

Hypertension Update

ACOI 2018

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Disclosures

Nothing to declare

Hypertension - Introduction

US population incidence – 30% and growing due to an aging and increasingly obese population

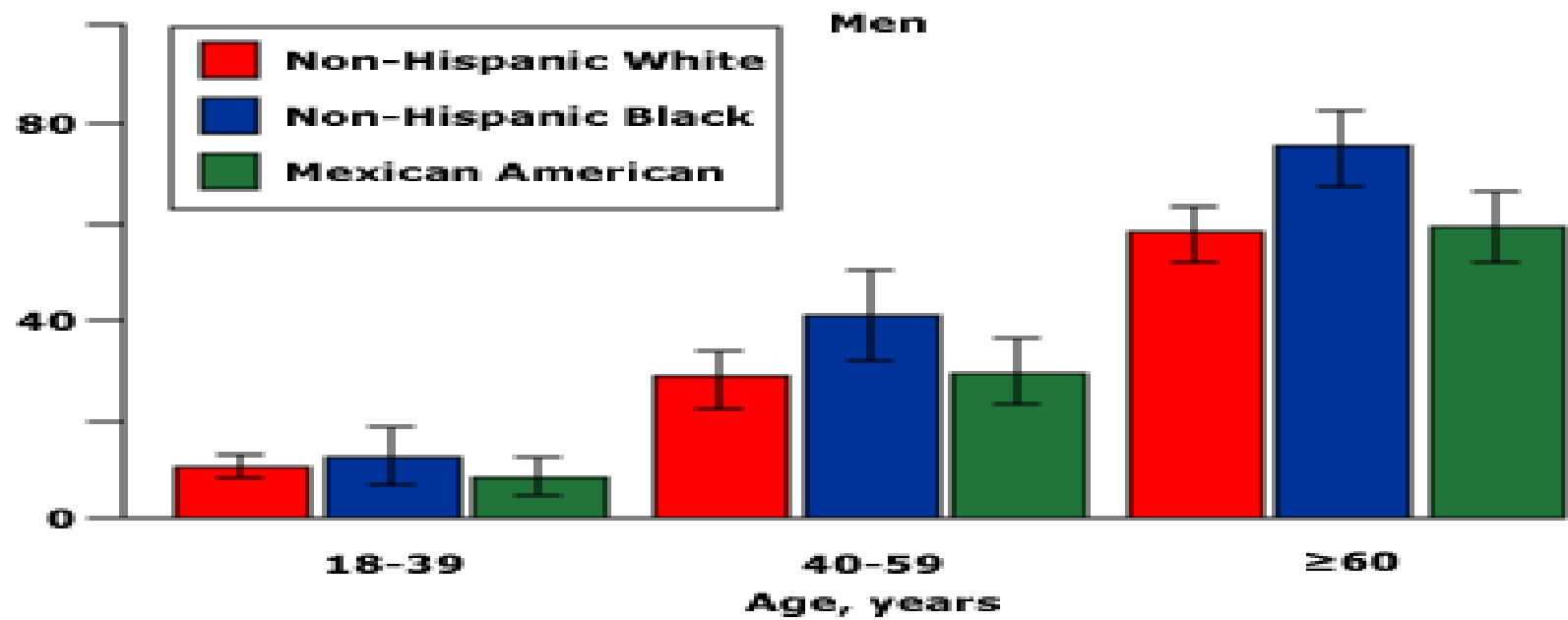
Poorly controlled

Most common risk for CVD

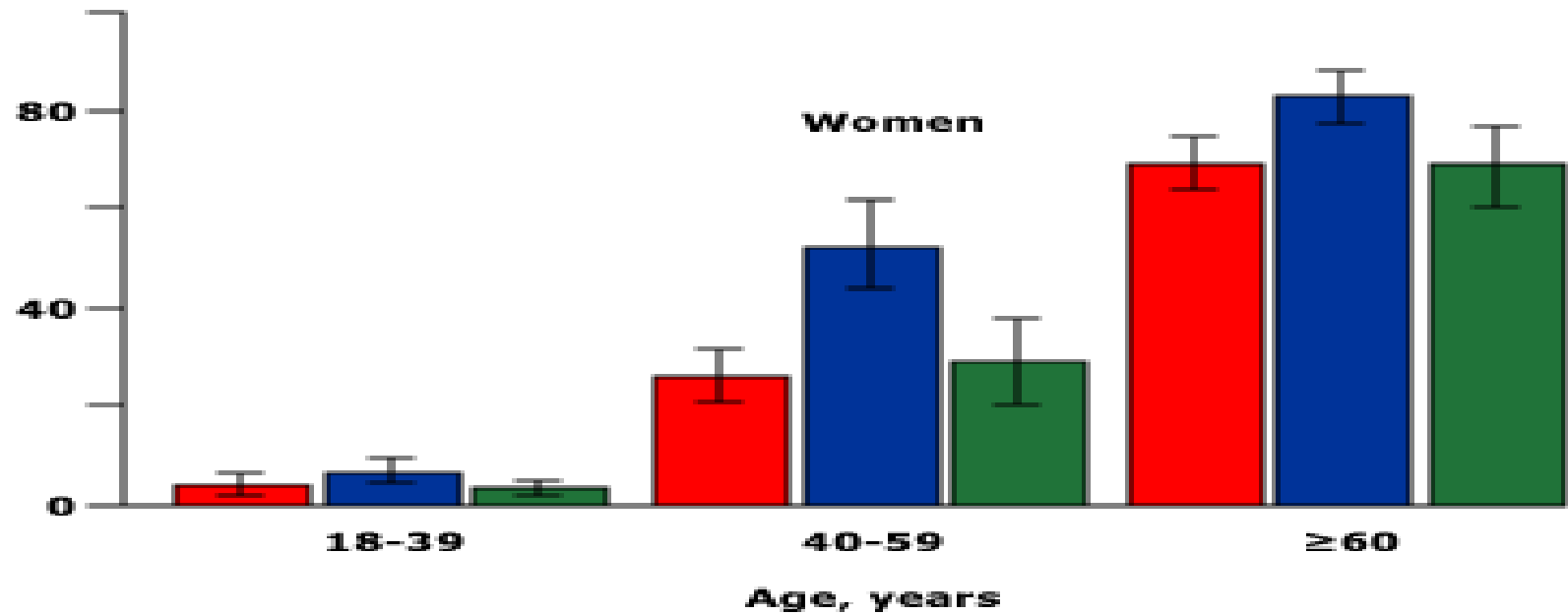
Global Burden of Disease Study 2010 – HTN is the leading risk factor for death and DALY

Despite poor control, treatment of HTN has positively influenced stroke, CVD and CHF

Hypertension prevalence, percent



Hypertension prevalence, percent



HTN - Definitions

Primary HTN – BP > 140/90 without secondary cause (Stg 1 140-159/90-99; Stg 2 > 160/100 (benign if criteria for malignant HTN not met)

White Coat HTN – BP > 140/90 in office and home BP < 135/85 at home

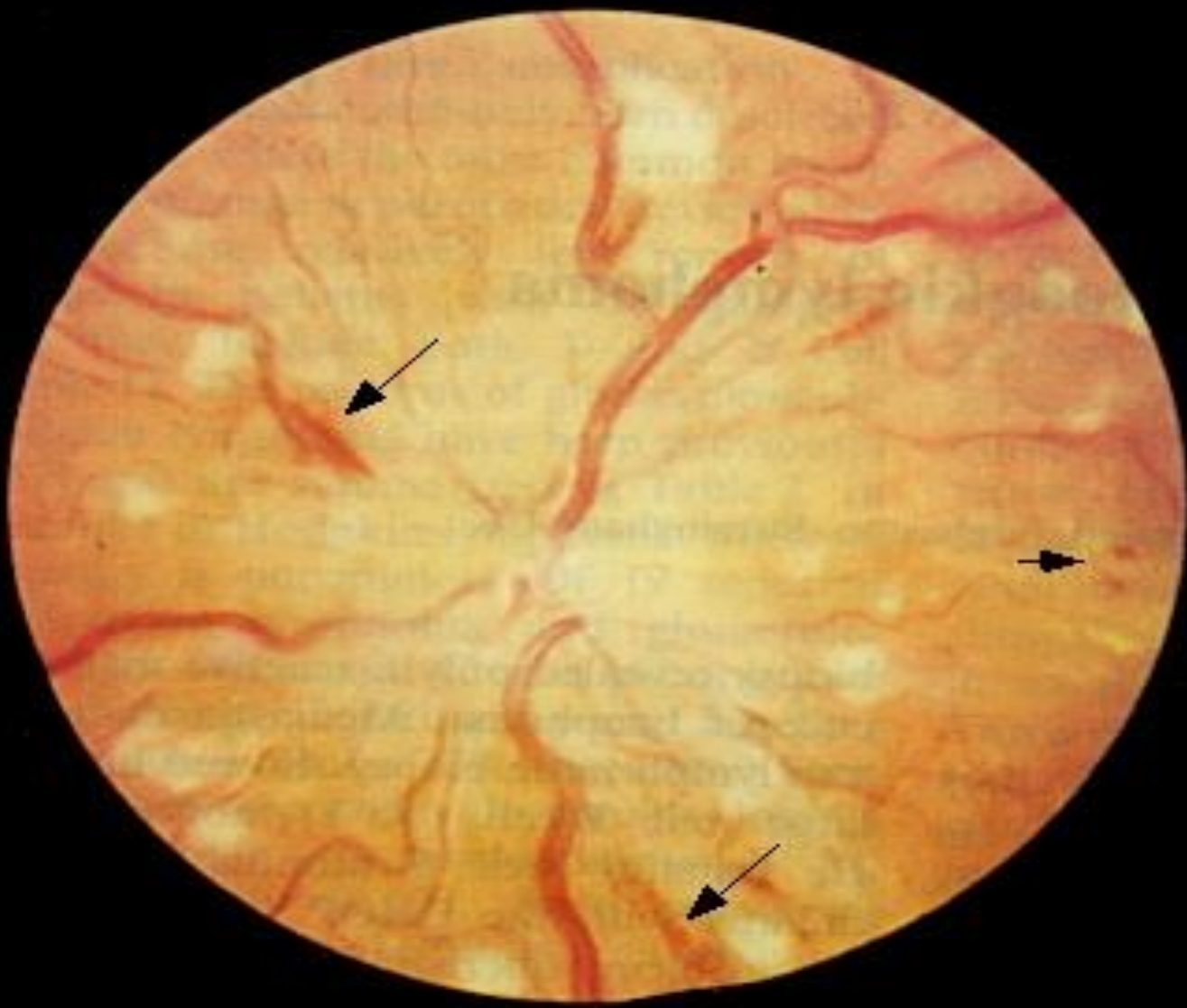
Masked HTN – BP normal in office but > 140/90 at home (end organ damage)

