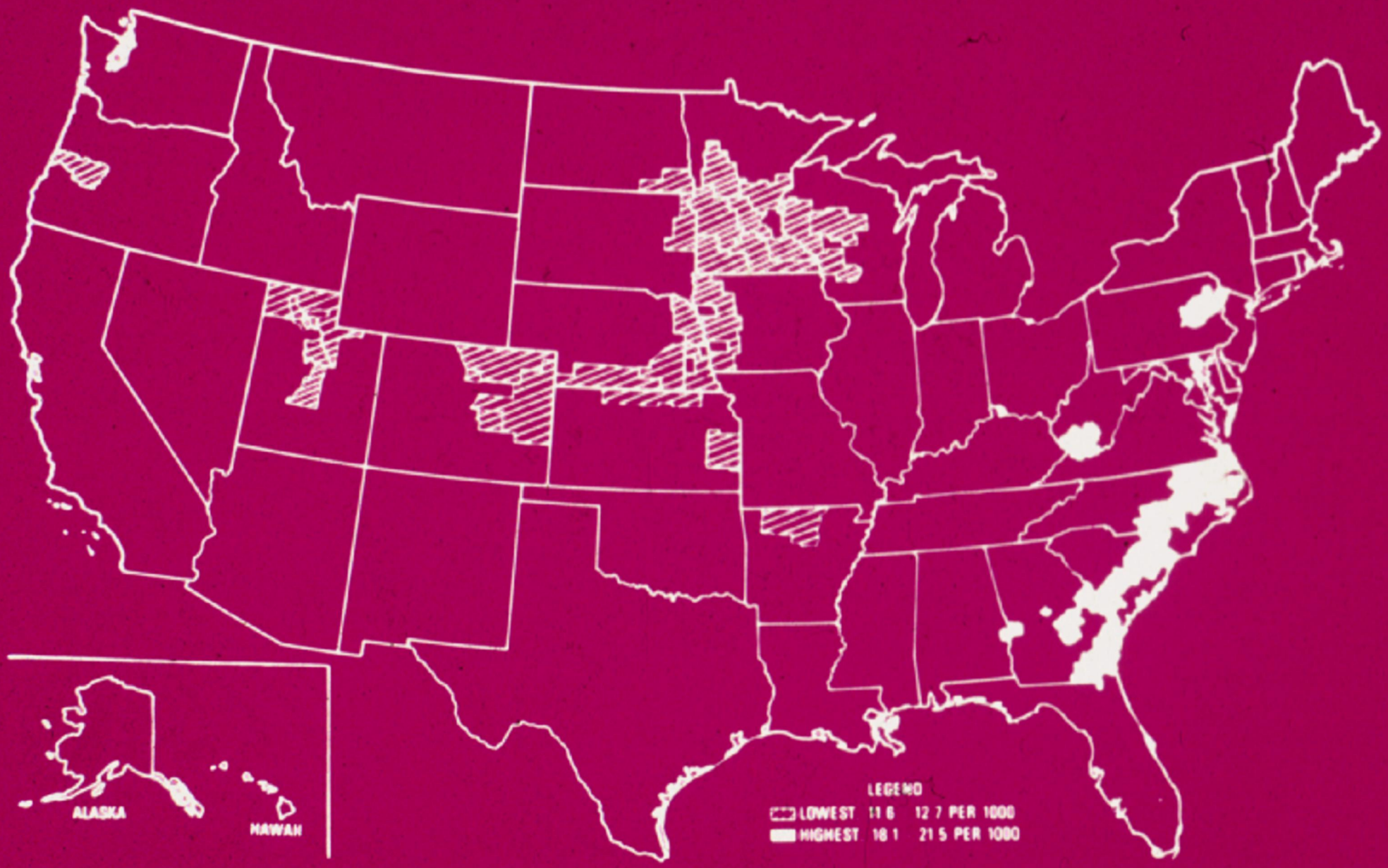
Hypertension: Concepts and Guidelines for Clinical Management

Daniel T. Lackland DrPH FAHA

National Library of Medicine


ALASKA
HAWAII
LEGEND
LOWEST 11 6 12 7 PER 1000
HIGHEST 18 1 21 5 PER 1000

Life Expectancy for Births: SC and United States, 2006

ÅSouth Carolina	74.8 years
ÅUnited States	77.5 years

Life Expectancy
South Carolina and US, 2006

	South Carolina	United States
White Males	72.8	75.3
White Females	78.0	80.5
Black Males	66.5	69.0
Black Females	73.7	76.1

Life Expectancy
Birth 2006

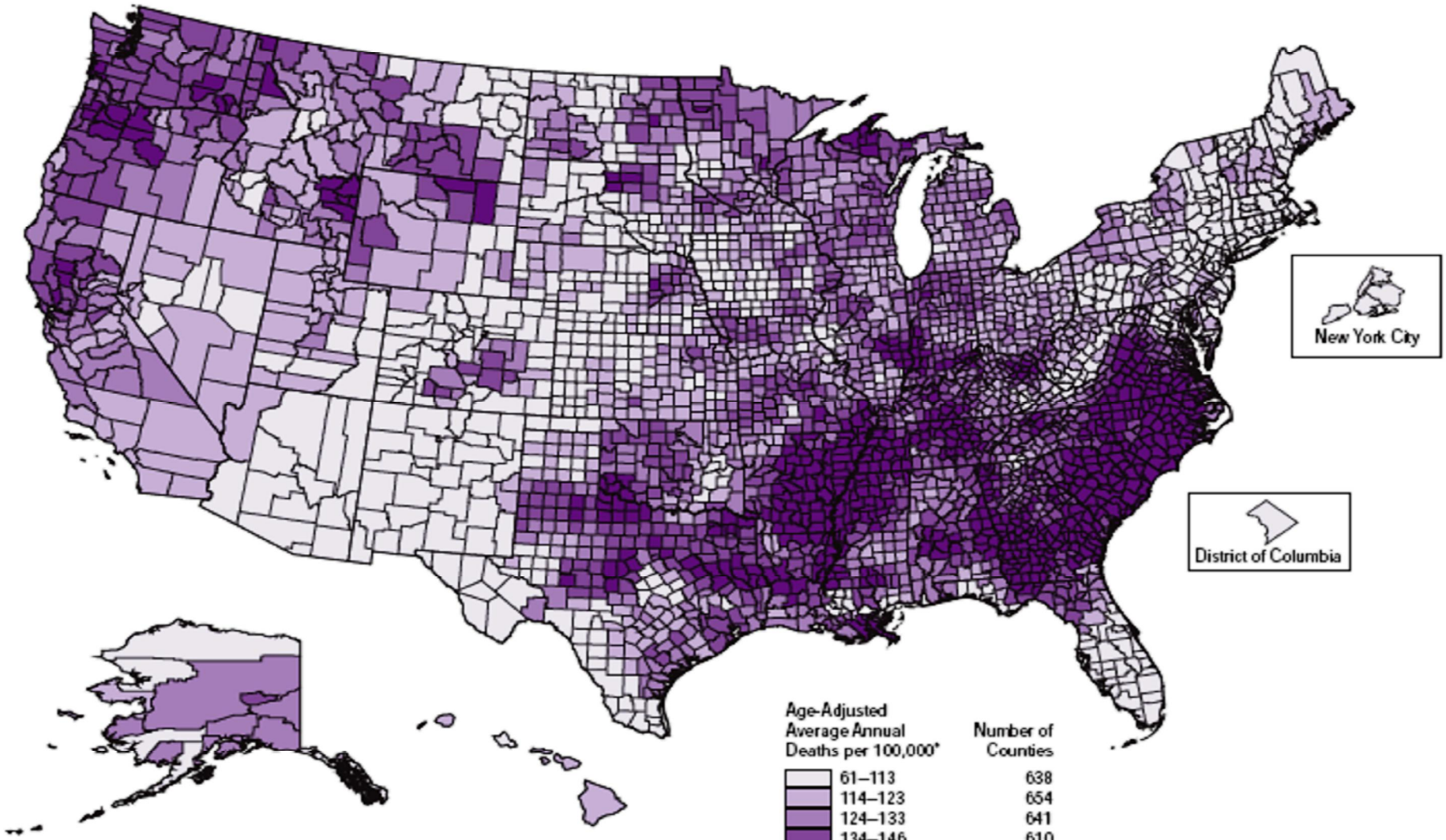
	Years
South Carolina	74.8
Connecticut	78.7
Minnesota	78.8

Leading Causes of Death, 2006

United States		South Carolina	Connecticut	Minnesota
Heart	211	208	146	213
Cancer	187	204	176	201
Stroke	46	53	43	44
COPD	42	45	34	42
Diabetes	24	26	22	22
Alzheimer	24	32	26	21
Influenza	19	19	12	22
Nephritis	15	20	14	16

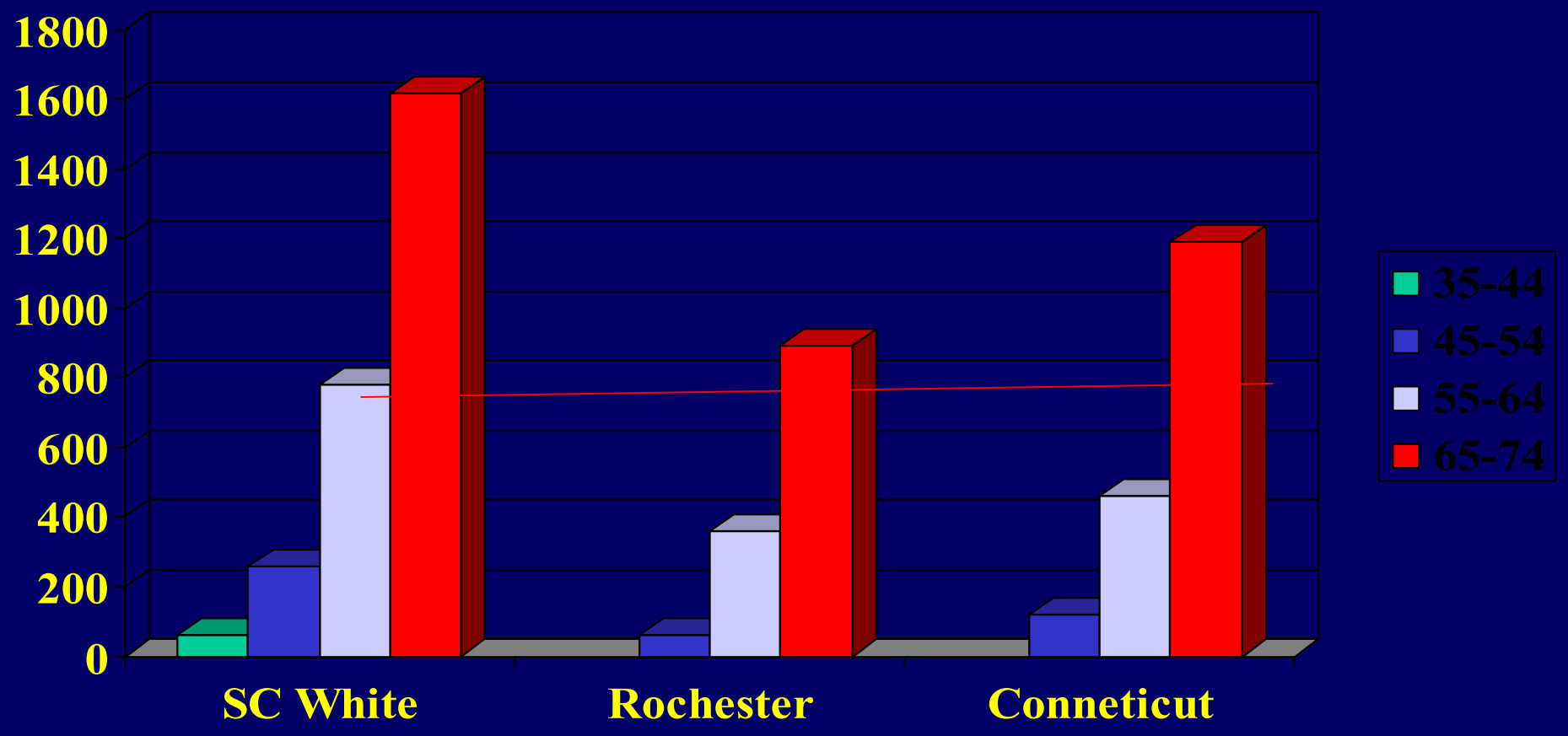
Smoothed County Stroke Death Rates
1991–1998

Total Population
Ages 35 Years and Older



*Stroke death rates are spatially smoothed to enhance the stability of rates in counties with small populations. See Appendix B for details.

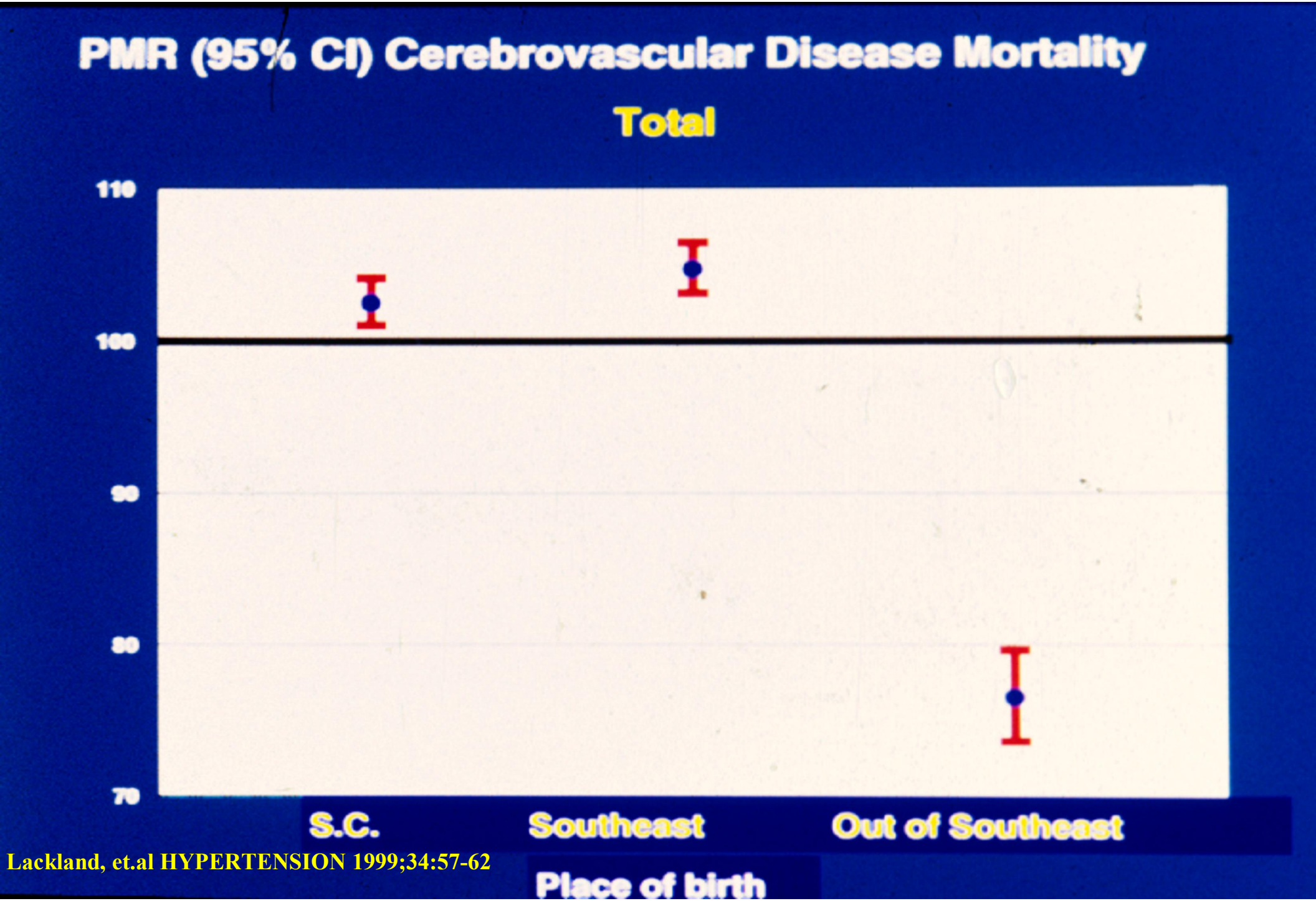
Stroke Incidence from Three US Populations, White Men



