

GUIDELINE-DRIVEN MANAGEMENT OF HYPERTENSION: AN EVIDENCE- BASED UPDATE

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Disclosures

- Chair, AHA Writing Committee for 2018 scientific statement on resistant hypertension.
- Member, AHA Writing Committee for 2019 scientific statement on BP measurement.
- Vice-Chair, ACC/AHA Writing Committee for the 2017 hypertension clinical practice guideline.
- Co-chair, Endocrine Society clinical practice guideline panel on primary aldosteronism (2022-).

“The recommendations and opinions presented by our guest speakers may not represent the official position of the American Heart Association. The materials are for educational purposes only, and do not constitute an endorsement or instruction by AHA/ASA. The AHA/ASA does not endorse any product or device.”.

OUTLINE

- Brief review of major guideline recommendations
- Optimal systolic BP and primordial disease prevention
- Current state of BP control
- Secondary hypertension: drug therapy
- Secondary hypertension: primary aldosteronism
- Treatment of hypertension in young adults at low short-term CVD risk
- Lifestyle management of BP
- Pharmacologic management of hypertension
- BP management in older adults
- Concluding comments

BRIEF REVIEW OF MAJOR GUIDELINE RECOMMENDATIONS

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BP CLASSIFICATION (2003 JNC 7 and 2017 ACC/AHA Guidelines)

SBP		DBP	2003 JNC7	2017 ACC/AHA
<120	and	<80	Normal BP	Normal BP
120–129	and	<80	Prehypertension	Elevated BP
130–139	or	80–89		Stage 1 hypertension
140–159	or	90–99	Stage 1 hypertension	Stage 2 hypertension
≥160	or	≥100	Stage 2 hypertension	Stage 2 hypertension

} Area of difference

- Blood Pressure should be based on an average of ≥ 2 careful readings on ≥ 2 occasions
- Adults with SBP or DBP in two categories should be designated to the higher BP category

Whelton PK, Carey RM, et al. *Hypertension*. 2018;71:1269-1324./ *J Am Coll Cardiol*. 2018;71:2199-2269.



2017 ACC/AHA BP Guideline: Thresholds for Drug Treatment

SBP	DBP	CVD Risk/other circumstances	Recommended Treatment
<120 and <80 (Normal)		N/A	Healthy Lifestyle
120–129 and <80 (Elevated)		N/A	Nonpharmacological therapy
130–139 or 80–89 (Stage 1 Hypertension)		- No CVD - 10-yr ASCVD risk <10%*	Nonpharmacological therapy
		- CVD, or - 10-year ASCVD risk ≥ 10%	Nonpharmacological therapy and Antihypertensive drug therapy
		Diabetes or CKD	
130–139 (Stage 1 Hypertension)		Age ≥65 years	Antihypertensive drug therapy
≥140 or ≥90 (Stage 2 Hypertension)		N/A	

* AHA/ACC 2013 Pooled Cohort CVD Risk Equations



2017 ACC/AHA BP Guideline: Treatment Targets

SBP		DBP	CVD Risk	Recommended BP Target
<120	and	<80	N/A	N/A
120–129	and	<80	N/A	N/A
130–139	or	80–89	No CVD and 10-year ASCVD risk <10%	SBP <130 (DBP <80 mm Hg)
130–139	or	80–89	Clinical CVD or 10-year ASCVD risk ≥ 10%	
≥130	or	≥80	Diabetes or CKD	
≥140	or	≥90	N/A	
≥130			Age ≥65 years	SBP <130 mm Hg

Whelton PK, Carey RM, et al. *Hypertension*. 2018;71:1269–1324./ *J Am Coll Cardiol*. 2018;71:2199–2269.

There was controversy surrounding the 2017 ACC/AHA guideline recommendations when they initially appeared.

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Have the major guideline recommendations been validated?



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COMPARISON OF CVD EVENTS AND DEATH PREVENTED WITH ADHERENCE TO 2 GUIDELINE RECOMMENDATIONS

- 1) Estimation of proportion of US adults in BP categories using NHANES
- 2) Incidence of major CVD events & all-cause mortality by modeling 4 large community-based cohort studies (ARCS, CV Health, Framingham, and MESA)
- 3) Network meta-analysis (42 RCTs) to estimate HRs for outcomes and determine population-attributable risks and events reduced.

Characteristic	2014 Evidence-Based Guideline	2017 ACC/AHA Guideline
BP threshold for initiation of antihypertensive drugs	$\geq 140/90$ (<age 60) $\geq 150/90$ (\geq age 60)	$\geq 140/90$ (gen. population) $\geq 130/80$ (high CVD risk)
BP goal of treatment	$< 140/90$ (<age 60) $< 150/90$ (\geq age 60)	$< 130/80$
Annual CVD event reduction (\geq age 40)	270,000	610,000 (NNT=70)
Annual reduction in death (\geq age 40)	177,000	334,000 (NNT=129)



SIMULATED POPULATION IMPACT OF ACHIEVING AND MAINTAINING 2017 ACC/AHA GL BP GOALS IN US ADULTS ≥ 45 Y WITH HYPERTENSION

Achieving and maintaining 2017 ACC/AHA guideline recommended BP goals compared to:

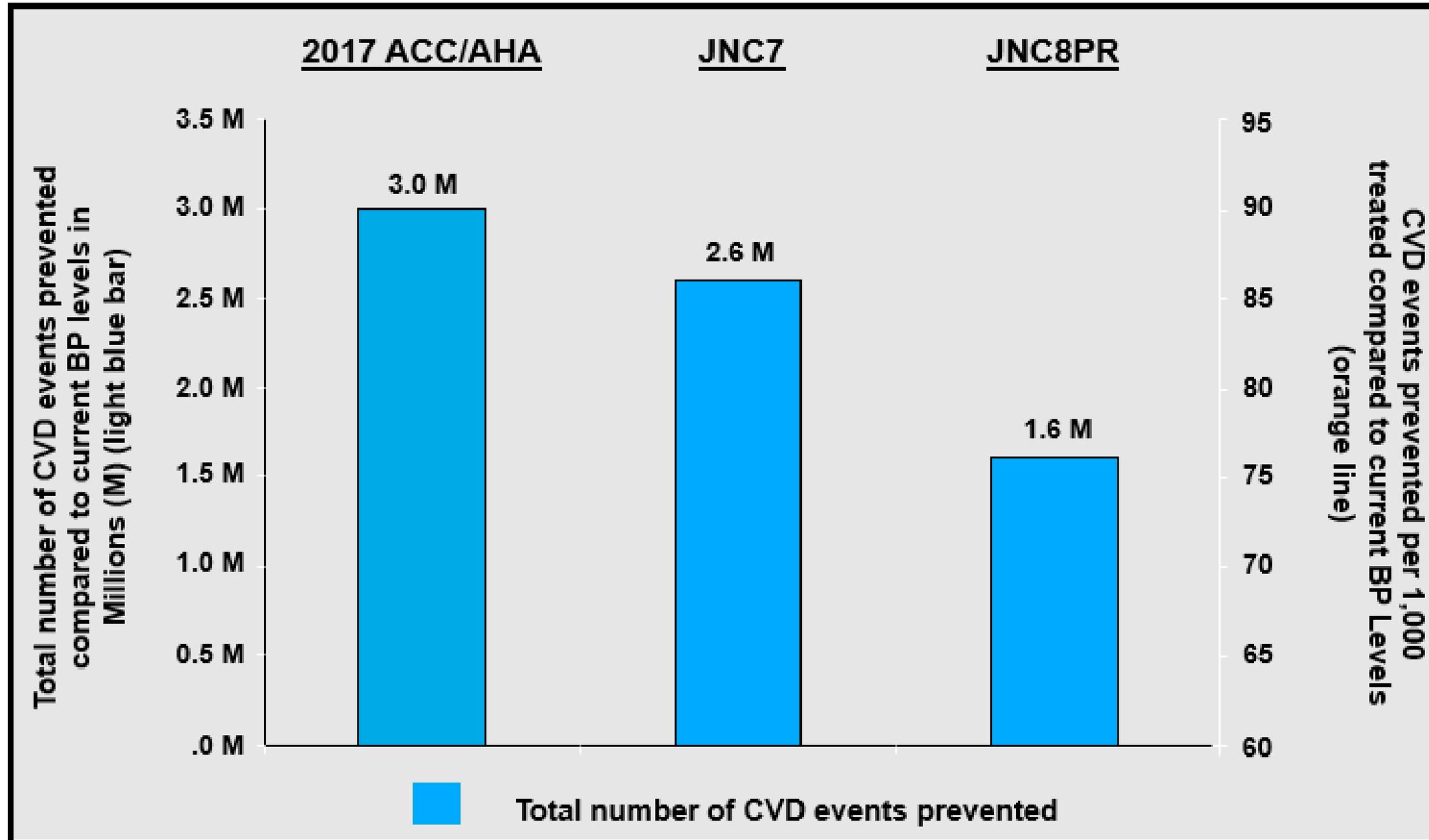
- Maintaining current BP treatment and control levels
- Achieving BP goals recommended in the 2003 JNC7 guideline
- Achieving 2014 Eighth Joint National Committee panel report BP goals

Estimated using the following inputs:

- 10-year CVD event rates in hypertension treatment groups using the REGARDS study, weighted to the US population.
- US adult population sizes for each group from NHANES
- Expected CVD risk reduction with BP lowering to goal based on response to treatment to current and recommended BP levels in a meta-analysis of antihypertensive drug treatment randomized trials from Bundy *et al. JAMA Cardiology*. 2017.
- Expected risk of treatment-related SAEs with BP lowering based on treatment-related harms observed in patients treated to standard and intensive BP goals using pooled data from SPRINT and ACCORD.

Bress AP *et al. Circulation*.2019;139:24-36

PROJECTED CVD EVENTS PREVENTED x 10Y



POPULATION MODELING STUDIES SUMMARY

- Two well-performed simulation studies demonstrate a highly positive population impact of following the 2017 ACC/AHA hypertension guideline recommendations for lowering BP in hypertensive persons compared to older guidelines.
- The increased risk of adverse events (largely reversible) with the lower BP target should not be equated to the risk reduction of major clinical events. Significant reduction in all-cause mortality shows that benefit of treatment outweighs risks.
- These results strongly support a lower BP target (<130/80 mmHg) in the management of hypertension.

Is there any association of BP levels within the normotensive range with cardiovascular events or disease?

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What does the data say about the importance of primordial prevention?



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WHAT IS PRIMORDIAL PREVENTION?

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Actions that inhibit the emergence of risk factors in the form of environmental, economic, social and behavioral conditions and cultural patterns of living.





ASSOCIATION OF NORMAL RANGE BP WITH SUBCLINICAL ASCVD

- The 2017 ACC/AHA guideline lowered the SBP goal of therapy from <140 to <130 mm Hg. This recommendation focused on the cut point at which there is likely to be benefit from antihypertensive drug therapy.
- But many individuals classified as low risk based on their ASCVD risk score have subclinical atherosclerosis (based on coronary artery calcium scores) and may not truly be at low risk.
- Is there an association between SBP, within the normal range as currently defined, and ASCVD in persons without traditional risk factors?

