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Health Disparities in the Age of Personalized Medicine

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Introduction and summary

The human genome sequence has been fully completed for a decade now and the price of full genome sequencing is dropping precipitously. Many believe that with these developments, a new era of personalized medicine is about to hit full speed. Personalized medicine is essentially "the use of genetic susceptibility or pharmacogenetic testing to tailor an individual's preventive care or drug therapy," although some definitions also include the development of patient outcomes research, health information technology, and care delivery models.[1] Put more simply, it means the development of medicines and therapies tailored to patients' unique genetic traits and risks.

The field is evolving rapidly but many hurdles still remain. Individually tailored drugs based on a patient's genetic makeup are far off, and the cost of developing drugs for genetic subpopulations with largely similar genetic traits for one or more diseases hinders developments in this arena. Similarly, the lack of standards surrounding direct-to-consumer genetic tests and the lack of robust, large-scale genomic data for many diseases and conditions are additional hurdles.

Nevertheless, personalized medicine is making its way into the mainstream. Estimates by PricewaterhouseCoopers indicate that the market for personalized medicine, currently a $232 billion industry, will grow at a rate of 11 percent annually.[2] Personalized medicine is also making serious strides in the pharmaceutical industry with drugs like the colon cancer drug Erbitux, which is most effective in patients with a certain genetic mutation.

Personalized medicine also has the potential to rein in rising health care costs. For instance, physicians can better prevent adverse drug reactions by using genetic information to calibrate the ideal dosage of the blood-thinning drug Warfarin for an individual patient. This alone could prevent 85,000 serious bleeding cases and 17,000 strokes, and save the health care system $1.1 billion annually.[3]

But the health care and scientific communities will still have to answer important questions about who will have access to these new medical advancements as they develop. Health disparities persist between different groups for various reasons including access to care, lifestyle factors, socioeconomic status, and genetics. Studies indicate that minorities have less access to health care and generally receive a lower quality of care. Studies show that African Americans have lower incidence of breast cancer than white women, for example, but suffer greater mortality.[4] Heart disease is widespread among minorities and a leading killer in the African-American community.

Personalized medicine can potentially alleviate these discrepancies since it could allow physicians to prescribe medication that treats the disease more effectively. African-American women suffer from a more aggressive form of breast cancer that tends to be estrogen resistant, for example.[5] Profiling the genes of the tumor and the genes of the patient could allow a doctor to prescribe the most effective drug regimen.

Yet certain issues regarding racial and ethnic health disparities need to be addressed in order for personalized medicine to offer the greatest benefit to all. This paper examines these issues in detail and then offers some ethical guidelines for policymakers to consider, among them:

- There must be a frank discussion of the social and methodological appropriateness of using race or ethnicity as disease proxies.

- Genetic variation research and clinical trials must systematically incorporate such discussions into their individual study designs and the research itself.

- We cannot ignore structural inequalities in access to health care and in fact should seek to reduce them through research that looks at social, environmental, and behavioral contributions to health status as well as research on the outcomes of different care delivery models for different populations.

In the pages that follow we will demonstrate why these proposed ethical guidelines are essential to the development of personalized medicine in our country.

Using race as a proxy

Genes and race do not line up. Geneticists since the 1950s have obtained scant evidence supporting the correlation between outward physical appearance—the typical determinant of racial categories—and underlying genetic correlations. The Human Genome Project, which was completed in 2003, came to the consensus that human beings are 99.9 percent similar on the molecular level. Some have estimated since then that it might be slightly lower at 99.5 percent.[6]

Many more studies have aimed to explain group differences in health in terms of genetics but they each have their own unique experimental designs and parameters for defining group membership. But it is safe to say that race cannot be defined in strictly biological terms given the great genetic diversity within certain groups as well as the genetic overlap among multiple groups. Indeed, all individuals have the same set of genes and all groups of people share the major variants of those genes. There is no genetic marker that takes the form of one variant in all members of one large group and takes the form of another variant in all members of another large group. Different variants of genes are distributed across human populations in gradations and not in discreet groupings.

