

Controversies in Hypertension: Testing What You Know

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Disclosure

Consultant: Alnylam; Blue Earth Diagnostics; Eli Lilly (SURPASS-CVOT); Idorsia (Hypertension); Medtronic (Renal Denervation Program); Mineralys; Novo Nordisk; ReCor (Renal Denervation); UpToDate (Hypertension Section)

Research Grant: Ablative Solutions (Target BP I); Corcept (MOMENTUM); Eli Lilly (TRIUMPH); ReCor (Radiance I and II)



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Which of the Following Statements Is *True* Concerning the Epidemiology of Hypertension?

- A. Elevated SBP is responsible for more Worldwide deaths and disability adjusted life-years than any other risk factor.
- B. According to the NHANES, hypertension control rates have improved between 2013-2018.
- C. Not having a designated health care provider leads to improved BP control rates.
- D. Non-Hispanic Blacks are more likely to be aware of their having hypertension, more likely to be treated for their hypertension, and more likely to have their hypertension controlled.
- E. Social determinants of health have little effect on BP control and CV outcomes.



CONTINUING EDUCATION COMPANY

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Question # 1

Which of the following statements is True regarding the epidemiology of hypertension?

- 1) **Elevated SBP in the adult is responsible for more worldwide deaths and disability adjusted life-years than any other risk factor.**
- 2) According to the NHANES, hypertension control rates have improved between 2013-2020.
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4

Uncontrolled HTN Is Responsible for More Deaths and Disability Adjusted Life Years Worldwide Than Any Other Risk Factor

High SBP # 1

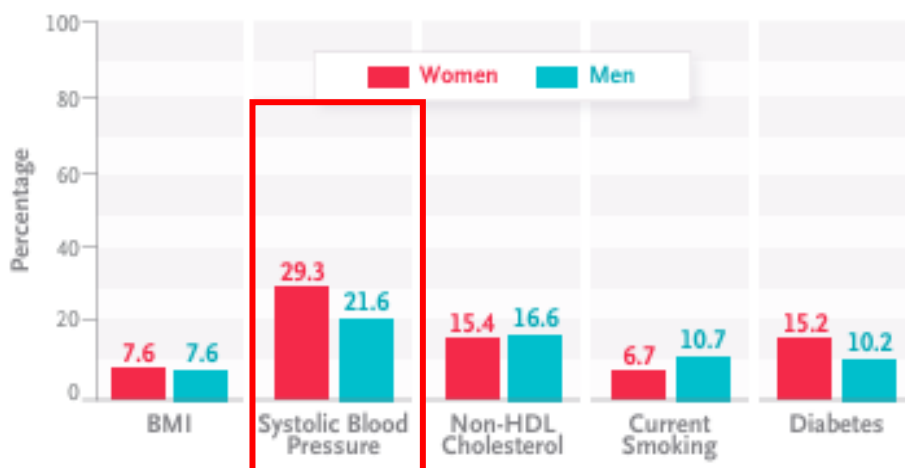
Rank	Cause of Death	Number of Deaths in 2021 (95% UI)	Number of DALYs (95% UI)
1	High systolic blood pressure	10,800,000 (9,150,000-12,100,000)	209,000,000 (172,000,000-236,000,000)
2	Dietary risks	6,580,000 (2,270,000-9,520,000)	142,000,000 (45,300,000-200,000,000)
3	High low-density lipoprotein cholesterol	3,810,000 (2,170,000-5,420,000)	86,300,000 (54,100,000-115,000,000)
4	Ambient particulate matter pollution	3,130,000 (2,310,000-3,930,000)	62,500,000 (45,700,000-78,400,000)
5	Smoking	2,370,000 (498,000-4,410,000)	59,600,000 (13,100,000-107,000,000)
6	High fasting plasma glucose	2,300,000 (2,030,000-2,650,000)	41,200,000 (36,600,000-47,600,000)
7	High body mass index	1,950,000 (1,120,000-2,910,000)	43,900,000 (23,800,000-65,400,000)
8	Kidney dysfunction	1,870,000 (1,440,000-2,340,000)	38,200,000 (30,700,000-45,900,000)
9	Household air pollution from solid fuels	1,610,000 (904,000-2,820,000)	36,200,000 (21,200,000-61,100,000)
10	Lead exposure	1,570,000 (-139,000-3,170,000)	29,700,000 (-2,780,000-61,200,000)
11	Low temperature	1,020,000 (915,000-1,100,000)	17,700,000 (15,900,000-19,200,000)
12	Secondhand smoke	743,000 (297,000-1,070,000)	16,700,000 (6,870,000-24,300,000)
13	High alcohol use	407,000 (179,000-708,000)	9,260,000 (3,830,000-16,300,000)
14	Low physical activity	397,000 (122,000-684,000)	7,220,000 (2,870,000-11,500,000)
15	High temperature	164,000 (114,000-205,000)	3,440,000 (2,370,000-4,300,000)

Vaduganathan M. et al. JACC VOL. 80, NO. 25, pg 2361-2371 Dec 20/27 2022.

DALYs-Disability Adjusted Life Years

5

Population-Attributable Fractions of the Individual Risk Factors for CV Disease



Global Effects of Modifiable Risk Factors on CV Disease and Mortality N,Engl.J.Med 2023;389:1273-1285..

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Question # 1

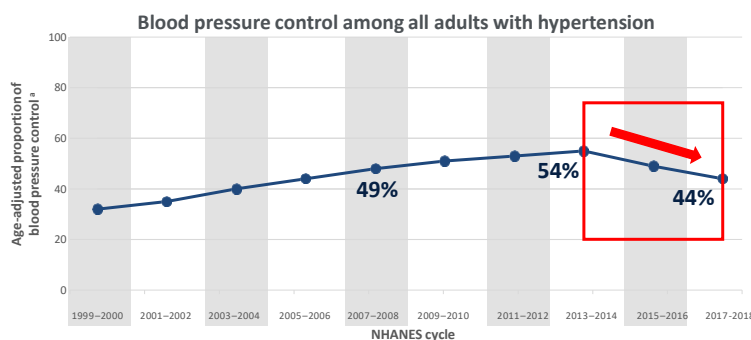
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Hypertension Control Rates Have Most Recently Been Falling¹

Age-Adjusted Trends in Blood Pressure Control (< 140/90 mm Hg)
Among US Adults 18 and Older With Hypertension,
NHANES 1999-2000 to 2017-2018 (N=18,262)



10 % reduction in control rate observed from 2013 to 2018
 -obesity and diabetes rates increased
 -fewer patients received BP medication
 -use of monotherapy increased
 -access to care was unchanged

An overall decline in quality of care.²

Despite our Best Efforts, hypertension control rates are not improving

1. Muntner et al. JAMA. 2020 Sep 22;324(12):1190-1200.

2. Egan B. and Myftari K. *Hypertension* VOL. 80, Issue 12, pg 2544-2546 Nov 15, 2023

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Hypertension Control Rates in US Adults (<130/80 mm Hg) Continue to Fall

Age-adjusted BP control among non-pregnant US adults who self-reported taking antihypertensive medication for hypertension

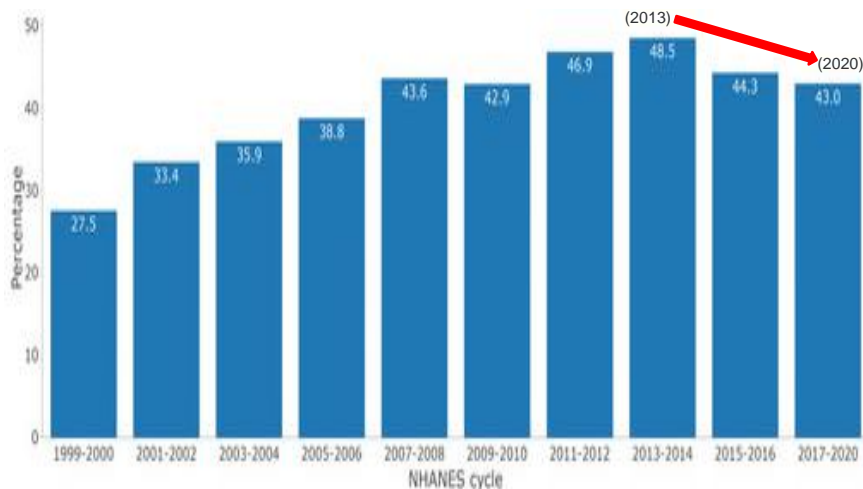


Fig 4. B. Jaeger B.C. et al. *Hypertension* June 2023 Vol 80, Issue 6: pages 1311-1320.

