AN OVERVIEW OF HEALTHCARE DISPARITIES IN THE AFRICAN AMERICAN COMMUNITY

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- Editor, Textbook of Black-Related Diseases
- Editor, Eliminating Healthcare Disparities in America
- Editor, Healthcare Disparities at the Crossroads with Healthcare Reform
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Presented to the

California Legislative Black Caucus

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Disclosure Statement

AstraZeneca: Grants, Speakers' Bureau

Pfizer: Advisory Group, Speakers' Bureau

Gilead Pharmaceuticals

Genentech

Forest Laboratories

Objectives

1. To provide the historical background of healthcare disparities
2. To create an awareness that the current health problems of minorities are rooted in slavery
3. To demonstrate evidence of healthcare disparities across multiple medical disciplines
4. To make recommendations for the elimination of healthcare disparities which all doctors can utilize

Dr. Martin Luther King, Jr. On Health Care Disparities

"Of all the forms of inequality, injustice in health is the most shocking and inhumane."

Dr. Martin Luther King, Jr.

Talmud Statement

By ten things is the world created,
By wisdom and by understanding,
And by reason and by strength,
By rebuke and by might,
By righteousness and by judgment,
By loving kindness and by compassion.

– Talmud Higaga 12A

Race And Ethnicity Definitions:

- **Race:** Derived from the Latin (generatio, a beginning). A term of taxonomic or biological classification which subdivides the human species (homo sapiens sapiens) into groups based upon phenotypical or physical similarities such as hair, skin, and eye color, facial features, and body proportions.

  Example: Black and white are racially relevant terms to describe people with darker or lighter skin color.

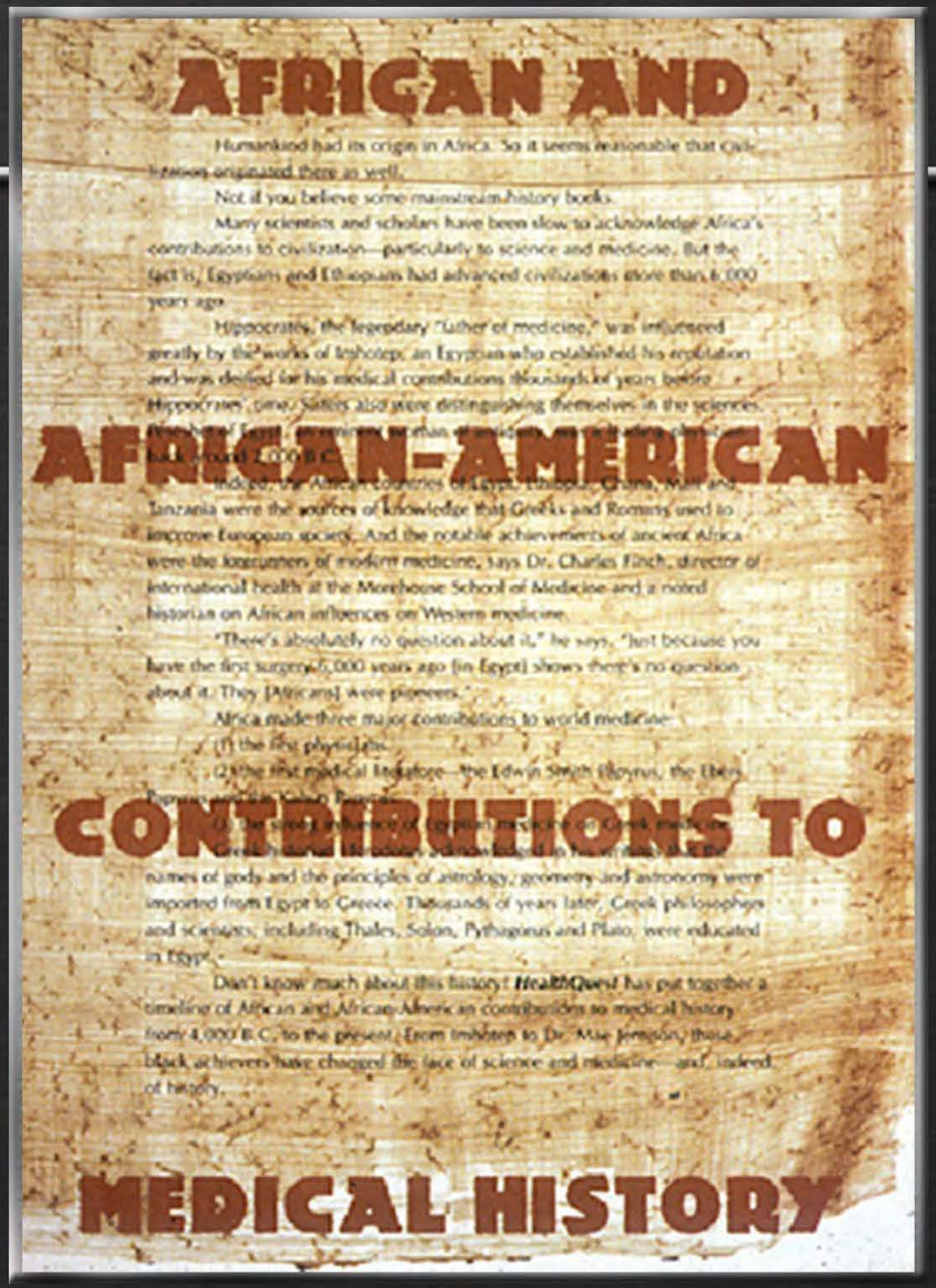
Race And Ethnicity Definitions:

- **Ethnic group/Ethnicity:** Terms invented by Ashley Montagu (1964) to subdivide humans according to their membership in socially distinct groups rather than according to shared physical characteristics.

  Example: African-American and Hispanic are ethnically relevant terms to describe population subgroups sharing certain sociological characteristics.

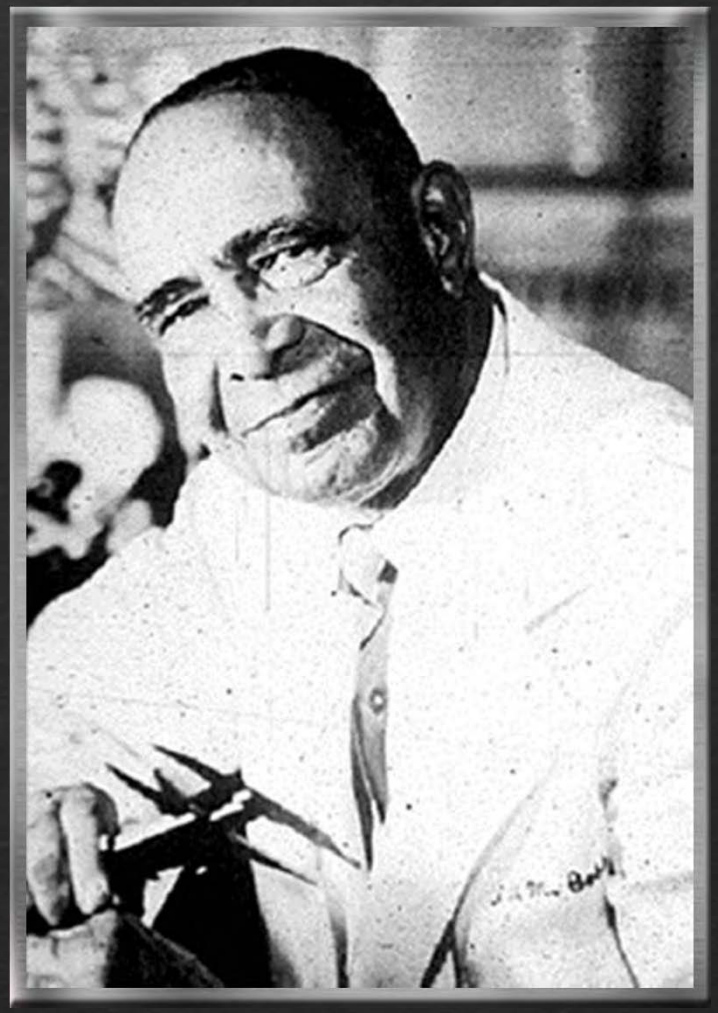
Race And Ethnicity Definitions:

- **Healthcare disparity**: A differential in outcomes of prevention and treatment of illness and disease which can be shown to vary according to the race, gender, and/or ethnic identity of patients. These differences may be ascribed to racism, denial of equal access to care, possession of different health-seeking behavior and idiosyncratic responses to treatment, or to poorly understood biological and genetic mechanisms.


AFRICAN AND
AFRICAN-AMERICAN
CONTRIBUTIONS TO
MEDICAL HISTORY


IMHOTEP, GOD OF MEDICINE


CITRATED WHOLE
HUMAN



Meharry Medical College and Howard University train most of the nation's black dentists and doctors.

W. Montague Cobb has been cited for his studies in anatomy and physical anthropology. He is the major historian of the Negro in medicine.

Dr. H.E. Gaskin (right) conducts a class in orthodontics at the Howard University School of Dentistry.

CARDIOLOGY

Richard Allen Williams

Daniel Hale Williams, M.D. (1858-1931). In 1893 he performed the first successful operation on the human heart, thus paving the way for the DeBakeys, Cooleys and Barnards of our day. *Schomburg Collection*

Historical Examples In Science and Medicine of Racist Attitudes

- Taxonomy: Linnaeus, 1735
- Anthropology: Dr. Samuel George Morton (1848); Carlton Coon
- Medicine: Drs. Meigs, Warren, Agassiz
- Politics: Sen. J.C. Calhoun of South Carolina and the fraudulent Census of 1840

J. MARION SIMS: GYNECOLOGIC SURGEON

Examples of Bigoted Medical Concepts

- "...the Negro's brain and nerves, the chyle and all the humora are tinctured with a shade of pervading darkness..."

Dr. Samuel Cartwright, *New Orleans Medical and Surgical Journal,* 1851

- ...the Negro has less chest discomfort because "more than moronic intelligence" is necessary to perceive the sensation of pain

Dr. MM Weiss, American Heart Journal, 1939

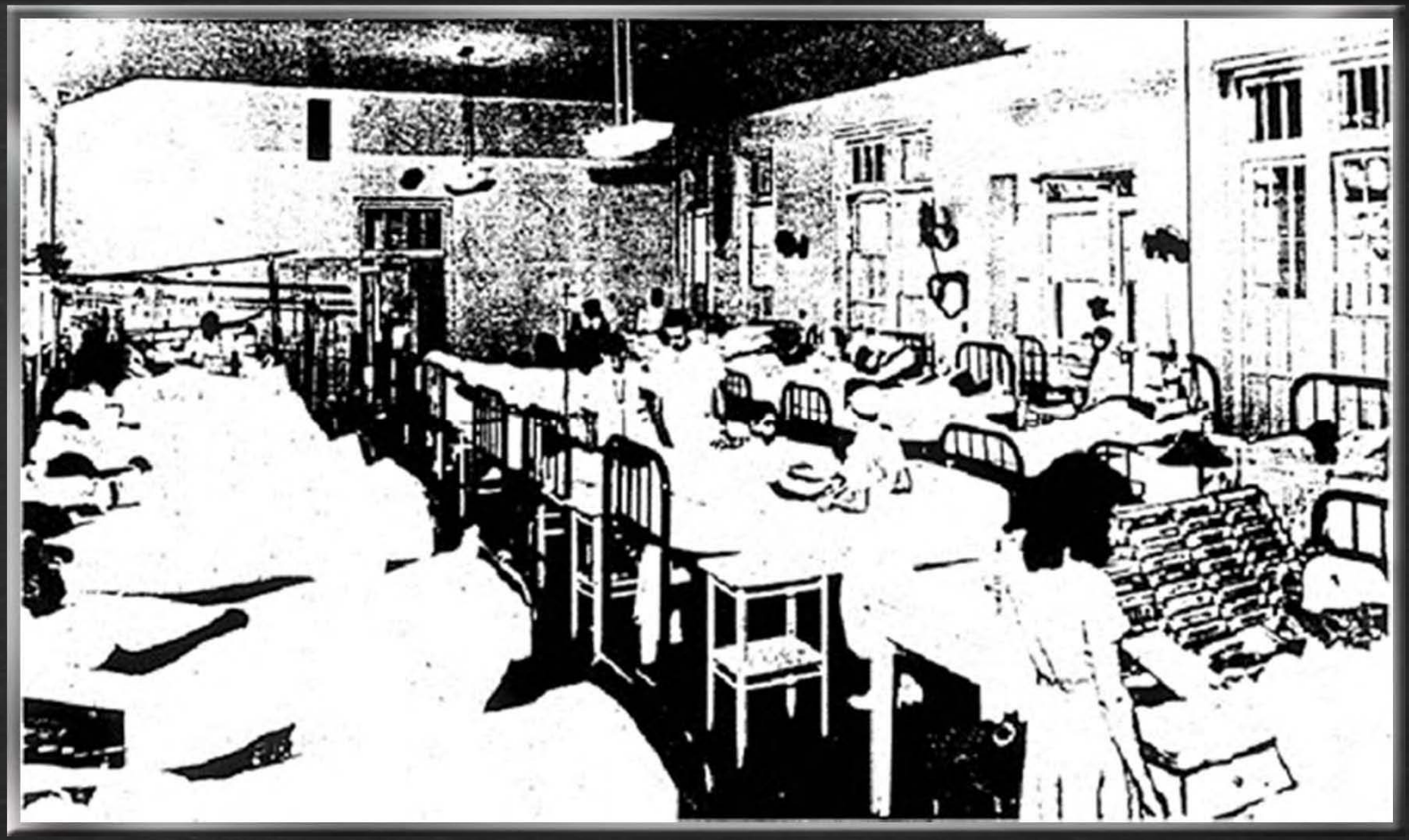
- Negros are a source of contagion and infection and they should be trained only as sanitarians to protect whites from their diseases

Dr. Abraham Flexner, 1910

Races	No. of Skulls	Mean Internal Capacity (cu. Inches)	Largest in Series	Smallest in Series
Caucasian	52	87	109	75
Mongolian	10	83	93	69
Malay	18	81	89	64
American	147	80	100	60
Ethiopian	29	78	94	65

Mortality Rates Per Thousand for Slaves and the Antebellum Population

Age	Slaves	Entire United States
0	350	179
1 – 4	201	93
5 – 9	54	28
10 – 14	37	19
15 – 19	35	28
20 – 24	40	39



A black surgical ward in Charleston's segregated "Old Roper" Hospital, c. 1950. Although patients were all black, the professional staff here were all white. Courtesy of the Waring Historical Library. Medical University of South Carolina.

Projected Survival of White and Nonwhite Cohorts Born in 1975

Year	White	Nonwhite
1974	1,000	1,000
1975	982	969
1984	977	961
2000	963	936
2039	738	581
2044	639	478

Source: National Center for Health Statistics, *Vital Statistics of the United States, Monthly Vital Statistics Report*, Vol. 20, no. 13, suppl.2, U.S. Public Health Service, Aug. 30, 1972.