HTN - Definitions

Secondary HTN – HTN with secondary cause such as renovascular HTN, ETOH etc

Malignant/Accelerated HTN – HTN associated with grade 3 or 4 hypertensive retinopathy with a thrombotic microangiopathy leading to acute tissue injury (brain, kidney, heart)

Resistant HTN - BP above goal (> 160/) despite 3 or more medications (including a diuretic)



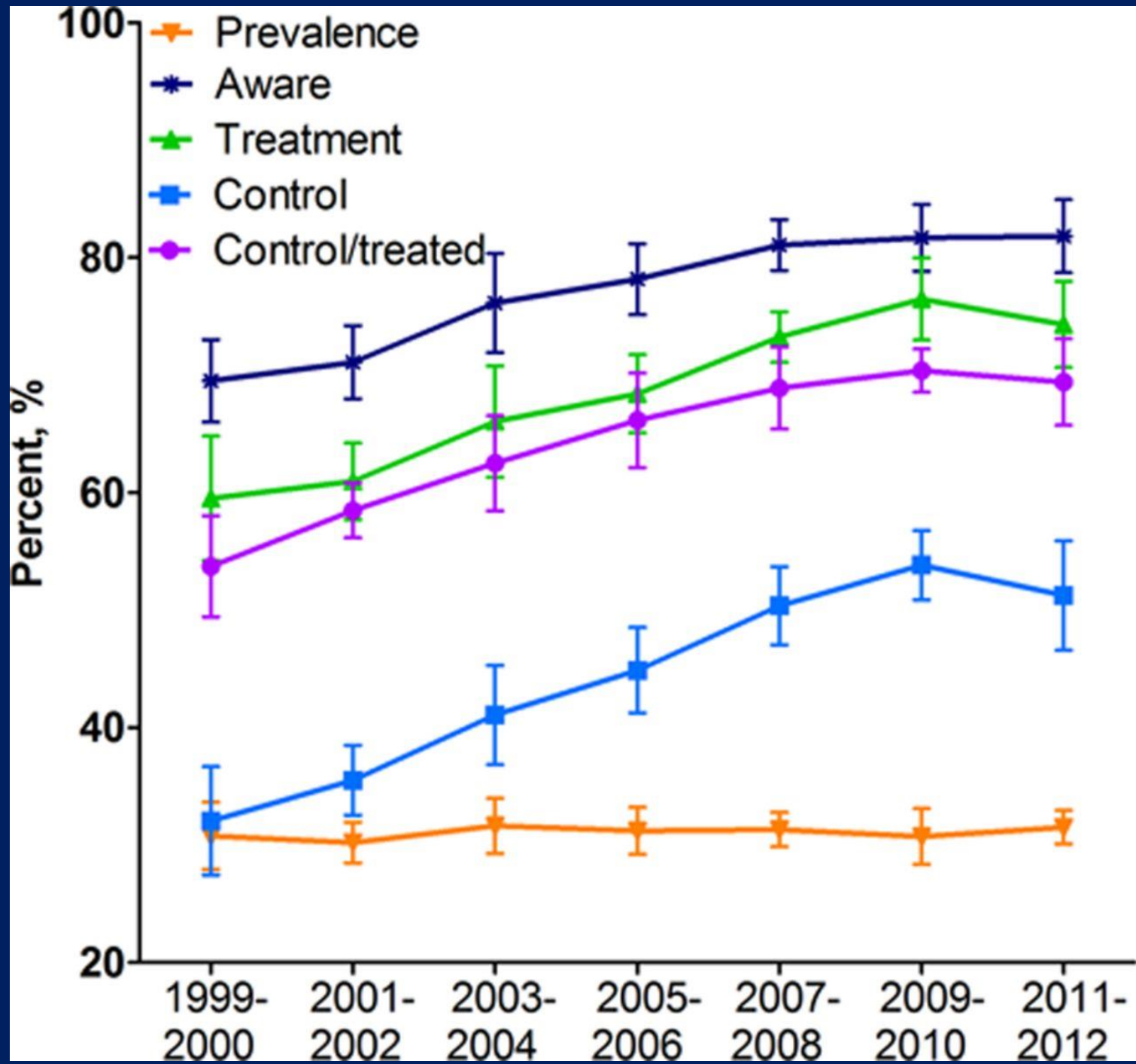
HTN - Definitions

HTN Emergencies – HTN and acute end organ disease (malignant HTN etc)

HTN Urgencies – asymptomatic elevation of BP > 180/

Non Dipper – loss of normal BP decrease during sleep (predicts CV disease)

Gestational HTN – BP > 140/90 that occurs after the 20th week (chronic HTN occurs before and lacks proteinuria) (preeclampsia has proteinuria)



Benefits of Lowering BP

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

HTN Evaluation

History and physical along with directed lab evaluation serve to screen for secondary HTN, assess end organ damage as well as assess CV risk. These serve to determine further workup and to tailor therapy types and goals.

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 albumin to creatinine ratio

*May be included in a comprehensive metabolic panel.
eGFR indicates estimated glomerular filtration rate.

Assess interarm difference when at first assessment of hypertension

Clark's meta-analysis included a number of published studies in hypertensive patients or subgroups of hypertensive patients, in which BPs were taken from both arms, plus some unpublished data from his own group.

Differences in mortality between those with large differences in interarm SBP readings

Outcome	HR, ≥ 10 -mm-Hg difference in SBP between arms ^a	Total subjects/deaths, n	p ^a	HR, ≥ 15 -mm-Hg difference in SBP between arms ^b	Total subjects/deaths, n	p ^b
All-cause mortality	1.60	1990/420	0.01	1.60	2231/456	0.008
Cardiovascular mortality	2.15	1516/151	0.007	1.34	2178/201	0.24

Ambulatory BP Monitoring

ABPM is warranted for evaluation of “white-coat” HTN in the absence of target organ injury. Also dx of masked HTN

Ambulatory BP values are usually lower than clinic readings.

Awake, individuals with hypertension have an average BP of $>135/85$ mmHg and during sleep $>120/75$ mmHg.

BP drops by 10 to 20% during the night; if not, signals possible increased risk for cardiovascular events. Non dipper

BP highest 6-8 AM and 5-7 PM

Self-Measurement of BP

Provides information on:

- Response to antihypertensive therapy

- Improving adherence with therapy

- Evaluating white-coat HTN

- BP variability

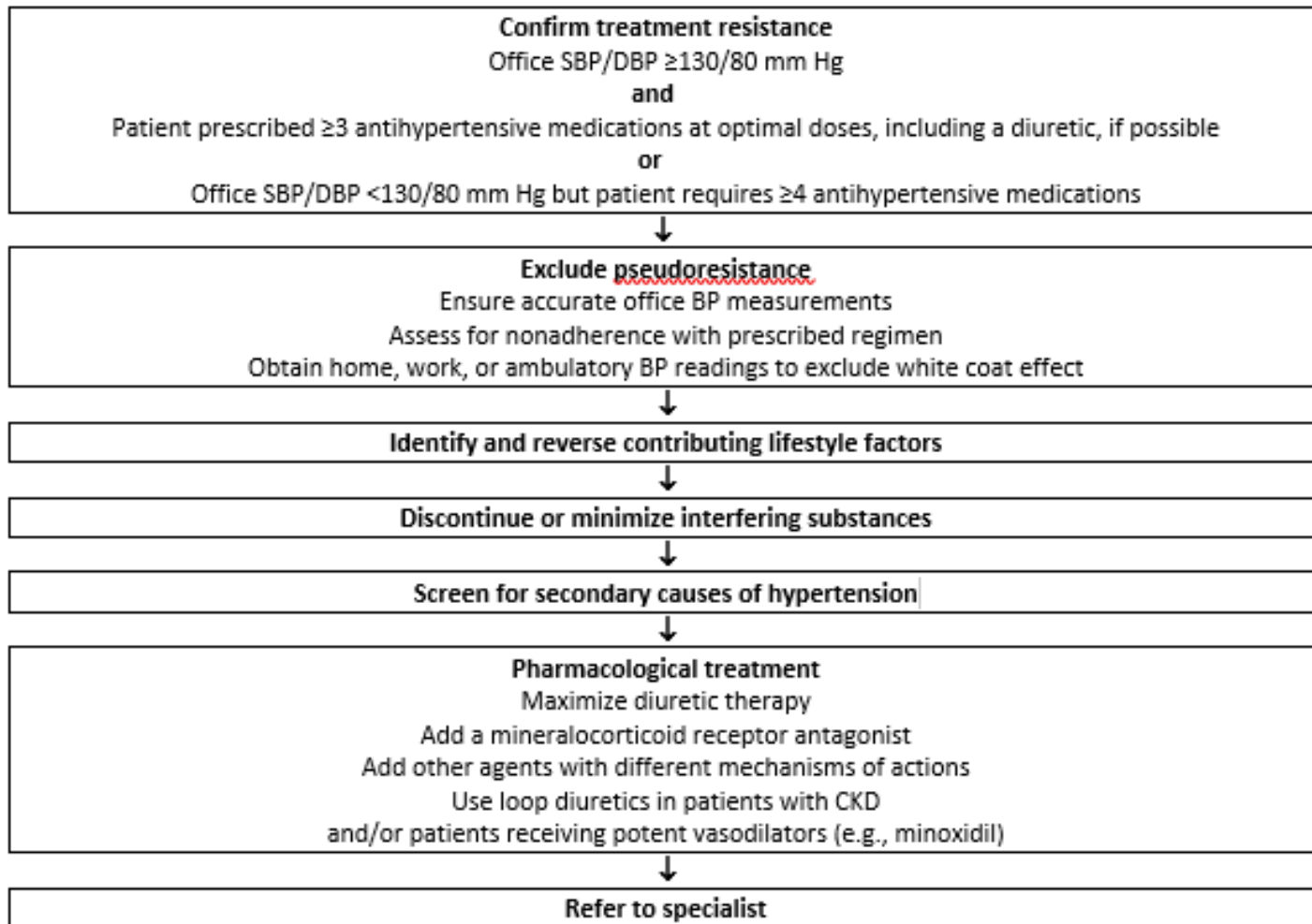
Home measurement of $>135/85$ mmHg is generally considered to be hypertensive.

