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Pharmacogenetics in Primary Care: The Promise of Personalized Medicine and the Reality of Racial Profiling

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Abstract

Many anticipate that expanding knowledge of genetic variations associated with disease risk and medication response will revolutionize clinical medicine, making possible genetically based Personalized Medicine where health care can be tailored to individuals, based on their genome scans. Pharmacogenetics has received especially strong interest, with many pharmaceutical developers avidly working to identify genetic variations associated with individual differences in drug response. While clinical applications of emerging genetic knowledge are becoming increasingly available, genetic tests for drug selection are not as yet widely accessible, and many primary care clinicians are unprepared to interpret genetic information. We conducted interviews with 58 primary care clinicians, exploring how they integrate emerging pharmacogenetic concepts into their practices. We found that in their current practices, pharmacogenetic innovations have not led to individually tailored treatment, but instead have encouraged use of essentialized racial/ethnic identity as a proxy for genetic heritage. Current manifestations of Personalized Medicine appear to be reinforcing entrenched notions of inherent biological differences between racial groups, and promoting the belief that racial profiling in health care is supported by cutting-edge scientific authority. Our findings raise concern for how pharmacogenetic innovations will actually affect diverse populations, and how unbiased treatment can be assured.

Keywords

Pharmacogenetics; Personalized Medicine; Race and Ethnicity; Racial Profiling

Introduction

New technologies have radically accelerated discovery of genetic variations associated with disease risk and medication response, and many anticipate that these discoveries will quickly revolutionize clinical medicine (AMA, 2011; Feero & Green, 2011; Timmermans & Oh, 2010). In current medical literature, review articles and commentary heralding the dawn of Personalized Medicine are abundant. The idea is that by scanning a person's genome, it will be possible to tailor health care based on the individual's genetic risk for developing various diseases, and their genetically governed reactions to specific medications (See for example: Chan & Ginsburg, 2011; Ginsburg & Willard, 2009). Pharmacogenetics[1], the study of the genetic variations affecting individual response to drugs to inform development of safer prescribing criteria and more effective drugs, has received especially strong interest in efforts to apply genetics to clinical practice.

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[1]Definitions of "pharmacogenetics" versus "pharmacogenomics" are difficult to distinguish. In that the distinction is not germane to our argument, we have chosen to use the more established term "pharmacogenetics" throughout this paper. (See also footnote #8 in Jones 2011).

Despite the prevalence of the notion that we are at the dawn of genetically based Personalized Medicine, the impact of genetics on primary care practice is only in its infancy. Genetic tests that might affect diagnosis and management of most common diseases are not widely available, and/or not covered by insurers (DHHS, 2006). Furthermore, few primary care clinicians are prepared to interpret genetic findings (Shields, Burke, & Levy, 2008). How do clinicians respond to this heavy emphasis on genomics, with limited knowledge of and access to genetic testing? The answer may lie in the routine clinical practice of assuming racial/ethnic identity can be used as a proxy indicator for genetic heritage. In this paper, we consider how concepts of racial difference are being integrated into emerging clinical applications of pharmacogenetics, then, drawing on interviews we conducted with a group of primary care clinicians, we present some illustrations of how clinicians interpret and apply these notions.

Pharmacogenetics and Racial Identities

The routine use of racial/ethnic identity in clinical medicine is by no means new, but instead reflects deeply entrenched practices. Consider, for example, that existing clinical guidelines for a number of common health conditions prominently feature race/ethnicity in standards for screening, diagnosis and treatment. (See for example: Chobanian et al., 2003; UpToDate, 2012; Wolf et al., 2010).

In the burgeoning arena of human genetic science, racial/ethnic identity has also been routinely employed as a fundamental construct. For example, genetic association studies regularly report frequencies using common racial/ethnic labels: Europeans, Asians, Africans, and Native Americans (Hunt & Megyesi, 2008a; Kahn, 2009). The widespread acceptance in medicine of the notion that race is an appropriate proxy for genetic variation (Fullwiley, 2011), is clearly evident in current medical literature: a recent Medline search for genetic research using these racial labels yielded nearly 4,000 articles for 2011 alone.