It is crucial to recognize that disease and health disparities are the product of complex interactions that are not solely limited to genes but also involve environmental factors, socioeconomic status, lifestyle factors, and the biases of health care providers. Yet Healthy People 2010, a Department of Health and Human Services initiative aimed at identifying preventable threats to public health, reports that many of these factors are sidelined and studies tend to mainly focus on race.[7] Researchers can use race as a convenient way to associate biological variables with social, geographic, and historical variables when obtaining more detailed biological information would be unfeasible. But studies should not overuse race as a proxy for assessing disease risk at the expense of gathering other biological or diagnostic information that could be just as relevant, if not more so.

Race can be a misleading proxy in clinical and research contexts since the physical traits society uses to categorize individuals by race are not reflected in genes. There is significant genetic overlap between different racial and ethnic groups and the differences that do exist between groups are mere graded variations in the frequencies of certain genes as opposed to distinctive genotypes. What's more, socially and physically defined racial groups do not accurately map on to the genes that may be exclusive to a single population. In other words, race is less a genetically determined characteristic and more a socially constructed one.

Yet the appearance of medicines such as BiDil and Travatan, both approved exclusively for African-American patients, raise questions of whether medicines tailored to particular genotypes can lessen health care disparities and how. Both hypertension and glaucoma-related blindness are more prevalent among African Americans. But science has not shown the reason for this is genetics. Instead it is likely that diet and poor access to medical facilities contribute to those conditions more than genetics do. A misattribution of the disease causes to genetics instead of other more easily remedied factors will mean failure to close the health care gap, and can potentially lead to "racialized diseases."

Additional problems arise with the use of race as a genetic or biomedical proxy since there is often genetic overlap between races and much genetic diversity within races. Indeed, an early and enduring finding about genetics is that there is more genetic diversity within races than between them. An especially large amount of diversity exists within and among various African populations, much of which has yet to be fully mapped. The genomes of African Americans have an estimated 10 percent to 20 percent level of European admixture, which complicates using race alone as a proxy.[8] And Latinos are an especially genetically diverse group since their genomes are comprised of varying combinations of European, African, and Native-American genes depending on the exact heritage of the individual. Medical professionals need to take precautions when prescribing medication based on African-American or Latino self-identification due to the diversity within these genomes.

The proxy of race is but one tiny window into the complex biological, social, and environmental forces that influence disparate health outcomes but it risks being overemphasized in fields where genetic technologies are becoming increasingly prevalent. This includes the field of health disparities as well as genealogy and forensic science. Professionals and the lay public could easily fall into the trap of fetishizing genetics and its connections to race and ethnicity in the context of public health, crime, and cultural history without a proper understanding of how genetics only tells part of the story.

Genetic research has and will continue to shed much light on human health but researchers and medical professionals should not interpret this as a reason to adopt a naive genetic essentialism where genes are understood to completely determine human health and physical traits.[9] Indeed, genetic markers themselves only indicate probability of risk or outcome, not certainty.

Scientists also need to be clear about how they employ racial and ethnic categories when doing research on genetics and/or health disparities. In an open letter in the journal *Genome Biology*, a group of scientists and ethicists from Stanford University listed a set of guidelines for using racial categories in genetic research. One guideline explicitly encourages researchers to "describe how individual samples are assigned category labels, to explain why samples with such labels were included in the study, and to state whether racial or ethnic categories are research variables."[10] The Stanford group calls upon

researchers to assess the purpose and impact of the use of racial categories and investigate alternative approaches.[11] Concurrently, leading journals such as *Nature Genetics* and the *American Journal of Medical Genetics* have issued publication guidelines for authors who make use of racial categories in their research findings.[12]

Researchers need to be careful about reifying race or transforming race from a social to a scientific category, which then reinforces pre-existing and incorrect understandings of race. This can create a circular feedback loop that uses science to perpetuate certain harmful assumptions about racial groups. These assumptions about the relation of genetics to social categories of race become particularly salient when the commercial viability of a product rests on them. Companies can easily oversell tenuous correlations between genes, race, and health disparities in order to market a new medical product to a particular racial demographic, albeit with racially inclusive intentions—even when the predominant causes of a disparity may in fact be social, economic, or environmental.[13]

Genetic variation research

Similar genetic history does not necessarily mean similar ethnic background

Technological advancements have allowed scientists to discover genetic complexities and variations with greater precision. Conducting genetic variation research can lead to better understanding of disease susceptibility and targeted personalized medicine. But one of the dangers of genetic research variation is it can potentially open avenues for scientific racism and genetic determinism, which could in turn underscore stereotypes plaguing minority communities.[14]

There has been some debate about whether and how to classify individuals according to race and/or ethnicity and whether patients are ultimately better served by scientists and physicians who employ a patient's genetic ancestry or self-identified ancestry. The dilemma is that even though there are geographical patterns of genetic variation that correspond to continental origin, these patterns do not map directly on to our socially defined notions of race or ethnicity.