Home measurement devices should be checked regularly.

PREDICTS CV OUTCOMES BETTER THAN OFFICE BP

Resistant Hypertension: Diagnosis, Evaluation, and Treatment

Figure 10. Resistant Hypertension: Diagnosis, Evaluation, and Treatment



Causes of Resistant Hypertension

Improper BP measurement

Excess sodium intake

Inadequate diuretic therapy

Medication

- Inadequate doses or timing

- Drug actions and interactions (e.g., NSAIDs, illicit drugs, sympathomimetics, oral contraceptives)

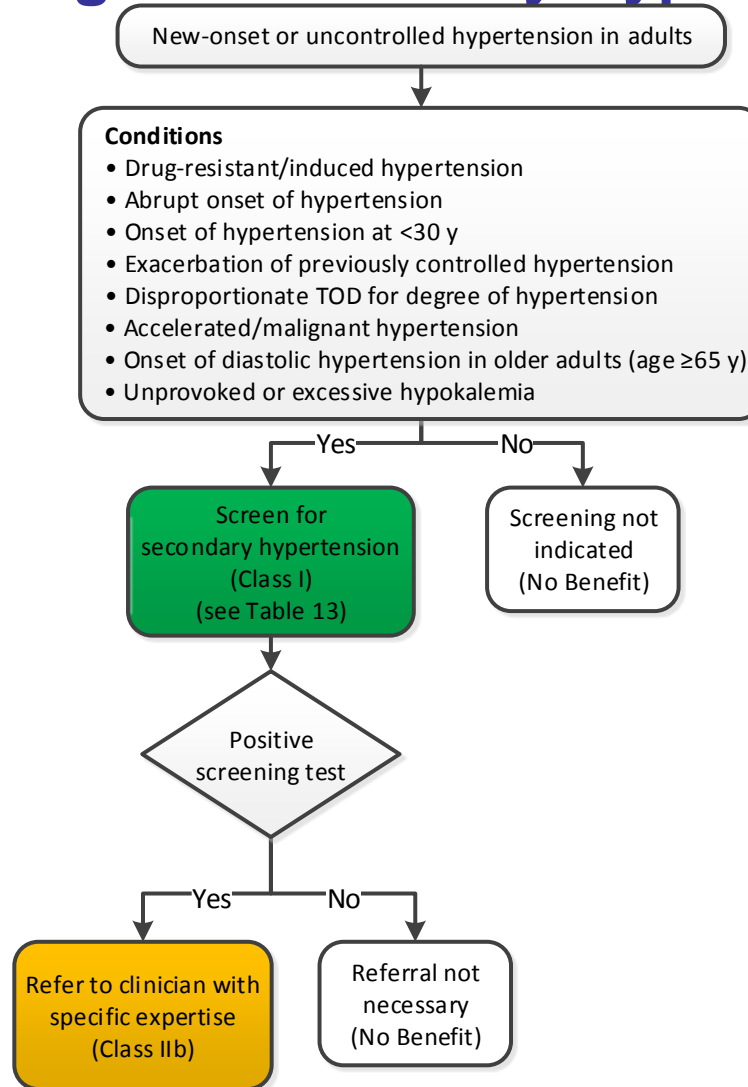
- Over-the-counter (OTC) drugs and herbal supplements

Excess alcohol intake - > 14/wk men, > 7/wk women

Identifiable causes of HTN – sleep apnea, RAS, primary aldosteronism etc

Secondary HTN

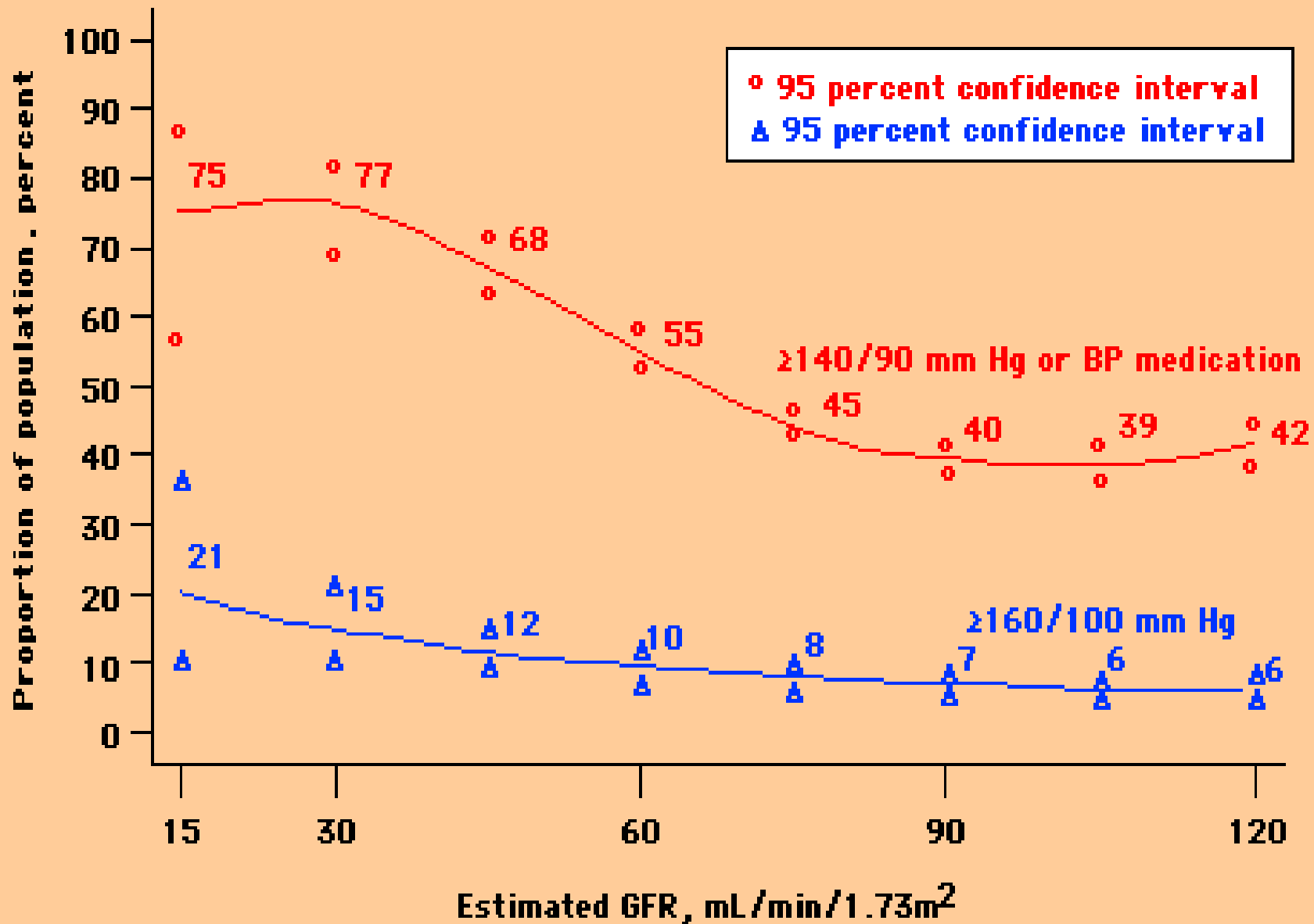
Screening for Secondary Hypertension



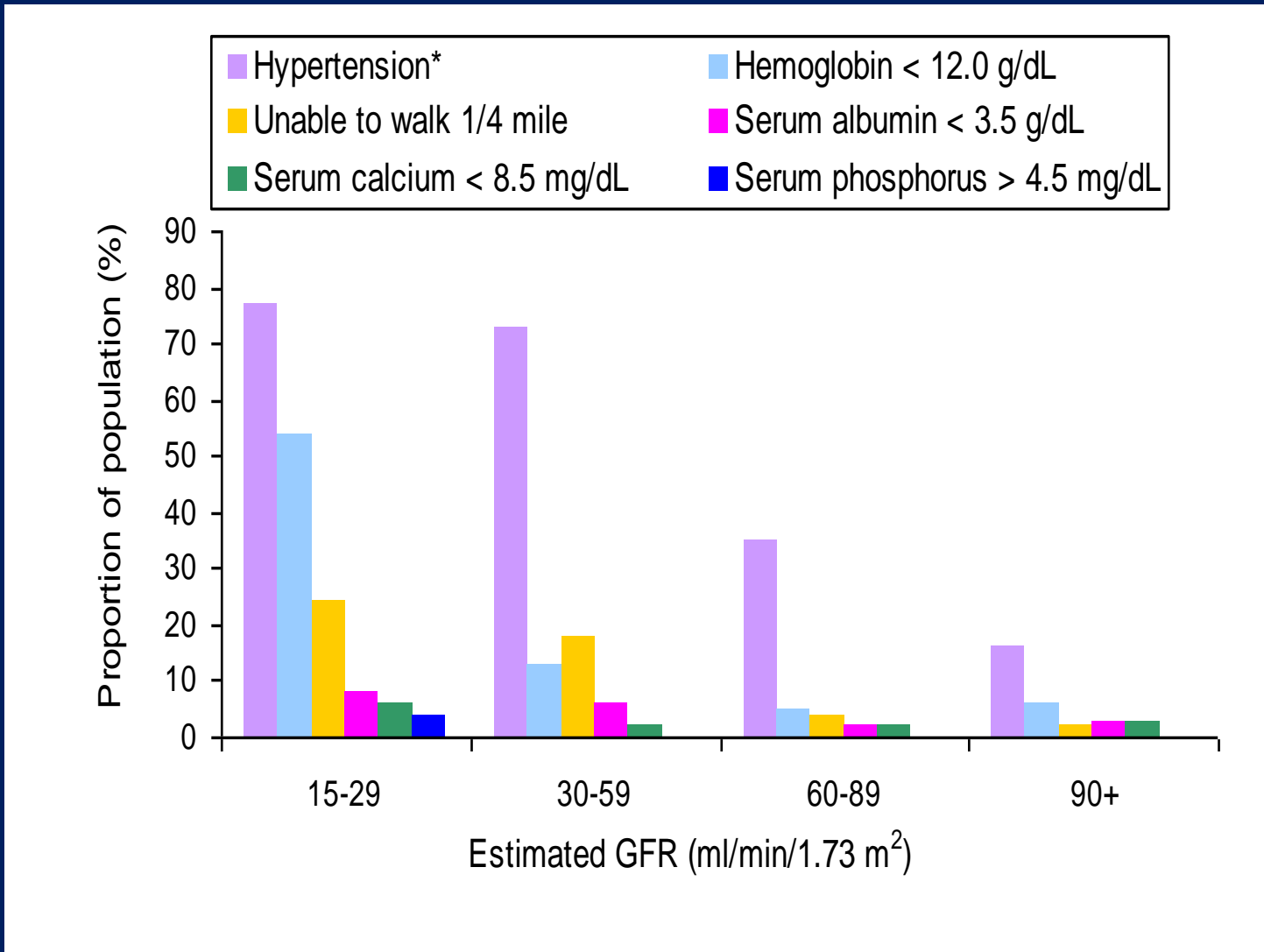
Colors correspond to Class of Recommendation in Table 1 .

