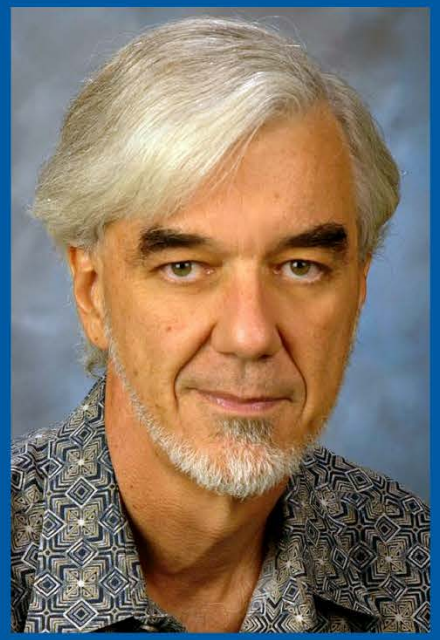
Lecture Series

2017
Genomics and Health Disparities

Exploring the Role of Genomics in Achieving Health Equity

Variation in Blood Pressure Across Populations – Chasing the Phantom of Race



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Variation in Blood Pressure across Populations – Chasing the Phantom of Race

Richard Cooper, MD
Public Health Sciences
Loyola University Medical School

Making use of transformative tools

. . and other

Faustian bargains for 21st Century scientists.

The complementary weakness of access to Big Data

is the temptation to engage in over-reach.

Including genomics in the pursuit of race.

Scientists threaten to boycott €1.2bn Human Brain Project

. . . it proved controversial from the start. Many researchers refused to join on the grounds that it was *far too premature to attempt a simulation of the entire human brain in a computer*. Now some claim the project is taking the wrong approach, wastes money and risks a backlash against neuroscience if it fails to deliver.

Guardian, May, 2014

Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016

*GBD 2016 Causes of Death Collaborators**

Summary

Background Monitoring levels and trends in premature mortality is crucial to understanding how societies can address prominent sources of early death. The Global Burden of Disease 2016 Study (GBD 2016) provides a comprehensive assessment of cause-specific mortality for 264 causes in 195 locations from 1980 to 2016. This assessment includes evaluation of the expected epidemiological transition with changes in development and where local patterns deviate from these trends.

Methods We estimated cause-specific deaths and years of life lost (YLLs) by age, sex, geography, and year. YLLs were calculated from the sum of each death multiplied by the standard life expectancy at each age. We used the GBD cause of death database composed of: vital registration (VR) data corrected for under-registration and garbage coding; national and subnational verbal autopsy (VA) studies corrected for garbage coding; and other sources including surveys and surveillance systems for specific causes such as maternal mortality. To facilitate assessment of quality, we reported on the fraction of deaths assigned to GBD Level 1 or Level 2 causes that cannot be underlying causes of death (major garbage codes) by location and year. Based on completeness, garbage coding, cause list detail, and time periods covered, we provided an overall data quality rating for each location with scores ranging from 0 stars (worst) to 5 stars (best). We used robust statistical methods including the Cause of Death Ensemble model (CODEm) to generate estimates for each location, year, age, and sex. We assessed observed and expected levels and trends of cause-specific deaths in relation to the Socio-demographic Index (SDI), a summary indicator derived from measures of average income per capita, educational attainment, and total fertility, with locations grouped into quintiles by SDI. Relative to GBD 2015, we expanded the GBD cause hierarchy by 18 causes of death for GBD 2016.

