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The justifiability of racial classification and generalizations in contemporary clinical and research practice

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This paper argues that racial classification and generalization may sometimes be justified in clinical treatment and research, in part to ensure better outcomes for the individual patients subject to such classification and generalization; in part to enable medicine to eliminate the need for racial categories. But race must be used carefully and sparingly because of the risk to the individual patient of overgeneralization, and the risk to society of reinforcing a false understanding of race as a biological category. Even if the use of racial categories in biomedical research subverts rather than reinforces those categories, that research may well lead to the recognition of non-racial, genetically based groups, which will be susceptible to harmful, if less invidious, stereotyping.

Keywords: race; classification; generalization; stereotyping; probability; treatment; research.

1. Introduction

Is it ever permitted, or even required, for a physician to take account of a patient's observed or self-described race in making testing or treatment decisions? Is it ever appropriate, or even required, for a clinical researcher to recruit or exclude subjects of an observed or self-described race? My answers are as follows: at present and in the near future, it will sometimes be permissible or even mandatory for a physician to take race into account, although there is good reason to hope that it will no longer be useful or permissible in the future. My answer to the second question is that researchers must in some cases select and exclude subjects on the basis of race to help bring about that future. In medical practice as in society at large, to get beyond race it is sometimes necessary to take race into account. At the same time, it is important to bear in mind that research into genetic markers may also reinforce racial classification, if, as seems likely, correlations are found between race and alleles associated with disease susceptibility and drug side effects. And even if the findings of that research do more to subvert than reinforce racial categories, they may foster the recognition of genetically based 'groups', groups that will almost certainly be subject to potentially harmful, if less invidious, stereotyping.

I will proceed as follows: first, I will briefly consider some of the different meanings of 'race' and their interplay in medical and research settings. I will then describe the ways in which taking

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account of race, understood in one or another of these ways, may be beneficial for the individual patient, for underserved minorities, and for the growth of medical knowledge. I will then discuss how some of these uses of race can be harmful or wrongful to the individual patient, the race(s) with which he is associated, and the larger society. Finally, I will discuss two reasons for continued anxiety about the growing field of pharmacogenomics—that it will promote rather than discourage the use of racial classification in clinical practice, and that even if it reduces the reliance on race, it may lead to other types of stereotyping and overgeneralization, less invidious but potentially as harmful in individual cases.

In clinical practice, the harms include the familiar ones of misdiagnosis, inattentive or perfunctory care and under- and overtreatment. The wrongs include disrespectful assumptions about risky behaviour and poor compliance, and more benign but still problematic assumptions about the patient's background and experience. In clinical research, the harm or wrong is not to the individual subject, but to any minority race with which he is associated—the reinforcement of the view that race is a biological category and a medically significant characteristic. But refusing to take race into account in clinical practice and research can also be harmful. In the present state of medical knowledge and health care delivery, some racial generalizations may improve the odds of successful outcomes or at least save the patient significant time and money. Refusing to recruit subjects by race or failing to promote minority-targeted research may reduce the odds of effective treatments for less healthy and underserved groups, neglect possible sources of health-outcome disparities, and delay the achievement of a level of genetic knowledge that may finally permit medicine to get beyond race.

In assessing the harms of using racial generalizations in medical diagnosis and research, I will argue that too much emphasis has been placed on the 're-biologization' of race. Even if it is appropriate for the Food and Drug Administration (FDA) to approve certain drugs only for use in certain races, race-specific drugs are likely to be rare, to be widely used off-label for patients of different races and to form only an insignificant part of the pharmacological armamentarium. Any adverse effects on the public perception of race will be countered more effectively by restrictions on their marketing than their development.

An equally great but less appreciated danger lies in the assumption that people of the same self-described or observed races will have had very similar 'social' backgrounds and experience. If it is easy for members of powerful and privileged groups to overlook or underestimate the impact of racism, it is also easy for them to assume that individuals of those races have uniform or very similar backgrounds and experiences, to overlook or underestimate the cultural and social diversity that is an increasing part of American life. A patient who classifies himself as African American may have few of the disease-associated alleles found disproportionately in members of his social group. But equally, he may possess few of the 'social factors' found disproportionately in that group—e.g. he may have been raised in a prosperous, stable and nurturing family in a friendly environment with little experience of hostility, exclusion or subtler forms of prejudice.