Words Of Wisdom

Those Who Fail To Heed

The Lessons Of History

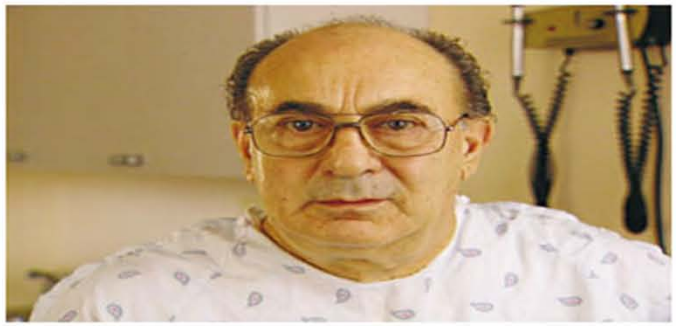
Are Destined To Repeat Them.

-Santayana

THE EFFECT OF RACE AND SEX ON PHYSICIANS' RECOMMENDATIONS FOR CARDIAC CATHETERIZATION

KEVIN A. SCHULMAN, M.D., JESSE A. BERLIN, SC.D., WILLIAM HARLESS, PH.D., JON F. KERNER, PH.D., SHYRL SISTRUNK, M.D., BERNARD J. GERSH, M.B., CH.B., D.PHIL., ROSS DUBÉ, CHRISTOPHER K. TALEGHANI, M.D., JENNIFER E. BURKE, M.A., M.S., SANKEY WILLIAMS, M.D., JOHN M. EISENBERG, M.D., AND JOSÉ J. ESCARCE, M.D., PH.D.

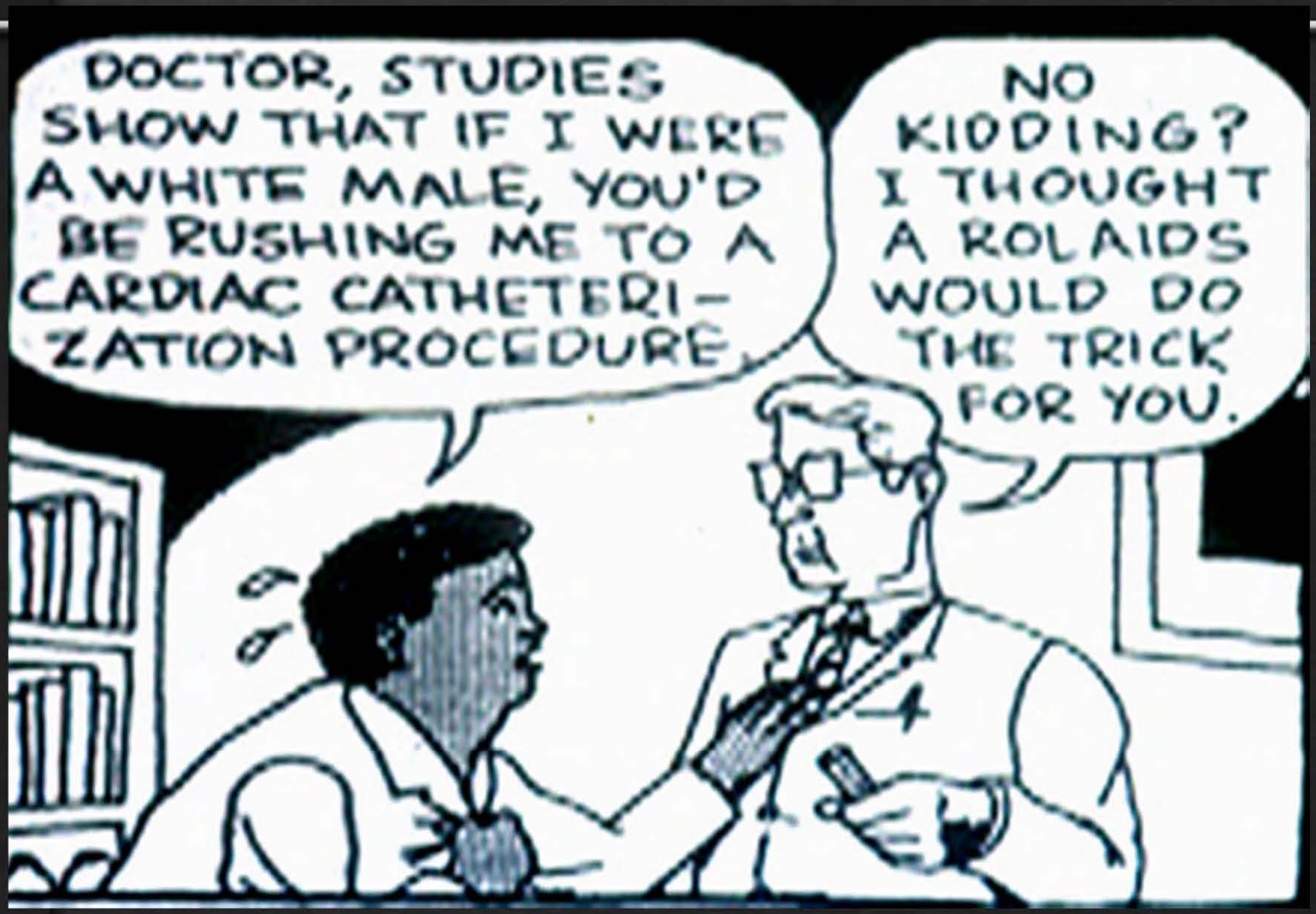
“Patients” experiencing symptoms of heart disease, from Schulman et al. (1999)



Evidence of Racial and Gender Bias in Medical Procedures and Treatment

1. Treatment of cardiac arrest
2. Selection of patients for cardiac catheterization
3. Coronary artery bypass graft surgery (CABG)
4. Thrombolytic therapy
5. Percutaneous transluminal coronary angioplasty (PTCA)
6. Selection of patients for treatment to prevent stroke

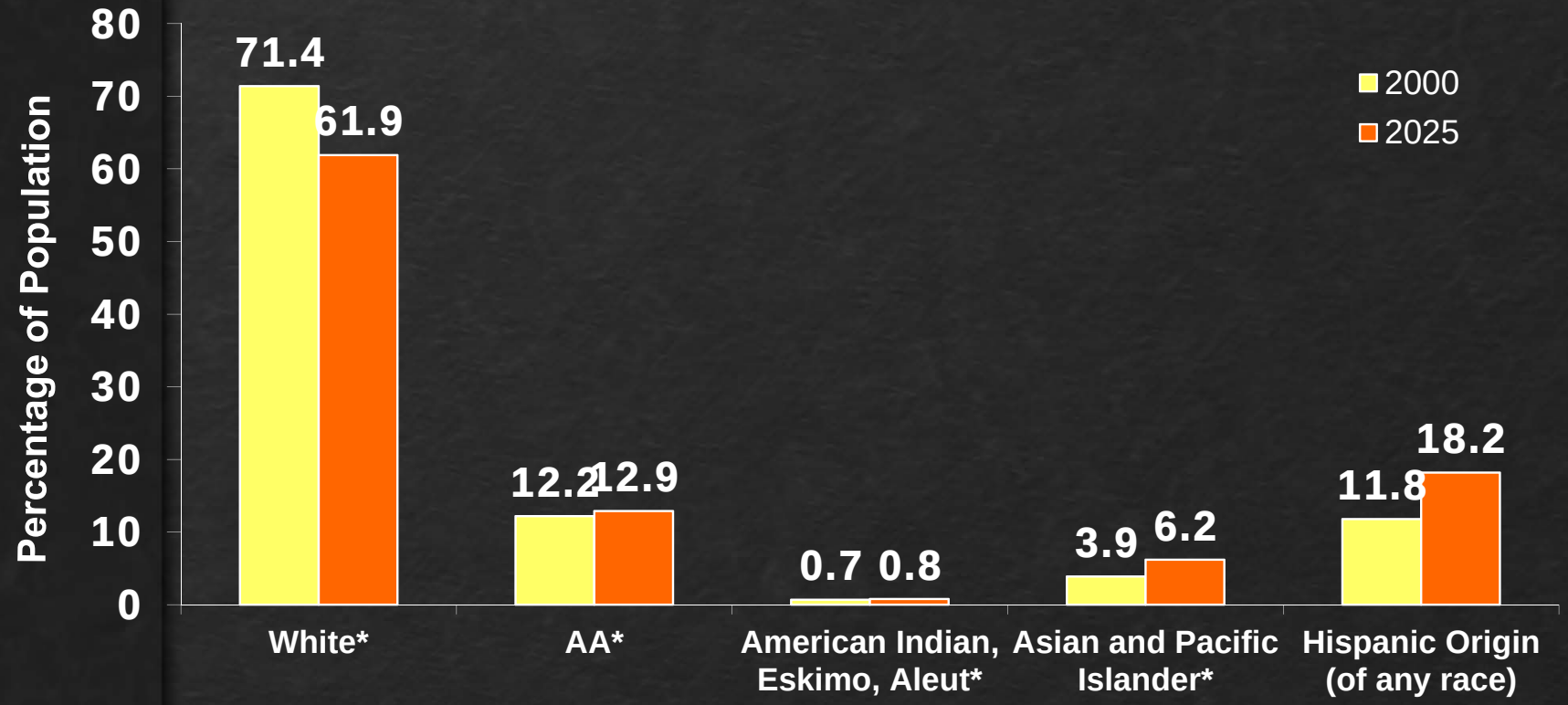

GIVE IT TO ME STRAIGHT, DOC.. I CAN TAKE IT.. WHAT'S WRONG WITH ME?
YOU'RE NOT A WHITE MALE.


DOCTOR, STUDIES SHOW THAT IF I WERE A WHITE MALE, YOU'D BE RUSHING ME TO A CARDIAC CATHETERI-ZATION PROCEDURE.
NO KIDDING? I THOUGHT A ROLAIDS WOULD DO THE TRICK FOR YOU.

PatientSpeak: Culturally Conditioned Medical Terms

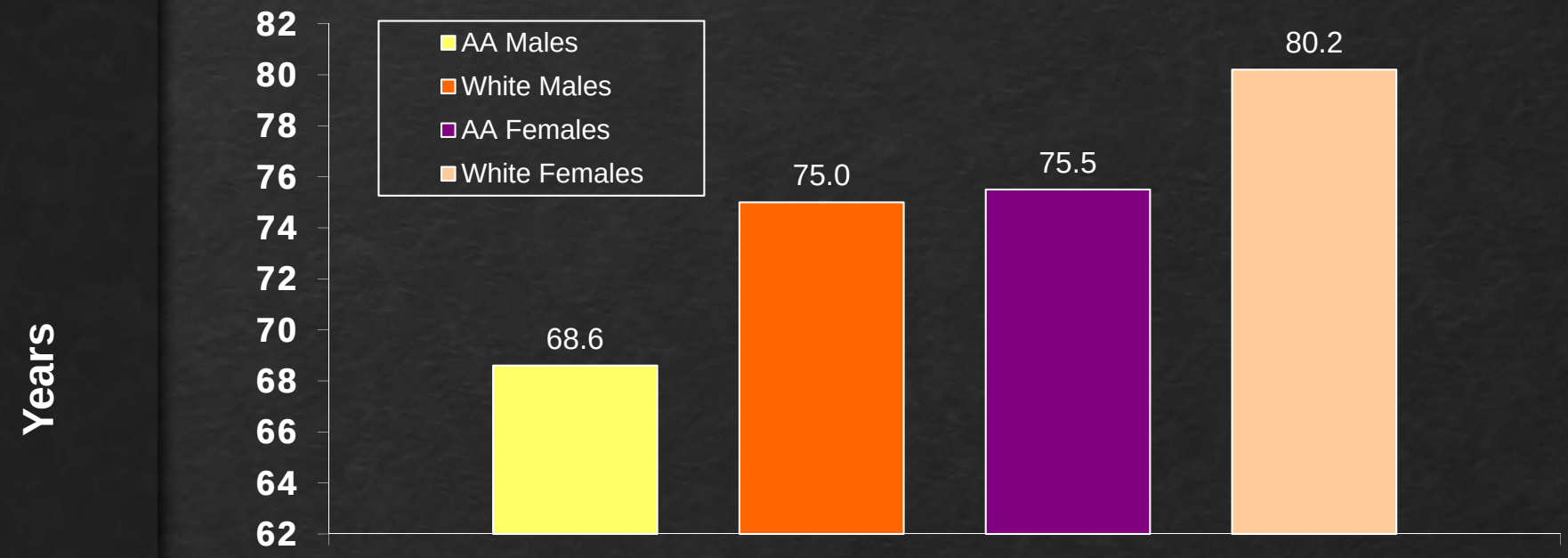
Expression	Translation
A Sedimentary Life	Sedentary
Emancipated	Emaciated
Genetic Drugs	Generic Drugs
Old-Timers' Disease	Alzheimer's Disease
Premarital Stress	Premenstrual Stress
Valium Stress Test	Thallium Stress Test
Public Hair	Pubic Hair
I had an Autopsy	Biopsy
Pep Smear	Pap Smear
Prostrate	Prostate
Tubal Litigation	Ligation
Cologne Trouble	Colon
Cardiac Coagulation	Catheterization
I was Castrated	Catheterized

Percentage of the Population by Race/Ethnicity: 2000 and 2025



*Indicates non-Hispanic.
AA=African American.
US Census Bureau, 2000.

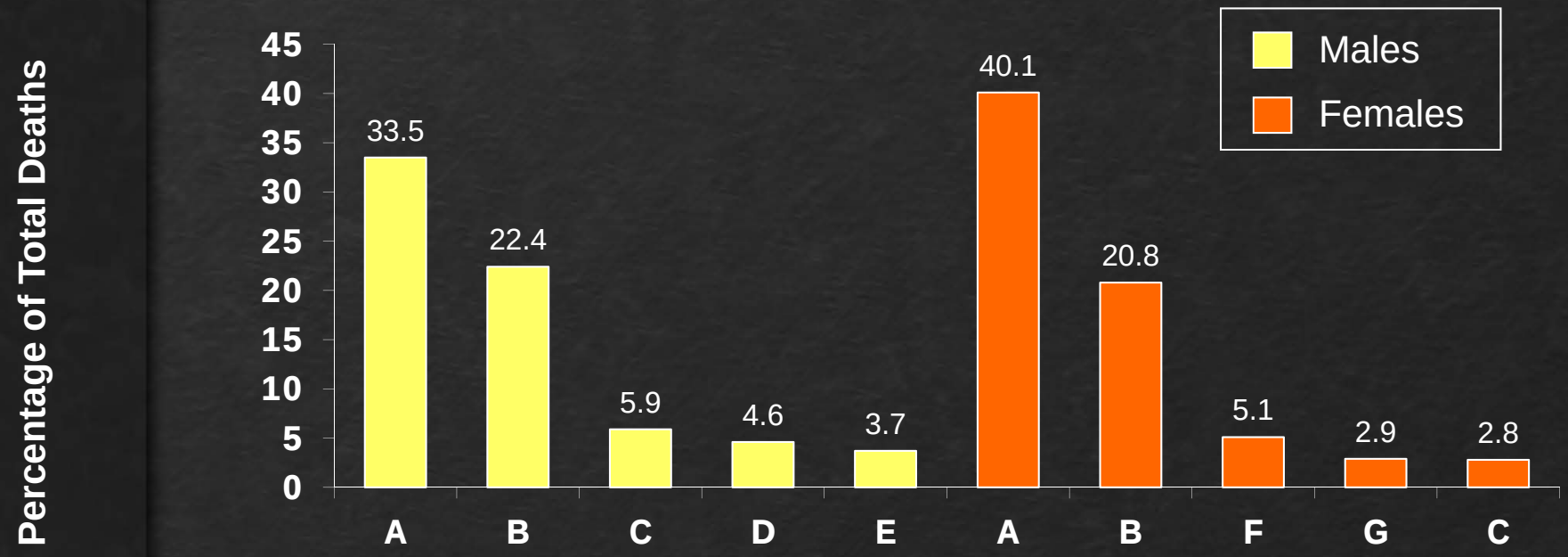
Estimated Life Expectancy: 2001



National Vital Statistics Reports. 2004;52:33–34.