Individuals have even been known to report different ethnic or racial identities in different contexts or at different points in their lives.[15] These self-defined groupings can also have little correlation to genetic ancestry. One study conducted in the American Southwest found that 85 percent of Hispanics underestimated their Native-American genetic ancestry and most Native Americans underestimated their European ancestry.[16] There will always be some groups that are genetic exceptions—no matter what categorical framework is used—and this makes it difficult to properly contextualize the genetic components of health disparities that occur across socially defined racial and ethnic lines.[17]

Some researchers and scholars believe genetic variation research based on genetic population groups or common ancestry groups will nevertheless help shed more light on the genetic component of health disparities. Even racial categories might be appropriate for the labeling of some drugs if those drugs meet strict standards for efficacy in one racial group and inefficacy in all other groups (see section on FDA regulation).[18]

These scholars argue that even though these groups are socially defined, disparities do occur along these racial and ethnic lines, and the biomedical community should allow for the possibility that disparities can be repaired along these lines as long as they are placed in a social justice framework and do not legitimize biological notions of race.[19]

Who benefits from genomic medicine?

Abdallah Daar and Peter A. Singer, two bioethicists from the University of Toronto, argued in a 2004 *Nature* commentary that if personalized medicine is to benefit the global population, including the populations of developing countries, scientists will need to conduct research studies on all population groups across the globe. Individual-level information would deliver the highest level of confidence about disease risk or treatment response, but Daar and Singer claim personalized medicine will only continue to reinforce existing disparities if it focuses solely on individual genetic profiles without proactive efforts to study and treat underrepresented groups specifically.[20]

There is some truth to this claim since researchers conduct genome-wide association studies on populations of European descent by a ratio of 10-to-1 versus all other groups combined, and so the gene-disease correlations that these studies bring to light mostly apply to people of European descent.[21] A person of Asian or African descent may possess similar traits or suffer from the same disease as a European but it might be caused by a different gene variant or another nongenetic cause altogether, simply because the gene variant that causes it in Europeans is less prevalent in Asian or African populations (see text box on page 8).[22]

There are, however, exceptions to this rule, such as responsiveness to hepatitis drugs where the favorable gene variant is present in different proportions in each continental group. But it still has the same effect for an individual who possesses it regardless of which continental group they belong to.[23]

Three scientists from the University of California, San Francisco, note that one of the least examined questions in population genetics is whether the level of risk conferred by a gene variant changes with the ancestral mixture of a given population. For instance, a gene variant that increases the risk for Alzheimer's disease might confer more or less risk depending on an individual's percentage of African ancestry.[24] This gene variant is known as a common variant and has continuous levels of prevalence across the global population but it is uncertain how it interacts with rare variants that are more specific to ancestral populations.

Common genetic variations so far seem to contribute very little to common disease risk by themselves, and rare, large-effect variants have been shown to make much greater contributions. The study of rare genetic variants will not kick into high gear, however, until whole genome sequencing comes down in price and researchers can compare individuals with a strong expression of a trait or disease to unaffected individuals from the same ancestral population group as a reference. Thomas Urban of Duke University anticipates these diverse reference genomes will become available once projects such as the 1000 Genomes Project are completed.[25]

Direct-to-consumer genetic testing and gene-disease correlation

Direct-to-consumer genetic testing aims to place consumers in control of their genetic information by exploring their genomes using the latest scientific research data. But the research data these companies provide does not always apply the same way to each individual consumer. As these companies further develop their services, they will need to use data from more diverse research pools and better communicate to consumers the caveats that come with the data.