2. Race are a biological and social category

There is still a lively scientific and philosophical debate about biology and race, but its terms have changed significantly in the past few decades. Few scholars defend the once-prevailing view that races are basic biological kinds, subspecies of homo sapiens. The contemporary debate largely concerns the question of how to understand the role played by differences in ancestry, geographic origins

and associated genetic differences in the social classification schemes of race and ethnicity.[1] Few scholars deny that socially classified races (of course, there is no one, uniform social classification scheme) differ statistically in some genetic features as a result of ancestry; but few believe that those differences are large enough to provide biological criteria for racial classification.[2] Nevertheless, those differences may have some predictive or diagnostic value. Certain symptoms, for example, are far more likely to be due to sickle-cell anaemia in a patient with African ancestry than in one without such ancestry. But even generalizations with some value for the patient can be harmful: the physician may place too much reliance on such generalizations. Moreover, there are reasons to believe that overreliance is likely. First, although race cannot be regarded as a biological category, humans may be disposed to racial essentialism.[3] Second, even if race has only slight predictive or diagnostic value, humans may rely on information-processing strategies that give it excessive weight.[4]

Let me try to state some features of an emerging consensus on racial groups and genetic variation that may present clinicians and researchers with the ethical challenges of race-based generalizations in the near future. First, the ancestors of all human beings came from Africa; second, health-relevant mutations have occurred since the main period of migration from Africa, in groups that stayed in Africa as well as those that migrated; third, there is more genetic variation within than between ancestry-based groups; fourth, there is more health-relevant genetic variation within populations that remained in Africa than within any other migratory population group; fifth, sociallydefined racial and ethnic groups, in the USA and elsewhere, correspond only roughly to ancestral groups; sixth; in the USA, an individual believed to have any African ancestry will be classified for some purposes as black/African American; seventh, there are significant differences in the incidence of some diseases and responsiveness to some drugs among self- or observer-classified racial groups; eighth and last, there are significant differences in many health-relevant social and environmental variables among self- or observer-classified racial groups.[5]

[1] CAULFIELD, T., FULLERTON, S., ALI-KAHN, S.E. ARBOUR, L., et al. (2009) "Race and Ancestry in Biomedical Research: Exploring the Challenges. *Genome Medicine* 1: 8; KOENING, B.A., SOO-JIN LEE, SANDRA, and RICHARDSON, S. (2008) "Introduction: Race and Genetics in a Genomic Age", in Koening, B.A., Soo-Jin Lee, Sandra, and Richardson, S. eds. *Revisiting Race in a Genomic Age* (New Brunswick, NJ: Rutgers University Press); COLLINS, F.S. (2004) "What We Do and Don't Know about 'Race', 'Ethnicity', Genetics and Health at the Dawn of the Genome Era". *Nature Genetics Supplement*, 36: S13-S15; FOSTER, M. & SHARP, R. (2004) (Opinion): Beyond Race; Towards a Whole-Genome Perspective on Human Populations and Genetic Variation. *Nature Reviews Genetics* 5: 790-796;.HARDIMON, M. (2003) The Ordinary Concept of Race. *Journal of Philosophy* 50: 437-455; GLASGOW, J. (2003) On The New Biology of Race. *Journal of Philosophy* 50: 456-474; ANDRAEASEN, A. (2000) Race: Biological Reality or Social Construct? *Philosophy of Science* 67 (Proceedings): S653-S666.

[2] Two important exceptions to the latter are RISCH, N., BURCHARD, E., ZIV, and TANG, H. (2007) "Categorization of Humans in Medical Research, Genes, Race, and Disease". *Genome Biology* 3: 12; and BURCHARD, E.G., ZIV, E. COYLE, N., GOMEZ, S.L. , TANG, H, KARTER, A.J., et al. (2003) "The Importance of Race and Ethnic Background in Biomedical Research and Clinical Practice ". *New England Journal of Medicine*, 348: 1170-1175. Although these authors defend the understanding of race as a biomedical category; their understanding of race is far more nuanced and qualified than that of earlier defenders of biological race.

[3] HOLDEN, C. (2008) "The Touchy Subject of 'Race"'. *Science* 322: 839; HIRSCHFELD, L. (1996) *Race in the Making: Culture, Cognition and the Child's Construction of Human Kinds* (Cambridge, MA: MIT Press).

[4] SMEDLEY, B., STITH, A., and NELSON, eds. (2003) "Assessing potential Sources of Racial and Ethnic Disparities in Care: The Clinical Encounter", Ch. 4 in *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care* (Washington, DC: The National Academies Press); KRIEGER, L.H. (1995) "The Content of Our Categories: A Cognitive Bias Approach to Discrimination and Equal Employment Opportunity". *Stanford Law Review*, 47: 1161-148, 1186-1216; HEWSTONE, M., BENN, W., and WILSON, H. (1987) "Bias in The Use of Base Rates: Racial Prejudice in Decision-Making". *European Journal of Social Psychology*, 18: 171-186.