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CVD Mortality Trends for US Males and Females, 1980-2022

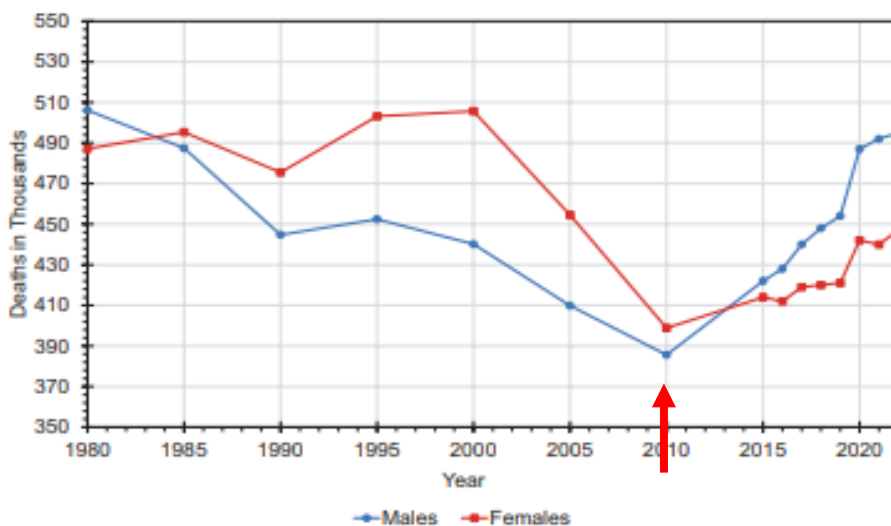
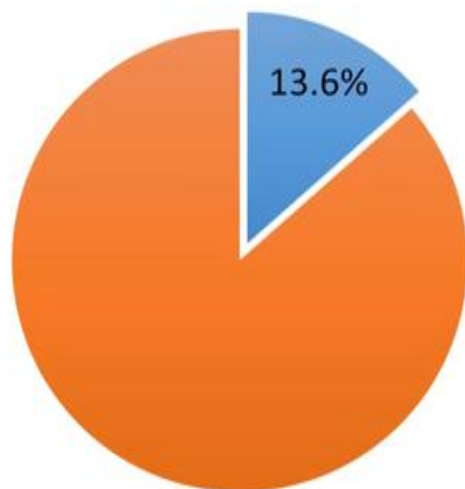


Chart 14-9. Martin et al. Heart Disease and Stroke Statistics 2025. *Circulation*; 151:e284. Feb 26, 2025.

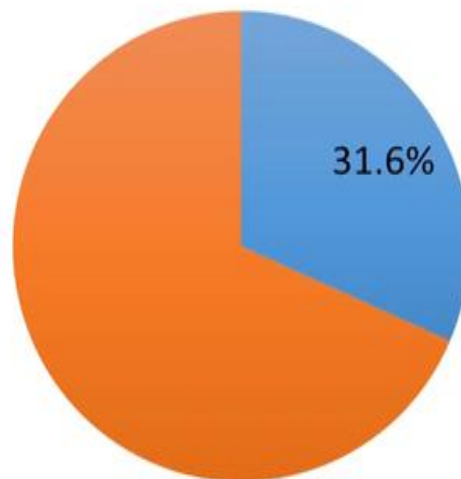
10

ESRD: USRD Racial Differences in Prevalence, 2019

US African American Population



US ESRD Population

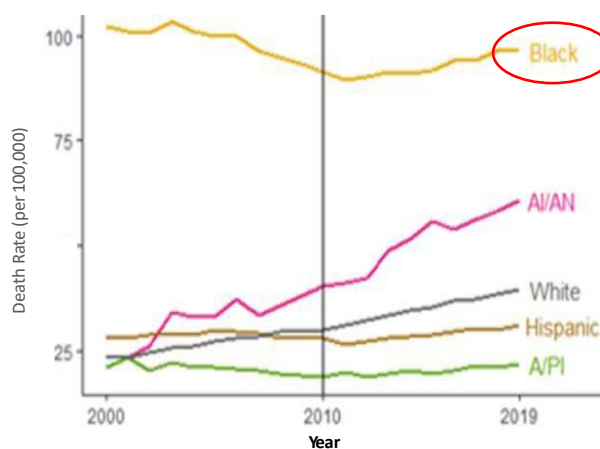


Access 8/17/24: <https://adr.usrds/2021/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-conditions>

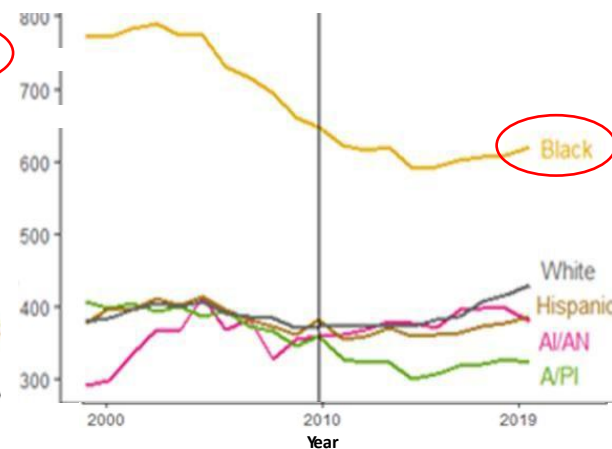
11

US Hypertension-Related CV Disease Mortality-2000-2019

Age 35-64 Years



Age ≥65 Years



Vaughan A et al. *JAHA* 2022;11:e024785.

Black-Non-Hispanic
AI/AN-American Indian/Alaska Native, Non-Hispanic
White-Non-Hispanic
A/PI -Asian/Pacific Islander, Non-Hispanic

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Which of the following statements is True regarding the epidemiology of hypertension?

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Who Is **More Likely** to Have Their BP Controlled to < 140/90 mm Hg:

- Younger (45-64) than older (75 or older)
- White (48%) vs Black (42%) participants
- Has Health Insurance (48%) vs No Health Insurance (24%)
- Has a Usual Healthcare Facility They Attend (48%) vs No Specific Healthcare Facility (26%)
- **6 times as likely to be controlled if seen in the last year by their healthcare provider**

Muntner P. et al. *JAMA*. 2020;324(12):1190-1200.

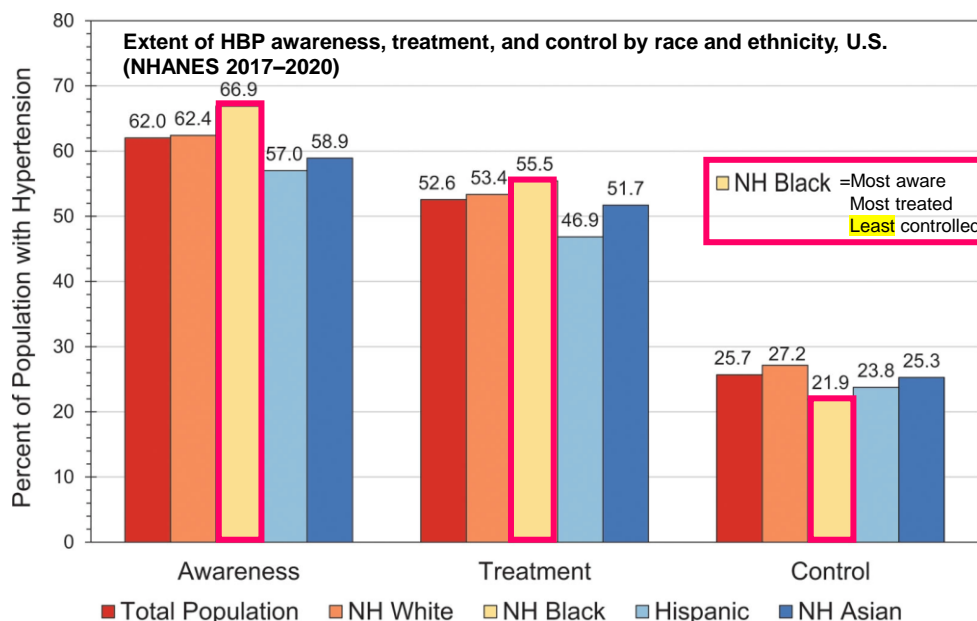
14

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15



Connie W. Tsao. Circulation. Heart Disease and Stroke Statistics—2023 Update: A Report From the American Heart Association.