Leading Causes of Death for African American Males and Females

United States: 2001



A	**Total CVD**	**E**	**HIV (AIDS)**
B	**Cancer**	**F**	**Diabetes Mellitus**
C	**Accidents**	**G**	**Nephritis, Nephrotic Syndrome, and Nephrosis**
D	**Assault (Homicide)**		

CVD=cardiovascular disease.

Adapted from *Heart Disease and Stroke Statistics—2004 Update.* American Heart Association; 2003:6.

Defining Health STATUS Disparities

- "...differences that occur by gender, race or ethnicity, education or income, disability, living in rural localities or sexual orientation." US Department of Health and Human Services, Healthy People 2010

- "...a population-specific difference in the presence of disease, health outcomes, or access to care." US Health Resources and Services Administration (2000)

- "...differences in the incidence, prevalence, mortality and burden of diseases and other adverse health conditions that exist among specific population groups in the United States. Research on health disparities related to socioeconomic status is also encompassed in the definition." National Institutes of Health (2000).

Defining Health CARE Disparities

- "…racial or ethnic differences in the quality of healthcare that are not due to access-related factors or clinical needs, preferences and appropriateness of interventions."

- Institute of Medicine (2002)

The Minority-Majority and the Future of Healthcare

Can a healthcare system created in segregation adjust to the minority-majority?

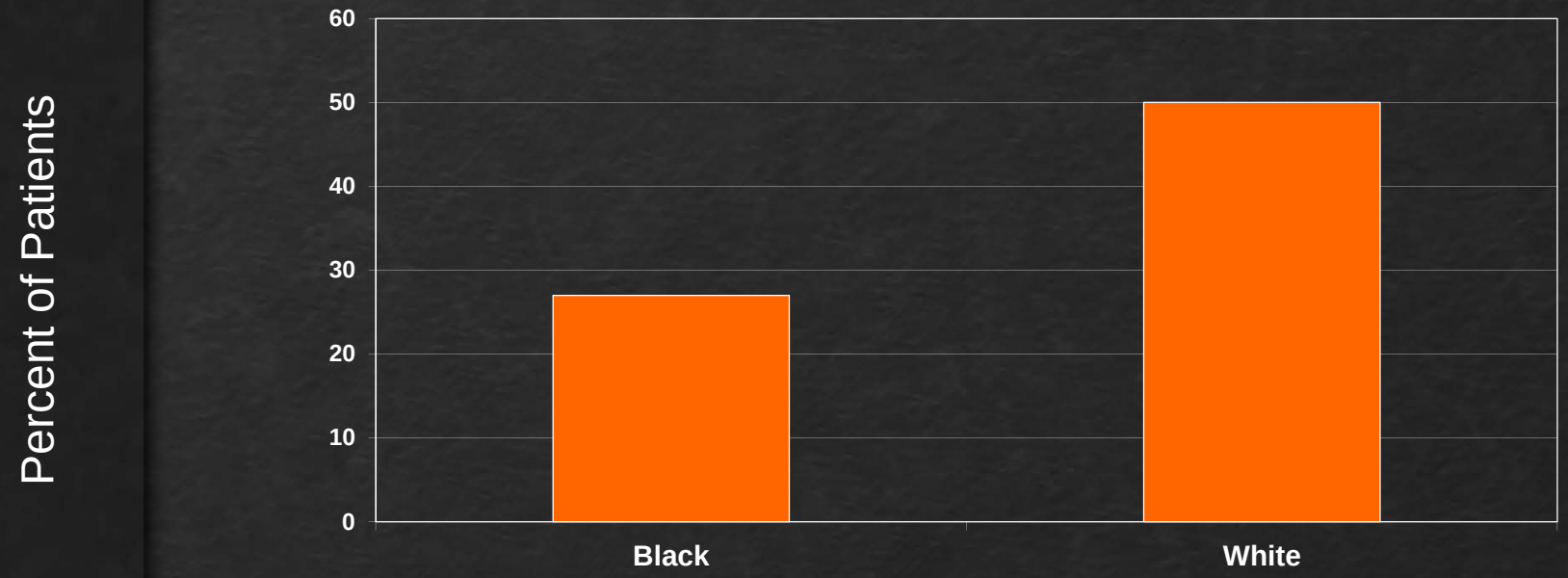
Risk Factors for Disparate Healthcare

- Poverty
- Racism
- Discrimination
- Bias
- Language barriers
- Geographical barriers
- Socioeconomic status
- Immigrant status
- TRUST (or lack thereof)

Institute of Medicine. Summary of: *Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare*. 2003.

Healthcare Disparity

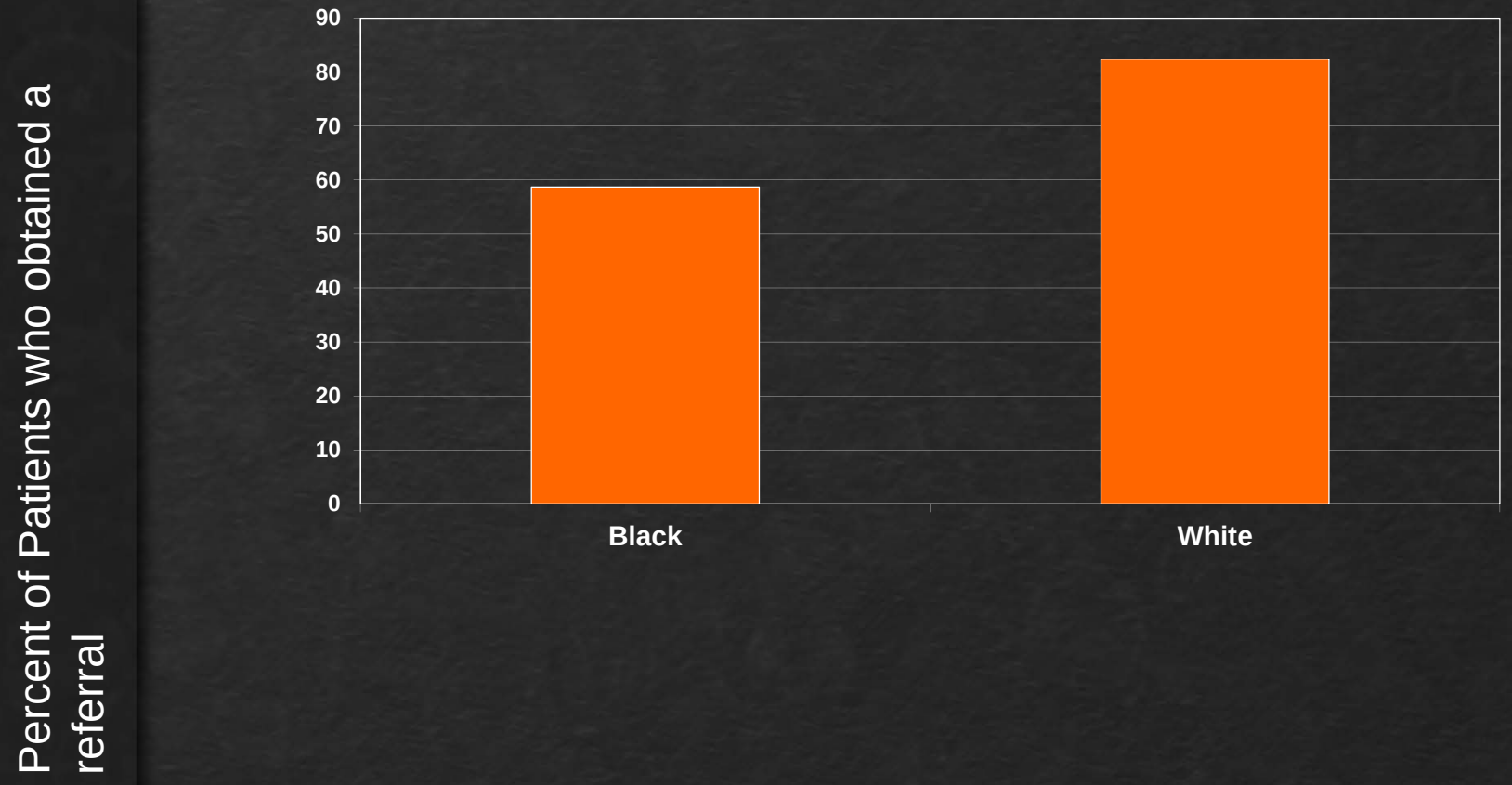
A race disparity in coronary revascularization **was found among patients in the** Veteran Affairs **health system, where there are no race differences in ability to pay and providers are paid a salary.**



Source: Ibrahim SA, Whittle J, Bean-Mayberry B, Kelley ME, Good C, Conigliaro J. Racial/ethnic variations in physician recommendations for cardiac revascularization. Am J Public Health. 2003 Oct;93(10):1689-93.

Healthcare Disparity

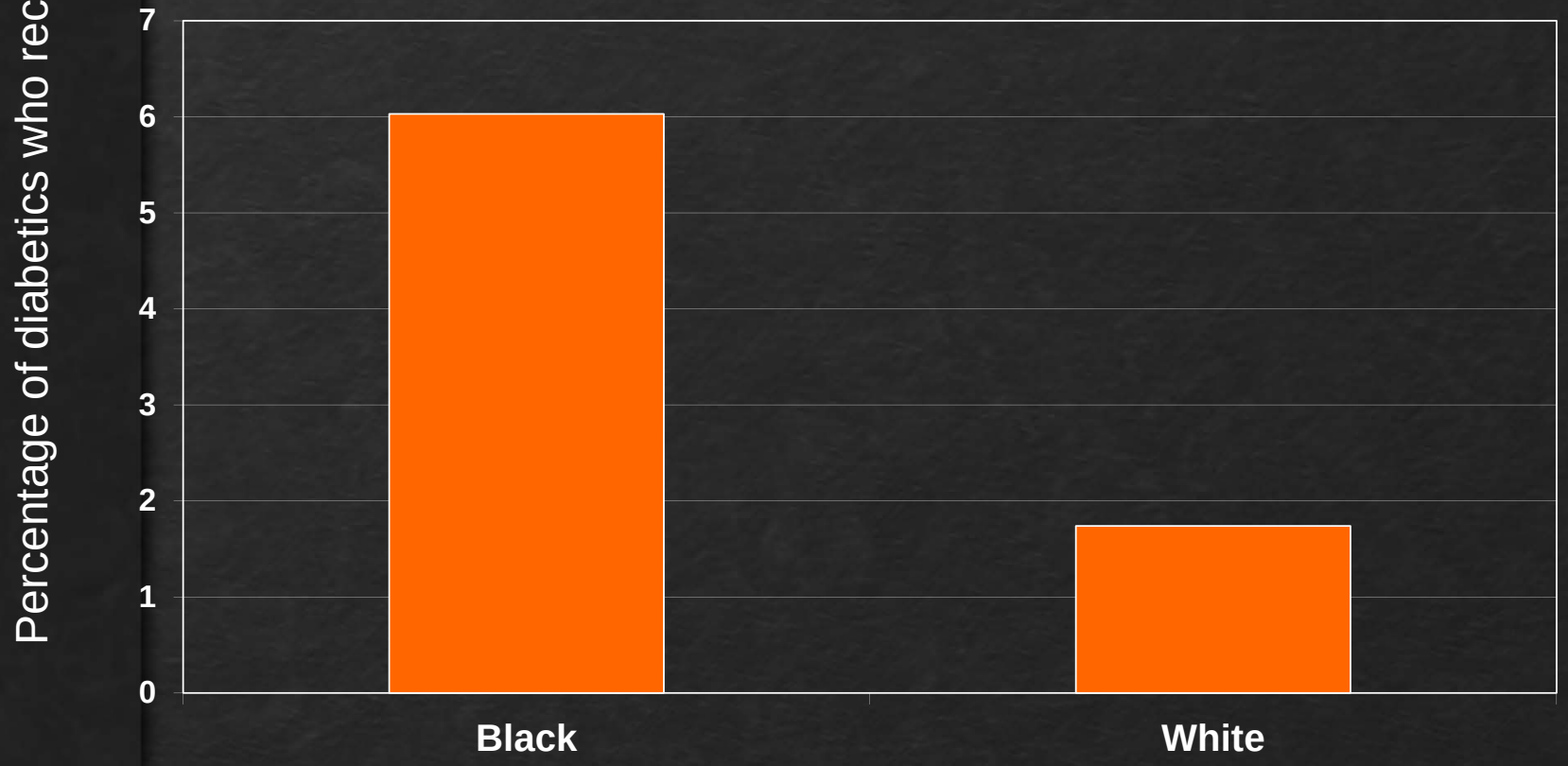
Studies of patients who were appropriate candidates for coronary angiography **have found race differences in obtaining a referral for this diagnostic procedure.**



Source: LaVeist TA, Arthur M, Morgan A, Rubinstein M, Kinder J, Kinney LM, Plantholt S. The cardiac access longitudinal study. A study of access to invasive cardiology among African American and white patients. J Am Coll Cardiol. 2003 Apr 2;41(7):1159-66.

