

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)



Hypertension with Diabetes

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Goals

Describe	Describe HTN and diabetes burden in the U.S.
Discuss	Discuss impact of SGLT2is on BP
Recognize	Recognize potential benefits of SGLT2is in HTN treatment

Diabetes Prevalence by Race/Ethnicity

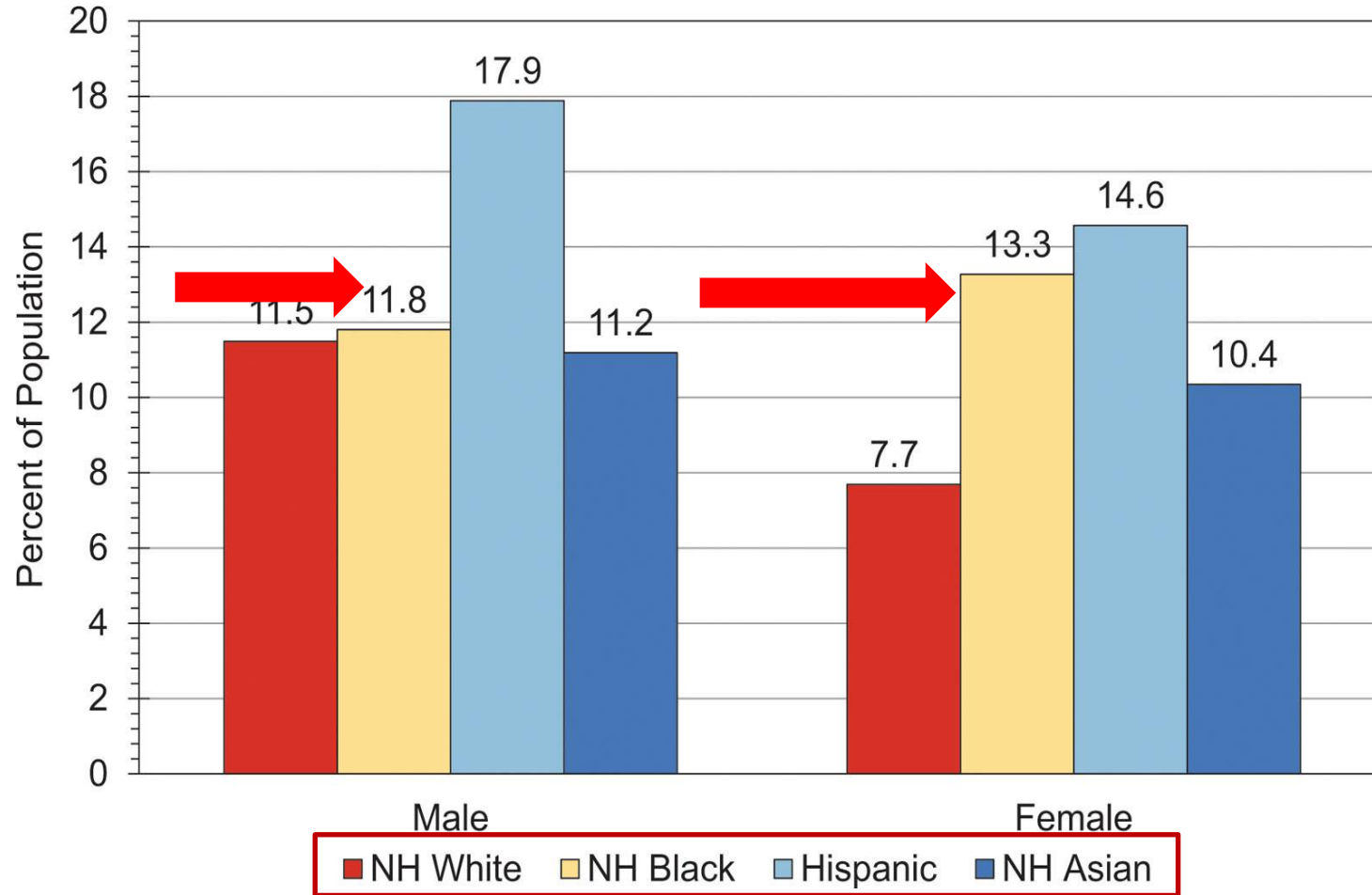


Chart 9-1. Age-adjusted prevalence of diagnosed diabetes in US adults ≥20 years of age by race and ethnicity and sex (NHANES 2017-2020)

Which of the following has the highest prevalence of diabetes by race/ethnicity?

- a) Non-Hispanic White male
- b) Hispanic Male
- c) Non-Hispanic Asian Female
- d) White Female

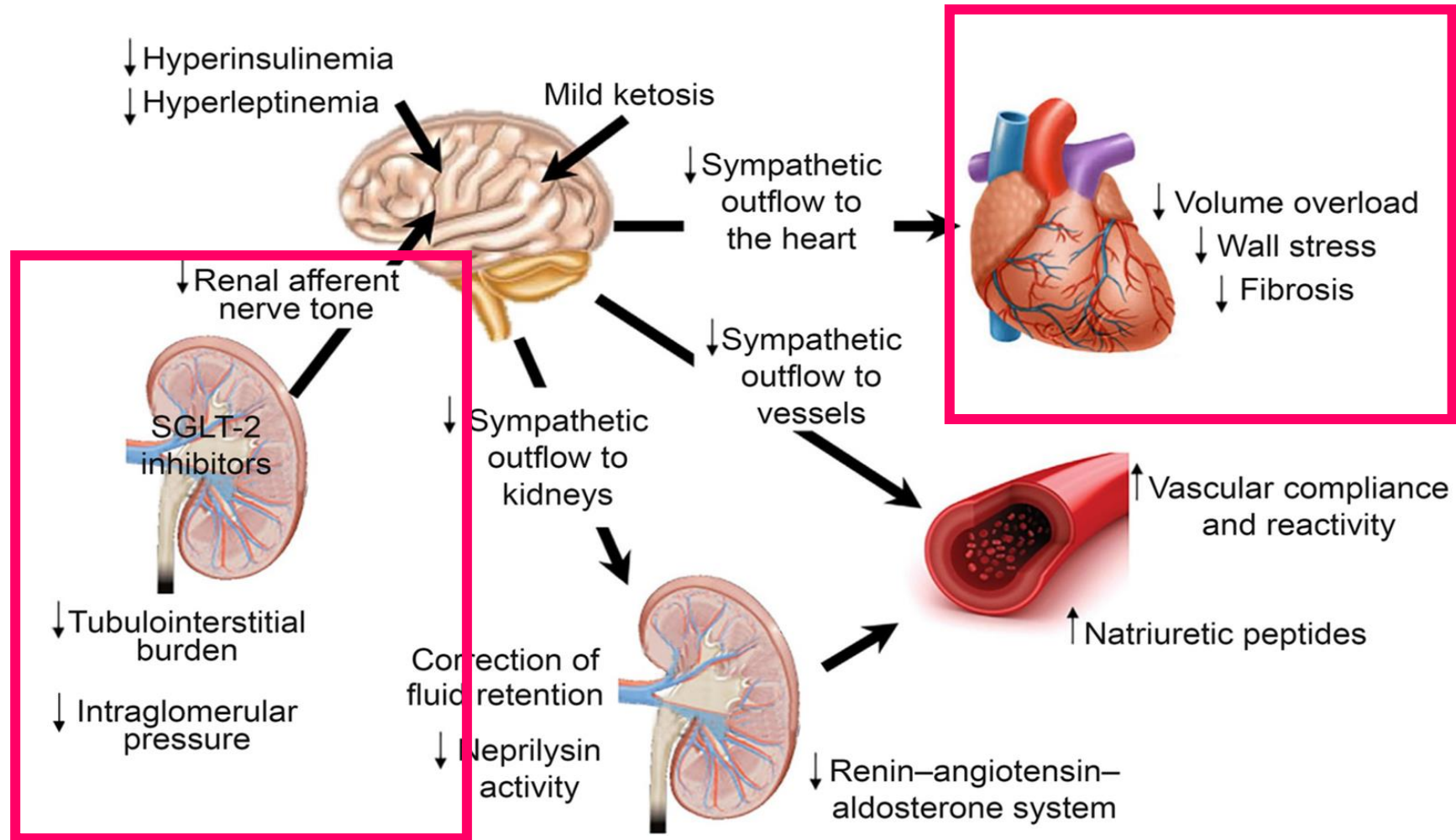
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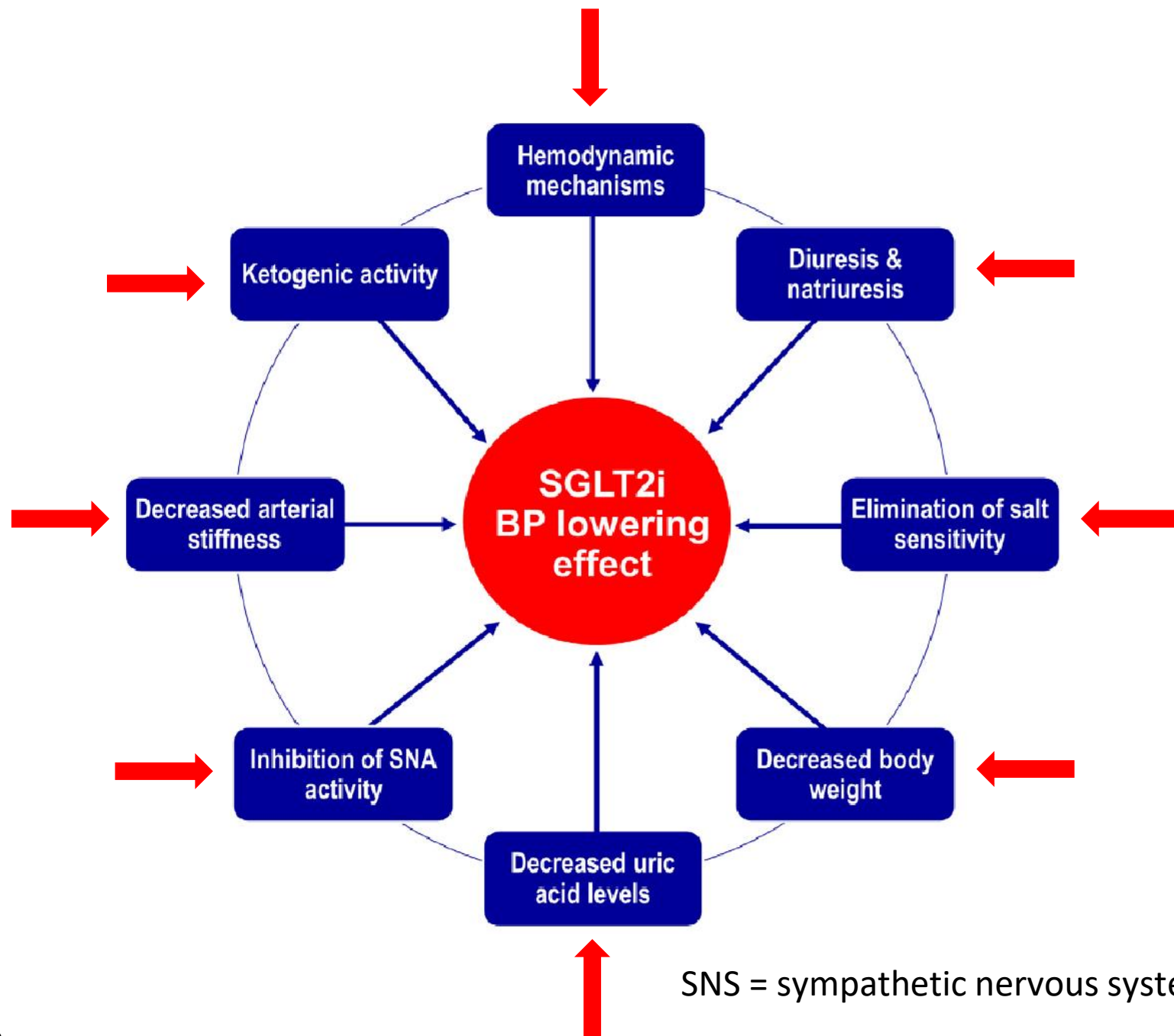
Impact of DM on CVD and All-Cause Mortality