16

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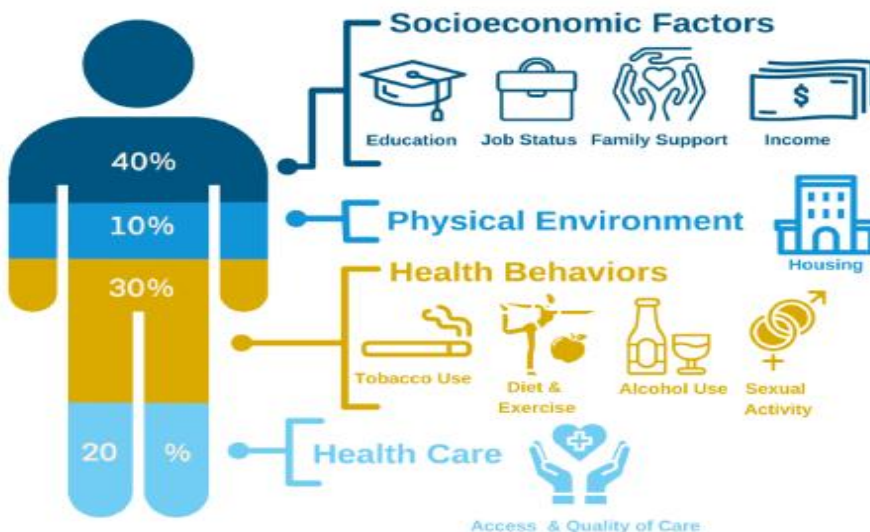
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Social Determinants of Health

- Eat
- Pray
- Work
- Stay



www.UCLAHEALTH.org/sustainability/social-determinants-of-health

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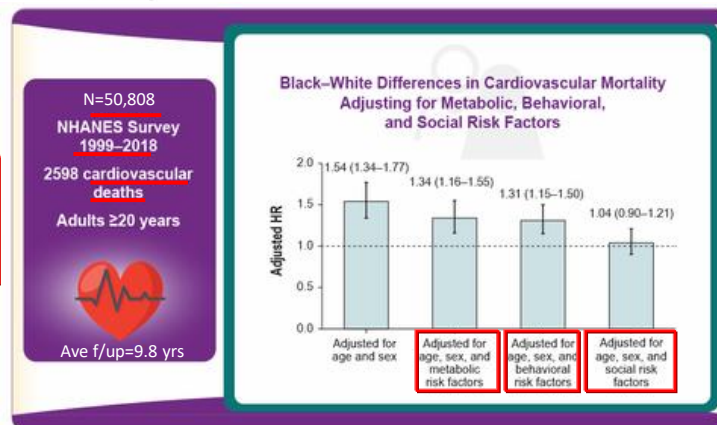
ORIGINAL RESEARCH

Annals of Internal Medicine

Social, Behavioral, and Metabolic Risk Factors and Racial Disparities in Cardiovascular Disease Mortality in U.S. Adults

An Observational Study NHANES (National Health and Nutrition Examination Survey 1999-2018).

Do Racial Differences in CV Mortality Persist after Metabolic, Behavioral, and Social Risk Factors are Accounted for?



- Metabolic risk factors included obesity, hypertension, diabetes, and total/HDL-C ratio ≥ 5 .
- Behavioral risk factors included current smoking, Healthy Eating Index score < 52 , no leisure-time physical activity, and sleep duration < 6 or > 8 h/d.
- Social risk factors included unemployment, family income/poverty ratio $< 300\%$, marginal or low food security, not owning a home, $<$ high school education, no regular health care access, no private health insurance, and not married nor living with a partner

He J. et al. *Ann Intern Med*; Vol. 176 No. 9 pg 1200-1208 September 2023.

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Which of the Following **Is Recommended** in the **Initial** Clinical Evaluation and Assessment of Hypertension-mediated Target Organ Damage in Patients with Hypertension, According to the 2017 ACC/AHA Hypertension Guideline?

- Echocardiography in all patients with hypertension.
- Measurement of plasma aldosterone/renin levels in all patients with hypertension
- Ultrasonography of the carotid arteries in asymptomatic patients with hypertension.
- An EKG in all patients with hypertension.
- A baseline plasma renin and aldosterone before antihypertensive drug therapy.



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Basic and Optional Laboratory Tests for Primary Hypertension

Basic testing	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR**
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
	Urinalysis
	Electrocardiogram
Optional testing	Echocardiogram
	Uric acid
	Urinary alb to creatinine ratio***

* Usually part of a Basic Metabolic Panel although Calcium often ordered separately

** Estimated glomerular filtration rate

*** Cost and lack of insurance coverage in non-diabetics makes this optional

2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*; JACC Nov 2017.

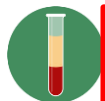
21

2024 ESC Guidelines for Managing Elevated BP and HTN

Screening for Secondary HTN



- Patients with signs on physical exam or history suggestive of secondary HTN should be appropriately screened—Like the ACC/AHA 2017 Guideline



- Renin and aldosterone should be measured in all patients with HTN:

This is new

-Primary aldosteronism and Hyperaldosteronism is common not only in secondary HTN but in early forms of hypertension.

McEvoy JW, et al; ESC Scientific Document Group. Eur Heart J. 2024:ehae178.

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Basic and Optional Laboratory Tests for Primary Hypertension

Basic testing	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR**
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
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2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*; JACC Nov 2017.

23

Screening and Diagnosis: KDIGO 2022

How



Spot UACR

and



eGFR

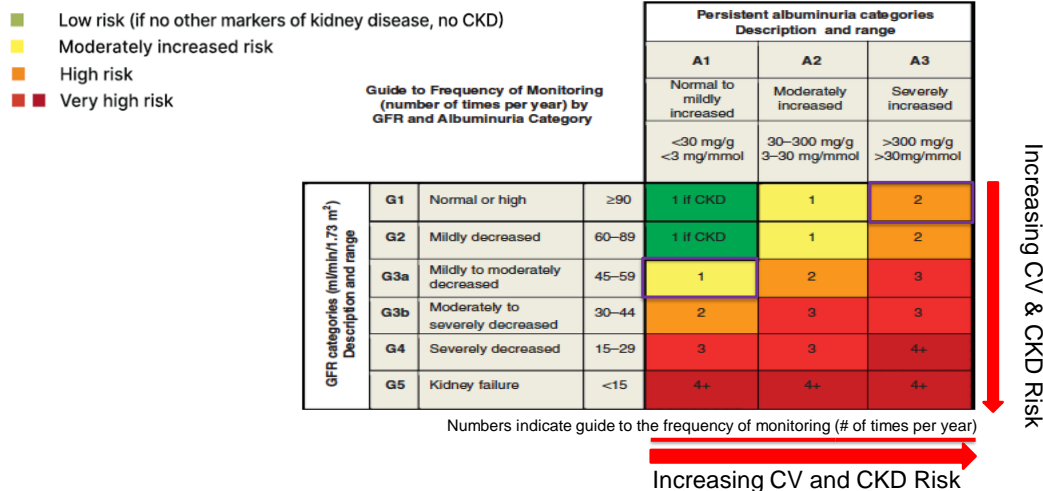
**In ALL
Patients at
Risk for CKD
-AODM
-HTN**

GFR=glomerular filtration rate, UACR=urine albumin/creatinine

de Boer IH et al. Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Diabetes Care*. 2022 45:3075-3090

24

Monitoring Disease Progression in Chronic Kidney Disease: Synopsis of the 2020 KDIGO Clinical Practice Guideline



- Recognize that small fluctuations in GFR are common and are not necessarily indicative of progression

Navaneethan SD et al. Synopsis of the 2020 KDIGO clinical practice guideline.
Ann Intern Med 2020 Nov 10; [e-pub]. (<https://doi.org/10.7326/M20-5938>)

25

Which of the Following Is Most Accurate Regarding Non-pharmacologic (Lifestyle) Management of Hypertension?

- Adult men and women with hypertension should be advised to consume a maximum of four standard alcoholic drinks per day.
- Increased dietary potassium is recommended for adults with hypertension unless they have CKD or are on medications that decrease potassium excretion.
- For weight loss to reduce BP in patients with hypertension, the reduction must typically be $\geq 10\%$ of body weight.
- Most patients with hypertension should be advised to discontinue even modest coffee consumption.
- Consumption of dietary potassium, calcium, or magnesium is associated with elevations in BP.