TOD indicates target organ damage (e.g., cerebrovascular disease, hypertensive retinopathy, left ventricular hypertrophy, left ventricular dysfunction, heart failure, coronary artery disease, chronic kidney disease, albuminuria, peripheral artery disease).

CKD and HTN



Prevalence of Abnormalities at each level of GFR



*>140/90 or antihypertensive medication

p-trend < 0.001 for each abnormality

Pathogenesis HTN – CKD

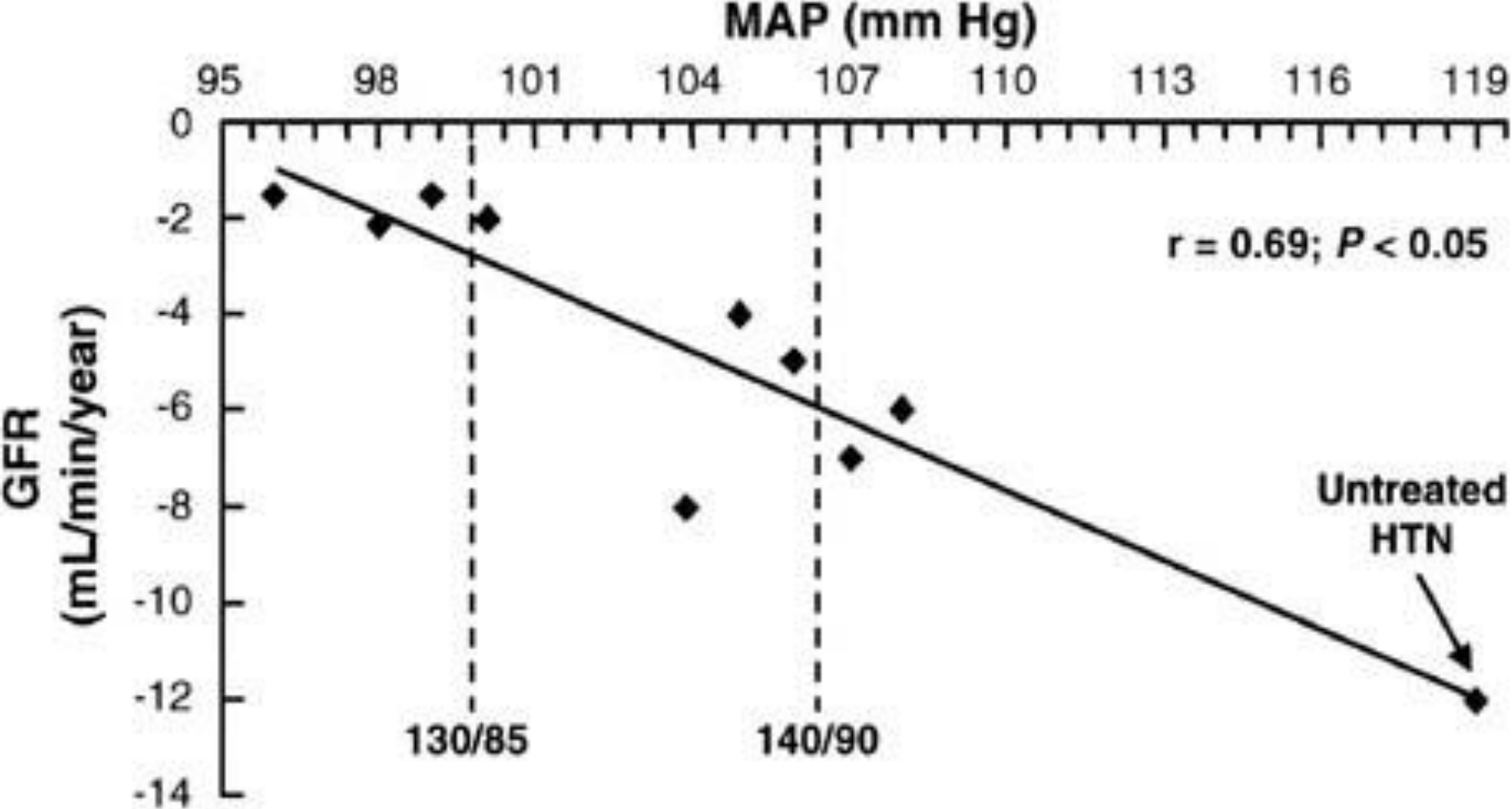
Na Sensitive HTN

Volume-dependent HTN is the most common type of HTN seen in CKD

Incidence inversely proportional to GFR

Defined as low or normal renin and response to dietary Na restriction

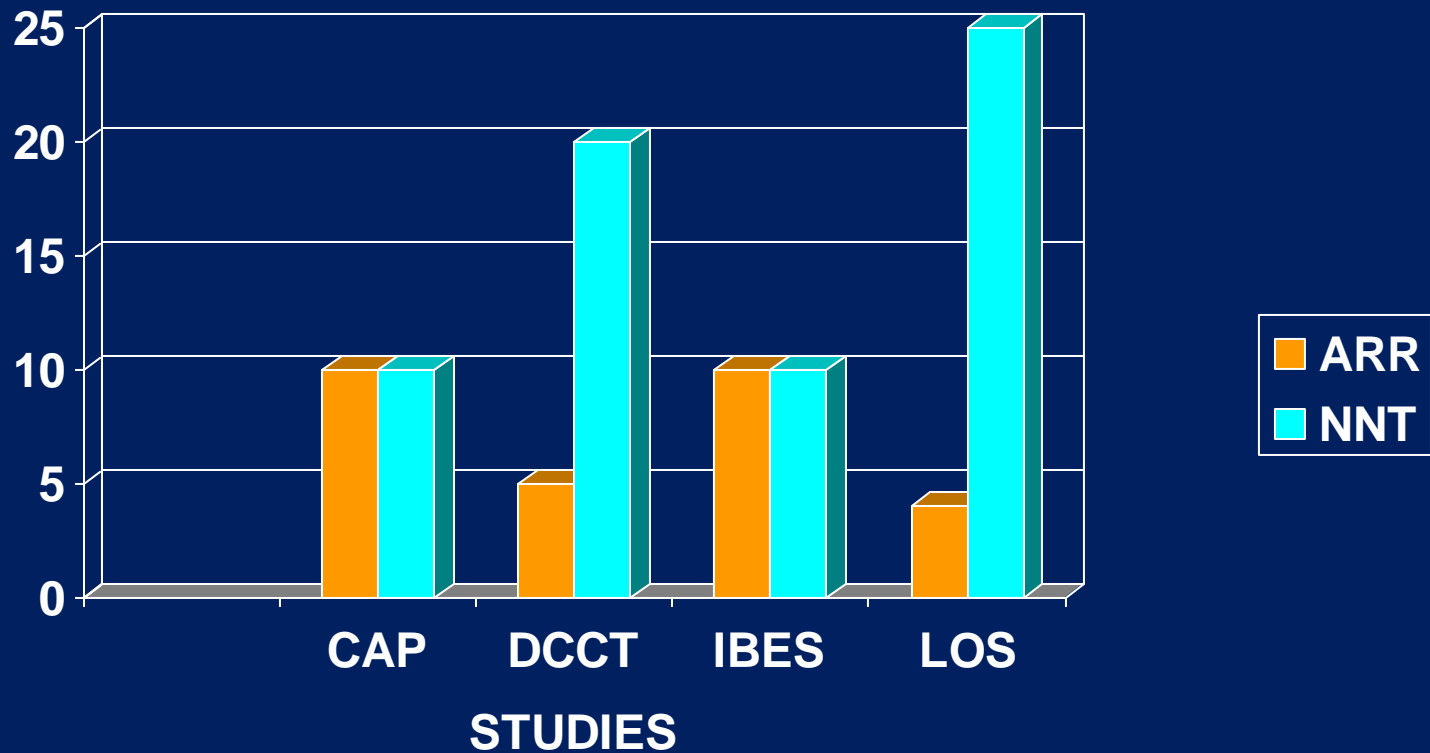
Always consider volume overload as a cause of poor HTN control (GFR < 30 and proteinuria)