Lancet 2017; 390: 1151–210

*Collaborators listed at the end of the Article

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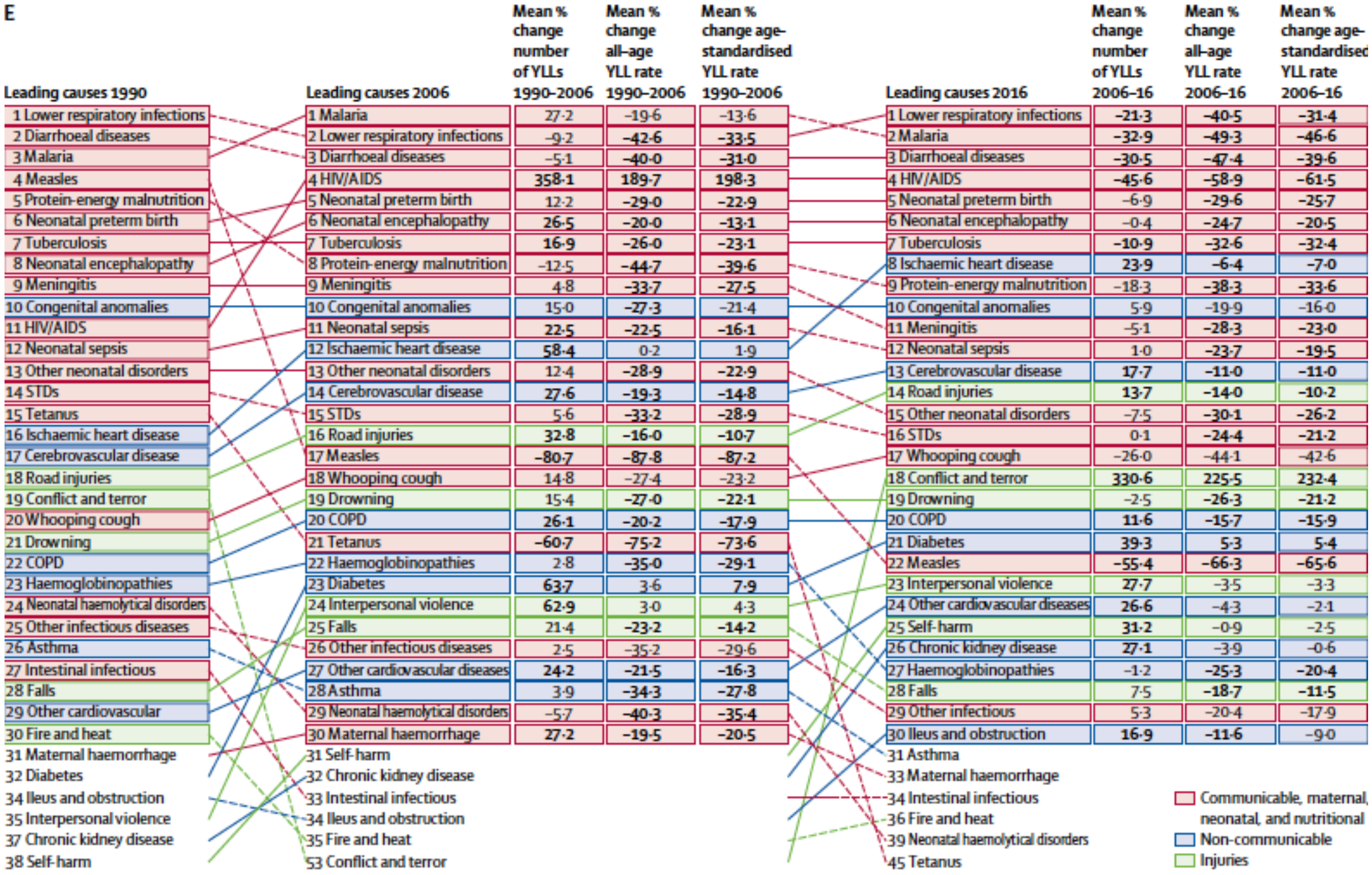
Leading causes 1990
1 Lower respiratory infections
2 Diarrhoeal diseases
3 Malaria
4 Measles
5 Protein-energy malnutrition
6 Neonatal preterm birth
7 Tuberculosis
8 Neonatal encephalopathy
9 Meningitis
10 Congenital anomalies
11 HIV/AIDS
12 Neonatal sepsis
13 Other neonatal disorders
14 STDs
15 Tetanus
16 Ischaemic heart disease
17 Cerebrovascular disease
18 Road injuries
19 Conflict and terror
20 Whooping cough
21 Drowning
22 COPD
23 Haemoglobinopathies
24 Neonatal haemolytical disorders
25 Other infectious diseases
26 Asthma
27 Intestinal infectious
28 Falls
29 Other cardiovascular
30 Fire and heat
31 Maternal haemorrhage
32 Diabetes
34 Ileus and obstruction
35 Interpersonal violence
37 Chronic kidney disease
38 Self-harm
Leading causes 2006
1 Malaria
2 Lower respiratory infections
3 Diarrhoeal diseases
4 HIV/AIDS
5 Neonatal preterm birth
6 Neonatal encephalopathy
7 Tuberculosis
8 Protein-energy malnutrition
9 Meningitis
10 Congenital anomalies
11 Neonatal sepsis
12 Ischaemic heart disease
13 Other neonatal disorders
14 Cerebrovascular disease
15 STDs
16 Road injuries
17 Measles
18 Whooping cough
19 Drowning
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21 Tetanus
22 Haemoglobinopathies
23 Diabetes
24 Interpersonal violence
25 Falls
26 Other infectious diseases
27 Other cardiovascular diseases
28 Asthma
29 Neonatal haemolytical disorders
30 Maternal haemorrhage
31 Self-harm
32 Chronic kidney disease
33 Intestinal infectious
34 Ileus and obstruction
35 Fire and heat
53 Conflict and terror
Mean % change number of YLLs 1990–2006
27·2
–9·2
–5·1
358·1
12·2
26·5
16·9
–12·5
4·8
15·0
22·5
58·4
12·4
27·6
5·6
32·8
–80·7
14·8
15·4
26·1
–60·7
2·8
63·7
62·9
21·4
2·5
24·2
3·9
–5·7
27·2
Mean % change all-age YLL rate 1990–2006
–19·6
–42·6
–40·0
189·7
–29·0
–20·0
–26·0
–44·7
–33·7
–27·3
–22·5
0·2
–28·9
–19·3
–33·2
–16·0
–87·8
–27·4
–27·0
–20·2
–75·2
–35·0
3·6
3·0
–23·2
–35·2
–21·5
–34·3
–40·3
–19·5
Mean % change age-standardised YLL rate 1990–2006
–13·6
–33·5
–31·0
198·3
–22·9
–13·1
–23·1
–39·6
–27·5
–21·4
–16·1
1·9
–22·9
–14·8
–28·9
–10·7
–87·2
–23·2
–22·1
–17·9
–73·6
–29·1
7·9
4·3
–14·2
–29·6
–16·3
–27·8
–35·4
–20·5
Leading causes 2016
1 Lower respiratory infections
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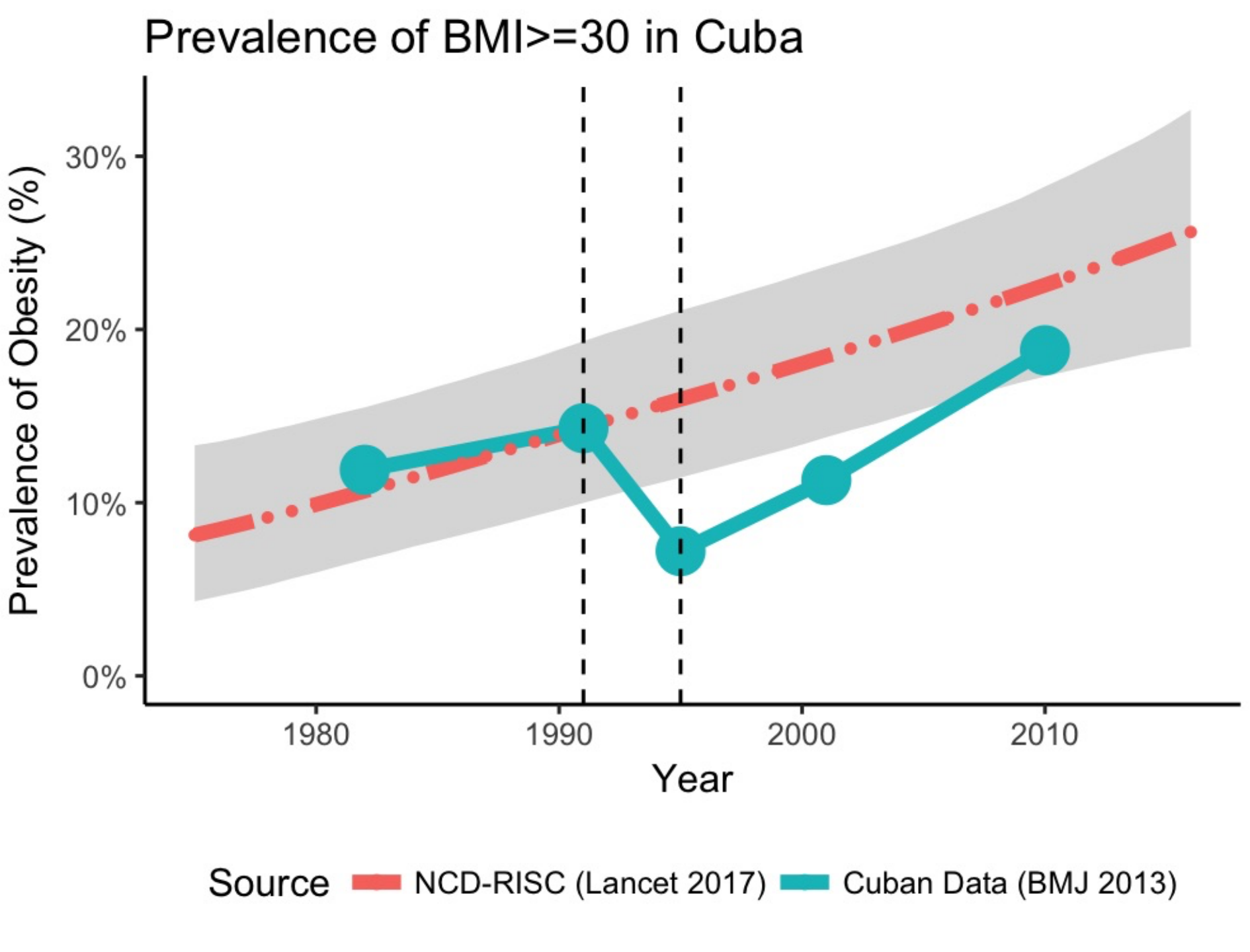
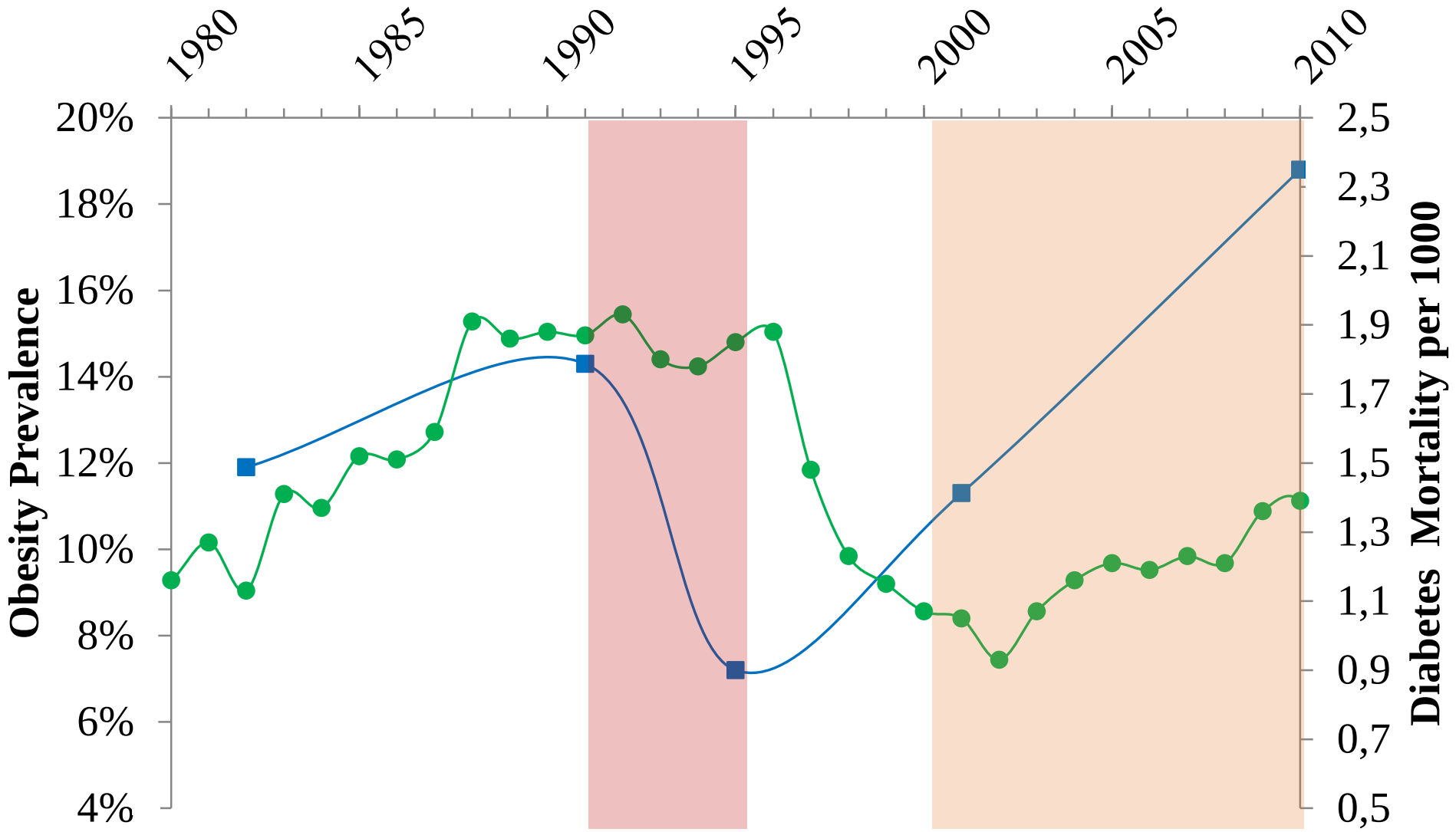
28 Falls
29 Other infectious
30 Ileus and obstruction
31 Asthma
33 Maternal haemorrhage
34 Intestinal infectious
36 Fire and heat
39 Neonatal haemolytical disorders
45 Tetanus
Mean % change number of YLLs 2006–16
–21·3
–32·9
–30·5
–45·6
–6·9
–0·4
–10·9
23·9
–18·3
5·9
–5·1
1·0
17·7
13·7
–7·5
0·1
–26·0
330·6
–2·5
11·6
39·3
–55·4
27·7
26·6
31·2
27·1
–1·2
7·5
5·3
16·9
Mean % change all-age YLL rate 2006–16
–40·5
–49·3
–47·4
–58·9
–29·6
–24·7
–32·6
–6·4
–38·3
–19·9
–28·3
–23·7
–11·0
–14·0
–30·1
–24·4
–44·1
225·5
–26·3
–15·7
5·3
–66·3
–3·5
–4·3
–0·9
–3·9
–25·3
–18·7
–20·4
–11·6
Mean % change age-standardised YLL rate 2006–16
–31·4
–46·6
–39·6
–61·5
–25·7
–20·5
–32·4
–7·0
–33·6
–16·0
–23·0
–19·5
–11·0
–10·2
–26·2
–21·2
–42·6
232·4
–21·2
–15·9
5·4
–65·6
–3·3
–2·1
–2·5
–0·6
–20·4
–11·5
–17·9
–9·0
Communicable, maternal, neonatal, and nutritional
Non-communicable
Injuries


Prevalence of BMI>=30 in Cuba
Prevalence of Obesity (%)
30%
20%
10%
0%
1980
1990
2000
2010
Year
Source
NCD-RISC (Lancet 2017)
Cuban Data (BMJ 2013)

Obesity and Mortality from Diabetes in Cuba



BMJ 2013

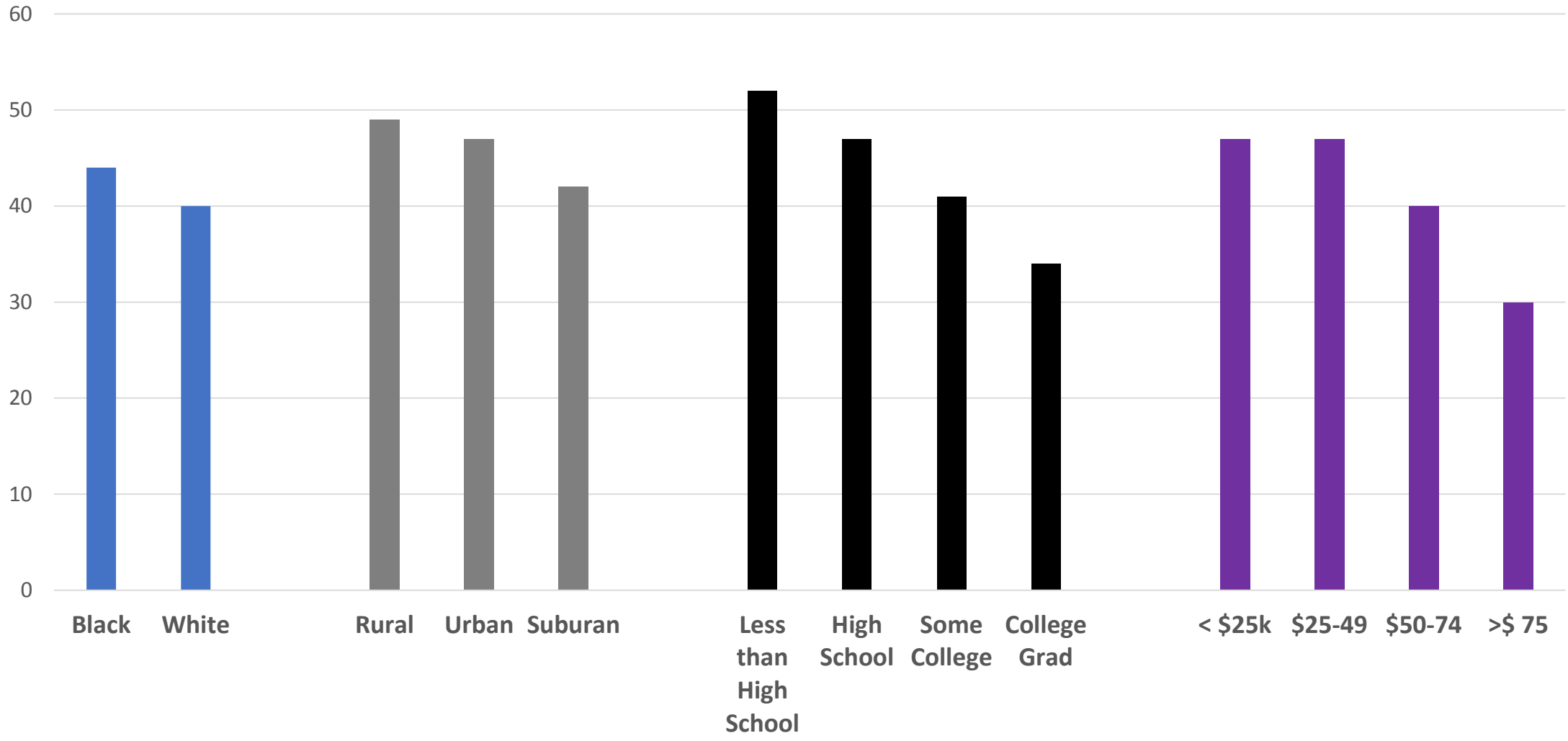
“Recent successes in programming machines to mine complex data to derive the fundamental laws of motion perhaps represent a glimpse into the future of biology, in which machines may be able to *derive fundamental rules in complex living systems,* given large-scale data sets.”