- DM patients more than without DM, had
- 1.56 times higher risk of death from all-cause
- 1.72 times higher from heart disease
- 1.48 times higher from cerebrovascular disease
- 1.67 times higher from CVD

Potential mechanisms: Cardioprotective & Renoprotective SGLT-2is effects in CV Outcomes Trials



Potential mechanisms: BP-lowering effects of SGLT2i

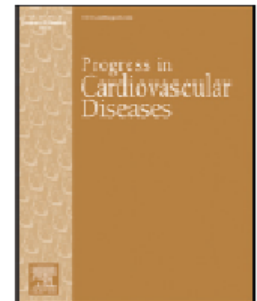




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Control of 24-hour blood pressure with SGLT2 inhibitors to prevent cardiovascular disease☆



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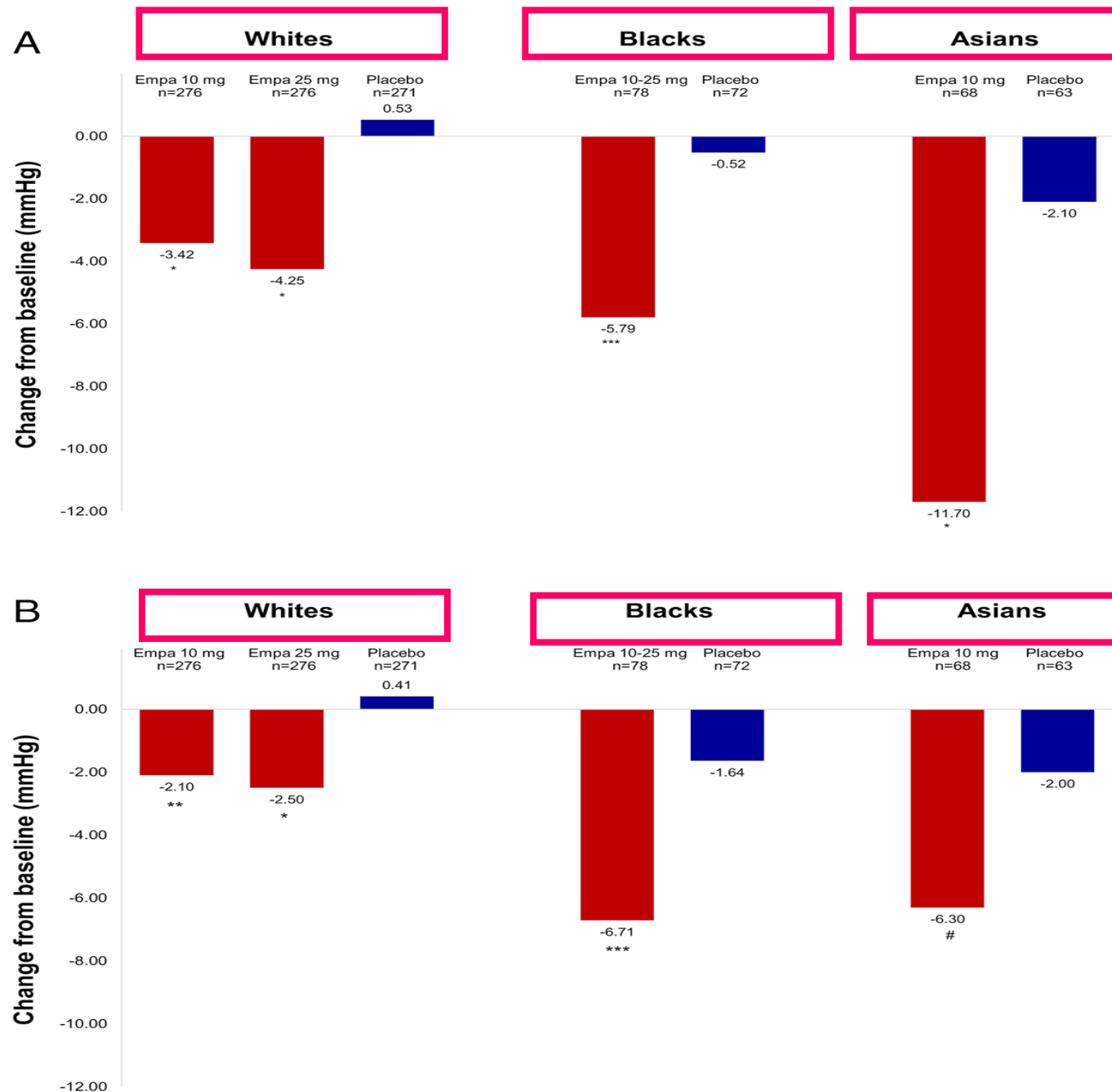
^b Hypertension Cardiovascular Outcome Prevention and Evidence in Asia (HOPE Asia) Network, Japan

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Changes from baseline in:
 Daytime (A) and nighttime (B)
 SBP based on ABPM during 12 weeks treatment with empagliflozin vs. placebo

*p <0.001,
 **p <0.01,
 ***p <0.05,
 p = 0.159





Antihyperglycemic and Blood Pressure Effects of Empagliflozin in Black Patients With Type 2 Diabetes Mellitus and Hypertension

Editorial, see p 2110

BACKGROUND: Empagliflozin, a sodium-glucose cotransporter 2 inhibitor indicated for type 2 diabetes mellitus (T2DM), can lower blood pressure (BP) and reduce cardiovascular mortality in patients with T2DM and preexisting cardiovascular disease. Its effects in blacks have been understudied.

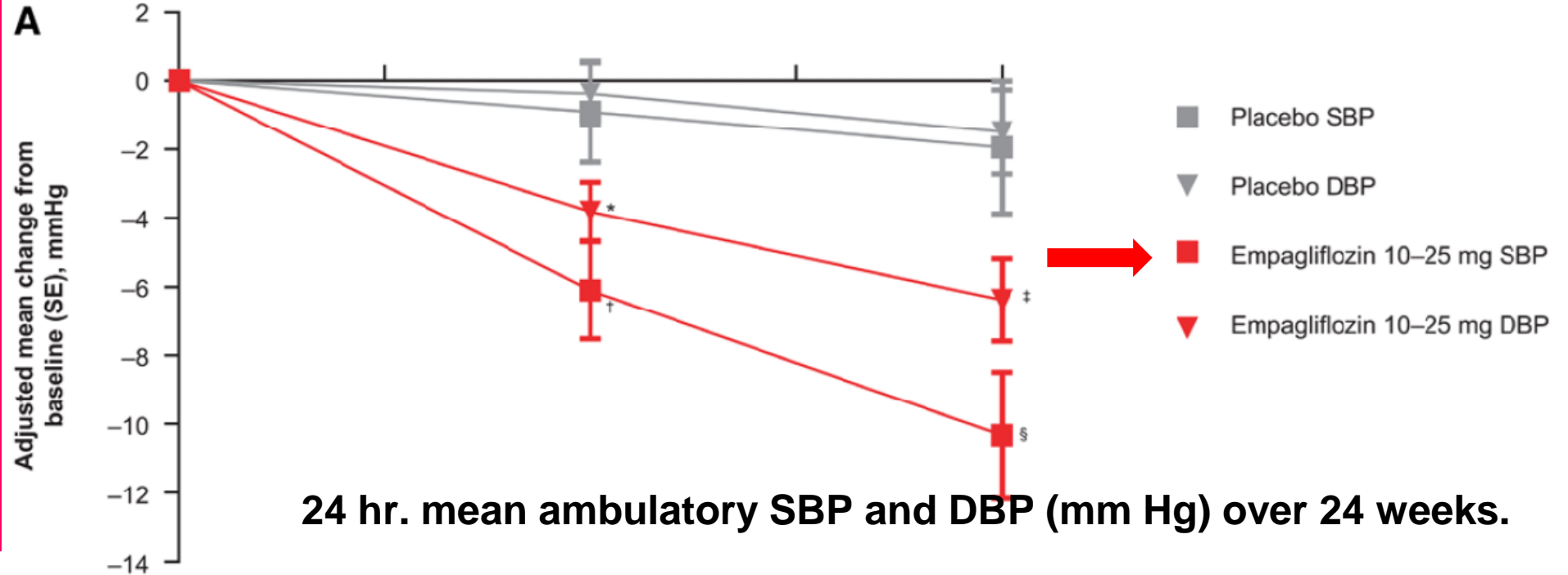
METHODS: In this 24-week study, 150 blacks with T2DM and hypertension

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Leo Seman, MD, PhD

24-hour ambulatory BP.

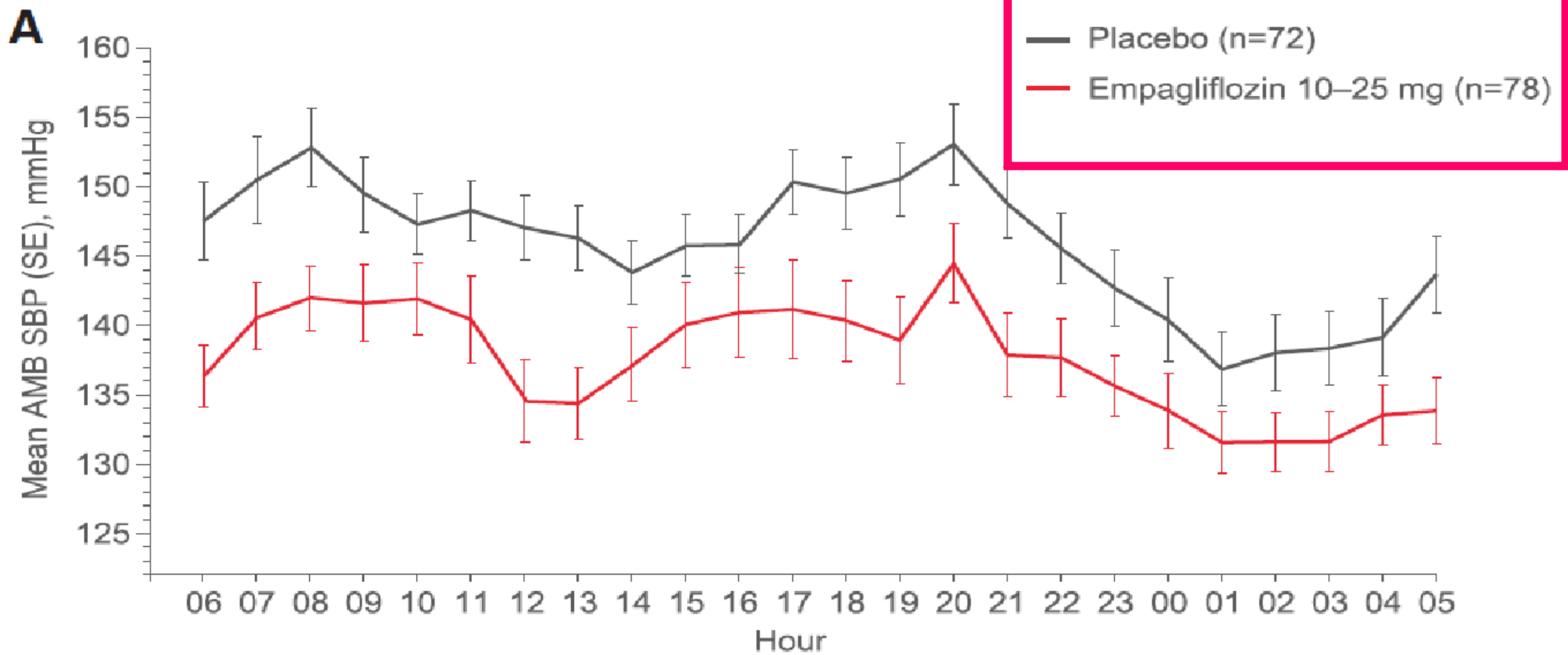
52.7% male,
mean (SD)
age, 56.8 (9.3) years

Mean duration of T2D,
9.3 (7.1) years.