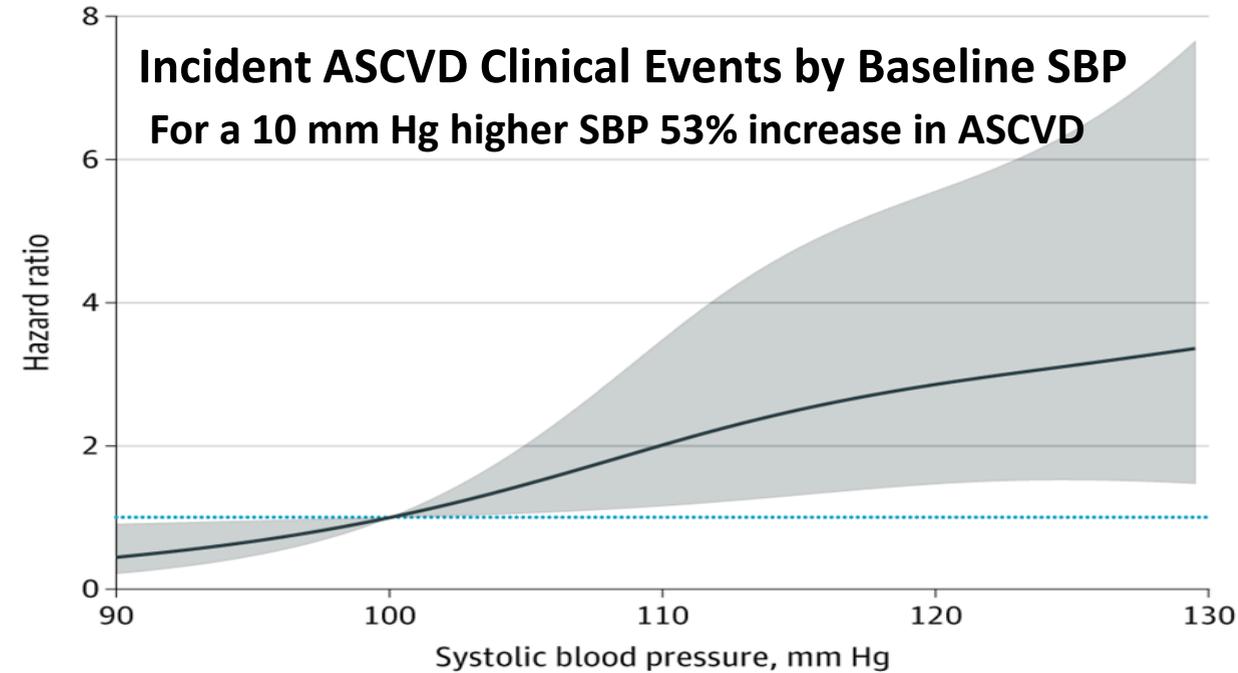
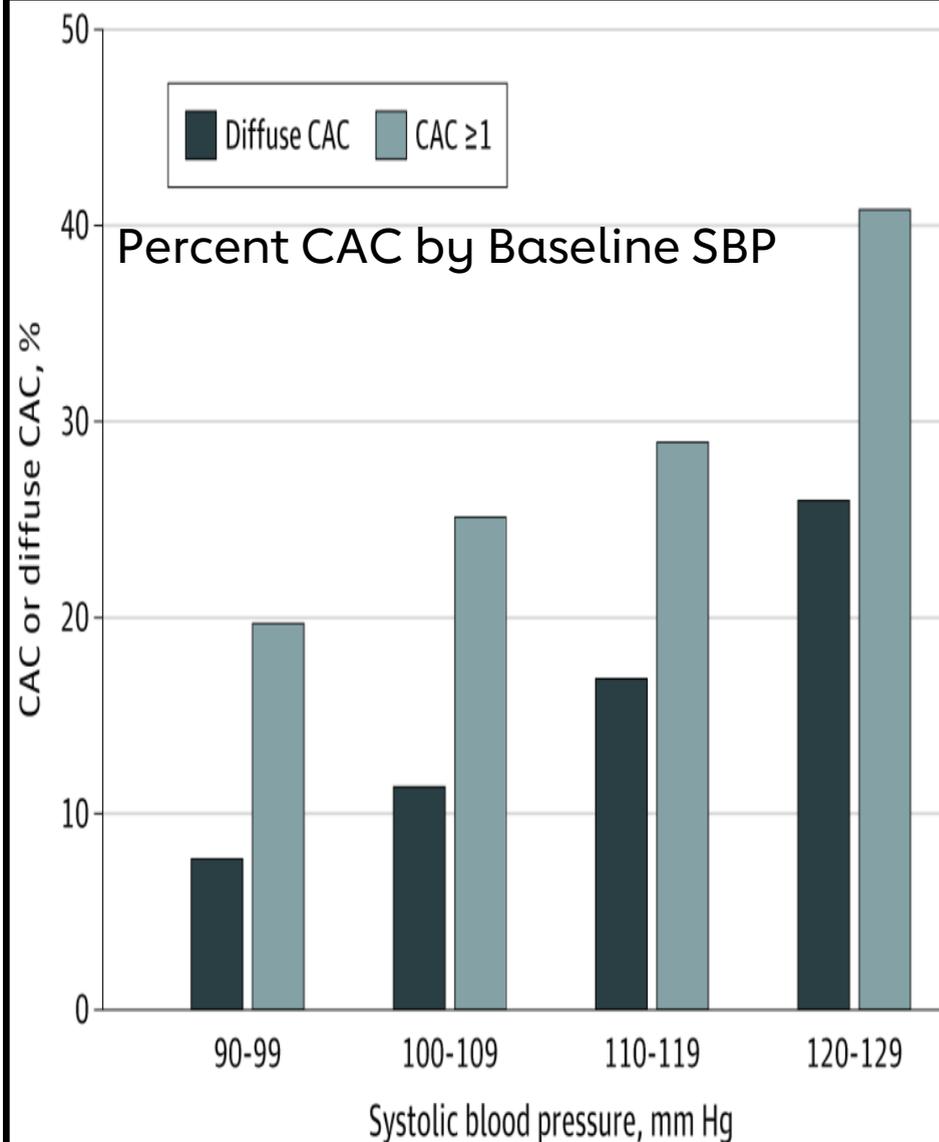
Whelton S *et al.* *JAMA Cardiol.* 2020;5:1011-1018.



ASSOCIATION OF NON-HYPERTENSIVE LEVELS OF SBP & CVD In the Absence of Traditional CVD Risk Factors

MESA FU of 14.5 years in 1457 adults, mean age 58 y and free of ASCVD with SBP 90-129 mm Hg, LDL-C <160 mg/dL, HDL-C 40+ mg/dL, no DM, no tobacco use, no treatment for hyperlipidemia or DM

Higher levels of SBP @ baseline associated with development of CVD Risk Factors



Adjusted for age, sex, race/ethnicity, diastolic blood pressure, total cholesterol level, high-density lipoprotein cholesterol level, fasting blood glucose level, body mass index, income, educational level, ever smoking, and prediabetes.

Hazard of Cardiovascular Disease by Systolic Blood Pressure Group

Table 2. Hazard of Cardiovascular Disease by Systolic Blood Pressure Group

Characteristic	Systolic blood pressure, mm Hg				P value for trend
	90-99	100-109	110-119	120-129	
Unadjusted	1 [Reference]	3.04 (1.05-8.80)	3.49 (1.23-9.90)	6.31 (2.24-17.73)	<.001
Model 1 ^a	1 [Reference]	2.70 (0.93-7.85)	2.64 (0.93-7.82)	3.76 (1.33-10.69)	.07
Model 2 ^b	1 [Reference]	3.00 (1.01-8.88)	3.10 (1.03-9.28)	4.58 (1.47-14.27)	.06

^a Adjusted for age, sex, race/ethnicity.

^b Model 1 adjustments plus diastolic blood pressure, total cholesterol level, high-density lipoprotein cholesterol level, fasting blood glucose level, body mass index, income, educational level, ever smoking, and prediabetes.

Whelton S
*et al. JAMA
Cardiol.*
2020;5:1011-
1018.



ASSOCIATION OF NORMAL RANGE BP WITH SUBCLINICAL ASCVD

- In this cohort study including 1457 participants without atherosclerotic cardiovascular disease, beginning with a SBP level of 90 mm Hg, there was a stepwise increase in the prevalence of traditional ASCVD risk factors, coronary artery calcium scores, and the risk of ASCVD.
- For every 10 mm Hg increase in SBP, there was a 53% higher risk for ASCVD.
- The results highlight the importance of primordial prevention to maintain optimal SBP levels as well as other traditional risk factors.

Whelton S *et al.* *JAMA Cardiol.* 2020;5:1011-1018.

Since the introduction of the current BP guidelines, is there any evidence for improvement in BP control?