Lackland DT, et.al Stroke 1998

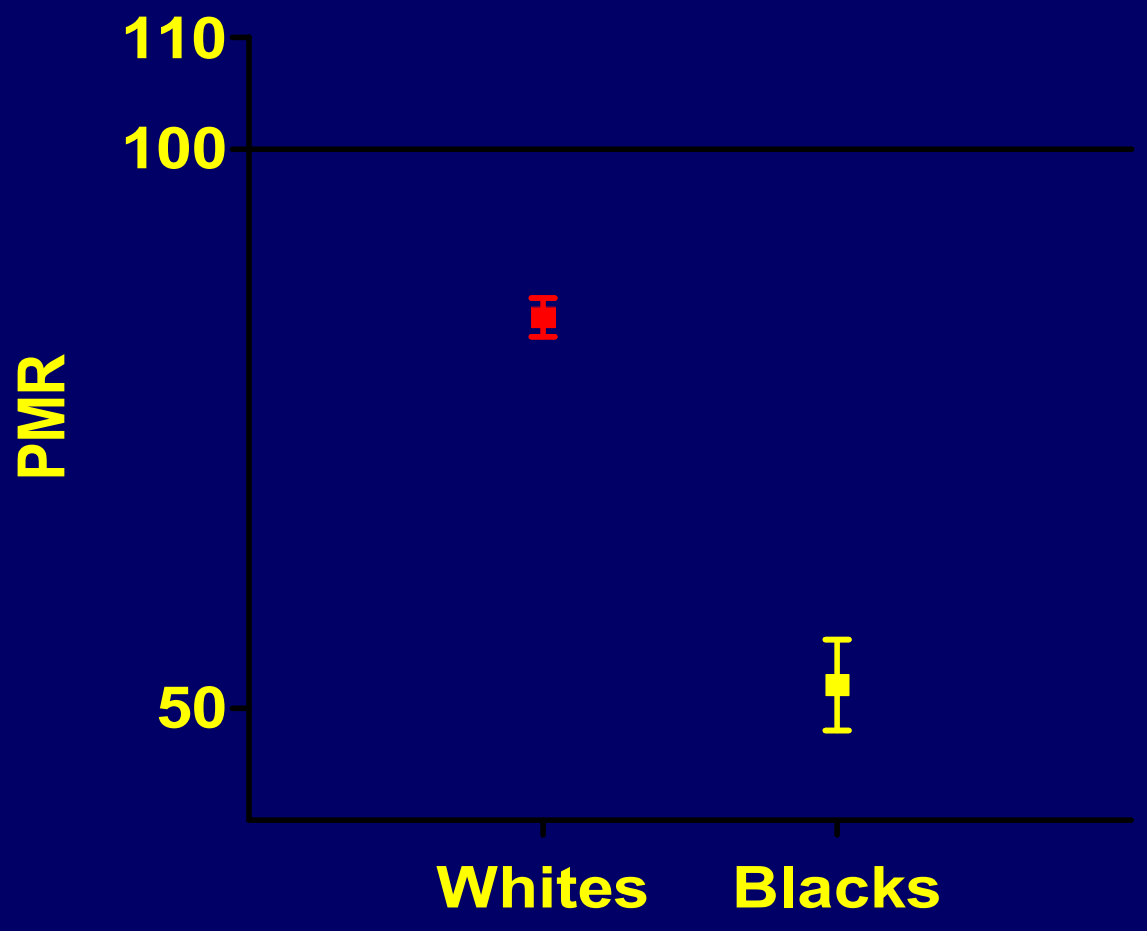
Nativity

Born in Southeast



Lackland, et.al HYPERTENSION 1999;34:57-62

Proportional Mortality Ratios for Stroke: South Carolinians born outside of the Southeast



* Hypertension 1999; 34. 57-62

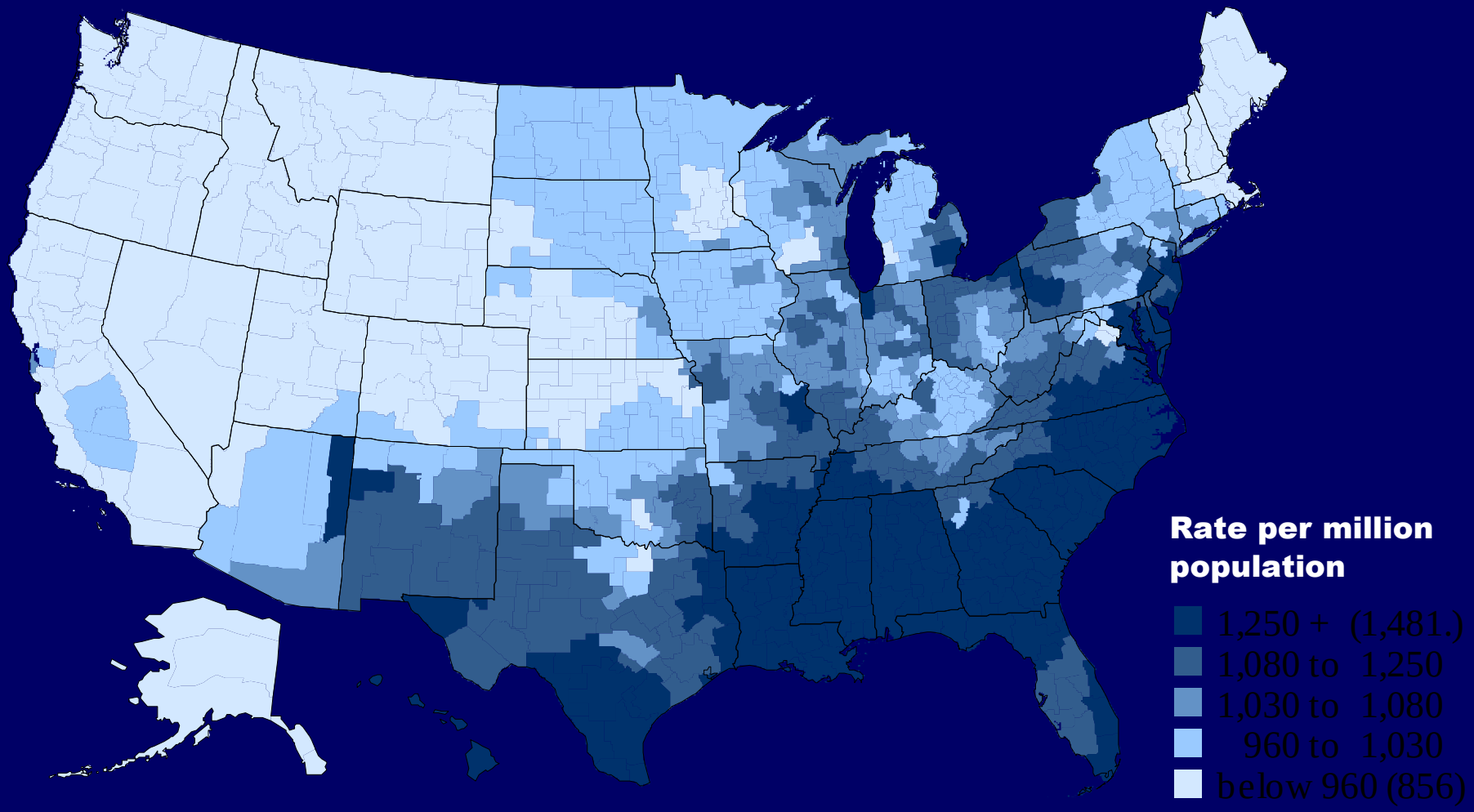
Residency

- **Å Time period in Southeast with greatest risks – birth through 20 years**

Å Virginia Howard, PhD - 2008

Prevalent rates: All

rate per million population, point prevalent ESRD patients alive on December 31, 1999, by HSA, smoothed



Diabetic Nephropathy Burden of Illness

- Incidence
  - Approximately 40% of all new cases of ESRD in the U.S. are due to diabetes[1]
  - Type 2 diabetes accounts for most cases of diabetic nephropathy[2,3]
    Prevalence of nephropathy 57% after 25 years of type 2 diabetes[4]
- Cost
  - In U.S. alone, total annual spending for ESRD > $15 billion[1]
    Cost/patient-year higher for diabetic ESRD ($51,000) than nondiabetic ESRD ($39,000)[5]

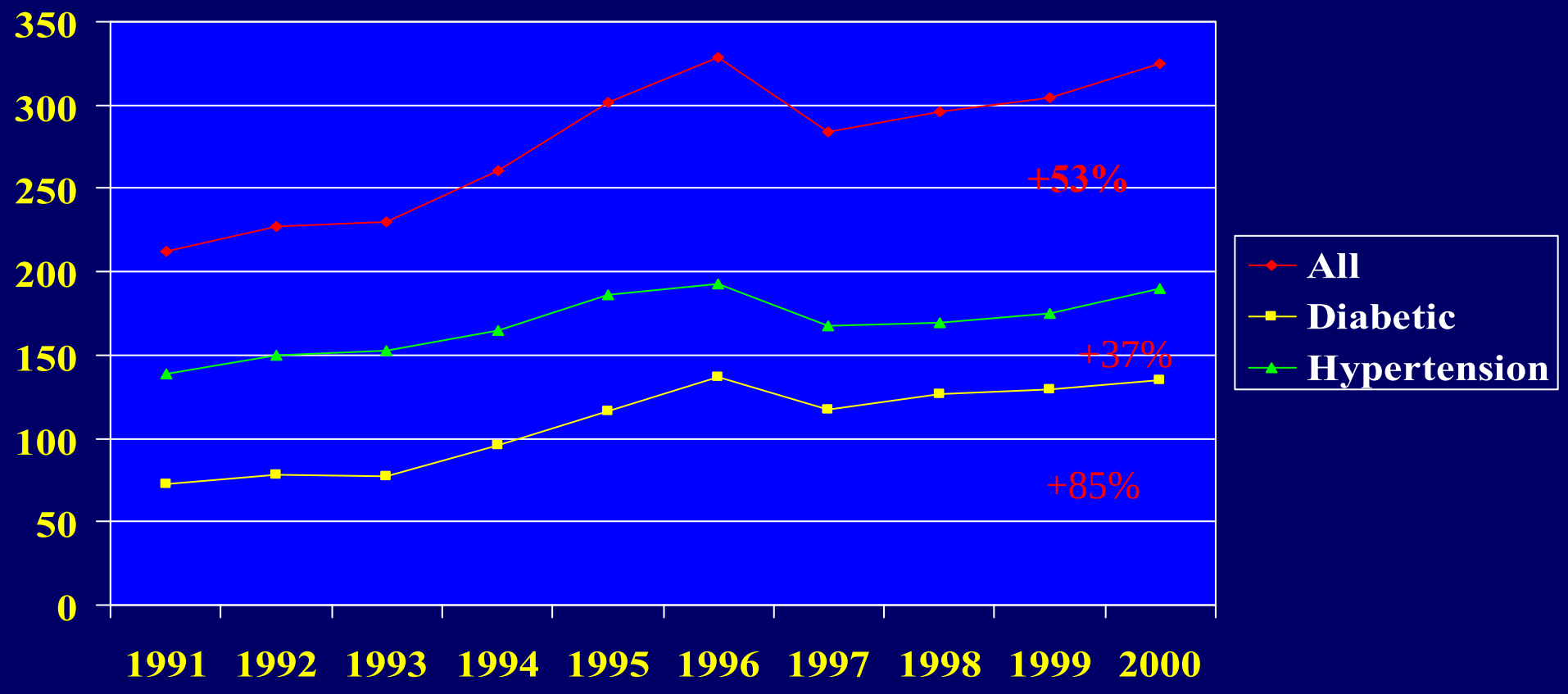
1. USRDS Coordinating Center. USRDS 1999 Annual Data Report. The Kidney Epidemiology and Cost Center of the University of Michigan; 1999. NIH Contract no. NO1-DK-3-2202.
2. American Diabetes Association. Diabetes Care. 2001;24 (supp 1):S69-72.
3. Ritz E, et al. Am J Kidney Dis. 1996;27:167-194.
4. Bakris GL et al. Am J Kidney Dis. 2000;36:646-661.
5. Ruggenenti P et al. J Am Soc Nephrol. 1998;9:2336-2343.

Diabetic Nephropathy Burden of Illness (continued)

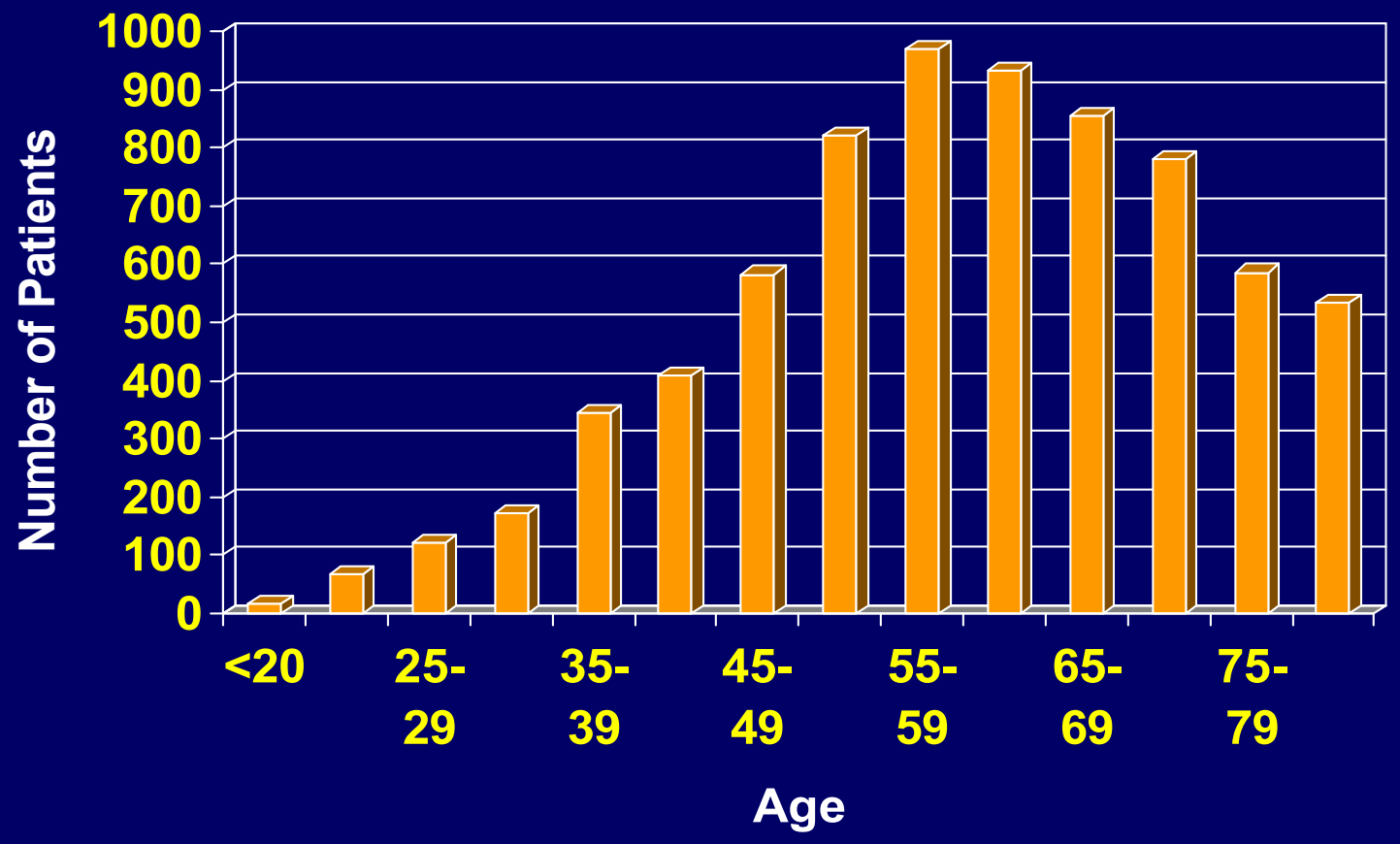
- Mortality
  - 1.5-2.5x greater mortality among diabetics with ESRD than nondiabetics[1]
    - < 20% of diabetics with ESRD survive 5 years after initiation of dialysis[1]
    - Cardiovascular complications the most common cause of death[2,3]

1. Koch M et al. Diabetologia. 1993;36:1113-1117.
2. Bakris GL. Diabetes Res Clin Pract. 1998;39:S35-S42.
3. Grundy SM et al. Circulation. 1999;100:1134-1146.

