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## What Race and Ethnicity Measure in Pharmacologic Research

**Jamie Mihoko Doyle**

From the Population Studies Center, University of Pennsylvania, Philadelphia, Pennsylvania.

### Abstract

Advances in genomic technology have put the utility of collecting racial and ethnic data into question. Some researchers are optimistic about the potential of moving toward “personalized medicine” by using a person’s genome to administer medications. Genetics will not erase the importance of race and ethnicity because race and ethnicity do not measure genetic composition. Unlike genes, race and ethnicity are social constructs; 2 persons with identical genetic makeup may self-identify as being of different race or ethnic origin. Race and ethnic categories have been subject to change over time; a person’s self-identification may vary according to the context, wording, and format of the question asked. Despite the fluid nature of the concept, self-identified race and ethnicity can capture something that genes cannot, namely, aspects of culture, behavior, diet, environment, and features of social status that commonly used measures of socioeconomic status, such as income, education, and occupation, cannot measure.

### Keywords

Race; ethnicity; clinical trials; measurement; FDA; genetics; regulations; pharmacology

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Developing novel drugs to improve the quality of life and eliminate illnesses among all human populations remains a cornerstone of pharmaceutical research. Yet one growing concern involves possible dissimilarities in drug response by race and ethnicity. Scientific evidence confirms that genetic variation within racial groups far outstrips the differences between groups.<sup>1–4</sup> However, with advances in genomic technology, some researchers suggest that collecting information on race for clinical trials will become unnecessary.<sup>5,6</sup> According to this perspective, science will soon move toward “personalized medicine,” whereby clinicians can tailor the course of treatment for each patient according to the patient’s particular genetic makeup.<sup>7,8</sup> Given the fluidity in the meaning and measurement of race, why should scientists continue to collect data on race and ethnicity, even with these technological advances? Race and ethnicity are important proxies for a person’s culture, diet, and health behaviors that cannot be captured by a person’s genetic profile. On a more macro level, race and ethnicity measure the extent to which a person is exposed to the forces of social stratification, which, in turn, impinges on human biological processes and, in turn, could create gene-environment interactions. Hence, accurate collecting, reporting, and interpreting data from clinical trials is particularly important and has profound implications for future research, even with genetic biomarkers.

## WHAT DO RACE AND ETHNICITY MEASURE?

It is important to emphasize that race and ethnicity are distinct from socioeconomic status (ie, income, education, and occupation). Race, ethnicity, and class are not interchangeable, in spite of popular media portrayals of destitute minorities.<sup>9,10</sup> In fact, non-Hispanic whites are well represented among the impoverished. For instance, in 2004 in the United States, households headed by whites constituted nearly 45% of households that reported incomes below the federal poverty line.<sup>11</sup> Although race, ethnicity and social class are not interchangeable, the synergistic combination of minority status and social class significantly impedes improvements in health outcomes among racial and ethnic minorities in the United States.<sup>12</sup> More information is contained in cited references.<sup>13,14</sup>

### Endogenous Factors

Despite the arbitrary and fluid nature of racial and ethnic categories, they are critical signposts and confound relationships between drugs and drug response for 2 reasons. First, beginning from an endogenous perspective, race and ethnicity capture important dimensions of a person's culture, diet, and health behaviors.<sup>2,15-17</sup> Prior studies provide compelling evidence that the 3 aforementioned characteristics affect both drug response measurements and dosing ranges for safety.<sup>18-22</sup> For instance, drug pharmacokinetics may be variable because of race-specific or ethnic-specific diets, which affect drug absorption and metabolism.<sup>15,23</sup> Furthermore, the interpretation of questions asked about adverse events and disease progress after administering a drug to patients may also vary because of cultural differences in beliefs about medicine and medical practice.<sup>24,25</sup> These factors can exert a powerful influence on the generalizability of clinical studies.<sup>15,24</sup>

### Exogenous Factors

Second, exogenous factors known as neighborhood or environmental effects are also intimately tied to race and ethnicity. This area of research focuses on how a given stratification system affects health. Exogenous factors should not be confused with individual-level measures of social class, although they can be closely related in some situations. To simplify and illustrate the potential importance of exogenous factors in the present context, I will amalgamate these perspectives into 2 related areas: psychosomatic responses and neighborhood effects. Psychosomatic responses refer to physical processes initiated by the mind in reaction to mental or emotional stress. Some researchers refer to these catalysts broadly as stressors. This perspective emphasizes the role of allostasis and, specifically, allostatic load. Allostasis refers to "physiological mediators such as adrenalin from the adrenal medulla, glucocorticoids from the adrenal cortex, and cytokines from cells of the immune system [that] act upon the receptors in various tissues and organs to produce effects that are adaptive in the short run but can be damaging if the mediators are not shut off when no longer needed."<sup>26(p10)</sup>