Recently, a report from the Government Accountability Office on direct-to-consumer genetic testing companies noted many of these companies provide disease probabilities based on gene-disease correlation data that have been generated from studies on mostly European-descended populations. Some of these companies do not inform their African-American and Asian customers of these data limitations until they release a customer's test result, which of course happens after the customer has paid for the test.[30]

The company 23andMe, which collects information on its customers' health status in the hopes of mining their genetic and health data to find new correlations, states on its blog that it is "actively seeking to initiate a large study of African American individuals that will seek to replicate genetic associations already known in European populations (or show that these associations do not hold)."[31]

The analysis of genetic ancestry might be seen as a useful way to obtain greater scientific clarity on genetic relatedness than the inaccurate and contentious proxies of race and ethnicity, but it can still result in the perpetuation or exacerbation of disparities since it sidesteps the interaction of biological and social factors that contribute to health.[26] The science of genetic ancestry can also reify racial distinctions by presenting genetic clusters that do not arise organically from the genetic data. This is because these studies sometimes analyze the raw genetic data by employing statistical methodologies or computer programs with built-in assumptions about how the data should be grouped.[27]

According to sociologist Tukufu Zuberi, this has long been a problem even in the social sciences as "social statisticians ignore the discussions about the meaning of race and the implications this meaning has for their statistical models."[28] This is because statistical theories are often not detailed enough to explain all variables and their relations. With racial statistics, this leads to an assumption that race is a static attribute and not a dynamic characteristic that depends on other social circumstances.[29]

Is there a right way to use race?

A group of scholars and scientists published a commentary in *Genome Medicine* in January 2009 in which they compiled existing recommendations from scientific publications regarding the use and reporting of race and ethnicity in biomedical research.[32] These recommendations call upon scientists to:

- Use race and ethnicity (and gender and socioeconomic status) only when the study collects and includes in the analysis data relevant to the underlying social mechanisms.

- Attempt to measure as many alternative variables as possible, including: "racism and discrimination, socioeconomic status, social class, personal or family wealth, environmental exposures, insurance status, age, diet and nutrition, health beliefs and practices, education level, language spoken, religion, tribal affiliation and country of birth."

- Create racial and ethnic categories that are as descriptive and specific as possible, avoiding catch-all terms in common use, and making sure to use groupings that are "precisely defined and of similar resolution."

- Assign subjects to research categories that are appropriate to the research question.

- Reflect on and explain precisely how data on race and ethnicity was collected and how it may affect the study—if it was self-reported or assigned by others, for example.

- Consider the "implied relationship between study populations and the populations to which findings are generalized."

These guidelines are important for how geneticists articulate their research to the scientific community, the medical community, and the public at large. They are also important for overcoming another major obstacle to a broadly inclusive genetic research enterprise: obtaining consent from donors of genetic material. Consent for genetic research is low compared to other forms of biomaterial donation, such as blood or tissues. The lower rate of consent can be attributed to factors such as lack of knowledge, mistrust of researchers, the gap between participants and beneficiaries, and concerns regarding discrimination and confidentiality.[33]

The passage of the Genetic Information Non-Discrimination Act of 2008 should help allay fears about employers or insurance companies obtaining genetic information as long as researchers clearly articulate these protections to subjects. Yet it is essential for researchers to address the concerns held by various communities regarding genetic variation research both in the collection and reporting of data.

Medical anthropologist Barbara Koenig has suggested the creation of medical DNA databases should be coupled with efforts to promote community understanding beyond the informed consent standard.[34] Indeed, in addition to questions such as "who should be sampled and what will their sample be used for?" and "who are the beneficiaries of research studies?", the scientific community needs to be ready to answer questions for underserved communities such as:

- How can discrimination stemming from future discoveries be prevented?
- How can I talk about genetics with my doctor in order to get the most health benefit?
- Who will benefit from the profits this data generates if the samples are collected by a private company?

Researchers can start by being more thorough and consistent. And the individual recruiting genetic samples should understand the research so he or she can answer subjects' questions.[35] Researchers, whether from the public or private domain, need to be transparent about the objectives of the study and the motivations of the researchers. They must also be aware of how their material is presented, simplify the consent documents, and ensure the research team members who are actually obtaining informed consent from the subjects have enough experience.

They must also be aware of the research institution's relationship to the community and how this shapes the subjects' perceptions. And research facilities should also allow the donors to be able to make key decisions such as what studies their samples can and cannot be used for.[36] Researchers should also share data and results with subjects whenever feasible, although this may be difficult in some studies where the research must be conducted blindly in order to ensure objectivity. At the very least, subjects should be able to share in the data at the end of the study. The more researchers can standardize these aspects of subject disclosure and involvement across research projects, the better.