*** $P=0.0069$; † $P=0.0117$; ‡ $P=0.0058$; § $P=0.0025$, all versus placebo.**

	Baseline Adjusted Mean	Week 12 Adjusted Mean Change From Baseline	Week 24 Adjusted Mean Change From Baseline
Placebo, SBP (mmHg)	145.78	-0.90	-1.94
Empa 10–25 SBP (mmHg)	146.81	-6.10	-10.33
Placebo, DBP (mmHg)	90.08	-0.37	-1.48
Empa 10–25 DBP (mmHg)	88.72	-3.80	-6.38

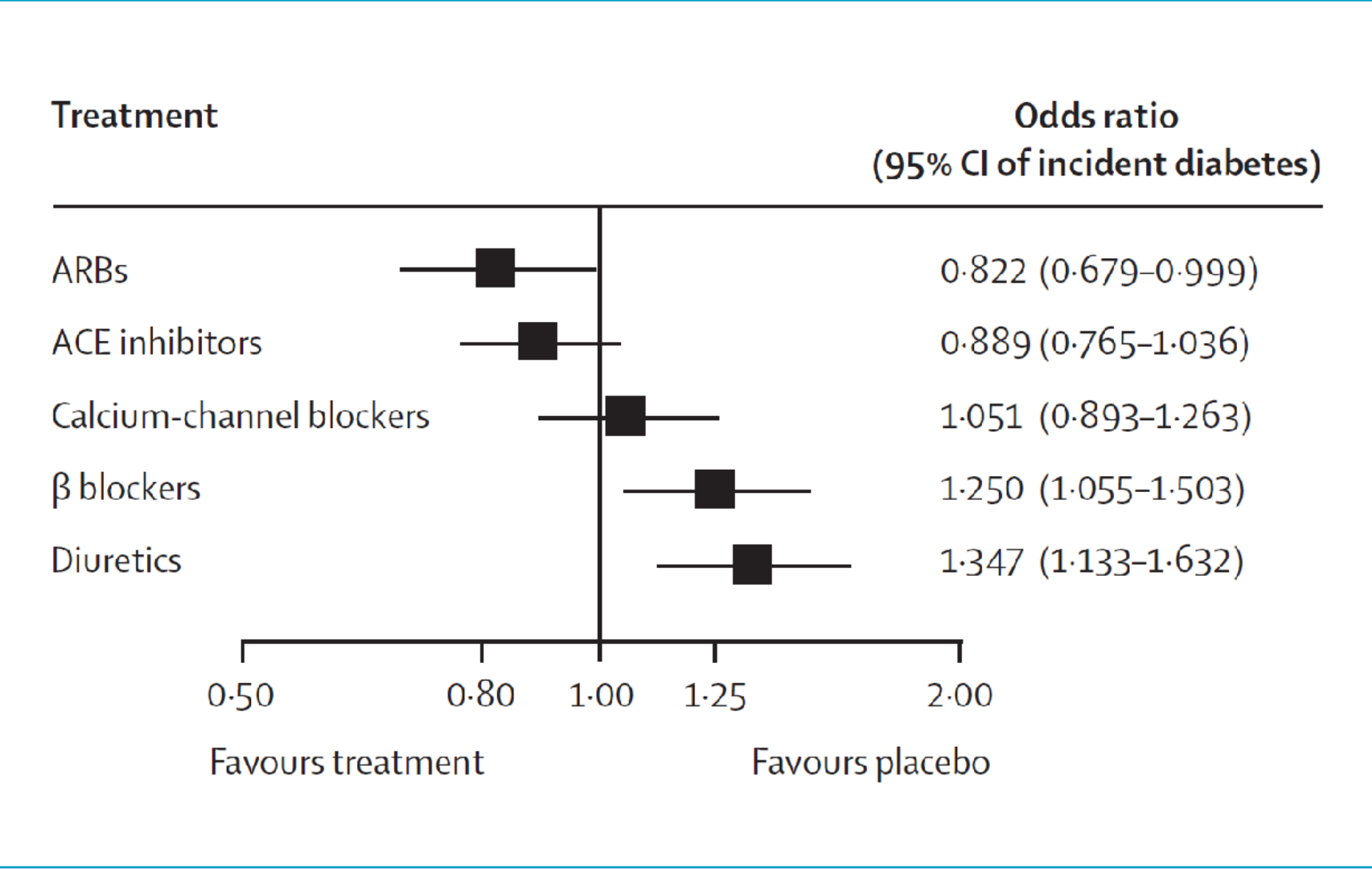


Number of patients with data:

Hour	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	00	01	02	03	04	05
Placebo	58	57	57	56	57	55	55	57	56	56	56	58	56	55	58	57	57	58	58	58	58	58	55	58
Empagliflozin	52	51	50	47	52	49	50	52	51	50	52	51	52	51	51	51	53	51	53	53	52	53	53	52

New-onset DM and Antihypertensives

Full Bayesian Network Meta-Analysis



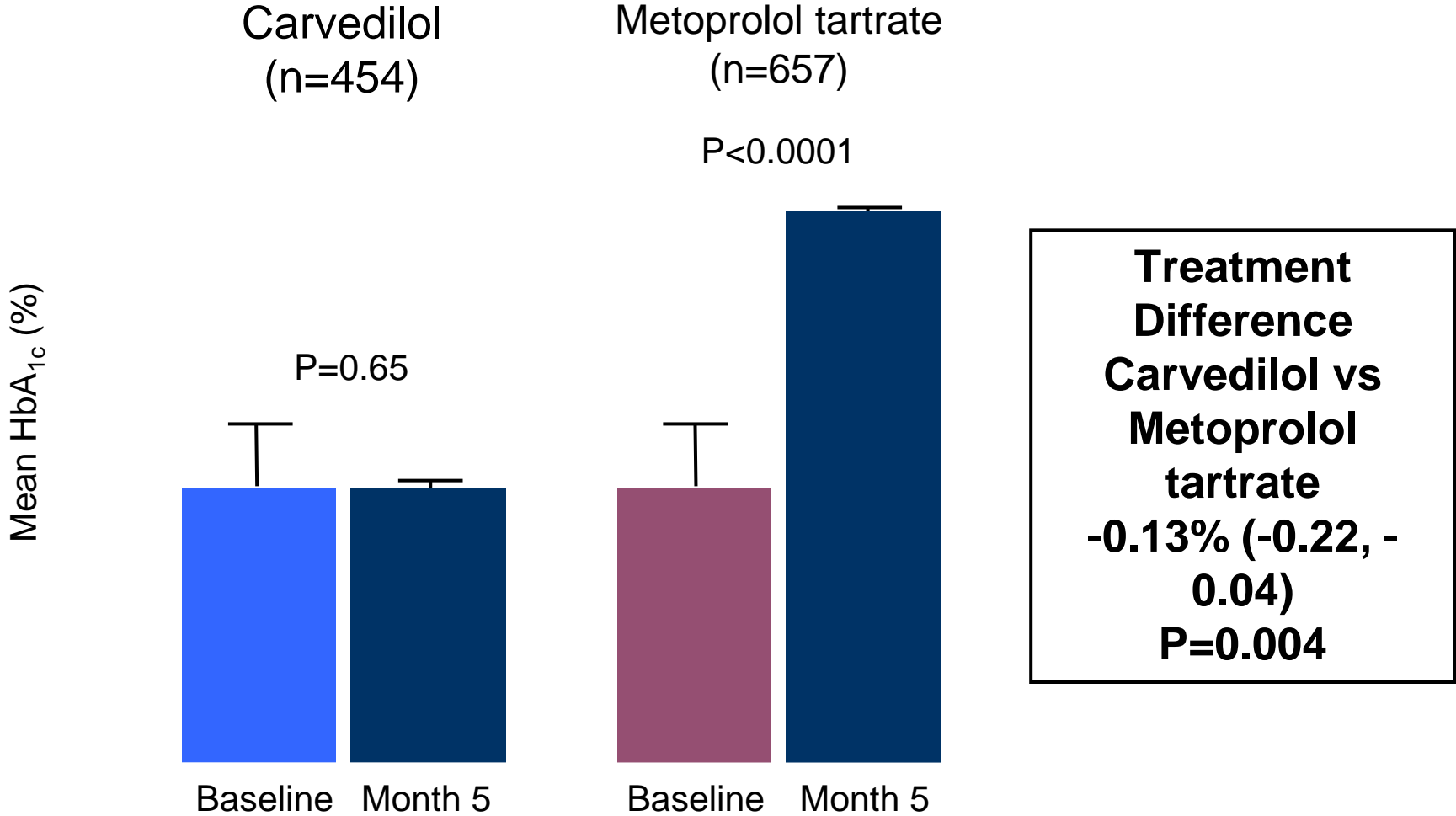
Which anti-hypertensive causes the highest rate of new onset diabetes?

- a) ARBs
- b) ACE inhibitors
- c) Calcium-channel blockers
- d) B-blockers
- e) Diuretics

Which anti-hypertensive causes the highest rate of new onset diabetes?

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- d) B-blockers
- e) Diuretics

GEMINI: Hemoglobin A_{1c}



1111 patients (90%) evaluable for efficacy, having both a valid baseline and at least one on-therapy HbA_{1c} .

Circulation

EDITORIAL

Are SGLT2 Inhibitors New Hypertension Drugs?

Kazuomi Kario^{id}, MD,
PhD

Keith C. Ferdinand, MD

Wanpen Vongpatanasin,
MD

Data on Changes in Ambulatory BP During Treatment With SGLT2 Inhibitors

† P<0.001.

‡ P<0.01.