Researchers hypothesize that racial and ethnic differences in many chronic diseases can be attributed to allostatic load, which is the physiologic costs of persistent allostasis<sup>27</sup> caused by persistent social inequality. The effects of allostatic load are linked to the progression of numerous diseases and biological processes from type 2 diabetes to the suppression of immune responses.<sup>26</sup> This framework has been particularly insightful for health disparities among African Americans because a growing body of literature documents that African Americans disproportionately experience race-related stressors, which, in turn, affects physical and mental health via allostatic load.<sup>28-31</sup> The lasting effects of racial stratification on physical health are also documented in other medical and sociologic literature.<sup>32-36</sup>

Alternatively, researchers focusing on neighborhood effects cite the potential importance of environmental influences and social context as fundamental causes of health disparities,<sup>12,37</sup>

<sup>38</sup> although direct evidence of the causal role of neighborhood context is still a matter of debate. <sup>39</sup> For example, several studies find that the concentration of poverty, substandard housing conditions, and deteriorating infrastructure in poor minority neighborhoods is associated with blacks having a higher prevalence of asthma as compared to other racial groups.<sup>40,41</sup> From an exogenous perspective, minority status is a proxy for external exposure to stressors and/or environmental toxins and allergens from neighborhood environments that can interact with genes, drug response, and health outcomes. Clearly, the information captured by asking the simple question, “What is your race?” entails greater complexity than commonly believed.

## CONCLUSION: RACE AND ETHNICITY IN LIGHT OF ADVANCES IN PHARMACOGENOMICS

Extraordinary advances in genomic research have provided greater depth to understanding disease pathology and drug metabolism. Groundbreaking studies of cancer exemplify the implementation of this technology into clinical practice. One example is *Trastuzumab*, which targets the overexpression of the human epidermal growth factor receptor (HER-2) gene in some forms of breast cancer.<sup>42</sup> Some scientists speculate that race and ethnicity will become obsolete in clinical practice as a result of these advancements in genomics. Because we can measure genes, why measure race and ethnicity?

Genetics will not erase the importance of race and ethnicity because race and ethnicity do not measure genetic composition; the 2 capture different phenomena. Unlike genes, racial and ethnic categories are social constructs, and 2 persons with identical genetic makeup may well self-identify as being of a different race or ethnic origin. Furthermore, race and ethnic categories have been subject to change over time, and a person’s self-identification may vary according to the context, wording, and format of the question asked. Yet, despite the fluid nature of the concept, self-identified race and ethnicity can capture something that genes cannot; namely, aspects of culture, behavior, diet, environment, and feature of social status that commonly used measures of socioeconomic status, such as income, education, and occupation, cannot measure. On the other hand, genetic biomarkers provide insight into disease pathology and drug response at the intra-cellular level. Yet neither is fully informative alone. If collected and interpreted correctly,<sup>\*</sup> both pharmacogenomics and race and ethnic indicators can synergistically improve measurements of drug efficacy and safety with the potential of attenuating health disparities by race and ethnicity.

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## REFERENCES

1. Bamshad M, Wooding S, Salisbury BA, Stephens JC. Deconstructing the relationship between genetics and race. *Nat Rev Genet* 2004;5:598–602. [PubMed: 15266342]

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<sup>\*</sup>Requirements on how to collect and interpret data on race and ethnicity are not currently outlined in the Code of Federal Regulations (CFR). For instance, 21CFR314.50 SS 5(V) states, “the effectiveness data shall be presented by gender, age, and racial subgroups and shall identify any modifications of dose or dose interval needed for specific subgroups”<sup>43</sup> but does not state which groups to include or how to collect such data. The Food and Drug Administration issued a guidance for industry, however.<sup>44</sup> Comments from the Clinical Data Interchange Standards Consortium Submission Data Standards are examples of how some researchers misunderstand what race and ethnicity measure in clinical trials research.<sup>45</sup> For instance, in their comments they state, “the selection of multiple [racial] categories will cause subjects who are not genetically alike to appear as if they are, and correlations that are indeed due to race will be missed (false negatives).”