Another option, in contrast to informed consent, is to adopt a gift model for genetic material donation just like the model used for organ donation. This model requires the subject or patient to waive all rights pertaining to the usage of their donated material. Implicit in this is the understanding that the genetic material could be used for research purposes that have yet to be determined. Trust and transparency will still be essential at the point of donation but this model will give the researchers more leeway with data usage, especially when much time has elapsed between data collection and analysis.[37]

Minority representation in clinical trials

Minorities are vastly underrepresented in biomedical clinical trials. The lack of clinical participation and recruitment entails severe consequences; most importantly, it will exacerbate the existing health care disparities if it continues. The lack of representation is disconcerting. Cancer is the second-leading cause of death among Latinos, and Hispanics are 14 percent of the U.S. population, yet they only make up 3 percent of cancer clinical trials in the United States. Asian Americans and African Americans also have significantly lower enrollment in clinical trials compared to whites.[38]

The poor representation can be attributed to many factors such as a lack of awareness, socioeconomic barriers, cultural issues, and provider bias. A survey by Harris Interactive found that 85 percent of cancer patients did not know they could participate in a trial or that it was an option.[39] One study cited in a recent report by the Institute of Medicine and National Cancer Institute found that "in two urban NCI-designated comprehensive Cancer Centers, patients were offered clinical trials in only 20 percent of the interactions, but when the patients perceived that they were offered a trial, 75 percent of patients assented to trial participation."[40]

Socioeconomic barriers such as cost of travel to specific locations, insurance coverage of clinical trials, and distrust of the medical community, as well as different cultural attitudes regarding chronic disease and language barriers also contribute to low participation. The American Society of Clinical Oncology acknowledges that recent studies show minorities are equally willing to participate in clinical trials as whites.[41] Efforts need to be directed toward eliminating the barriers and increasing participation from all groups.

Representation of other groups is necessary to provide complete and adequate care. Studies have found on multiple occasions that drugs affect various racial and ethnic groups differently. For instance, African Americans with hypertension respond better to calcium channel blockers and diuretics than whites. Those of Asian descent, particularly Chinese, are more sensitive to beta blockers than whites and may require a lower dosage.[42] Full representation is needed as the field of pharmacogenomics advances in order for treatments to cater to as many unique individuals as possible.

Provisions in various pieces of legislation have been aimed at countering the problem of the lack of minority representation in clinical trials. This has led to policies at both the National Institutes of Health and the Food and Drug Administration aimed at

the inclusion of minorities and women in research. The National Institutes of Health Revitalization Act of 1993, for example, requires that women and minorities are included in NIH-funded clinical trials and requires all of its grantees to report the total number of subjects along with a racial/ethnic and sex/gender breakdown. When a therapy undergoes a Phase-3 clinical trial, NIH guidelines require researchers to review previous data for the existence of gender- or minority-based differences in the effects of the therapy. If there is evidence supporting the existence of differences, then researchers are required to design the trial to assess differential demographic effects as primary research questions. If there is no evidence supporting differences, then demographic analysis is not required, but inclusion and analysis of all genders and minorities is strongly encouraged. If the evidence neither supports nor denies the existence of differences, then the researchers are required to ensure sufficient representation of all genders and minorities in order to conduct analysis of differential effects.[43]

Similarly, the Food and Drug Modernization Act of 1997 directed the FDA to examine issues related to the inclusion of racial and ethnic groups in clinical trials of new drugs. The FDA formed the Women and Minorities Working Group as a result and in 1998 issued the Demographic Rule. This regulation requires companies to collect gender, race, and age data for drug application annual reports and advises clinical trial sponsors to ask their subjects to volunteer such information and, if desired, to use the demographic categories issued by the Office of Management and Budget. OMB last updated these categories in 1997, which classify five races—white; black or African American; Asian; American Indian and Alaska Native; Native Hawaiian or other Pacific Islander—and two ethnicities: Hispanic or Latino, and not Hispanic or Latino.