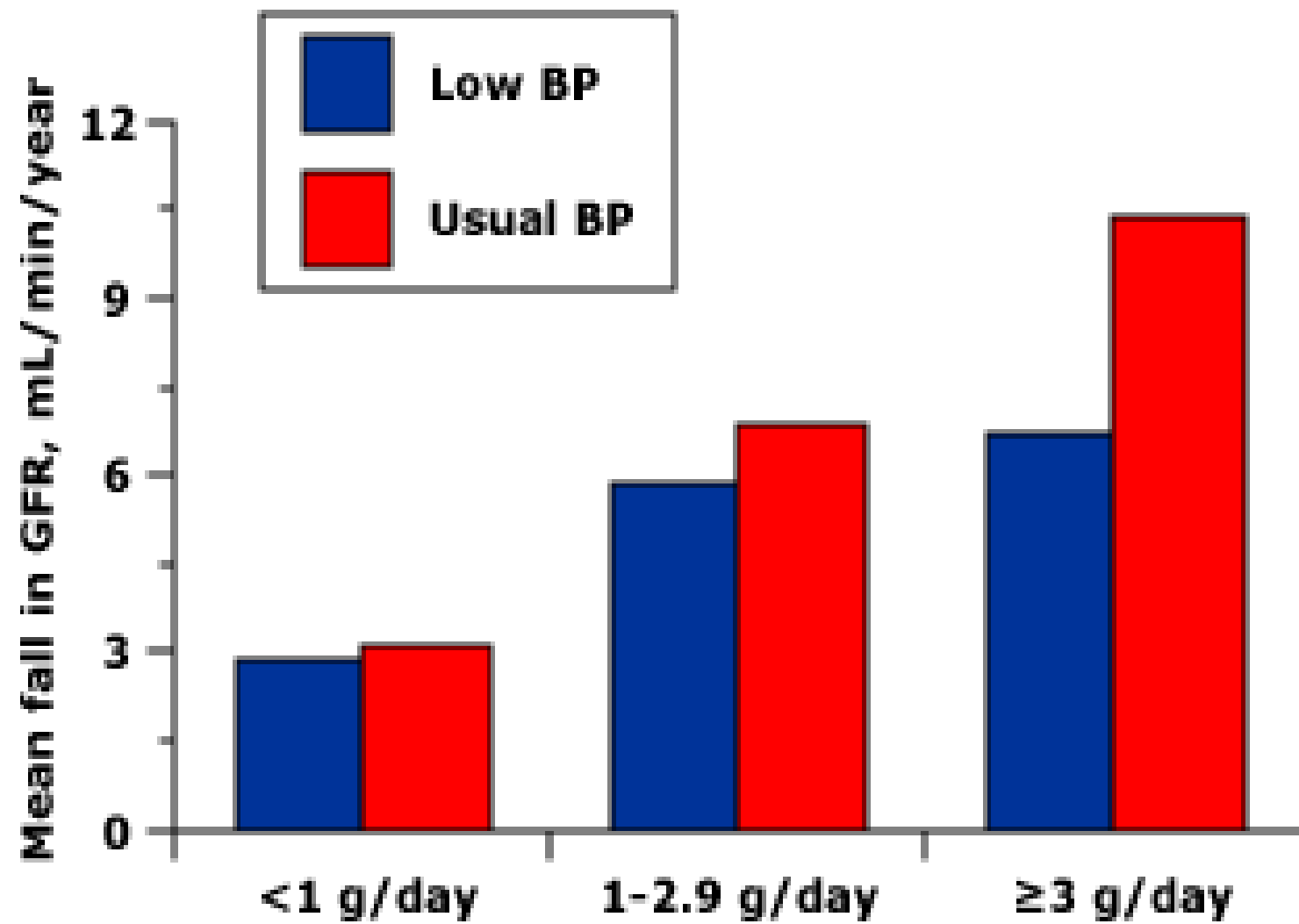


Summary of studies on nephropathy progression used in figure

- Parving HH et al. *Br Med J*, 1989
- Moschio G et al. *N Engl J Med*, 1996*
- Viberti GC et al. *JAMA*, 1993
- Bakris GL et al. *Kidney Int*, 1996
- Klor S et al. *N Eng J Med*, 1993*
- Bakris GL. *Hypertension*, 1997
- Hebert L et al. *Kidney Int*, 1994
- GISEN Group, *Lancet*, 1997*
- Lebovitz H et al. *Kidney Int*, 1994

Summary of ACE or ARBs in Diabetic CKD





Summary of ACEI/ARB in Stage 3-5 CKD – Non Diabetic

EFFICACY – proteinuric best

Stage 3 – ARR 8-10%; NNT 10-11 for ACE or ARB (ARR 20%) (ARR 20%: NNT 5 if U P/C > 3)

Stage 4 – ARR 20%; NNT 5 for ACE

Stage 5D – ACE will preserve residual function even when on PD

The worse the kidney function, the worse the proteinuria - the better the response

ACE and ARBs should be continued at all stages of CKD
A trial of ACE and/or ARBs should be considered for proteinuric patients regardless of the stage of CKD

Stopping ACE in nonproteinuric CKD may delay RRT

Initiation and Dose Escalation

Summary of Recommended Intervals to Monitor for Side Effects after Initiation or Change in Dose of ACE Inhibitor or ARB Therapy According to Baseline Values

Baseline Value	SBP (mm Hg)	$\geq 120^*$	110-119	< 110
	Baseline GFR (mL/min/1.73 m ²)	≥ 60	30-59	< 30
	Early GFR Decline (%)	< 15	15-30	> 30
	Serum Potassium (mEq/L)	≤ 4.5	4.6-5.0	> 5.0
Interval (Weeks)		4-12	2-4	≤ 2

Renovascular HTN

Clinical Clues Suggesting Renovascular Hypertension

- Onset of hypertension under age 25 or over age 55
- An abdominal bruit, particularly in diastole
- Refractory, accelerated, or malignant hypertension or worsening of previously controlled hypertension
- Undiagnosed renal failure, with or without hypertension (particularly with normal urine sediment)
- Acute renal failure precipitated by hypertension treatment, particularly with ACE inhibitors
- A unilateral small kidney (by any prior investigational procedure)
- "Flash" pulmonary edema

Sensitivity and Specificity of Tests for Renovascular Hypertension

Test	Sensitivity (%)	Specificity (%)
Doppler flow ultrasonography	80	80
Magnetic resonance angiography	90	90
CT Angio	90	90

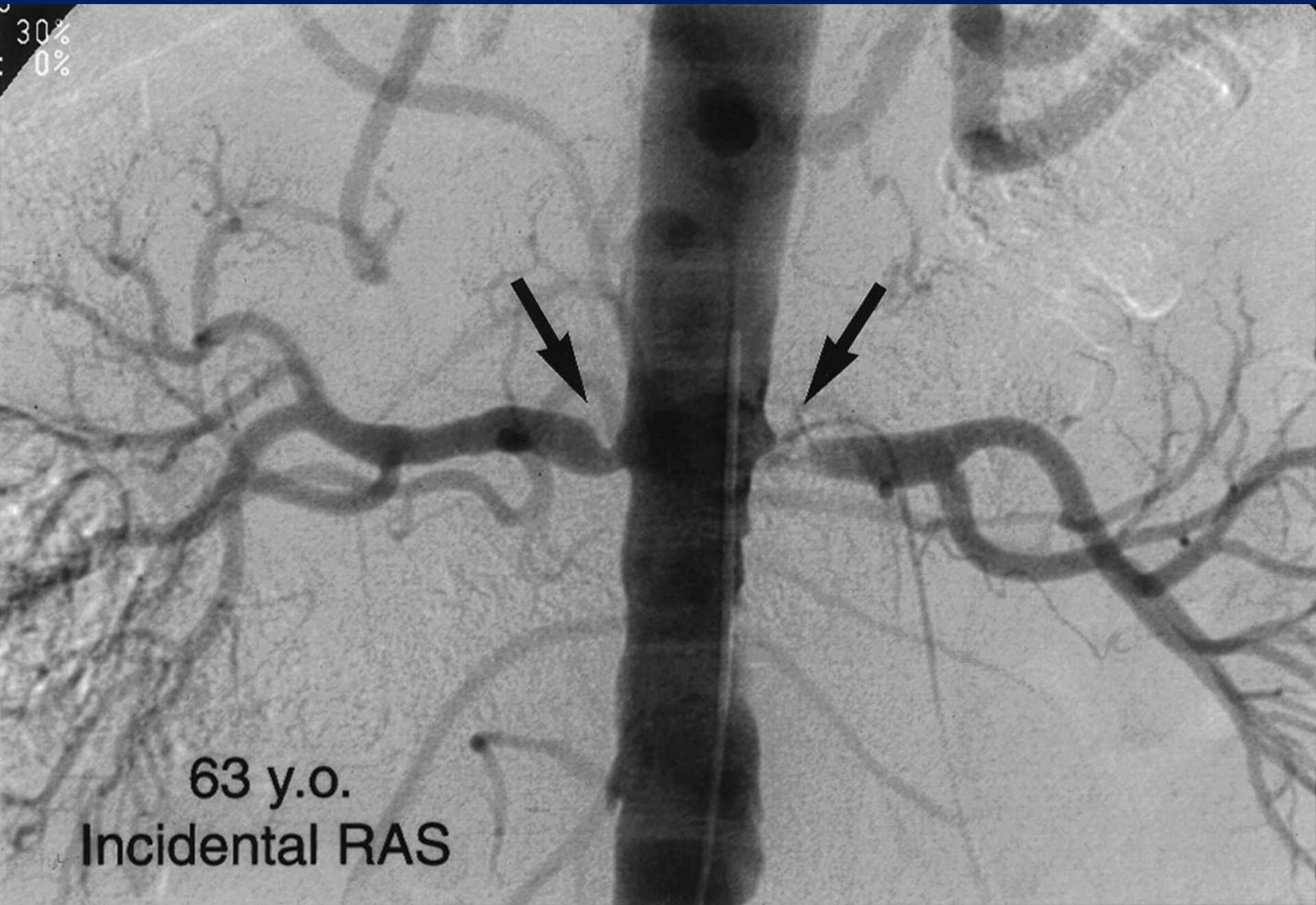
Anatomic Diagnosis not functional diagnosis

Renovascular Disease

Angiography, with or without digital subtraction, is the “gold standard” for diagnosis for renovascular disease

Drive by angio

30%
0%



63 y.o.
Incidental RAS

Renovascular HTN

Outcomes

Patency Rate at 12 months > 80%

Progression of CKD – medical = intervention

HTN Control – intervention = medication

Controversy – patient selection is key and we don't have enough data to make recommendations

Recurrent flash pulm edema, refractory HTN and med intolerance

(7660 1996 to 35000 2005)