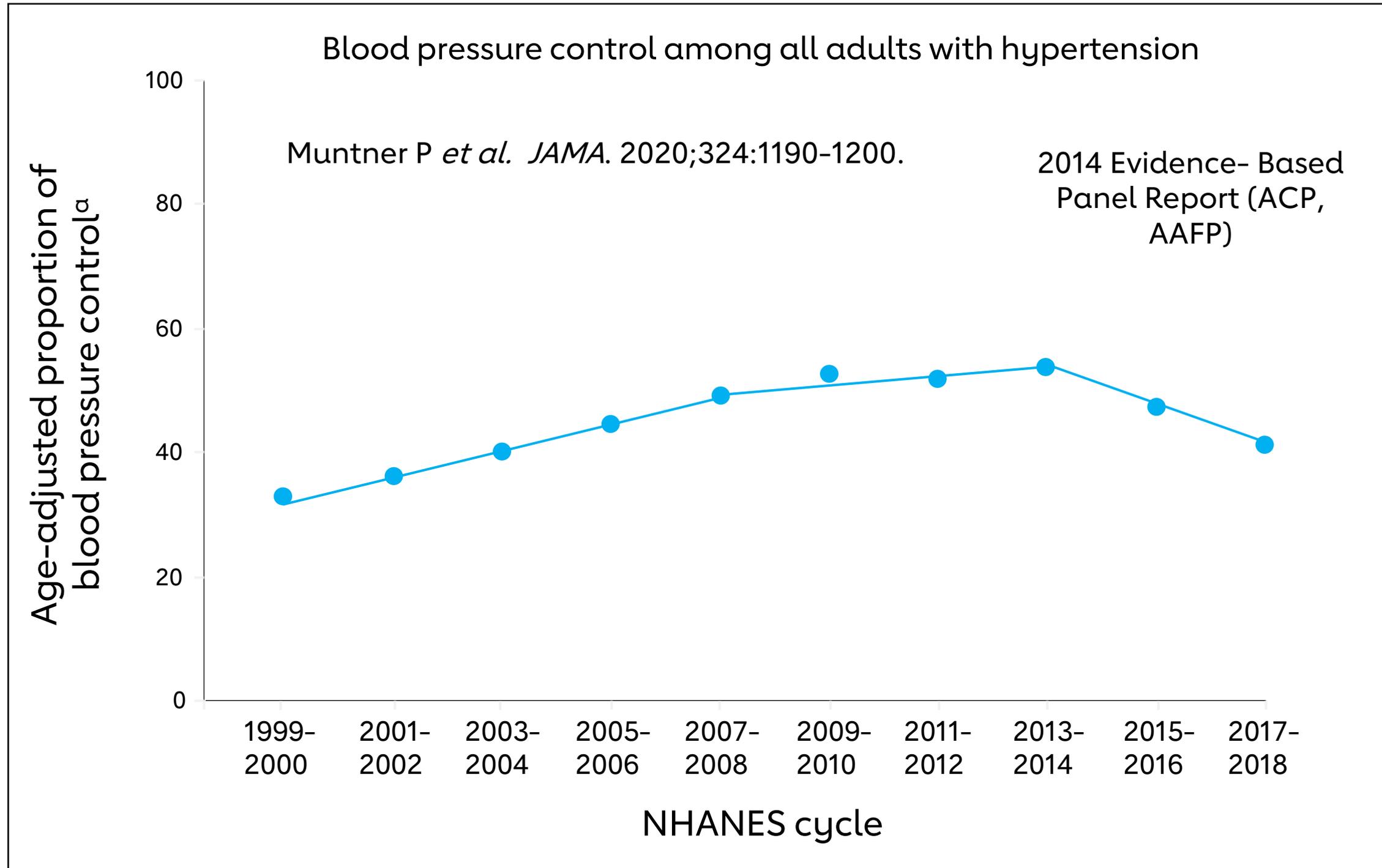
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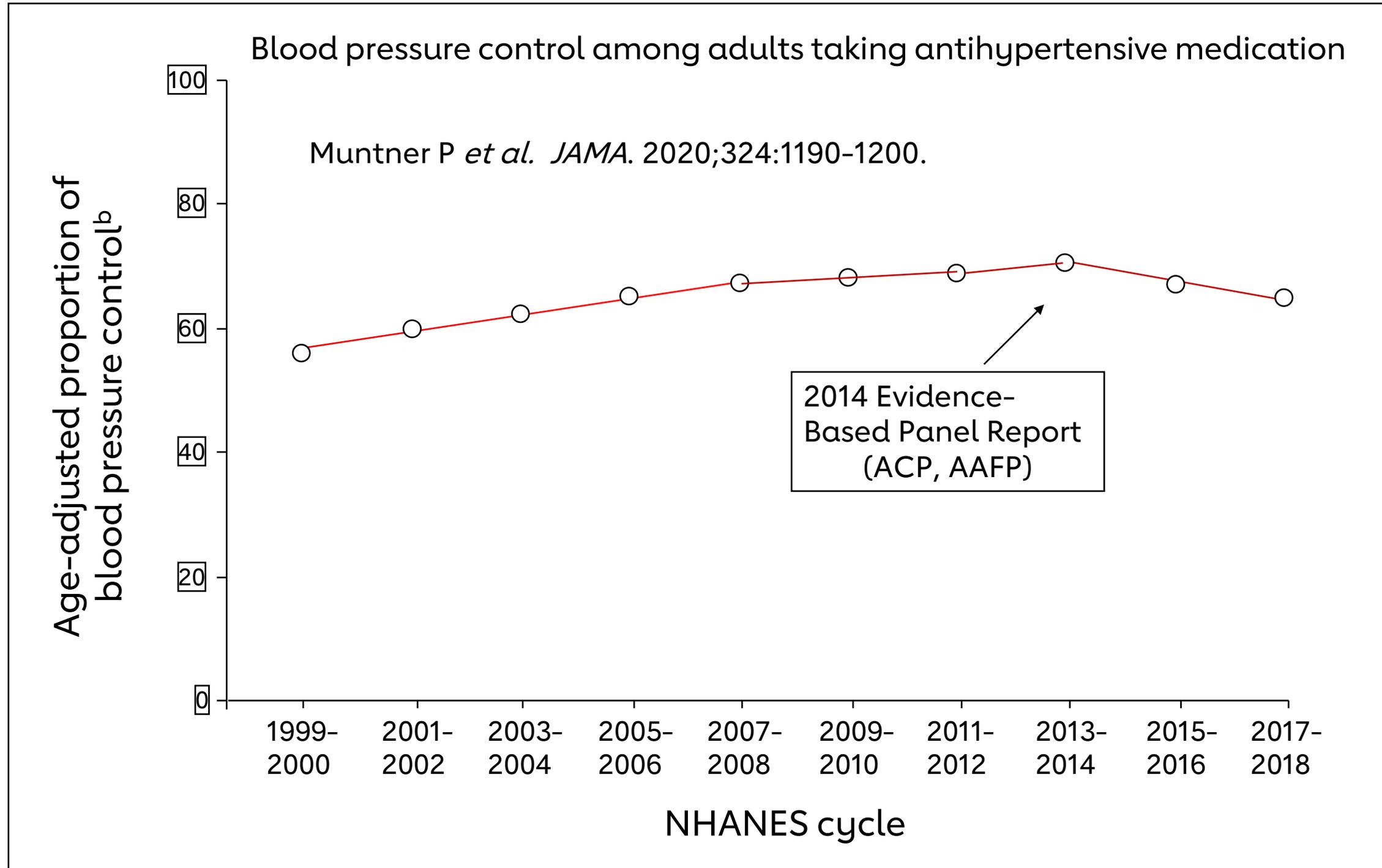
AGE-ADJUSTED ESTIMATED PROPORTION OF ADULTS WITH HYPERTENSION AND CONTROLLED BP (<140 mm Hg)



Muntner P, *et al.*, *JAMA*. 2020;324:1190-1200.



AGE-ADJUSTED ESTIMATED PROPORTION OF ADULTS WITH HYPERTENSION AND CONTROLLED BP (<140 mm Hg)



Muntner P, *et al.* *JAMA*. 2020;324:1190-1200.



What drugs should I worry about that might induce secondary hypertension or aggravate BP levels in hypertensive patients?

- Non-steroidal anti-inflammatory agents (NSAIDs) – *the most important category; at any dose level that controls pain, BP is elevated. NSAIDs interfere with antihypertensive actions of ACEIs, ARBs, diuretics & β -blockers.*
- Oral contraceptives and hormone replacement therapy
- Immunosuppressive agents: cyclosporine
- Recombinant human erythropoietin
- Tyrosine kinase inhibitors
- Cocaine
- Amphetamines
- Antidepressants

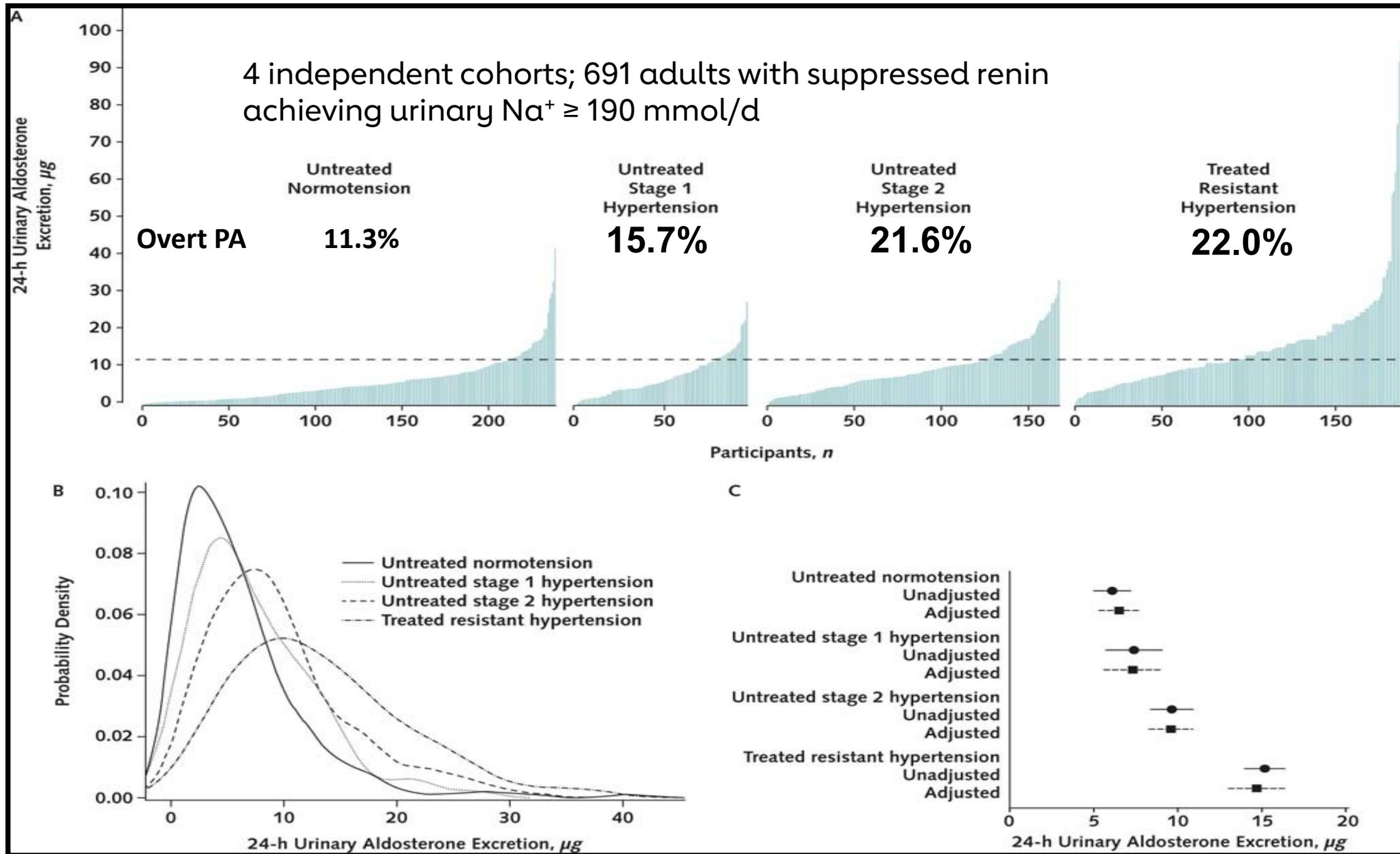
Is there anything new in screening for secondary hypertension due to primary aldosteronism?

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DISTRIBUTION OF RENIN-INDEPENDENT ALDOSTERONE PRODUCTION



STUDY CONCLUSIONS

- A continuum of autonomous and renin-independent aldosterone production can be found across the spectrum from normotension to resistant hypertension.
- The frequency of PA (primary aldosteronism) by confirmatory testing ranged 6-12.7% in normotensives, 6.3-19.4% in stage 1 hypertensives, 14.9-25.2% in stage 2 hypertensives, and 17.8-52.4% in resistant hypertensives, depending on the PA definition used.
- In the context of renin suppression, autonomous 24h urine aldosterone is associated with blood pressure and urinary potassium excretion, consistent with activation of MR.
- Unrecognized, and/or subclinical, primary aldosteronism likely explains the pathogenesis of a substantial proportion of primary hypertension.

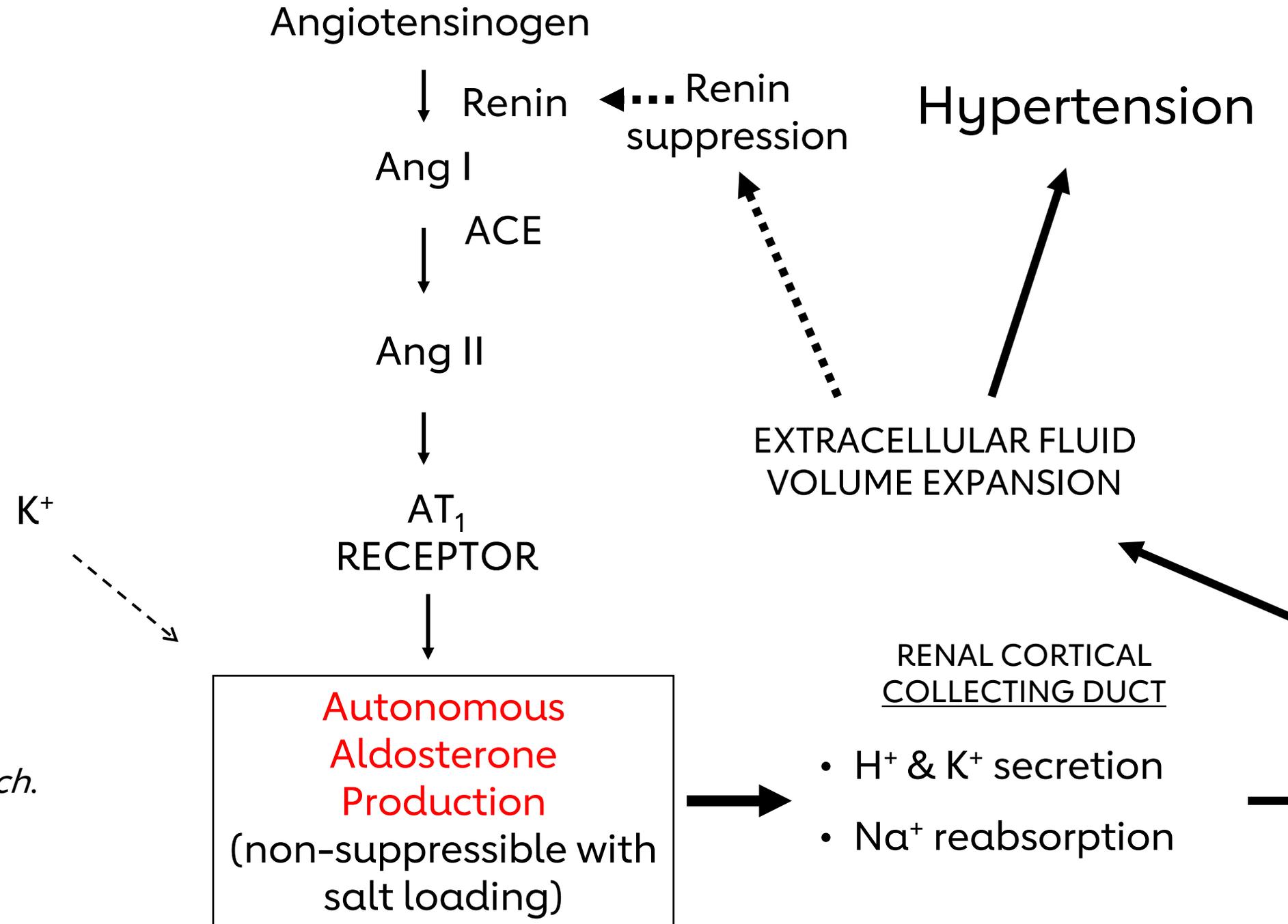


HOW MANY PATIENTS WITH PRIMARY HYPERTENSION ARE EVER SCREENED FOR PRIMARY ALDOSTERONISM?

