

Section 1: Introduction to Genetic Research on Racial and Ethnic Groups

I. The History of Race/Ethnicity in Medical Research

Pre-World War II: Throughout the 19th and early 20th centuries scientists widely understood race to represent objective biological divisions of humanity. (Ethnic groups were viewed either as racial groups in and of themselves or as racial sub-groups). Race was both essentialist and hierarchical with racial groups believed to display measurable physiological, behavioral, and intellectual differences. Seen in this manner, racial differences had obvious implications for health and many physician researchers of the era sought associations between racial groups and disease susceptibility, occupational injuries, and hygiene. When federal and state health departments began to collect health statistics in the early 1900s it went unquestioned that data should be divided by racial categories. The use of race in early medical research often drew heavily on social assumptions of racial superiority and fears of immigrant populations, and many prominent physicians used such research to provide scientific support for segregation and eugenics policies, both in the United States and abroad.

Byrd and Clayton 1992 (pp. 189-200) and Haller 1970 (pp. 154-167) provide an overview of 19th and early 20th century scientists' views and use of race.

Krieger and Fee 1996 (pp. 391-418) discuss the ways in which racial and ethnic categories were applied in the efforts to collect health data.

McBride 1991 (pp. 9-68) writes on how early 20th century physicians linked race and disease contagion in order to facilitate segregation.

Provine 1973 (pp. 790-796) and Sofair and Kaldjian 2000 (pp. 312-319) provide an overview of the effect of early 20th century views of race on the development of eugenics policies.

The Rise of Population Genetics: In the years following World War II, leading scientists from the fields of evolutionary biology, population genetics, and physical anthropology publicly disavowed the biological validity of race as previously understood. In its place they advanced the concept of the population as a more accurate representation of how genetic diversity was structured within the human population. However, the degree to which human populations might themselves constitute taxonomic races or how closely they overlapped with traditional racial categories remained contested. During the same period, the concept of ethnicity emerged as an increasingly popular alternative to race, especially among social scientists, because of its emphasis on cultural criteria. In medical research, however, race, as well as ethnicity, continued to be used largely as biological variables and the premise that racial and ethnic groups displayed meaningful biological differences in terms of disease susceptibility, hormone production, and drug response remained the subject of substantial research. Growing research in the 1960s and 1970s on hereditary genetic diseases, such as sickle cell disease and Tay-Sachs disease, occurring in specific racial and ethnic groups, further supported the medical importance of race and ethnicity.

Dobzhansky 1951 (pp. 264-266) and Cavalli-Sforza 1966 (pp. 362-379) provide representative scientific arguments for the replacement of race with population.

Reardon 2005 (pp. 17-73) and Marks 2000 (pp. 241-249) provide an overview of the emergence of population genetics and the new discipline's claims about race and human genetic diversity.

Montagu 1962 (pp. 919-928) presents an early call for the use of ethnicity instead of race in science.

Oppenheimer 2001 (pp. 1049-1055) examines current debates surrounding the use of ethnicity versus race in medical research.
 Damon 1969 (pp. 69-80) argues for a continued biological view of race and ethnicity in medical research.

II. Racial and Ethnic Groups and Human Genetic Variation

In-Group Variation is Greater than Between-Group Variation: In a 1972 paper, the geneticist Richard Lewontin reported that the majority of human genetic variation (~85%) occurred within a given population opposed to between populations. In line with these findings, Lewontin and others have argued that racial categories have little biological validity as 1) between group genetic variation represents little of the total genetic variation between any two individuals and 2) racial categories correspond poorly to underlying patterns of human genetic diversity. This position was bolstered in 1999 when the Human Genome Project published findings that 99.9% of all genetic material is shared among all individuals. However, recently some geneticists have argued against Lewontin's conclusions, claiming that his methodology misconstrued genetic differences that do exist along racial classifications.