Schadt EE. Molecular networks as sensors and drivers of complex diseases. Nature 2009;46:218-226.

UAMS®

For a Better State of Health

Hypertension by Demographic Group, Arkansas, 2016; BRFS



358 U.S. 27

3 L.Ed.2d 1

John AARON et al., petitioners,
v.
William G. COOPER et al.

No. 1, Misc.

Supreme Court of the United States

August 28, 1958

Having considered the oral arguments, the Court is in agreement with the view expressed by counsel for the respective parties and by the Solicitor General that petitioners' present application respecting the stay of the mandate of the Court of Appeals and of the order of the District Court of June 21, 1958, necessarily involves consideration of the merits of the Court of Appeals decision reversing the order of Judge Lemley. **The Court is advised that the opening date of the High School will be September 15.** In light of this, and representations made by counsel for the School Board as to the Board's plan for filing its petition for certiorari, the Court makes the following order:

“I very early got the idea that what I was going to do was prove to the world the Negroes were just like other people.”

W. E. DuBois

Health Status Measures in US Racial/Ethnic Groups, 2014

Cause of Death	*White*		*Black*	*Hispanic*	*Asian*
	[Age – Adjusted Death Rates]				
All Causes	742.8	<	870.7	523.3	390.5
Heart Disease	165.5	<	203.1	113.9	85.0
Coronary Heart Disease	101.2	<	114.8	75.3	55.3
Stroke	35.4	<	50.9	30.2	28.5
Cancer	170.9	<	194.2	115.2	102.6
COPD	41.8	>	24.7	15.6	10.4
Pneumonia / Influenza	15.1	<	16.3	12.8	12.9
Diabetes mellitus	18.6	<	38.2	25.1	15.1
HIV infection	0.9	<	8.6	2.0	0.3
Infant Mortality (/1000)	5.1	<	11.1	5.0	4.1
Life Expectancy at Birth	78.9	>	75.1	81.6	85?

Data Source Age-Adjusted Rates: CDC Wonder, Hispanic includes All Races

Date Source Infant Mortality: NCHS, NVSR, Vol 64, Number 9

Date Source Life Expectancy at birth: Health United States 2014, Table 16

Health disparities in the US by race . .

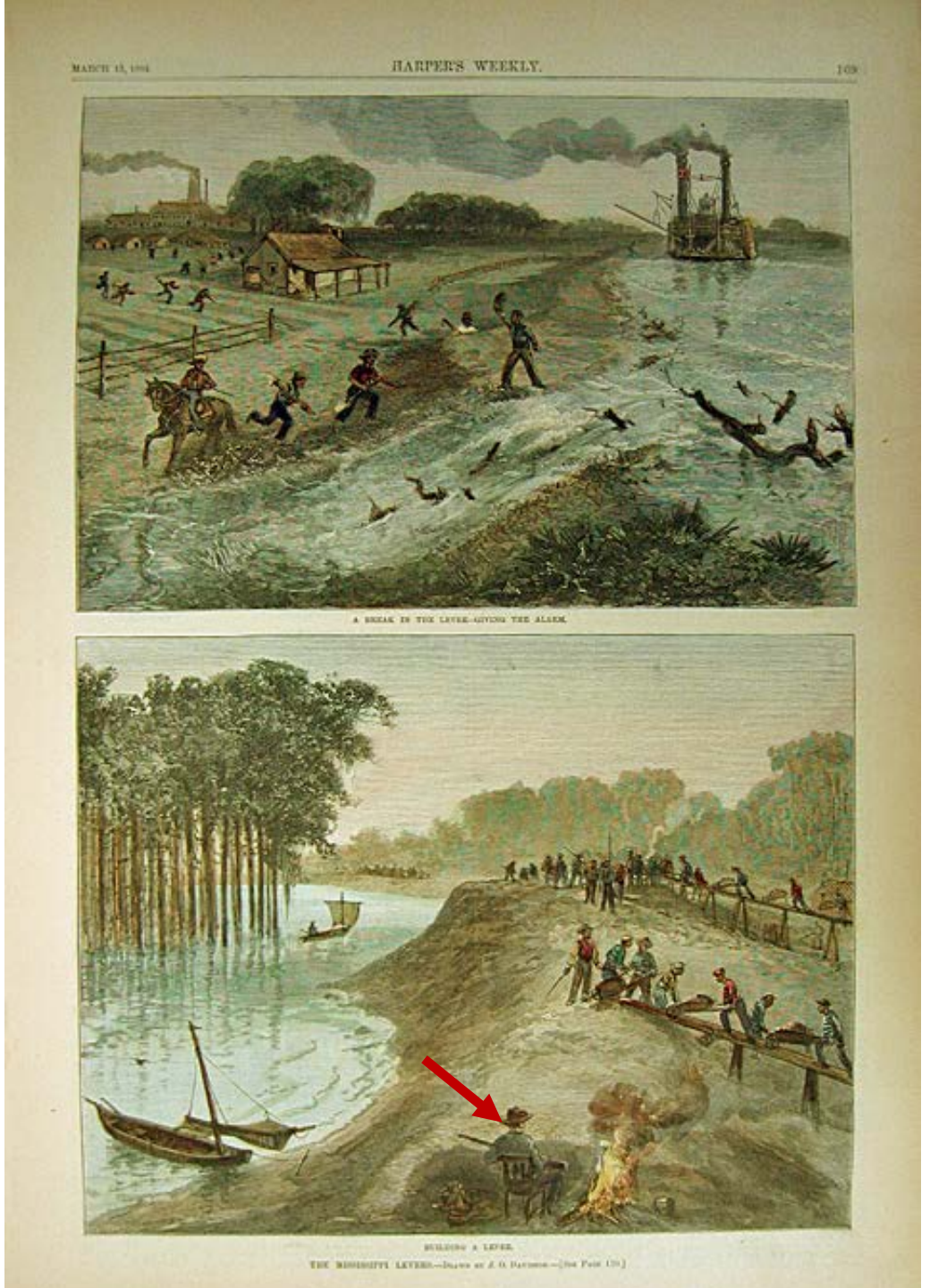
are rooted in structural inequality - unequal educational opportunity, occupation/wages, housing, etc.

Racial inequality is a result of widespread belief in the inferiority of "minority" groups, which allows employers and politicians to use racism for *economic* and – eg, "super-exploitation" (ie, low wages) –

and *political* advantage – engendering false allegiance to the power structure among white workers through white nationalism.

The Great Mississippi

Flood of 1927



Cooper R. Blacks and hypertension: A theoretical exploration. Urban Health 1975;4:9-12.

“…Hypertension has been found to exist more often among our American Negroes. . . The frequency of hypertension in a given population ... (is determined by)... the frequency in that population of a hypertensive gene. . .

I used to ask my medical friends about the situation in West Africa as to the prevalence of hypertension in the jungle. . “

Paul Dudley White, 1968

“Blood pressure seems to be higher among African, American, Caribbean and other black populations at the same level of sodium intake...(and this)... difference is likely to be genetically determined.”

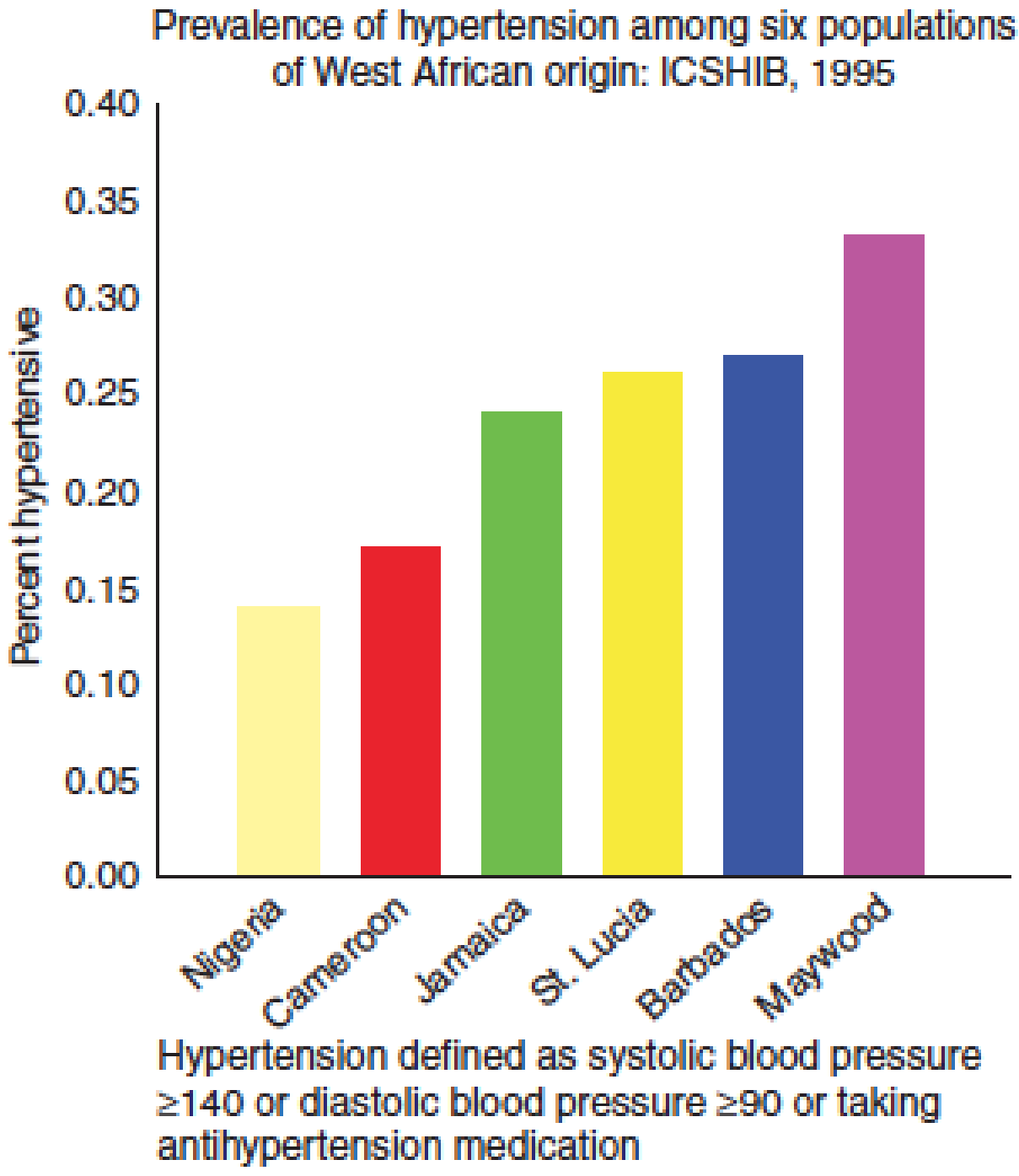
Law, et al. BMJ, 1991

International Collaborative Study of Hypertension in Blacks (ICSHIB)

