

Whence Social Determinants of Health?: Effective Personalized Medicine and the 2010 Patient Protection and Affordable Care Act

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Abstract

Personalized medicine consists of targeted genetic testing leading to diagnostic, preventive and treatment outcomes. In its consideration of genetic predisposition, personalized medicine may not completely account for social determinants of health in its implementation. Effectively coordinating certain provisions of the 2010 Patient Protection and Affordable Care Act would mitigate this gap in personalized medicine. Personalized medicine would affect health disparities as well as provide information on genetic illness through the recommendations outlined here.

Keywords: Personalized medicine; Social determinants of health; 2010 Patient protection and affordable care act

Introduction

When the human genome was officially mapped in 2003 (a preliminary map of the genome was published in 2000) through both public and private ventures, it was anticipated that the public would greatly benefit from the advancement of genomics. This anticipation arose from the emergence of technologies through the Human Genome Project, including more advanced genetic testing and genome wide association studies. The advent of a branch of medical science whereby patients could be diagnosed and treated based on the genotype of their individual genomes, personalized medicine, was weakly articulated during the heyday of the sequencing of the human genome. Nonetheless, personalized medicine became a direct beneficiary of the Human Genome Project.

Fast forward nearly 11 years, and we have health care reform, arising out of political struggle and widespread public debate. The upshot of this debate was the passage of the 2010 Patient Protection and Affordable Care Act, passed on partisan grounds but currently law.

What is the impact of personalized medicine on health care reform? How personalized medicine is reflected in the 2010 Patient Protection and Affordable Care Act (henceforth ACA)? How does the incorporation of personalized medicine in the ACA improve patient outcomes and reduce health care costs? This paper addresses these questions and in doing so, argues that personalized medicine, as articulated in the ACA, makes some advances in improving patient care and reducing health care costs, (even though it has been argued that further reform must be implemented in the conduct of clinical trials with respect to the pharmaceutical industry for the ACA, as it currently stands, to fully realize the enormous potential of personalized medicine¹). But the thrust of this essay is that the ACA must improve on the current implementation of personalized medicine so as to address the social determinants of health. That is, the ACA to some extent does address both personalized medicine and health disparities separately, but these provisions should accordingly be assimilated such that personalized medicine, through pharmacogenetic and individual diagnostic testing, accounts for the sociological contexts of

health and disease. As it is currently articulated, particularly through the recommendations of the Personalized Medicine Coalition, and discussion by other commentators [1,2], personalized medicine does not reflexively incorporate the addressing of health disparities or the social factors contributing to disease and illness. In doing such, ACA's intent to improve patient outcomes and decrease health care costs should be commensurate with the goals of personalized medicine.

According to my analysis, there are four crucial areas where personalized medicine has influential bearing on the ACA:

1. comparative effective research, or patient centered outcomes research, because the individualized treatment provided by personalized medicine may be reflected in comparative effectiveness research;
2. the expansion of electronic health records, since the data resulting from the implementation of personalized medicine may be stored electronically;
3. the establishment of Accountable Care Organizations, since treatment through personalized medicine may be catalogued through these organizations and;
4. the reform of the health insurance industry, because personalized medicine may be paid for by health insurance;
5. each of these areas addresses personalized medicine's goals to directly connect genomic makeup and testing with patient health, however these areas accomplish this task incompletely, since there exists a gap in fulfilling the potential of personalized medicine in addressing the social determinants of health. The ACA does address the social determinants of health as evidenced by certain provisions detailing health disparities, community health and prevention, but the incorporation of personalized medicine remains a glaring gap in the ACA's apparatus to

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¹This is based on A. Jayadev and J. Stiglitz article in a 2009 issue of *Health Affairs*, vol. 28, 1 where Jayadev and Stiglitz write that "Public funding of clinical trials likewise can reduce both pharmaceutical costs and prices and direct research effort in a manner that is more socially productive than the current state of affairs" (Jayadev and Stiglitz 2009).

address the sociological contexts of disease. For personalized medicine to fully achieve maximal health outcomes, it is argued that this should be addressed. In other words, personalized medicine should account for racial, ethnic, educational and socioeconomic disparities in health in addition to genomic variation, and this consideration should be reflected in the ACA. The best way to achieve this, as I will argue, is through the implementation of preventive care through personalized medicine and coordination of the efforts of the Patient-Centered Outcomes Research Institute (PCORI), Community Health Center programs and the US Preventive Services Task Force (USPSTF), all of which are infrastructurally provided for by the ACA.