Healthcare Hyper-Disparity

African American Medicare patients are more likely than white Medicare patients to have a lower limb amputation **as a result of poor management of** diabetes**.**



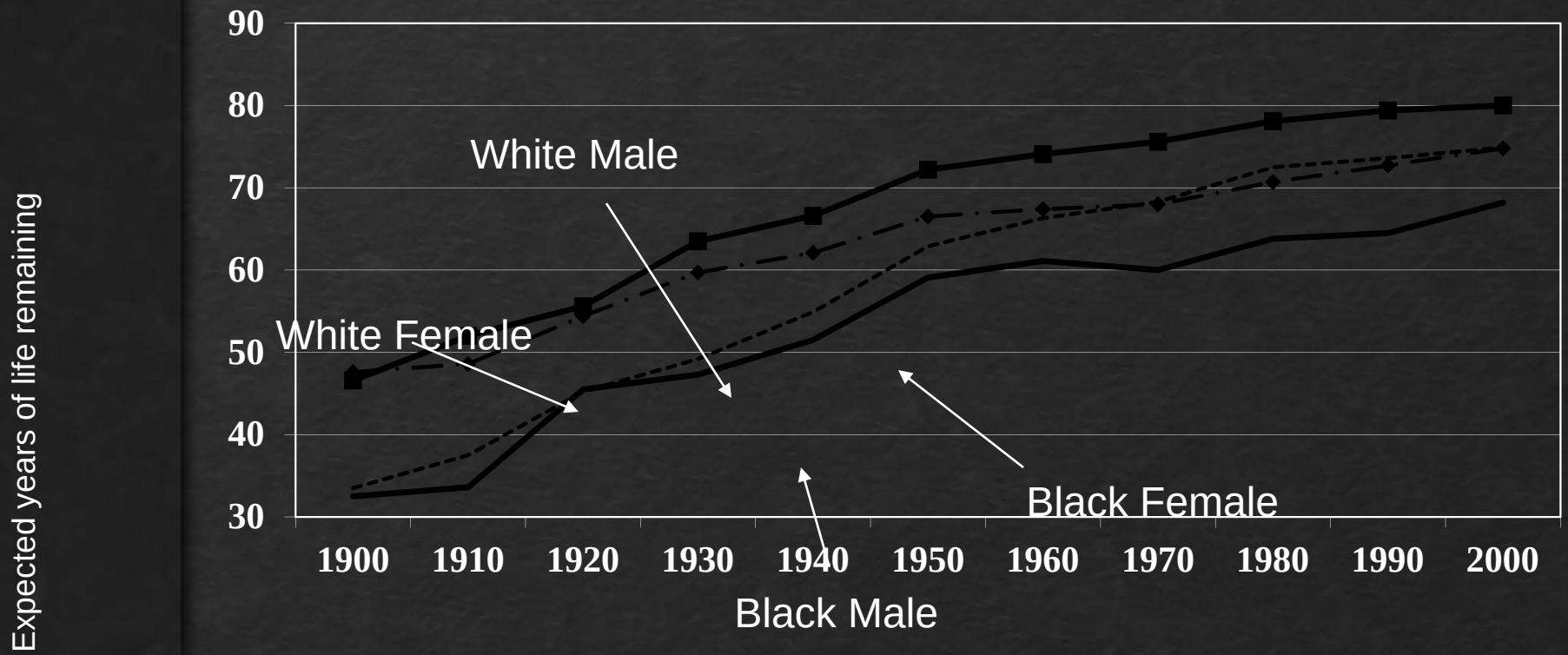
Source: Gornick M (2000) “Vulnerable Populations and Medicare Services: Why do disparities exist?” New York: The Century Foundation Press

Physician-patient Race Concordance in the 1994 Commonwealth Minority Health Survey

	Patient's Race			
Physician's Race	White (n = 910)	Black (n = 745)	Hispanic (n = 676)	Asian American (n = 389)
White		58.5%	60.1%	45.0%
Black	1.5%		2.2%	1.3%
Hispanic	2.1%	2.3%		.5%
API	7.5%	10.1%	10.5%	
Other	3.3%	7.4%	8.3%	1.0%

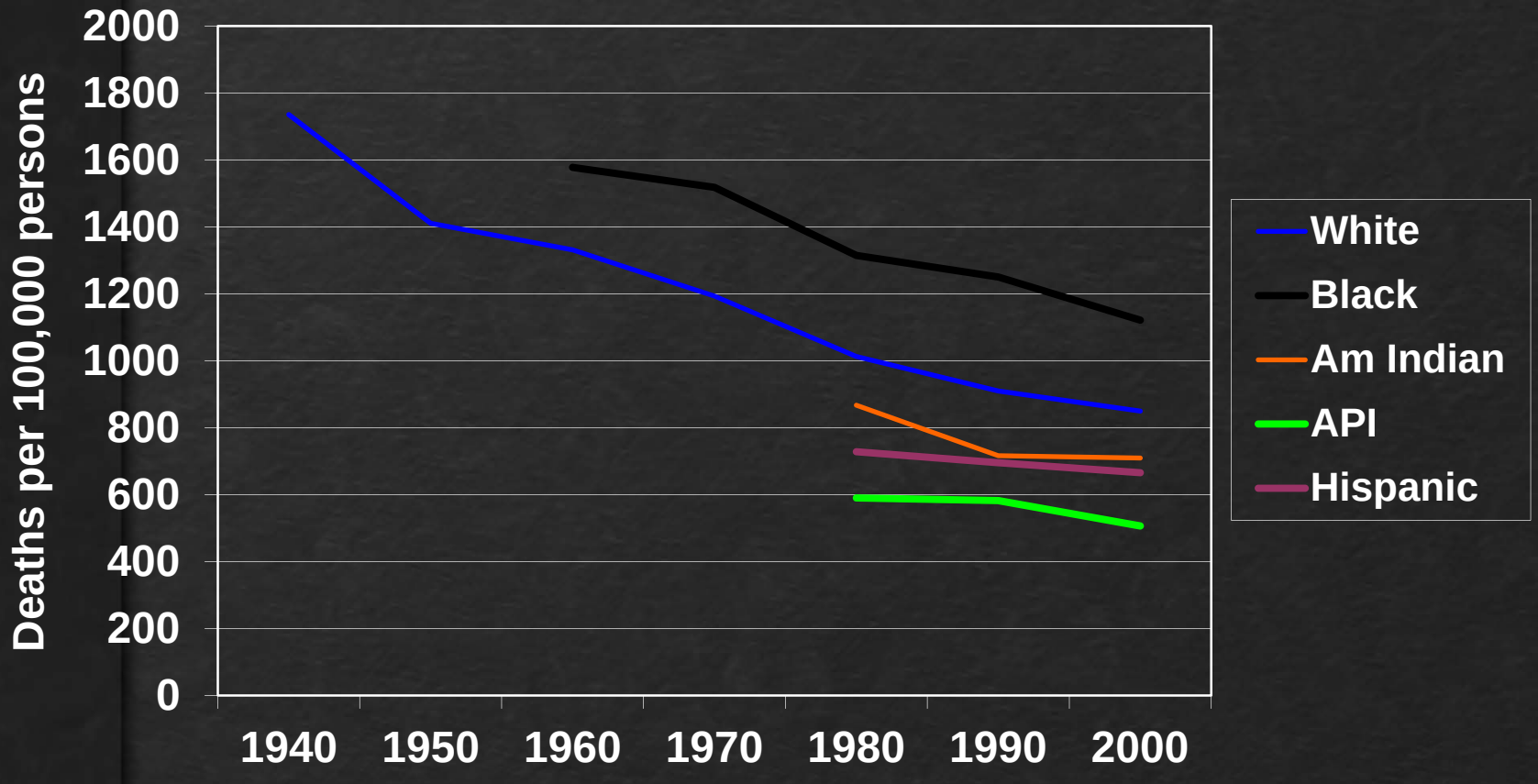
LaVeist, Thomas A., Nicole C. Rolley, and Chamberlain Diala. "Prevalence and patterns of discrimination among US healthcare consumers" (2003) *International Journal of Health Services* Vol 33, No 2, Pages 331-344

Life Expectancy at birth by race and gender, U.S. 1900-2000



Source: U.S. National Center for Health Statistics, “Health, United States, 2003”, Table 27

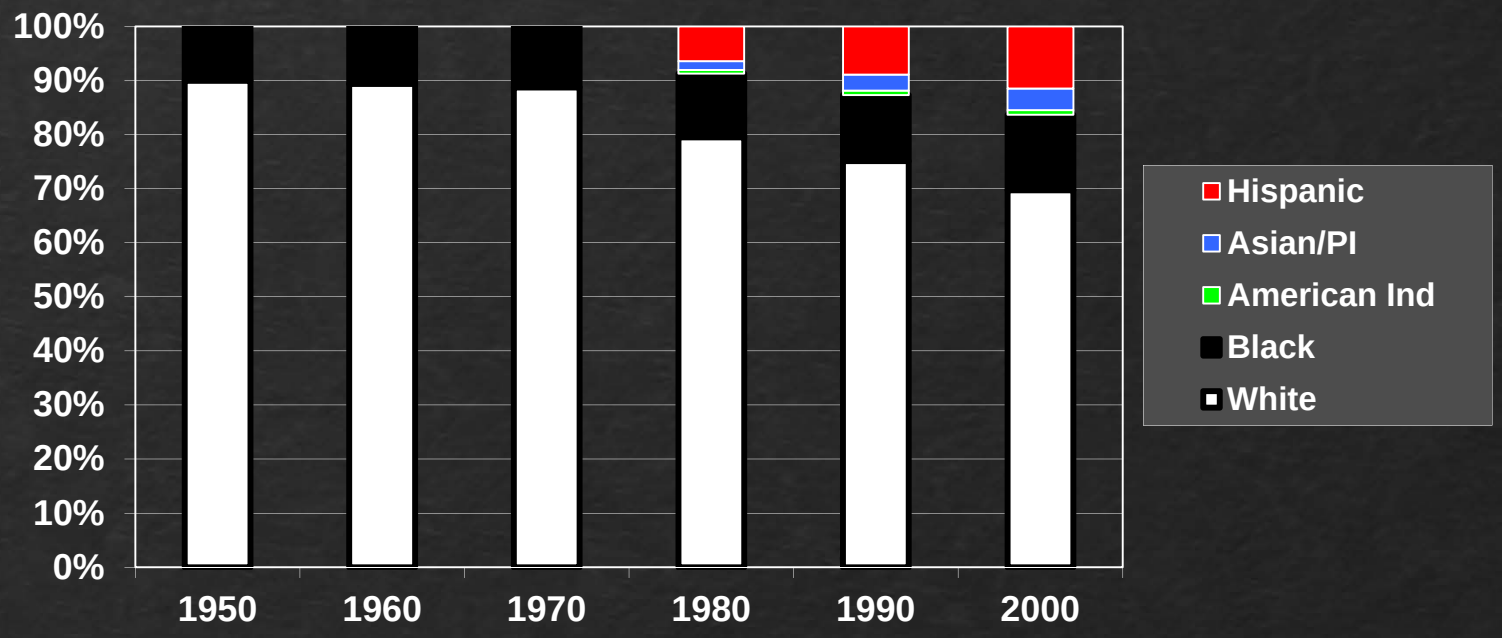
Age-adjusted mortality rates by race/ethnicity, 1940-2000



Source: U.S. National Center for Health Statistics, "National Vital Statistics Reports, Volume 52, Number 3, September 18, 2003

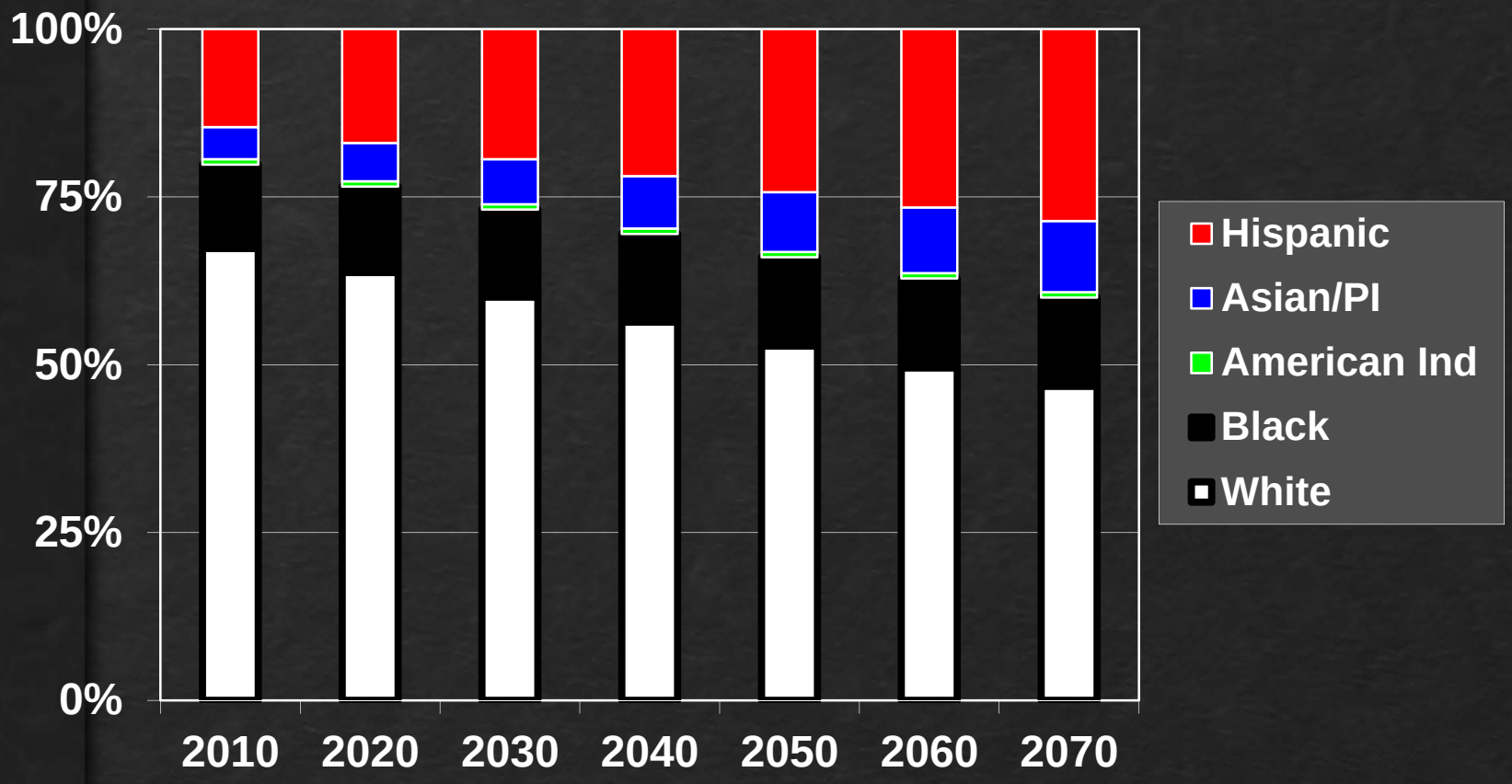
[1] Data for Hispanics is based on estimates