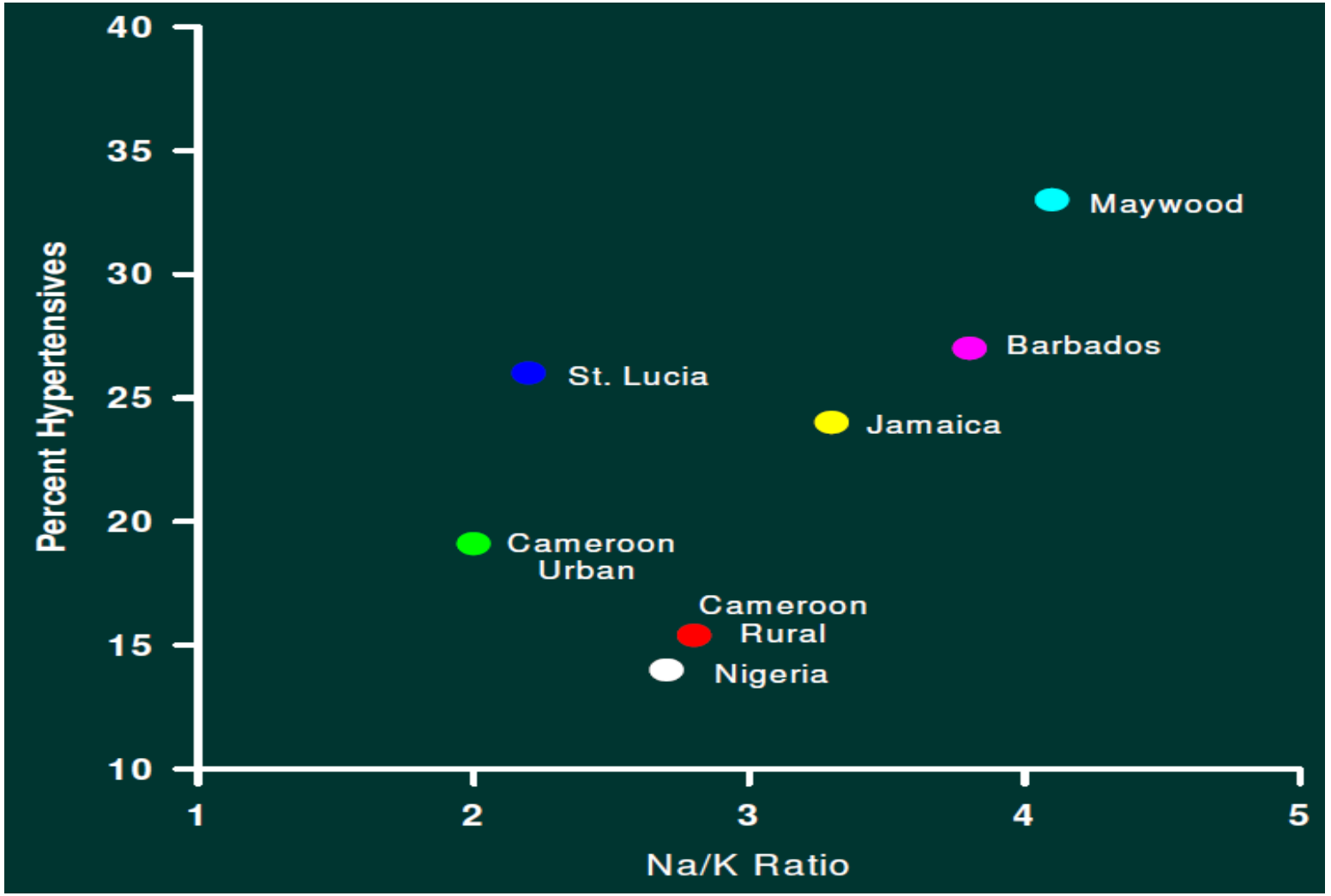
Africa **- Nigeria Cameroon**
Caribbean **- Jamaica Barbados St. Lucia**
United States **(Maywood/Chicago)**
United Kingdom **(Manchester)**

12,000 individuals examined 1992 - 1995

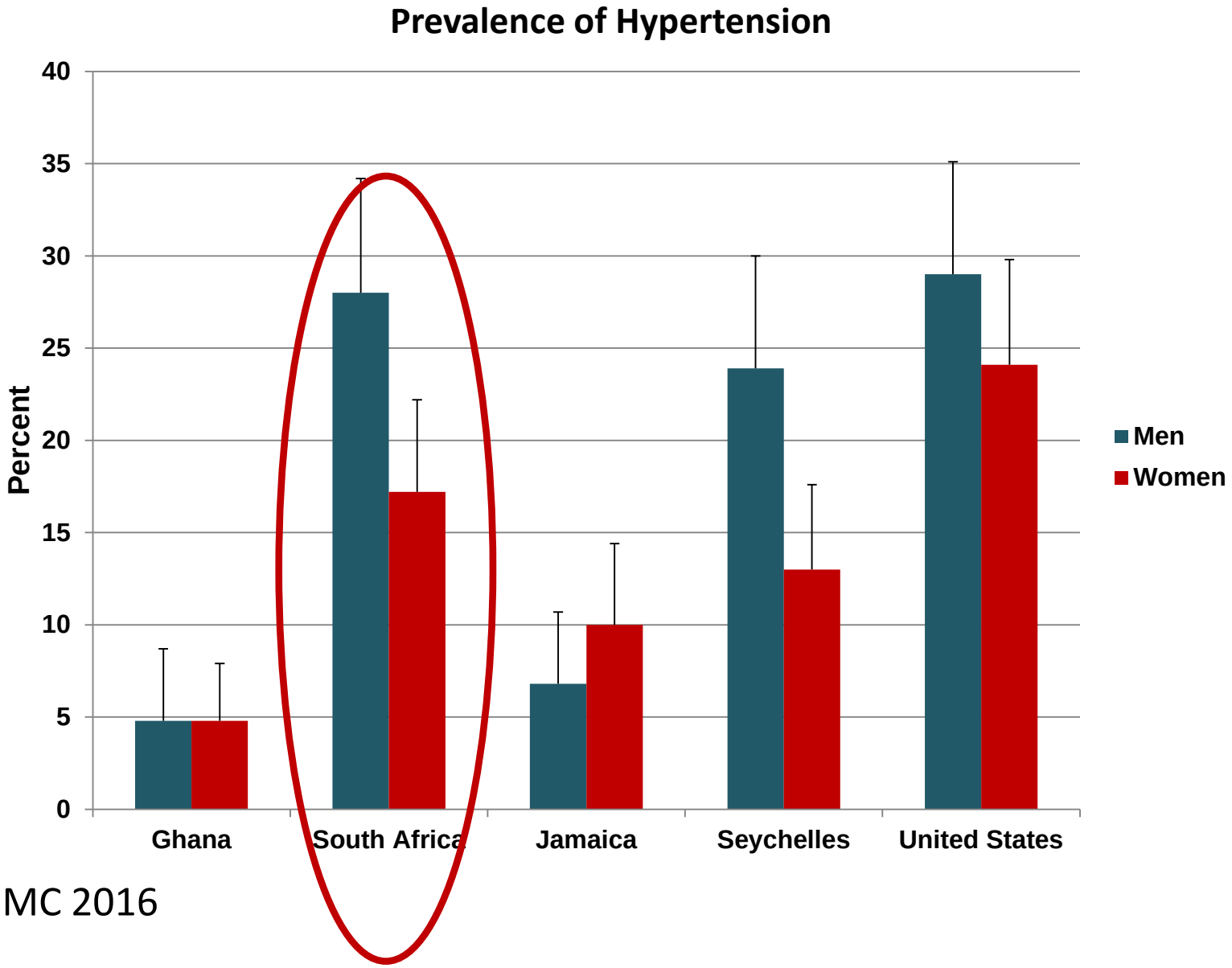
ICSHIB Investigators Meeting, Ibadan, Nigeria, 1993


Prevalence of hypertension among six populations of West African origin: ICSHIB, 1995
Percent hypertensive
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Nigeria
Cameroon
Jamaica
St. Lucia
Barbados
Maywood
Hypertension defined as systolic blood pressure ≥140 or diastolic blood pressure ≥90 or taking antihypertension medication

Prevalence of Hypertension by Na/K Ratio Among Seven Populations of West African Origin

