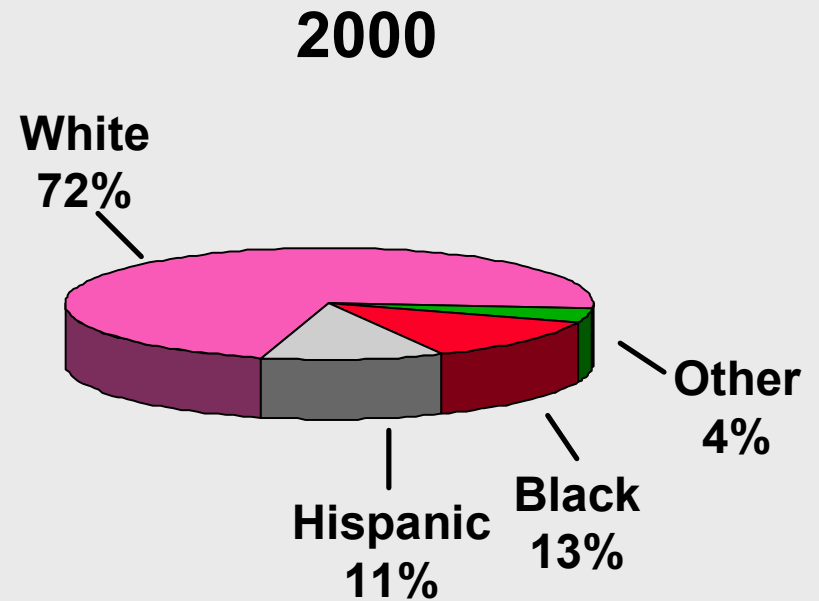
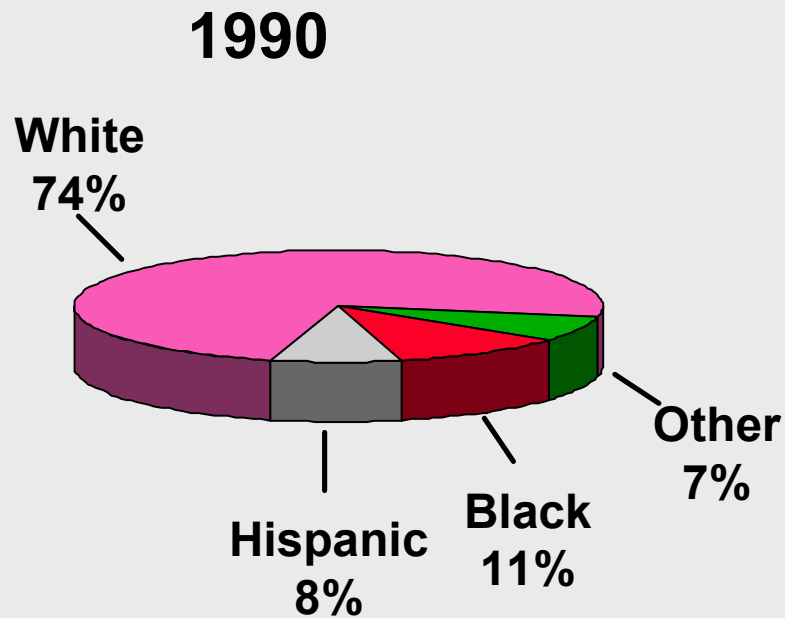