Percentage Resident Population by race/ethnicity, U.S. 1950-2000



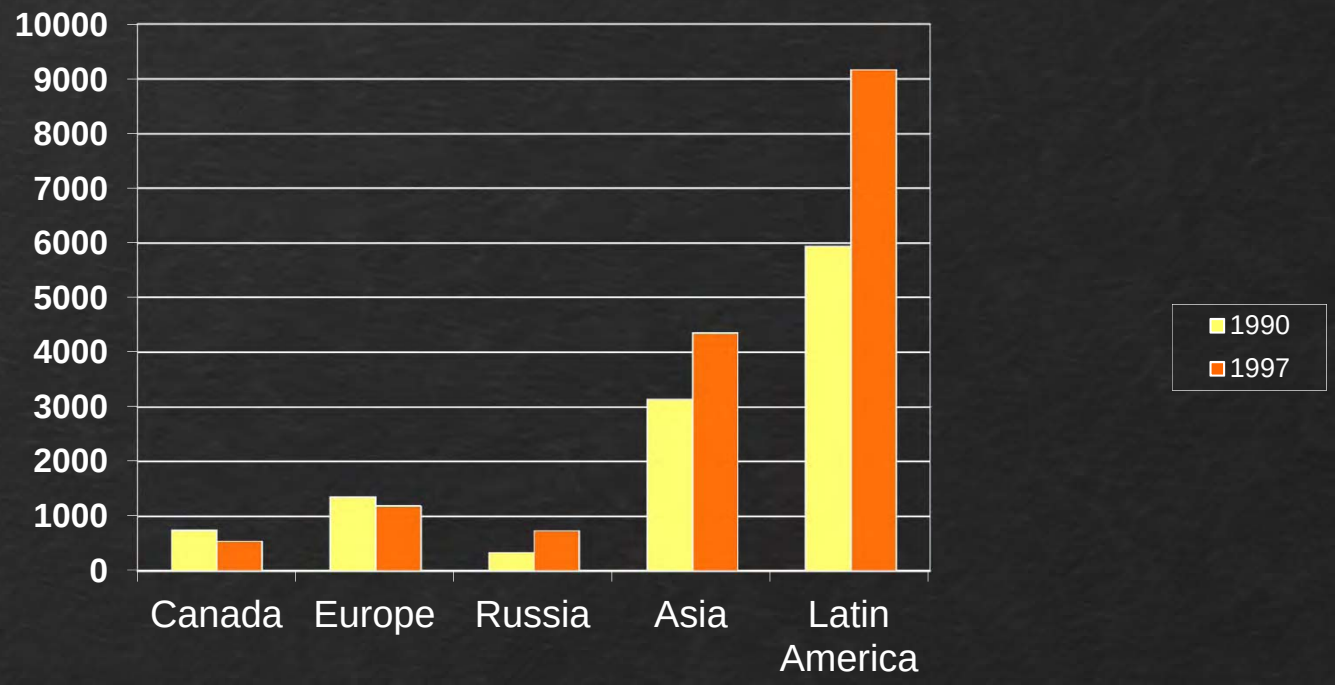
Source: National Center for Health Statistics (2002)

Projected Percentage Resident Population by race/ethnicity, U.S. 2010-2070

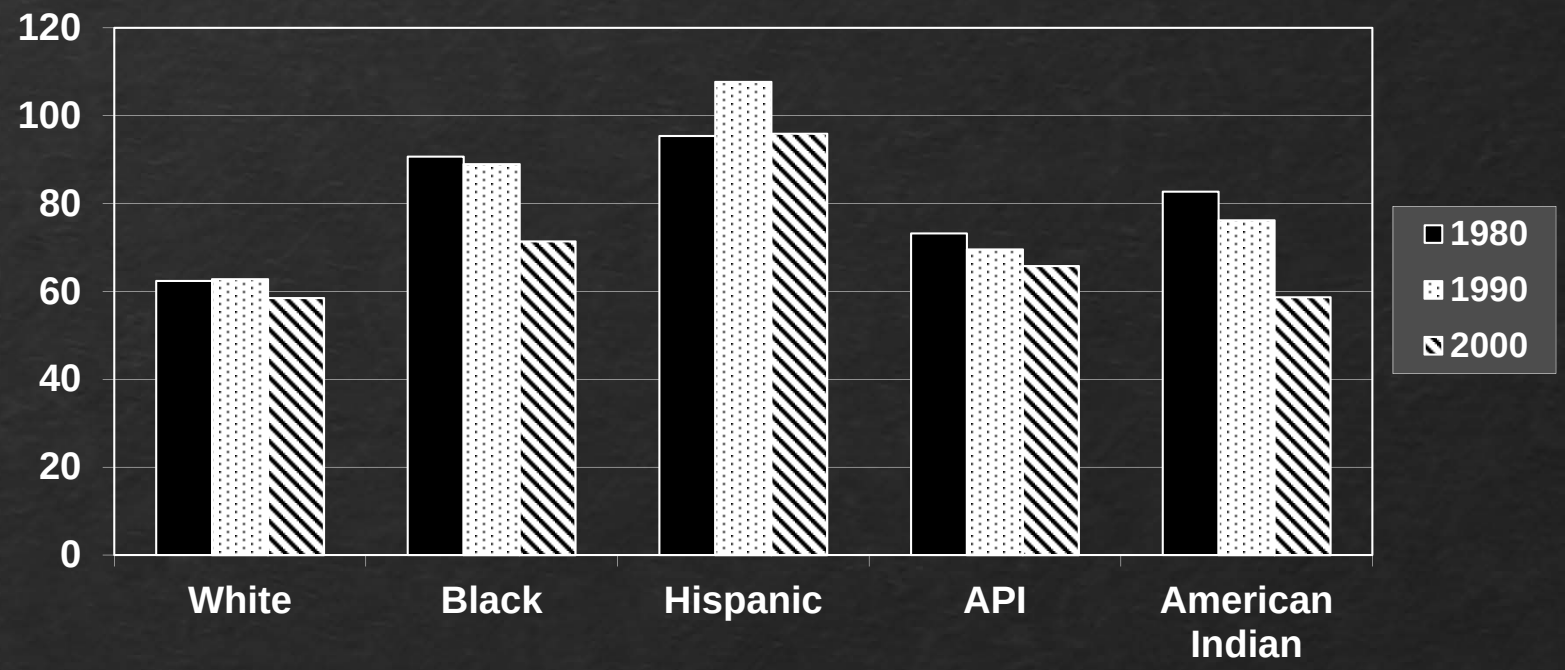


Source: U.S. Bureau of the Census:(NP-T5) Projections of the Resident Population by Race, Hispanic Origin, and Nativity: Middle Series, 1999 to 2100

Region of birth for foreign-born U.S. population, 1990-1997



Fertility Rates by race/ethnicity, 1980-2000



Source: National Center for Health Statistics, 2002

Table 1. Definition and basic characteristics of the eight Americas

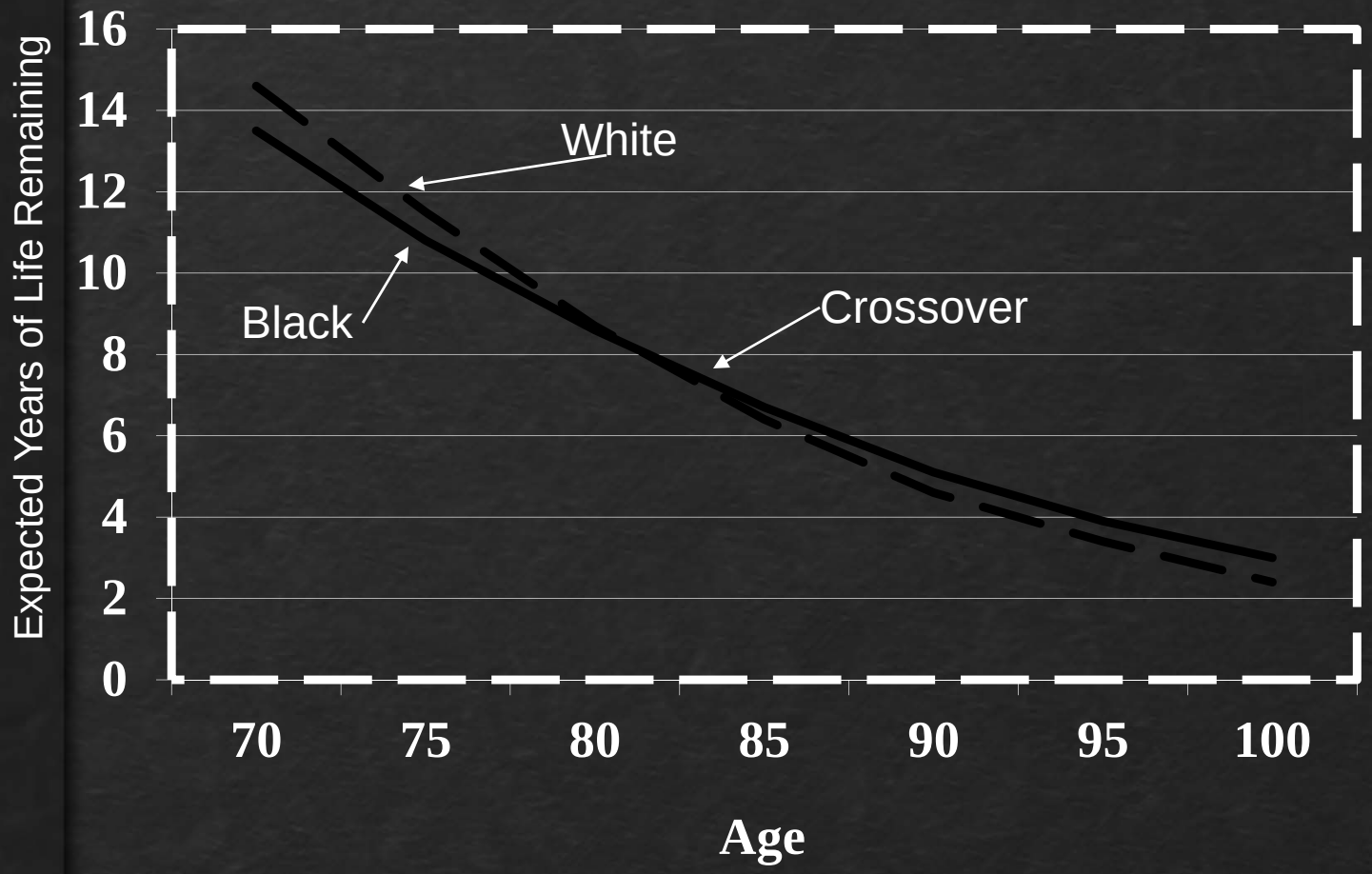
America	General description	2000 Census population (millions)	2000 Census income per capita	2000 Cen completi school
1	Asians	10.1	$21,675	80
2	White low-income rural Northland	3.6	$17,758	83
3	Middle America	219.0	$24,463	84
4	White poor Appalachia/Mississippi Valley	11.0	$15,451	70
5	Western Native Americans	1.0	$10,008	69
6	Black middle America	23.4	$15,407	75
7	Black poor rural South	5.8	$10,432	61
8	Black high-risk urban	7.5	$14,798	71

individual characteristics, community attributes, and access to and interaction with the healthcare system interact to determine health outcomes.

Critical to the formulation of effective policies to

(2) had a population large enough to facilita analysis of causes of death, risk factors, acces care services and other factors over time. T ment of each race/ethnicity subgroup w

The Mortality Crossover



Source: National Center for Health Statistics :National Vital Statistics Reports, Deaths: Final Data for 2001, Vol 52, No 3, September 18, 2003, Table 7

Table 2. Male and female life expectancy at birth for 2001 in eight Americas

America	General description	Male life expectancy at birth	Female life expectancy at birth	F di li ex
1	Asians	82.8	87.7	4.
2	White low-income rural Northland	76.2	81.8	5.
3	Middle America	75.2	80.2	5.
4	White poor Appalachia/Mississipi Valley	71.8	77.8	6.
5	Western Native Americans	69.4	75.9	6.
6	Black middle America	69.6	75.9	6.
7	Black poor rural South	67.7	74.6	6.
8	Black high-risk urban	66.7	74.9	8.

the other seven Americas. America 4 is made up of poor white populations in Appalachia and the Mississippi Valley. Thirty percent of these populations have not

In other words, millions of Americans in health-disadvantaged groups have life expect are similar to some poor developing countr

SUMMARY OF FINDINGS
From IOM Report

Racial and ethnic disparities in health care exist and, because they are associated with worse outcomes in many cases, are unacceptable.

Racial and ethnic disparities in health care occur in the context of broader historic and contemporary social and economic inequality, and evidence of *persistent* racial and ethnic discrimination in many sectors of American life.

Many sources – including health systems, health care providers, patients, and utilization managers – contribute to racial and ethnic disparities in health care.

SUMMARY OF FINDINGS

From IOM Report (Continued)

Bias, stereotyping, prejudice, and clinical uncertainty on the part of healthcare providers may contribute to racial and ethnic disparities in healthcare.

Racial and ethnic minority patients are more likely than white patients to refuse treatment, but differences in refusal rates are generally small, and minority patient refusal does not fully explain healthcare disparities.

John F. Kennedy

If we cannot end our differences,
at least we can make
the world safe for diversity,
for in the final analysis,
our most basic link
is that we all inhabit
this small planet.
We all breathe the same air,
we all cherish our children's future,
and we are all mortal.

John F. Kennedy

- “WE MAY HAVE COME HERE ON DIFFERENT SHIPS, BUT WE’RE IN THE SAME BOAT NOW.”

- “Insanity is when people continue to repeat the same mistakes over and over with the same bad results”
- -Albert Einstein

Where There Is No Vision,

The People Perish.

Proverbs 29:18

Cardiovascular Disease Statistics in African Americans

- African Americans (AA) are about 2.5 times as likely as the general US population to die from complications of hypertension.
- Approximately one third of AA adults have hypertension (age-adjusted), among the world's highest rates.
- The prevalence of MI in AA women is 3.3% compared with 2.0% in white women.
- AA have a 1.3 and 1.8-fold increased risk of suffering a nonfatal or fatal stroke, respectively, compared with whites.
- AA are about twice as likely as Americans in general to die from diabetes. Diabetes is the third leading cause of death in AA women

Source: Nash, DT, Cardiovasc Rev Rep, 2003, 24(9): 458-463, 467

Hypertension

- The African American prevalence of hypertension is highest in the World
- Stage 3 hypertension is more common among African Americans than Whites
- AA have a higher incidence of LVH
- AA have a 4 fold greater incidence of end stage renal disease than other Americans
- 75% of AA women are overweight or obese

Heart Failure

- HT is the leading cause of HF in AA
- HF affects 3.5% of AA men and 3.1% of AA female over 20 years, and 5% of over 65 years
- HF outcome is poorer in AA patients with 45% higher rate of functional decline or death in 6 months c/w white

Atherosclerosis Risk in Communities Study (ARIC) Study 1987-1997

Multivariant analysis

- HT was a particularly strong risk factor in AA women
- Diabetes was somewhat more predictive in white women
- LDL was similarly predictive in all race-sex groups
- HDL was somewhat more protective in white

(2298 black women,5686 white women,

1096 black men,4682 white men)

"Under-use" in African Americans or "Over-use" in Whites?