- One in 1,000 in the United Kingdom and Germany
- 2.1% of resistant hypertensives in the U.S.
- The cardiometabolic risk profile for patients with primary aldosteronism without targeted therapy is at least 3-fold higher than that for patients with primary hypertension matched for age, sex and BP.
- Therefore, we need a new simplified diagnostic approach, one that can be endorsed by the primary care community.

Jaffe G et al. Hypertension. 2020;75:650-659.

AUTONOMOUS ALDOSTERONE PRODUCTION IN PRIMARY HYPERTENSION



Carey RM *et al.*
Circulation Research.
2021;128:827-846.

**Should all patients with primary
(essential) hypertension be screened
for primary aldosteronism?**

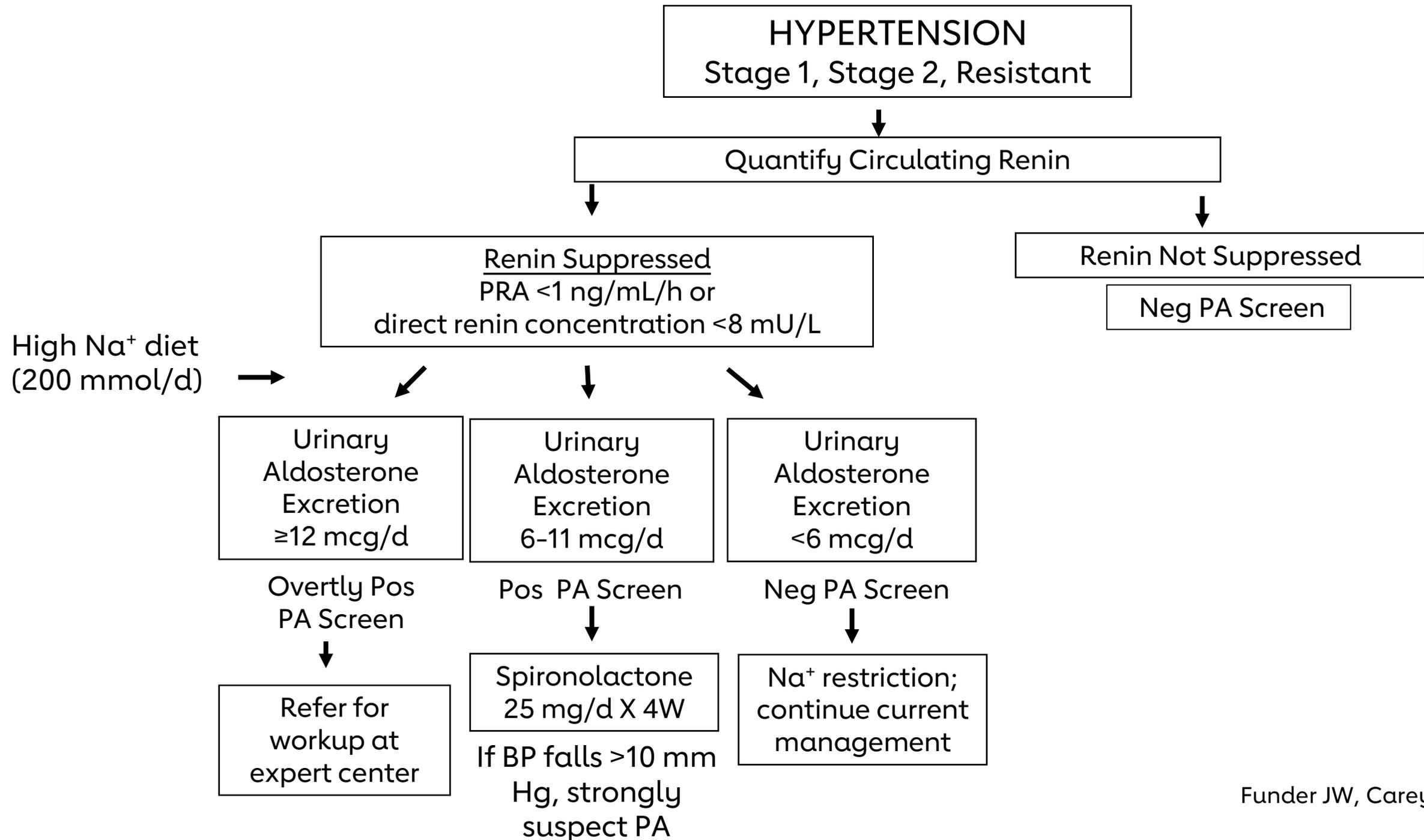
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If so, how?



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PROPOSED SCREENING FOR AUTONOMOUS ALDOSTERONE PRODUCTION IN HYPERTENSIVE ADULTS



Treatment of hypertension in young and low risk groups was not well covered in the 2017 ACC/AHA guideline.

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How should we manage young low-risk adults in the absence of RCT evidence?



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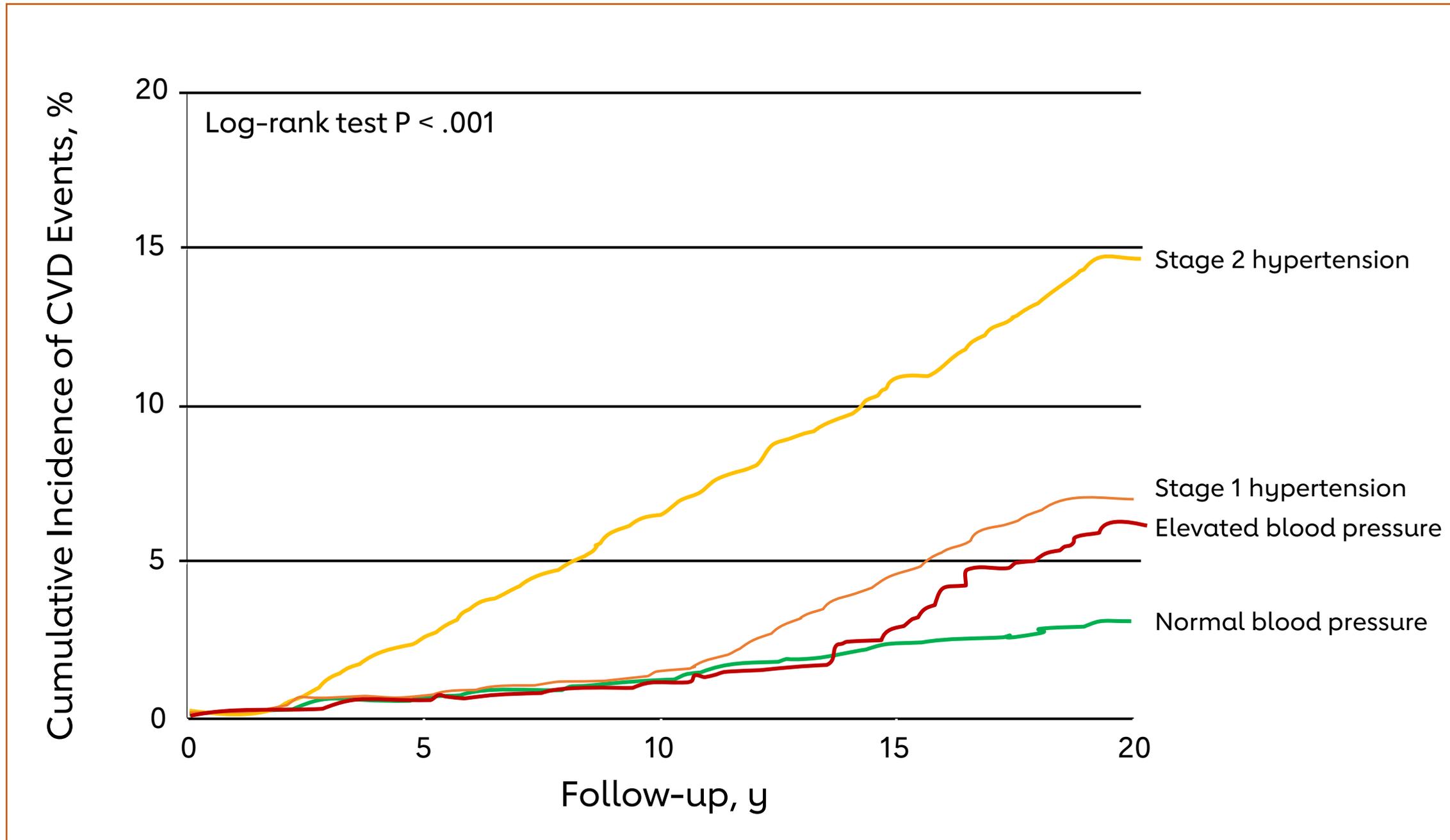
DOES HIGH BP CONFER INCREASED CVD RISK EVEN IN "LOW RISK" YOUNG ADULTS?

- For young adults with isolated hypertension, lifetime risk of ASCVD is high although 10-y ASCVD risk may be low.
- As the overall population BP level has shifted to a lower average value, more CVD events are occurring at lower BP levels.
- This was demonstrated for young adults with hypertension who have earlier onset of coronary heart disease, heart failure, stroke, transient ischemic attacks and peripheral arterial disease requiring intervention.
- In the CARDIA (Coronary Artery Risk Development in Young Adults) study of 3,851 adults followed 18.8 years, only 4% were taking antihypertensive medication.
- Adjusted hazard ratios for CVD events were 1.67 , 1.75 and 3.49 for elevated BP, stages 1 hypertension and stage 2 hypertension, respectively, compared to controls with normal BP.