Cardiology vs. Nephrology

CORAL TRIAL

CORAL Trial - Results

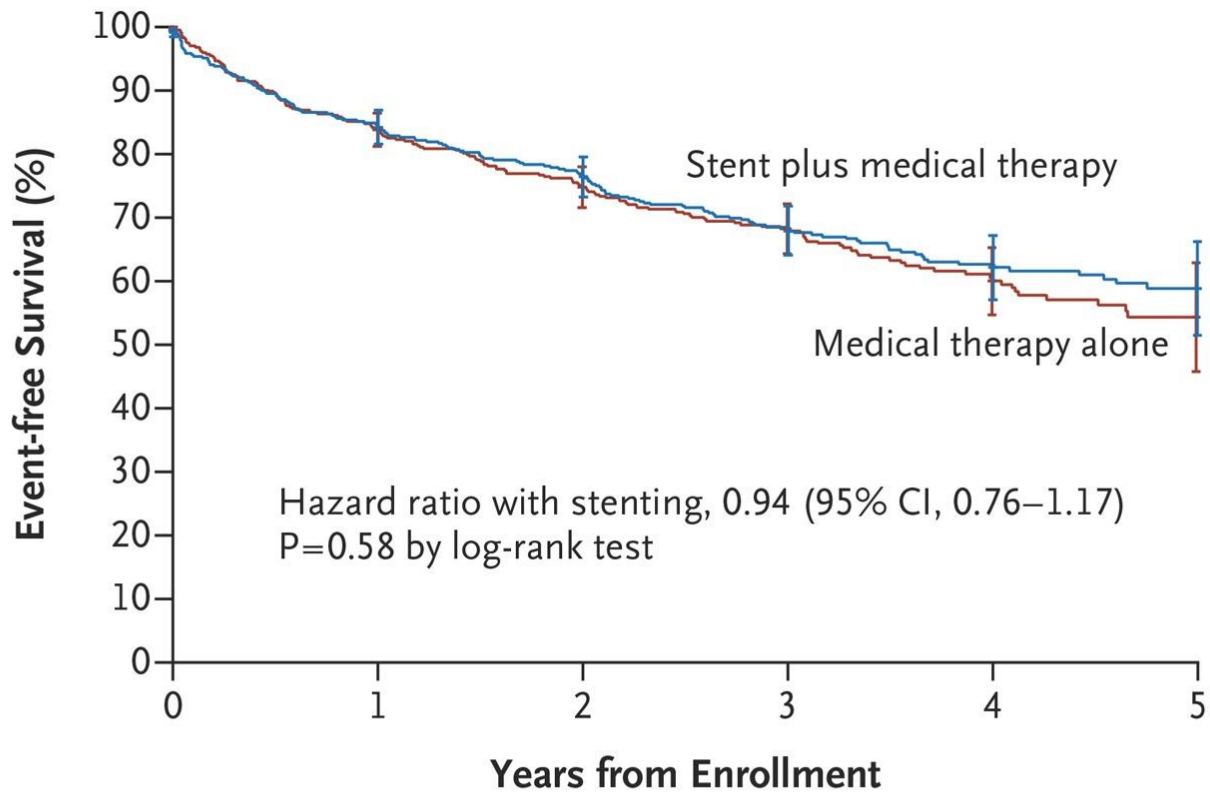
BP goal met with medical treatment:

No DM or CKD – 93%

DM or CKD – 80%

2 year follow up

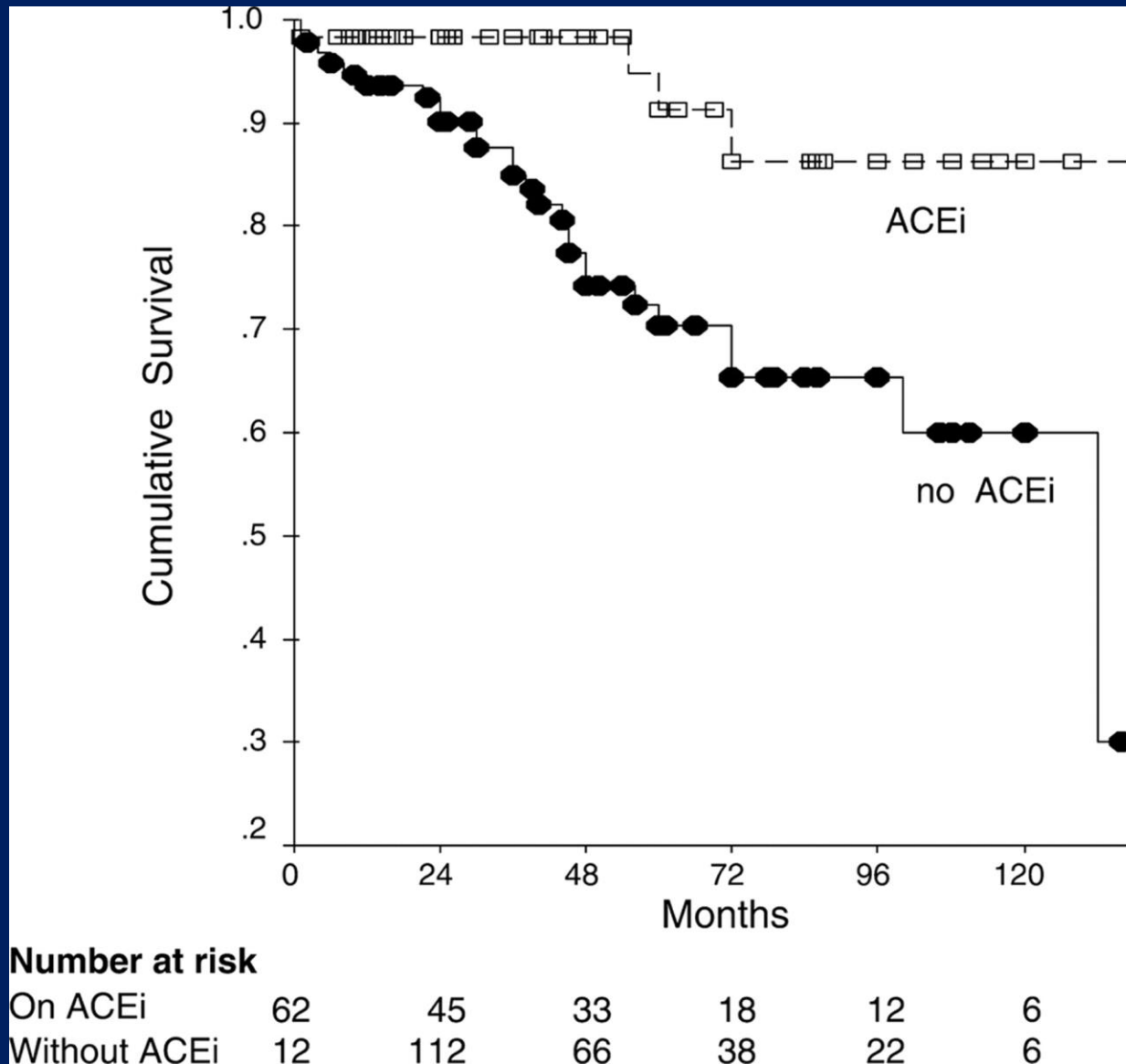
CORAL Kaplan–Meier Curves for the Primary Outcome.



No. at Risk

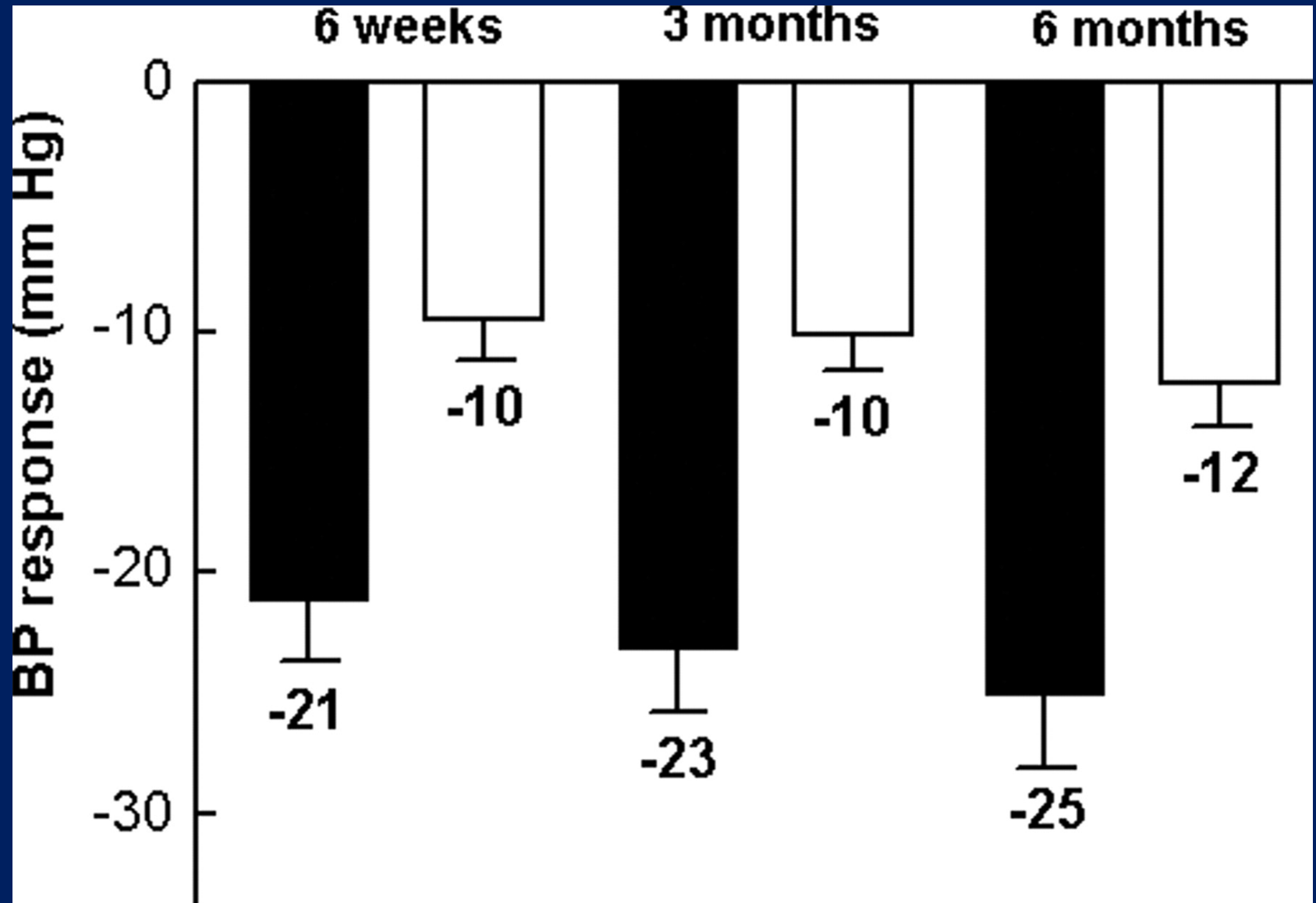
Medical therapy alone	472	371	314	214	115	40
Stent plus medical therapy	459	362	318	224	131	59