- Do those with 'most to gain' (ie sickest) get procedures?
  - Patients with baseline symptoms (angina)
  - Estimated incremental survival benefit
- Are there measurable differences in Long-term patient outcomes?
  - Actual Survival Rates
  - Functional Outcomes

Impact of Racial Differences on Downstream Functional Status and Angina

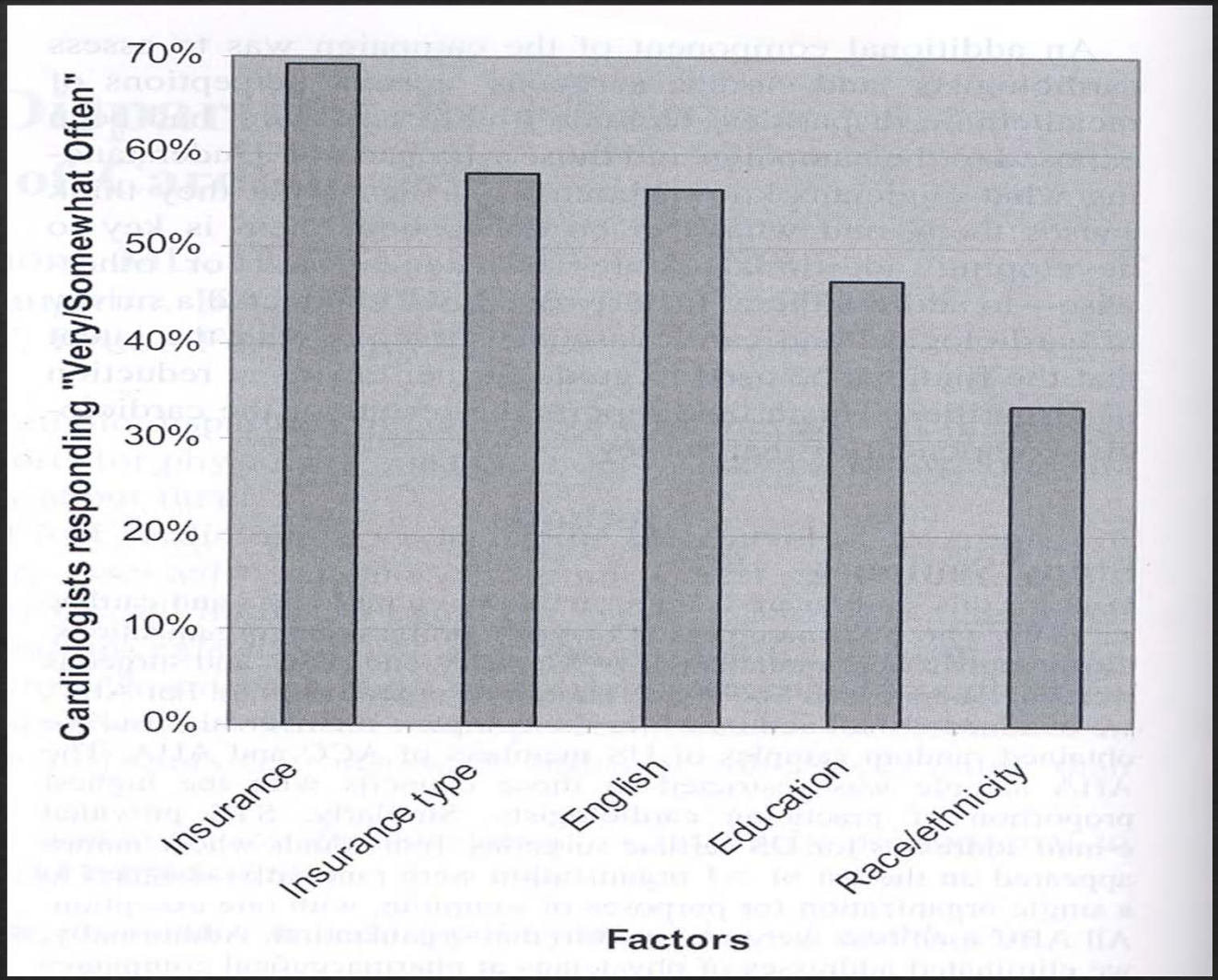
Model Components	Estimated Coefficient (P value)
SF -36 Physical Function	
Race	- 2.3 (<0.01)
Race + Clinical	- 1.5 (0.03)
Race + Clinical + Treatment	- 1.3 (0.69)
Angina Frequency Score	
Race	-3.9 (<0.01)
Race + Clinical	-2.7 (0.03)
Race + Clinical + Treatment	-2.3 (0.07)

Source: Kaul P Circulation 2005;111:1184-90

Conclusions

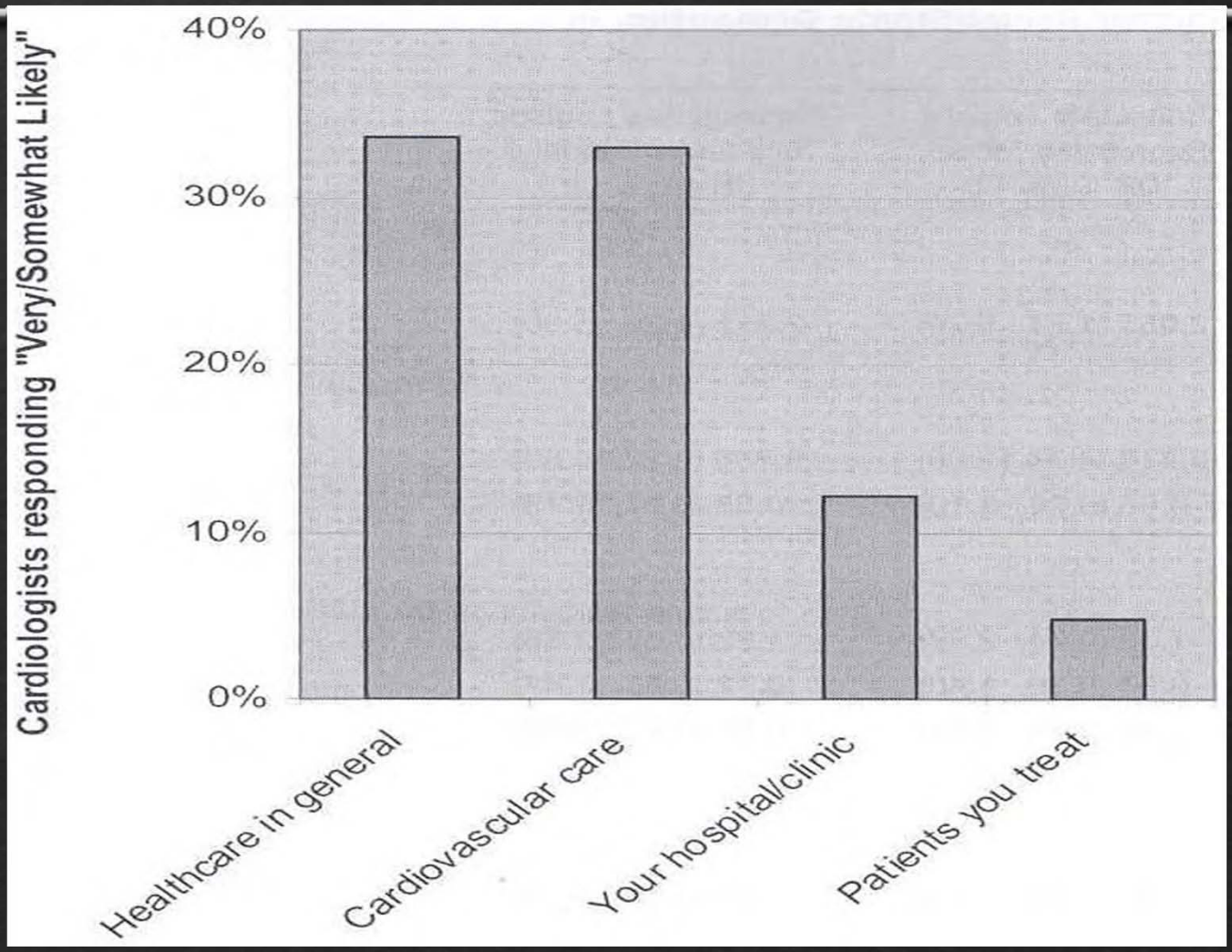
- AA with CVD are less likely to receive revascularization than whites after adjusting for clinical factors, etc.
- Differences most marked among those who stood the most to gain from the procedure.
- These differences in care appear to have resulted in worse long-term survival for blacks.
- These difference in care were also associated with more downstream angina and worse functional status

Perceived Factors Influencing Health Care



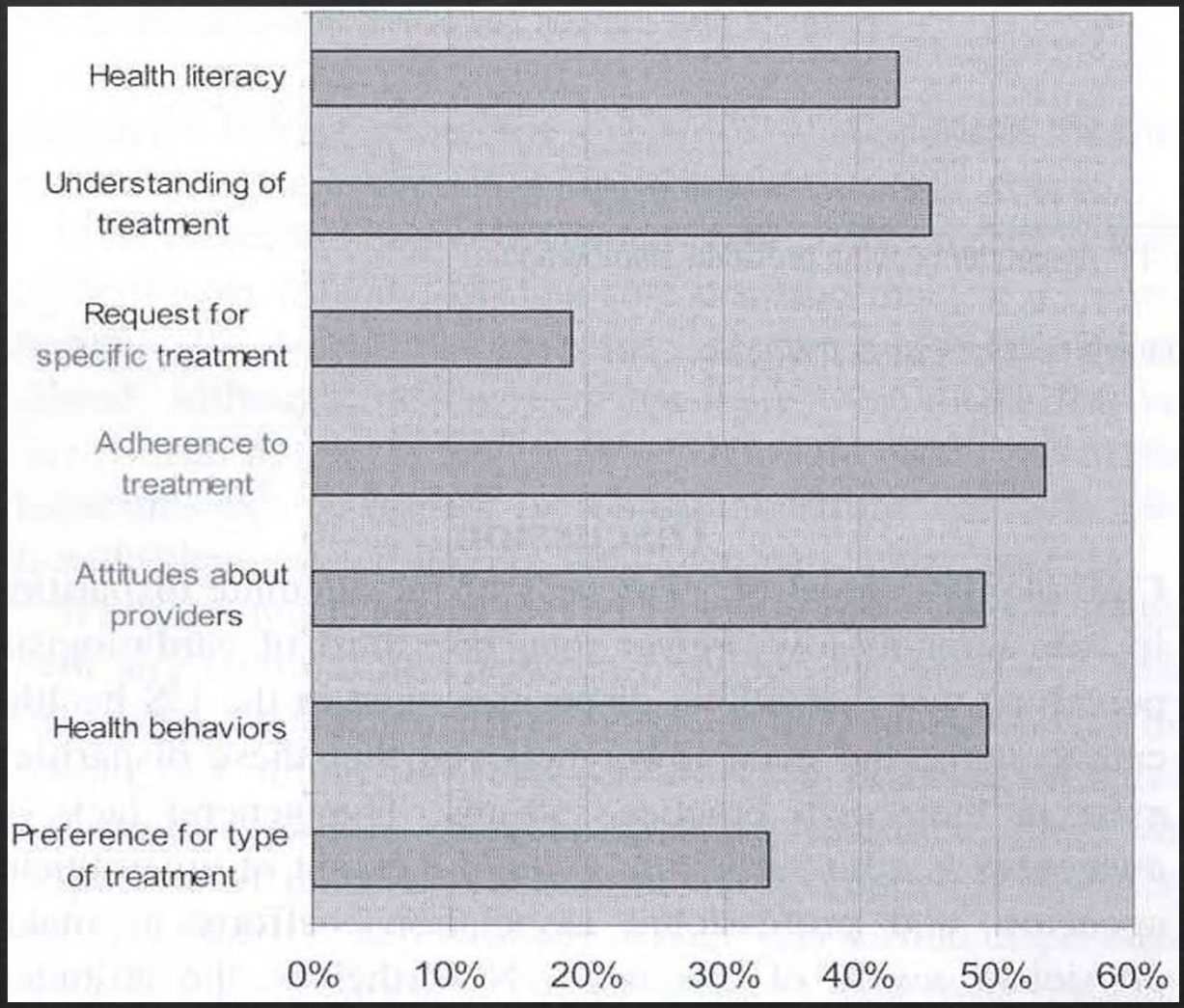
Source: Lurie N et al. *Circulation* 2005;111:1264-1269

Does Race Impact Care Decisions?



Source: Lurie N et al. *Circulation* 2005;111:1264-1269

What Factors Cause Racial Disparities in CV Procedures ?

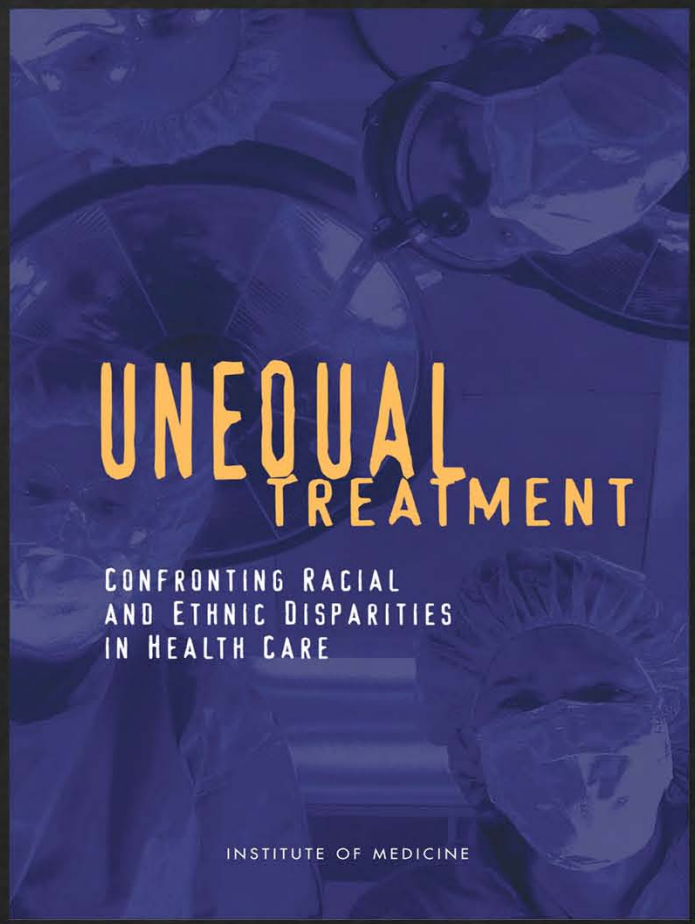


Source: Lurie N et al. *Circulation* 2005;111:1264-1269

IOM Report, 2002: Assessing the Quality of Minority Health Care

"Disparities in the health care delivered to racial and ethnic minorities are real and are associated with worse outcomes in many cases, which is unacceptable."

-- Alan Nelson, retired physician, former president of the American Medical Association and chair of the committee that wrote the Institute of Medicine report, *Unequal Treatment: Confronting Racial and Disparities in Health Care*



Conclusions

After 20 years of research…

- Racial differences in use of CV care persist..
  - Most marked in interventional procedures (e.g.,CABG) and newer, high cost drugs (GP, Clop, statins)
- These differences in care NOT explained fully by clinical or other patient factors
- Differences appear to impact on patient outcomes
- Answers to overcoming disparities remain unclear,
  - Patient involvement in decision-making
  - Efforts to measure and promote ‘evidenced-based care’ for all!