In this paper, I have discussed the aspects of personalized medicine, which may lead to changes in disease outcomes. In the second section, I argued that personalized medicine possesses some shortcomings in adequately predicting health outcomes. I then made clear how personalized medicine is reflected in the ACA and how this incorporation will affect patient health and health care costs. I will argue that the Patient Protection and Affordable Care Act should address some of the shortcomings of personalized medicine, and in doing so, make possible the full health and economic gains of personalized medicine. I also point to portions of the ACA that are relevant for personalized medicine.

Personalized Medicine: A Gradual Revolution in Health Care

Though not articulated in any of the health care discussions, according to Arthur Feldman, personalized medicine or pharmacogenomics also has an enormous potential for lowering health care costs by identifying those patients that will benefit from a specific drug, thereby allowing physicians to target drugs to selected populations. Finally, he asks, will regulatory groups recognize that personalized medicine is not just a fad but might in fact be able to substantially lower the cost of medical care? This becomes important in view of the fact that the pharmaceutical industry has been reluctant to include genotyping in their clinical trials because it is far more cost-effective for a drug to be marketed to the entire population than to a select population.

Feldman cites the discovery of the drug Herceptin as an excellent example of how pharmacogenetics could impact costs through more selective prescription of drugs. The expensive new agent for treating women with breast cancer, Herceptin, is only beneficial in patients whose tumors overexpress the her2 receptors. Cost savings could also result from studies similar to the recent finding that one's genotype can predict how one responds to the cardiovascular agent clopidogrel [3].

Personalized medicine is based on the uniqueness of the individual: each patient's genome reveals patterns of risk susceptibility to disease, variation in treatment regimens, and information leading to tailored screening and diagnosis. In addition to the Human Genome Project, advances in proteomics, metabolomics and epigenomics also led to the development of personalized medicine. Thus as Chan and Ginsburg state (2011), "personalized medicine is a broad and rapidly advancing field of health care that is informed by each person's unique clinical, genetic, genomic, and environmental information". According to Hong and Oh (2010), there are four fundamental components of personalized medicine:

As the first component, personalized medicine requires standard

health risk assessment (HRA) tools capable of evaluating an individual's likelihood of developing a certain disease. One well-known HRA tool is the Diabetes Risk Calculator (5), the objective of which is the calculation of the probability that an individual has either diabetes or prediabetes. The second component is family health history (FHH), which is a complex combination of shared genetic, environmental and life style risk factors. FHH has tremendous potential for improving preventive healthcare in a personal manner. Regarding the third component, personalized medicine needs to integrate information on genomes and their derivatives, such as the transcriptome, proteome and metabolome. The fourth component is the clinical decision support (CDS) system. CDS systems are interactive computer programs designed to assist clinicians in their decisions about disease care, and they are defined as 'Clinical Decision Support systems link health observations with health knowledge to influence health choices by clinicians for improved healthcare' [4].

Risk susceptibility tests include the BRCA1 and BRCA2 genes for breast cancer, the PTEN gene for sarcomas and the KTF6 gene for coronary artery disease. Pharmacogenomics indicate individual patient response to treatment regimens and have been developed for Herceptin (Her2/neu), Statins (SLCO1B1, KIF6), Irinotecan (UGT1A1), Cetuximab (KRAS), Warfarin (DMET) and Erlotinib (EGFR).

Thus, at the nexus of patient histories, genetic uniqueness and clinical diagnosis, personalized medicine is predicated upon a synthesis of new and old variations in medical science, where cutting edge technology in the form of genetic tests meets standard techniques in patient care. This association between risk susceptibility, as evidenced for example by BRCA testing for breast cancer and health history makes demands upon health care providers which clinical decision support systems addresses to some extent. Even more so, direct to consumer genetic testing by private companies such as 23 and Priya Venkatesan Hays and Navigenics has obviated the need for genetic health care teams, (although not completely blunting the necessity of genetic counselors).