§ P<0.05

Drug and dose	Number of patients SGLT2i/placebo	Office SBP (mm Hg)			24-h ambulatory SBP (mm Hg)			Nighttime ambulatory SBP (mm Hg)		
		Baseline*	Change from baseline	Placebo-subtracted change from baseline	Baseline*	Change from baseline	Placebo-subtracted change from baseline	Baseline*	Change from baseline	Placebo-subtracted change from baseline
Kario et al, 2019 (SACRA) ³	68/63	141	-9.9†	-8.6‡	139	-10.0†	-7.7‡	130	-6.3‡	-4.3
Empagliflozin 10 mg/d										
Ferdinand et al, 2019 ⁴	78/72	149	-10.3	-7.4‡	146	-10.3	-8.4‡	144	-6.7	-5.1§
Empagliflozin 10–25 mg/d										
Tikkanen et al, 2015 (EMPA-REG BP) ⁵	276/271	142	-5.5	-4.8†	131	-3.7	-4.2†	123	-2.5	-2.9†
Empagliflozin 25 mg/d										
Papadopoulou et al, 2021 ⁶	43/42	130	NR	NR	129	-5.8‡	-5.7	NR	NR	NR
Dapagliflozin 10 mg/d										

BP Goals for Patients With Diabetes

Blood pressure should be measured at every routine clinical visit. When possible, individuals found to have elevated blood pressure (systolic blood pressure 120–129 mmHg and diastolic <80 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension

Hypertension is defined as a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 80 mmHg based on an average of ≥ 2 measurements obtained on ≥ 2 occasions

Individuals with blood pressure $\geq 180/110$ mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit

All people with hypertension and diabetes should monitor their blood pressure at home

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Diabetes, Obesity, and CKD

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Diabetes Prevalence by Race/Ethnicity

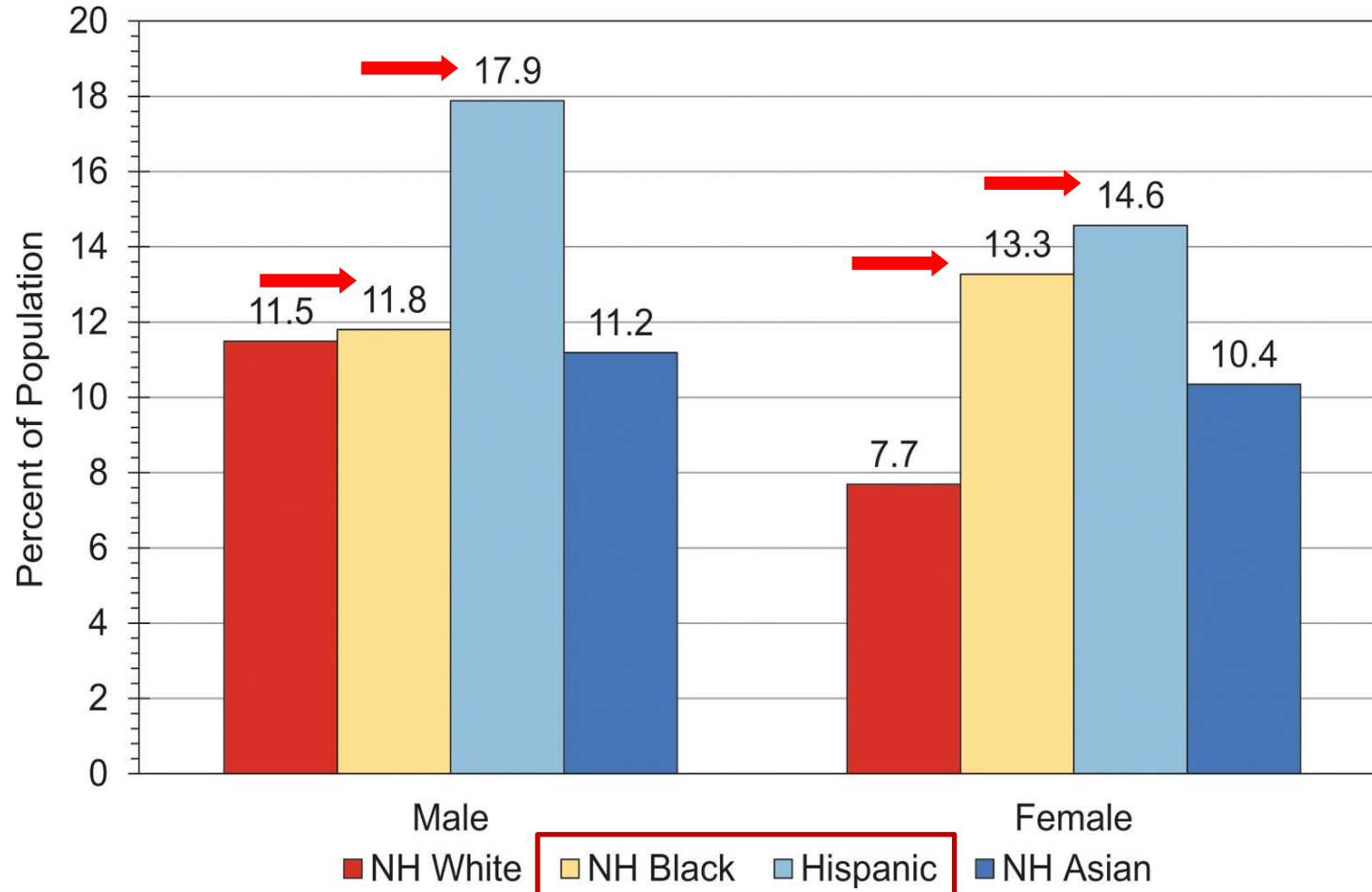
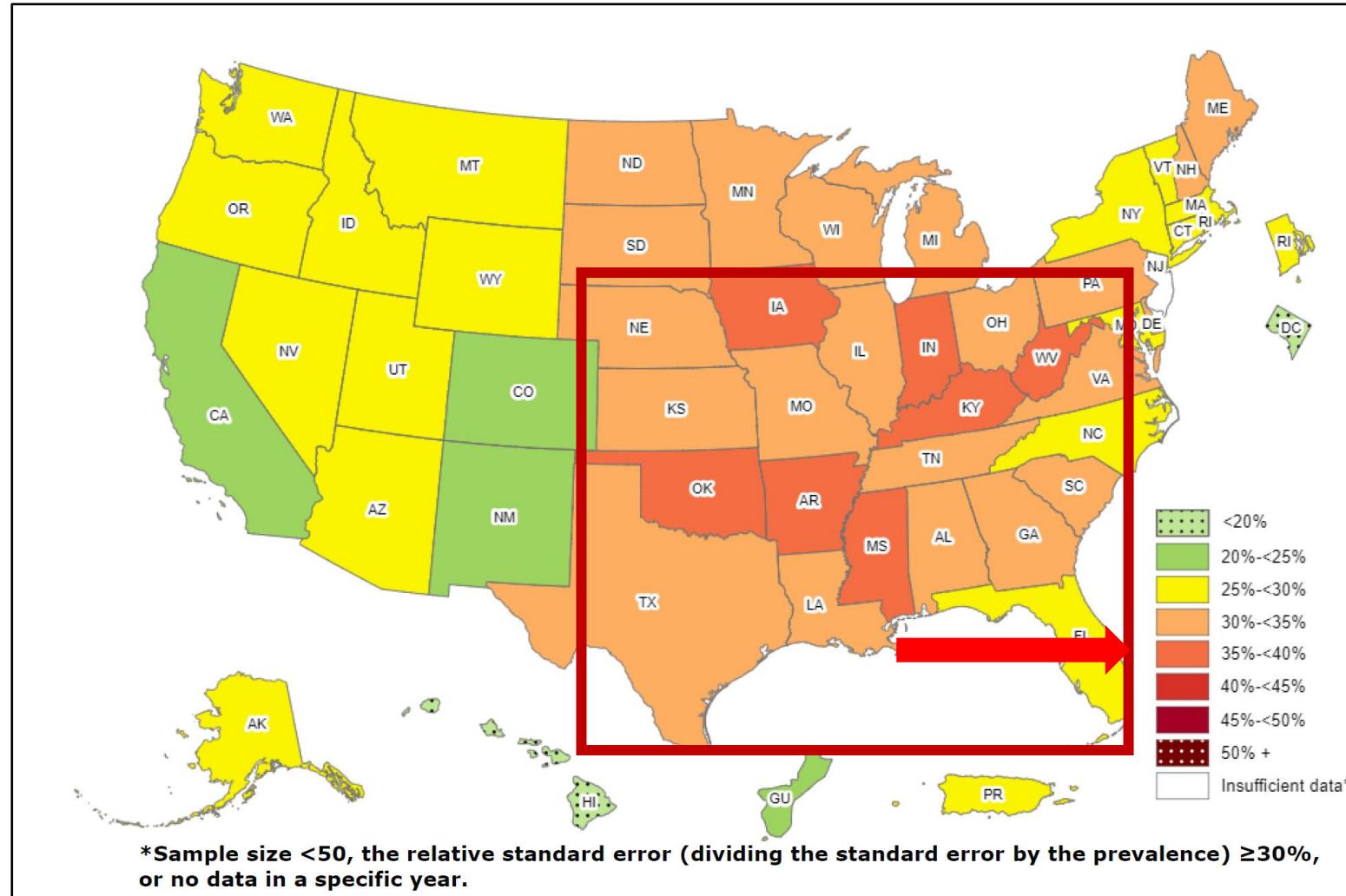


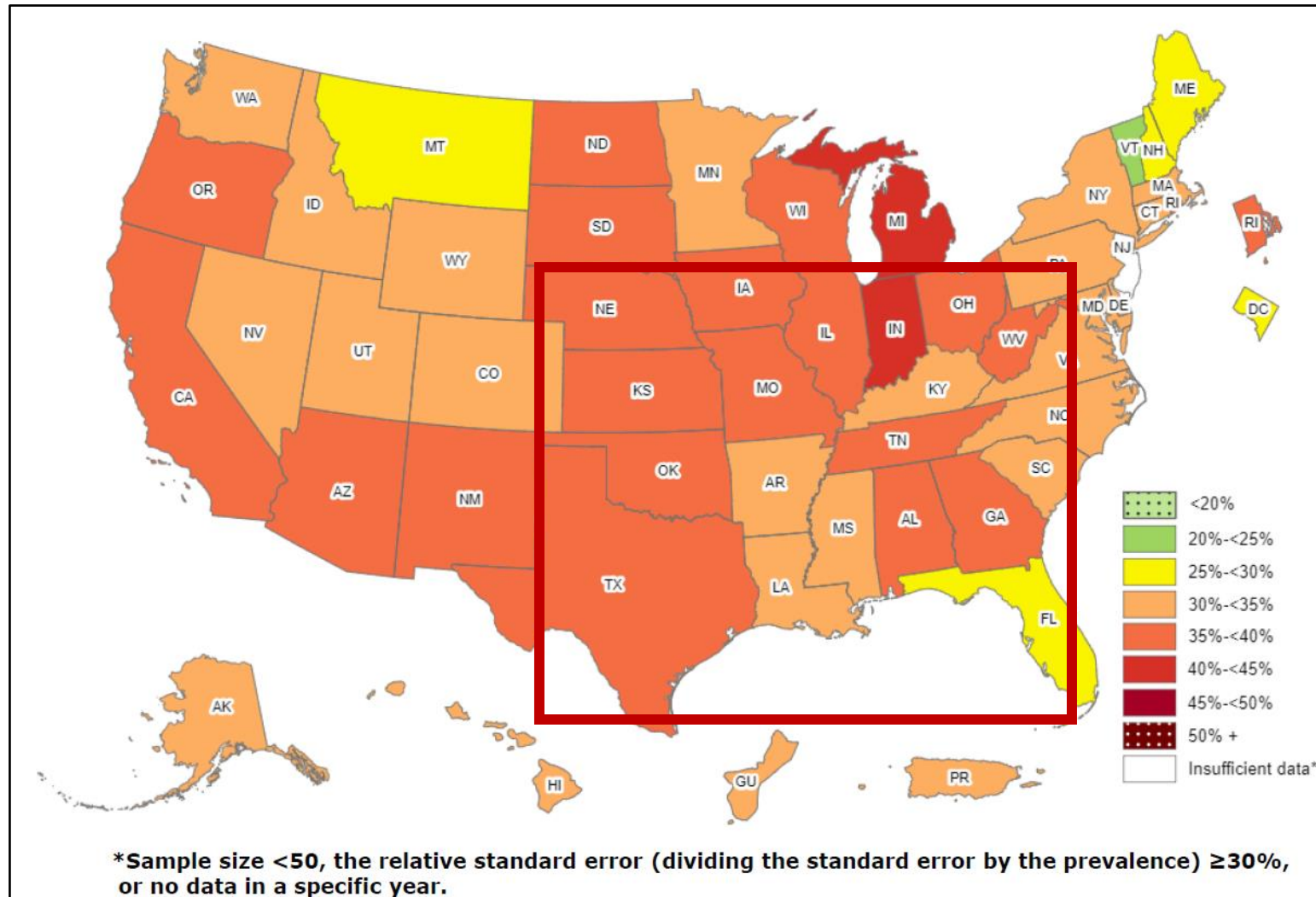
Chart 9-1. Age-adjusted prevalence of diagnosed diabetes in US adults ≥20 years of age by race and ethnicity and sex (NHANES 2017-2020)