From its outset, pharmacogenetics has likewise placed a heavy emphasis on the assumption that genetic variations follow along racial/ethnic lines. In what Jones (2011) refers to as a self-fulfilling prophecy, from the first forays into understanding differential drug metabolism, researchers assumed the existence of genetic and racial variations and they searched for them (Gaines, 1998). That patients of different racial/ethnic groups will have different genetically determined drug responses remains a central notion in the field.

Pharmacogenetics is an area of especially avid innovation, with a myriad of pharmaceutical developers diligently working to identify genetic variations associated with individual differences in drug response. Why such fervent interest in what one might think is a relatively obscure field of endeavor? In addition to the laudable goal of improving the quality of medical care for diverse groups of patients, there are at least two important marketing factors that may be motivating the great interest in pharmacogenetics. One is that people who are not sick, but who carry a specific so-called “susceptibility” genetic variant could be prescribed medications as a preventative measure. Another important entrepreneurial opportunity is that drugs that do not show sufficient effect in a general population or that are dangerous for some people, could be salvaged for FDA approval, and labeled for use or avoidance by people with specific genetic variations.[2] Indeed, the FDA has already approved specific genetic recommendations on the labeling of at least 200 drugs (Ginsburg & Willard, 2009).

[2]The controversial drug BiDil provides a case in point, where presumed racial genetics has been successfully used to gain approval of a drug not shown to be sufficiently effective in the general population Kahn (2004).

To date, however, pharmacogenetics remains largely a promissory science (Cheng et al., 2010). There are only a few specific clinical applications of pharmacogenetics: Some genes have been identified within certain cancer tumors which render them appropriate targets for certain medications. There are also genetically governed variations in so-called "drug metabolizing enzymes" that can affect how individuals respond to certain drugs. (For a useful review of some current trends in the study of drug metabolizing enzymes see: Ninnemann, 2012). The few established therapeutic applications of pharmacogenetics are frequent topics in medical literature which encourages clinicians to recognize the clinical relevance of genetic traits in selecting and prescribing medications.

Consider for example a pamphlet published in July of 2011 by the American Medical Association titled: "Pharmacogenomics: Increasing the Safety and Effectiveness of Drug Therapy" (AMA, 2011). After noting that the goal of personalized health care is to tailor clinical decisions to individual history, environment, behavior and "most importantly, genetic variation," it reviews in detail the enzyme actions affecting metabolism of four specific drugs, identifying specific genetic variations associated with those enzyme variants.

New FDA drug labeling practices similarly promote the notion that individual genetic profiles are important to the selection of medications (FDA, 2010). For example, the following instruction appears on a number of drug labels recently approved by the FDA:

> Patients with ancestry in genetically at-risk populations should be screened for the presence of [specific allele variant] prior to initiating treatment with [drug name]. Patients testing positive for the allele should not be treated with [drug name].

In that genetic tests for these variants are not readily available, and are rarely covered by insurance, what exactly clinicians can do with this information is not altogether clear. The AMA pamphlet concludes with the following advice:

> Pharmacogenomics is still developing… In the meantime, physicians and health care providers should be familiar with the concept that genetic variations can cause their patients to respond unexpectedly to drug therapy and that in some cases, it may be appropriate to guide therapeutic decisions. (p.10)

So once escorted to the door of Personalized Medicine, but in the absence of access to the key to that door: genetic testing, what do physicians do? The answer to this question is strangely ironic. It seems to lie in an important phrase in the FDA labeling quoted above: "at-risk population." In practice, it appears that medicine is being "Personalized" by assigning individuals to "at-risk populations," and responding accordingly.

What exactly are "at-risk populations"? It is standard practice in reports of genetic variations, to note different frequencies of genetic markers, using common racial/ethnic labels such as Asian, African American or Caucasians. Put less-euphemistically, "at-risk populations" refers to racial or ethnic groups, and promoting so-called Personalized Medicine may in actual practice amount to promoting racial profiling in medicine.