In short, personalized medicine has led to a gradual revolution in health care.

Personalized Medicine and the Social Determinants of Health

As currently implemented, personalized medicine and direct to consumer testing do not necessarily consider the social contexts of health and disease. Later in this paper as an example, I showed how personalized testing for prostate cancer takes into account genome variation, but outside of laboratory testing, personalized medicine remains inconclusive and incomplete in predicting health factors and preventing illness.

In terms of variation in the genome, three terms play a role in defining the benefits of a laboratory genetic test. Analytic validity, the first term, is the accuracy with which a given laboratory test identifies a particular genetic variant. Clinical validity, the second term, is considered when the genetic variant being analyzed also must correlate with a specific disease or condition in the patient (a phenotype) or with heightened risk of disease. The third term, clinical utility is the likelihood that using the test results will lead to a beneficial outcome. All of these terms are factors that would lead to valid outcomes in pharmacogenetic testing. A genetic predictor of health must have analytic validity, the laboratory test must identify the genetic variants in question, the genetic variant must correlate with a specific disease or

condition (clinical validity) and the clinical utility must be high for any personal direct to consumer or individual diagnostic test.

While it may be apparent that analytic validity and clinical validity are addressed by personalized medicine, the clinical utility for applications of personalized medicine such as direct to consumer testing remains marginal to moderate at best. This will be demonstrated in this paper by using genomic variation and prostate cancer as a case study.

Several studies have associated genomic variation with race in prostate cancer. For example, there is an association of 8q variants with prostate cancer risk in Caucasian and Hispanic men. Genotyping of a 615 kb region within 8q24 with 49 haplotype tagged SNPs in 2109 samples (797 cases and 1312 controls) of two ethnic/racial groups found SNPs (single nucleotide polymorphisms, or base sequences that have been mutated from the “normal” gene) that are significantly associated with the risk for prostate cancer [5]. In addition, from looking at recent scientific studies of genetic variation and prostate cancer, one finds that there are SNPs associated with prostate cancer that differ between ethnic and racial groups. Genome-wide association studies have identified multiple common alleles associated with prostate cancer risk in populations of European ancestry. The studies suggest that multiple interacting SNPs within 8q24 may confer increased risk of prostate cancer. The studies also support that a large fraction of prostate cancer variants that have been identified in populations of European ancestry are global markers of risk [6].

However, in a recent paper by Freedland and Isaacs [7], the authors argue that in addition to genetic differences in the predisposition to prostate cancer between black and white men (differences all the more marked since prostate cancer is a disease that has much higher morbidity and mortality rates in black men), multiple reasons have been postulated to explain differences in cancer risk: access to care, attitudes to care, socioeconomic and education differences, differences in type and aggressiveness of treatment and dietary differences. These factors constitute the social contexts of a disease, and they may not be revealed by a direct to consumer genetic or pharmacogenetic test, because the test would not fully account for the sociological contexts of health care. In other words, the clinical utility of the test would be limited. Clinical utility should include sociological contexts in health care as well as analytic and clinical validity, which reveal variation in the genome. However, personalized medicine as it is currently understood would only take into account analytic and clinical validity.

In short, clinical utility is not completely tantamount to analytic and clinical validity, however screening and testing for disease variants makes this assumption since it makes sole use of the concept of genomic variation. This may be a misguided assumption.

In other words, pharmacogenetic testing (or other types of personalized genetic medicine) cannot explain the social impact of differences between prostate cancer morbidity and mortality between black and white men. This may potentially lead to a “do it yourself ethic” in which individuals bear the burden of preventing illness, and any incentive to improve health disparities that are a result of the patient’s social or cultural environment would be obviated. In the case of prostate cancer, because there is a genetic component to the differences in occurrence, morbidity and mortality between black men and white men, this component would be revealed by individual genetic testing. Yet, such testing would, of course, neither explain nor consider some of the social determinants of health and disease.

However, personalized medicine should normatively address the

social determinants of health. Tailored therapies remain inchoate without considerations of health disparities, including race, ethnicity and socioeconomic status, all factors causative of health status and outcomes. It is through the family health history component of personalized medicine as articulated by Hong and Oh, however, that most of the gains in personalized medicine addressing the social determinants of health are met.