Prospective observational cohort study comparing RAS patients treated (n=62) or not treated (n=133) with ACEs inhibitors (mean follow-up: 4.5 years)

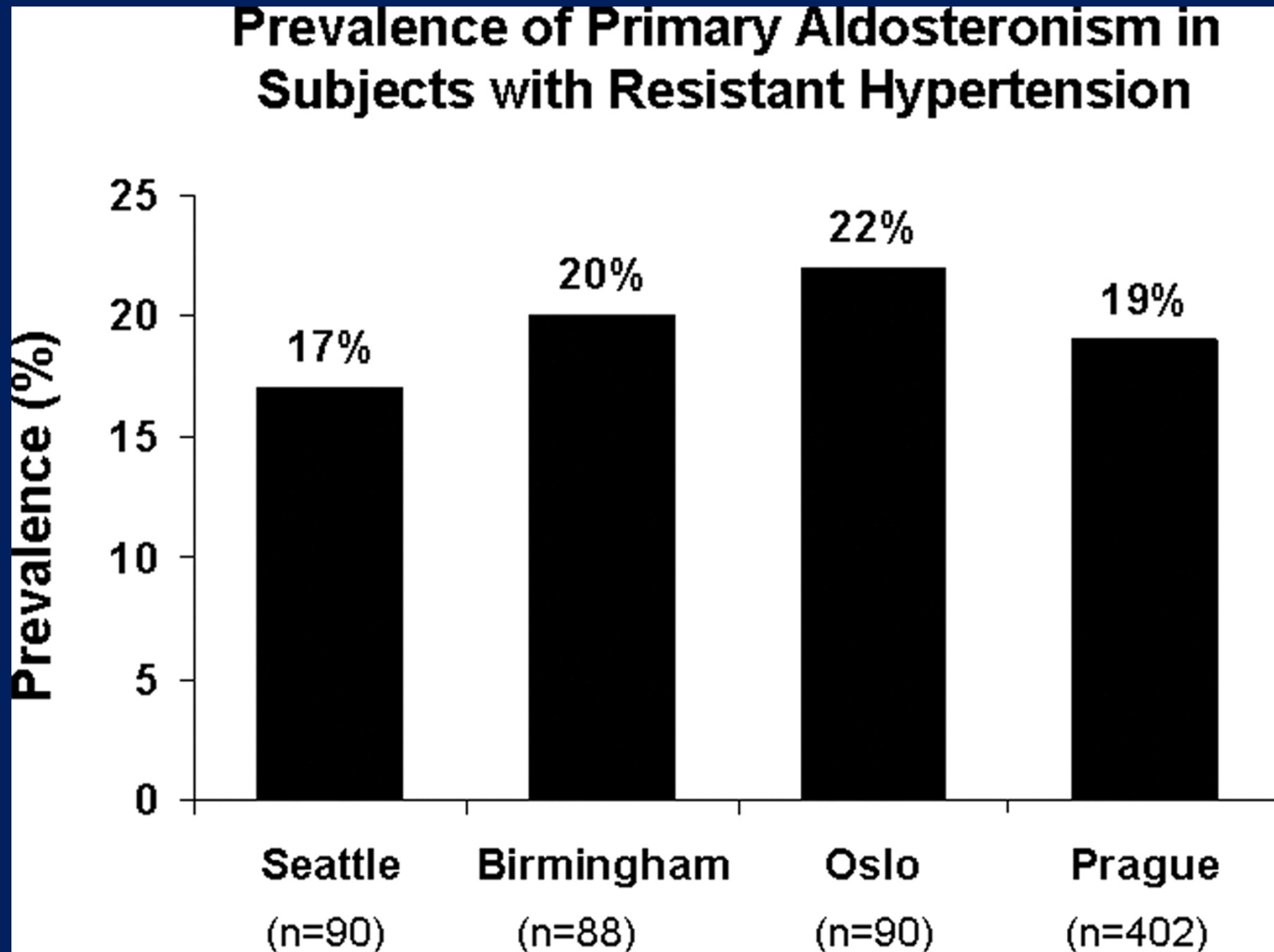


Primary Aldosteronism

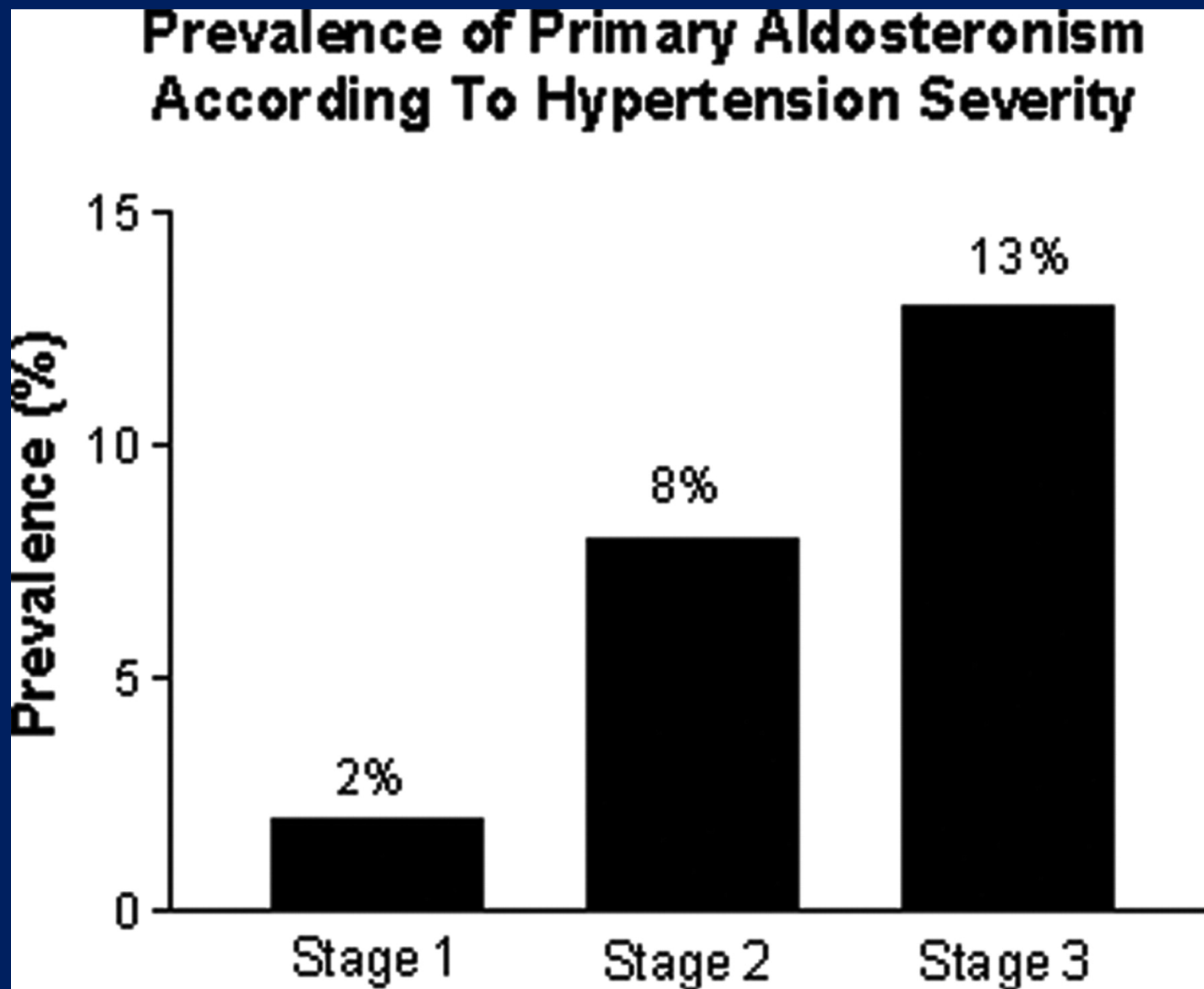
Spironolactone-induced reduction in systolic (■) and diastolic BP (□) at 6-wk, 3-mo, and 6-mo follow-up in patients with resistant hypertension



Prevalence of primary aldosteronism in patients with resistant hypertension from multiple clinics worldwide



Prevalence of primary aldosteronism in patients according to Sixth Joint National Committee (JNC VI) stages of severity of hypertension



Diagnosis of Primary Aldosterone Excess

AM plasma aldosterone/ plasma renin ratio of >30 (esp. if aldo > 20) = 90% sens/spec