[5] In addition to the articles cited in n. 1, see those cited in nn. 6, 8, 11, and 17.

3. The uses of race in biomedical research and practice

Taken together, these widely accepted claims suggest a number of circumstances in which clinicians and researchers will have reason to take race into account in the performance of their professional roles. Consider the clinician first. A self- or doctor-classified black patient 'presents' with a collection of symptoms consistent with several underlying conditions for which the treatment would be very different. Some of these conditions are more common in some socially defined racial groups than others. Tests for all the conditions are expensive, and the doctor wants to economize by testing for the most likely first. As Tishkoff and Kidd observe:

> [M]any different disorders have similar symptoms, and the process of differential diagnosis can use ethnicity to prioritize testing according to the most likely etiology. Whether genetic, infectious, or environmental, the causes of disorders vary among ethnic groups. Economics and common sense argue that one would attempt to confirm (or reject) the most likely cause before attempting to confirm a very remote etiology. Taking "ethnicity" (genetic ancestry and sociocultural characterization) into account can be good medical practice . . . .[6]

It thus seems clear that is some cases, the patient's race should play a role in determining which test the doctor orders first. It also seems clear that the doctor may give too much weight to race in setting the order. Thus, she may be likely to test first for a condition with a much higher incidence in blacks than whites, even if it is a very rare condition, and the baseline odds that a black patient has this condition are less than the odds that he has one or more of the others. This error might not reflect racism or even racial overgeneralization, but the widely documented tendency to ignore base rates.[7]

Or consider a patient with a known diagnosis and a doctor with a choice of FDA-approved drugs equally effective in the general population. If the patient is black, self-classified or doctor classified, and several recent studies have found the drug to be more effective in blacks or to have fewer side effects, should the doctor take the patient's race into account in deciding which drug to try first? Of course, she may not be in 'equipoise' because she may not regard the drugs as equally effective, or the patient may have strong preferences among the possible side effects of different drugs. But suppose not. It seems clear that there will be some such cases in which it is reasonable for the doctor to start with drugs that have reported racial differences in effectiveness. And it also seems clear that the doctor will often give the patient's race too much weight, relying on a 'representative heuristic'—basing a decision on mere category membership rather than statistical likelihood—in prescribing a 'black drug' for a black patient.

While recognizing the need to take ethnicity into account, Tishkoff and Kidd warn that 'one must be wary of racial profiling and ignorance of the continuous nature of genetic variation and high levels of admixture in modern populations, which can result in misclassification and misdiagnosis'. But is in unclear how effectively even the most conscientious practitioner can bring that caution to bear in avoiding misclassification and misdiagnosis. Thus, consider the suggestions recently made by Feldman and Lewontin for an appropriately focused preliminary inquiry into a patient's genotype:

[6] TISHKOFF, S.A., and KIDD, K.F. (2004) "Implications of Biogeography of Human Populations for 'Race' and Medicine". *Nature Genetics Supplement* 36: S21-S27, 526.

[7] HEWSTONE, et al. (1987) op cit, n. 4.

> Do you have any African ancestors? If so, do you know from what part of Africa they came? Do you have any European ancestry? If so, from what part of Europe do they come? Were there any Ashkenazi Jews among your ancestors? And so on.[8]

Feldman and Lewontin recognize that 'detailed information about local geographical origins will often be unavailable', but they insist that 'categorical racial assignments are not a substitute for some kind of more informative history'.[9] This is undoubtedly true, but not very helpful. A physician who begins the prescribed genealogical inquiry may not get a 'yes' to any question but the first. What should she do with the knowledge that her patient has some African ancestry? If she uses that admittedly very sketchy ancestral information to decide which diagnostic test to begin with, or which drug to try out first, has she made a 'categorical racial assignment' or simply done the best she can with the available information?

Now turn to the researcher. Consider a study designed to look for genetic variations that affect susceptibility to a certain disease or drug side effect. Significant differences in susceptibility have been found between self-identified blacks and other races. Our researcher wants to get beyond race, to identify the genetic and/or socio-economic differences that may be responsible for this difference. She wants to enroll subjects from as many ancestral backgrounds as possible, particularly African. She is well aware that any contributing genetic variations are likely be found in some African populations but not others, and that different alleles may affect susceptibility in African and, say, northern European populations. She is also well aware that genetic differences may account for only some, or perhaps none, of the differences by race; that even if various socio-economic variables were "controlled for" in the recent studies, not all were, and that the health-relevant effects of American racial attitudes and practices may be hard to capture in discrete, quantifiable variables. So whom, and how, should our researcher recruit?