The association between family health history and social determinants of health is most exemplified in a study by Hariri et al. [8] conducted a survey based on 1999-2002 NHANES (The National Health and Nutritional Examination Survey, the NHANES is an annual survey designed to provide nationally representative estimates of the health and nutritional status of the civilian non-institutionalized U.S. population data, Hariri et al. 2006) for assessing evidence of undiagnosed Type II diabetes. They factored participants’ race, educational attainment, age and family history to predict the occurrence of undiagnosed Type II diabetes. This study indicates that certain aspects of personalized medicine can potentially account for social determinants of health.

The Patient Protection and Affordable Care Act and Health Disparities

The Patient Protection and Affordable Care Act does address health care disparities, but should consider the sociological contexts of health into its implementation and incorporation of personalized medicine.

The Patient Protection and Affordable Care Act of 2010 (ACA), which was signed into law on March 23, 2010, will undoubtedly bring the most sweeping changes to American health care since the enactment of Medicare and Medicaid. ACA was designed to accomplish three important goals: (1) expand access to health insurance coverage, (2) improve affordability and sustainability for those who have health care insurance, and (3) control the rising costs of health care while improving quality [2].

The Affordable Care Act accomplishes these objectives primarily through (1) subsidies provided to low income families under certain percentages of the Federal Poverty Line to purchase insurance, (2) expansion of Medicaid, (3) a health insurance mandate requiring individuals and families to purchase insurance or pay a penalty, (4) the passage of excise taxes (the “Cadillac tax”) and the provision to reduce provider payment rates for generating revenue, (5) health insurance exchanges to provide a clearinghouse for implementing the mandate and Accountable Care Organizations to allow for efficient provider reimbursement and (6) health insurance industry reform through the prohibition of considering pre-existing conditions as a criteria for denying insurance and of varying premiums on the basis of health status. The ACA “bends the cost curve” by bundling, or paying medical providers for a defined bundle of services.

The ACA also establishes the Patient-Centered Outcomes Research Institute (PCORI), a private, nonprofit institute to identify national priorities and provide for research to compare the effectiveness of health treatments and strategies. Overseen by a board of governors with broad stakeholder involvement and assisted by expert advisory panels, its methodology is to develop a standard set of methods that requires that research take into account subpopulations, genetic and molecular subtypes, and the phase in the innovation cycle of the treatment modality [2].

According to the “HHS Action Plan to Reduce Racial and Ethnic Health Disparities: A Nation free of disparities in health and health

care², the Affordable Care Act addresses health disparities in the following ways:

- The Affordable Care Act expands access to primary health care by investing \$11 billion into the HRSA Community Health Center program over the next five years. Together with funds from ARRA, the Affordable Care Act will enable the Community Health Center programs to nearly increase the number of patients served over the next five years. A key component of the health center program will be the implementation of the New Access Points (NAPs) grant program. For fiscal year 2011, HRSA has committed to support 350 NAPs to increase preventive and primary healthcare services for eligible public and nonprofit entities including tribal, faith-based and community-based organizations. Additional funding of up to \$335 million will be available this year for expanded services in existing health centers and \$10 million for 125 planning grants to help communities without a health center to develop one. The Community Health Center program provides care to vulnerable populations by assuring access to comprehensive, culturally competent, quality primary healthcare services. Of the nearly 19 million patients currently served through these HRSA-funded health centers, 63 percent are racial and ethnic minorities, and 92 percent are below the federal poverty level.
- The Affordable Care Act authorizes Community Transformation Grants to state and local governmental agencies, tribes and territories, and national and community-based organizations for the implementation, evaluation, and dissemination of evidence-based community preventive health activities to reduce chronic disease rates, prevent the development of secondary conditions, and address health disparities. This program is intended to build on CDC's "Communities Putting Prevention to Work" program.
- Section 4302 of the Affordable Care Act contains provisions to strengthen federal data collection efforts by requiring that all federally funded programs to collect data on race, ethnicity, primary language, disability status, and gender.