"Personalizing" Clinical Practice

In order to examine this notion more closely, we will present case material from interviews we conducted with a purposive sample of 58 primary care clinicians from 44 clinics in Michigan. (See Table 1). The interviews focused on their concepts of the importance of genetics to clinical practice, and the relevance of racial/ethnic identity to clinical decision making.

Consistent with the prevailing anticipation of the advent of Personalized Medicine, when discussing their expectations about the promise of genetics for clinical medicine, many of

these clinicians (40%, 23/58) talked about a future in which medication choice could be tailored to individual needs, based on a person's genetic profile. As one family practice doctor commented:

> I've been really fascinated by some of the new research that's going on— pharmaceutical companies are looking at a person's biochemical make-up to try to determine what pharmaceutical agent is going to work best for them. And I imagine in the future we're going to be able to run blood tests on people and say, "Okay, this is what your cytochrome P450[3] system looks like, so I'm going to avoid this medication and I'm going to choose this."

While many confidently asserted that such genetically based differential prescribing is "just down the road" or "coming down the pike," it is not yet a reality for any of those we interviewed. While a small number mentioned that the oncologists they refer patients to might sometimes run genetic tests on tumors to select chemotherapeutic drugs, only two said they had ever themselves considered genetic tests for medication selection. Neither had actually ordered the test because they did not know which lab offered them, or how to get them paid for. Instead, they just did what they have always done: started the person on a low dose of the medication, watched to see how they react, then increased or decreased the dose accordingly.

Still, most of these clinicians try to bring pharmacogenetic concepts into their practices. However, this is not based on genetic testing, but instead on their assumptions about genetic ancestry. Nearly all (86%, 50/58) cited family history as a simple way to get a sense of a patients' genetic background.

However, when talking about minority patients, rather than consider family history as an indicator of an individual's specific genetic inheritance, it was most often invoked as an indication of presumed group genetic characteristics. Discussion of family history for these patients was readily transformed into a discussion of racial ancestry.

Consider, for example, the view of geneticized racial ancestry described by this family practice physician, when asked if race/ethnicity is important to clinical practice:

> It's part of the diagnostic tool. It's part of the basic general work up… If you look at them and they are American Indian or Hispanic— if they're very dark-complected, they probably have the glu/katE gene. Versus if they're German, or Irish— if they're redhaired they probably have the ob/ob gene… To me it is very important to ask background and heritages and their general appearance and genotypes.

This physician was unique in making such specific claims about the relationship between particular genes and specific racial/ethnic identity. More often, clinicians expressed a more abstract notion that racial groups share a particular gene pool. A common extension of this logic was to assert that, due to their genetically determined metabolic profile, certain racial/ethnic groups require caution in the choice of drugs. Consider this remark, from a family practice physician: "I know there's different drug metabolism, particularly in Asians that I have to be cautious of." Similarly, another family practice physician stated:

> The side effect profile that you see in African Americans, some of them will have more cough secondary to the ACE inhibitor[4] than other populations will. There's a

[3]This is a class of enzymes involved in drug metabolism.
[4]ACE (angiotensin-converting enzyme) inhibitors are a class of drugs commonly used to treat high blood pressure.

> ton of studies just looking at African Americans that they had to take off ACE inhibitors because of cough, as opposed to Whites ….

These quotes refer to the often-cited notion that genetically determined variants of drug metabolizing enzymes vary between racial/ethnic groups, requiring different drug dosages or avoidance of certain drugs for members of these groups. While such concerns were mentioned by many, no one in our study said they had actually tested for these genes or had differentially prescribed based on these enzymes.

However, the vast majority of the clinicians (86%, 50/58) did say they had been taught to differentially prescribe anti-hypertensive medications for their African American patients, and most (76%, 45/58) reported that they did so. (However, it should be noted that there was high variability in the specific drugs they say are recommended or should be avoided for African Americans (For further discussion of these findings see: Hunt, Truesdell, & Kreiner, In Press).