Trends in Diabetes and Hypertension ESRD ï NC, SC and GA



ESRD Dialysis Patients, SC 2007 N=7199

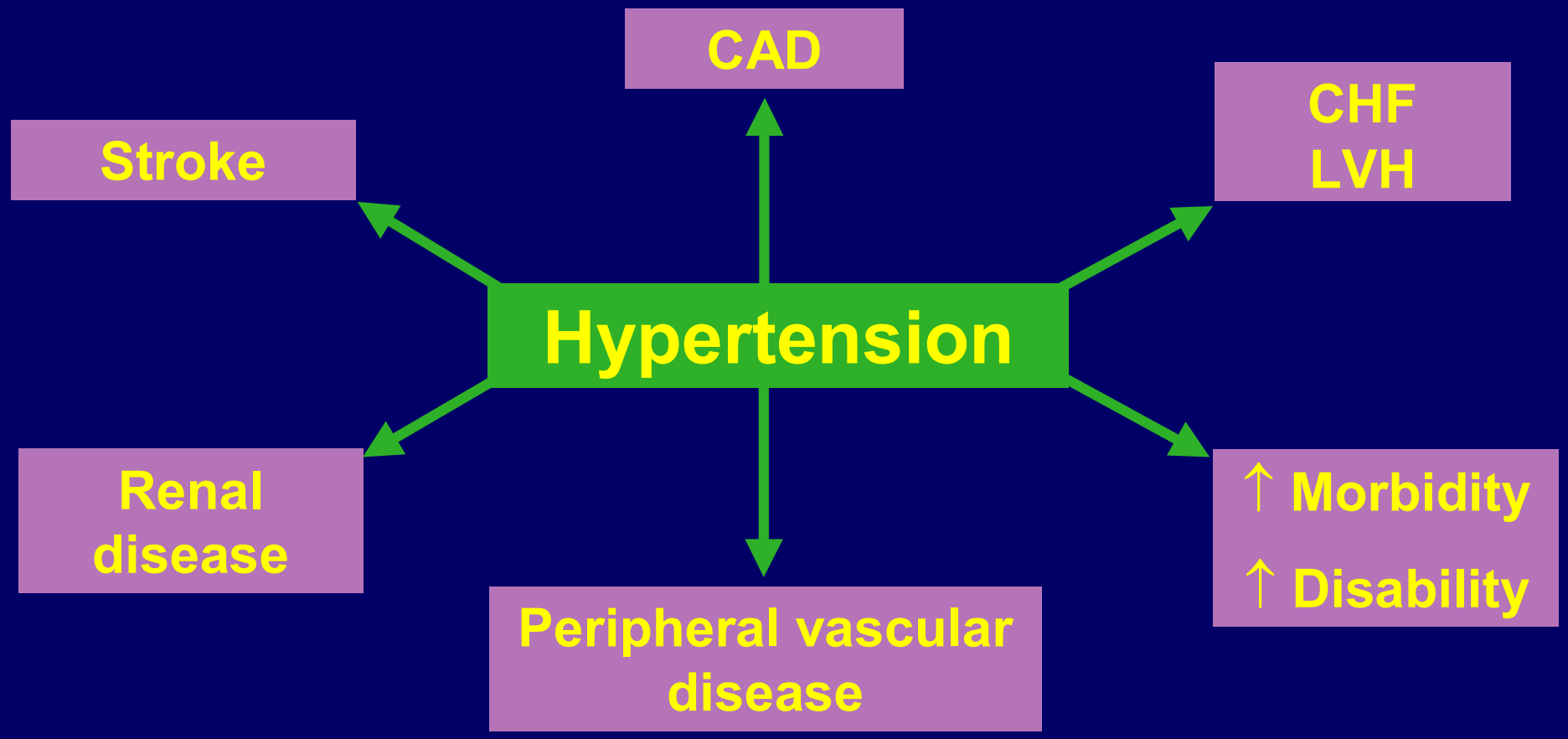


30-year Population Attributable Risks for Hypertension: Charleston and Evans County Heart Study

White Males	**23.8%**
White Females	**18.3%**
Black Males	**45.2%**
Black Females	**39.5%**

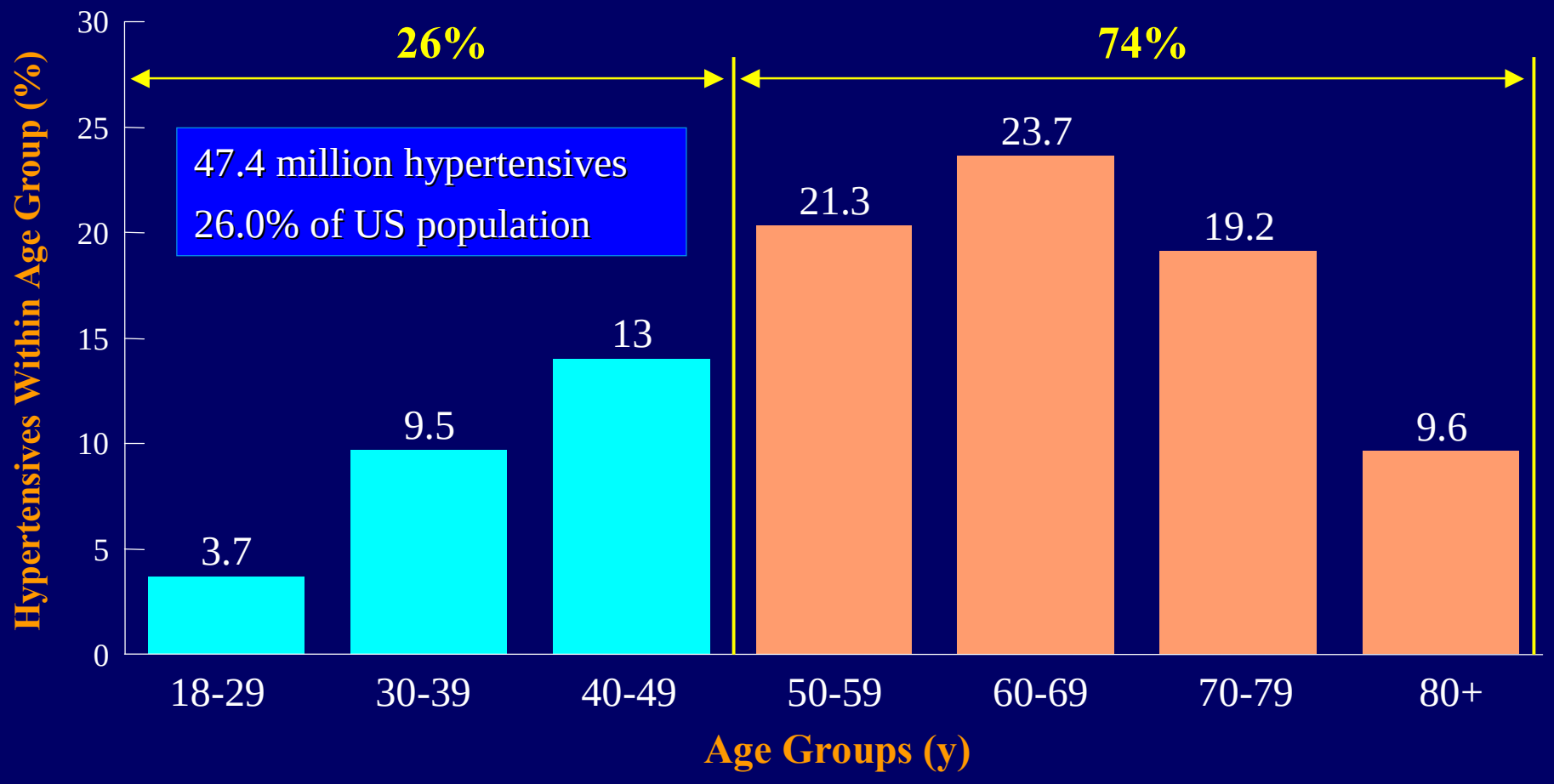
Lackland Clinical and Experimental Hypertension, 1995

Hypertension: A Significant CV and Renal Disease Risk Factor



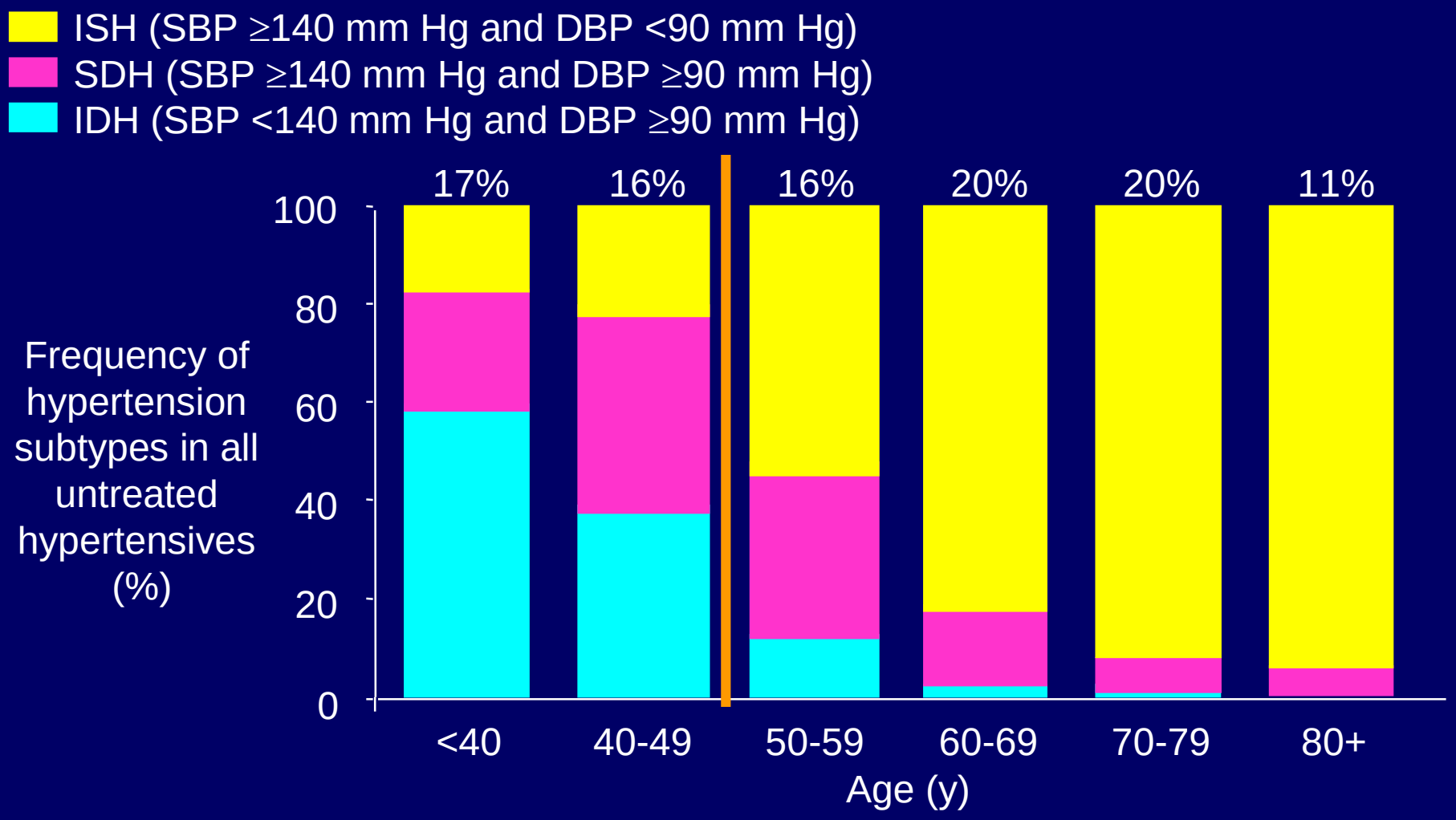
National High Blood Pressure Education Program Working Group. *Arch Intern Med.* 1993;153:186-208.

Age Distribution of Hypertensives in US Population (NHANES III and the 1991 Census)



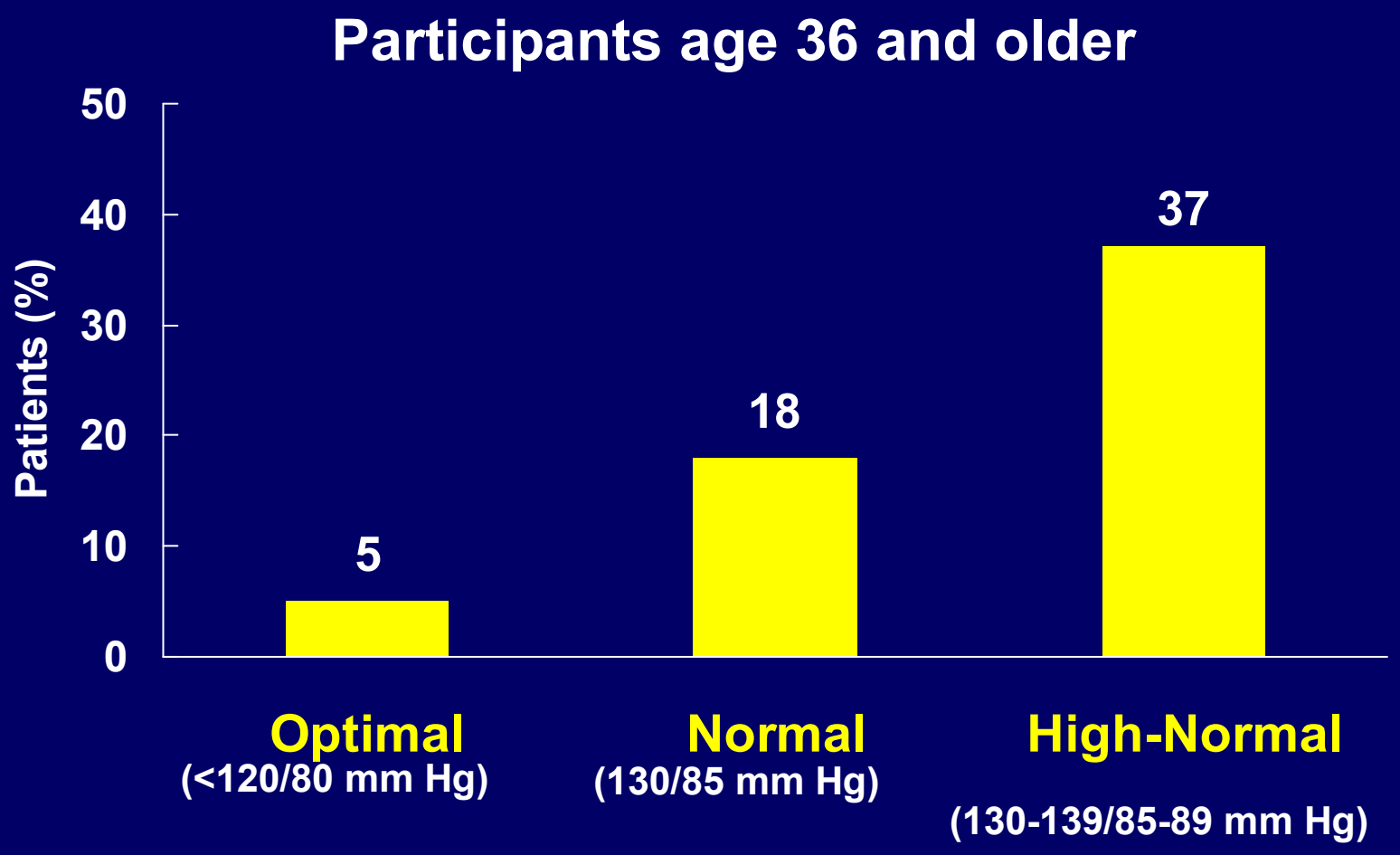
Franklin SS. *J Hypertension.* 1999;17(suppl 5):S29-S36.