NH White Adults Obesity Prevalence



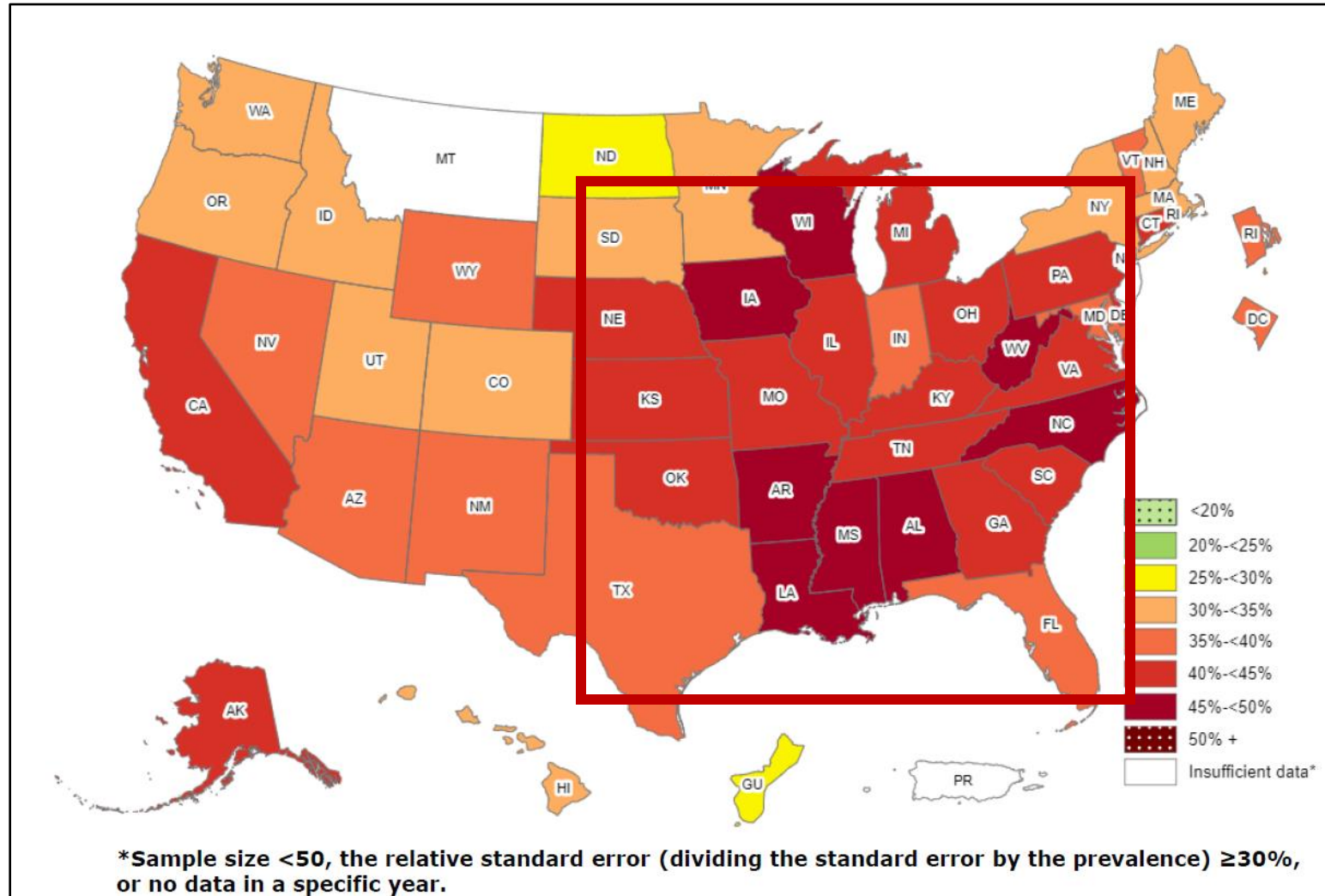
Prevalence of Self-Reported Obesity Among Non-Hispanic White Adults, by State and Territory, BFRSS, 2018 - 2020

Hispanic/Latinx Adults Obesity Prevalence



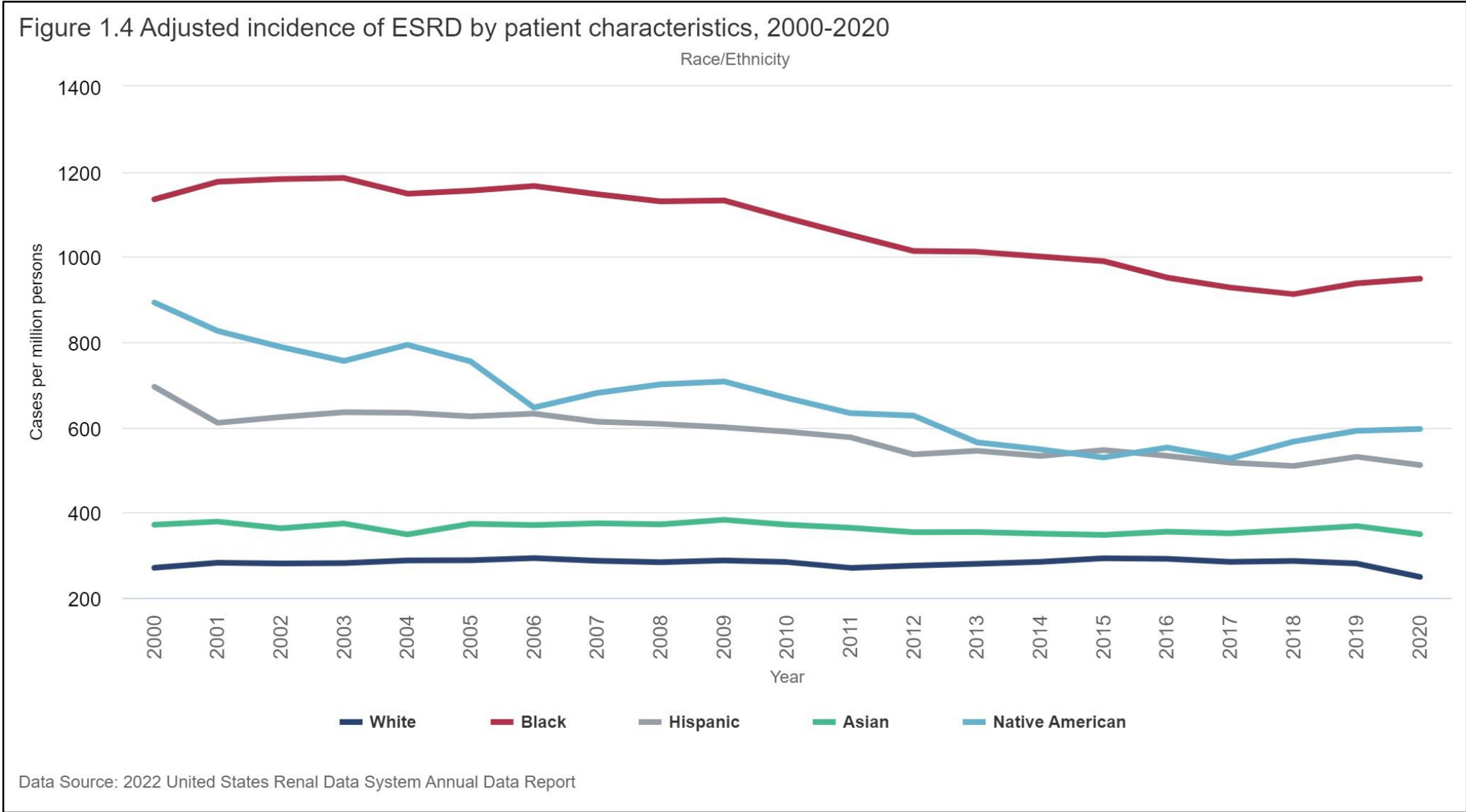
Prevalence of Self-Reported Obesity Among Hispanic White Adults, by State and Territory, BFRSS, 2018 - 2020

NH Black Adults Obesity Prevalence



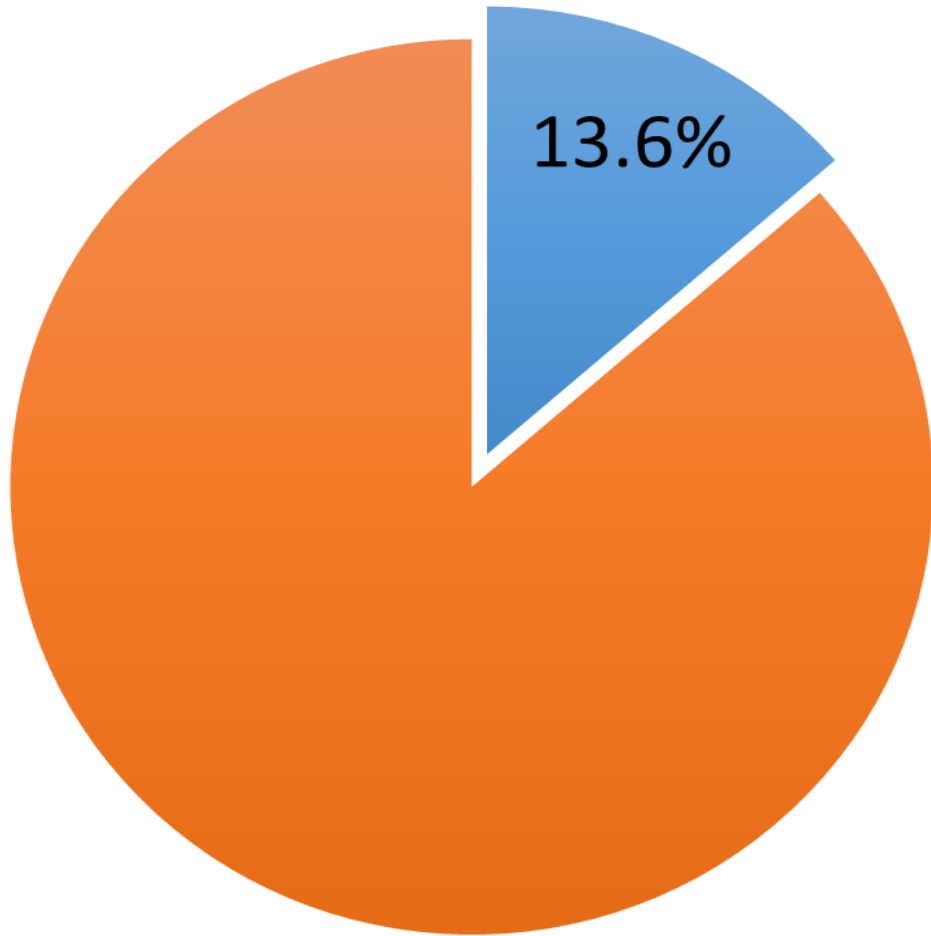
Prevalence of Self-Reported Obesity Among Non-Hispanic Black Adults, by State and Territory, BFRSS, 2018 - 2020