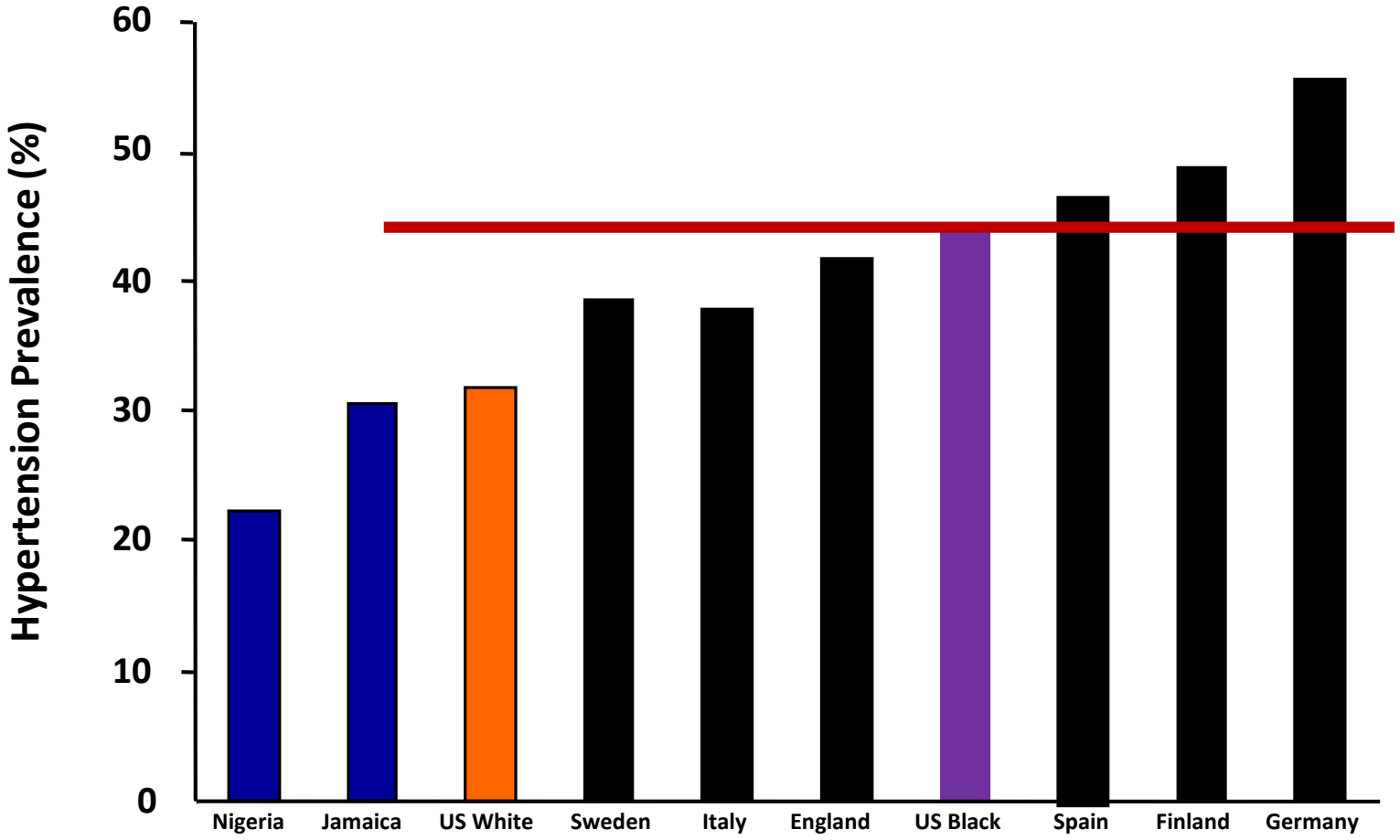


Hypertension Burden in METS, 2009-2011



Cooper et al BMC 2016

Age- and Gender- Adjusted Hypertension Prevalence, by Country and Race, 1990's

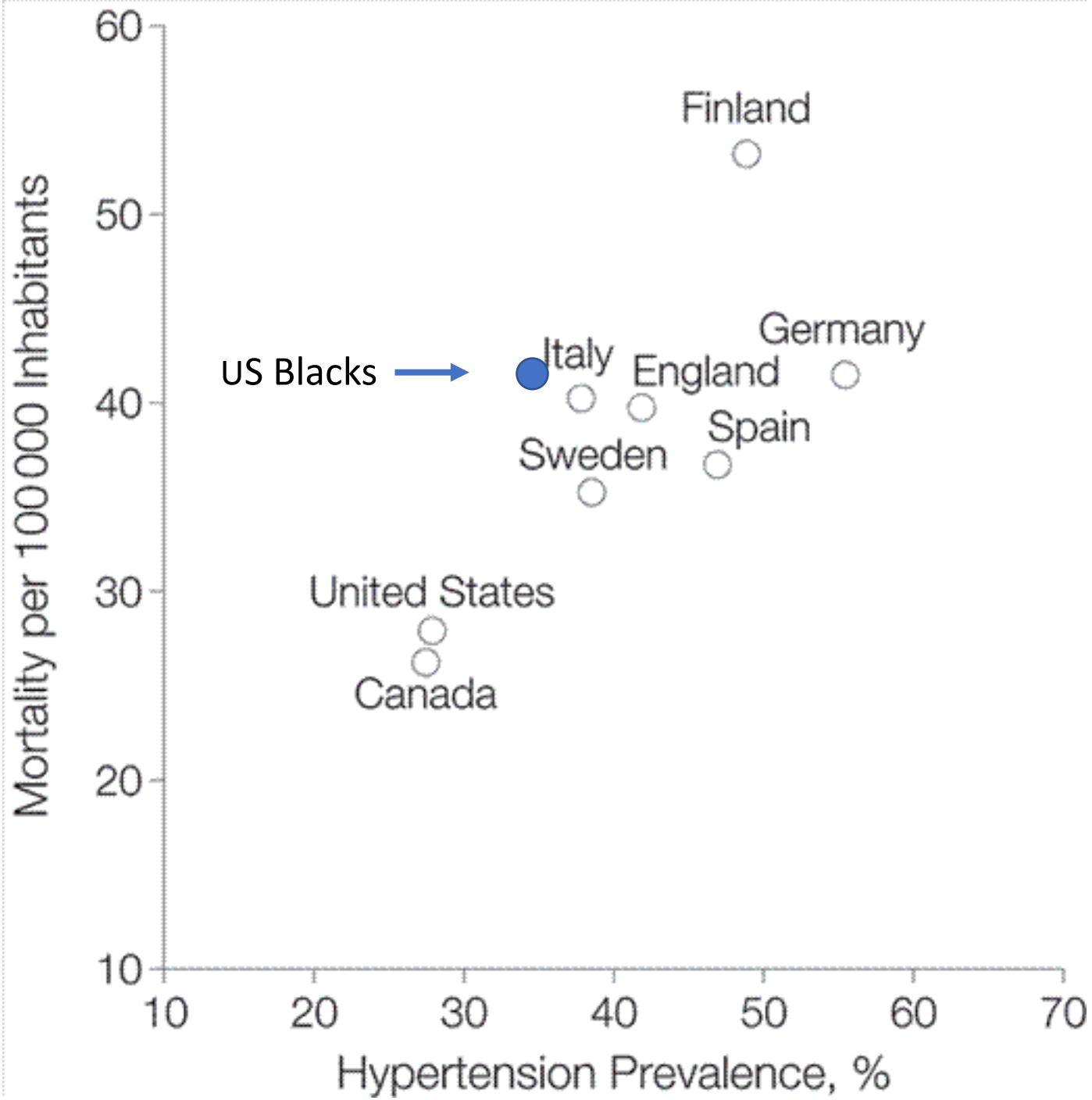


*Ages 35-64

Cooper et al, BMC, 2005

Hypertension Prevalence and Stroke Mortality

JAMA Wolf-Maier et al 2003



Systolic Blood Pressure in Finns and U.S. Blacks

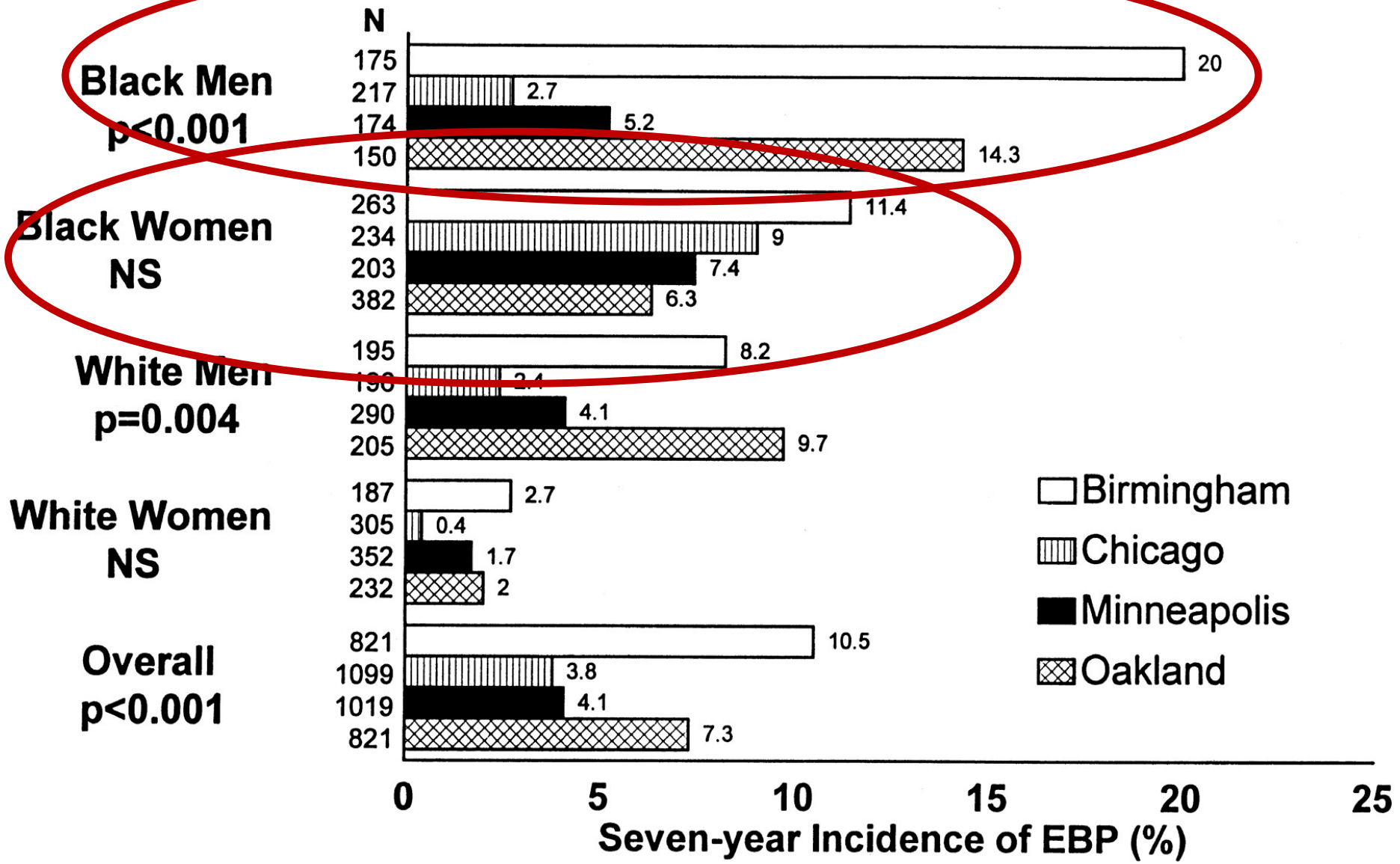
(Ages 30 – 59)

	Finland[1]	US Blacks[2]
Men	144	127
Women	138	120

[1]North Karelia, 1988: Varitiainen, et al. Int J. Epidemiol 1991:20;1961

[2]Maywood IL, 1992: Cooper et al.; Am J Public Health 1997

Elevated BP 7-year incidence, CARDIA Study, 1985-1993.