The FDA also issued a nonbinding guidance in 2005 recommending that researchers use "a standardized approach [i.e. the OMB categories] for collecting and reporting race and ethnicity information in clinical trials conducted in the United States and abroad for certain FDA regulated products."[44] The FDA acknowledged the usefulness of obtaining more detailed race and ethnicity data beyond the Office of Management and Budget classifications but asked that such "data be related to the identified OMB categories of all clinical trial participants when submitting such data to the Agency."[45]

The benefit of using the OMB categorizations for clinical trials is that it creates consistency in the analyses of data submitted to the FDA and other government agencies, and it allows the FDA to evaluate safety and efficacy differences for drugs across different racial and ethnic groups. The drawback to relying on these categories is that they are, as the OMB itself states, "social-political constructs and should not be interpreted as being scientific or anthropological in nature," which is certainly important for addressing the broad socioeconomic causes of health disparities but does not adequately approximate genetic differences on the individual level.[46] CAP's report "Measuring the Gaps" advocates for increased granularity in the way we collect and use racial information.

Charles N. Rotimi, the director of the Center for Research on Genomics and Global Health at the NIH, has suggested clinical trials should be based on patient groups characterized directly and specifically by genetic variation information since humans cannot be divided into distinct groups biologically according to common notions of "race" or "ethnicity." Multiple racial and ethnic groups should therefore be included in clinical trials, especially pharmacogenomics research, because there are subtle differences in allele frequencies between these groups that may be important in how members of these groups respond to drugs at the individual level.

Once it becomes feasible to incorporate whole-genome sequencing into clinical trials, researchers will have more information on subtle genetic differences to construct these more accurate patient groups for subsequent clinical trials.[47] The NIH and FDA will then need to make an effort to redefine the subpopulation categories for clinical trials according to genetic variation as opposed to using the social-political categories used by OMB.

Access to care and representation in research

For personalized medicine to truly be inclusive and beneficial to everyone, the scientific community including doctors, researchers, and pharmaceutical companies needs to make the effort to include all members of the society at every step from clinical trials to drug therapies to genetic testing. Underrepresented groups in the patient community often tend to suffer from economic inequalities, provider bias, lack of awareness, distrust, and cultural and linguistic barriers.[48] These factors result in lower participation and contribute to growing health care disparities. The scientific community should work to overcome these boundaries by extending a hand via community outreach. Underrepresented groups need to be made aware of their risk factors, ongoing clinical trials, and new genetic tests as well as the possible risks, benefits, and uncertainties of each in ways that are inguistically and culturally appropriate.

Researchers also need to address the question of access. Some federal programs currently mandate a certain percentage of minority participation, but studies frequently fail to meet these mandates because of the lack of knowledge about ongoing studies as well as factors such as insurance or transportation. Neglecting minority groups in studies can be detrimental for medical research and treatments. The cost of taking part in a trial or study needs to be reduced or offset to encourage participation.

Programs such as the National Cancer Institute's Minority-Based Community Clinical Oncology Program, which requires that 40 percent of enrolling cancer patients are from minority groups, are particularly successful in recruiting patients to clinical trials. The program is able to effectively integrate academic centers where clinical trials are managed and conducted with community physicians.[49] The system allows patients with physician supervision to take part in new clinical trials while remaining in their communities, thus eliminating issues of travel, access, and minority representation.

Doctors can also be a crucial link to easing health care disparities because they are close to the patient and are actively caring for the patient's health. Doctors can inform patients about ongoing clinical trials, introduce patients to new treatments, and provide genetic test recommendations for at-risk patients.

The medical community must also recognize recruitment challenges. The difficulty is often dispelling doubts within minority groups who may fear future discrimination in both employment and insurance, or may simply be unfamiliar with research participation. All groups need to be made aware of current laws such as the Health

Insurance Portability and Accountability Act of 1996 and the Genetic Information Nondiscrimination Act of 2008. HIPAA ensures confidentiality and restricts the disclosure of private health information, while GINA prohibits health insurance companies and employers from discriminating on the basis of genetic information.[50]

Patients and participants need to be made aware of existing laws that protect their interest and privacy. The scientific community can gain the trust and consent of historically underrepresented groups by ensuring protection. Indeed, these concerns relating to privacy, data ownership, and information security will only become more prevalent as the shift toward evidence-based personalized medicine leads to the merging of clinical care and medical research.