Distribution of Hypertension Subtype in the untreated Hypertensive Population in NHANES III by Age



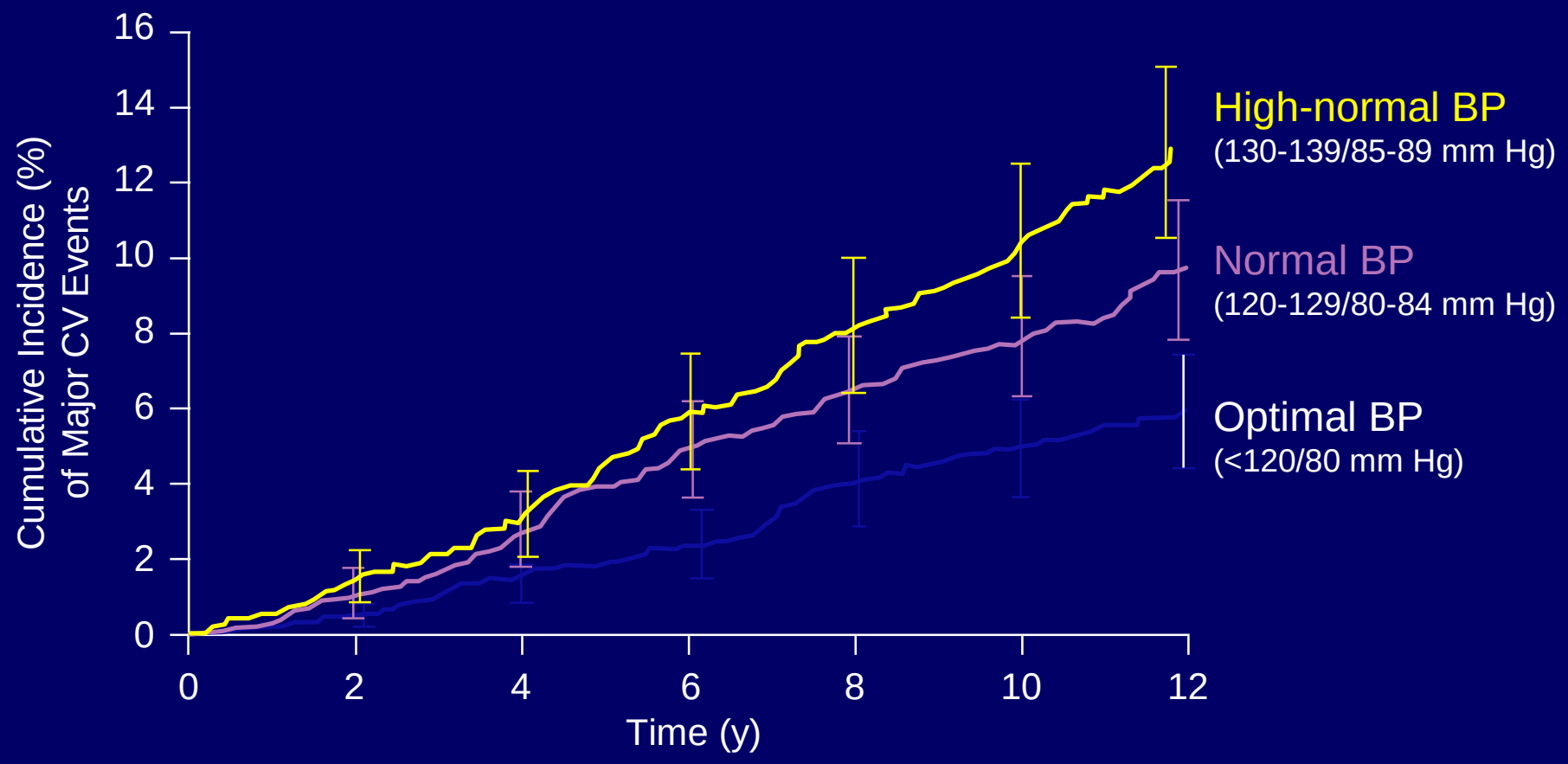
Numbers at top of bars represent the overall percentage distribution of untreated hypertension by age.
Franklin et al. *Hypertension 2001;37: 869-874*.

4-Year Progression To Hypertension: The Framingham Heart Study



Vasan, et al. *Lancet 2001;358:1682-86*

Impact of High-Normal BP on Risk of Major CV Events* in Men



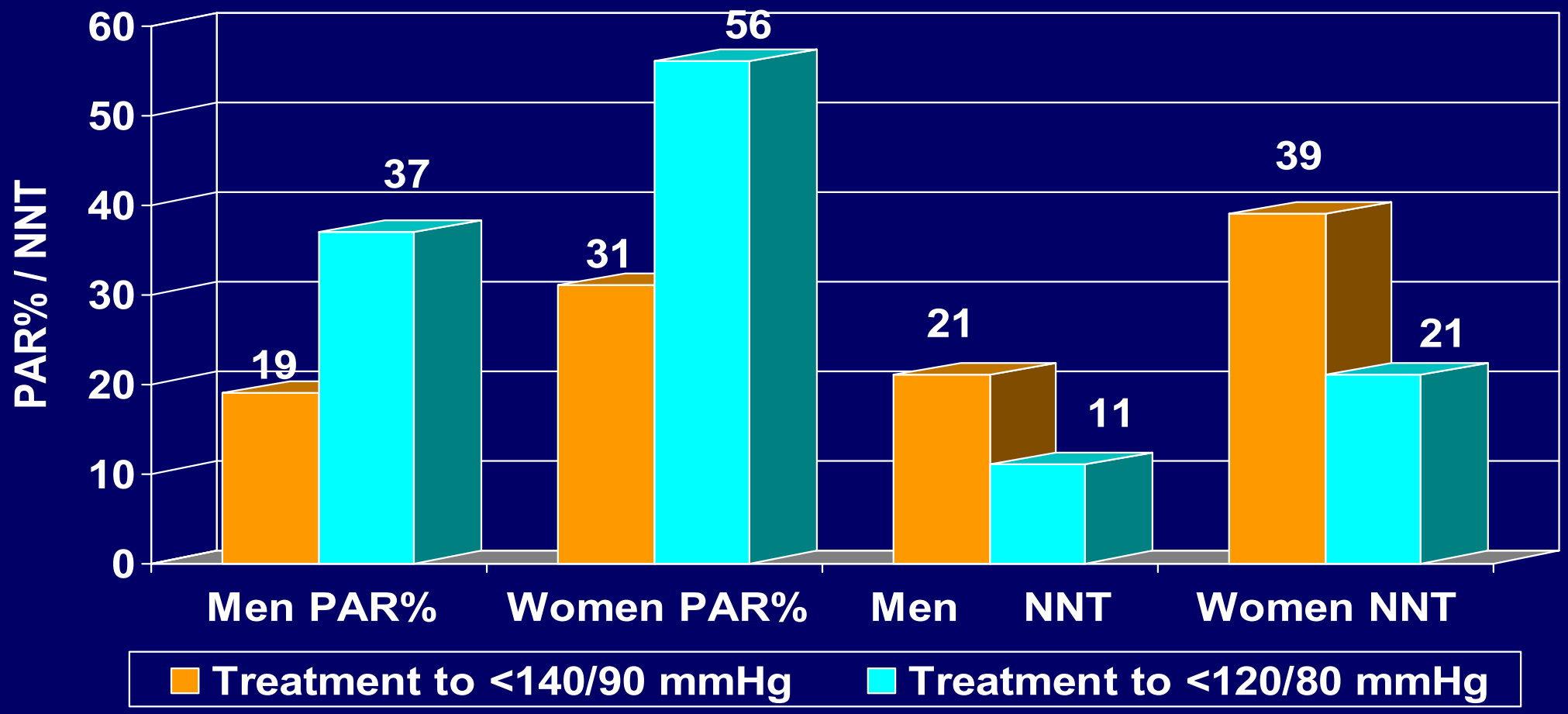
* Defined as death due to CV disease; recognized myocardial infarction (MI), stroke, or congestive heart failure (CHF).
Adapted from Vasan RS. *N Engl J Med.* 2001;345:1291-1297.

Benefits of Lowering BP

	Average Percent Reduction
Stroke incidence	35–40%
Myocardial infarction	20–25%
Heart failure	50%

Preventable CHD Events from Control of Hypertension in US Adults

(Wong et al., Am Heart J 2003; 145: 888-95)



PAR% = population attributable risk (proportion of CHD events preventable), NNT = number needed to treat to prevent 1 CHD event ; <0.01 comparing men and women for PAR%

Preventable CHD Events from Control of Hypertension in US Adults

(Wong et al., Am Heart J 2003; 145: 888-95) (cont.)

- The greatest impact (absolute numbers) from control of hypertension occurs in men, older persons, and those with isolated systolic hypertension
- The greatest proportion of preventable CHD events from control of hypertension occurs in women
- Optimal control of blood pressure could prevent more than one third of CHD events in men and more than half of CHD events in women

In a 56 male, which bllod pressure measure has the greatest predictive value

ÅA] Diastolic blood pressure

ÅB] Systolic blood pressure

ÅC] Mean arterial pressure

ÅD] Pulse pressure

ÅE] All have equal value

Elevated SBP Alone Is Associated With Increased Risk of Cardiovascular and Renal Disease

Disease	Relative Risk
Kidney failure (ESRD)	≥2.8
Stroke	≥2.7
Heart failure	≥1.5
Peripheral vascular disease	≥1.8
Myocardial infarction*	=1.6
Coronary artery disease	≥1.5

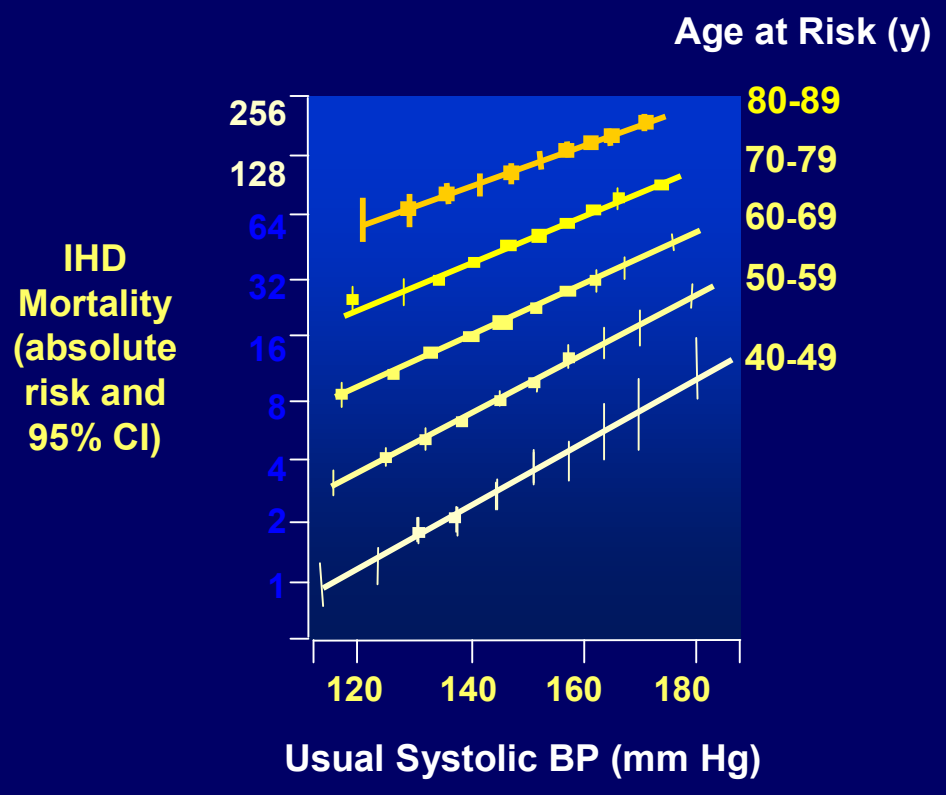
ESRD = end-stage renal disease; SBP ≥165 mm Hg.
*Men only.

Adapted from Kannel WB. *Am J Hypertens*. 2000;13:3S-10S; Perry HM Jr et al. *Hypertension*. 1995;25(part 1):587-594; Klag MJ et al. *N Engl J Med*. 1996;334:13-18; Nielsen WB et al. *Ugeskr Laeger*. 1996;158:3779-3783; Neaton JD et al. *Arch Intern Med*. 1992;152:56-64.

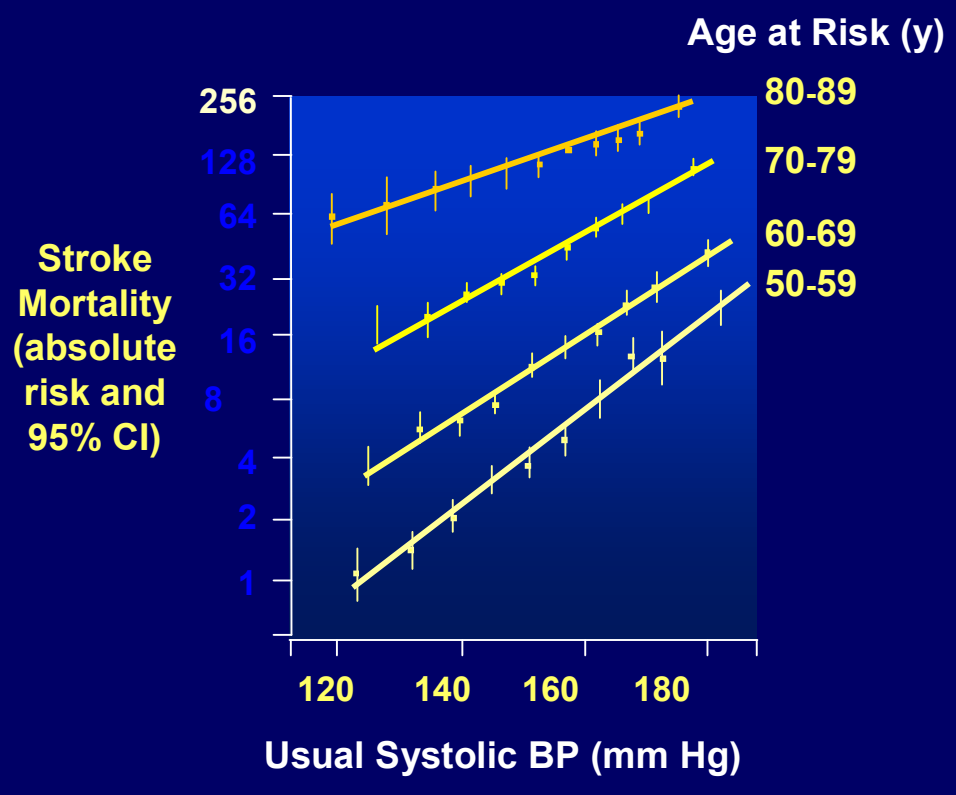
Risk of increased systolic blood pressure consistent through all age groups

One Million Adults, 61 Prospective Studies

Ischemic Heart Disease Mortality

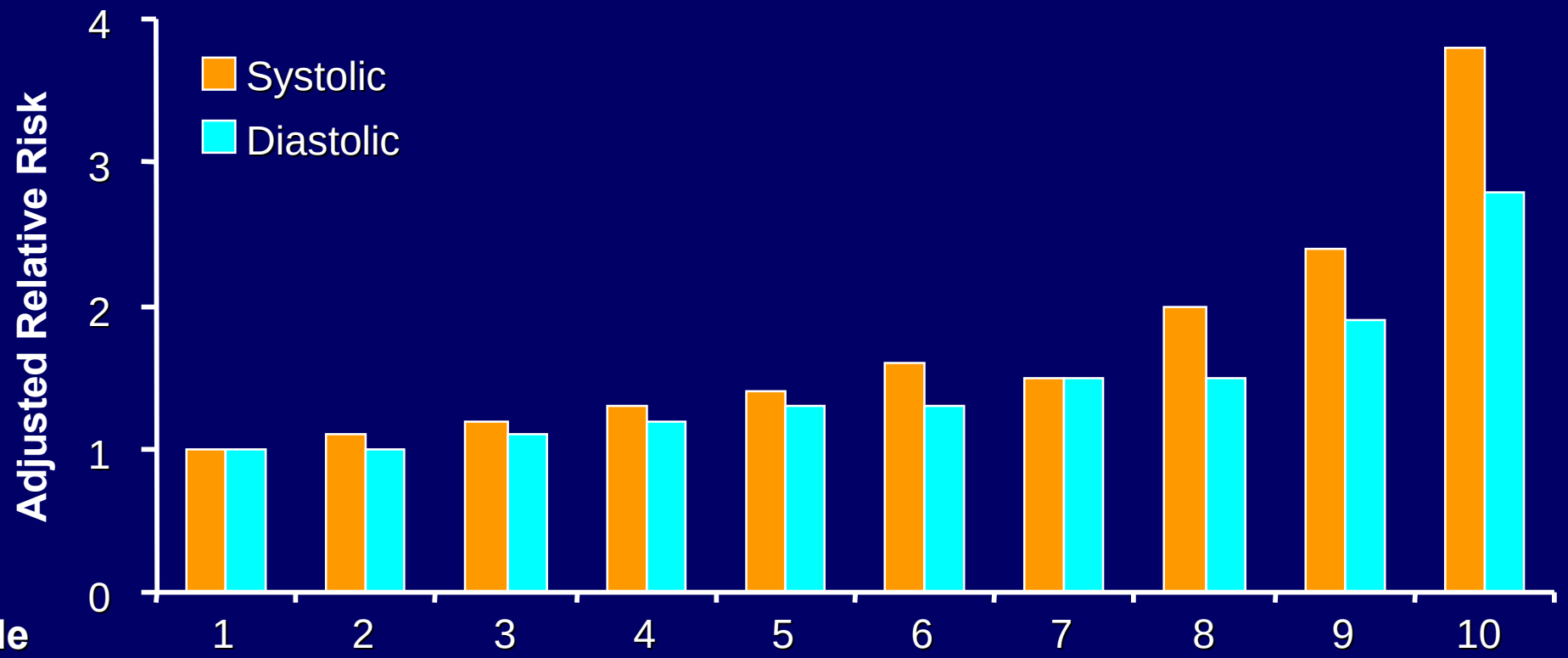


Stroke Mortality



IHD = ischemic heart disease.
Lewington S et al. *Lancet*. 2002;360:1903-1913.