PHARMACOGENETICS OF RACIAL AND ETHNIC MINORITIES

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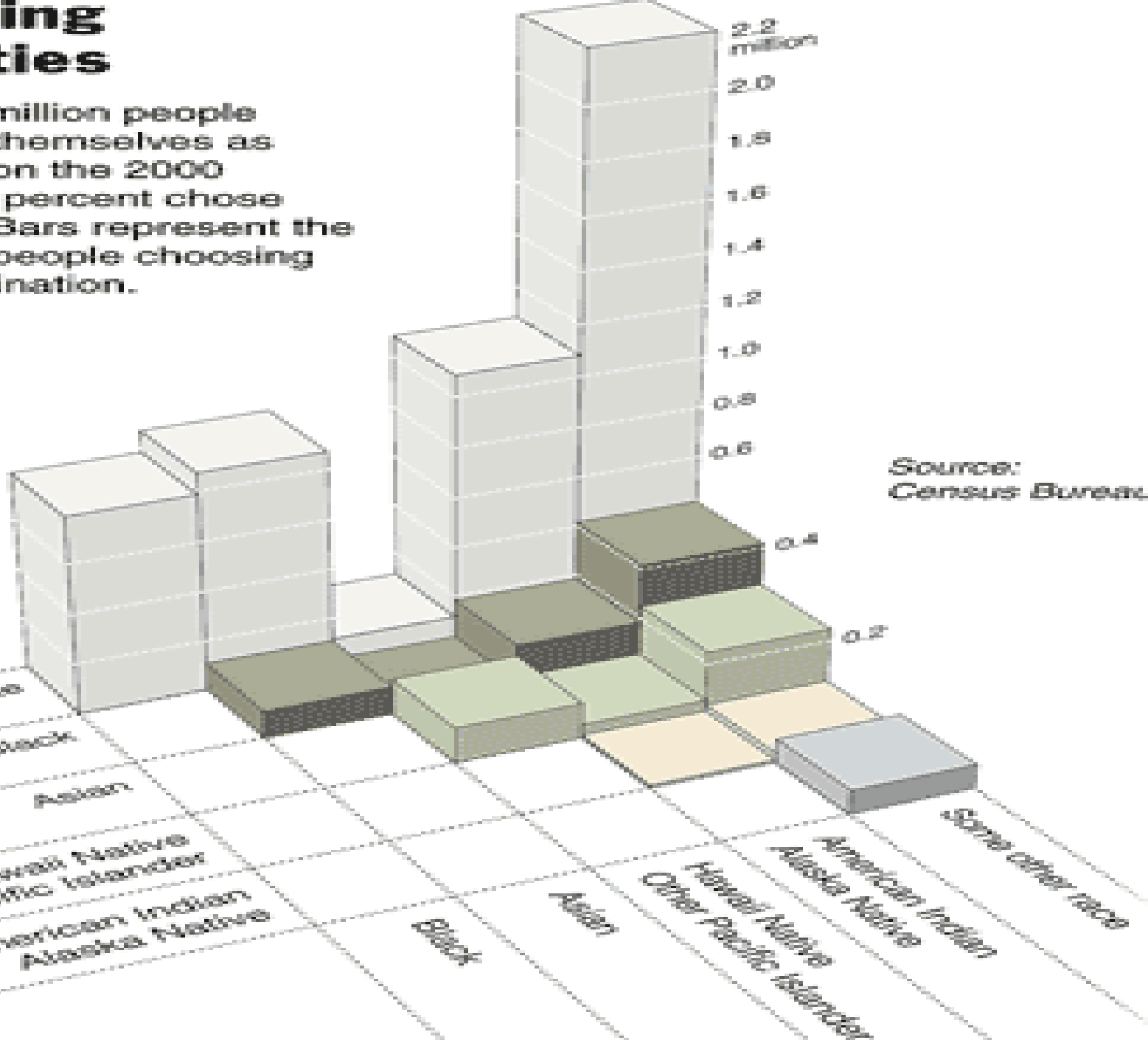
Racial and Ethnic Composition of the American Population



Source: U.S. Census figures and projections

Choosing Identities

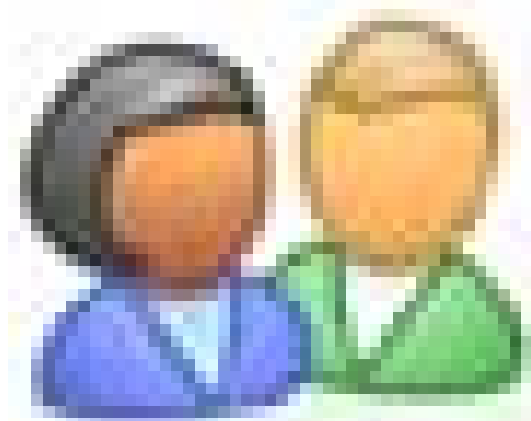
Of the 6.8 million people identifying themselves as multiracial on the 2000 census, 93 percent chose two races. Bars represent the number of people choosing each combination.