Quality of care

Care providers also need to acquire certain cultural competencies so they can effectively deal with minority groups. A recent example of poor outreach is a Native-American tribe from Arizona that believed scientists were taking their DNA samples solely for diabetes research, but later found out the DNA was also used to determine their prevalence of schizophrenia and their genetic ancestry, which clashed with their origin story.[51] Another is the story of Henrietta Lacks, which was recently recounted in a popular book and shows how a person's cells can be taken without their knowledge and then reproduced on a mass level due to the cells' unique viability, leaving the donor's family with no ownership rights and confusion about how their own biology or health status might complement or relate to the research done with those cells.[52]

Comparative effectiveness research also will be a major component of developing best practices for interacting with various ethnicities, linguistic communities, or faith communities in order to build trust in both care and research settings. HHS has been planning to reach out to these "priority populations" since mid-2009 after the American Recovery and Reinvestment Act of 2009 authorized it to devise such plans. The HHS Committee's report recommended:

- Language and communication services
- The building of a diverse scientific and health care workforce
- Community outreach by identifying trusted community members who can promote the benefits of research
- Cultural competency concerning diet, work/life balance, and environmental access to resources

The committee also elaborated on a research model known as community-based participatory research, which involves the community in the design and conduct of the research, resulting in a community's sense of "ownership" of the results and greater adherence to the outcomes.[53]

The Patient Protection and Affordable Care Act of 2010 takes a significant step toward establishing these approaches by creating the Patient Centered Outcomes Research Institute and directing it to take into account subpopulation differences in health care effectiveness. This means that as the Institute conducts its research on the effectiveness of various treatments, services, items, and interventions, it will design its methodology to focus on different demographic groupings such as racial and ethnic minorities, women, different age groups, people with different comorbidities, quality of life preferences, and genetic and molecular subtypes.[54]

This will avoid "one size fits all research" that just assesses the "average patient" (which has historically been white, male, and healthy), and steer our health care system to a more personalized model. The challenge will be to decide exactly when and how these demographic breakdowns will be most appropriate.

Different demographic lenses—whether genetics, race, age, or gender—all have various levels of usefulness depending on the situation and the purpose. More than one will usually be important to deciphering the causes of a medical condition and how to best intervene. It is important for demographic groupings such as race and genetics to complement and build on, rather than obscure, one another. Above all else, the patient must be treated as an individual by being given the care they need when they need it. Population-based studies and the data they produce will never be perfect, no matter how robust, and are simply a means for zeroing in on the best individual care regimen.

Next steps for genetic research

It is essential that this new path of personalized medicine is all-inclusive and beneficial to all as scientists develop new biomedical and medical technologies. Drug companies and health care providers will be faced with questions about what factors are most reliable for assessing disease risk and how much should depend on genetic information. Health care providers should avoid the trap of geneticizing identities and diseases as well as using inadequate proxies, and use a holistic approach. Factors such as environment, socioeconomic status, access to care, diet, and other lifestyle risks are easily masked and difficult to distinguish, but all these factors contribute strongly to disease prevalence in a specific population and to following the trajectory of the illness. Personalized medicine can be a particularly useful tool and can better cater to individual health needs but it should be seen that everyone benefits from such medical advancements.

The Genomics and Personalized Medicine Act, introduced in Congress in 2006 but never passed, provided a unique opportunity to initiate dialogue on issues such as the availability of personalized medicine to all, the infrastructure and technology needed for further advancement, and the status of race and ethnicity in personalized medicine. The original bill directly focused on issues such as genetic variation research and utilizing race as a proxy, including an entire section entitled "Race, Genomics, and Health," which called for the formation of a Genetics and Personalized Medicine Interagency Working Group that would be responsible for:

> *(i) determining appropriate definitions and use of categories of race and ethnicity, (ii) determining ways to increase access to pharmacogenomic and related clinical genetic services for minority populations, (iii) providing research opportunities and funding support in the area of race and genomics, (iv) enhancing integration of federal wide effort and activities, and (v) recommending privacy protection of genetic information.*[55]

When the bill was resubmitted to Congress in 2008, the entire section of "Race, Genomics, and Health" was eliminated, but some of the issues were addressed in the revised version of the Minority Health Improvement and Health Disparity Elimination Act of 2007 (S. 1576), which ultimately was not passed and has not been reintroduced. Nevertheless, it might have been a better legislative context for such provisions because if racial categories are to be used at all in personalized medicine, it is best that they are used for eliminating disparities instead of as proxies for individual genotypes. But it still used the OMB categories and did not make any efforts to move toward other gene-based categories that might be more useful.