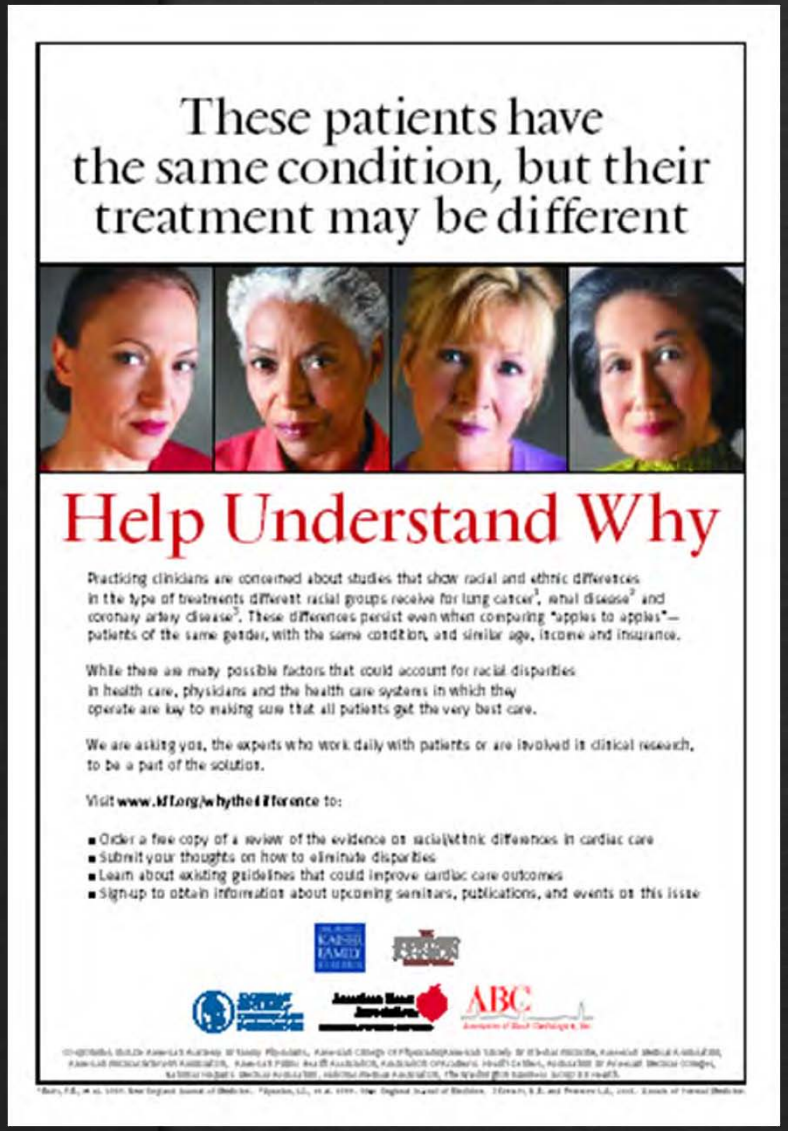
CDC Eliminate CVD disparities by 2010

- Reduce deaths from heart disease among AA by 30%
- Reduce deaths from stroke among AA by 47%

Means of Reducing Disparities GAP

- Better patient education about disease and treatment options. Patient activism
  - Shared Decision Project
- Physician education
  - Rand/ACC/AHA/STS Study
- Performance measurement

Kaiser Family Foundation Ad Campaign



Ad appeared in leading medical publications:

Journal of the American Medical Association

Today in Cardiology

Journal of the American College of Cardiology

Circulation – The Journal of the American Heart Association

Treatment Pearls: Management of High Blood Pressure in African Americans

- Obtain BP and assess risk of CVD at regular intervals
- Increase awareness of links between lifestyle choices and CV outcomes
- Increase dietary potassium while moderating sodium intake
- Increase awareness of obesity and inactivity as major risk factors
- Provide DASH diet information to patients
- Provide intensive intervention to lower LDL of those with type 2 diabetes
- Eliminate misperception that it is more difficult to lower blood pressure in African Americans
- Combination therapy may be required to achieve and maintain target blood pressure
- As monotherapy, beta blockers and ACE inhibitors may produce less blood pressure-lowering effects in AA than whites
- Diuretics and calcium channel blockers may have greater blood pressure lowering efficacy than other classes
- Where compelling indications have been identified for prescribing specific classes of agents, indications should be equally applied to AAs
- AA appear to be at increased risk for ACE inhibitor associated angioedema, cough or both. Patients should be instructed to report symptoms

Source: Douglas, J. G. et al. Arch Intern Med 2003;163:525-541.

TABLE 2. CAUSES OF DEATH IN THE PREVENTION TRIAL.

CAUSE OF DEATH	BLACKS (N=404)		WHITES (N=3658)		P VALUE*
	NO. OF DEATHS (%)	INCIDENCE/ 100 PERSON-YR†	NO. OF DEATHS (%)	INCIDENCE/ 100 PERSON-YR†	
All causes	89 (22.0)	8.1	532 (14.5)	5.1	<0.001
Pump failure	29 (7.2)	2.6	157 (4.3)	1.5	0.003
Arrhythmia	22 (5.4)	2.0	176 (4.8)	1.7	0.40
Myocardial infarction	13 (3.2)	1.2	84 (2.3)	0.8	0.20
Stroke or pulmonary embolism	10 (2.5)	0.9	25 (0.7)	0.2	<0.001
Other	15 (3.7)	1.5	90 (2.5)	0.9	0.08

*Two-sided P values for the comparison between blacks and whites were derived with the log-rank statistic.

†The unadjusted incidence is expressed as the rate per 100 person-years of follow-up.

Dries DL, et al.

Source: Dries D.L. et al. NEJM 1999; 340: 609-616.

AHeFT

- 1050 patients with Class III or IV HF
- Primary endpoint:

  Compsite score of all cause mortality, hospitalizations for HF & change in QOL
- Study terminated early :

  10.2 % mortality in placebo vs 6.2% in BiDil gorup (p=0.02)

  43% reduction in all cause mortality (p=0.01)

  33% reduction in hospitalization for HF (p=0.0001)

  Significant improvement in QOL (p 0.02)

Race/Ethnicity and Genetics in Drug Response

- At least 29 medicines have been claimed to work differently among racial/ethnic groups
- While it is not clear how many of these differences are real, this suggests a potentially important issue in the use of prescription medicines

Race and Cardiovascular Drug Response

Drug Class	Examples	Difference in Drug Response
ACE inhibitor	Enalapril, Lisinopril, Trandolapril	Lesser / no response in AAs compared with CAs
A combination of two vasodilators (the antihypertensive hydralazine and isosorbide dinitrate)	BilDil	Greater efficacy in AAs than CAs with CHF
Vasodilator antihypertensive	Sodium nitroprusside	Attenuated response in normotensive AAs compared to CAs
Beta-adrenoceptor blocker	Propranolol, Nadolol, Atenolol, Oxprenolol	More effective in CAs than AAs
Vasopeptidase inhibitor	Omapatrilat	Increased risk of angioedemas in AAs than CAs
Anticoagulant	Danaparoid	Significantly more CAs had favourable outcome than AAs
Alpha-adrenoceptor blocker	Prazosin	More effective in CAs than AAs
Thiazide (diuretic)	Hydrochlorothiazide	Greater response in AAs than CAs
Calcium channel blocker	Diltiazem	More effective in AAs than CAs

Race and Drug Response – Others

Class	Name	Difference in Drug Response
Alpha(1)-adrenoceptor agonist	Phenylephrine	Increased response in AAs compared to CAs
Alpha(2)-adrenoceptor agonist	Clonidine	AAs have reduced hypotensive response compared to CAs
Beta-adrenoceptor agonist	Isoproterenol	Attenuated vasodilation and heart-rate increase, in normotensive AAs compared to CAs.
Immunosupressant	Tacrolimus, Cyclosporine	AAs require higher dose than CAs, and have poorer response, resp.
Glucocorticoid	Methylprednisolone	Adverse effects more common in AAs than CAs
HepC Antiviral treatment	Ribavirin, Interferon	Poorer response in AAs than CAs
Prostaglandin analogue	Travoprost	Response greater in AAs than CAs
Cytotoxic agents	1. 6-MP and methotrexate 2. Docetaxol and Carboplatin	1. Significant difference in response by ethnicity for childhood ALL, with Asians > CAs> Hispanics > AAs. 2. Greater response in Asians than CAs with advanced NSCLC
Insulin	Insulin	AAs and Hispanic children more resistant than CAs
Antipsychotic	1. Haloperidol 2. Clozapine	1. Hispanics require greater mean dose than CAs or AAs 2. AAs require greater mean dose than CAs

- Could average genetic differences among racial or ethnic groups contribute to differences in drug response?

- Consider 42 gene variants that have been implicated in drug responses. How many have important differences in frequency between African Americans and Americans of European ancestry?

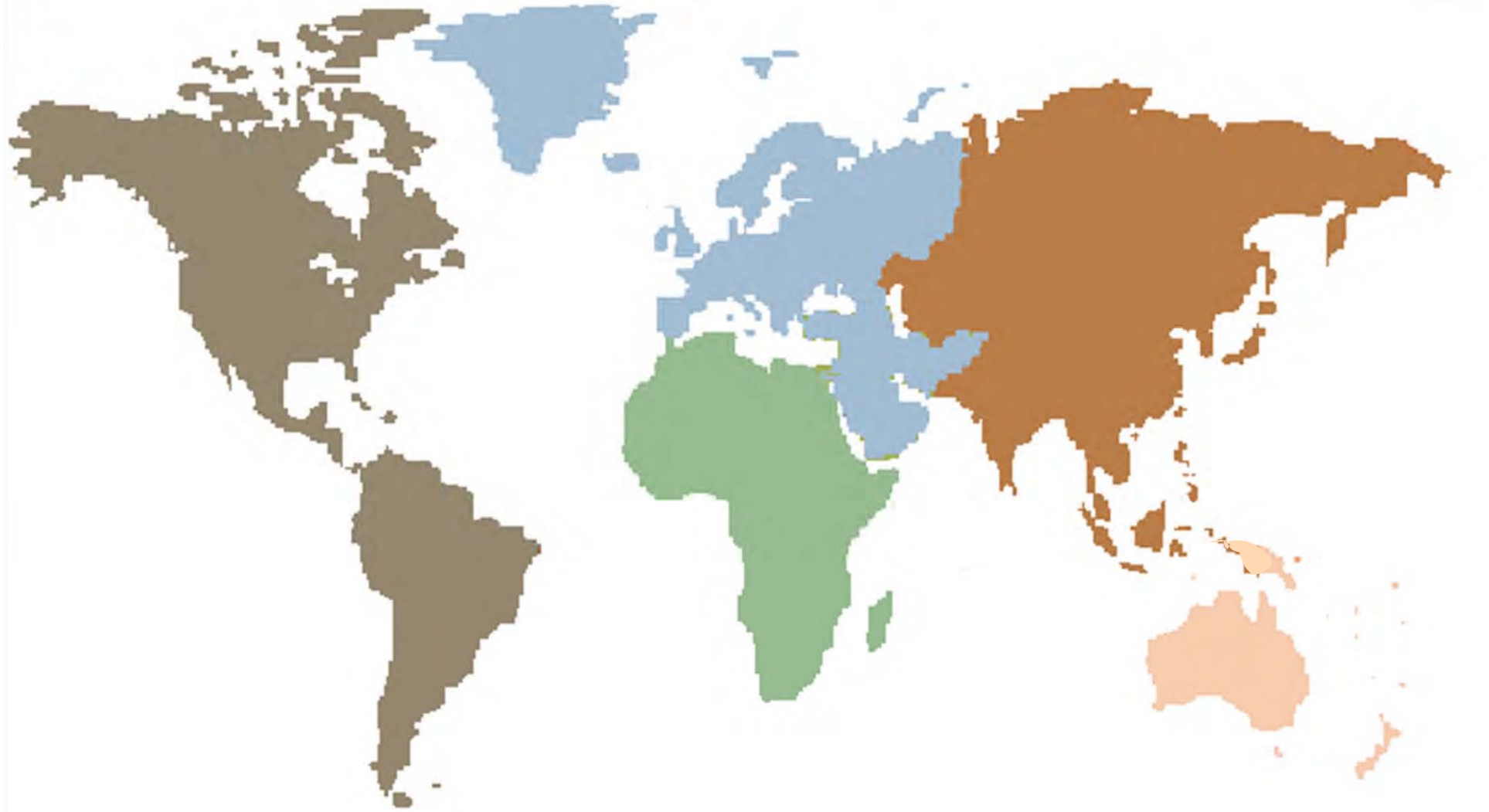
- Should race, ethnicity, or some other measure of group membership be used to guide treatment regimes?

Population Structure

- ***Ethnic or racial labeling*** uses racial labels to describe the structure of human genetic variation. Risch and colleagues (2002) propose five major racial groups based on continental ancestry. Whilst this method is easy to implement, it assumes a rather simplistic view of human genetic history.

- ***Explicit genetic inference*** ignores geographic, racial or ethnic labels and instead groups individuals using genetic data (e.g. Wilson et al 2001). However, such a scheme misses genetic variation *within* a group.

Current NIH Guidelines on Race

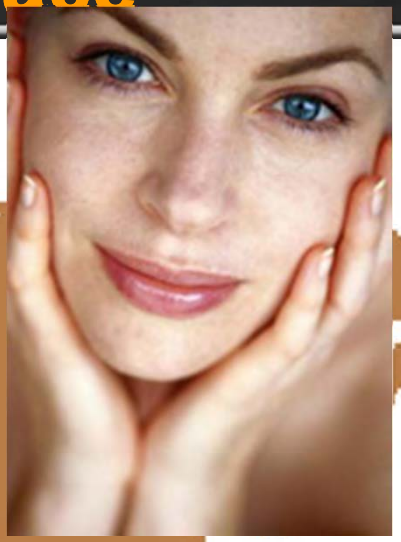


Current NIH Guidelines on Race

5 categories of race based on continental ancestry:

- African
- Caucasian (Europe and Middle East)
- Asian
- Pacific Islander
- Native American

Current NIH Guidelines on Race



Guidelines Ignore Variation Within Groups

e.g. African Bantu and San

What is wrong with using the five “races”?