If she has an unlimited budget, she could travel around African and other continents, looking for as many geographically isolated (sub-)populations as she can and trying to find an allele or alleles in each of those groups associated with the susceptibility in question. If she does, she can then test for the various alleles she has identified on her global trek, to see how they interact with various socio-environmental factors, without relying on the self- or other-classified race of the subject. But this strategy may not be feasible or adequate, for several reasons. First, she may not have the money. Second, the condition of interest may only be found in the racial/ethnic/ancestral stew of the USA or other northern countries. Third, even if she has the money, and the condition can be found in isolated populations, she may not find any associations, or only very weak ones, because differences in susceptibility may arise from the interaction between genetic differences and social and environmental conditions that rarely obtain in the areas occupied by these isolated populations. And finally, even if she does identify alleles that she can test for in the general American population without asking about race, she may still want to know about race.[10] That is because, as suggested above, the contribution of genetic variations may be mediated by racial discrimination and other 'factors' that are not easily captured as socio-environmental variables. The use of race for this purpose is not fraught with the same dangers of 're-biologizing' race as its use for other purposes.

[8] FELDMAN, M. and LEWONTIN, R. (2008) "Race, Ancestry, and Medicine", in Koening, B.A., Soo-Jin Lee, Sandra, and Richardson, eds. *Revisiting Race in a Genomic Age* (New Brunswick, NJ: Rutgers University Press).

[9] FELDMAN and LEWONTIN, op. cit. 98.

[10] See the discussion of the "colorblind" DNA Polymorphism Recovery Resource in SOO-LIN LEE, S. "Racial Realism and the Discourse of Responsibility for Health Disparities in a Genomic Age", in Koening, B.A., Soo-Jin Lee, Sandra, and Richardson, eds. *Revisiting Race in a Genomic Age* (New Brunswick, NJ: Rutgers University Press).

The researcher could recruit by ancestry, but in the case of African Americans of more than a couple of generations, any ancestry beyond 'African' would almost always be unknown. At the same time, the use of 'ancestry' rather than 'race' would signal the researcher's interests, and would permit more targeted recruitment for other groups. But 'ancestry' may still be seen merely as a euphemism for race and ethnicity, and to the extent it was not, it might give rise to confusion and misunderstanding: does a descendant of Transvaal Boers have African ancestry? Does a London resident whose great-grandparents immigrated to England from Trinidad have European ancestry? Does the scion of an old British banking family that has lived in Hong Kong for many generations have Asian ancestry? If the answer to questions like these are consistently 'no', then it looks like the use of 'ancestry' relies, at least covertly, on race.

Information about ancestry would also not be enough for research that sought to examine social and environmental effects on disease. Some diseases, such as type II diabetes, that are very rare in African communities with rural lifestyles and traditional diets, have a disproportionately high incidence in individuals of African ancestry in mainstream U.S. communities. Obviously, environment plays a role in these striking differences. Almost as obviously, however, changes in environment may interact with genetic differences. Not only would it be helpful in studying such interactions to know how long the subjects' ancestors had been in the USA, it might be useful to know if, and how long, they identified themselves as African American.

More broadly, Sankar and Cho provide a nice summary of the ways that race may enter into the design of genetic research:

> [P]harmacogenetic studies may be inventorying the genotypes occurring in human populations and may ideally sample from a diverse set of populations to attempt to represent a broad range of genetic differences. Association studies seek genetic differences between those with and without a particular phenotype. The more genetically similar they are, the easier it is to find the specific genetic differences that account for differences in phenotype. Race is used as a proxy for genetic relatedness to control for potential confounding that occurs if the study populations differ genetically in ways not related to the phenotype in question. In contrast, epidemiological studies seeking to determine risk factors for disease may want to use race to control for population stratification, but also as a proxy for environmental exposure, including social interactions (e.g. people of certain races may be more or less likely to be referred for treatment). . . . In all but the final example, the research is using race as a way of grouping subjects by similarity or difference of genetic sequence, which reflects population history.[11]

The justification for using race as a proxy variable will depend on a variety of considerations, including how good or indispensable a proxy it is, and how its use as a proxy may affect those classified as belonging to one race or another. It does not seem problematic to use race as a vehicle for exploring the range of human genetic variation. Race is used only as a conduit; once the variations are found, or once they become directly accessible, it is no longer needed. Perhaps certain racial descriptions would be more effective than others in yielding the maximum diversity, but this seems a strictly empirical issue. A by-product of such research, however, may be the association of particular alleles with particular racial descriptions, and then with race simpliciter, after those findings are