Interestingly, although the science underlying these recommendations is controversial and contradictory (Kahn, 2003; Nguyen et al., 2009), the clinicians often confidently invoked the scientific authority of genetics when describing these practices. As one family physician put it:

> Not all drugs work the same in different ethnic populations. There's something called genetic polymorphism, where people in [a given] ethnic group really don't respond well to that medication.

Another physician was even more resolute in citing the genetic science she believed to be behind racialized medicine:

> The Human Genome Project has proved beyond a doubt that African American males get prostate cancer at younger ages, African American hypertensive patients respond better to certain classes of medications. So to operate blindly, literally, blind to the ethnic and racial is, I think, ridiculous. Because the medical science is there now to say, 'No you have to consider it." It is politically incorrect in some circles to say that. But as far as delivering good health care I think it's essential. You know, "You happen to be Black so we should put you on this." … You <u>have</u> to take that into account, in light of the developments that have come out in the last 36 months.

In fact, this physician is mistaken. The Human Genome Project showed none of this. Differential prescribing recommendations for African American hypertensives are primarily based on clinical trials that involve no genetic testing, but instead consist of documenting different responses to medications in different sub-populations. Critics have noted that, in this line of research, when differences are observed between racially labeled groups, genetic variation is often assumed in the absence of genetic data, while other variables well-known to influence drug response are routinely neglected (Cooper, Kaufman, & Ward, 2003; Fiscella, 2011; Ninnemann, 2012; Shields et al., 2005; Tate & Goldstein, 2004).

For our interests in this paper, it is noteworthy that racial/ethnic group differences are so readily equated with presumed genetic differences, and that the idea of "Personalized Medicine" can so ironically be converted into carte blanche for practicing racialized medicine. In fact, when discussing their vision of the future contribution of genetics to primary care, a number of clinicians in our study (21%, 12/58) skipped the whole idea of using genetics to personalize prescribing, and instead indicated they looked forward to pharmacogenetics leading to more and better race-based treatment recommendations. As one physician expressed it, when we asked what could make genetic science more useful in clinical practice:

When they develop drugs, if they could tell us how the drugs react with different races. We already know that some diseases are more prevalent in different races. So to know the effects that drugs have on different races would be quite useful.

Conclusion

Thus we see that, despite the enthusiasm for the clinical revolution of genetically based Personalized Medicine, what seems to be developing in practice is quite the opposite. In the 11 absence of accessible, reliable genetic tests for the genes involved, clinicians turn to the familiar practice of using racial/ethnic ancestry not only as an indicator of inherited risk for disease, but also as an indicator of genetically determined drug response. Many critics have warned against the inclusion of racial/ethnic classification in the genetic databases upon which this emerging science is based, due to the inadequacy of the classifications themselves, and the high potential for lending unearned legitimacy to the mistaken idea that racial/ethnic groups are biologically distinct (See for example: Duster, 2005; Gaines, 2005; Hunt & Megyesi, 2008b; Lee, 2007). In our interviews we have seen that for these clinicians, developments in pharmacogenetics have not led to individually tailored treatment, but instead have fortified their belief that racial profiling in health care is supported by cutting-edge scientific authority (Ellison & Jones, 2002).

The trend toward so-called Personalized Medicine is being heralded as a potential weapon in the battle against health disparities: the unequal burden of disease carried by racial/ethnic minorities (Conrad, 2005; Fine, Ibrahim, & Thomas, 2005; Fiscella, 2011; Thayer & Kuzawa, 2011; Thorlby et al., 2011; Torres & Kittles, 2007). However, our findings raise concern for how diverse populations will actually be affected by these innovations, and how unbiased health care can be assured. So far, the impact of Personalized Medicine in primary care is limited to reinforcing the dubious belief that there are inherent biological differences between racial groups, and that emerging genetic science mandates differential health care for racially labeled patients.