Adjusted ESRD incidence rate, by race categories (2000-2020)

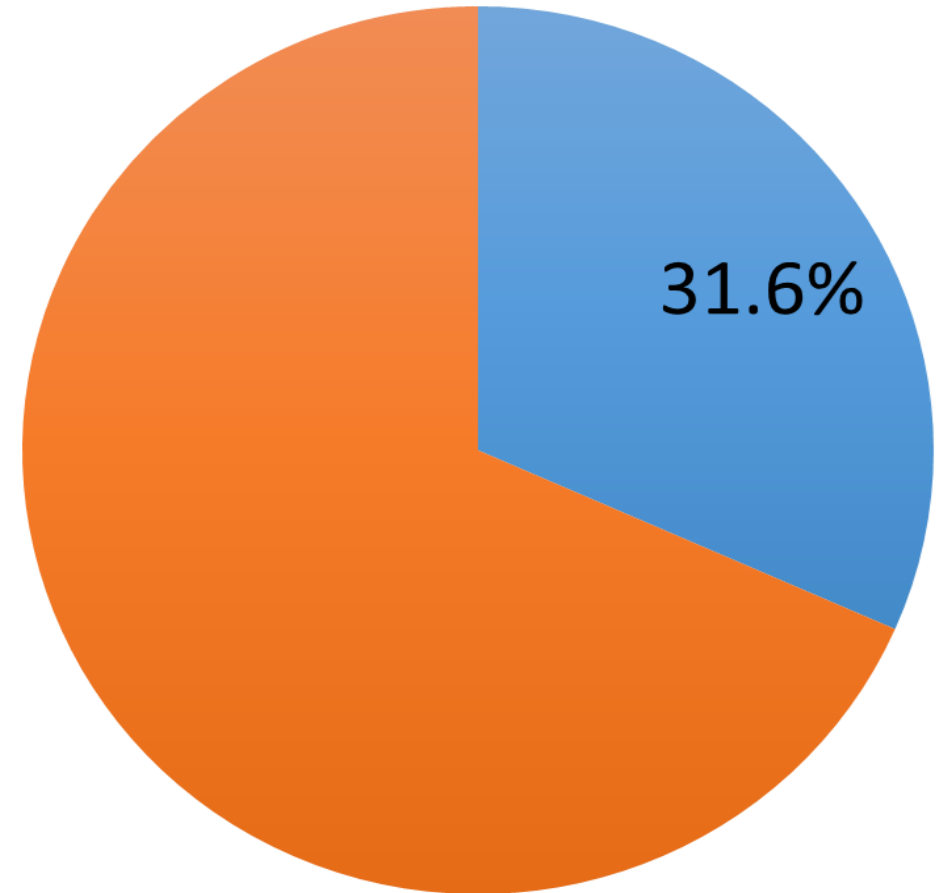


ESRD: Racial differences in prevalence USRD, 2020

US African American Population



US ESRD Population



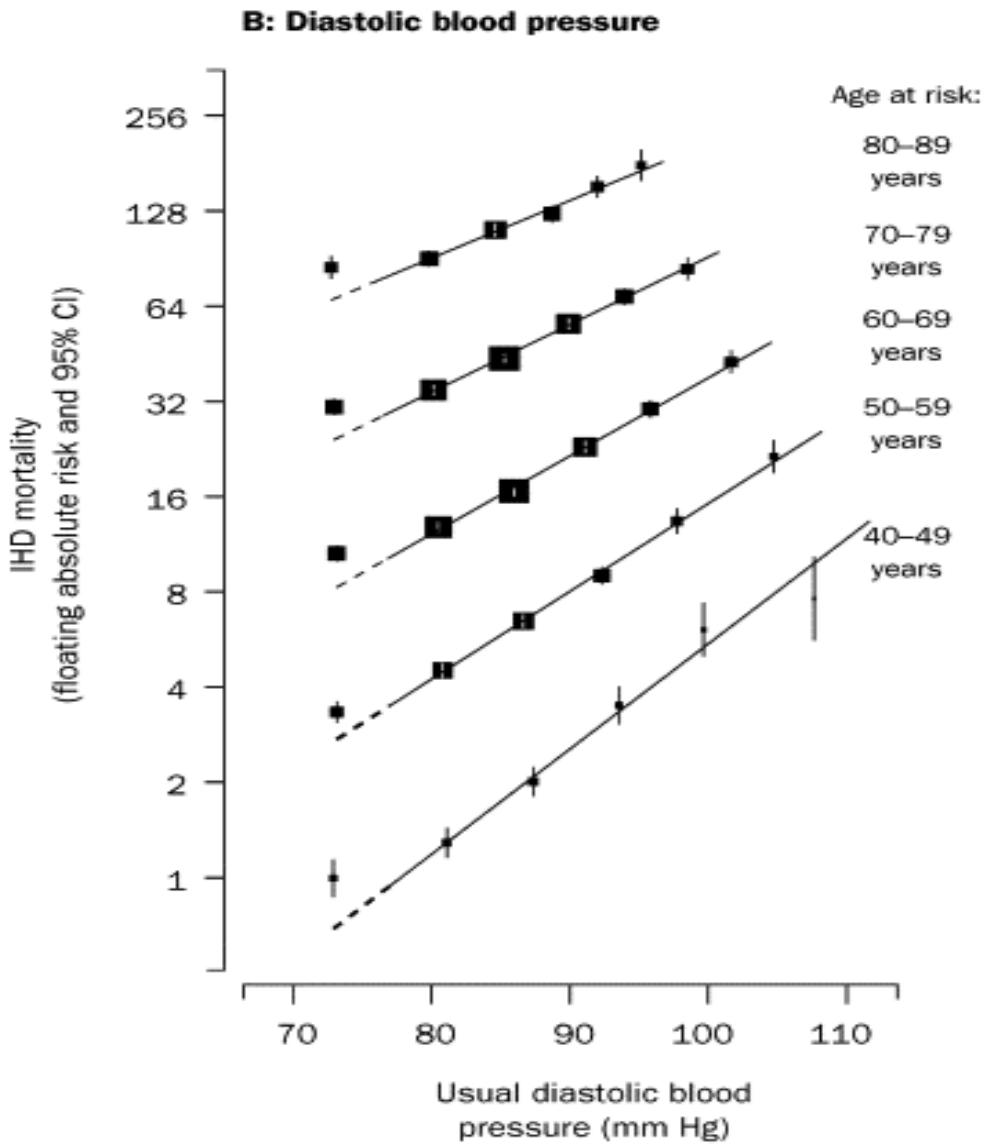
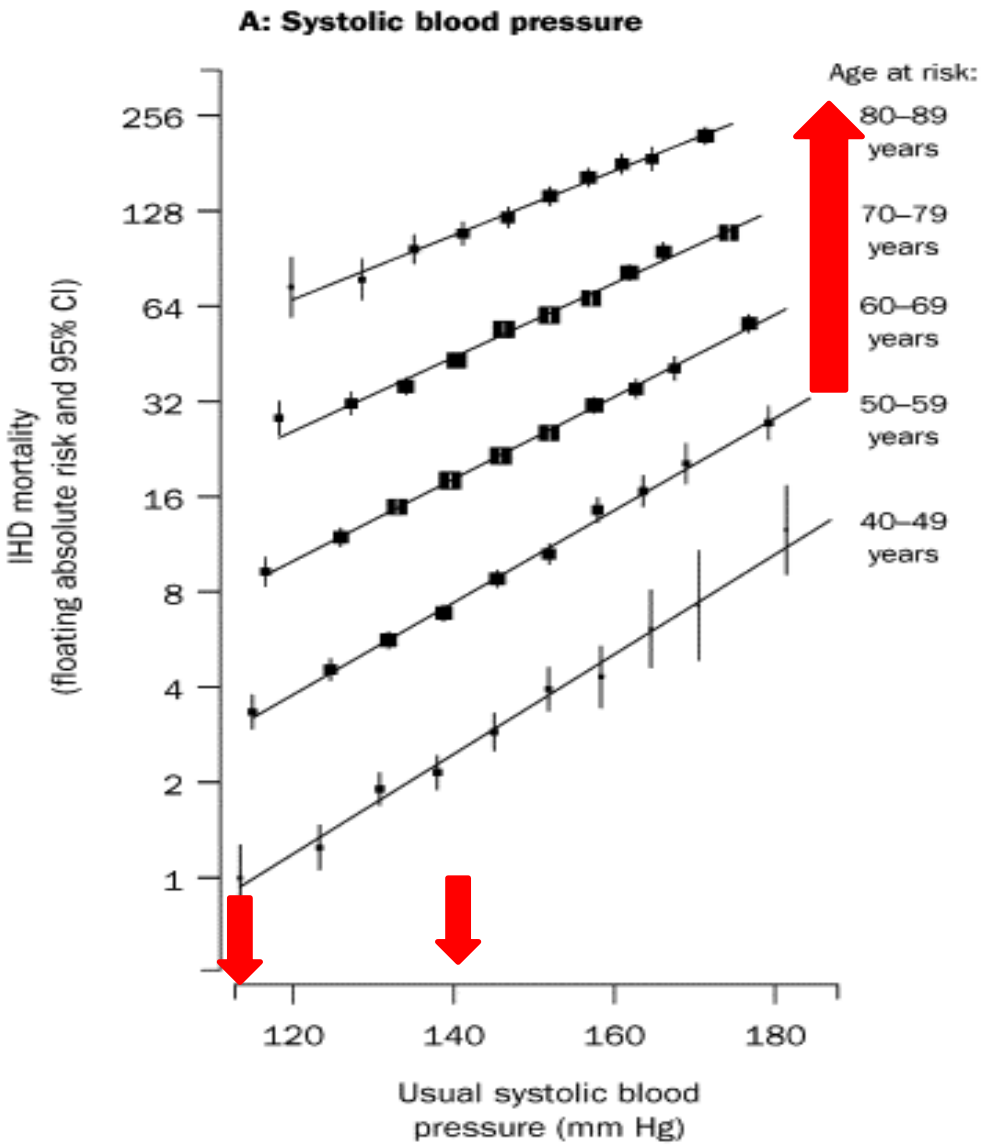
Reconsidering The Consequences of Using Race To Estimate Kidney Function

Estimated GFR equations are distinct because they assert that existing organ function is different between individuals who are identical except for race.