2. Chaturvedi N. Ethnicity as an epidemiological determinant—crudely racist or crucially important? *Int J Epidemiol* 2001;30:925–927. [PubMed: 11689494]
3. Goodman AH. Why genes don't count (for racial differences in health). *Am J Public Health* 2001;90:1699–1702. [PubMed: 11076233]
4. Reiner AP, Ziv E, Lind DL, et al. Population structure, admixture, and aging-related phenotypes in African American adults: the cardiovascular health study. *Am J Hum Genet* 2005;76:463–477. [PubMed: 15660291]
5. Nature Genetics [editorial]. Genes, drugs, and race. *Nat Genet* 2001;29:265–269. [PubMed: 11685208]
6. Wilson JF, Weale ME, Smith AC, et al. Population genetic structure of variable drug response. *Nat Genet* 2001;29:265–269. [PubMed: 11685208]
7. Young D. Scientists focus on pharmacogenomics at FDA science forum. *American Journal of Health System-Pharmacy* 2005;62:1226–1228. [PubMed: 15947120]
8. Service RF. Going from genome to pill. *Science* 2005;308:1858–1860. [PubMed: 15976283]
9. Bullock HE, Wyche KF, Williams WR. Media images of the poor. *J Soc Issues* 2001;57:229–246.
10. Gilens M. Race and poverty in America—public misperceptions and the American news media. *Public Opin Q* 1996;60:515–541.
11. DeNavas-Walt C, Mills R, Procter B. Income, poverty, and health insurance coverage in the United States: 2003. U.S. Census Bureau Web site. Available at: <http://www.census.gov/prod/2004pubs/p60-226.pdf>.
12. Williams DR, Collins C. U.S. socioeconomic and racial differences in health: patterns and explanations. *Annu Rev Sociol* 1995;21:349–386.
13. Adler NE, Boyce WT, Chesney MA, Folkman S, Syme SL. Socioeconomic inequalities in health—no easy solution. *JAMA* 1993;24:3140–3145. [PubMed: 8505817]
14. Krieger N, Williams DR, Moss NE. Measuring social class in US public health research: concepts, methodologies, and guidelines. *Annu Rev Public Health* 1997;18:341–378. [PubMed: 9143723]
15. Bjornsson TD, Wagner AJ, Donahue SR, et al. A review and assessment of potential sources of ethnic differences in drug responsiveness. *J Clin Pharmacol* 2003;43:943–967. [PubMed: 12971027]
16. Frank R. The misuse of biology in demographic research on racial/ethnic differences: a reply to Van Den Oord and Rowe. *Demography* 2001;38:563–567. [PubMed: 11723952]
17. Hummer RA, Rogers RG, Eberstein IW. Sociodemographic differentials in adult mortality: a review of analytic approaches. *Popul Dev Rev* 1998;24:553–578.
18. Dominick KL, Bosworth HB, Hsieh JB, Moser BK. Racial differences in analgesic/anti-inflammatory medication use and perceptions of efficacy. *J Natl Med Assoc* 2004;96:928–932. [PubMed: 15253323]
19. Yang CS, Brady JF, Hong JY. Dietary-effects on cytochromes-P450, xenobiotic metabolism, and toxicity. *FASEB J* 1992;6:737–744. [PubMed: 1537464]
20. Miners JO, Mackenzie PI. Drug glucuronidation in humans. *Pharmacol Ther* 1991;51:347–369. [PubMed: 1792239]
21. Kaminsky LS, Fasco MJ. Small intestinal cytochromes-P450. *Crit Rev Toxicol* 1992;21:407–422. [PubMed: 1801846]
22. Armstrong TL, Swartzman LC. Asian versus western differences in satisfaction with western medical care: the mediational effects of illness attributions. *Psychol Health* 1999;14:403–416.
23. Evelyn B, Toigo T, Banks D, et al. Participation of racial/ethnic groups in clinical trials and race-related labeling: a review of new molecular entities approved 1995–1999. *J Natl Med Assoc* 2001;93(suppl 12):18S–24S. [PubMed: 11798060]
24. Kagawa-Singer M. Improving the validity and generalizability of studies with underserved U.S. populations expanding the research paradigm. *Ann Epidemiol* 2000;10(suppl 8):S92–S103. [PubMed: 11189098]
25. Giuliano AR, Mokuau N, Hughes C, et al. Participation of minorities in cancer research: the influence of structural, cultural, and linguistic factors. *Ann Epidemiol* 2000;10(suppl 8):S22–S34. [PubMed: 11189089]
26. McEwen BS. Interacting mediators of allostasis and allostatic load: towards an understanding of resilience in aging. *Metabolism* 2003;52(suppl 10):10–16. [PubMed: 14577057]