[11] SANKAR, PAMELA and CHO, MILDRED K. (2002) "Enhanced: Towards a New Vocabulary of Human Genetic Variation" *Science*, 298: 1337-1338.

disseminated. But such uses can be discouraged by treating the initial racial categories as strictly pragmatic and heuristic, insufficiently grounded to support such association claims. Similarly, it does not seem problematic to use race to avoid confounding between affected and unaffected groups in association studies. Many other variables might serve as well, or better, but there is no theoretical limit to the number of variables that could be used. In both cases, the poorer race is as proxy for genetic similarity and difference, the worse it will serve the researcher's purpose. This may give the researcher an incentive to use more refined recruitment categories, e.g. to all, or some subset, of the 64 combinations yielded by the mark-all-that-apply instructions of the 2000 Census rather than the six of seven underlying categories, even if considerations of statistical power may favour the latter.

The use of race as a proxy for 'environmental exposures' is more problematic. While this use of race treats it as a social category, it may make unwarranted assumptions about the experiences of people in that category.[12] Clearly, it would be indefensible to use race as a proxy for low income or education, especially since it would be easy to assess the latter directly. But just because the discrimination faced by patients of minority races may be subtle or difficult to detect, it may be more defensible to use race as a control variable for differences in quality of treatment. Because there is still much uncertainty about the treatment differences that contribute to health disparities among socially defined racial groups,[13] enquiries about specific treatment differences, e.g. referrals to specialists, may be a less adequate control that race, at least at present. And while the psychological stress of perceived racism could be assessed by self-report, there may be reason to doubt that self-report is more reliable an indicator here than in other areas of protracted exposure to external stressors. On the other hand, it may be that the level of stress experienced by individuals of the same social groups varies enormously, and that self-report can help to reduce the variation.

If it can be psychologically burdensome to attribute similar backgrounds or environments to people of the same socially defined race, it is far more problematic to attribute similar behaviours to them, especially risky health behaviour. As I have argued elsewhere, it denies or disrespects the autonomy of the individual to infer his morally significant behaviour from the average behaviour of a reference group.[14] The offense or insult to autonomy will, of course, vary with the nature of the behaviour: the more dangerous, immoral or illegal the behaviour, the more objectionable a race-based inference. The inference that a poor young urban African American uses crack is far more troublesome that the inference that a poor young rural African American eats a high-fat diet (a matter of 'exposure' as much as behaviour), although the latter inference may be as unwarranted and dispensable as the former. The offence or insult will also vary with the nature of the group. It is more problematic to make an inference based solely on the baseline frequency of the behaviour in a random collection of people (e.g. in the much-discussed gatecrasher hypothetical, the rodeo management claims that it is warranted in inferring from the very small proportion of paying spectators that that any given spectator is a gatecrasher, in the absence of other evidence), than to make an inference based on causal assumptions about the psychology or behaviour of a stigmatized group. The worst possible outcome, in terms of medical accuracy as well as social justice, would be the

[12] WASSERMAN, D. (1997) "Diversity and Stereotyping", *Report from the Institute for Philosophy and Public Policy* Winter/Spring, 1997.

[13] SMEDLEY, et al. (2003) op. cit., n. 4.

[14] WASSERMAN, D. (1991) "The Morality of Statistical Proof and the Risk of Mistaken Liability". *Cardozo Law Review*, 13: 935-976.

over-attribution of health disparities to differences in behaviour, and the over-attribution of such behavioural differences to genetic differences.

4. Racial generalizations and individual patients

What harm is done by the kind of threshold racial generalizations likely to be made in the clinical practice of the next generation, where race serves as a proxy for an increasing number of differences in disease and drug susceptibility whose genetic causes have yet to be determined? It may be instructive, as my colleague Robert Wachbroit suggests, to compare the physician's use of family history. No one (or almost no one) objects to inquiries about the health and disease histories of one's parents, siblings and other close relatives. Those histories have, or are thought to have, considerable predictive value, and are the basis for many decisions about whether, how, or how often to test the patients for various conditions, and about whether to prescribe certain drugs and other treatments presymptomatically. These histories are partial proxies for genetic similarity (partial because diseases may be caused or exacerbated by 'risky behaviours' that may be 'transmitted' by nurture more than nature, and may also be caused or exacerbated by a shared environment, e.g. by exposure to pathogens or by patterns of family interaction). But even if a doctor places excessive reliance on these proxies, and thereby harm his patient in large or small ways, he does not appear to slight or disrespect him—his inferences largely concern the biological transmission of disease-associated genes.