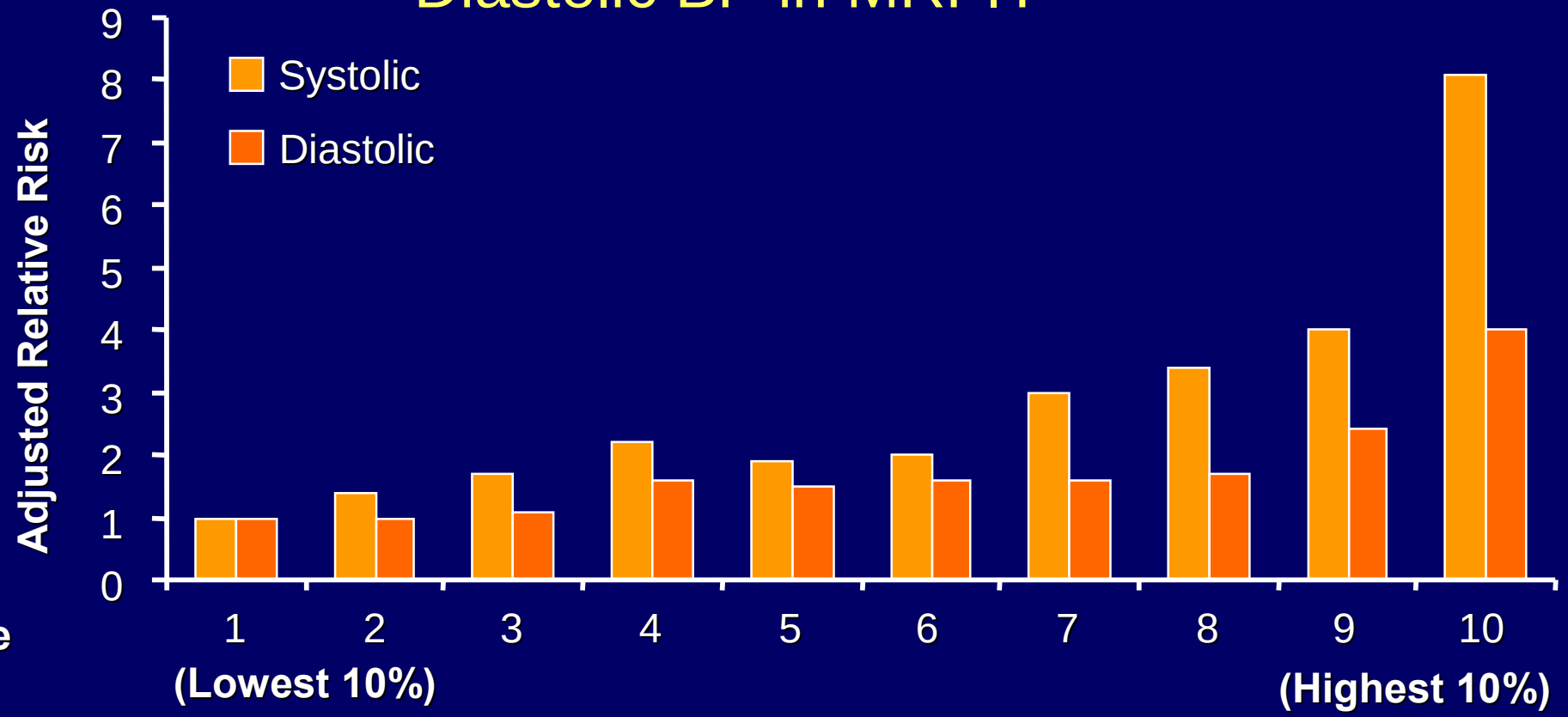
Risk of CHD Death According to Systolic BP and Diastolic BP in MRFIT



Decile	1 (Lowest 10%)	2	3	4	5	6	7	8	9	10 (Highest 10%)
Systolic BP (mm Hg)	<112	112-	118-	121-	125-	129-	132-	137-	142-	≥151
Diastolic BP (mm Hg)	<71	71-	76-	79-	81-	84-	86-	89-	92-	≥98

Stamler, Stamler, Neaton. *Arch Intern Med*. 1993;153:598-615.

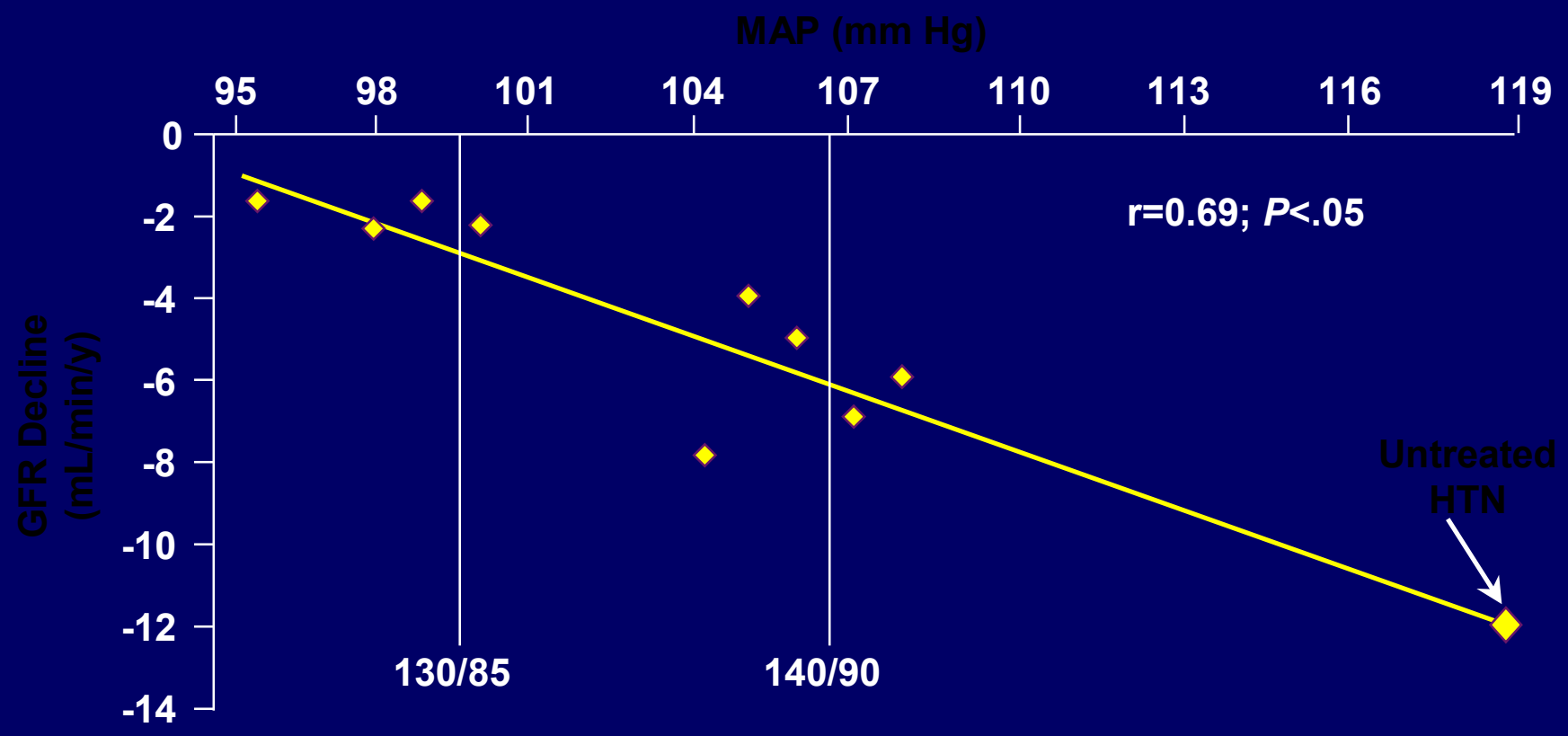
Risk of Stroke Death According to Systolic BP and Diastolic BP in MRFIT



Systolic BP (mm Hg)	<112	112-	118-	121-	125-	129-	132-	137-	142-	≥151
Diastolic BP (mm Hg)	<71	71-	76-	79-	81-	84-	86-	89-	92-	≥98

Stamler, Stamler, Neaton. *Arch Intern Med*. 1993;153:598-615.

Correlation Between MAP & Renal Function



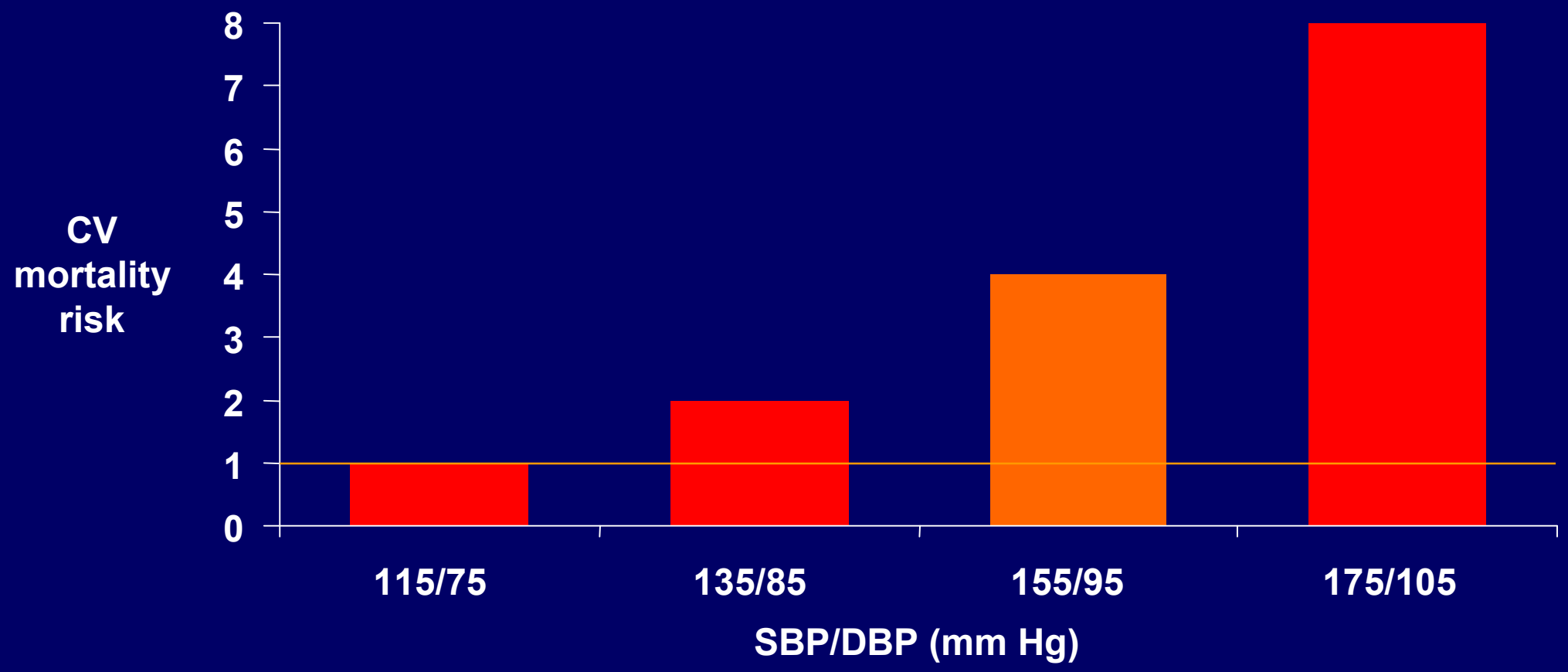
GFR, glomerular filtration rate; HTN, hypertension; MAP, mean arterial pressure.
Adapted from Bakris GL et al. Am J Kidney Dis. 2000;36:646-661.

30-year Population Attributable Risks for Hypertension

White Males	**23.8%**
White Females	**18.3%**
Black Males	**45.2%**
Black Females	**39.5%**

Lackland, et.al Clincal and Experimental Hypertension 1995

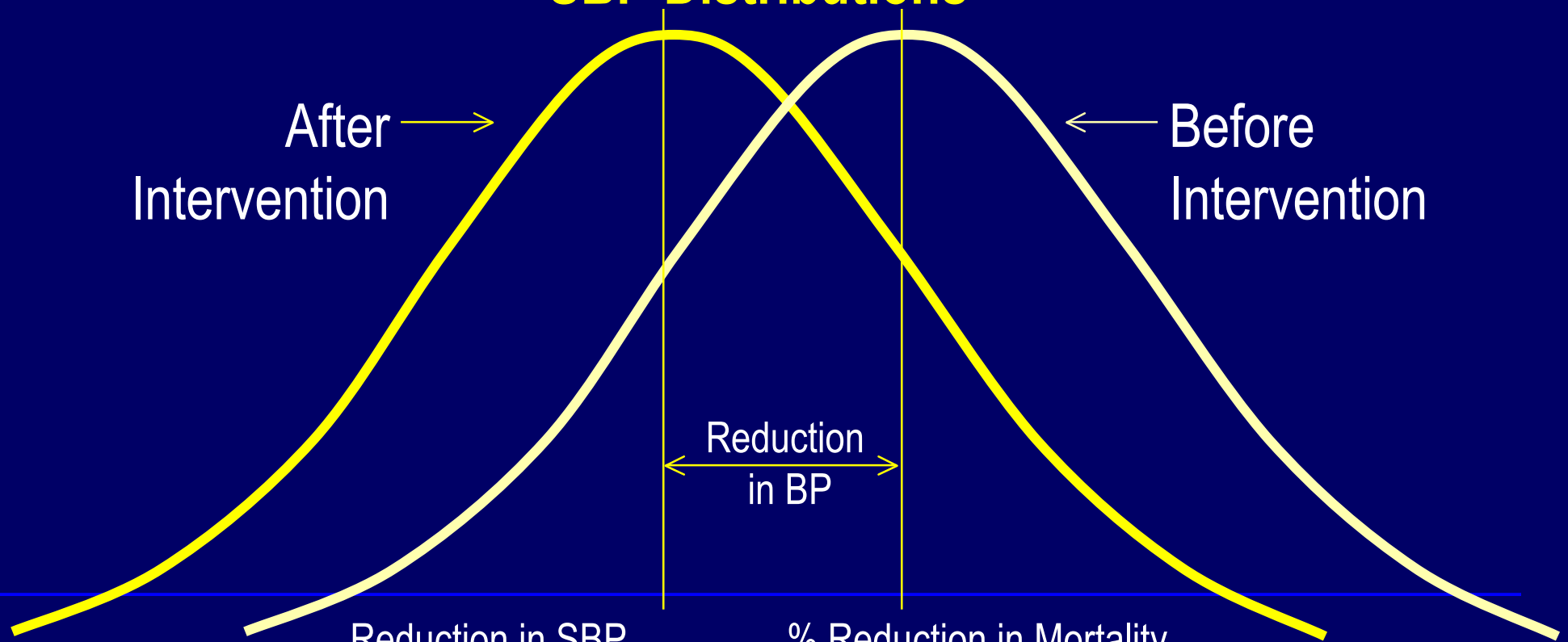
CV Mortality* Risk Doubles with Each 20/10 mm Hg BP Increment*



Age 40-70 years
Ref: Lancet. 2002; 60:1903-1913.
JNC 7 Express. JAMA. 2003;289:2560-2572.