CUMULATIVE INCIDENCE OF CVD EVENTS IN THE CARDIA STUDY BY BP GROUP

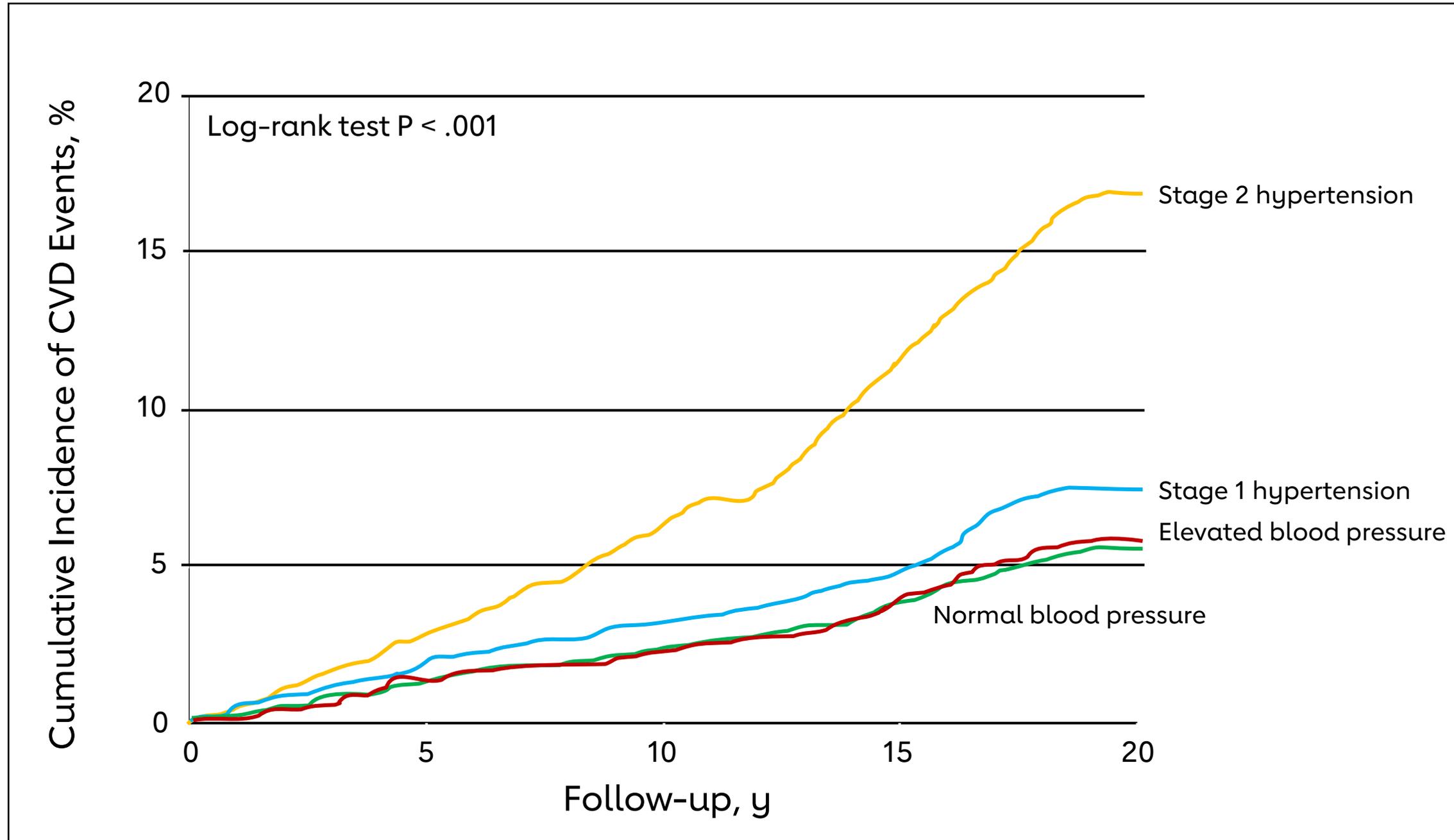
Yano Y *et al.*
JAMA.
2018;320:
1774-1782





CUMULATIVE INCIDENCE OF ALL CAUSE MORTALITY IN THE CARDIA STUDY BY BP GROUP

Yano Y *et al.*
JAMA.
2018;320:
1774-1782





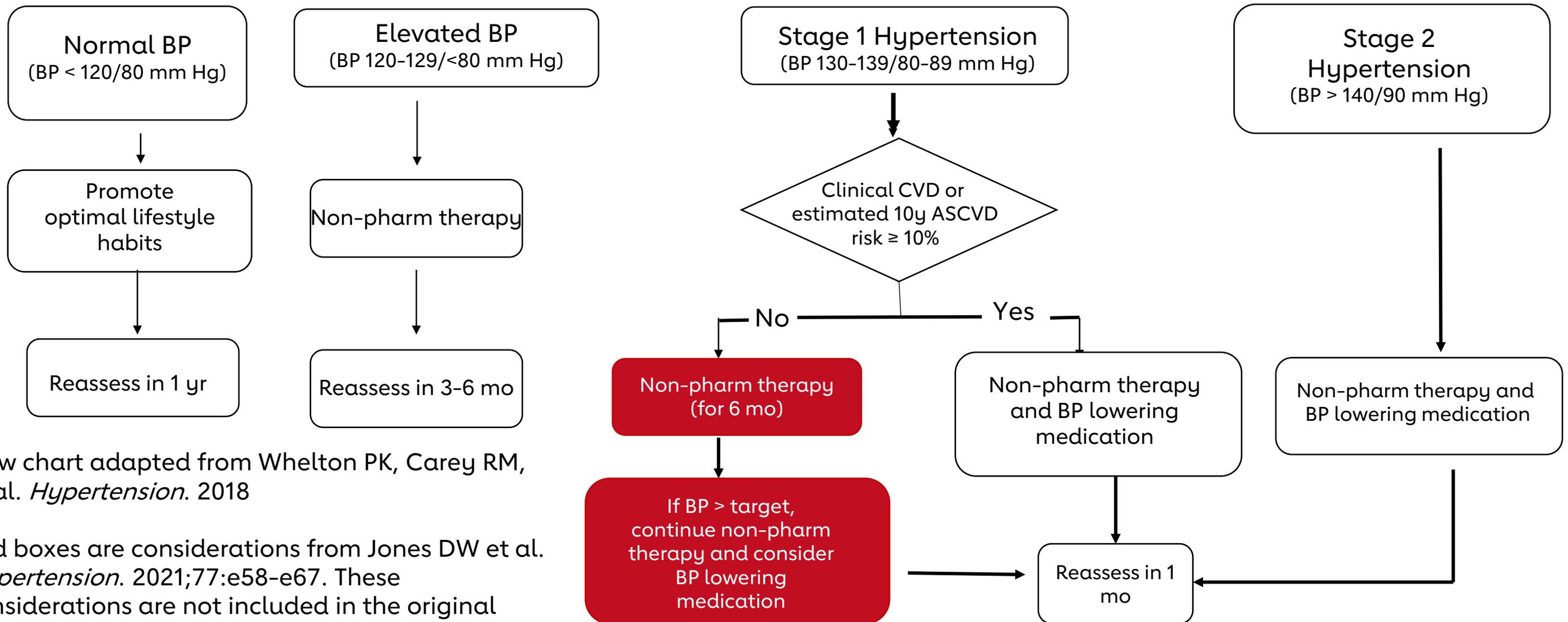
AHA SCIENTIFIC STATEMENT: MANAGEMENT OF STAGE 1 HYPERTENSION IN YOUNG ADULTS WITH LOW 10-YEAR ASCVD RISK

- Start with 6 months of vigorous lifestyle change.
- In all patients with stage 1 hypertension not achieving BP goal <130/80 mm Hg within 6 months, lifestyle therapy should be continued and consideration of first-line antihypertensive drug therapy.
- Special consideration should be given to use of antihypertensive agents in individuals with a family history of premature CVD, a history of hypertension during pregnancy, or a personal history of premature birth.
- 10-y ASCVD risk should be assessed every 4-6 years in patients with 10-y ASCVD risk <10%



2020 AHA Scientific Statement Considerations for Clinical Practice for Low-Risk Younger Adults

BP thresholds for treatment initiation and follow-up



Flow chart adapted from Whelton PK, Carey RM, et al. *Hypertension*. 2018

Red boxes are considerations from Jones DW et al. *Hypertension*. 2021;77:e58-e67. These considerations are not included in the original 2017 Guidelines.

**How important is lifestyle modification
in the treatment of hypertension?**

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**Is there any new evidence supporting the
efficacy of dietary sodium restriction?**

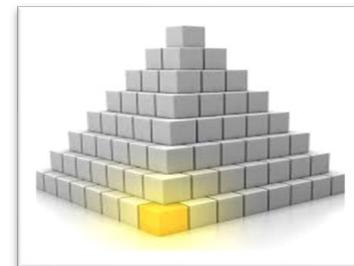


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LIFESTYLE MODIFICATION: THE CORNERSTONE FOR PREVENTION AND TREATMENT OF HYPERTENSION

<u>Lifestyle Intervention</u>	<u>Dose</u>	<u>Impact on SBP</u>	
		<u>Hypertension</u>	<u>Normotension</u>
Weight loss	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg
Healthy diet	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	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5/6 mm Hg	-2/3 mm Hg
Enhanced intake of dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg



All 4 Recommendations COR:1; LOE:A



LIFESTYLE MODIFICATION: THE CORNERSTONE FOR PREVENTION AND TREATMENT OF HYPERTENSION

Nonpharmacological Intervention		Dose	Effect on SBP	
			Hypertension	Normotension
Physical activity	Aerobic	<ul style="list-style-type: none"> ● 90–150 min/wk ● 65%–75% heart rate reserve 	-5/8 mm Hg	-2/4 mm Hg
	Dynamic resistance	<ul style="list-style-type: none"> ● 90–150 min/wk ● 50%–80% 1 rep maximum ● 6 exercises, 3 sets/exercise, 10 repetitions/set 	-4 mm Hg	-2 mm Hg
	Isometric resistance	<ul style="list-style-type: none"> ● 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk ● 8–10 wk 	-5 mm Hg	-4 mm Hg
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol to: <ul style="list-style-type: none"> ● Men: ≤2 drinks daily ● Women: ≤1 drink daily 	-4 mm Hg	-3 mm

Both Recommendations COR:1; LOE:A





BLOOD PRESSURE EFFECTS OF SODIUM REDUCTION

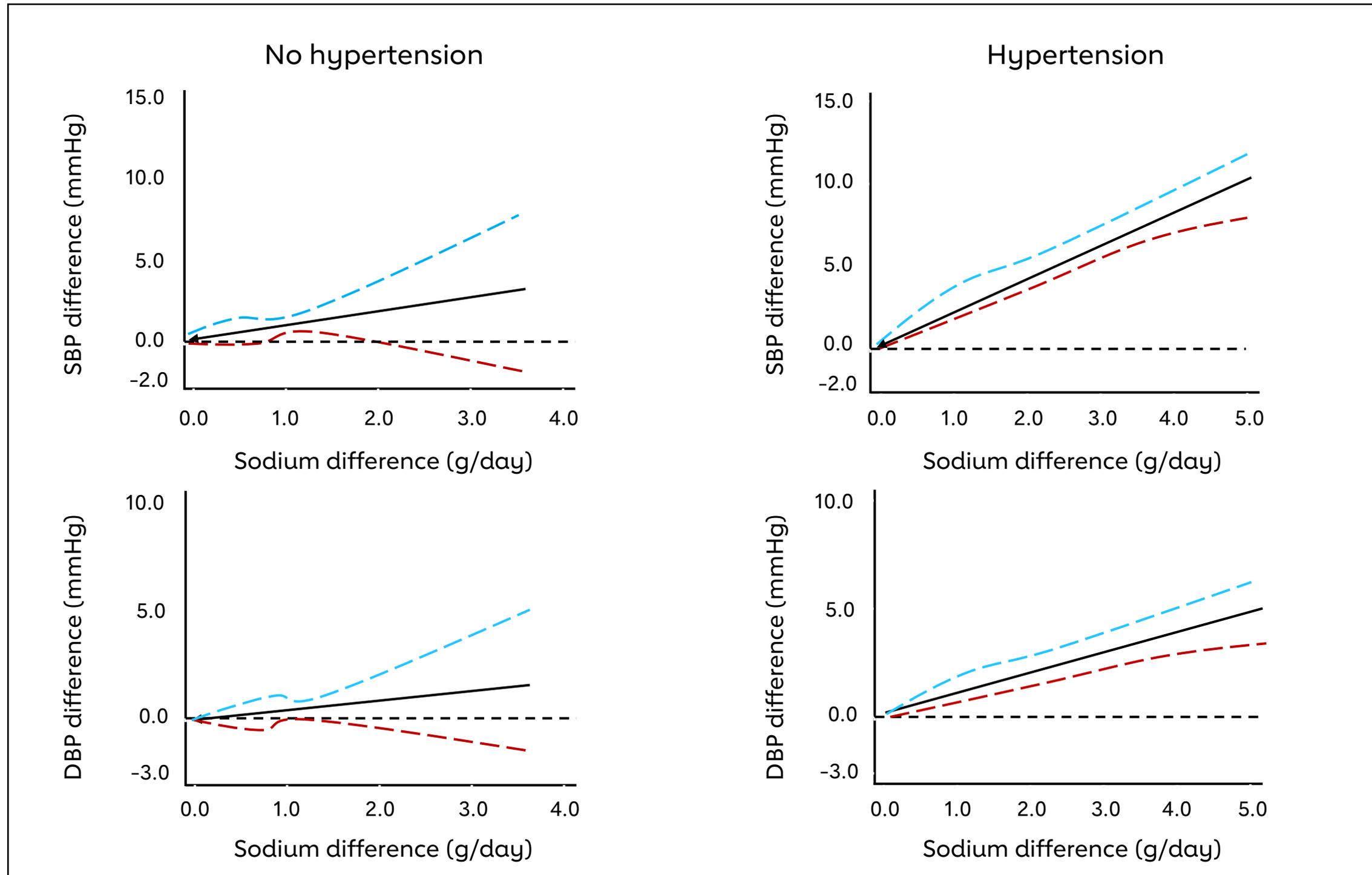
Dose-Response Meta-Analysis of Experimental Studies