No responsible doctor would rely on race, however assessed, to the same extent. But as discussed earlier, the patient's self- or doctor-classified race may place a role in some testing and treatment decisions. Are these uses of race more objectionable than similar uses of family history? Are errors made by overreliance more objectionable, wronging the patient in a way that overreliance on family history does not?

Clearly, in individual cases, an overreliance on family history can be almost as oppressive and dangerous as an overreliance on race or ethnicity. The assumption that 'the apple never falls far from the tree' can be demeaning and harmful when it concerns a disposition to risky health behaviour or bad eating habits, especially when accompanied by scepticism about the patient's self-reported behaviour or diet. Such an assumption may be especially demeaning to an individual who has made a concerted effort to avoid the excesses of his kin or associates. It would be less demeaning, but potentially as harmful, to assume that an individual will display the same biomedical susceptibilities as his kin. There is no disrespect to his autonomy but a considerable threat to his health in assuming that he will have the same genetic susceptibilities to disease as his parents or siblings, or even the same environmental exposures.

Both the insult and the potential injury may be magnified when the doctor relies on race or ethnicity, in contrast to family history. Few assumptions more demeaning than the assumption that an individual from a stigmatized group will, whatever the details of his personal history, behave in stereotypical ways, especially when the expected behaviour is foolish or destructive. And there are few assumptions more harmful from a medical perspective than the expectation than an individual from a stigmatized group will have the typical genetic susceptibilities and environmental stresses of the members of that group, given the variation in ancestry and social circumstances within the group.

The recognition that certain racial generalizations can be harmful in the context of medical treatment still leaves two difficult questions: first, does the physician make such a harmful generalization if she decides to prescribe a particular drug or test 'indicated' for patients of a particular race?

second, how should the harm of such a generalization be balanced against the benefits to the patient that may accrue from its use?

To start with the first: the research that led the FDA to approve the use of Bildil for black patients did not reveal anything about the causal mechanisms underlying the racial correlations. Future research is likely to uncover similar race-specific efficacy with no more insight into the underlying mechanisms.[15] The FDA, the drug companies, and the prescribing physicians may remain ignorant or agnostic about the reason the drug works better for those races; they need not attribute that effect to any particular factors, whether genetic, biological, environmental, or sociocultural. This seems to make the prescription of the drug innocent of any offensive assumption, at least if the membership of the patient in the racial group is not in question.

At the same time, research that aims to eliminate race as a medical category by identifying the underlying conditions it is a proxy for—an allele, an environmental insult, or a certain kind of stigmatization—may invite the use of such assumptions about causal mechanisms as testable hypotheses. Thus, the reason why the drug works better for blacks as a group may be that they have a higher frequency of a particular allele, more frequent exposure to an environmental toxin, less healthy diets or higher incidence of unhealthy behaviour. Testing such hypotheses does not seem offensive, even if it may be awkward, when prompted by significant statistical associations and motivated by a desire to dispense with race as a proxy variable. If the research is successful at identifying the source or sources of the association, it should reduce the use of racial generalization by yielding a means of ascertaining whether the patient has the specific allele, exposure or disease variant.

But the basis for prescribing a race-specific drug or test may not always be so innocent. It may be widely believed in the medical community that a particular cause or mechanism underlies the correlation, and physicians may assume that all their patients of the race in question have that underlying condition. If the source of the different reaction to the drug is a genetic factor like a predisposition to obesity or high blood pressure; an environmental condition associated with poverty, like lead exposure or a sociocultural factor like unhealthy diet or risky behaviour, the use of that assumption to prescribe the drug or test may be problematic in its reliance on an unflattering medical stereotype. Moreover, once the causal condition is established, the process of exempting individual patients may be awkward or painful for them. A black patient may be asked to take a genetic test or give a social history not requested of white patients. He may see it as being asked to prove that he does not fit a stereotype, an exercise that may be painful because of its association with efforts to exclude himself from more invidious stereotypes. And if the test or history takes time that the physician cannot spare, or imposes costs that the patient cannot pay, it may be that the physician ends up relying on the generalization. Indeed, such reliance might be best for the patient if the costs of 'exclusion' are significant, and the harm from a mistaken assumption minor. But this recourse to racial generalization would still be troubling.