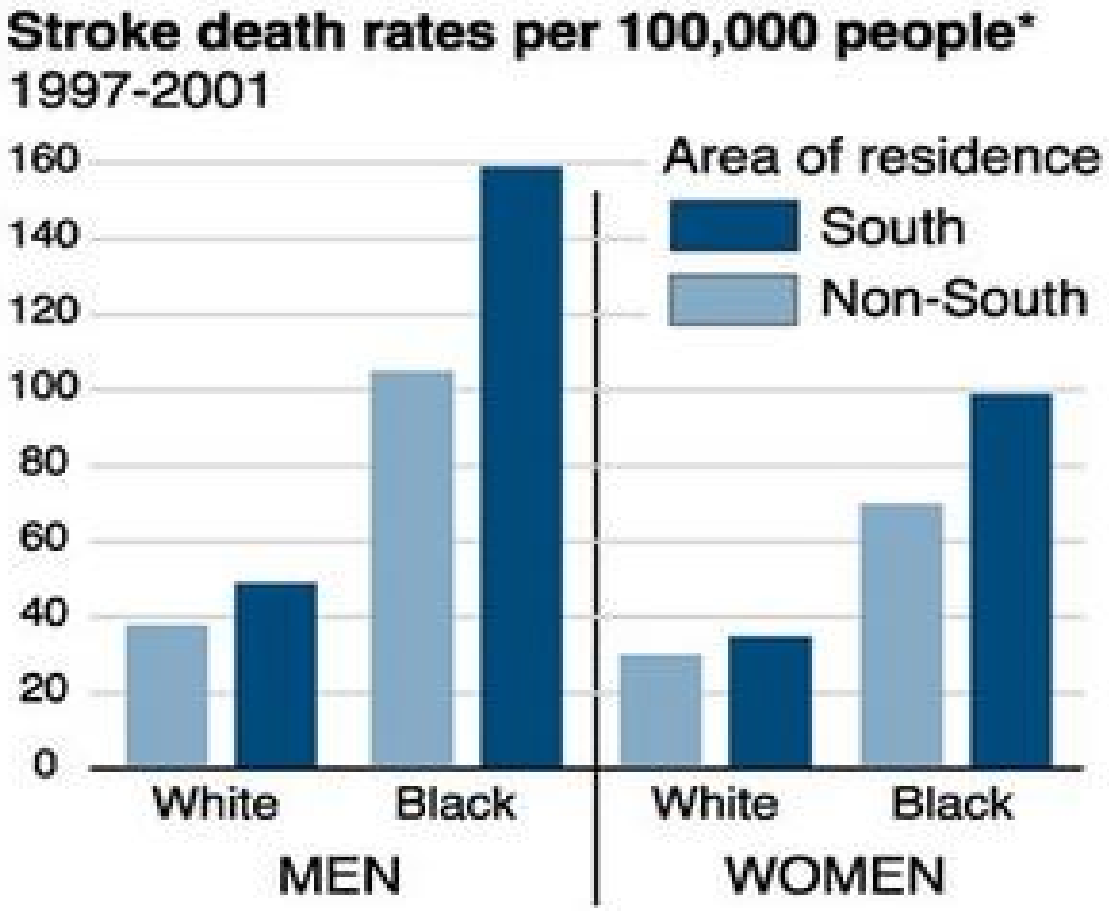


Catarina I. Kiefe et al. Circulation. 1997;96:1082-1088

Stroke death rate higher in South

Blacks in the South have a higher risk of dying from a stroke than white Southerners or blacks living elsewhere.

*Ages 55-64



SOURCE: National Center for Health Statistics

AP

Dietary and Urinary Metabonomic Factors Possibly Accounting for Higher Blood Pressure of African-Americans Compared to White Americans – – The INTERMAP Study

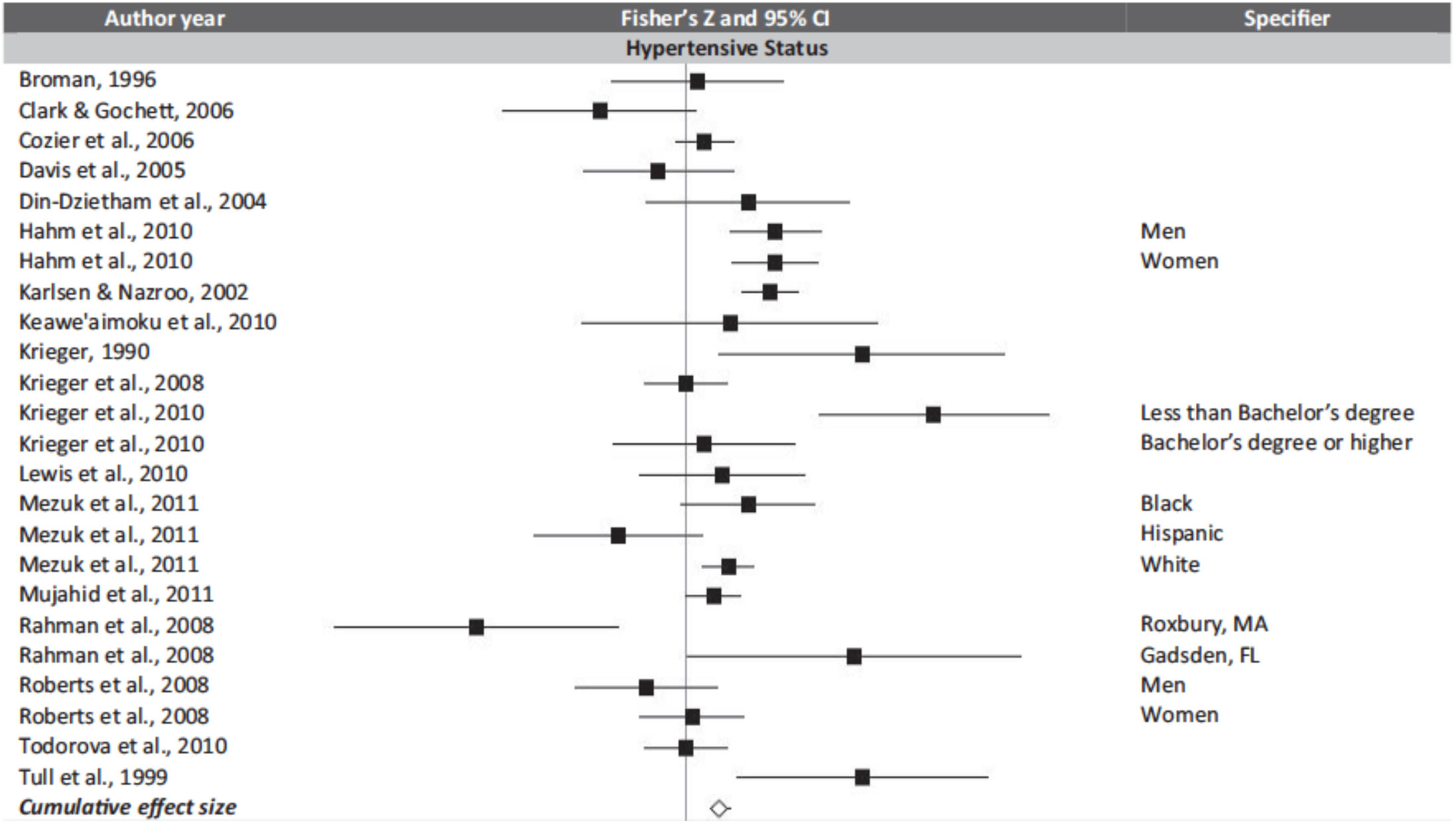
African American intake of multiple foods, nutrients related to blood pressure was less favorable - - less vegetables, fruits, grains, vegetable protein, glutamic acid, starch, fiber, minerals, potassium; more processed meats, pork, eggs, sugar-sweetened beverages, cholesterol, higher sodium to potassium ratio. Control for 11 nutrient and 10 non-nutrient correlates reduced higher African-American systolic/diastolic pressure to 2.3/2.3 mm Hg (52% and 33% reduction) (men) and to 5.3/2.8 mm Hg (21% and 27% reduction) (women).

Stamler, et al. Hypertension, 2013

“If you have negative biases toward people of color you are not a bad person – you are a normal American.”

David Williams
New York Times

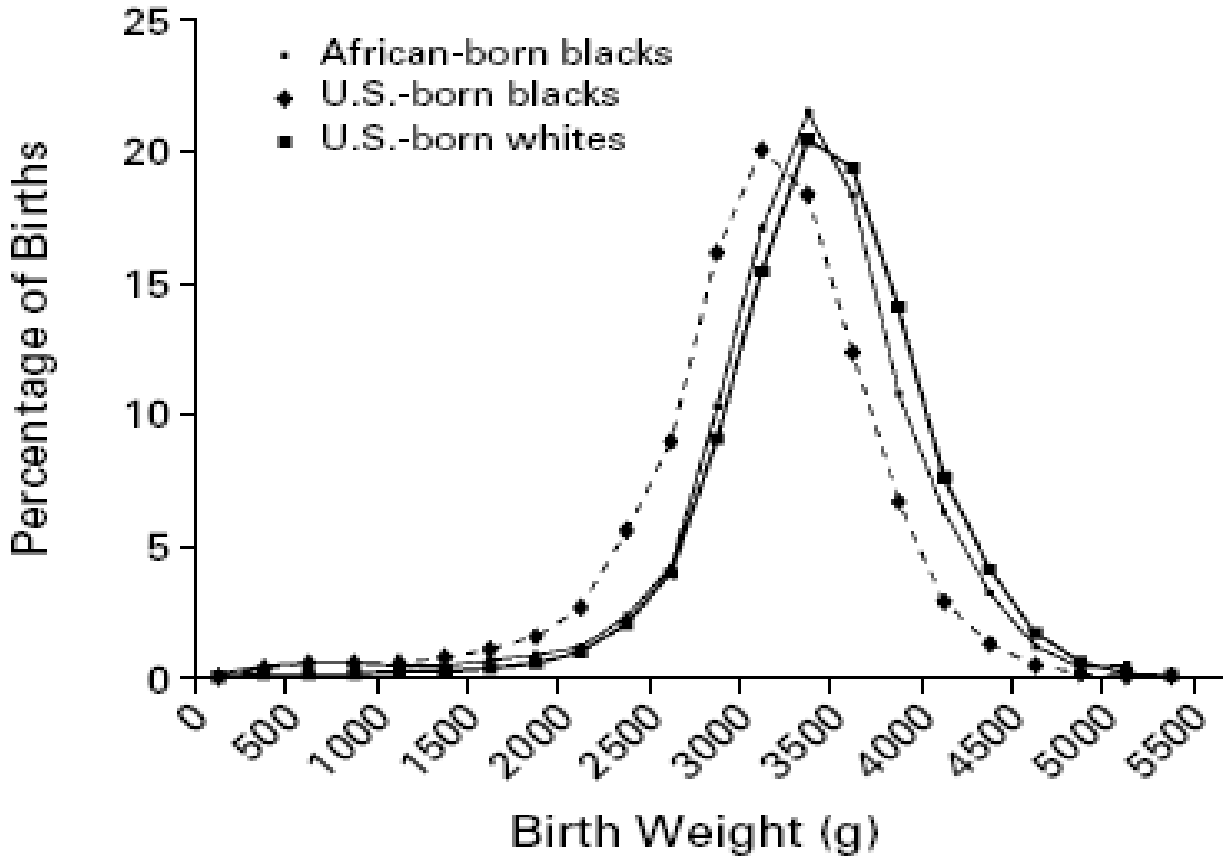
Perceived Racism and Hypertension in Blacks; Meta-analysis



Non-US Born Populations of the African Diaspora

DIFFERING BIRTH WEIGHT AMONG INFANTS OF U.S.-BORN BLACKS, AFRICAN-BORN BLACKS, AND U.S.-BORN WHITES

RICHARD J. DAVID, M.D., AND JAMES W. COLLINS, JR., M.D., M.P.H.