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Treatment Starts with Non-Pharmacologic (Lifestyle) Management Each with a 1A LOE

Goal	Nonpharmacological Interventions	Dose	Systolic BP Impact in Hypertension	Systolic BP Impact in Normotension
Weight loss	Weight/body fat	<ul style="list-style-type: none"> Best goal is ideal body weight Expect about 1 mm Hg for every 1 kg reduction in body weight 	-5 mm Hg	-2/3 mm Hg
Healthy diet	DASH dietary pattern	<ul style="list-style-type: none"> Consume a diet rich in fruits, vegetables, whole grains and low-fat dairy products with reduced content of saturated and total fat 	-11 mm Hg	-3 mm Hg
↓ ↑ Reduced intake of dietary sodium	Dietary sodium	<ul style="list-style-type: none"> Optimal goal is <1500 mg/day, most Americans 3400 mg/day Aim for at least a 1000 mg/day reduction in most adults 	-5/6 mm Hg	-2/3 mm Hg
↑ Enhanced intake of dietary potassium	Dietary potassium (not KCL)	<ul style="list-style-type: none"> Aim for 3500-5000 mg/day, preferably by consumption of a diet rich in potassium 	-4/5 mm Hg	-2 mm Hg
Physical activity	Aerobic	<ul style="list-style-type: none"> 90-150 min/week 65%-75% heart rate reserve 	-5/8 mm Hg	-2/4 mm Hg
Physical activity	Dynamic resistance	<ul style="list-style-type: none"> 90-150 min/week; 50%-80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set 	-4 mm Hg	-2 mm Hg
Physical activity	Isometric resistance	<ul style="list-style-type: none"> 4 x 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/week; 8-10 weeks 	-5 mm Hg	-4 mm Hg
Moderation of alcohol intake	Alcohol consumption	<ul style="list-style-type: none"> ≤1 drink daily for women ≤2 drinks daily for men <div>Drink= 5 oz of wine, 12 oz of beer 1 oz 100 proof or 1.5 oz of 70 proof</div>	-4 mm Hg	-3 mm Hg

Adapted from Whelton PK et al. *J Am Coll Cardiol.* 2018;71:e127-e248.

LOE=Level Of Evidence

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Foods Rich in Potassium

**Fruits-Raisins, Prunes, Apricots, Dates, Strawberries,
Bananas, Watermelon, Cantaloupe, Citrus Fruits**

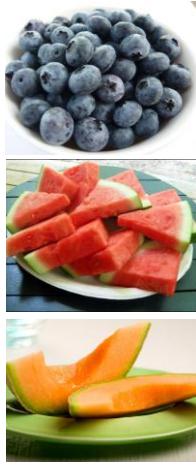
**Vegetables-Beets, Greens, Spinach, Tomatoes,
Mushrooms, Peas, Beans**

Fish-Salmon, Cod

Soy products, Veggie Burgers, Turkey, Beef

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Fresh Fruits



FRUIT	Serving	K(mEq)
Blueberries, raw	1/2 cup	1.7
Grapes	10	2.4
Pineapple, raw	1/2 cup	2.9
Plum	1	2.9
Strawberries	1/2 cup	3.2
Cherries, sweet, raw	10	3.9
Apple	1 medium	4.1
Peach	1	4.4
Peaches, canned	1/2 cup	4.1
Pear	1	5.3
Orange	1	6.1
Banana	1 medium	11.6
Raisins	1/4 cup	14.2
Watermelon	1/8	14.4
Avocado	1/2	15.4
Grapefruit	1/2	21.2
Cantaloupe	1/2	21.2

Highest

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The New England Journal of Medicine

24-Hour Urinary Sodium and Potassium Excretion and CV Risk

- Data from 6 studies of nearly 10,000 adults
- Mean age 52, followed median 9 years
- No evidence of CV or renal disease
- Multiple 24-hour urine collections (ave 3-4)
- Results applied to those w and w/o HTN
- Primary CV outcome-MI, stroke, coronary revascularization occurred in 6% of adults

Data from Six Studies

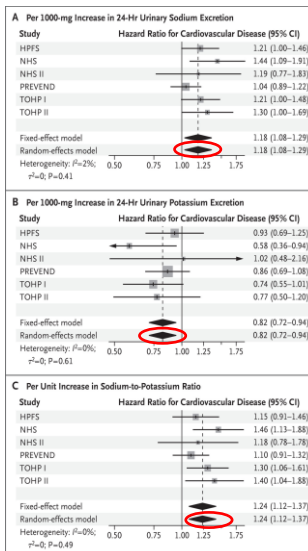
HFPS= Health Professionals Follow-up Study

NHS= Nurses' Health Study

NHS II=Nurses' Health Study II

PREVEND=Prevention of Renal and Vascular End-Stage Disease

TOHP I and II=Trials of Hypertension Prevention I and II



each additional 1000 mg of Na⁺ excretion per 24-hr urine (Panel A) was associated with an 18% increase in CV risk

each additional 1000 mg of K⁺ excretion per 24-hour urine (Panel B) was associated with an 18% decrease in CV risk

Increasing the excretion of more Na⁺ than K⁺ in the 24-hr urine (Na/K) per unit was associated with a 25% increase in CV risk

Ma Y et al. N Engl J Med 2021. DOI: 10.1056/NEJMoa2109794 Nov 15, 2021

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In America, It Is Processed, Canned, And Frozen Foods Where We Get 70% of Our Salt!

Salt vs Salt Substitute

Morton Plain Salt
26 oz=\$1.23

Nutrition Facts	
Serving Size 1/4 tsp (1.5g)	
Servings Per Container 491	
Amount Per Serving	
Calories 0	
% Daily Value*	
Total Fat 0g	0%
Sodium 590mg	25%
Total Carbohydrate 0g	0%
Protein 0g	
*Percent Daily Values are based on a 2,000 calorie diet.	



Morton Lite Salt 11 oz=\$2.71

Nutrition Facts	
Serving Size 1/4 tsp (1.4g)	
Servings Per Container 222	
Amount per serving	
Calories 0	
% Daily Value*	
Total Fat 0g	0%
Sodium 290mg	12%
Potassium 350mg	10%
Total Carbohydrate 0g	0%
Protein 0g	
Iodine	40%
Not a significant source of calories from fat, saturated fat, <i>trans</i> fat, cholesterol, dietary fiber, sugars, vitamin A, vitamin C, calcium and iron.	
*Percent Daily Values are based on a 2,000 calorie diet.	

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Based on the Most Recent ACC/AHA 2017 Hypertension Guideline, Your BP Goal Should Be < 130/80 mm Hg. But Should All Patients with HTN Above This Target Be Treated with Drugs?

- A. Yes
- B. No
- C. I am unsure

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BONUS DIGITAL CONTENT

Practice Guidelines

Blood Pressure Targets in Adults With Hypertension: A Clinical Practice Guideline From the AAFP

Sarah Coles, MD, FAAFP, Colorado Plateau Family and Community Medicine Residency Program, North County HealthCare, Flagstaff, Arizona; University of Arizona College of Medicine, Phoenix, Arizona

Lynn Fisher, MD, FAAFP, University of Kansas School of Medicine, Wichita, Kansas

Kenneth W. Lin, MD, MPH, Lancaster General Hospital Family Medicine Residency Program, Lancaster, Pennsylvania

Corey Lyon, DO, FAAFP, University of Colorado School of Medicine, Denver, Colorado

Alexis A. Vosooney, MD, Allina Health Group, West Saint Paul, Minnesota

Melanie D. Bird, PhD, MSAM, American Academy of Family Physicians, Leawood, Kansas

Am Fam Physician. 2022;106(6):721-722

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TABLE 4

Comparison of Recommended Blood Pressure Targets in Recent Guidelines

Guideline	18 to 59 years of age (mm Hg)	60 to 69 years of age (mm Hg)	70 to 79 years of age (mm Hg)	Older than 80 years (mm Hg)
2022 American Academy of Family Physicians*	< 140/90	< 140/90	< 140/90	< 140/90
2022 National Institute for Health and Care Excellence ¹³	< 140/90	< 140/90	< 140/90	< 150/90
2021 European Society of Hypertension Council ¹⁴	< 130/80†	< 130/80†	< 140/80	< 140/80
2020 International Society of Hypertension‡ ⁴⁴	< 130/80	< 140/90§	< 140/90	< 140/90
2020 U.S. Department of Veterans Affairs/U.S. Department of Defense ¹⁵	< 130/90¶	< 150/90	< 150/90	< 150/90
2017 American College of Cardiology/American Heart Association* ¹⁶	< 130/80	< 130/80	< 130/80	< 130/80
2017 American College of Physicians and American Academy of Family Physicians ¹¹	—	< 150/90	< 150/90	< 150/90
2014 Eighth Joint National Committee ¹⁰	< 140/90	< 150/90	< 150/90	< 150/90

*—Lower targets are reasonable based on clinical judgment and patient preferences or values.