REPORTS

- REPORT OF THE SECRETARY'S TASK FORCE ON BLACK AND MINORITY HEALTH 1985
- DISPROPORTIONATE MORBIDITY AND MORTALITY
- EXCESS DEATHS
- RESULT OF LACK OF ACCESS
- LIFE STYLE





REPORTS

- REPORT ON MENTAL HEALTH: A REPORT OF THE SURGEON GENERAL 1999
- MENTAL DISORDERS ARE COMMON AND TREATABLE
- LACK OF ACCESS: MEANS MANY GROUPS DO NOT GET THE BENEFITS



REPORTS

- SUPPLEMENTAL SURGEON GENERAL'S REPORT ON MENTAL HEALTH OF MINORITIES 2001
- NO SUBSTANTIAL DIFFERENCE IN PREVALENCE
- SIGNIFICANT ILLNESS BURDEN
- LACK OF ACCESS



HUMAN GENOME PROJECT

- TEASE OUT THE HUMAN GENOME
- IDENTIFY ALL GENES
- DETERMINE THEIR FUNCTION





DEFINING ISSUES

- NIGHT DOCTORS
- TUSKEGEE INCIDENT
- PSYCHOSURGERY
- EUGENICS
- IQ AND RACE

PHARMACOGENETICS



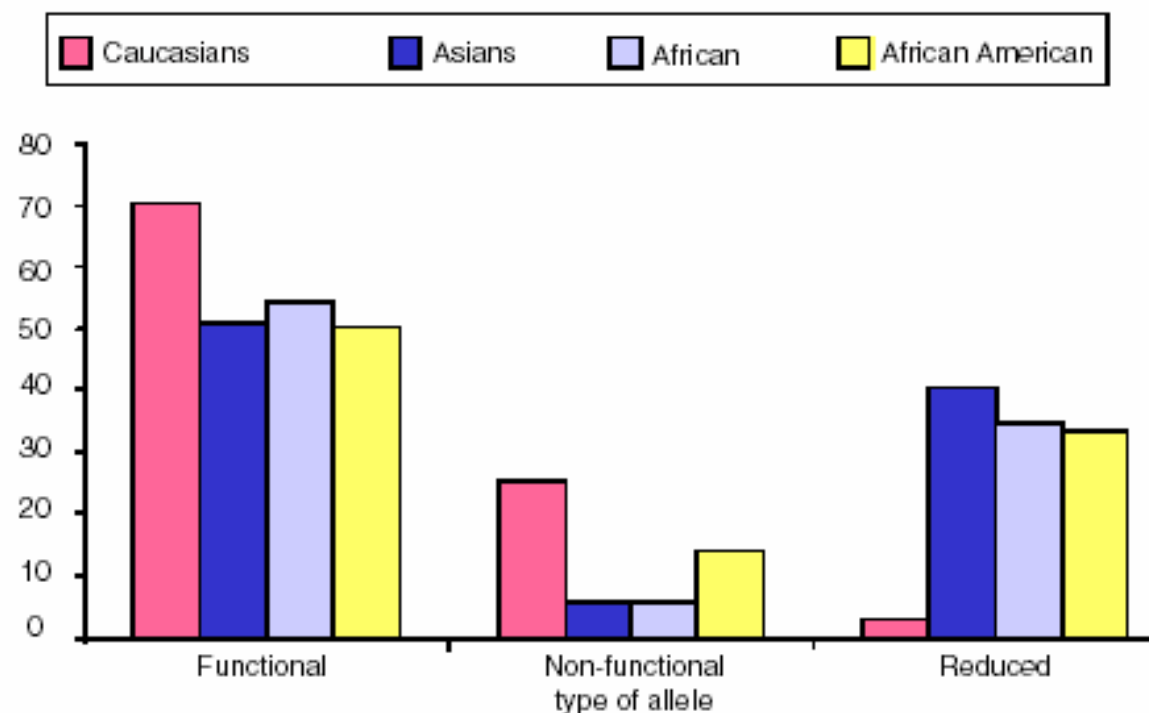
Clinical Findings

- More EPS in Asians
- Lower doses of antipsychotics and antidepressants in Asians and Latinos
- More tardive dyskinesia in African Americans
- More lithium side effects in African Americans

■ **Genotypical Differences**

- Shift to the Right for African Americans and Asians for CYP2D6 for antidepressants and antipsychotics
- Fewer Rapid Metabolizers
- Fewer Poor Metabolizers
- More Slow Metabolizers (Bradford, 2000; Mendoza et al, 1999)
- Lithium and differences in RBC/plasma ratio for African Americans

Figure 1. Median frequency for *CYP2D6* alleles classified as functional, non-functional and reduced functioning in Caucasians, Asians, Africans and African Americans.