Population-Based Strategy

SBP Distributions



Reduction in SBP mmHg	% Reduction in Mortality Stroke	CHD	Total
2	–6	–4	–3
3	–8	–5	–4
5	–14	–9	–7

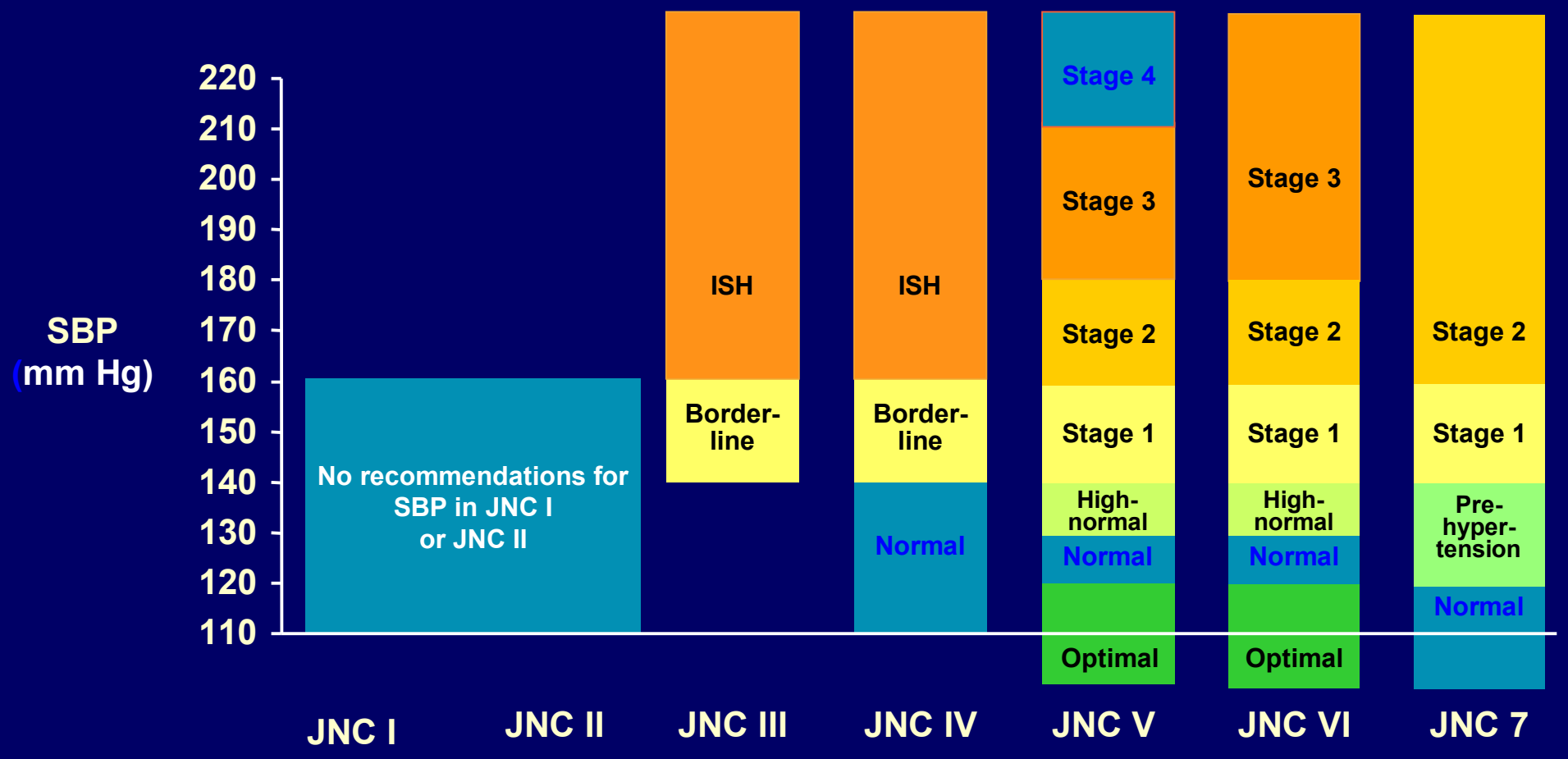
JAMA. 2003;289:2560-2572

Evolution of Treatment Recommendations

JNC I	JNC II	JNC III	JNC IV	JNC V	JNC VI	JNC 7
1977*	1980†	1984‡	1988§	1993¶	1997¶	2003#
Stepped care diuretic to methyldopa reserpine, or propranolol	Stepped care diuretic to adrenergic-inhibiting agents	Thiazide diuretics or BBs	Thiazide diuretics, BBs, ACE-Is, or CCBs	Thiazide diuretics or BBs	Thiazide diuretics or BBs; for reno- and cardio-protection ARBs recommended in patients intolerant of ACE-Is	Thiazide diuretics, ARBs, ACE-Is, BBs, or CCBs; combination therapy for Stage 2

BB = ß-blocker; ACE-I = angiotensin-converting enzyme inhibitor; CCB = calcium-channel blocker;
ARB = angiotensin-receptor blocker.
*JNC I. *JAMA*. 1977;237:255-261; ÀJNC II. *Arch Intern Med*. 1980;140:1280-1285; ÿJNC III. *Arch Intern Med*. 1984;144:1045-1057; §JNC IV. *Arch Intern Med*. 1988;148:1023-1038;
¶JNC V. *Arch Intern Med*. 1993;153:154-183; #JNC VI. *Arch Intern Med*. 1997;157:2413-2446; **Chobanian AV et al. *JAMA*. 2003;289:2560-2572.

Evolution of SBP Classification



SBP = systolic blood pressure; ISH = isolated systolic hypertension.

JNC I. *JAMA.* 1977;237:255-261; JNC II. *Arch Intern Med.* 1980;140:1280-1285; JNC III. *Arch Intern Med.* 1984;144:1045-1057; JNC IV. *Arch Intern Med.* 1988;148:1023-1038; JN V. *Arch Intern Med.* 1993;153:154-183; JNC VI. *Arch Intern Med.* 1997;157:2413-2446; Chobanian AV et al. *JAMA.* 2003;289:2560-2572.

JNC 7: Guidelines for Hypertension

- **Goal: To reduce cardiovascular and renal morbidity and mortality through prevention and management of hypertension**

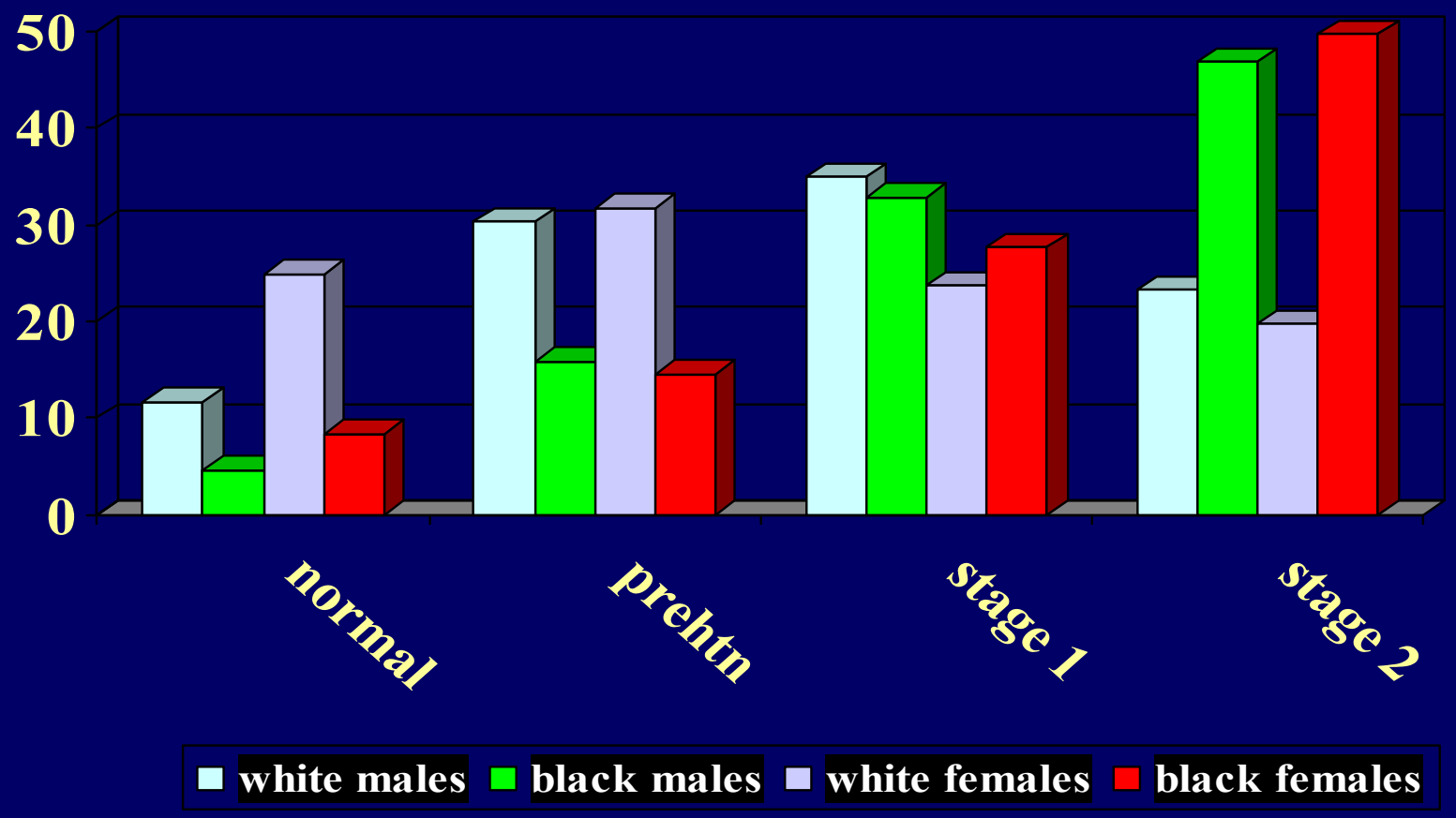
Classification of Blood Pressure

Category	SBP (mm Hg)		DBP (mm Hg)
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Hypertension, Stage 1	140-159	or	90-99
Hypertension, Stage 2	≥160	or	≥100

JNC 7, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Adapted from the JNC 7 Slide Deck. Available at: http://www.nhlbi.nih.gov.

Blood Pressure Levels



Lackland, 2005

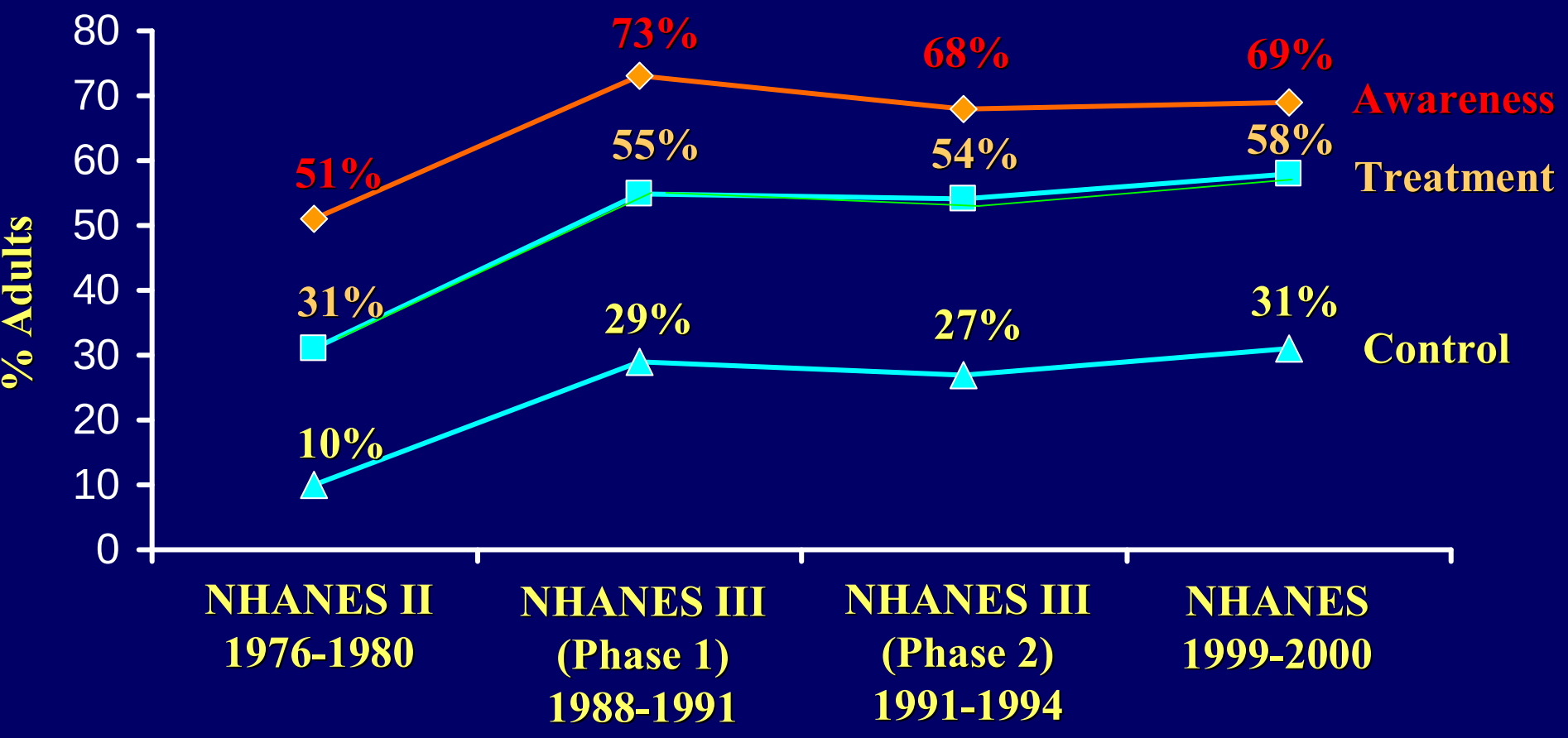
Patients Not at JNC 7ï Recommended BP Goals

NHANES (1999-2000)

Patient Type	Goal BP (mm Hg)	% Not at Goal* Systolic BP	% Not at Goal* Diastolic BP
Total hypertensives	<140/90	57%	26%
African American	<140/90	60%	32%
Mexican American/ Hispanic	<140/90	63%	30%
Older patients (≥60 years)	<140/90	71%	9%
Symptomatic CHD	<140/90	47%	4%
Patients with diabetes†	<130/85	81%	24%

*Includes those ≥17 years of age with diagnosed and undiagnosed hypertension. National Center for Health Statistics. NHANES 1999-2000 (CD-ROM); †NHANES III.

Hypertension Awareness, Treatment, and Control: US 1976 to 2000



Burt et al. *Hypertension*. 1995;25:305-313; Hyman et al. *N Engl J Med*. 2001;345:479-486; National Center for Health Statistics. NHANES 1999-2000 (CD-ROM); NIH. *The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*; 1997. NIH publication 98-4080.

Case 1

ÅAn overweight 55-year-old man with type 2 diabetes and no history of physical findings of vascular disease has blood pressure 145-150/90-95 mmHg. His fasting glucose level is 138 mg/dl and his hemoglobin A!C level is 7.8%. He has normal renal function and no proteinuria. He stopped smoking one year ago.

Which of the following is the most appropriate goal of antihypertensive therapy in this patient?

ÅA] BP < 140/90 mmHg

ÅB] BP < 140/85 mmHg

ÅC] BP < 130/80 mmHg

ÅD] BP < 120/75 mmHg

Hgb A1c By Hypertension Status among Diabetics

	Hypertensive	Non-Hypertensive
White Males	8.55	8.09
White Females	8.28	6.45
Black Males	10.25	9.63
Black Females	10.64	7.92

Lackland, et.al International Journal of Epidemiology, 1992

Cardiovascular Disease Relative Risks for Diabetes

Å2-3 males

Å3-4 females

Stamler Diabetes Care 16:434-444, 1993

UK Prospective Diabetes Study

	More Intensive	Less Intensive
Goal	< 150/85 mm hg	< 180/105 mm hg
Average BP after 9 years	144/82 mm hg	154/87 mm hg

BMJ 317:703-713, 1998

UKPDS Relative Risk Reduction with Intensive Blood Pressure Control

ÅDiabetes-related outcomes	34%
ÅDeath	32%
ÅStroke	44%
ÅMicrovascular complications	37%

BMJ 317:703-713, 1998

Stop Atherosclerosis in Native Diabetics Study (SANDS)
N= 499 Native Americans 40+ years with diabetes

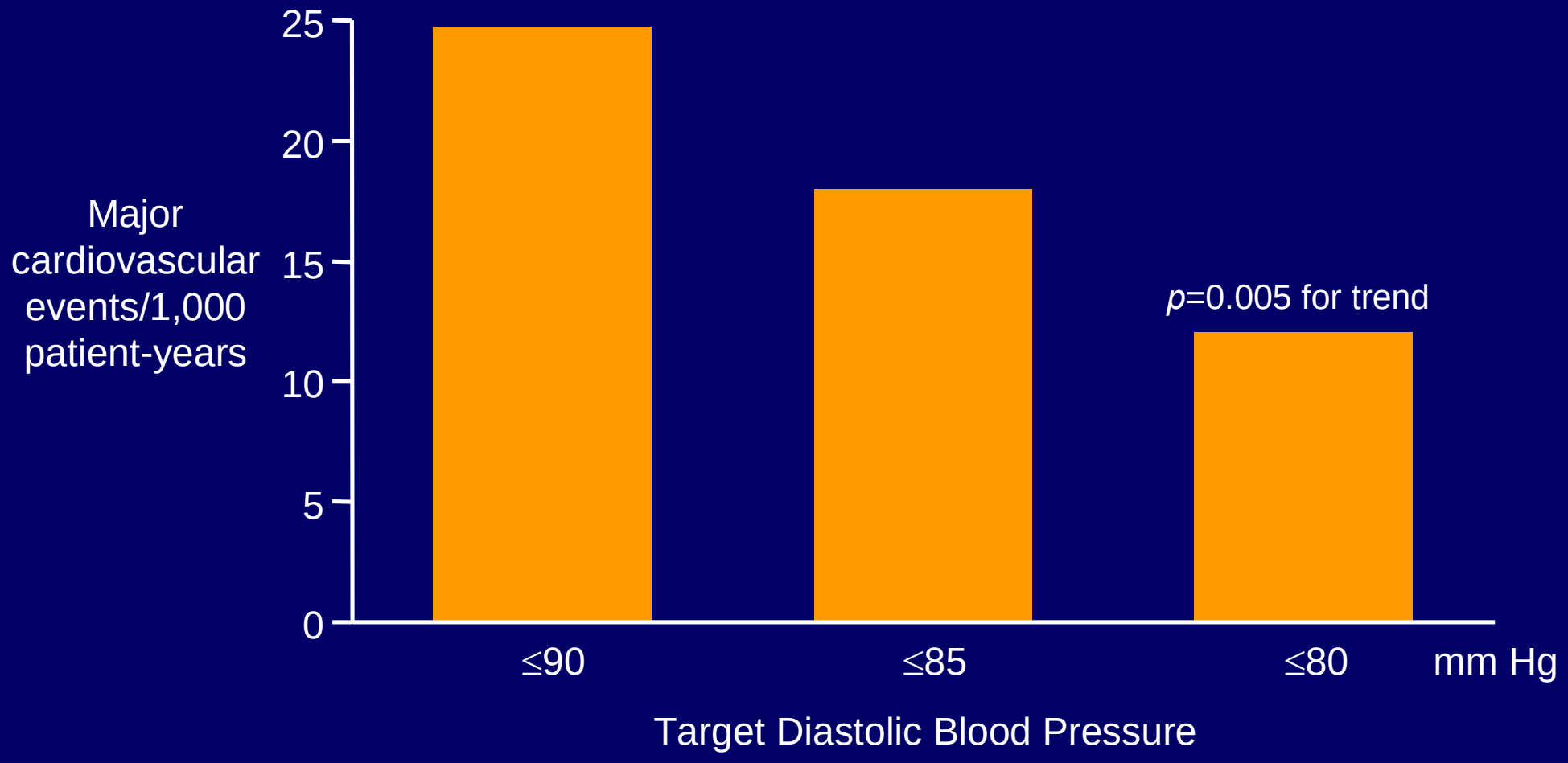
	Aggressive	Standard
Goal Blood Pressure	< 115 mm Hg	< 130 mm Hg
Achieved Blood Pressure	104 mm Hg	117 mm Hg
LV Mass reduction	-2.4 $g/m^{2.7}$	-1.2 $g/m^{2.7}$
Carotid IMT	-0.012 mm	0.038 mm