†—A target of less than 140/90 mm Hg is recommended for patients with chronic kidney disease.

‡—Recommendation is to treat all patients to less than 140/90 mm Hg but states it is optimal to treat persons younger than 65 years and people with coronary artery disease, chronic kidney disease, heart failure, previous stroke, chronic obstructive pulmonary disease, or diabetes mellitus to less than 130/80 mm Hg (less than 140/80 mm Hg in older patients).

§—Recommendation is to transition from target of 130/80 mm Hg to 140/90 mm Hg at 65 years of age.

||—A target of less than 140/90 mm Hg is recommended in patients with diabetes.

¶—Recommendation is to treat all patients 18 to 59 years of age (including those with diabetes) to a systolic blood pressure target of less than 130 mm Hg. For patients 30 years and older, a diastolic blood pressure target of less than 90 mm Hg is recommended.

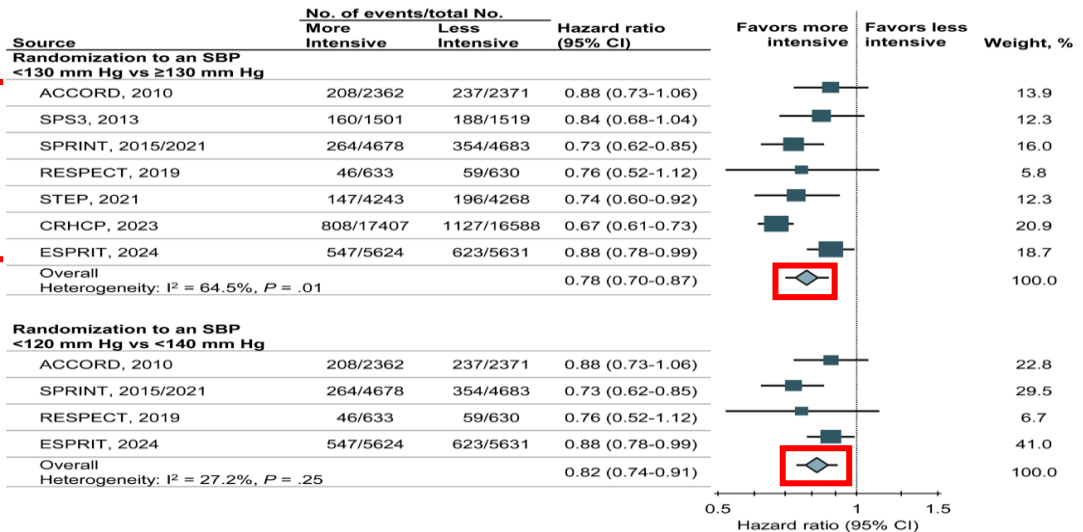
Information from references 10, 11, 13–16, and 44.

Am Fam Physician. 2022;106(6):721-722

34

Optimal Antihypertensive SBP: A Systematic Review and Meta-Analysis

Reduces the risks of Major CVD and All-Cause Mortality

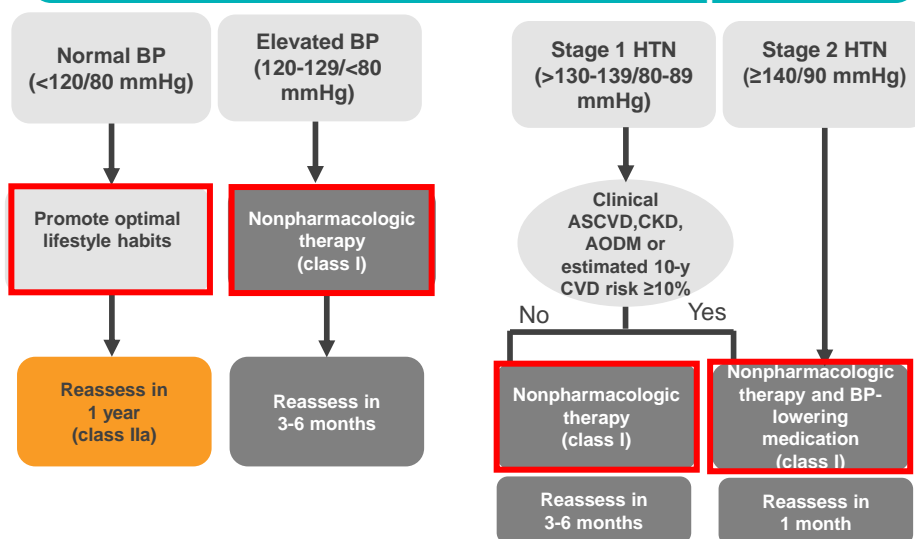


Based on a smaller # of trials, the studies support a SBP target of < 120 mm Hg

Whelton PK et al. *Hypertension*; Vol 81, Issue 11, Nov 2024. pgs 2329-2339.

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Algorithm: BP Thresholds and Recommendations for Treatment and Follow-Up



2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*: JACC Nov 2017

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ACC/AHA ASCVD Risk Estimator

Optimal risk factors

- Age, sex, race,
- TC
- HDL-C
- LDL-C
- Systolic BP mmHg
- Diastolic BP mmHg
- Not taking medications for HTN
- Not a diabetic
- Not a smoker
- On a statin, on ASA

<http://tools.acc.org/ASCVD-Risk-Estimator/>
Goff DC, et al. *J Am Coll Cardiol* 2014;63:2935-59

10-year risk of non-fatal MI, coronary heart disease death, and fatal and non-fatal stroke

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NEW PARADIGM FOR CVD RISK: PREVENT™

<https://professional.heart.org/prevent>

PREVENT™ Online Calculator

Welcome to the American Heart Association Predicting Risk of cardiovascular disease EVENTS (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

Sex: ☒ Male ☐ Female

Age: years

Total Cholesterol: mg/dL

HDL Cholesterol: mg/dL

SBP: mmHg

BMI:

eGFR:

Diabetes: ☒ No ☐ Yes

Current Smoking: ☒ No ☐ Yes

Anti-hypertensive medication: ☒ No ☐ Yes

Lipid-lowering medication: ☒ No ☐ Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available, please click on yes and enter the value

UACR: ☒ No ☐ Yes

HbA1C: ☒ No ☐ Yes

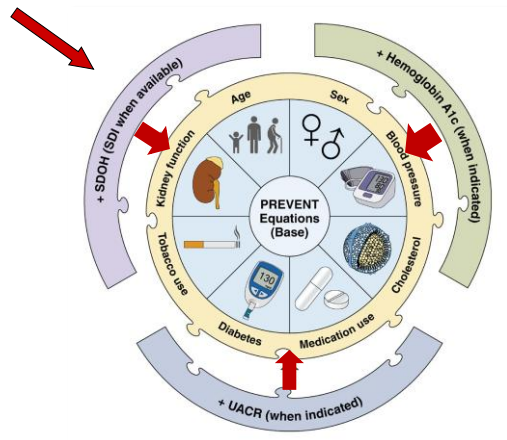
Zip Code (for estimating social deprivation index [SDI]): ☒ No ☐ Yes

☒ Risk of CVD ☐ Risk of ASCVD ☐ Risk of Heart Failure

Khan SS et. al. *Circulation* 2023

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NEW PARADIGM FOR CVD RISK: PREVENT™



Abbreviations: CVD indicates cardiovascular disease; PREVENT, Predicting Risk of CVD Events; SDI, social deprivation index; SDOH, social determinants of health; and UACR urine albumin-to-creatinine ratio.