NEJM 1997

Figure 1. Distribution of Birth Weights among Infants of U.S.-Born White and Black Women and African-Born Black Women in Illinois, 1980–1995.

Hypertension among Blacks and Non-Blacks in Latin America, the Caribbean and the US

Country	Rate Ratio, Black: Non-Black Men	Women
Brazil	1.16	1.49
Trinidad	1.32	1.02
Cuba – 1	1.17	1.04
Cuba - 2	0.99	1.61

Average	Men	Women	Both Sexes
Non-US	**1.2**	**1.3**	**1.2**
US	**1.4**	**1.8**	**1.6**

Socioeconomic Position, But Not African Genomic Ancestry, Is Associated With Blood Pressure in the Bambui-Epigen (Brazil) Cohort Study of Aging

Characteristics	Total (n=1272)	African Ancestry Proportion in Quintiles: Lowest (<4.2%; n=253)	Intermediate* (4.3%–19.7%; n=764)	Highest (≥19.8%; n=255)
Sociodemographic and health indicators				
Age, y, mean (SD)	68.8 (6.9)	69.9 (7.3)	68.7 (6.8)	68.2 (6.5)†
Women, %	61.2	57.3	61.1	65.1
<4 y of schooling, %	63.4	45.1	64.7	77.7‡
Monthly household income per capita <USD 180.00, %	46.7	37.9	46.7	55.3‡
Blood pressure and related measures				
Systolic blood pressure (SBP), mm Hg, mean (SD)	137.6 (22.3)	139.5 (21.2)	136.5 (21.7)	139.2 (25.0)
Diastolic blood pressure (DBP), mm Hg, mean (SD)	83.5 (12.6)	84.6 (12.4)	82.7 (12.4)	84.8 (13.3)†
Current use of antihypertensive drugs, %	48.9	54.6	46.6	50.2
Controlled hypertension among treated, # %	46.1	44.2	48.9	40.6

Lima-Costa, Circ, 2016

Canadian Health Survey, 2009

Table 3
Binary logistic regression models on the presence of hypertension.

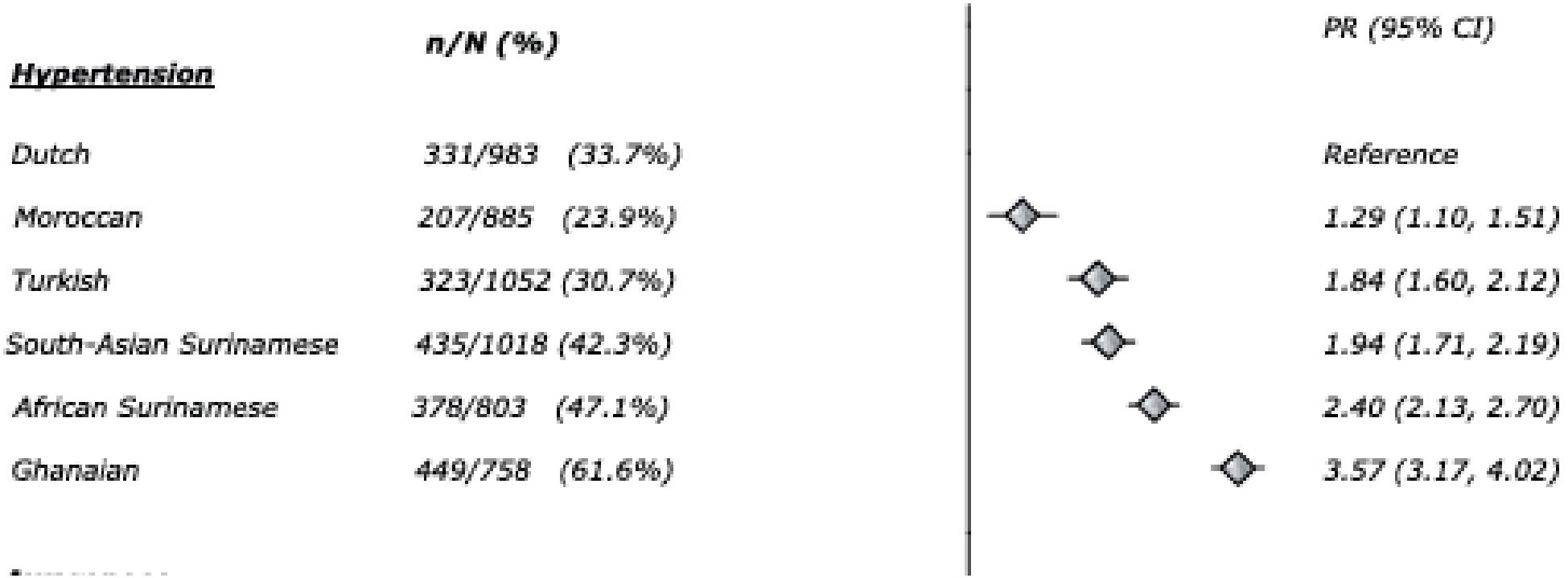
	Model I	Model II	Model III	Model IV
	OR	OR	OR	OR
Racial/cultural identification				
Aboriginal	1.327*	1.324*	1.203	1.248
Aboriginal/White	1.009	1.006	0.971	0.981
Black	1.558**	1.587**	1.503*	1.453*
Chinese	1.037	1.093	1.084	1.109
Filipino	1.727**	1.833**	1.867**	1.872**
Latin American	1.015	1.060	1.018	1.009
South Asian	1.148	1.231	1.219	1.211
White (reference)	1.000	1.000	1.000	1.000

Veenstra, et al Racialized identity and health in Canada. Soc Scie Med 2009

Hypertension control in a large multi-ethnic cohort in Amsterdam, The Netherlands: The HELIUS study

Charles Agyemang [a,*], Suzanne Kieft [a], Marieke B. Snijder [a], Erik J. Beune [a], Bert-Jan van den Born [b], Lizzy M. Brewster [b], Joanne J. Ujcic-Voortman [c], Navin Bindraban [d], Gert van Montfrans [b], Ron J. Peters [d], Karien Stronks [a]

A) *Prevalence ratios of hypertension, awareness, treatment, and control ethnic group in men*



Int J Cardiol 2015

Panethnic Differences in Blood Pressure in Europe

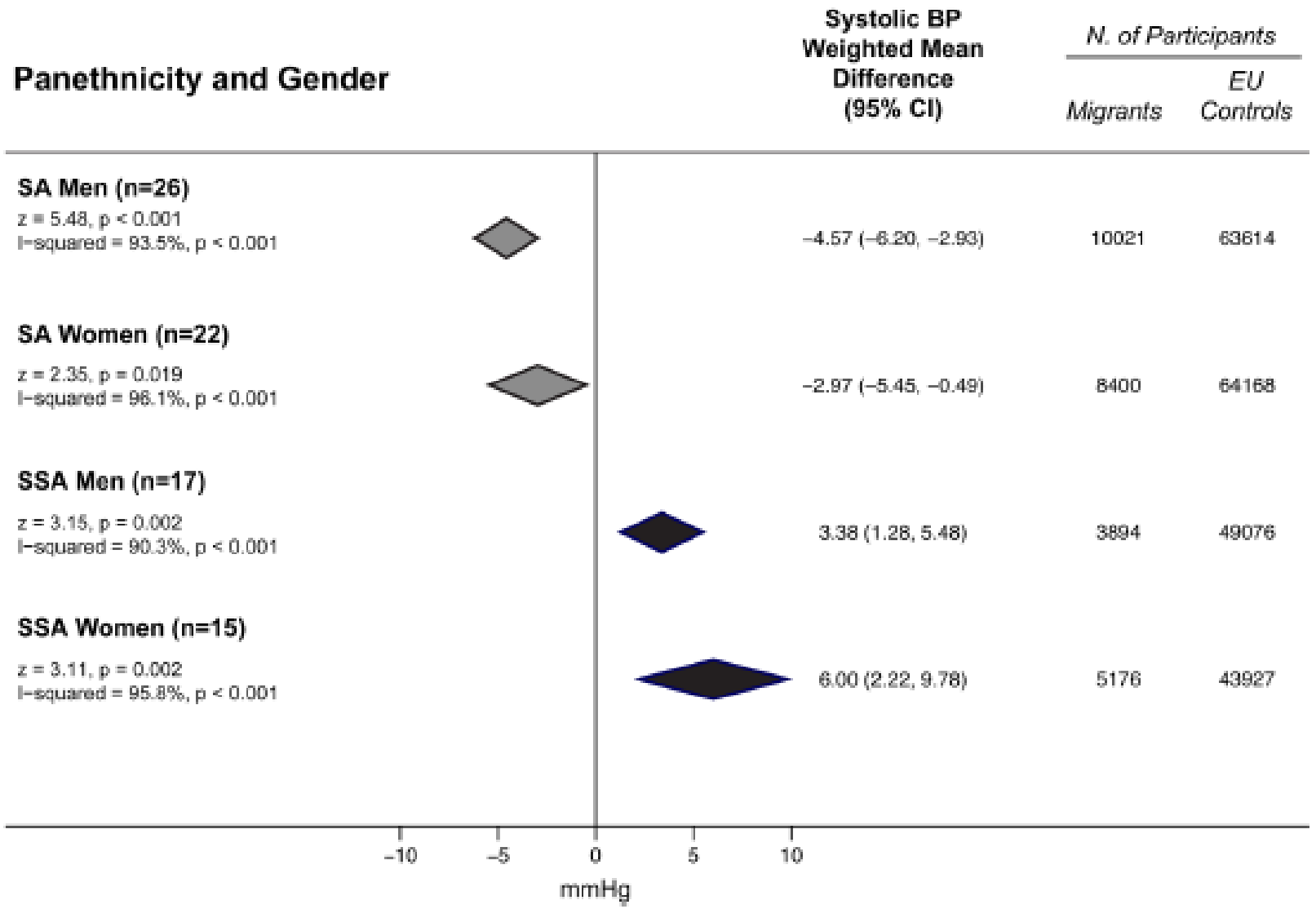


Fig 2. SBP differences between minority groups and EU participants by panethnicity and gender. Subgroup comparisons of the weighted mean difference of systolic blood pressure (BP) between minority groups and EU participants by panethnicity and gender. Diamonds denote the pooled estimates and 95% confidence intervals. SSA = Sub-Saharan Africans; SA = South Asians; EU = Europeans, "n" is the number of comparisons available for each subgroup.

doi:10.1371/journal.pone.0147601.g002

Modesty et al PLOS1 2016

Blood Pressure in US-Born and Foreign-Born Blacks and US Whites, Ages 18 and Older, NHANES 1999-2014

	US Born Blacks	Foreign-Born Blacks	US Whites
N	*12558*	*1148*	*24736*
Sys BP*	126.7	126.3	121.9
Dias BP	73.2	71.9	72.1
BMI	29.1	27.0	22.7

*Adjusted for age, BMI and sex

Cooper et al, unpublished data

Premise of “Genetic Predisposition” Theory

Blood pressure is a polygenic trait; if variation in genetic susceptibility to high BP exists across geographic populations, the physiologic basis of this trait must have been under positive selection.