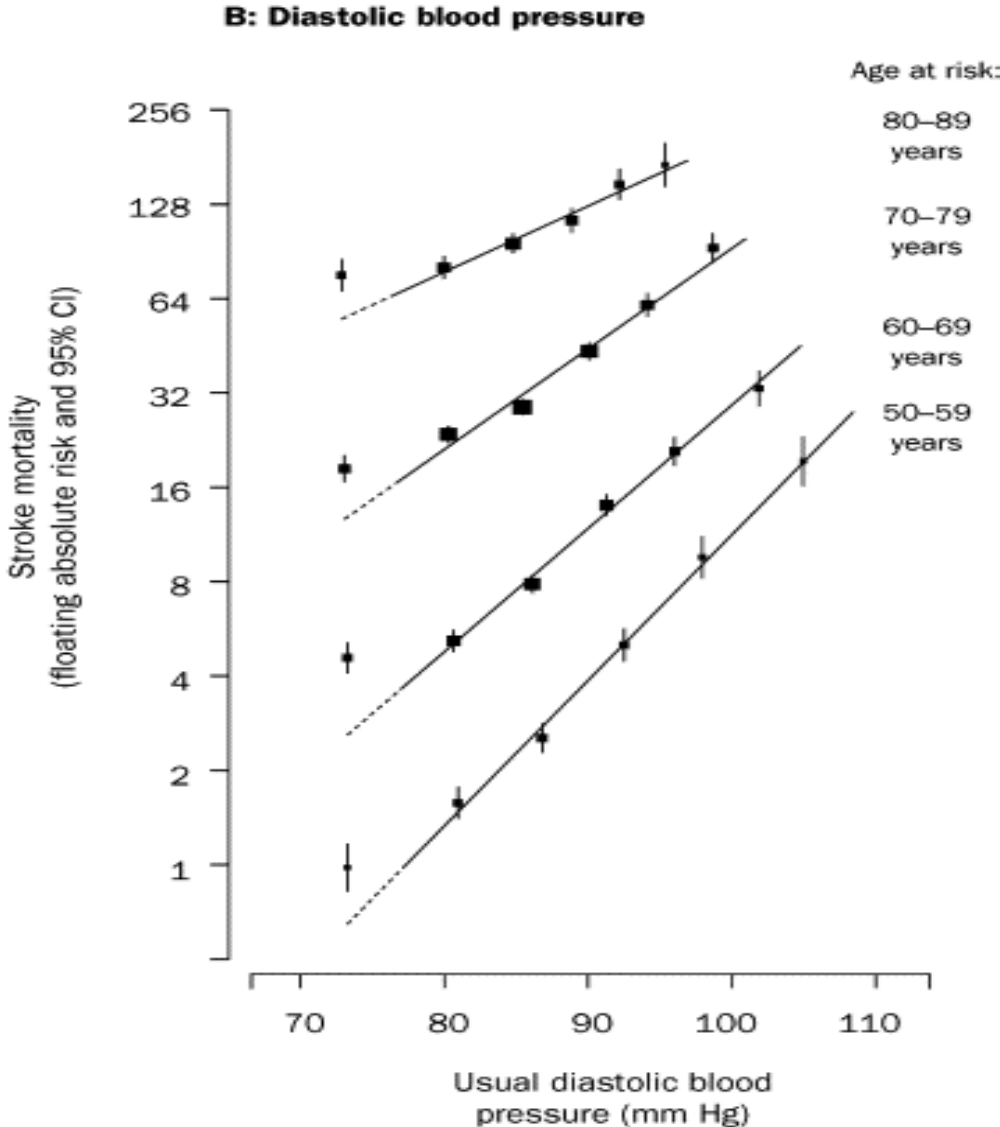
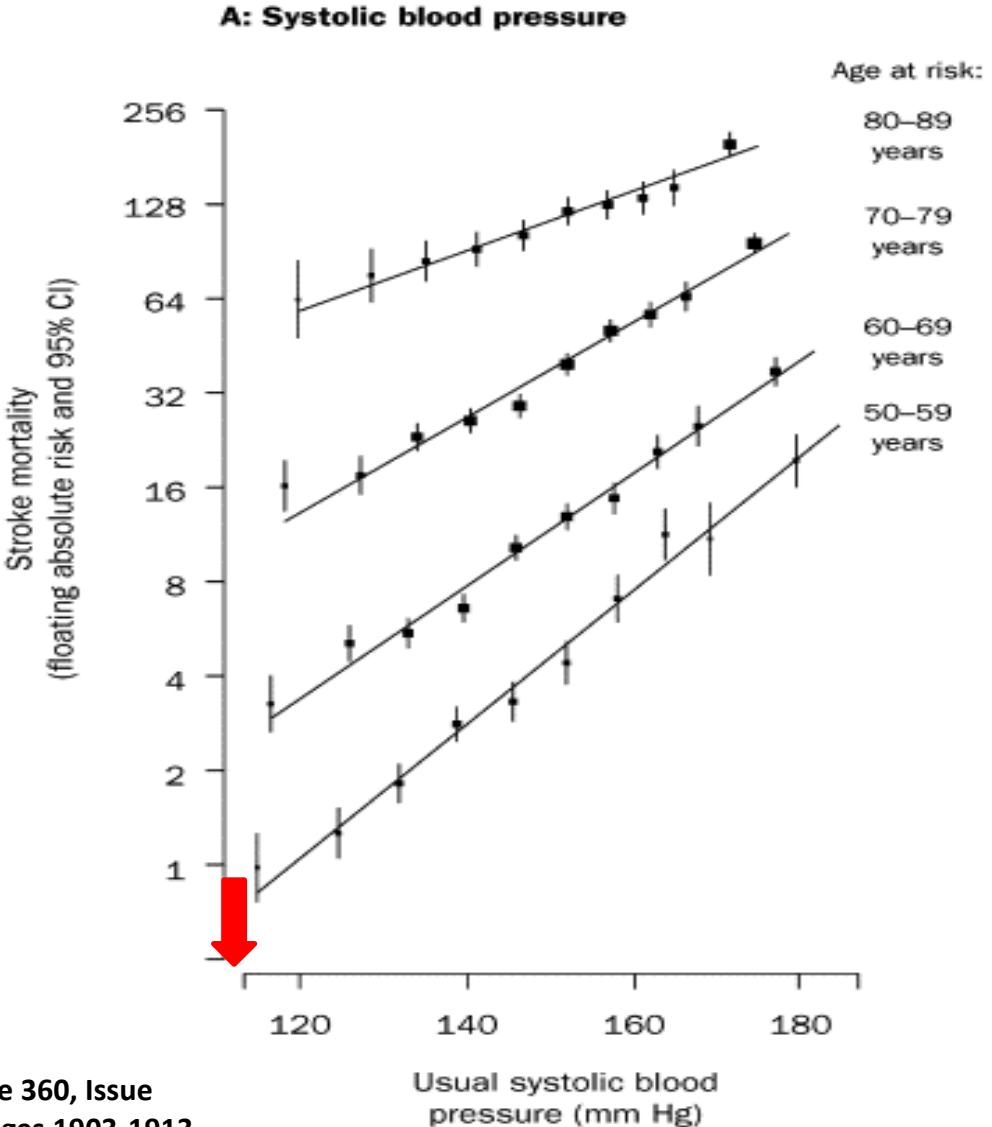
HTN and DM

- **HTN is common with DM**, with prevalence depending on type and duration of DM, age, sex, race/ethnicity, BMI, Hx of glycemic control, and presence of CKD, among other factors
- **HTN is a strong risk factor for ASCVD, HF, and microvascular complications.**
- **Numerous studies: anti-HTN therapy reduces ASCVD events, HF, and microvascular complications in people with DM.**
- Large benefits are seen when multiple risk factors are addressed simultaneously

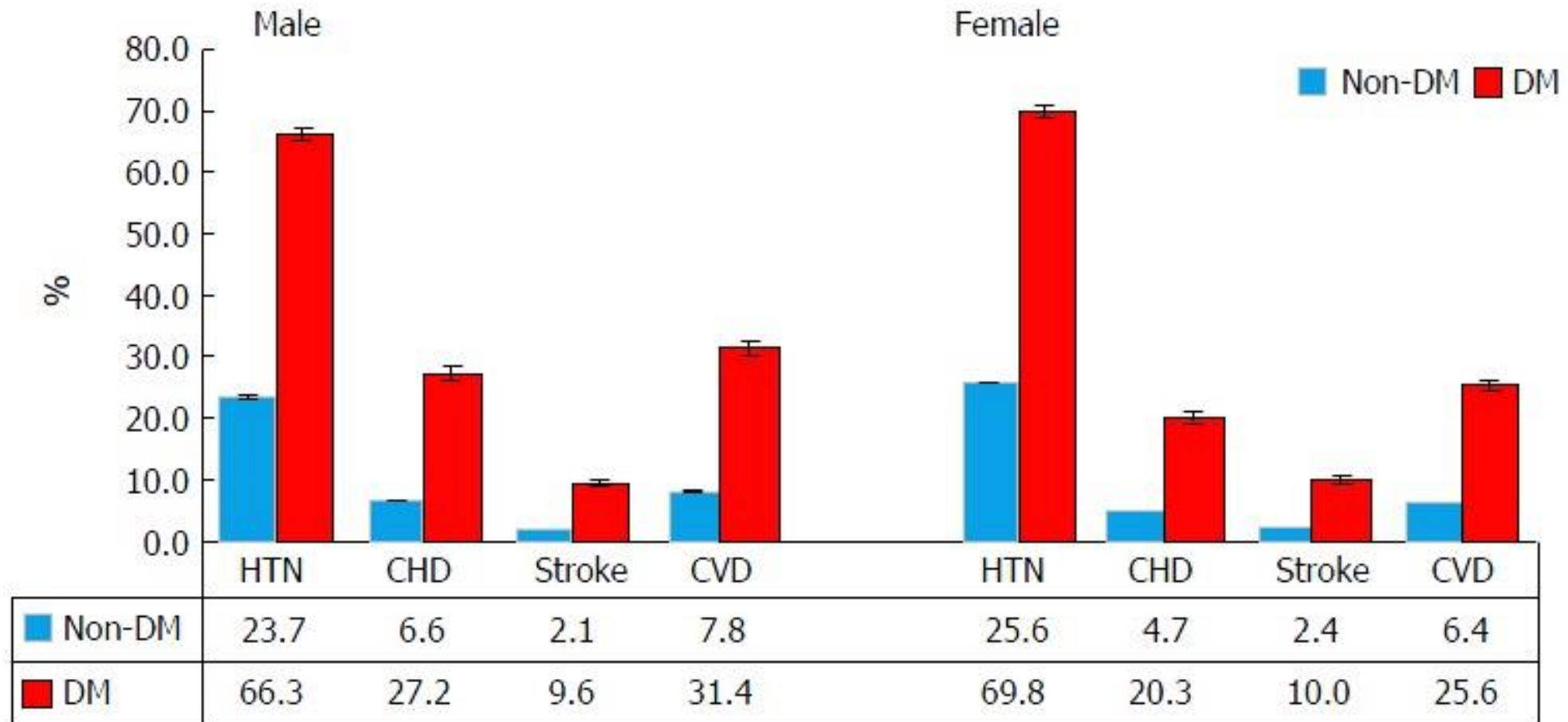
Ischemic Heart Disease (IHD) Mortality Rate In Each Decade Of Age