5. Racial generalizations, racial groups, and the public perception of race

One reason that even relatively benign racial generalizations in medical practice may be troubling is that they will sometimes reinforce the notion of race as a biological category. Of course, the use of

[15] TUTTON, R., SMART, A., MARTINE, P.A., ASCHCROFT, R. and ELLISON, T.H. (2008) "Genotyping the Future: Scientists' Expectations about Race/Ethnicity after Bildil" *Journal of Law, Medicine, and Ethics*, 36: 464.

the generalization does not require such a belief—one can regard races as fluid social groups and still believe that membership in them is correlated closely enough with some biological characteristics to guide certain preliminary steps in diagnosis or prescription. But research suggests that we may be genetically predisposed to racial essentialism—to seeing certain visible features as reliable indicators of essential or important 'internal' characteristics.[16] For many doctors, unschooled in the vagaries of racial classification, the repeated use of race-based generalizations, based on nothing more than useful but ungrounded associations, may reinforce a racial essentialism they have never questioned. And the widespread use of such generalizations in the medical community may thereby contribute to the 'rebiologization' of race.[17]

The danger, then, is not merely in the use of race as an interim category, to be discarded once we identify a sufficiently large number of medically relevant alleles. As Parker, et al. observe in a discussion of 'Tailored Medicine', the identification of such alleles may exacerbate as well as alleviate racial stereotyping and generalization.[18] The balance between the two will depend on what is actually discovered, and how the discoveries are used.

Researchers will undoubtedly find significant correlations between socially defined race and medically relevant alleles, although many or most of those correlations are likely to be fairly weak. In theory, such findings may suggest that the biological basis of racial classification is even more tenuous or complicated than previously recognized. But in practice, they may reinforce the over-reliance on race as a diagnostic category and its continued treatment as a biological category by the general public. These dangers are especially great because the associations found between race and disease susceptibility or drug responsiveness will be doubly probabilistic first, the link between membership in a racial group and possession of the allele; second, the link between possession of that allele and the occurrence of particular medical effects. Even conscientious physicians may be disposed to assume that patients of a given race possess both the allele and the susceptibility or responsiveness. How strong and harmful an assumption will depend on how quick, and cheap it is to test for the allele, and to assess its penetrance or expression in the individual patient. Regulations (e.g. requiring genetic testing as a prerequisite to prescribing genetically tailored drugs) and practice guidelines may help to reduce the risks of clinical overreliance. It will be considerably harder to protect against the public misunderstanding of associations between race and health.[19] Restrictions on marketing may well suppress the most irresponsible and unsupported claims, but they cannot prevent the public exaggeration or oversimplification of technically accurate claims. And they can do even less to reduce the indirect support that the medical reliance on racial classification will give to the recalcitrant belief that race is a biological category.

Another danger in the association of socially defined race and medically relevant alleles lies in what a colleague calls (only somewhat facetiously) the 'rebiologization of racial disparities in

[16] HIRSCHFELD, op. cit., n. 3.

[17] KOENING, B. A., SOO-JIN LEE, SANDRA, and RICHARDSON, S. (2008), op. cit., n. 1; KAHN, J. (2006) "Genes, Race, and Populations: Avoiding a Collision of Categories". *American Journal of Public Health*, 96: 1965-1970; JORDE, L. B. and WOODING, S. P. (2004) "Genetic Variation, Classification, and "'Race"' *Nature Genetics Supplement*, 36: S28-S33; ROTIMI, C (2004) "Are Genetic and Nonmedical Uses of Genomic Markers Conflating Genetics and 'Race'? *Nature Genetics Supplement*, 36: S43-S47.

[18] SMART, A, MARTIN, H., & PARKER., M. (2004) Tailored Medicine: Whom Will It fit? The Ethics of Patient and Disease Stratification. *Bioethics*, 18, 322-342.

[19] But cf. STEVENS, J. (2008) "The Feasibility of Government Oversight of NIH Funded Population Genetics Research", in Koening, B.A., Soo-Jin Lee, Sandra, and Richardson, S. eds. *Revisiting Race in a Genomic Age* (New Brunswick, NJ: Rutgers University Press).

health'. Those disparities remain a striking feature of the American health profile. According to a recent report from the Agency for Healthcare Research and Quality (AHRQ) 'Among nonelderly adults . . . 17 percent of Hispanic and 16 percent of black Americans report than are in only fair or poor health, compared with 10 percent of white Americans'. The report suggests that much of the disparity, which persists even when income and insurance access are taken into account, can be attributed to striking differences in health care, such as access to primary care, screening for breast cancer and the provision of such treatments as angioplasty, asthma medications and antiretroviral drugs.[20]

The view that much of the disparity in health among racial groups is due to disparities in health care would not be challenged by findings of statistical differences among racial groups. Indeed, the failure to identify or take account of genetically based differences in disease susceptibility or drug responsiveness itself can be seen as a form of neglect or discrimination. Much like the neglect of women's health, it may reflect the inordinate attention paid by the research and clinical communities to the health of white males.