REFERENCES

AMA (American Medical Association). Pharmacogenomics: Increasing the Safety and Effectiveness of Drug Therapy. 2011. http://www.ama-assn.org/resources/doc/genetics/pgx-brochure-2011.pdf.

Chan IS, Ginsburg GS. Personalized medicine: progress and promise. Annu Rev Genomics Hum Genet. 2011; 12:217–244. [PubMed: 21721939]

Cheng YJ, Kahn HS, Gregg EW, Imperatore G, Geiss LS. Recent Population Changes in HbA1c and Fasting Insulin Concentrations among US Adults with Preserved Glucose Homeostasis. Diabetologia. 2010; 53:1890–1893. [PubMed: 20517591]

Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003; 42(6):1206–1252. [PubMed: 14656957]

Conrad, Peter. The shifting engines of medicalization. Journal of Health and Social Behavior. 2005; 46(1):3–14. [PubMed: 15869117]

Cooper RS, Kaufman JS, Ward R. Race and genomics. New England Journal of Medicine. 2003; 348(12):1166–1170. [PubMed: 12646675]

DHHS, (Department of Health and Human Services). Coverage and Reimbursement of Genetic Tests and Services. Report of the Secretary's Advisory Committee on Genetics, Health and Society. 2006. http://oba.od.nih.gov/oba/sacghs/reports/CR_report.pdf

Duster, Troy. Medicine. Race and reification in science. Science. 2005; 307(5712):1050–1051. [PubMed: 15718453]

Ellison, George TH.; Jones, Ian Rees. Social identities and the 'new genetics': scientific and social consequences. Critical Public Health. 2002; 12(3):265–282.

FDA (Food and Drug Administration). Drug Safety Newsletter: EQUETRO® (carbamazepine) Extended-Release Capsules Prescribing Information. 2010. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021710s008lbl.pdf.

Feero, W Gregory; Green, Eric D. Genomics Educations for Health Care Professionals in the 21st Century. American Medical Association. 2011; 306(9):989–990.

Fine MJ, Ibrahim SA, Thomas SB. The role of race and genetics in health disparities research. American Journal of Public Health. 2005; 95(12):2125–2128. [PubMed: 16257933]

Fiscella K. Health care reform and equity: promise, pitfalls, and prescriptions. Annals of Family Medicine. 2011; 9(1):78–84. [PubMed: 21242565]

Fullwiley, Duana. The Enculturated Gene: Sickle Cell Health Politics and Biological Difference in West Africa. Princeton: Princeton University Press; 2011.

Gaines, Atwood D. Culture and Values at the Intersection of Science and Suffering: Encountering Ethics, Genetics and Alzheimer Disease. In: Post, SG.; Whitehouse, PJ., editors. Encountering Ethics, Genetics and Alzheimer Disease. In G enetic Testing for Alzheimer Disease: Ethical and Clinical Issues. Baltimore: Johns Hopkins University Press; 1998. p. 256-274.

Gaines, Atwood D. Race: Local Biology and Culture in Mind. In: Casey, C.; Edgerton, R., editors. Companion to Psychological Anthropology: Modernity and Psychocultural Change. Oxford: Blackwell; 2005. p. 255-278.

Ginsburg GS, Willard HF. Genomic and personalized medicine: foundations and applications. Transl Res. 2009; 154(6):277–287. [PubMed: 19931193]

Hunt, Linda M.; Megyesi, Mary S. The ambiguous meanings of the racial/ethnic categories routinely used in human genetics research. Social Science & Medicine. 2008a; 66(2):349–361. [PubMed: 17959289]

Hunt, Linda M.; Megyesi, Mary S. Genes, race and research ethics: who's minding the store? Journal of Medical Ethics. 2008b; 34(6):495–500. [PubMed: 18511627]

Hunt, Linda M.; Truesdell, Nicole; Kreiner, Meta J. Race, Genes and Culture in Primary Care: Racial Profiling in the Management of Chronic Illness. Medical Anthropology Quarterly. In Press.