Modification of Dietary Protein in Renal Disease (MDRD)

	Usual Target	Lower Target
Goal Blood Pressure	<140/90 mm Hg	< 125/75 mm Hg
Achieved Blood Pressure	128/72 mm Hg	134/81 mm Hg
Developed Kidney Failure	70%	62%

Annals of internal Medcine 142:342-351, 2005

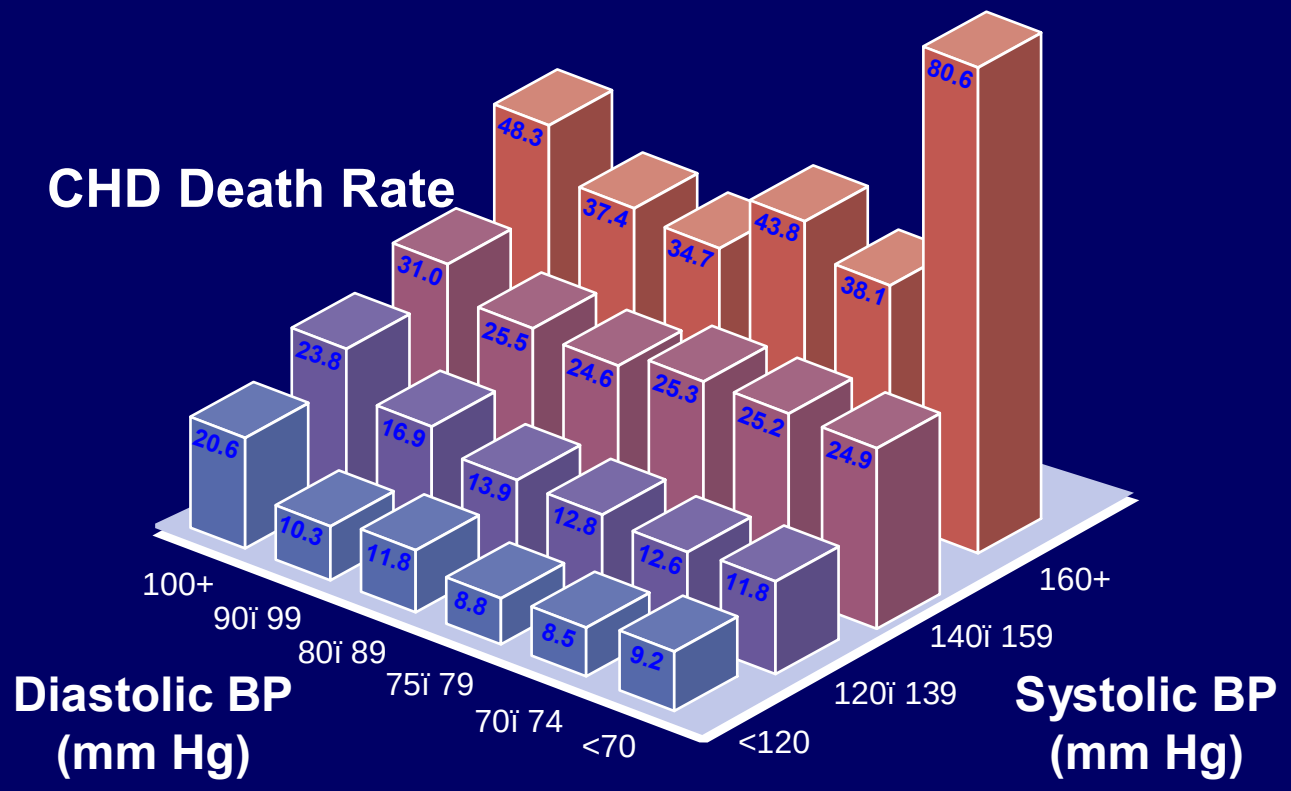
HOT Study: Significant Benefit From Intensive Treatment in the Diabetic Subgroup



Hansson L et al. *Lancet.* 1998;351:1755-1762.

SBP-Associated Risks: MRFIT

SBP versus DBP in Risk of CHD Mortality



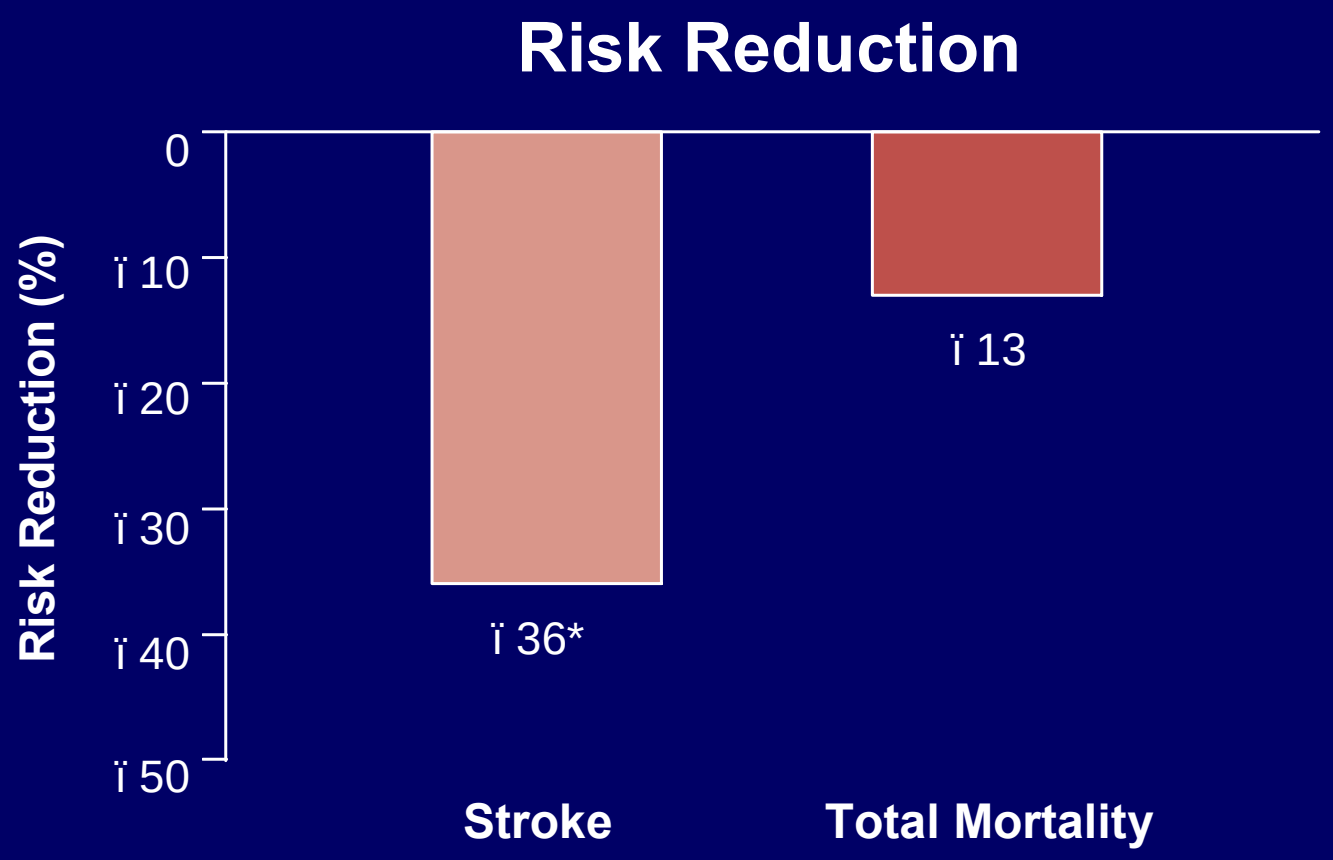
Adapted from Neaton JD et al. *Arch Intern Med*. 1992;152:56-64.

Lowering SBP Benefits Older Patients

- Clinical trials document importance of controlling elevated SBP to prevent cardiovascular disease
  - SHEP (Systolic Hypertension in the Elderly Program)
  - Syst-Eur (Systolic Hypertension in Europe)

Adapted from SHEP Cooperative Research Group. *JAMA*. 1991;265:3255-3264; Staessen JA et al. *Lancet*. 1997;350:757-764.

SHEP: Outcomes



***P=.0003 vs placebo.**

Adapted from SHEP Cooperative Research Group. *JAMA*. 1991;265:3255-3264.

Systolic Hypertension in Europe (Syst-Eur)

Objective: To determine whether antihypertensive treatment reduces cardiovascular complications in older patients with elevated SBP

Patients: 4695 patients, ≥60 years of age, with SBP 160ï 219 mm Hg and DBP <95 mm Hg

Treatments: Nitrendipine (10ï 40 mg/day) with possible addition or substitution of:

- ï Enalapril (5ï 20 mg/day)
- ï Hydrochlorothiazide (12.5ï 25 mg/day)

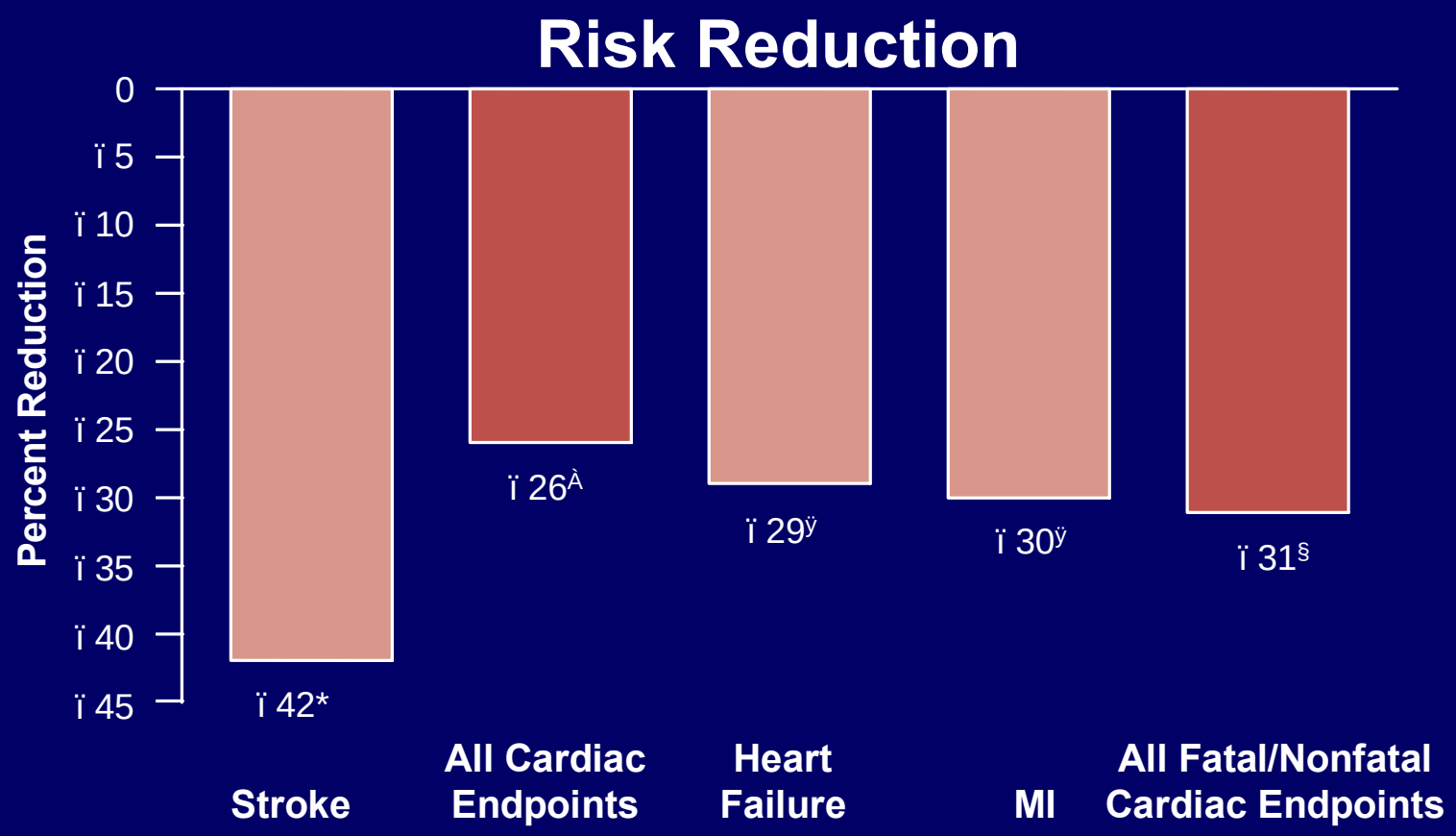
Placebo

Follow-up: 2 years (median)

Endpoint: Total stroke
Myocardial infarction

Adapted from Staessen JA et al. *Lancet.* 1997;350:757-764.

Syst-Eur: Outcomes



*P=.003; ÀP=.03; ÿP=.12; §P<.001.

Adapted from Staessen JA et al. *Lancet*. 1997;350:757-764.

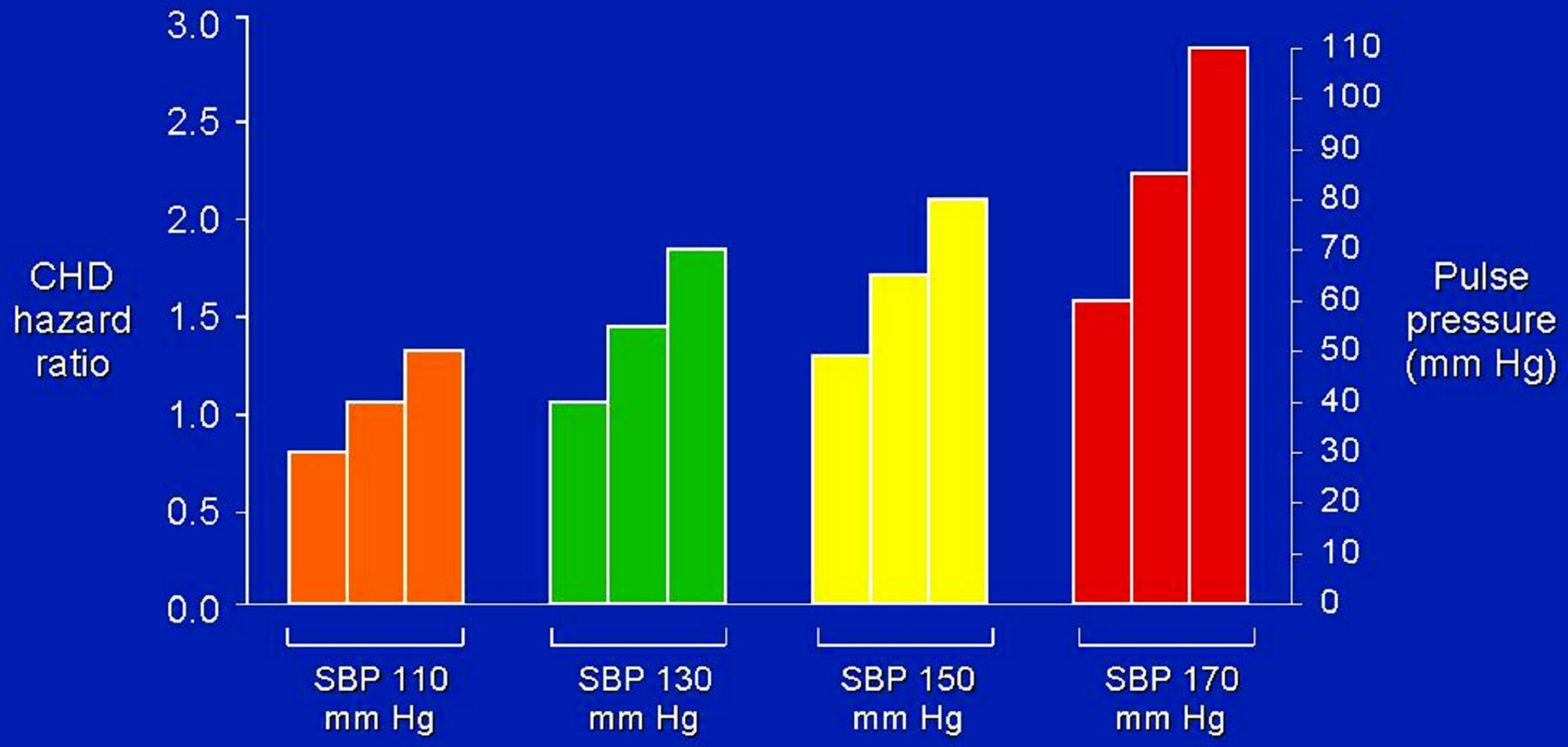
Pulse Pressure

PP = SBP – DBP

- Increase in *pulse pressure* **(PP)** indicates greater stiffness in large conduit arteries, primarily the thoracic aorta.
- **PP**, therefore, is a surrogate measure of dynamic, cyclic stress during systole.
- **PP** may be a better marker of increased CV risk than either systolic BP or diastolic BP alone in older persons.