- A comprehensive dose-response meta-analysis of trials detailing the effects of change of dietary sodium on BP, using the most up-to-date statistical dose-response modeling, shows that the relationship is positive, and almost but not entirely linear.
- Progressively large reduction in BP can be expected with decreases in NaCl consumption down to 1 to 1.5 g/d, with no evidence for a threshold benefit.
- The results suggest that this relationship is generally true for both SBP and DBP, for adults with and without hypertension, and during shorter and longer periods of sodium reduction.



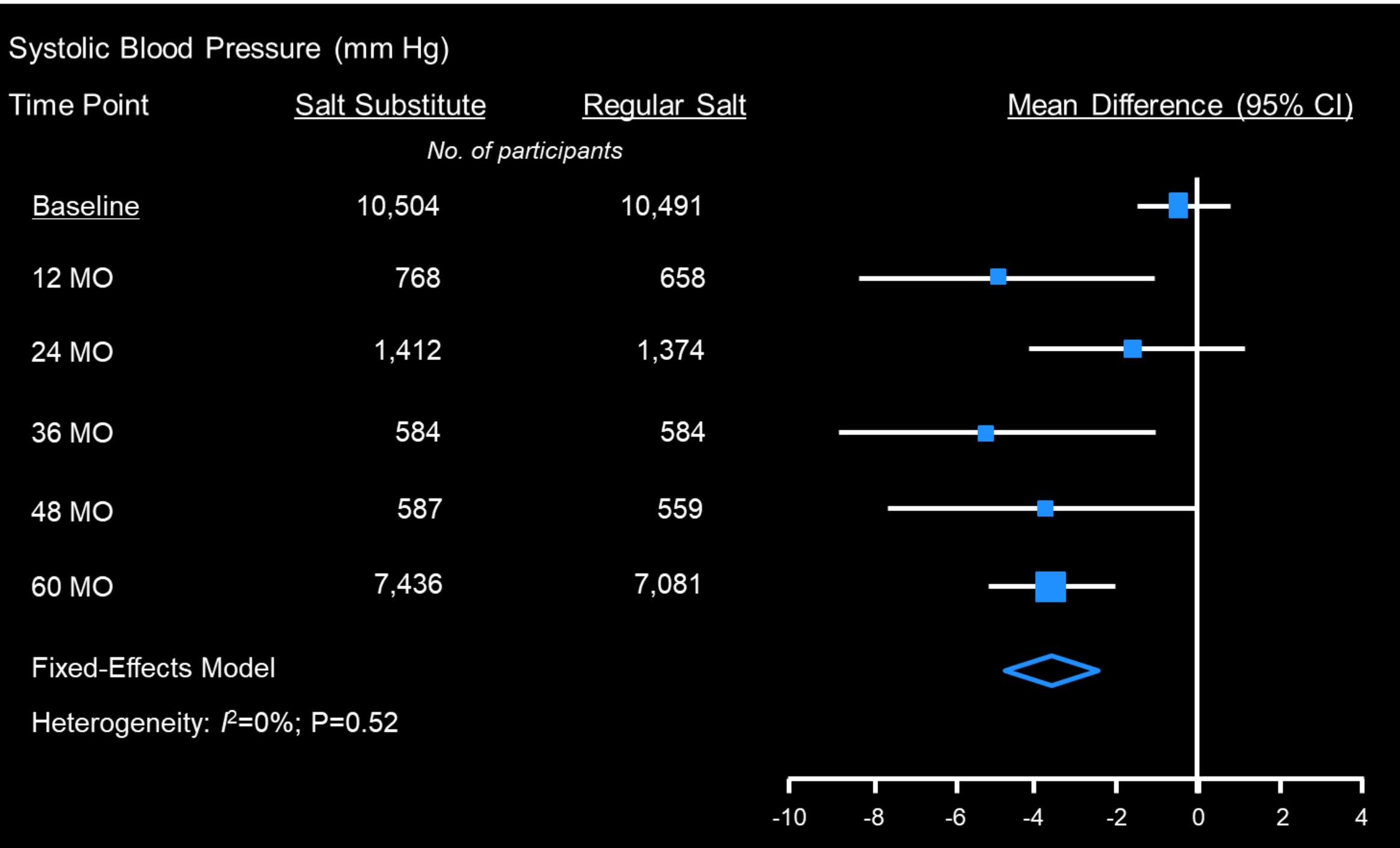
DOSE-RESPONSE META-ANALYSIS OF CHANGES IN SBP & DBP ACCORDING TO DIFFERENCES IN SODIUM EXCRETION

Filippini T *et al.* .
Circulation.
2021;143:
1542-1567.



- Salt substitutes with reduced Na^+ and increased K^+ levels have been shown to lower BP, but their effects on CVD and safety outcomes have been uncertain.
- Neal *et al.* conducted an open-label, cluster randomized trial involving 600 villages in rural China. Participants had hypertension and a history of stroke or were \geq age 60.
- Villages were randomly assigned to an intervention group (a salt substitute containing 75% NaCl and 25% KCl by mass) or a control group continuing to use regular salt (100% NaCl).
- The primary outcome was stroke, the secondary outcomes were major adverse cardiovascular events and death from any cause, and the safety outcome was hyperkalemia.

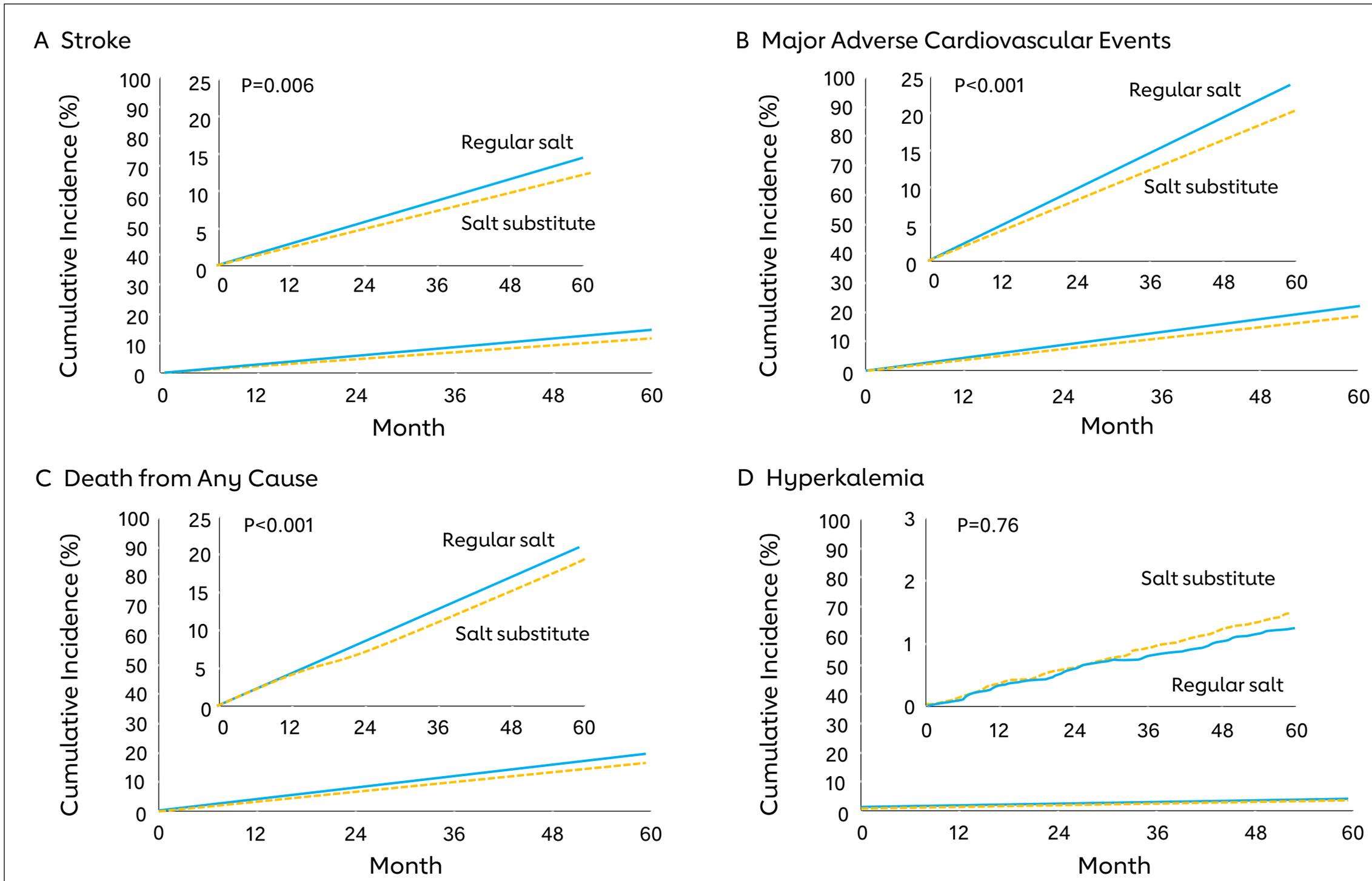
EFFECT OF SALT SUBSTITUTION ON CVD EVENTS AND DEATH



Neal B *et al.*
N Engl J Med.
 2021;385:106
 7-1077.

EFFECT OF SALT SUBSTITUTION ON CVD EVENTS AND DEATH

Neal B *et al.* *N Engl J Med.* 2021;385:1067-1077.



What are the latest principles for the pharmacological management of hypertension?

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PHARMACOLOGICAL TREATMENT OF HYPERTENSION

Agree (patient and clinician) on BP goal

First-line therapeutic classes

- CCB* and/or
- ACEI or ARB and/or
- Thiazide-like** or thiazide diuretic

Monthly visits
until BP goal
achieved

- Measure (minimum 2 readings in am & pm 3 d/week), record and report home BP readings at each office visit.
- Use fixed-dose drug combinations and 90-day prescription refills if possible
- If BP not at goal, assess for social barriers and non-adherence to treatment.
- Dose-titrate and/or add another first-line agent from a different class if needed to achieve goal.