Jones, DS. How Personalized Medicine Became Genetic, and Racial: Werner Kalow and the Formations of Pharmacogenetics. 2011. http://www.ncbi.nlm.nih.gov/pubmed/21908852

Kahn, Jonathan. Getting the numbers right: statistical mischief and racial profiling in heart failure research. Perspectives in Biology and Medicine. 2003; 46(4):473–483. [PubMed: 14593217]

Kahn, Jonathan. Beyond Bidil: The Expanding Embrace Of Race In Biomedical Research And Product Development. Saint Louis University Journal Of Health Law & Policy. 2009; 3(61):61–92.

Lee, Sandra Soo-Jin. The ethical implications of stratifying by race in pharmacogenomics. Clinical Pharmacology and Therapeutics. 2007; 81(1):122–125. [PubMed: 17186010]

Nguyen TT, Kaufman JS, Whitsel EA, Cooper RS. Racial differences in blood pressure response to calcium channel blocker monotherapy: a meta-analysis. American journal of hypertension. 2009; 22(8):911–917. [PubMed: 19498341]

Ninnemann KM. Variability in the efficacy of psychopharmaceuticals: contributions from pharmacogenomics, ethnopsychopharmacology, and psychological and psychiatric anthropologies. Culture, medicine and psychiatry. 2012; 36(1):10–25.

Shields AE, Burke W, Levy DE. Differential use of available genetic tests among primary care physicians in the United States: results of a national survey. Genet Med. 2008; 10(6):404–414. [PubMed: 18496223]

Shields AE, Fortun M, Hammonds EM, King PA, Lerman C, Rapp R, et al. The use of race variables in genetic studies of complex traits and the goal of reducing health disparities: a transdisciplinary perspective. American Psychologist. 2005; 60(1):77–103. [PubMed: 15641924]

Tate SK, Goldstein DB. Will tomorrow's medicines work for everyone? Nature Genetics. 2004; 36(11 Suppl):S34–S42. [PubMed: 15508001]

Thayer ZM, Kuzawa CW. Biological memories of past environments: epigenetic pathways to health disparities. Epigenetics : official journal of the DNA Methylation Society. 2011; 6(7):798–803. [PubMed: 21597338]

Thorlby R, Jorgensen S, Siegel B, Ayanian JZ. How health care organizations are using data on patients' race and ethnicity to improve quality of care. The Milbank Quarterly. 2011; 89(2):226–255. [PubMed: 21676022]

Timmermans S, Oh H. The Continued Social Transformation of the Medical Profession. Journal of Health and Social Behavior. 2010; 51(Suppl):S94–S106. [PubMed: 20943586]

Torres JB, Kittles RA. The relationship between "race" and genetics in biomedical research. Current hypertension reports. 2007; 9(3):196–201. [PubMed: 17519124]

UpToDate. Evidence-Based Clinical Decision Support Resource. 2012. http://www.uptodate.com/index

Wolf AM, Wender RC, Etzioni RB, Thompson IM, D'Amico AV, Volk RJ, et al. American Cancer Society guideline for the early detection of prostate cancer: update 2010. CA Cancer J Clin. 2010; 60(2):70–98. [PubMed: 20200110]

Table 1

Selected Characteristics for 58 Clinicians Interviewed

	No.	%
Sex		
Male	26	45
Female	32	55
Race/Ethnicity		
Non-Hispanic White	37	63
African American	10	17
Native American	2	3
Pacific Islander	2	3
Asian	5	9
Hispanic	2	3
Age *range: 27–77 median: 43*		
24–34	12	21
35–44	19	33
45–55	16	27
>55	11	19
Degree		
MD	34	59
DO	17	29
PA	2	3
NP	5	9
Genetics Training		
Formal Genetics Course	13	22
Part of a Non-Genetics Course	24	41
No Relevant Genetics Training	20	35
Missing	1	2
Type of Clinic		
University	3	3
Hospital/Health System	21	36
Physician Owned	21	36
FQHC	8	14
Other	5	9