Additionally, and perhaps most importantly, the Affordable Care Act requires health plans and encourages state Medicaid programs to place a strong emphasis on prevention, specifically by encouraging coverage for: i) any clinical preventive service recommended with a grade A or B by the U.S. Preventive Services Task Force (USPTF); and ii) for immunizations recommended by the Advisory Committee on Immunization Practices (ACIP). Through the Medicare program, beneficiaries can now receive personalized prevention plans, an initial preventive physical examination, and any Medicare-covered preventive service recommended (grade A or B) by the USPTF.

Personalized Medicine and the Patient Protection and Affordable Care Act: Clinical Utility and the Sociological Contexts of Health

As Chan and Ginsburg (2011) point out, if personalized medicine is to be widely practiced, having health insurers, both private and governmental, willing to provide coverage for genetic tests will be essential for moving toward integration. To this point, health insurers have been unwilling because they have not been provided with incentives that would help them gain long-term cost benefits. However, recent progress has been made to incentivize personalized medicine: New models have shown a method for coordinating prevention with

favorable disease outcomes and reduced costs [9]. These models, according to Whellan et al. [10], offer disease management that would presumably lead to greater use of personalized medicine.

Personalized health care offers the potential for widespread adoption of risk-stratification techniques and preventive health strategies inclusive of pharmacogenomic testing aimed at reducing clinical events. However, it is not clear whether this technology will bring cost savings to the health care system. As more products are brought to market for smaller subsets of patients, the cost of pharmaceutical therapy is likely to increase. When personalized medicine leads to tailoring of existing therapies, it is likely to be cost saving. However, when pharmacogenomics is integrated into clinical development programs, the result is likely to be greater efficacy or safety at additional cost [11].

In a similar vein, the Personalized Medicine Coalition addresses the implementation of personalized medicine by calling for the provision of coverage of individual diagnostic tests through expansion of Medicaid and Medicare coverage. Thus, the Personalized Medicine Coalition suggests the following ways to ensure the ACA advances the goals of personalized medicine³:

1. Ensuring Adequate Representation of Personalized Medicine Perspective⁴ through Advisory Committees
 - (A) Health and Human Services Personalized Medicine Advisory Committee
 - (B) Medicare Payment Advisory Commission
 - (C) National Healthcare Workforce Commission
2. Incentivize Personalized Medicine by Creating a Transparent and Predictable Regulatory Environment for Personalized Medicine Products
 - (A) Requiring a Coordinated Review of Related Personalized Medicine Products
 - (B) Concurrent Review of Qualified Companion Diagnostics
3. Medicare Coverage of Personalized Medicine Diagnostics and Related Items and Services
 - (A) Medicare Coverage of Personalized Medicine Diagnostics
 - (B) Medicare Coverage of Genetic Condition Diagnostic Tests.

Although the Personalized Medicine address the costs of implementing and covering personalized medicine (particularly through Medicaid), the Coalition does not extensively consider the social determinants of health or health disparities. For personalized medicine to have the most clinical utility, personalized medicine should be reflected in the ACA so as to address the social determinants of health. The ACA thus must go beyond the Coalition's recommendations. The ACA should allow for the implementation of personalized medicine through an expansion of insurance coverage for personalized medicine diagnostics that incorporates the ACA's current strategies to reduce health disparities among Americans, which include the establishment of Health Insurance Exchanges that reach target populations.

²http://minorityhealth.hhs.gov/npa/files/Plans/HHS/HHS_Plan_complete.pdf

³This section is quoted directly from <http://www.personalizedmedicinecoalition.org/sites/default/files/files/PMC%20Legislative%20Specifications.pdf>

⁴which includes identification of the methods of personalized medicine and the benefits of its implementation

Personalized medicine by revealing an individual's genetic code would allow for disease prevention strategies for the individual. One of the most optimal ways of enhancing this aspect of personalized medicine should be through (1) the coordination of efforts of the Patient-Centered Outcomes Research Institute (PCORI) with the Community Health Center programs and the US Preventive Services Task Force, and through (2) the expansion of health information technology and electronic health records, the latter considered a provision of the ACA.

The PCORI addresses family health history in determining the social factors causing disease (by cataloguing disease for patients and integrating them into a database), in addition to helping to promote personalized health outcomes. Alongside the Community Health Center programs and the US Preventive Services Task Force, the PCORI should be able to coordinate the implementation of both personalized and preventive medicine concurrently. The PCORI ascertains genomic variation (by taking into account and cataloguing the genetic characteristics of patients): aligned with CHC programs and the USPSTF this information may remain more meaningful in the context of addressing health disparities, as well.