Second-line therapeutic classes

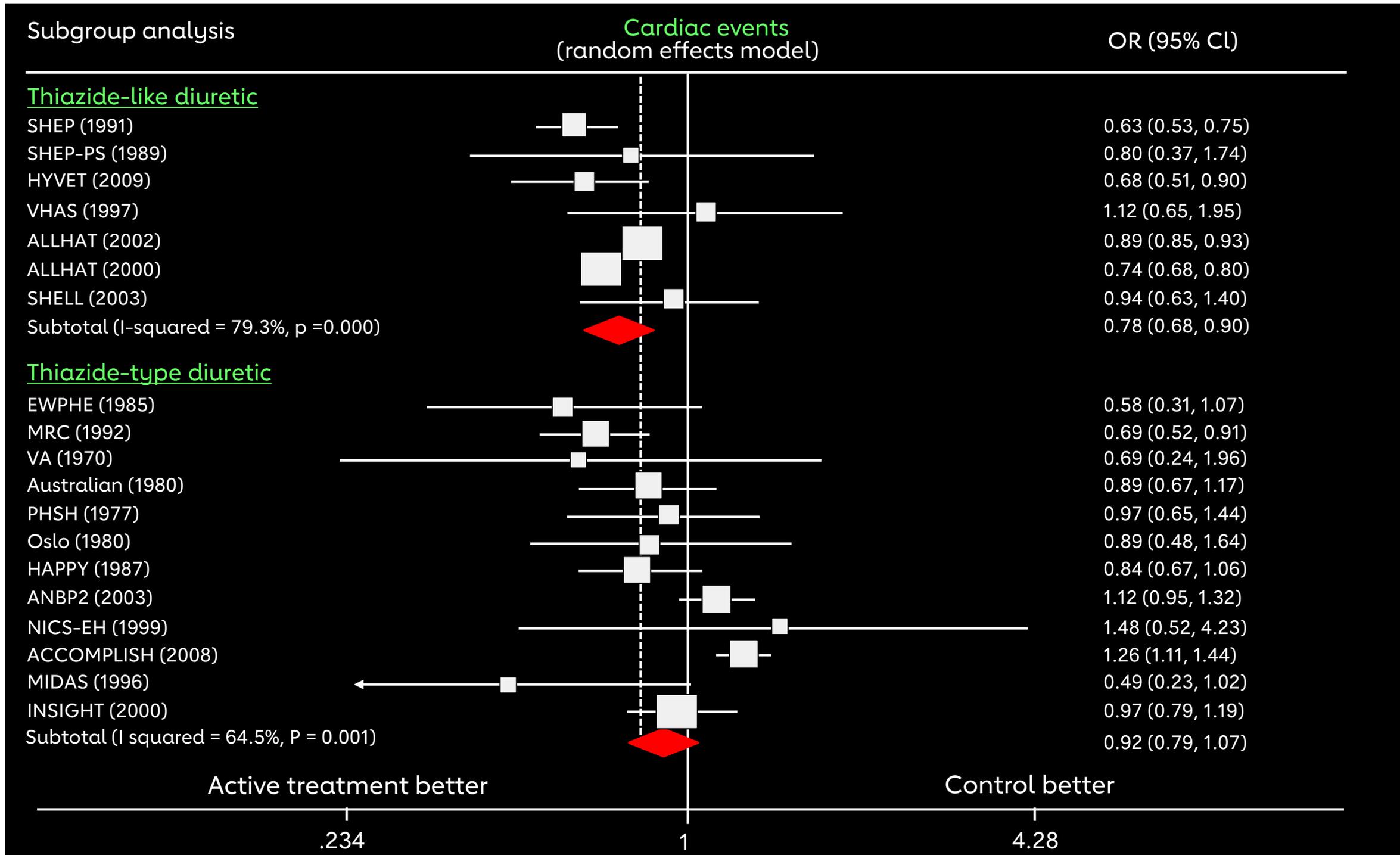
- β -blocker (first-line only in IHD and HF)
- MRA (preferred in low renin states and resistant HT)
- α_1 -antagonist
- Direct vasodilator (use with diuretic and β -blocker)
- K^+ -sparing diuretic (minimally effective in BP reduction)
- Loop diuretic (preferred in CKD with GFR < 30, in symptomatic HF and when using potent direct vasodilator minoxidil)
- Central α_2 -agonist (last-line due to CNS effects and potential for hypertensive crisis on withdrawal)

KEYS TO EFFECTIVE BP LOWERING IN HYPERTENSION

- Agree (patient and provider) on BP target .
- Use fixed dose combinations.
- Substitute long-acting chlorthalidone for hydrochlorothiazide.
- Use long-acting amlodipine as first line calcium channel blocker.
- Monthly visits until blood pressure target achieved
- Replace prescriptions of 30 day with 90-day refills, if allowed.
- Use telehealth strategies to augment office-based management.
- Enhance connectivity between patient, provider and electronic health record for better feedback and communication.
- Screen for social determinants of health and consideration of obstacles to care.
- Use multidisciplinary team-based care to enhance lifestyle and medication adherence and to solve social issues.

CARDIOPROTECTIVE EFFECTS OF THIAZIDE-LIKE DIURETICS

Chen P *et al.*
Am J Hypertens.
 2015;28:1453-1463



Intensive BP lowering in hypertensive older adults has been controversial, especially in light of risks, such as orthostatic hypotension, electrolyte abnormalities and increased renal failure.

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Is there any new evidence supporting the efficacy of intensive BP lowering in older adults?



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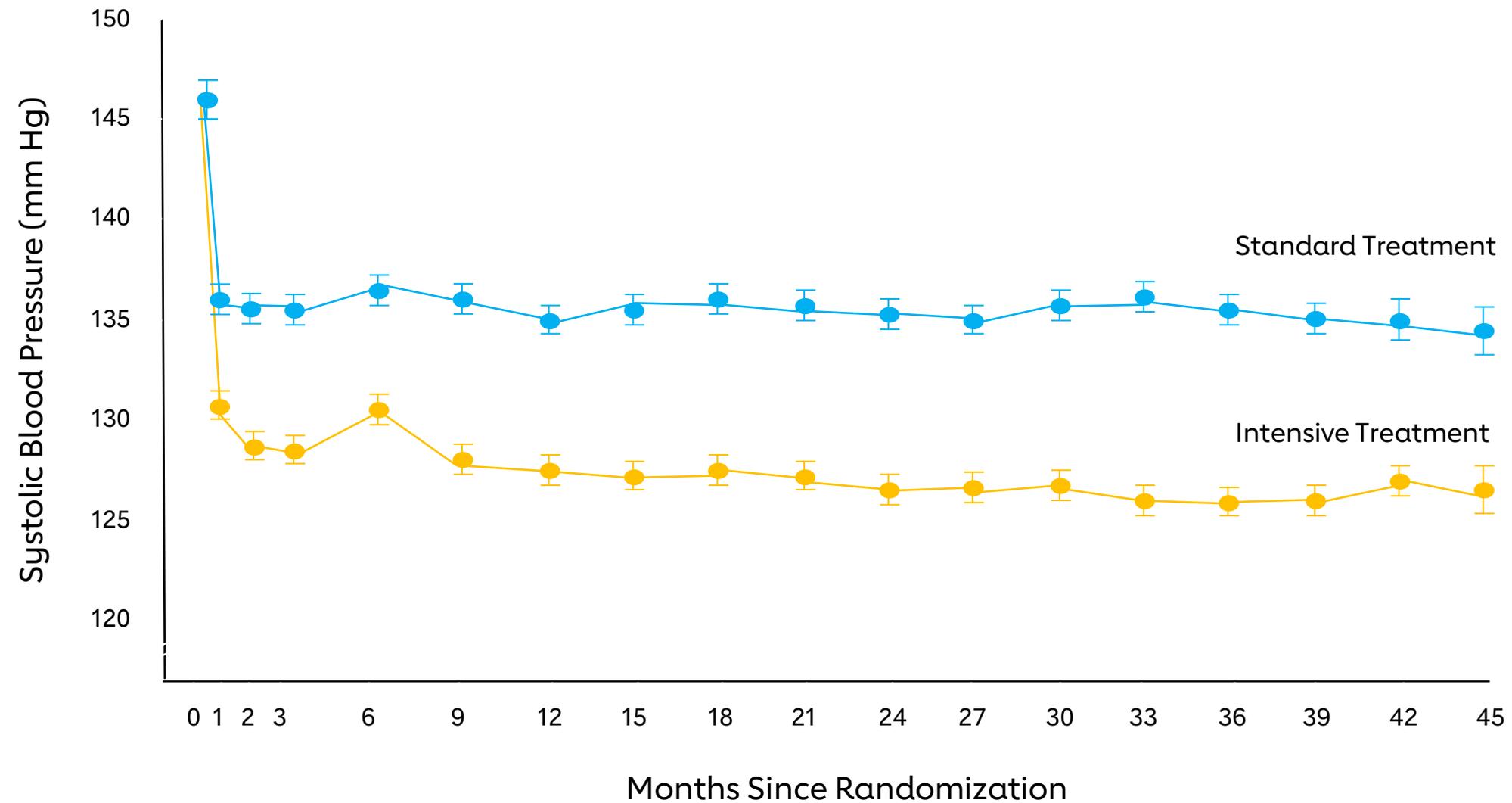
MANAGEMENT OF HYPERTENSION IN OLDER ADULTS

THE STEP STUDY

- Chinese patients (9,624) ages 60-80 with hypertension (including diabetics) randomized to SBP target 110-130 mm Hg (intensive treatment) or 130-150 mm Hg (standard treatment).
- Primary outcome: composite of stroke, acute coronary syndrome, acute decompensated heart failure, coronary revascularization, atrial fibrillation or death from a cardiovascular cause.
- Median follow up 3.34 years

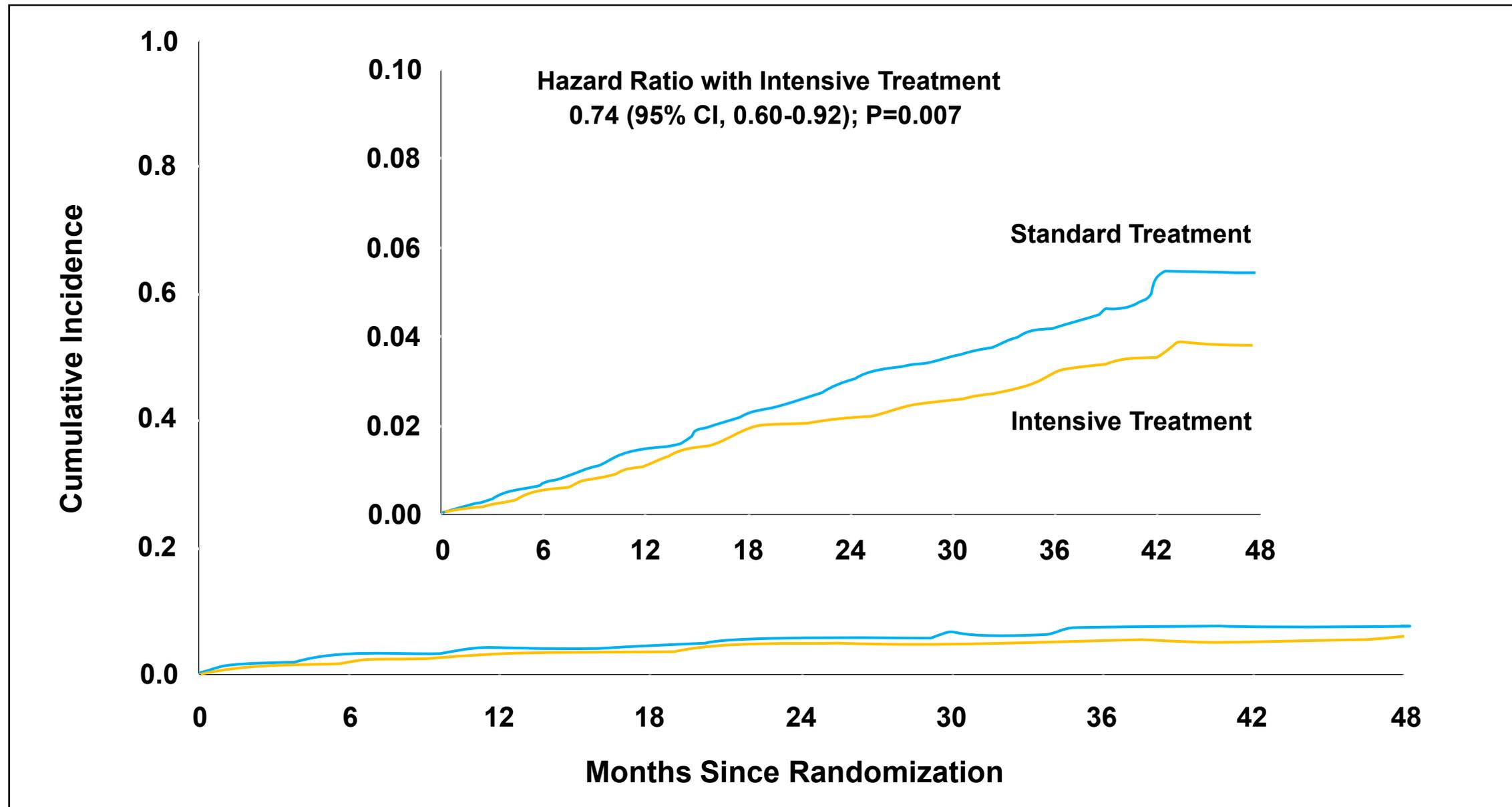
MANAGEMENT OF HYPERTENSION IN OLDER ADULTS