Lewontin 1972 (pp. 381-398) presents findings on human genetic variation.
 Cooper 1984 (pp. 715-722) and Condit 2001 (pp. 85-108) argue that Lewontin's findings support the claim that racial categories have little biological validity.
 IHGSC 2001 (pp. 860-921) and Collins and Mansoura 2000 (pp. 221-225) introduce findings on shared genetic material from the Human Genome Project.
 Edwards 2003 (pp. 798-801) argues that Lewontin's conclusions about human genetic classification are incorrect and based on fallacious statistical reasoning.

Are Race and Ethnicity Suitable Proxies for Meaningful Genetic Differences?: Over the past decade an increasing number of scientists have challenged the position that race and ethnicity are genetically meaningless. While acknowledging that 99.9% of genetic material is shared between individuals, they argue that the remaining 0.1%, approximately 3 million base pairs, can, through statistical analysis, be shown to congregate in clusters that correlate significantly with racial categories. Other geneticists have responded that the statistical analysis used to produce such clusters is often biased by its selection criteria and that while genetic differences between geographically distinct population groups do exist, the overall structure of human genetic diversity is better characterized by a genetic continuum or cline, in which genetic variation changes incrementally over geographic distance.

Bamshad 2004 (pp. 598-609) and Fausto-Sterling 2004 (pp. 1-37) provide an overview of recent research on whether human genetic diversity is aligned with racial categories.
 Risch 2002 (pp. 1-12), Rosenberg 2002 (pp. 2381-2385), and Jorde and Wooding 2004 (pp. S28-S33) argue that human genetic diversity is organized in genetic clusters that approximate racial categories.
 Kaufman and Cooper 2001 (pp. 291-298), Kittles and Weiss 2003 (pp. 33-67), and Serre and Paabo 2004 (pp. 1679-1685) argue that human genetic diversity is best represented by clines.

III. Genetic Research and Health Disparities

Social Explanations for Health Disparities: Beginning with the civil rights movement significant attention has been given to discrepancies between the health of minorities and

the white population in the United States. In the 1985 the Department of Health and Human Services published the first comprehensive report on health disparities and under the Clinton administration the elimination health disparities became a major health care objective. Much of the public health research undertaken on the roots of health disparities has focused on social factors, either the socioeconomic status of minority communities or personal and structural biases within the health care system.

Mayberry 2000 (pp. 108-145) , Clayton and Byrd 2001 (pp. 35S-54S) and Smith 2005 (pp. 317-324) provide historical overviews of health disparities as a political issue and a focus of public health research.

Nickens 1986 (pp. 577-580) and McCord and Freeman 1990 (pp. 173-177) summarize early influential reports on health disparities.

Smedley 2003 (pp.) Williams and Jackson 2005 (pp. 325-334) , and Kawachi 2005 (pp. 343-352) review recent research on health disparities.

Genes and Health Disparities: Over the past decade there has emerged significant debate over the degree to which genetic differences between racial and ethnic groups might contribute to health disparities. In the 1990s epidemiological studies on a number of diseases concluded that racial/ethnic differences in health outcomes could not be explained solely by social factors, leading to the hypothesis that genetic differences that exist between racial and ethnic groups are likely to explain some percentage of health disparities. Since the completion of the Human Genome Project research has accelerated on identifying genes that disproportionately predispose particular racial and ethnic groups to specific diseases or decrease the effectiveness of drug treatments in such groups. However, some researchers have argued that available evidence suggests that social factors remain the primary cause of health disparities and that research seeking genetic explanations for health disparities is an inefficient means of addressing the problem.

Fine 2005 (pp. 2125-2128) summarizes the debate over whether genetic differences contribute to health disparities.

Burchard 2003 (pp. 1170-1175) , Collins 2003 (pp. 835-847) , and Mountain and Risch 2004 (pp. S48-S53) argue for a genetic role in health disparities.

Cooper 2003 (pp. 1166-1170) , Lee 2001 (pp. 33-75) , and Sankar 2004 (pp. 2985-2989) argue against a genetic role in health disparities.