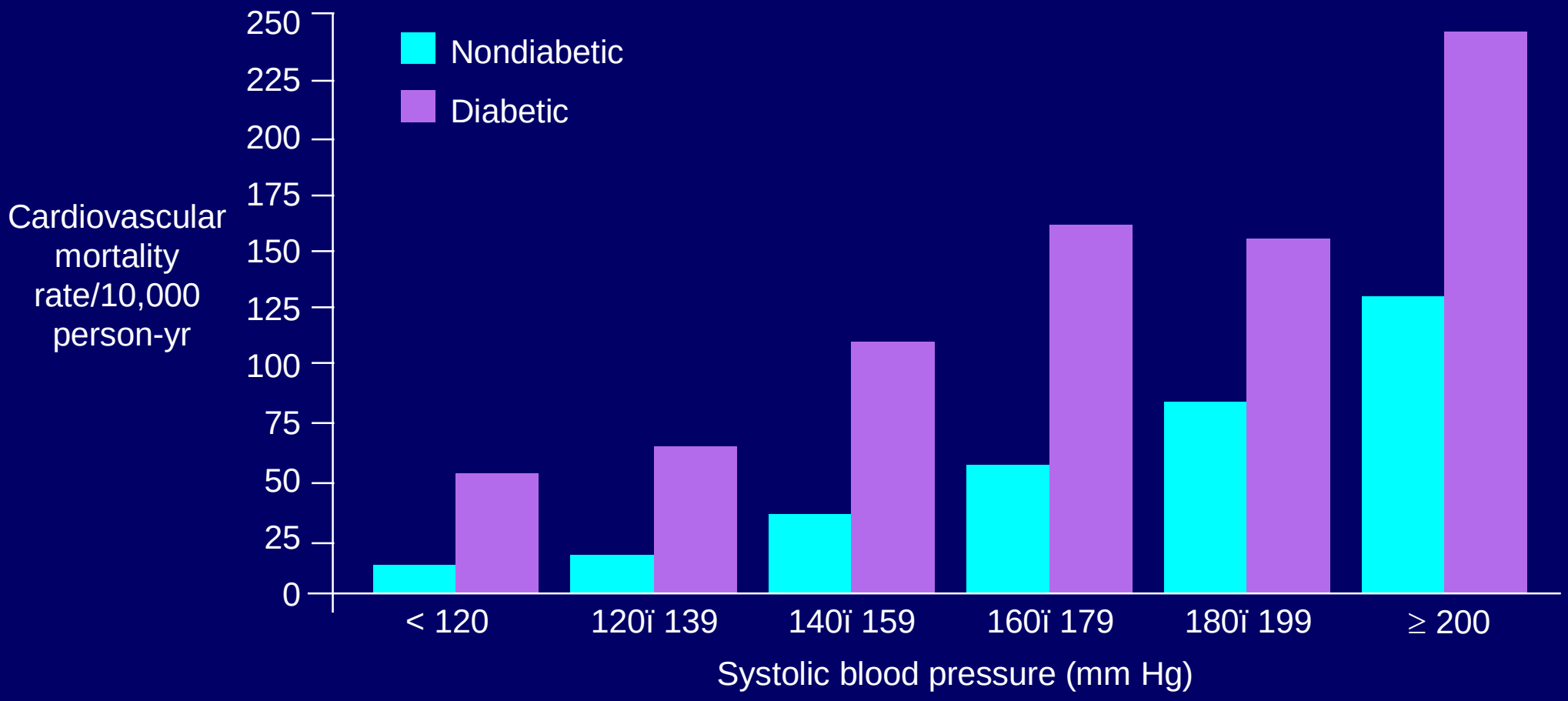
Independent Influence of Pulse Pressure (PP) on Coronary Heart Disease Risk

The Framingham Heart Study



Modified from Franklin S et al. *Circulation*. 1999;100:354-360.

MRFIT: Association of Systolic BP and Cardiovascular Death in Type 2 Diabetes



Stamler J et al. *Diabetes Care*. 1993;16:434-444.

Veterans Administration Hypertension and Screening Clinics

15-Year ESRD Rates and Risk Ratios by Baseline Systolic Blood Pressure

SBP (mm Hg)	Risk Ratio
≤ 140	1.00
> 140 but ≤ 151	1.00
> 151 but ≤ 165	1.08
> 165 but ≤ 180	2.07
> 180	5.62

Number of screenees: 11,912 (5,730 black; 6,182 white)

Source: Perry HM, et al. **Hypertension.** 1995;25:587-594

Veterans Administration Hypertension and Screening Clinics

15-Year ESRD Rates and Risk Ratios by Baseline Diastolic Blood Pressure

DBP (mm Hg)	Risk Ratio
≤ 94	1.00
> 94 but ≤ 100	1.05
> 100 but ≤ 106	0.89
> 106 but ≤ 118	1.54
> 118	4.18

Number of screenees: 11,912 (5,730 black; 6,182 white)

Source: Perry HM, et al. **Hypertension.** 1995;25:587-594

United Kingdom Prospective Diabetes Study (UKPDS): Results

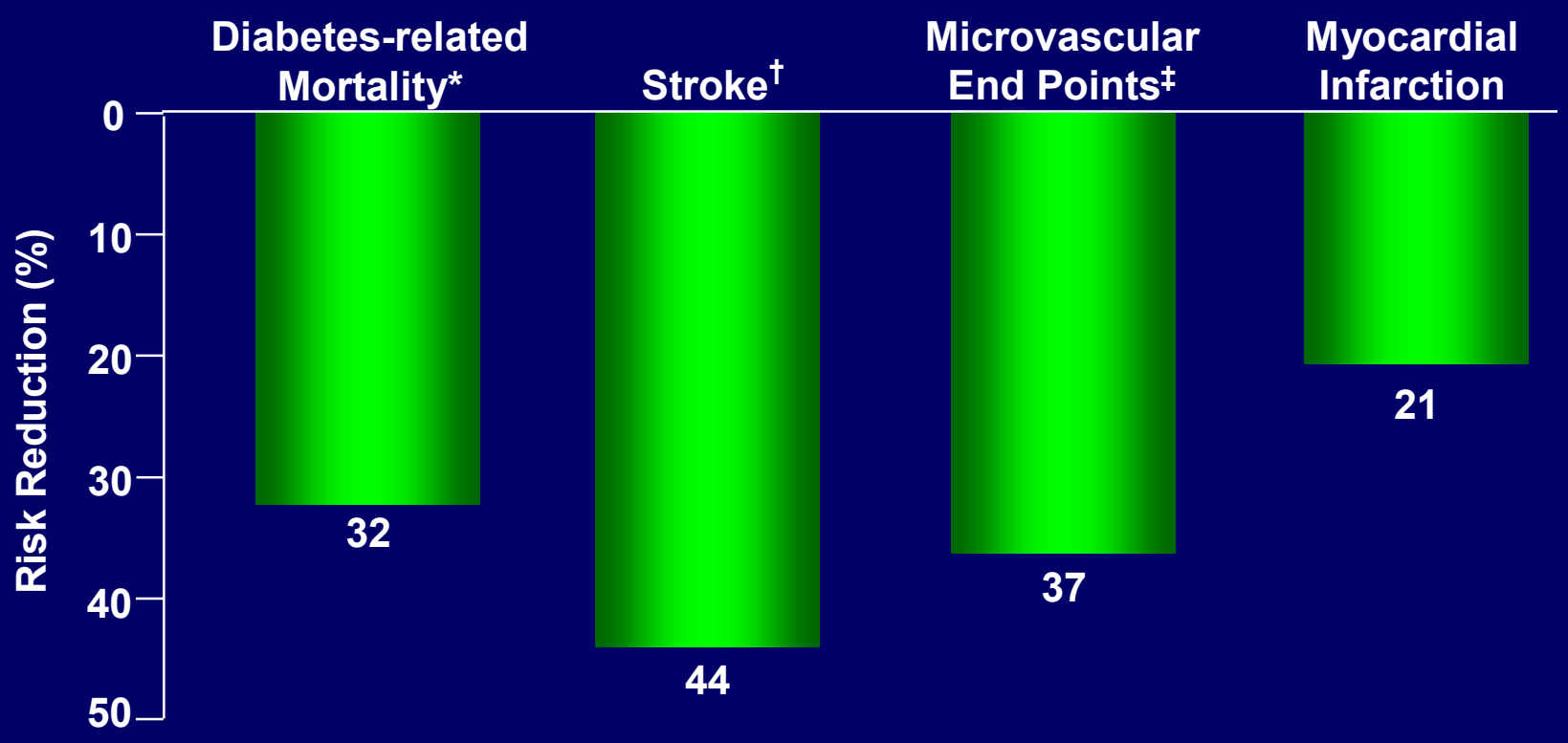
Å Tight blood pressure control* with captopril- or atenolol-based therapy reduces risk of

	Risk reduction	*p*-value
ï Any diabetes-related endpoints	24%	0.005
ï Diabetes-related deaths	32%	0.019
ï Stroke	44%	0.013
ï Microvascular endpoints	37%	0.009

* Mean blood pressure achieved: 144/82 vs 154/87 mm Hg.

UK Prospective Diabetes Study Group 38. *BMJ.* 1998;317:703-713.
UK Prospective Diabetes Study Group 33. *Lancet.* 1998;352:837-853.

Risk Reduction of Diabetes-Related End Points with Tight BP Control



* Death due to MI, sudden death, stroke, peripheral vascular disease, renal disease, hyperglycemia, or hypoglycemia.
À Fatal or nonfatal.
ÿ Retinopathy requiring photocoagulation, vitreous hemorrhage and fatal or nonfatal renal failure.
Mean BP achieved with captopril- or atenolol-based therapy: 144/82 mm Hg (tight BP control) vs 154/87 mm Hg (less tight BP control).
Adapted from UK Prospective Diabetes Study Group. BMJ. 1998;317:703-713.

Stop Atherosclerosis in Native Diabetics Study (SANDS)
N= 499 Native Americans 40+ years with diabetes

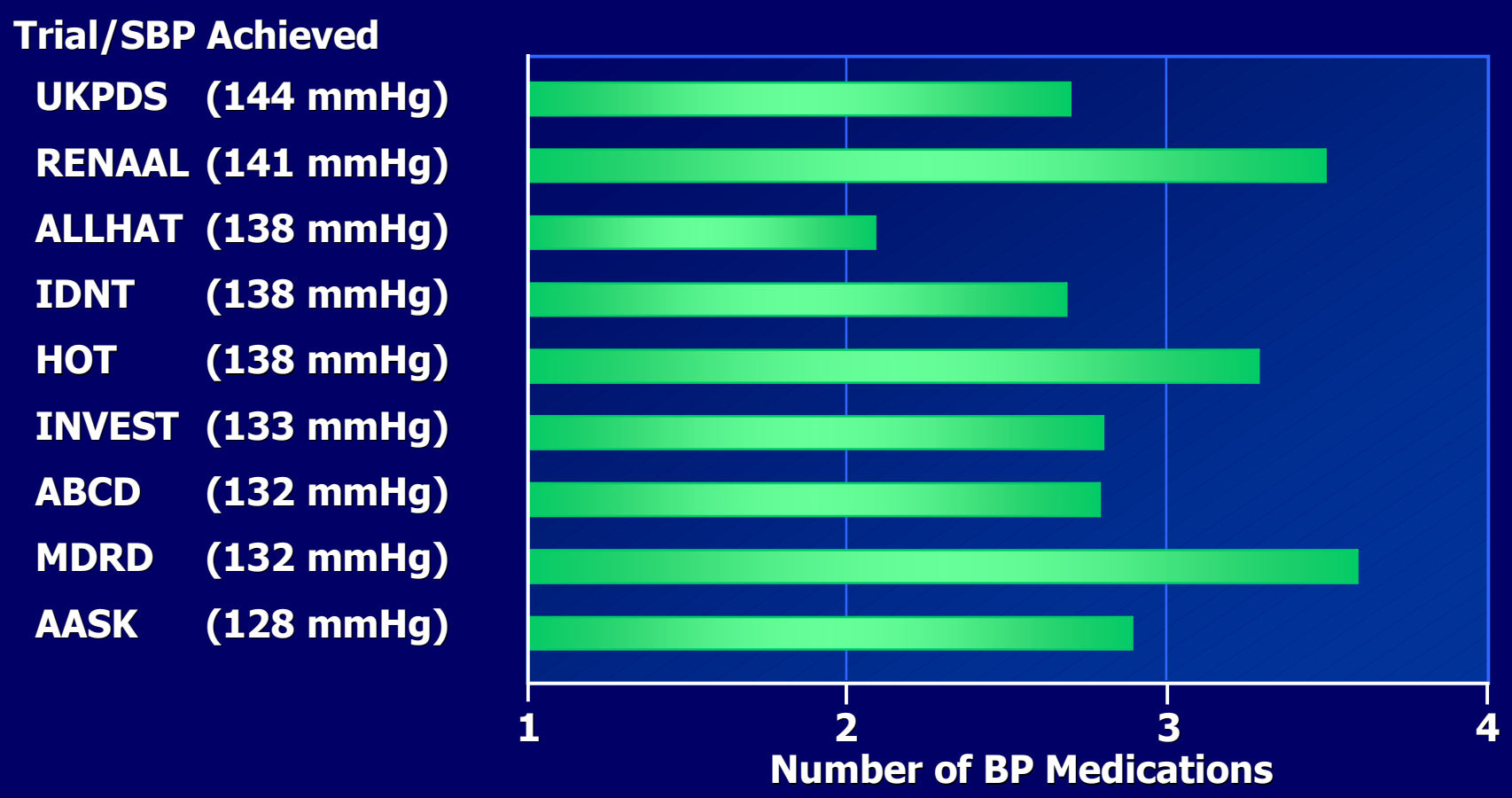
	Aggressive	Standard
Goal Blood Pressure	< 115 mm Hg	< 130 mm Hg
Achieved Blood Pressure	104 mm Hg	117 mm Hg
LV Mass reduction	-2.4 $g/m^{2.7}$	-1.2 $g/m^{2.7}$
Carotid IMT	-0.012 mm	0.038 mm

SANDS Conclusions

- It is possible to lower blood pressure to an "optimal" level without harm in patients with diabetes
- Better outcomes were seen with lower blood pressure in patients with diabetes.

BP Control Usually Requires Combination Therapy

Most patients require ≥2 antihypertensives to reach BP goal



BP=blood pressure; SBP=systolic blood pressure.

Copley JB, Rosario R. *Dis Mon*. 2005;51:548–614.

1300

650

TOTAL Calories
2250

$7.41

24 oz. Beverage
300

2/3 LB** Double Bacon Cheese Thickburger

Serving size (grams) = 462

Calories = 1300

Calories from fat = 860

Total fat = 96 grams

Saturated fat = 40 grams

Cholesterol = 205 mg

Sodium = 2110 mg

Total Carbohydrates = 51 grams