action Plan

Personalized healthcare promises to be curative, predictive, and preventive. Our qualitative survey of patient organizations and patients themselves found a shared anticipation of the cutting-edge possibilities of personalized healthcare advances, especially as seeds of innovation yield tangible tools that move this approach forward. However, patient involvement is central to generating a sea-change in the traditional model of healthcare delivery.

Realigning the promise of personalized healthcare requires effectively and efficiently shifting some responsibility to the consumer while simultaneously requiring healthcare providers to process even more information.

We offer a framework for multiple stakeholders in the healthcare delivery system to act on to make personalized healthcare a reality:

- **Involve Patients in Medical Research.** An individual's genetic and molecular profile has the potential to predict predisposition to certain diseases, guide prevention strategies, and develop customized therapies. It is crucial for patients to understand their value to medical research and to actively participate by donating their biological specimens, being a part of clinical trials, and advocating for the use of EHRs. Accelerating and rewarding patient involvement in medical research will allow us to seize personalized healthcare's promise to affect real change in short- and long-term patient outcomes.
- **Transform the Drug Development Process.** Personalized healthcare challenges the long-held belief that randomized clinical trials are the gold standard for testing the safety and efficacy of new diagnostics and drugs. Understanding evidence emerging from personalized medicine will require a different set of skills than those used in traditional clinical trials, combining diagnostic evidence with safety and efficacy evidence. One of the challenges of personalized healthcare lies in

³⁵ Health Resources and Services Administration, Maternal Health Bureau, Consumer Initiatives for Genetic Resources and Services Abstract search, <https://perfddata.hrsa.gov/mchb/DGISReports/Abstract/AbstractSearch.aspx>, Last Accessed September 10, 2008.

³⁶ See Genetic Alliance Access to Credible Genetics Resources Network <http://geneticalliance.org/atcg>.

³⁷ See National Human Genome Research Institute Active Grants Database, <http://www.genome.gov/10001799> Last accessed August 25, 2008.

assessing outcomes because some of these interventions are being offered directly to the consumer and because the very nature of clinical evidence will become more focused on individuals and subpopulations.

- **Protect Patient Privacy.** Key to the widespread adoption of personalized healthcare is addressing public anxiety about misuse of personal health information. The privacy protections realized through the passage of GINA will lead to improvements in care and more participation in research that involves the collection of genetic information. We need to ensure that the application of GINA's protections is clear and consistent.
- **Focus on and Deliver Patient-Centered Care.** Personalized healthcare elevates the role of the patient to that of data source, proactive partner, and decision-maker. The role of the healthcare provider will evolve as well. The provider becomes the information filter, translating medical breakthroughs into real-world scenarios applicable at a personal level. However, our ability to deliver patient-centered care, and therefore personalized healthcare could be held back by the existing insufficiencies within our healthcare system.