Pharmacogenetics as a Solution to Health Disparities: The undertaking of the Human Genome Project produced much discussion regarding the prospect of “personalized medicine” or pharmacogenetics, whereby in order to produce optimal efficacy and safety, an individual’s drug therapy would be determined by their genotype. This vision of “personalized medicine” has yet to be realized. However, some researchers have argued that by identifying genes that disproportionately affect drug metabolism or toxicity in particular racial and ethnic groups, more effective drugs can be designed for specific use in those groups. In 2005, the FDA approved the first race-specific drug, BiDil, as a treatment for heart failure in African-Americans. Supporters of the decision have heralded it as “a step towards the promise of personalized medicine,” and have argued that it will assist in eliminating mortality differences between black and white individuals with heart failure. Opponents have countered that the decision was based on flawed research and represents more a marketing coup than a medical advancement.

Nebert and Menon 2001 (pp. 19-22) and Tate and Goldstein 2004 (pp. S34-S42) review the use of race and ethnicity in pharmacogenetic research.
 Wilson 2001 (pp. 265-269) examines the affect of population genetic structure on drug response.
 Taylor 2004 (pp. 2049-2057) provides study data used to support BiDil.
 Carlson 2005 (pp. 464-468) and Daar and Singer 2005 (pp. 241-246) argue in favor of BiDil and race/ethnicity-specific drugs.
 Kahn 2004 (pp. 1-46) and Lee 2005 (pp. 2133-2138) argue against the approval of BiDil.

IV. Case Study: African Americans and Prostate Cancer

That African American men in the United States have the highest incidence and mortality rates for prostate cancer in the world, and that these rates diverge significantly from those of white men in the United States, has been a central feature of prostate cancer epidemiology research from the 1960s onward. Through the early 1990s most such research focused on environmental or behavioral risk factors thought to be responsible for these differences, most prominently diet and sexual activity. Prostate cancer also received attention in the 1980s within early reports on health disparities, which attributed the racial differences in disease largely to the socioeconomic differences between African Americans and whites. In the 1990s these disparities began to draw the attention of genetic researchers. A 1996 study by researchers from the National Human Genome Research Institute and Johns Hopkins University examined 91 families at high risk for prostate cancer and found that one-third of these families, including the two African American families participating in the study, manifested a linkage to an area on chromosome 1q labeled HPC1. This finding was buttressed by a second, smaller confirmatory study that included six African American families. The second study substantiated the idea of a susceptibility gene at this locus and “hint[ed] that mutations in the HPC1 gene are more prevalent in African Americans than in Caucasian Americans.”

To explore this gene and others possibly involved in hereditary prostate cancer in African American men, Howard University received funding in 1997 from the NIH to initiate the African American Hereditary Prostate Cancer (AAHPC) Study Network. The study represented a collaboration of seven medical centers across the United States seeking to recruit at least 100 African American families at high risk for prostate cancer. It was advertised as not simply an effort to identify prostate cancer genes, but as an initiative designed and carried out by African American scientists to investigate a serious, but neglected, African American health problem. Despite the efforts of the AAPHPC study, however, a prostate cancer gene that explains the racial differences in the disease has yet to be identified. Many researchers have continued to maintain that genetic factors play a large role in the high incidence and mortality of the disease in African Americans, but that probably a number of weaker genes instead of one powerful gene are responsible. Some critics have suggested, however, that in focusing on African Americans as a single group researchers failed to account for the genetic heterogeneity of the group, and that future research must be designed to better reflect the genetic diversity present in African Americans.

Brawley 1998 (pp. 184-186) reviews past and current research on African Americans and prostate cancer.
 Henschke 1973 (pp. 763-768) , Schuman and Mandel 1980 (pp. 630-649) , and Nomura and Kolonel 1991 (pp. 200-227) provide examples of early research investigating the high rates of prostate cancer in African Americans.

Whittemore 1995 (pp. 732-740) , Smith 1996 (pp. 1371-1374) , and Cooney 1997 (pp. 955-959) present key genetic prostate cancer studies in African Americans.

Powell 2001 (pp. 120-123) and Ahaghotu 2004 (pp. 165-169) describe and present data from the AAPHC study.

Freedland and Isaacs 2005 (pp. 243-252) address the inability of recent studies to identify a prostate cancer gene in African Americans and outline new approaches to research on the group.