And yet the public and policy makers may respond to findings of such genetically based differences by shifting responsibility for persistent health disparities from society to biology and the individual.[21] It is, of course, profoundly mistaken to assume that there is a fixed amount of responsibility to be assigned for health disparities, so that assigning some causal role to genetic differences reduces the importance of discriminatory biomedical practices. Yet, as the debate over human behavioural genetics suggests, calling attention to one source of differences is likely to draw attention from others—unlike responsibility, attention may be in limited supply.

Assessing such risks requires a balancing that is in one respect the reverse of the type typically engaged in by institutional review boards (IRBs). There, the risks or harms are all to the subject, in the expenses and discomforts of adherence to a research protocol and the risks of unpleasant or dangerous side effects. The benefits, on the other hand, are largely to the society, in clinically useful generalizable knowledge that may not avail the individual subject. Here, in contrast, the benefits of race-based generalizations, in the more efficient use of tests or drugs, accrue to the individual patient, while the harms of reinforced racial essentialism and responsibility shifting are incurred as much or more by his social group. But IRBs are not expected, trained or staffed to engage in this kind of balancing.

6. Non-racial genetic stereotyping

It is possible that most of the medical relevant alleles identified by genomic medicine will have too little association with sociallydefined racial groups to support racial stereotyping and generalization, particularly if they could be grouped into a small number of distinct genetic profiles that have only weak correlations with race. But the development and use of genetically based groups might raise significant problems of stereotyping and overgeneralization even if it reduced reliance on racial categories. The promise of a completely individualized medicine is illusory.[22] As Parker, et al. point out:

[20] AGENCY FOR HEALTHCARE RESEARCH and QUALITY, "Addressing Racial and Ethnic Disparities in Health Care (http://www.ahrq.gov/research/disparit.htm, accessed 2/11/2010).

[21] SOO-LIN LEE, S. (2008) op. cit. n. 10.

[22] FEERO, W. GREGORY, GUTTMACH, ALAN E., and COLLINS, FRANCIS S. (2008) "The Genome Gets Personal–Almost" *Journal of the American Medical Association*, 299: 1351-1352.

> While its proponents initially claimed that 'personalized medicine' would replace the 'one-size-fits-all' paradigm of drug development and usage, it now seems more likely that pharmacogenetics will tend to direct drugs toward genetically-defined *groups*; if you like, 'off-the-peg' medicine rather than individually 'bespoke' medicine.[23]

At best, pharmacogenetics can improve the group generalizations on the basis of which drug development and treatment decisions are made. It cannot hope to eliminate group-based generalizations altogether, but it can replace more stigmatizing and less accurate generalizations with more benign and clinically useful ones. On the other hand, the greater accuracy of genetic profiling, and its greater acceptability, compared to racial profiling, could easily lead to overreliance. Physicians reluctant to talk to their patients for personal or financial reasons will have a better excuse for doing less talking. They may find it easy to convince themselves that the information yielded by genetic testing makes their patients' own observations or experiences less important.

Moreover, although medical generalizations based on non-racial genetic groups may be less inaccurate and invidious, they will still lend themselves to exaggeration and caricature. Consider the careless use of such recent biopsychological categories as the 'Type A personality'. To be subject to popular stereotyping, of course, a genetic profile must have at least some rough correspondence to observable health and health-related characteristics. But I suspect we already have a large number of informal stereotypes, e.g. the otherwise healthy individual chronically afflicted with mild or minor indispositions, which are likely to acquire spurious credibility by their association with genetic 'types'. While physicians may resist such crude stereotyping, a generation of research on decision making under uncertainty suggests that professional overreliance on genetic profiling will only be more esoteric, not less significant.[24]

The extent to which genetically based grouping is benign and clinically useful will depend on many other factors besides their overlap with racial categories and their susceptibility to stereotyping and overgeneralization. Among other factors will be the correlations that are found between various alleles associated with disease susceptibility and drug responsiveness. Genetic grouping will be more benign to the extent that they are NOT generally predictive of health or treatability; to the extent that individuals with some susceptibilities lack others, so that the possession of any single allele cannot serve as a proxy for poor overall health prospects. Those genetic groups will be more clinically useful if they are more predictive, and if their interactions with other genetic variations (epigenetics) do not preclude reliable generalizations about particular health effects.

[23] SMART, A, MARTIN, H., & PARKER., M. (2004), op. cit., n.___.

[24] See cites, n. 4.