Genome-wide association analyses using electronic health records identify new loci influencing blood pressure variation

Thomas J Hoffmann[1,2], Georg B Ehret[3,4], Priyanka Nandakumar[3], Dilrini Ranatunga[5], Catherine Schaefer[5], Pui-Yan Kwok[2], Carlos Iribarren[5], Aravinda Chakravarti[3] & Neil Risch[1,2,5]

All previously described and new loci explained 2.9%, 2.5%, and 3.1% of the variation in SBP, DBP, and PP in GERA non-Hispanic whites, respectively, with estimated greater (but not significantly different) variance explained in Latinos (3.4%, 2.6%, and 3.6%) and less variance explained in East Asians (2.4%, 1.7%, and 2.6%) and African Americans (2.0%, 1.3%, and 2.1%), who similarly had the lowest GRSs.

*Who similarly had the **lowest** GRSs . . . .*

Darwin, on the Races of Man -

Every naturalist who has had the misfortune to undertake the description of a highly varying organism, has encountered cases precisely like that of man . . . .

And if of a cautious disposition he will end by uniting all the forms that graduate into each under a single species; for he will say to himself he has no right to give names to objects he cannot define.

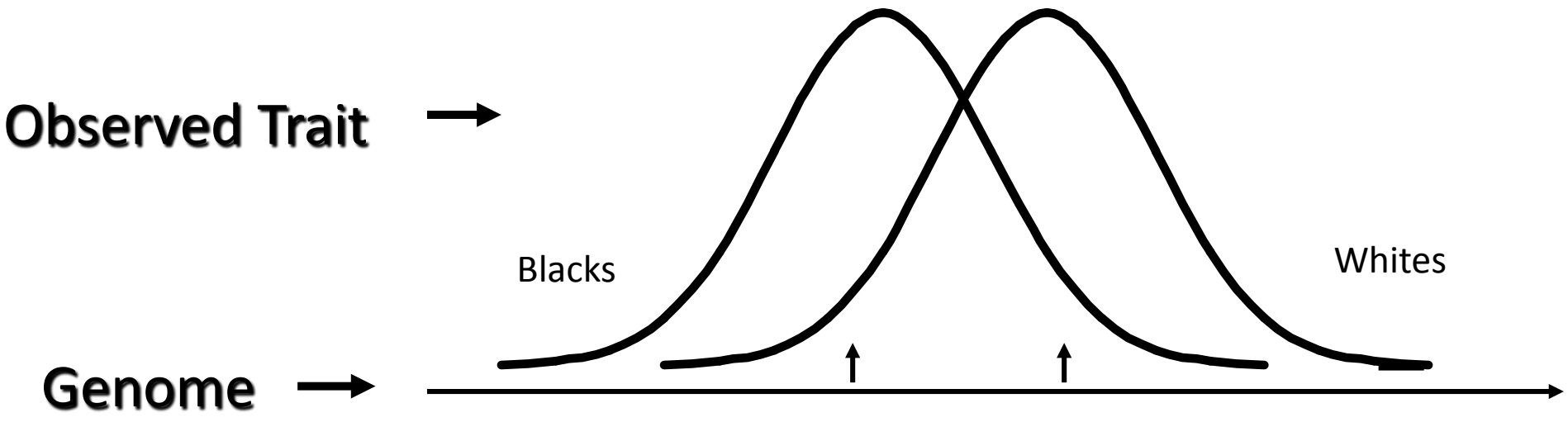
The Descent of Man

Science is supposed to provide us with safeguards against over-reach by asking for hypotheses . .

And thereby prevent us from getting lost in the land of nescience . .

- the unknown and the unknowable

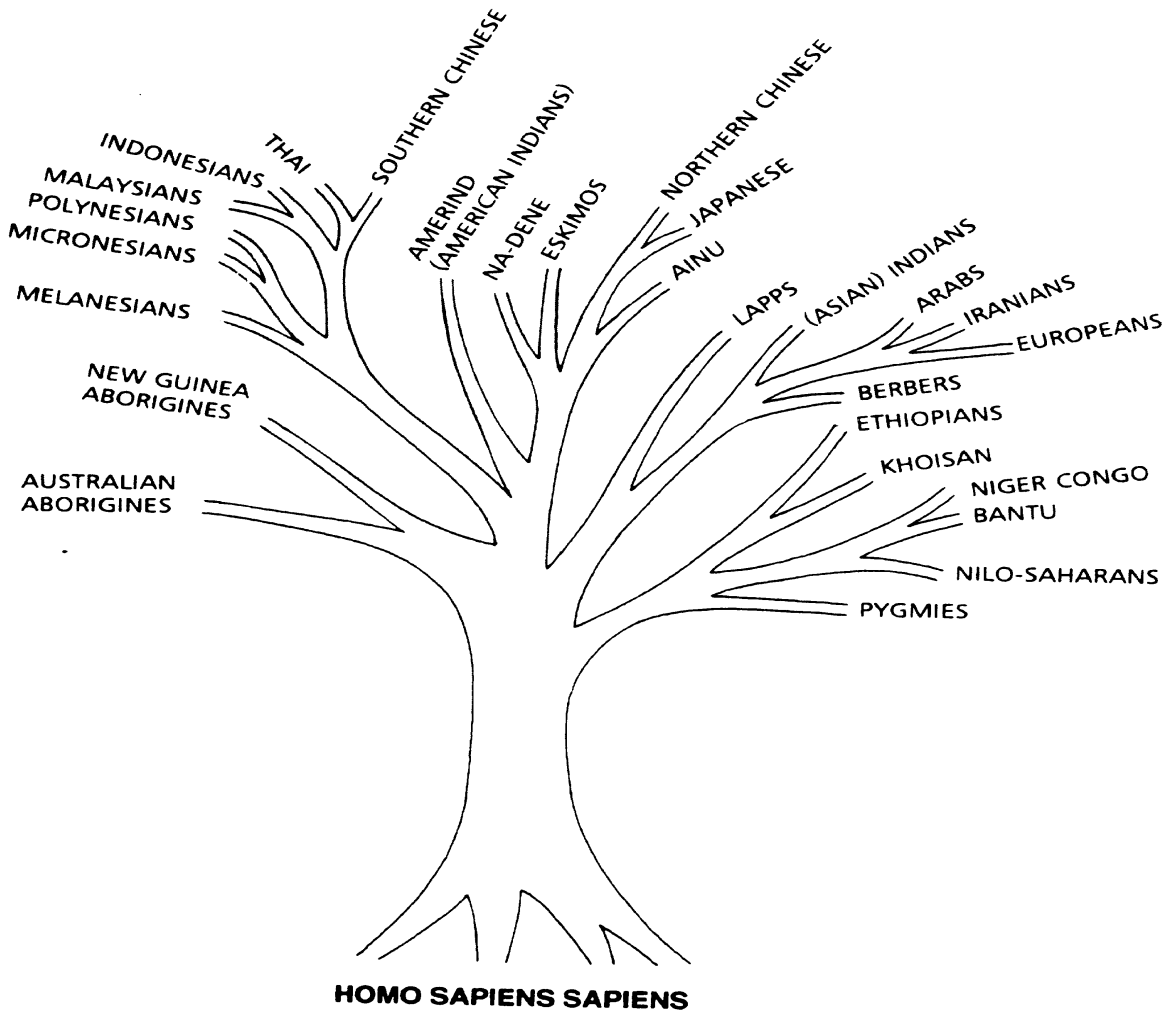
In the Beginning . . there was the Jeffersonian Genome



? IQ

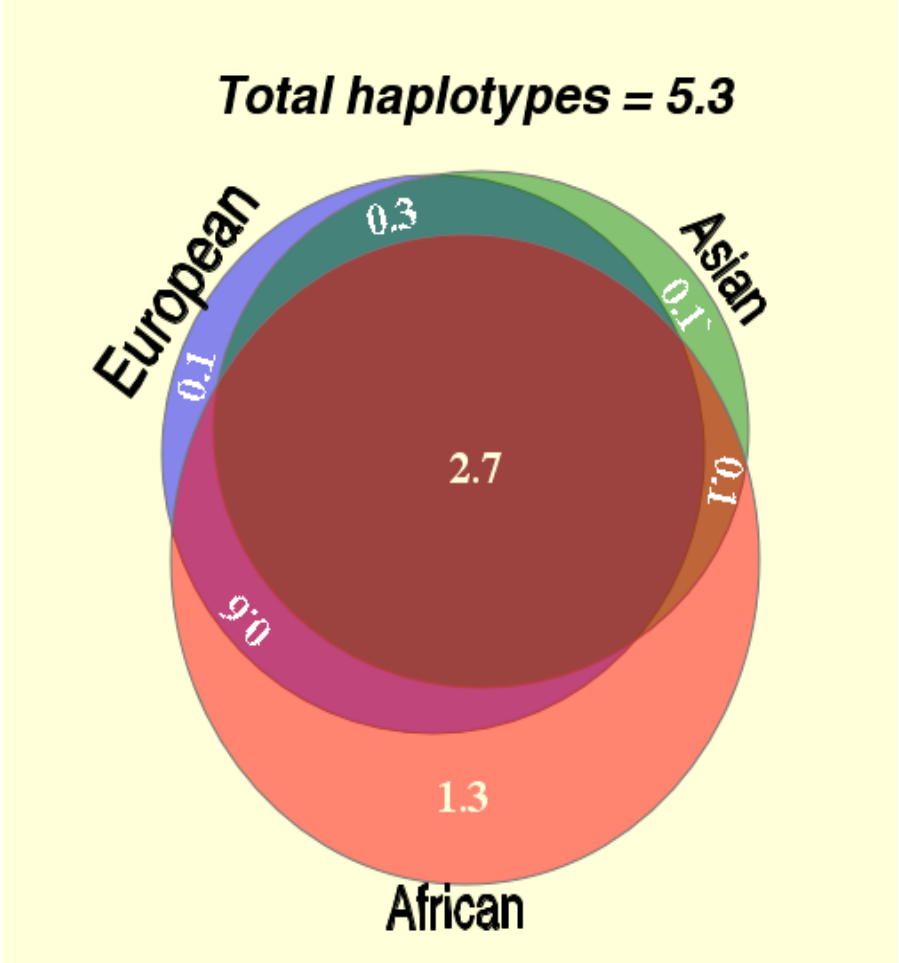
? BP

Then, the Anthropologist's Genome



Cavalli-Sforza, *The Great Human Diasporas*

Comparison of Haplotype Blocks Across Population Samples



One Genome, One Species