Validation of SBP Goal <130 mm Hg



MANAGEMENT OF HYPERTENSION IN OLDER ADULTS

Validation of SBP Goal <130 mm Hg



MANAGEMENT OF HYPERTENSION IN OLDER ADULTS

- The 2017 ACC/AHA BP Guideline recommends a systolic BP treatment goal of <130 mm Hg for non-institutionalized ambulatory free-living older adults (≥ 65 y of age) and an individualized team-based approach, based on clinical judgement and patient preference, for those with higher burden of comorbidity and limited life expectancy.
- Concerns have been raised that the CVD event and all-cause mortality benefit of intensive BP control may be offset by an increased rate of adverse effects, especially in older adults.
- Several studies in the past 2 years have addressed this question and also have provided evidence for protection from mild cognitive impairment and dementia with SBP <130 mm Hg.

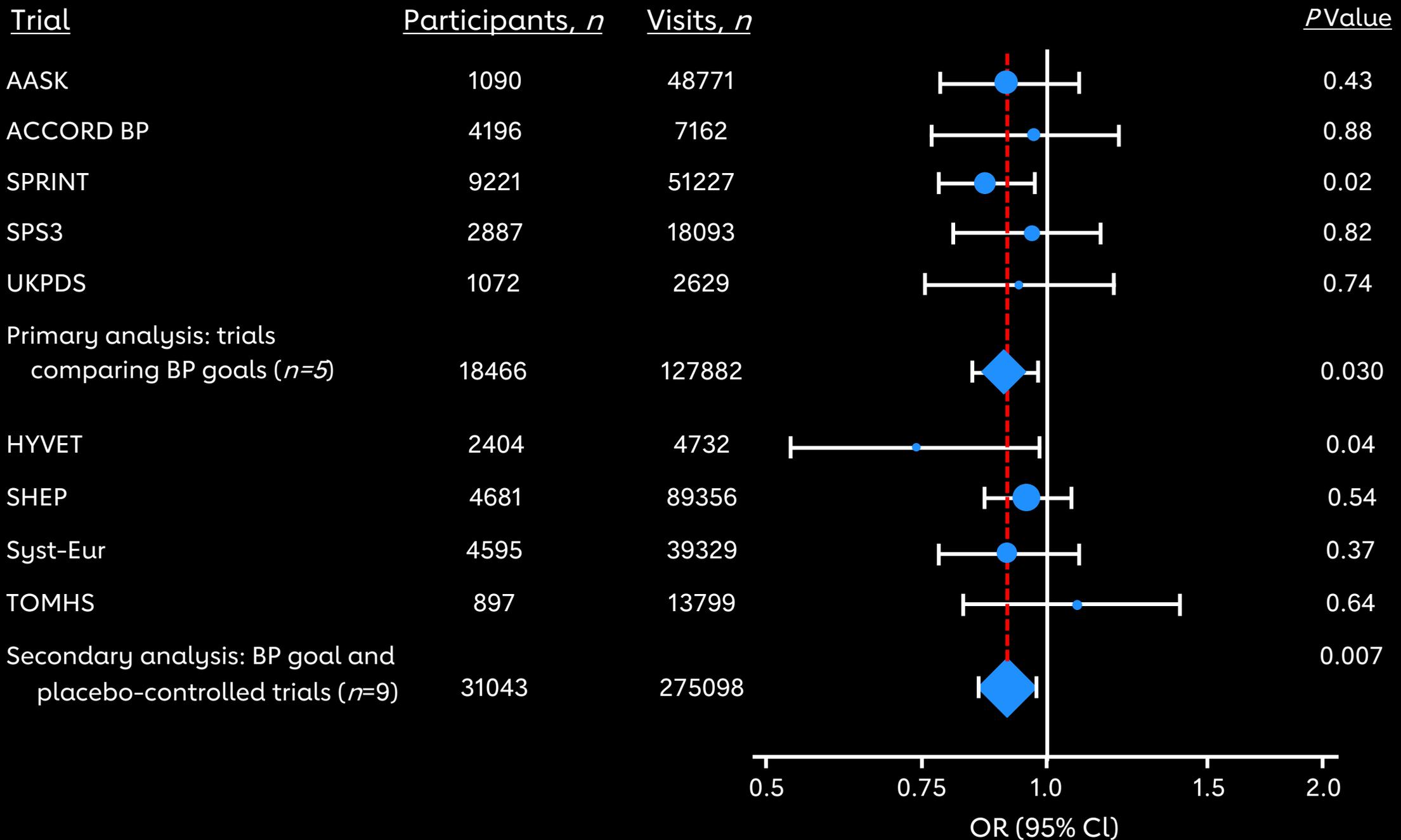
MANAGEMENT OF HYPERTENSION IN OLDER ADULTS

- The concern about SAEs was put to rest by 2 reports by Juraschek *et al.* Examining the SPRINT data and the aggregated individual patient data from multiple clinical trials for association of intensive BP lowering with orthostatic hypotension.
- In SPRINT, orthostatic hypotension was more common in the standard treatment group and was not associated with a higher rate of CVD events or with syncope, electrolyte abnormalities, injurious falls or acute renal failure.
- In the Juraschek *et al.* meta-analysis of 18,466 participants, intensive BP lowering actually reduced the incidence of orthostatic hypotension, possibly due to improved baroreceptor function.
- Thus, asymptomatic orthostatic hypotension during hypertension treatment should not trigger automatic down-titration of therapy, even in the setting of a lower BP goal.



EFFECTS OF BP TREATMENT ON RISK OF ORTHOSTATIC HYPOTENSION

Effects of BP treatment on risk for orthostatic hypotension, by study



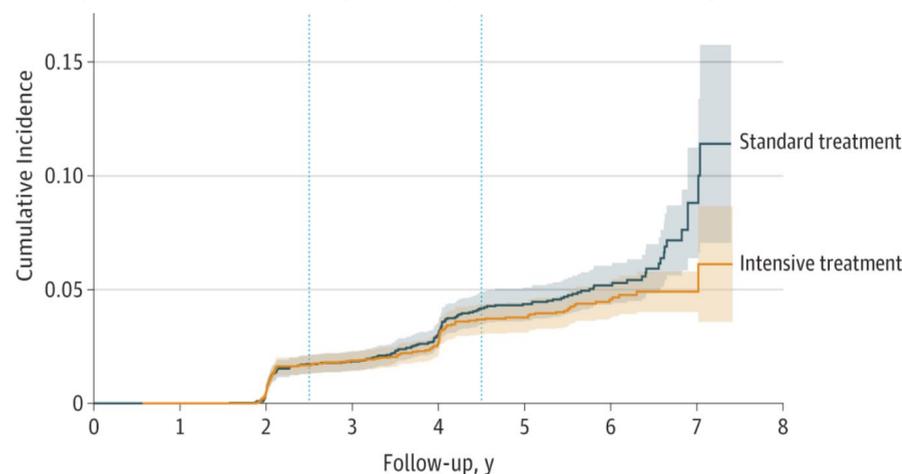
Juraschek SP
et al. Ann Int Med.
2021;174:58-68.



EFFECT OF INTENSIVE (SBP <120 mm Hg) VS STANDARD (SBP <140 mm Hg) BP CONTROL ON DEMENTIA & MILD COGNITIVE IMPAIRMENT

Disorder	Cases per 1000 person-years (Number of events)		Hazard Ratio (95% CI) (Number of events)	P value
	Intensive	Standard		
Dementia	7.2 (149)	8.6 (176)	0.83 (0.67-1.04)	0.10
Mild cognitive impairment (MCI)	14.6 (287)	18.3 (353)	0.81 (0.69-0.95)	0.007
Dementia and MCI	20.2 (402)	24.1 (469)	0.85 (0.74-0.97)	0.01

Probable Dementia by Treatment Group (Trial and post-trial analysis by randomized groups)



No. at risk	0	1	2	3	4	5	6	7	8
Standard treatment	4285	4282	4168	3886	2829	2107	989	87	0
Intensive treatment	4278	4277	4171	3917	2893	2189	1027	93	0

} Separation by treatment arm occurs later than for CVD events

MRI Sub-study (N=454)

Significantly smaller increase in cerebral white matter lesions in the Intensive BP-lowering treatment group compared with the Standard BP-lowering treatment group (p<0.004)

MAJOR TAKE AWAY POINTS

- BP control rates increased steadily until 2013-14 after which they have declined.
- Be careful to avoid NSAIDS patients with high BP, substituting another class of agents to control pain.
- Autonomous aldosterone production almost certainly plays a role in the pathogenesis of Stages 1 and 2 hypertension and resistant hypertension. All adults with hypertension should be screened for primary aldosteronism. If renin is low, consider 24-hour urine aldosterone measurement during salt loading (high sodium diet) conditions.
- Young adults with hypertension have earlier onset of CVD events compared with those with normal BP. Thus, delay of treatment may be inappropriate, even though RCT evidence is lacking. The evidence supports initial management with lifestyle modification for 6-12 months followed by antihypertensive drug therapy if BP remains above goal.
- Lifestyle modification is the cornerstone of antihypertensive therapy. Each nonpharmacological intervention is effective in lowering BP, and concurrent use of 2 or more interventions results in additive effects. Lifestyle modification improves the effectiveness of pharmacologic therapy.

MAJOR TAKE AWAY POINTS

- The relationship of dietary NaCl to BP is positive and almost linear. Decreases in BP can be expected with decrease in dietary NaCl down to 1-1.5 g/d. Salt substitutes are effective in lowering BP and improving outcomes.
- Intensive BP control is not associated with increased hospitalization and does not increase the risk of orthostatic hypotension. Asymptomatic orthostatic hypotension in hypertensive adults is not associated with higher rates of CVD events, syncope, injurious falls or acute renal failure and should not be a reason to withdraw or down-titrate treatment.
- For older adults with hypertension, intensive treatment with an SBP target 110-130 mmHg substantially lowers the incidence of CVD events over standard treatment with a target 130-150 mm Hg. In addition, intensive BP lowering may prevent or at least partially arrest cognitive decline with aging.
- Home BP self-monitoring and telemonitoring are effective in facilitating antihypertensive drug titration leading to achievement and maintenance of BP goal.