- The scheme cannot represent the diversity within groups
- The scheme is unlikely to reflect the real pattern of global human diversity
  - The sample used that have been used to date are far from comprehensive and incomplete sampling may generate a false impression of discrete groups

The BEST Population

- 833 Caucasians and 207 African-Americans who entered a clinical trial for the non-selective beta-blocker bucindolol, for congestive heart failure
- Overall, only survival benefit for Caucasians
- Ask whether drug response is associated with the genetic ancestry of the individuals and if so, can this be explained by frequency differences of haplotypes or SNPs in the drug targets

ADRB2 Genetic Variation and Response to Bucindolol

ADRB2 SNP	Associated Phenotype	P Value
Upstream – 1023	Treatment success for G/A patients	0.00034
	Change in LVEF by genotype (A allele better response) for African-Americans	0.00723
Arg16Gly	Baseline LVEF by genotype for African-Americans (Gly higher),	0.00595
Gln27Glu	Treatment success for Gln/Glu patients	0.00046

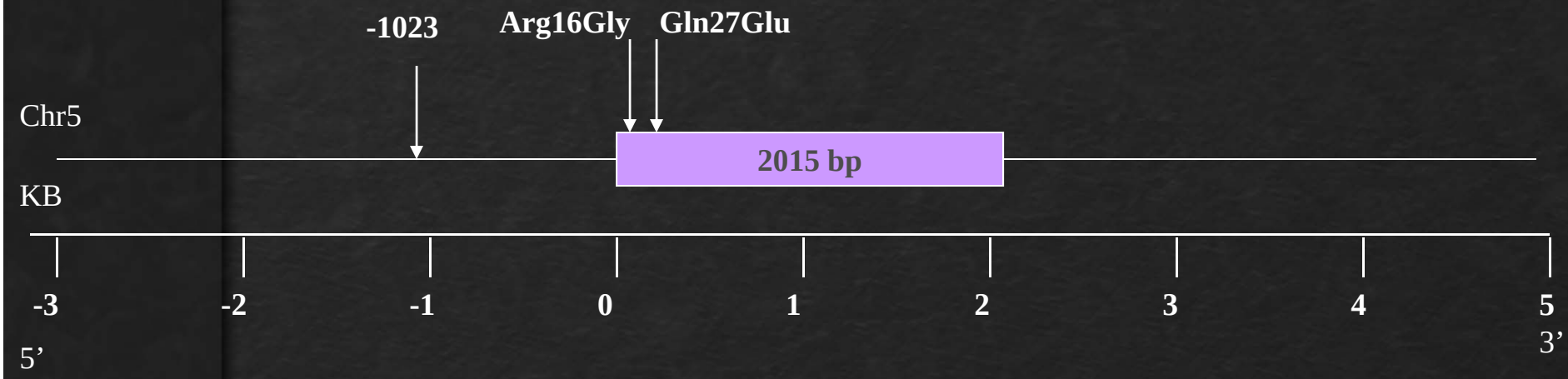
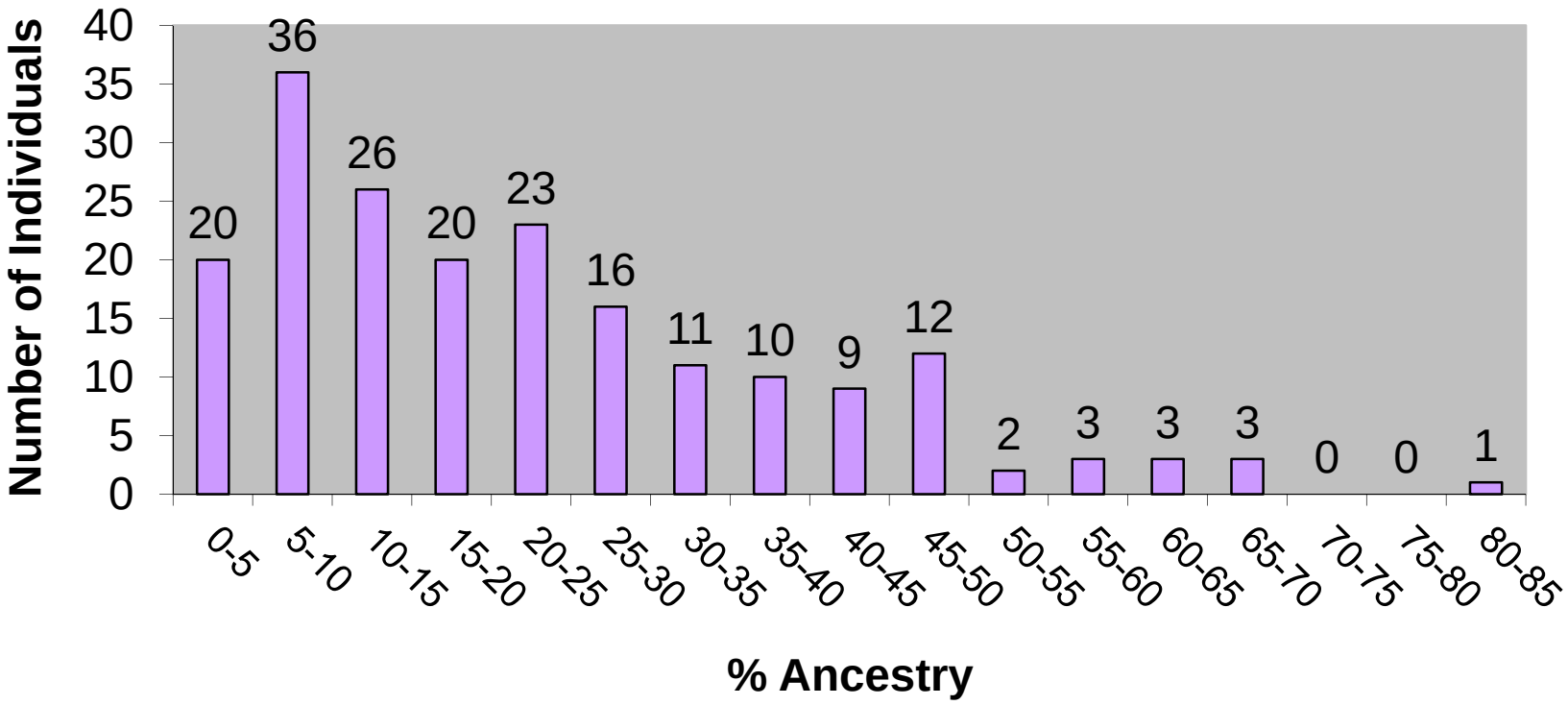
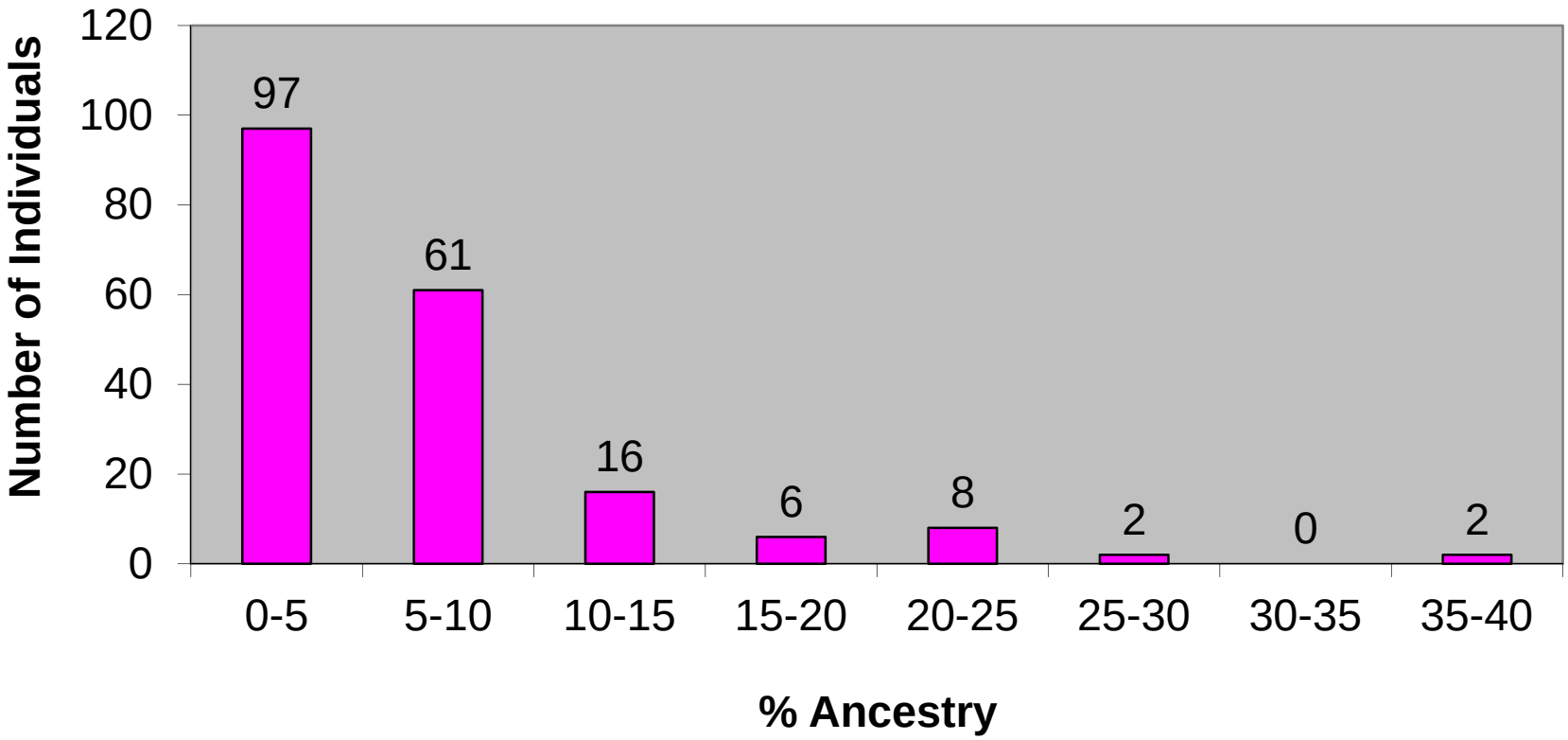


Fig 2. % European Ancestry for African-Americans



This figure shows that the African-Americans have a broad range of ancestry proportions indicating substantial genetic structure. This may be relevant to drug response

Fig 1. % African Ancestry for Caucasians



This figure demonstrates that there is little internal structure within the Caucasians.

PONDERING THE PROBLEM OF PONDEROUS PEOPLE

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OBESITY FACTS

- 65 % of U.S. adults over age 20 are overweight or obese.
- 30 % (60 million) are obese.
- Black female girls have highest prevalence: 37.6% overweight, 22.2% obese. Black adolescent girls 12-19 are 45.5% overweight, 26.6% obese.
- Mexican American boys 6-11: 43% overweight, 27.3% obese; adolescents 44.2% overweight, 27.5% obese.
- Californians have gained 360 million pounds in the last decade.

GENDER, RACE, AND OBESITY

- Black women 40-59: 58% obese.
- White women: 38% obese.
- Adult men: Whites and Blacks equally obese.

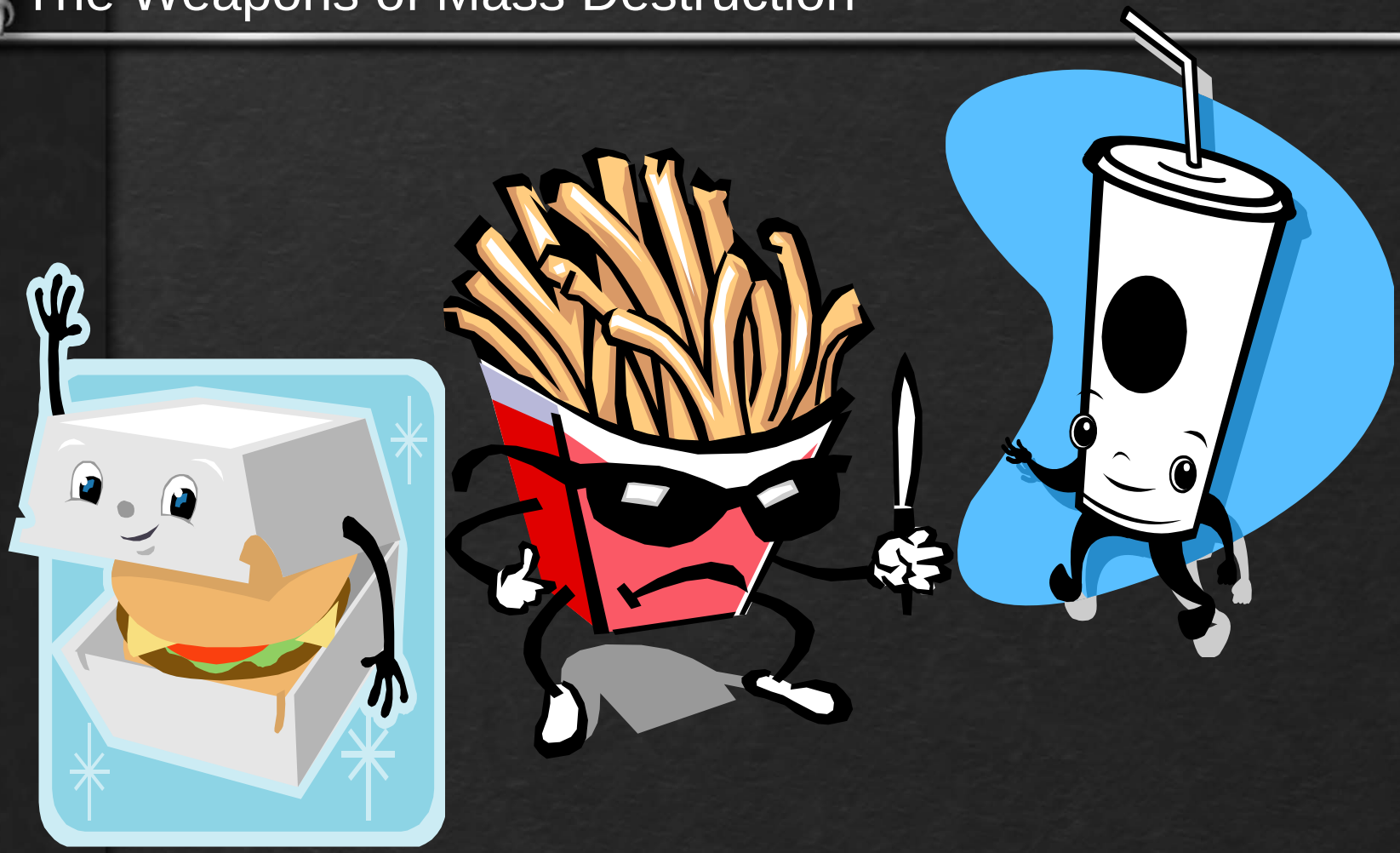
Other Effects of Adiposity

- Insulin resistance
- Dyslipidemia
- Low-grade inflammation
- Increased growth factor and hormone levels
- ACCELERATED AGING
- 30% caloric restriction prevents or retards chronic diseases and PROLONGS MAXIMAL LIFE SPAN (In lab animals)

Diseases Associated With Obesity

- Hypertension
- Dyslipedemia
- Diabetes
- Coronary heart disease
- Stroke
- Gallbladder disease
- Sleep apnea
- Cancer (endometrial, breast, colon)

The Weapons of Mass Destruction



Conclusions

1. Although Risch et al propose that racial groupings based on continental ancestry be used to represent population structure, real data from the BEST population, as seen in Fig 1., demonstrates that this classification is insufficient for African-Americans. African Americans are highly heterogeneous.

2. The ADRB2 upstream –1023 SNP is associated with change in left ventricular ejection fraction in the BEST African-Americans.

Implications

- Racial / ethnic groups are not homogeneous entities
- If there is association between drug response and race or ethnicity this is a pointer that individual (environmental or genetic) variables are important to drug response
- Identifying the individual determinants will also provide better diagnostic information than the group designation

Social Causes of Disparity

- Socioeconomics
- Limited access especially in rural areas
- Culture and trust
- Lack of diversity of healthcare providers
- Shortage of training of minority providers

Steps to be taken by Medical Institutions:

- Clear mission statement that recognizes the value of diversity
- Appoint URM to leadership position to influence change
- Articulate the vision for diversity to all levels
- Hold leaders accountable
- Institutional objectives must be consistent with the goal to increase diversity including efforts to ease financial and nonfinancial obstacles

Summary

- Biologic & Genetic factors
- Environmental factors
- Socioeconomic factors
- Access & Cost
- Practice Bias
- Lack of Diversity in Providers
- Need for Leadership and commitment