Discovering and investigating individual genetic markers holds great promise for eliminating the distinction of race in research. But the imminent commercial reality is there are currently 700 drugs in research and development that are specifically intended for African-American patients, and the idea of race in medicine needs to be addressed rather than ignored. So-called "race-based" therapeutics and racialized medicine cannot be left without any standards.[56]

The Genomics and Personalized Medicine Act of 2010, which is now dead, contained a few provisions that should contribute to a socially equitable and scientifically accurate transition from racial/ethnic categories to gene-based categories. The bill instructs the FDA to improve the development of diagnostic tests in companion with drugs by conducting postmarket surveillance to "identify genetic and other biological, social, behavioral, and environmental factors that may underlie the differential drug effects when drugs are shown to be more or less effective in certain racial and ethnic subpopulations."[57] Yet it also instructs the FDA to issue guidance on "the collection and analysis of genetic and other biological factors that may be better biological predictors of individual differences in drug response than broad categories such as race, ethnicity, and gender."[58]

This is a promising first step; closing persistent health care disparities requires dialogue that leads to a concrete understanding of the legal and regulatory standing that race and ethnicity will have in medical research and practice.

One of the more robust recommendations concerning a legal approach to the regulation of race-based pharmaceuticals comes from Osagie K. Obasogie of the Center for Genetics and Society. Obasogie calls for a "strict scrutiny" model of approval for drugs with racial indications. This model was originally adopted as a Supreme Court doctrine for dealing with cases involving racial classifications. It requires that racial classifications established by the state should be "narrowly tailored to further compelling state interests."[59]

Obasogie argues the FDA should adopt this model when devising regulations for drugs that are to be approved for use only in certain racial or ethnic subgroups. This means the FDA will need to go beyond its traditional standards of safety and efficacy and examine the social effect of such categorizations, probably by instituting an advisory committee for this express purpose. Since the use of racial categorizations has such a horrific history, especially in a biological context, they must only be utilized when narrowly tailored to achieve maximum health benefits. This means racial categories should only be used for drugs when more specific genetic markers are not available and not simply as a convenient proxy. Other types of population group categories might have a stronger overlap with specific genetic markers and may function as better proxies for situations when more detailed genotyping in the clinical setting is unfeasible.[60]

Jonathan Kahn of Hamline University School of Law argues for this "tight fit" model in clinical and biomedical research so as to avoid easy conflation of genetic population groups with socially defined population groups. Drugs run the risk of becoming both over- and underinclusive unless there is this "tight fit." This means medical professionals may overprescribe the drug to some members of a drug's approved population group even though other therapies may be more effective, and those who are not within the drug's approved population group may not be prescribed the drug even though they may have a genotype that indicates they would benefit from the drug.[61]

Obasogie and his colleague David Winikoff come to the conclusion that "race-specific indications should be rejected unless clinical trials demonstrate convincingly that the drugs are both better than existing treatments for a specified group and no better than existing treatments for non-specified groups."[62] Some drugs that do not meet these strict standards for single-race approval could still have information on race-related efficacy on the label.[63] A regulatory regime that follows this model would allow for a much more rationalized approval process for drugs aimed at specific genetic population groups that may or may not overlap with conventional categories of race and ethnicity.

Conclusion

Genetics are a breakthrough tool in our scientific understanding of human biology but it can easily lead to a naïve, restrictive view of health care that exacerbates disparities if not placed in its proper context. The most important principles to bear in mind as the biomedical community goes forward with genomics and personalized medicine research are:

- The scientific inadequacy and social perniciousness of biological definitions of race and ethnicity
- The importance of a geographically and genetically diverse research pool so the developing body of genetic knowledge applies to as broad a swath of humanity as possible
- The importance of placing genetic factors in context with social, environmental, and economic factors for the purpose of resolving health disparities between populations
- The need to reach out to various racial and ethnic communities so research and health care protocols can be designed with their cooperation in order to achieve maximum trust, compliance, and effectiveness while protecting the rights of research subjects and patients

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