Predictors:

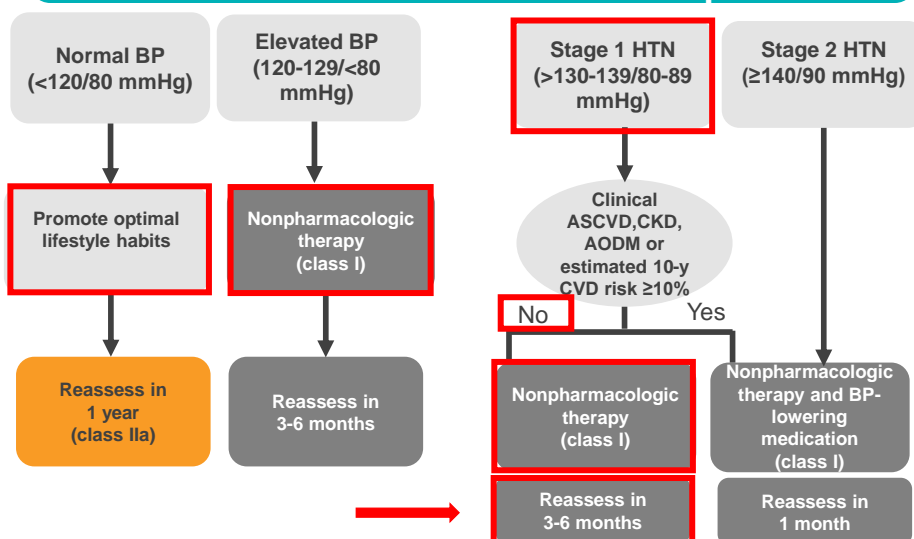
- Base: Traditional risk factors (Gender, Age, SBP, Total and HDL cholesterol, diabetes, use of anti-hypertensive and lipid-lowering medication, smoking, eGFR, and BMI)
- Add-on: UACR, HbA1c, SDI

Will PREVENT™ be Adopted in the July 2025 ACC/AHA Updated HTN Guideline?

Khan SS et. al. *Circulation* 2023

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Algorithm: BP Thresholds and Recommendations for Treatment and Follow-Up



2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*: JACC Nov 2017

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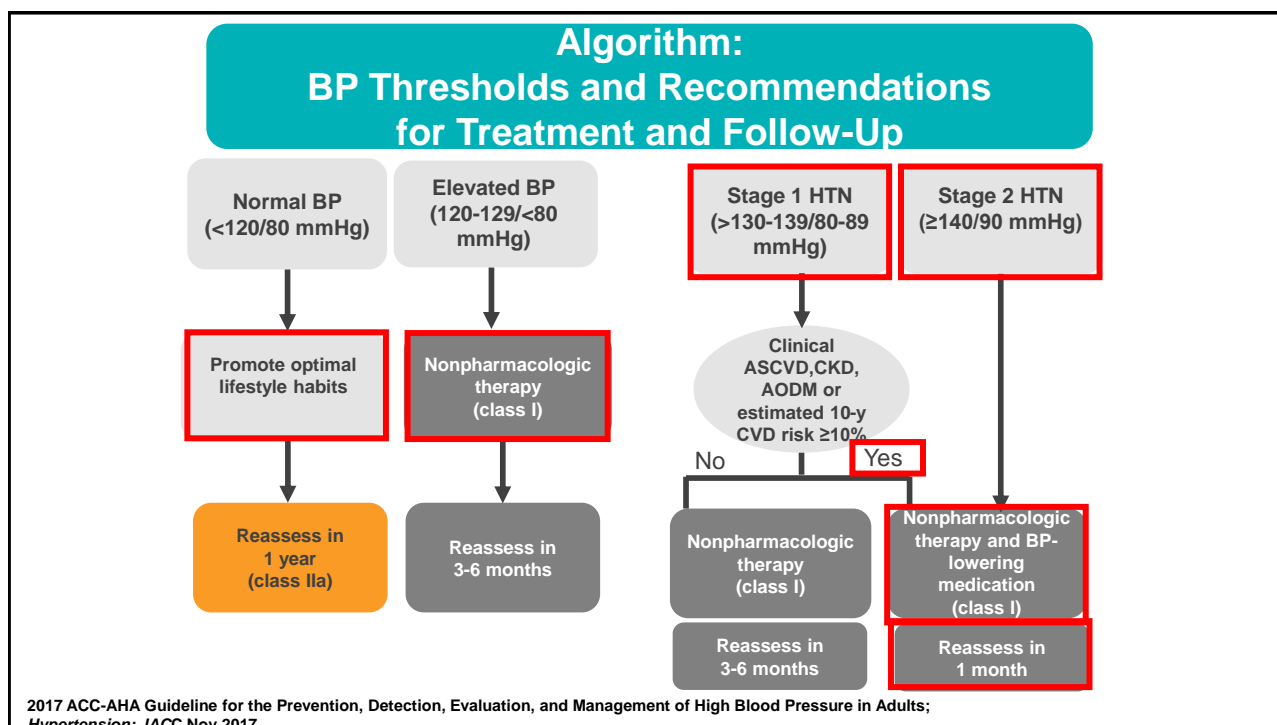
BP Management in Patients with Low 10-Year CVD Risk (<10%)

Thoughts to consider beyond the guidelines:

- Initiate drug therapy for all with SBP > 130 mm Hg after 6 months of attempt at lifestyle therapy alone.
- Consider the same for SBP 120-130 mm Hg when:
 - Antihypertensive Rx as an Adolescent or Young Adult
 - Family History of Hypertension
 - Family History of Premature CVD
 - Personal Hx of HTN during Pregnancy or Personal Hx of Premature Birth
- In addition, always use lifestyle therapy

Jones, DW et al. *Hypertension* 2021;77:e58–e67.

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Which of the Following Is the Best Initial Monotherapy for Hypertension?

- A. Ras-blocking Drugs
- B. Thiazide/Thiazide like diuretics
- C. Calcium Channel Blockers
- D. Beta-blockers which are particularly good for reducing stroke
- E. A, B, or C



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ORIGINAL CONTRIBUTION

JAMA-EXPRESS

Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group

TREATMENT AND COMPLICATIONS among the 50 to 60 million people in the United States with hypertension are estimated to cost \$37 billion annually, with antihypertensive drug costs alone accounting for an estimated \$13.9 billion per year. Antihypertensive drug therapy substantially reduces the risk of hypertension-related morbidity and mortality.¹⁻⁶ However, the optimal choice for initial pharmacotherapy of hypertension is uncertain.

Earlier clinical trials documented the benefit of lowering blood pressure (BP) using primarily thiazide diuretics or β -blockers.^{1,2} After these studies, several newer classes of antihypertensive agents (ie, angiotensin-converting enzyme [ACE] inhibitors, calcium channel blockers [CCBs], α -adrenergic blockers, and more recently angiotensin-receptor blockers) became available. Over the past decade, major placebo-controlled trials have documented that ACE inhibitors and CCBs reduce cardiovascular events in individuals with hypertension.³⁻¹⁰ However, their relative value compared with older, less expensive agents remains unclear. There has been considerable uncertainty regarding effects of some classes of antihypertensive drugs on risk of

Context Antihypertensive therapy is well established to reduce hypertension-related morbidity and mortality, but the optimal first-step therapy is unknown.

Objective To determine whether treatment with a calcium channel blocker or an angiotensin-converting enzyme inhibitor lowers the incidence of coronary heart disease (CHD) or other cardiovascular disease (CVD) events vs treatment with a diuretic.

Design The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), a randomized, double-blind, active-controlled clinical trial conducted from February 1994 through March 2002.

Setting and Participants A total of 33 357 participants aged 55 years or older with hypertension and at least 1 other CHD risk factor from 623 North American centers.

Interventions Participants were randomly assigned to receive chlorthalidone, 12.5 to 25 mg/d (n=15 255); amlodipine, 2.5 to 10 mg/d (n=9048); or lisinopril, 10 to 40 mg/d (n=9054) for planned follow-up of approximately 4 to 8 years.

Main Outcome Measures The primary outcome was combined fatal CHD or nonfatal myocardial infarction, analyzed by intent-to-treat. Secondary outcomes were all-cause mortality, stroke, combined CVD (primary outcome), coronary revascularization, or angina with hospitalization, and combined CVD (combined CHD, stroke, treated angina without hospitalization, heart failure [HF], and peripheral arterial disease).