The median frequencies for the functional classes of alleles in Caucasians, Asians, Africans and African Americans are shown. The frequency of functional alleles in Caucasians is predominant (71%), followed by non-functional alleles at 26% (mainly the 2D6*4 but also the *5 contributes). The reduced function Asian allele, the 2D6*10 variants importance has long been known in Asian populations. For both Asian and Black populations, the functional allele class assumes a less dominant role, with scarcely 50% of the variability of the alleles being accounted for. The reduced function alleles in Black populations (both African and African American) may increase in importance if other mutants, like the 2D6*29, occurring up to 20% in Africans [10] and 7% in African Americans [12] are discovered. The importance of assembling a review of allele frequencies underscores the predictability of drug response, due to the functionality that the allele bestows on the enzyme. The next research programs should include not only larger population studies for accurate assessment of allele frequency but also studies on individual clinical response and predictability of genotype.

CYP: Cytochrome P450.



AFRICAN AMERICANS

- Receive more prn medication
- Receive higher doses of psychotropic medication
- Receive more different medications
- Receive more injections of medication
- More likely to receive depot medication
- (Chung et al. 1995; Flaherty & Meagher 1980; Lawson 1986; Price et al.1985; Segal et al. 1996; Strakowski et al.1993)

Ramifications of a Misdiagnosis of Schizophrenia

Antipsychotic Prescribing in new onset Bipolar disorder

Measure	White (n=34)	Afr.-Amer. (n=24)
% f/u on any AP*	34	70
% f/u on conv. AP*	3	18
% f/u on AP w/o psychosis*	25	35
% f/u on AP w/ remission	20	24