27. Taylor SE, Repetti RL, Seeman T. Health psychology: what is an unhealthy environment and how does it get under the skin? *Ann Rev Psychol* 1997;48:411–447. [PubMed: 9046565]
28. Whitfield KE, Weidner G, Clark R, Anderson NB. Socio-demographic diversity and behavioral medicine. *J Consult Clin Psychol* 2002;70:463–481. [PubMed: 12090363]
29. Steffen PR, McNeilly M, Anderson N, Sherwood A. Effects of perceived racism and anger inhibition on ambulatory blood pressure in African Americans. *Psychosom Med* 2003;65:746–750. [PubMed: 14508015]
30. Brosschot JF, Thayer JF. Anger inhibition, cardiovascular recovery, and vagal function: a model of the link between hostility and cardiovascular disease. *Ann Behav Med* 1998;20:326–332. [PubMed: 10234427]
31. Waldstein SR, Burns HO, Toth MJ, Poehlman ET. Cardiovascular reactivity and central adiposity in older African Americans. *Health Psychol* 1999;18:221–228. [PubMed: 10357503]
32. Geronimus AT, Bound J, Waidmann TA, Colen CG, Steffick D. Inequality in life expectancy, functional status, and active life expectancy across selected black and white populations in the United States. *Demography* 2001;38:227–251. [PubMed: 11392910]
33. Hayward MD, Heron M. Racial inequality in active life among adult Americans. *Demography* 1999;36:77–91. [PubMed: 10036594]
34. Coutinho R, David RJ, Collins JW. Relation of parental birth weights to infant birth weight among African Americans and whites in Illinois: a transgenerational study. *Am J Epidemiol* 1997;146:804–809. [PubMed: 9384200]
35. Schoendorf KC, Hogue CJR, Kleinman JC, Rowley D. Mortality among infants of black as compared with white college-educated parents. *N Engl J Med* 1992;326:1522–1526. [PubMed: 1579135]
36. Krieger N. Embodying inequality: a review of concepts, measures, and methods for studying health consequences of discrimination. *Int J Health Serv* 1999;29:295–352. [PubMed: 10379455]
37. Buka SL, Brennan RT, Rich-Edwards JW, Raudenbush SW, Earls F. Neighborhood support and the birth weight of urban infants. *Am J Epidemiol* 2003;157:1–8. [PubMed: 12505884]
38. Morenoff JD. Neighborhood mechanisms and the spatial dynamics of birth weight. *Am J Sociol* 2003;108:976–1017. [PubMed: 14560732]
39. Yen IH, Syme SL. The social environment and health: a discussion of the epidemiologic literature. *Annu Rev Public Health* 1999;20:287–308. [PubMed: 10352860]
40. Lwebuga-Mukasa JS, Oyana TJ, Wydro P. Risk factors for asthma prevalence and chronic respiratory illnesses among residents of different neighborhoods in Buffalo, New York. *J Epidemiol Community Health* 2004;58:951–957. [PubMed: 15483313]
41. Aligne CA, Auinger P, Byrd RS, Weitzman M. Risk factors for pediatric asthma: contributions of poverty, race, and urban residence. *Am J Resp Crit Care Med* 2000;162(pt 1):873–877. [PubMed: 10988098]
42. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *N Engl J Med* 2001;344:783–792. [PubMed: 11248153]
43. Code of Federal Regulations. Title 21, Vol. 5. U.S. Food and Drug Administration Web site. [Accessed September 16, 2005]. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.50&SearchTerm=racial>.
44. U.S. Department of Health and Human Services. Guidance for industry collection of race and ethnicity data in clinical trials; *Fed Regist*. 2003. p. 68
45. Clinical Data Interchange Standards Consortium, Submission Data Standards (CDISC SDS). Comments on draft guidance for industry: collection of race and ethnicity data in clinical trials. Division of Dockets Management. [Accessed September 16, 2005]. Available at: <http://www.fda.gov/ohrms/dockets/dockets/02d0018/02D-0018-emc00004-01.pdf>.