Results Mean follow-up was 4.9 years. The primary outcome occurred in 2956 participants, with no difference between treatments. Compared with chlorthalidone (6-year rate, 11.5%), the relative risks (RRs) were 0.98 (95% CI, 0.90-1.07) for amlodipine (6-year rate, 11.3%) and 0.99 (95% CI, 0.91-1.08) for lisinopril (6-year rate, 11.4%). Likewise, all-cause mortality did not differ between groups. Five-year systolic blood pressures were significantly higher in the amlodipine (0.8 mm Hg, $P=.03$) and lisinopril (2 mm Hg, $P<.001$) groups compared with chlorthalidone, and 5-year diastolic blood pressure was significantly lower with amlodipine (0.8 mm Hg, $P<.001$). For amlodipine vs chlorthalidone, secondary outcomes were similar except for a higher 6-year rate of HF with amlodipine (10.2% vs 7.7%; RR, 1.38; 95% CI, 1.25-1.52). For lisinopril vs chlorthalidone, lisinopril had higher 6-year rates of combined CVD (8.3% vs 7.0%; RR, 1.10; 95% CI, 1.05-1.16); stroke (6.3% vs 5.6%; RR, 1.15; 95% CI, 1.02-1.30); and HF (8.7% vs 7.7%; RR, 1.19; 95% CI, 1.07-1.31).

Conclusion Thiazide-type diuretics are superior in preventing 1 or more major forms of CVD and are less expensive. They should be preferred for first-step antihypertensive therapy.

JAMA. 2002;288:2891-2997

www.jama.com

Author Affiliations: ALLHAT Authors. Their Financial Disclosures, and Group Members are listed at the end of this article.
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See also pp 2998 and 3039.

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(Reprinted JAMA, December 18, 2002—Vol 288, No. 25, 2981)

JAMA. 2002;288:2891-2997

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Randomized Design of ALLHAT

High-risk
hypertensive
patients

Consent /
Randomize
(42,418)

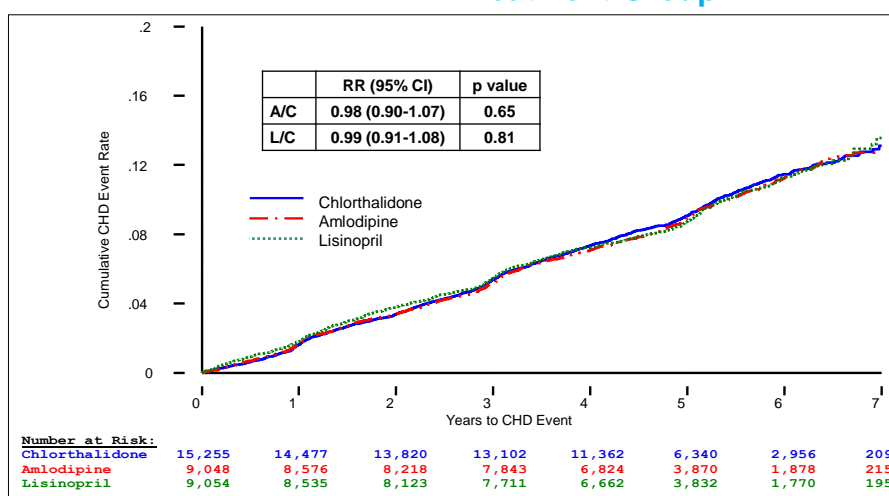
Amlodipine
Chlorthalidone
~~Doxazosin~~
Lisinopril

JAMA. 2002;288:2891-2997

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Cumulative Event Rates for the Primary Outcome (Fatal CHD or Nonfatal MI) by ALLHAT Treatment Group

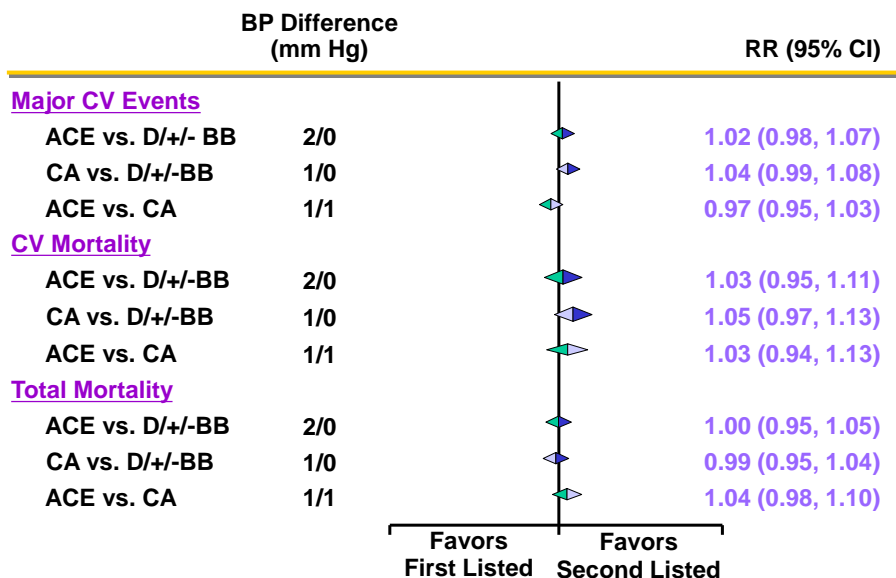


JAMA. 2002;288:2891-2997

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BP-Lowering Treatment Trialists Group

Comparisons of Different Active Treatments

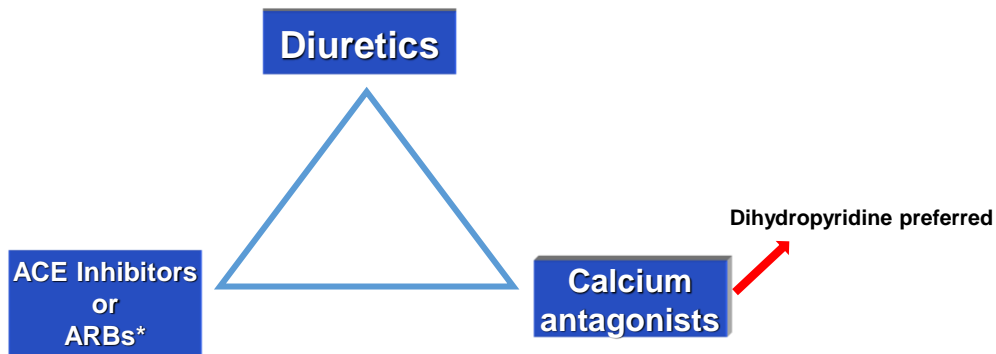


Adapted from Lancet 2000; Vol 356, Issue 9246, pgs 1955-1964.

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Initial Medications for the Management of Hypertension

Lifestyle Modification—Especially Diet and Exercise



* Recommended for CKD or Clinical Proteinuria
Combining ACEI with ARB discouraged—Class 3, Harm

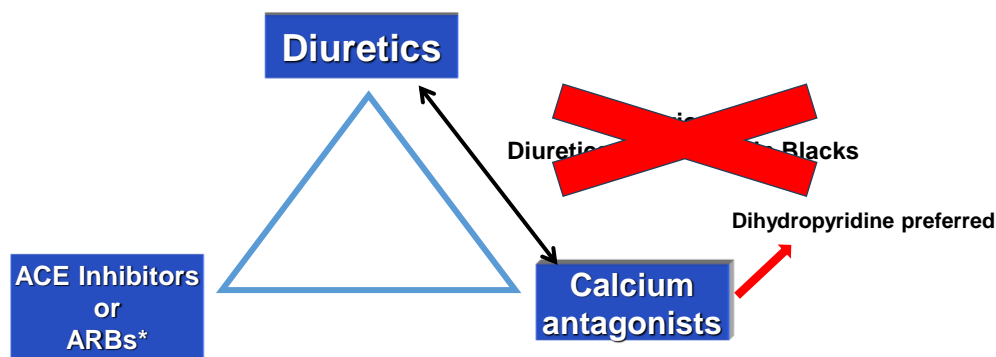
2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311(5): 507-520. Feb 5, 2014

2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. Whelton PK, Carey RM et al. Hypertension 2018; 71:e13-e115.

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Initial Medications for the Management of Hypertension

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2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. Whelton PK, Carey RM et al. Hypertension 2018; 71:e13-e115.

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Which of the Following Statements Is *True* Regarding Antihypertensive Drug Therapy for Hypertension?