* $p < .05$; up to 24 months of follow-up



THERAPIST'S ATTITUDES ABOUT THE PATIENT AFFECT TREATMENT

- RACIAL DIFFERENCES IN PRESCRIBING RELATED TO PHYSICIANS'S WILLINGNESS TO ENGAGE THE PATIENT Segal et al, 1996



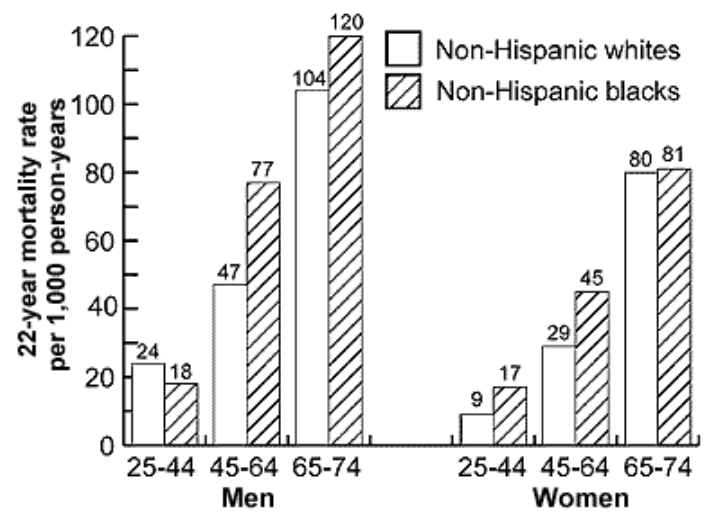
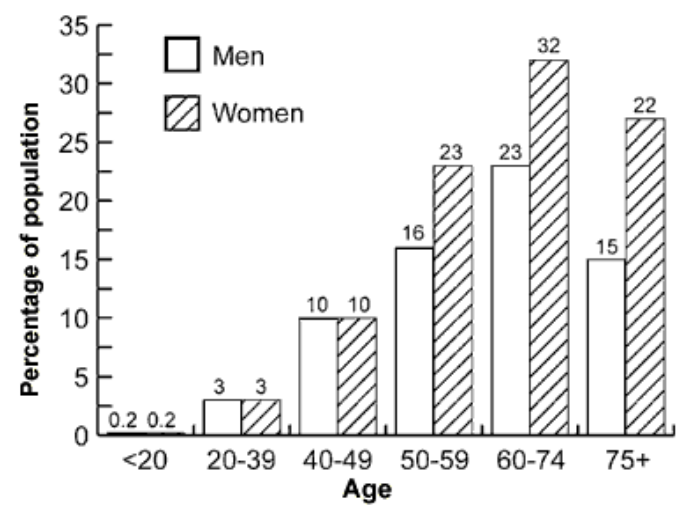
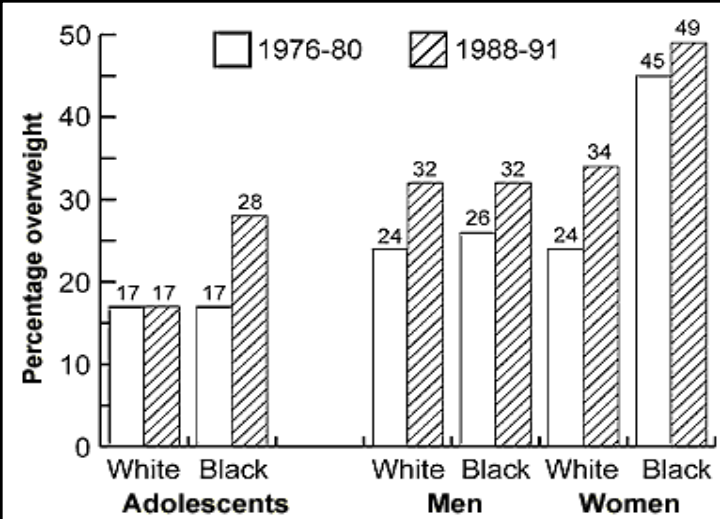
LITHIUM IN AFRICAN AMERICANS

- Greater RBC/Plasma ratio
- More side effects
- Poorer compliance?
 - (Okpaku et al. 1980; Strickland et al. 1993; 1995)



HEALTH CARE DISPARITIES

- African Americans and /or low SE show greater risks for:
- Diabetes and complications Clozapine, Olanzapine
- Cardiovascular disease Geodon
- Low WBC (benign leucopenia) Clozapine
- Eye disease-glaucoma, cataracts Seroquel





African Americans and Hispanics

- Often do not receive evidence based psychotherapy
- Often do not receive antidepressants
- Often do not receive second generation antipsychotics
- More likely to receive older antidepressants
- More likely to receive older antipsychotics and in excessive doses

Minority Representation in Clinical Trials of Recently Approved Drugs

- **Little data available for clinical trials of recently approved drugs**
- **Estimated to average substantially less than 5% in pivotal trials supporting drug safety and efficacy**
- **< 1% of studies in biological psychiatry when ethnicity is identified**

(Lawson, 1990)





African American Researchers are Rarer

- <1% of Academic Physicians
- Rare recipients of R01 grants and career development awards