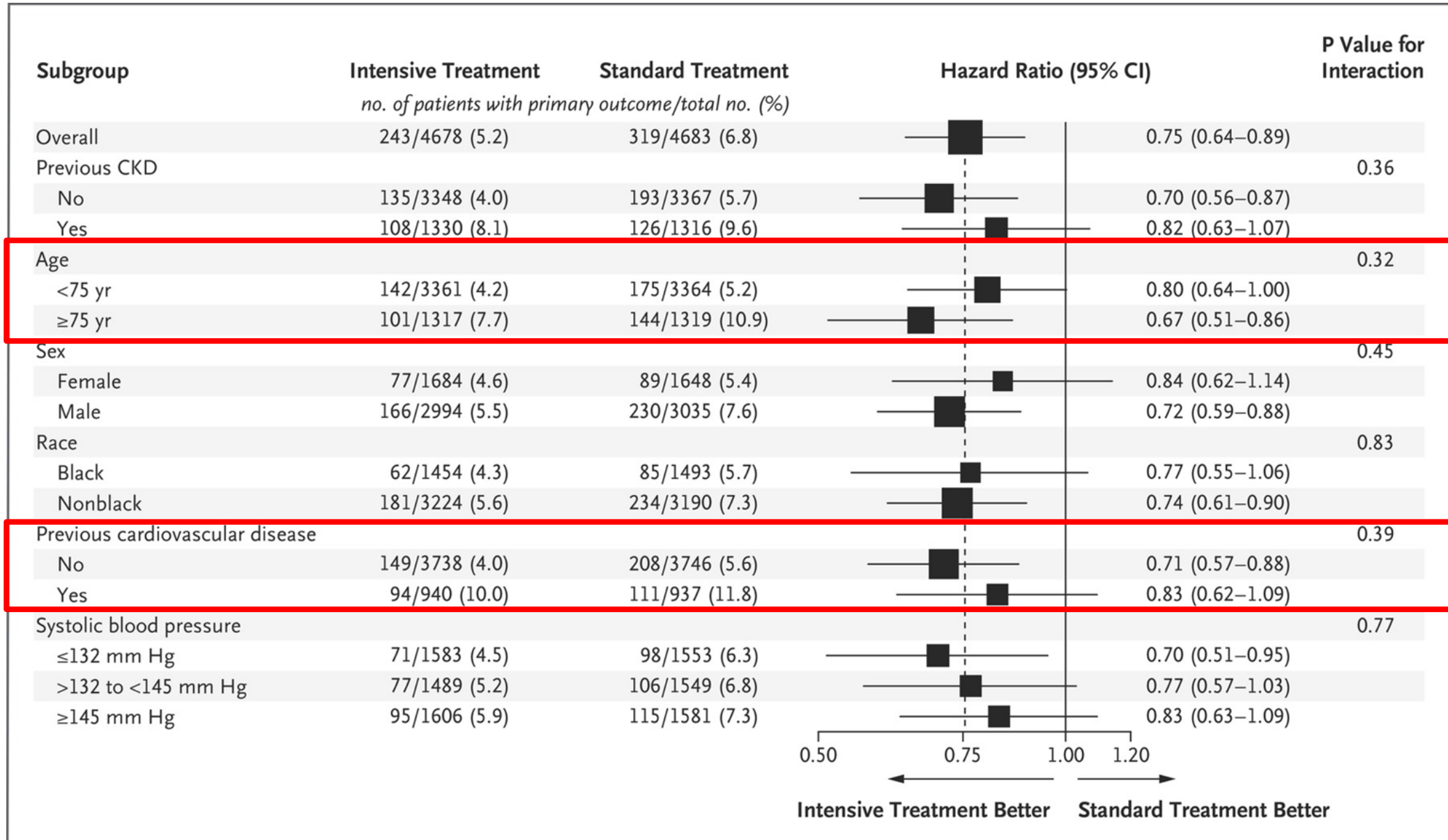
Stroke Mortality Rate in Each Decade of Age Versus Usual BP



Prevalence Co-morbid HTN, CHD, Stroke and CVD with and without DM, U.S. National Health Interview Surveys 2000-2009.



SPRINT: Primary Outcome Pre-specified Subgroups



ACC/AHA DM and HTN

- As a matter of convenience, it can be assumed vast majority of adults with DM have 10-year ASCVD risk $\geq 10\%$, placing them in high-risk category
- That requires initiation of antihypertensive drug therapy at BP $\geq 130/80$ mm Hg

ADA Blood Pressure Target Recommendations

- For people with diabetes and hypertension, the on-treatment target blood pressure goal is <130/80 mmHg, if it can be safely attained
- For people with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences

ADA Blood Pressure Target Recommendations

Epidemiologic analyses show that $BP \geq 115/75$ mm Hg is associated with increased rates of ASCVD, HF, retinopathy, kidney disease, and mortality in a graded fashion, contributing to the evidence that BP control is important in the clinical outcomes of diabetes

Important Differences: ACCORD vs. SPRINT

- SPRINT: older cohort
- Mean SPRINT 68 vs. 62 years in ACCORD,
- 28% of SPRINT was 75 years of age or older.
- SPRINT also included CKD
- Sample size of ACCORD only half that of SPRINT
- ACCORD=4,733 vs. SPRINT=9,361).

Research

JAMA Cardiology | **Original Investigation**

Association of Normal Systolic Blood Pressure Level With Cardiovascular Disease in the Absence of Risk Factors

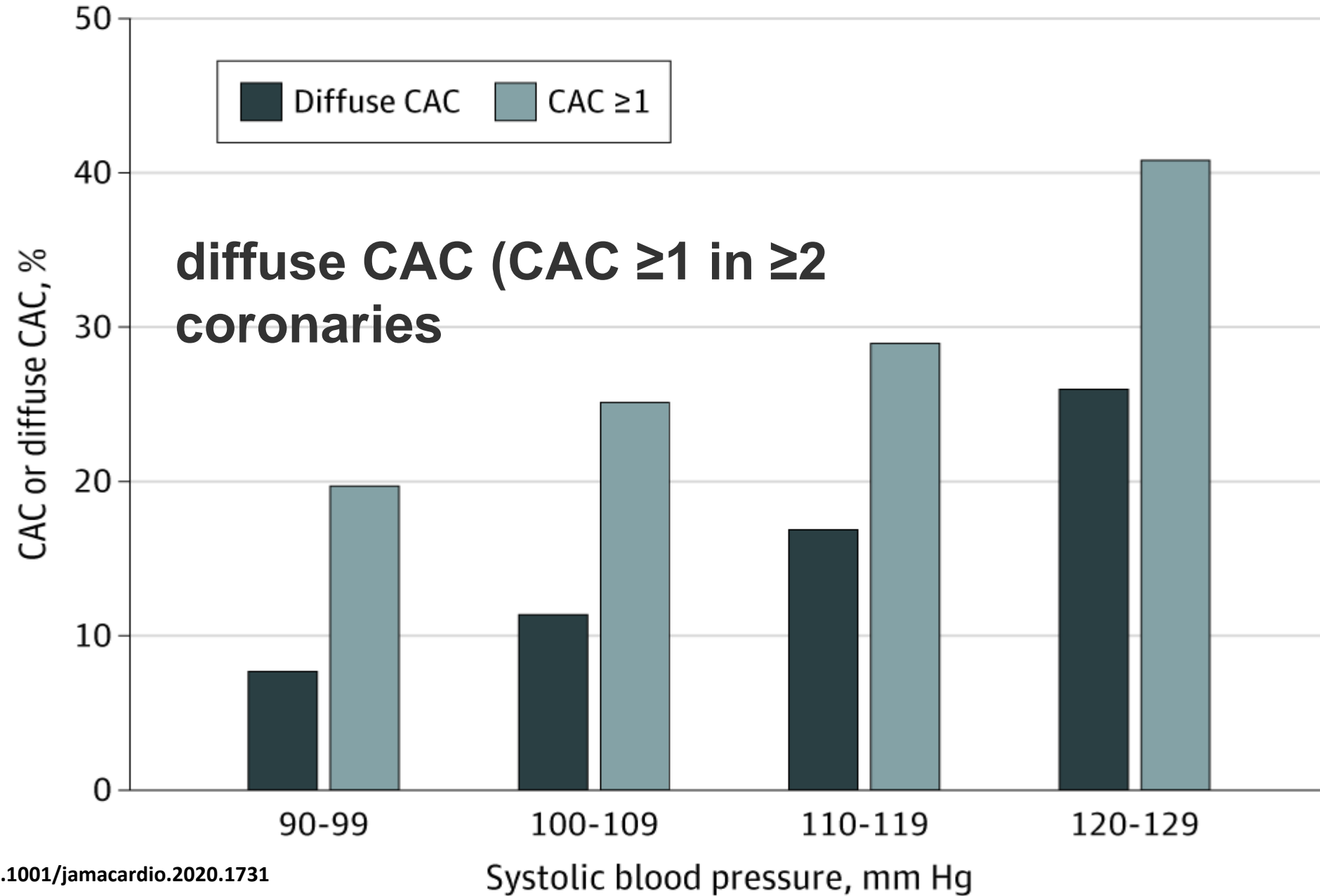
Seamus P. Whelton, MD, MPH; John W. McEvoy, MB, BCh, MHS; Leslee Shaw, PhD; Bruce M. Psaty, MD, PhD; Joao A. C. Lima, MD, MBA; Matthew Budoff, MD; Khurram Nasir, MD, MPH; Moyses Szklo, MD; Roger S. Blumenthal, MD; Michael J. Blaha, MD, MPH

IMPORTANCE The risk of atherosclerotic cardiovascular disease (ASCVD) at currently defined normal systolic blood pressure (SBP) levels in persons without ASCVD risk factors based on current definitions is not well defined.

OBJECTIVE To examine the association of SBP levels with coronary artery calcium and ASCVD in persons without hypertension or other traditional ASCVD risk factors based on current definitions.



Proportion of Participants With CAC and Diffuse CAC by SBP Group



ACC/AHA Classification of BP

BP Category	Systolic BP		Diastolic BP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Hypertension: stage 1	130-139 mm Hg	or	80-89 mm Hg
Hypertension: stage 2	≥140 mm Hg	or	≥90 mm Hg

ACC/AHA Diabetes Mellitus

COR	LOE	Recommendations for Treatment of Hypertension in Patients With DM
I	A ^{SR}	All first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective.
IIb	B-NR	ACE inhibitors or ARBs may be considered in the presence of albuminuria .

ADA Recommendations for treatment of confirmed HTN in people with DM

- ***An ACEi or ARB is suggested to treat HTN with urine albumin-to-creatinine ratio 30–299 mg/g creatinine and strongly recommended with urine albumin-to-creatinine ratio ≥ 300 mg/g creatinine.**
- ****Thiazide-like diuretic; long-acting agents shown to reduce CV events, such as chlorthalidone and indapamide, are preferred. ***Dihydropyridine CCB.**

Conclusions

- ➔ HTN and DM are major risk factors for increasing CVD mortality.
- ➔ However, achieving optimal BP control with DM is challenging
- ➔ SGLTis CVD and CKD benefits demonstrated, including HFrEF and HFpEF
- ➔ Early and sustained reductions in SBP

Conclusions

- ➔ SGLT2i lower clinic and out-of-office BP, attributed to natriuresis and osmotic diuresis.
- ➔ Mechanisms linking SGLT2i and neurohormonal activity likely through multiple indirect effects and the sympathetic nervous system.
- ➔ SGLT2is are attractive choices for glycemic control, weight reduction, and BP-lowering with HTN and with and without T2D.