Conclusion

In the context of these recommendations, by focusing on preventive care and family health history, (as provisionally documented by the implementation of electronic health records), personalized medicine may more readily affect social determinants of health. Since the ACA provides for HRSA Community Health Centers, one may envision that genetic diagnostic testing becomes a service of these centers as a New Access Point (a grant program run by the HRSA, the HRSA has committed to support 350 NAPs to increase preventive and primary healthcare services for eligible public and nonprofit entities including tribal, faith-based and community-based organizations). PCORI, combined with Section 4302, could potentially determine a patient's treatment regimen as indicated by the patient's genetic makeup and compared on a nationwide basis with comparative effectiveness methods and by the results of treatment regimens previously administered to patients with similar genetic makeup. Implementing both of these recommendations would effectively enable personalized medicine to reduce health disparities. Thus personalized medicine could improve community health outcomes through its focus on preventive genetic medicine and family history.

This may be illustrated by the following case study. Consider Patient X who has a genetic predisposition for breast cancer. Personalized medicine would reveal this predisposition through genomic/genetic testing. Perhaps the BRCA1 mutation is present in Patient X, conferring increased susceptibility to breast cancer. Family (medical) history, ethnicity, diet, socioeconomic status may also have a bearing on a diagnosis of breast cancer in Patient X. PCORI would potentially coordinate the genetic information with the social determinants of breast cancer. PCORI may then provide Patient X and her clinician with the necessary clinical knowledge to make a fully informed decision (in terms of what she should do about her medical diagnosis, e.g., changes in diet, environment) about the prospects for developing breast cancer.

Thus, the ACA may affect health disparities by accounting for both genomic variation and social determinants of health. The recommendations outlined here are provisional and may require further delineation to more effectively promote the desired potential of personalized medicine. However, it may be time to start to consider these suggestions for effectively implementing the full capacity of the ACA.

References

1. Ginsburg GS, Konstance RP, Allsbrook JS, Schulman KA (2005) Implications of Pharmacogenomics for Drug Development and Clinical Practice. *Arch Intern Med* 165: 2331-2336.
2. Dalton WS, Sullivan DM, Yeatman TJ, Fenstermacher DA (2010) The 2010 Health Care Reform Act: A Potential Opportunity to Advance Cancer Research by Taking Cancer Personally. *Clin Cancer Res* 16: 5987-5996.
3. Feldman AM (2010) Health Care Reform and Translational Medicine. *Clinical and Translational Science* 3: 63-64.
4. Hong KW, Oh B (2010) Overview of personalized medicine in the disease genomic era. *BMB Rep* 43: 643-648.
5. Beuten J, Gelfond JA, Martinez-Fierro ML, Weldon KS, Crandall AC, et al. (2009) Association of chromosome 8q variants with prostate cancer risk in Caucasian and Hispanic Men. *Carcinogenesis* 30: 1372-1379.
6. Waters KM, Le Marchand L, Kolonel LN, Monroe KR, Stram DO, et al. (2009) Generalizability of associations from prostate cancer genome-wide association studies in multiple populations. *Cancer Epidemiol Biomarkers Prev* 18: 1285-1289.
7. Freedland SJ, Isaacs WB (2005) Explaining racial differences in prostate cancer in the United States: sociology or biology? *Prostate* 62: 243-252.
8. Hariri S, Yoon PW, Moonesinghe R, Valdez R, Khoury MJ (2006) Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. *Genet Med* 8: 752-759.
9. Chan IS, Ginsburg GS (2011) Personalized Medicine: Progress and Promise. *Annu Rev Genomics Hum Genet* 12: 217-244.
10. Whellan DJ, Gauden L, Gattis WA, Granger B, Russell SD (2001) The Benefit of Implementing a Heart Failure Disease Management Program. *Arch Intern Med* 161: 2223-2228.
11. Fox JL (2007) Despite glacial progress, US government signals support for personalized medicine. *Nat Biotechnol* 25: 489-490.

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