- A. For patients with significant hypertension, simultaneous use of an ACE inhibitor and ARB is often recommended.
- B. Beta-blockers are particularly good for reducing stroke.
- C. Mineralocorticoid Receptor Antagonists (MRAs) are contraindicated in patients with resistant hypertension.
- D. Women receiving medication for BP control who become pregnant or are planning to become pregnant should be transitioned to labetalol, long-acting nifedipine, or methyldopa.
- E. Calcium-channel blockers are not associated with gingival hyperplasia.



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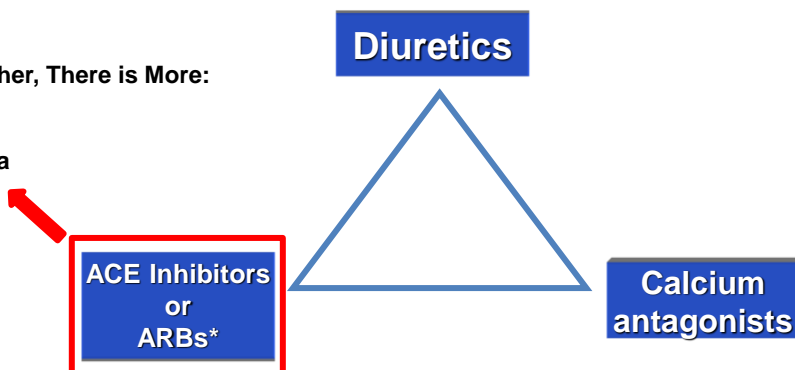
50

Initial Medications for the Management of Hypertension in the 2017 ACC-AHA Guideline

Lifestyle Modification—Especially Diet and Exercise

If Used Together, There is More:

- Syncope
- Hypotension
- Hyperkalemia
- AKI



* Combining ACEI with ARB discouraged-Class 3, Harm

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311(5): 507-520. Feb 5, 2014

2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. Whelton PK, Carey RM et al. Hypertension 2018; 71:e13-e115.

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Cochrane Review:

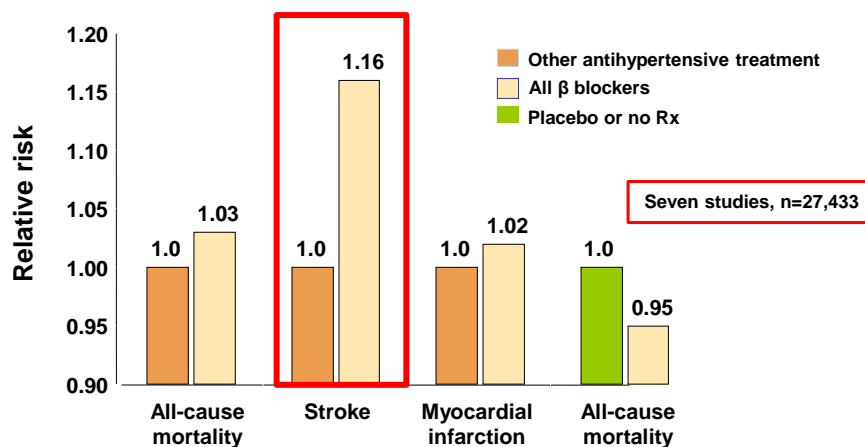
Beta-blockers Should Not Be First Line for Hypertension

- The available evidence does not support the use of beta-blockers as first-line drugs in the treatment of hypertension.

Cochrane Database of Systematic Reviews. Published by John Wiley & Sons, Ltd. January 24, 2007.

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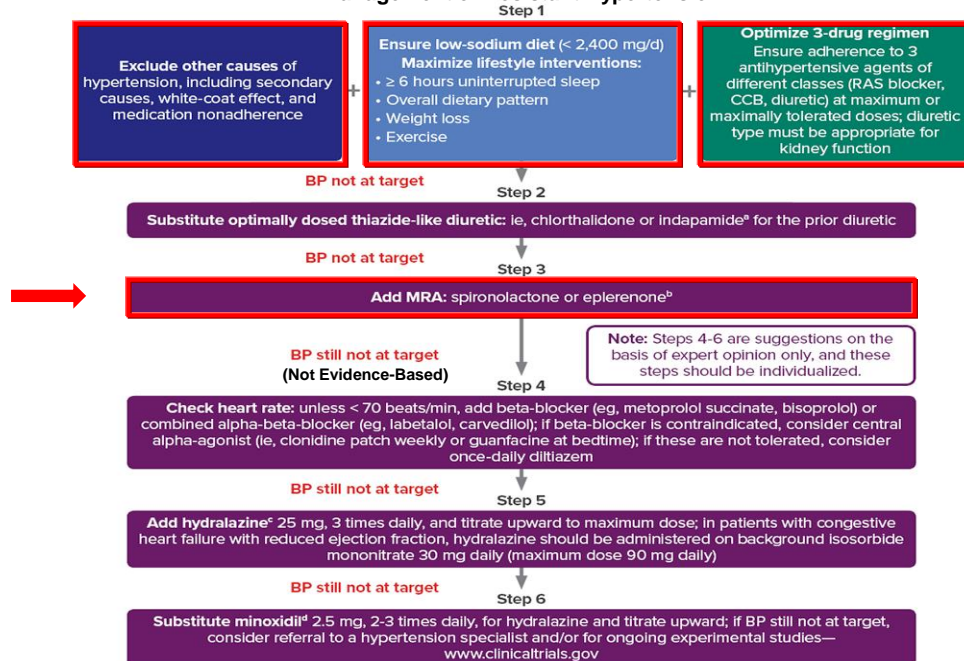
β Blockers and Clinical Outcomes



Lindholm LH et al. *Lancet*. 2005;366(9496):1545-1553.

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Management of Resistant Hypertension



Carey RM et al. *Hypertension*. 2018;72:e53–e90

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Pregnancy

COR	LOE	Recommendations for Treatment of Hypertension in Pregnancy
I	C-LD	Women with hypertension who become pregnant, or are planning to become pregnant, should be transitioned to methyldopa, nifedipine, and/or labetalol during pregnancy.
III: Harm	C-LD	Women with hypertension who become pregnant should not be treated with ACE inhibitors, ARBs, or direct renin inhibitors.

Adapted from 2017 ACC-AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; *Hypertension*; JACC Nov 2017.

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Oral Antihypertensive Therapy

Labetalol 100-200mg BID, increase Q2-3d; max 2400 mg/24h
Nifedipine ER 30-60mg QD, increase Q7-14d; max 120 mg/24h
Methyldopa 250 mg BID-TID, increase Q2d; max 3000 mg/24h

Hydralazine* 10mg QID, increase Q2-5d; max 200 mg/24h

Thiazide diuretics-Hctz 12.5-50 mg daily, second or 3rd line agent

CONTRAINDICATED: ACEI/ARB, Renin Inhibitors, MRAs

**Hydralazine should not be used in isolation due to reflex tachycardia*

ACOG Practice Bulletin Nos. 202 and 203. Obstet Gynecol, 133 (1): e26-e50, January 2019

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Society of Maternal-Fetal Medicine (SMFM) Statement 2022 Antihypertensive Therapy for Mild Chronic Hypertension in Pregnancy

Key Recommendations-Rx Goals in Pregnancy:

- In conclusion, the CHAP trial provides evidence that treating mild chronic hypertension in pregnancy reduces the risk for maternal and peri-natal morbidity without increasing the risk for SGA infants or other neonatal morbidities compared with no treatment unless hypertension becomes severe.

- **Based on the available evidence, SMFM recommends treatment of mild chronic hypertension in pregnancy with antihypertensive therapy to a goal BP of < 140/90 mm Hg.**

Society of Maternal-Fetal Medicine Publication Committee. August 2022.

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CCBs Are Most likely to Cause This Condition



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Resolution of His Gingivitis



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IN SUMMARY:

1. Take a good history on all patients and understand that social determinants of health (SDOH) may strongly influence BP control.
2. Blood Pressure control rates have recently fallen.
3. The basic workup for hypertension after a complete history and physical examination is basic and simple. Don't spend money on the workup if it will not improve patient outcome. Look for renin and aldo as early lab tests in the future?
4. We should endorse lifestyle modification in all patients for effective BP control with a special emphasis on dietary potassium supplementation and sodium restriction.
5. Remember the first three classes of drugs to use when pharmacologic therapy is required do not include *B*-blockers unless there is a compelling reason for their use.
6. Patients who are planning to or who become pregnant should be taken off ACEi's, ARBs, or DRIs and transitioned to either labetalol or long-acting nifedipine with a BP target of < 140/90 mm Hg.

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