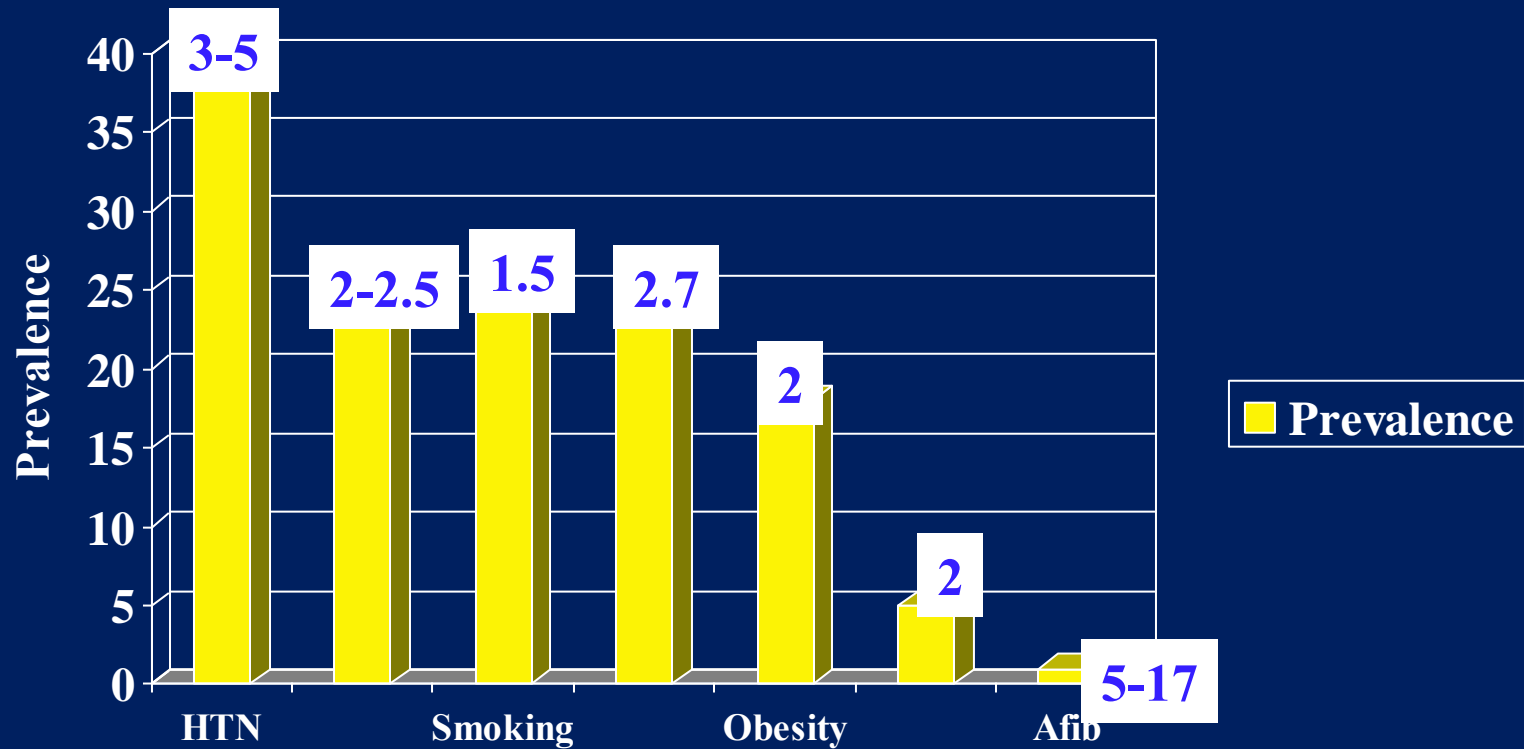
Confirmation

24 hr urine for aldosterone after 72 hrs of > 5 grams/day Na diet

plasma aldosterone after 2000 cc NSS
(<6 nl, > 10 primary aldo)

CT – hyperplasia more common than adenoma

Importance of Stroke Risk Factors



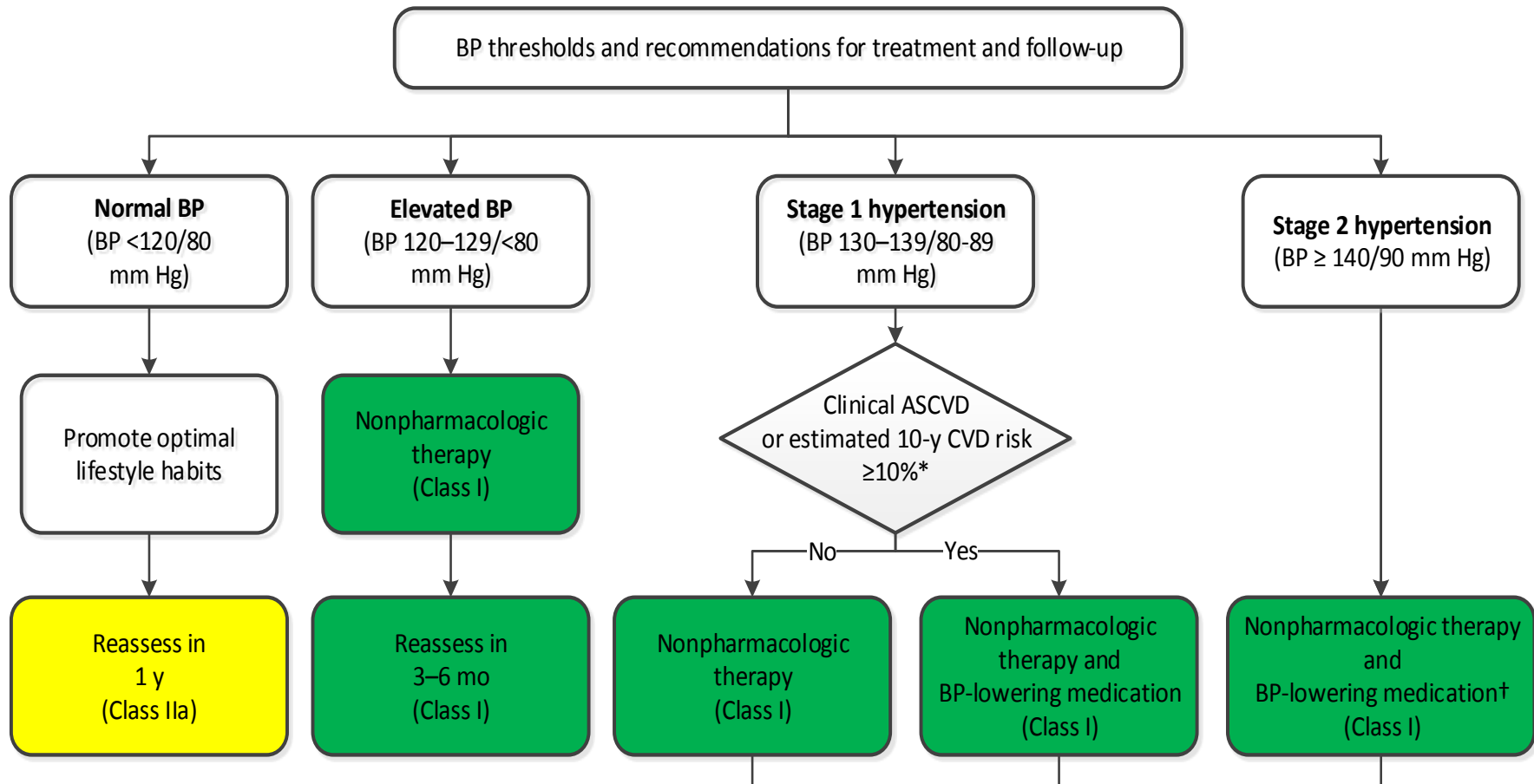
Primary Prevention

<u>Treatment</u>	<u>RRR</u>	<u>NNT (1 stroke/yr)</u>
HTN	42%	7937
Statins	25%	13,333
Aspirin	7% increase	NA
ACE-I	30%	11,111

Secondary Prevention

<u>Treatment</u>	<u>RRR</u>	<u>NNT (1 stroke/yr)</u>
HTN	28%	51
Statins	25%	57
Aspirin	28%	77
Thieno vs ASA	13%	64
Smoking D/C	33%	43
CEA	44%	26

Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up (continued on next slide) |



Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Weight loss	Weight/body fat	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	DASH dietary pattern	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	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	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.

DASH indicates Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

Resources: Your Guide to Lowering Your Blood Pressure With DASH—How Do I Make the DASH?

Available at: <https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to>.

Top 10 Dash Diet Tips. Available at: http://dashdiet.org/dash_diet_tips.asp

Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension* (cont.)

	Nonpharmacological Intervention	Dose	Approximate Impact 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

*Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.

†In the United States, one “standard” drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).

Diet Durability

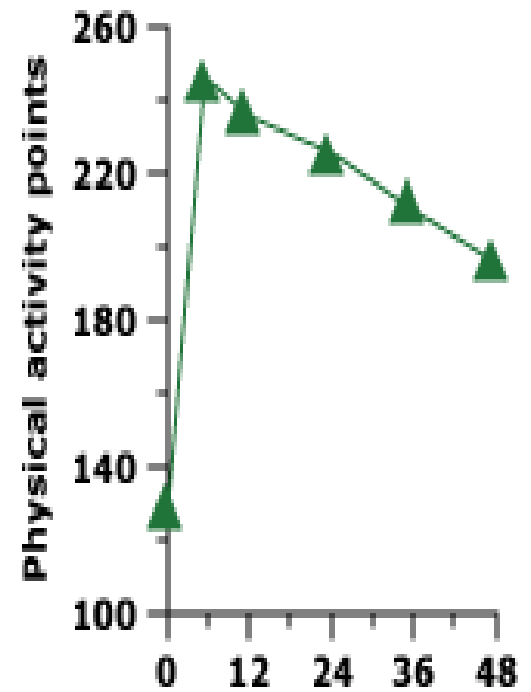
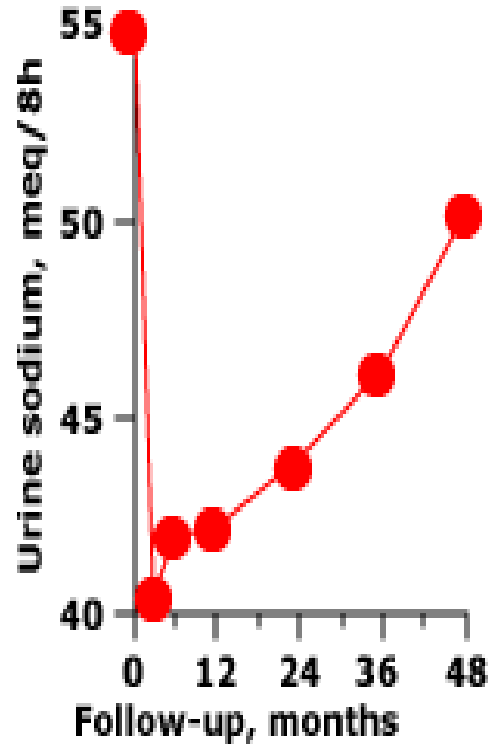
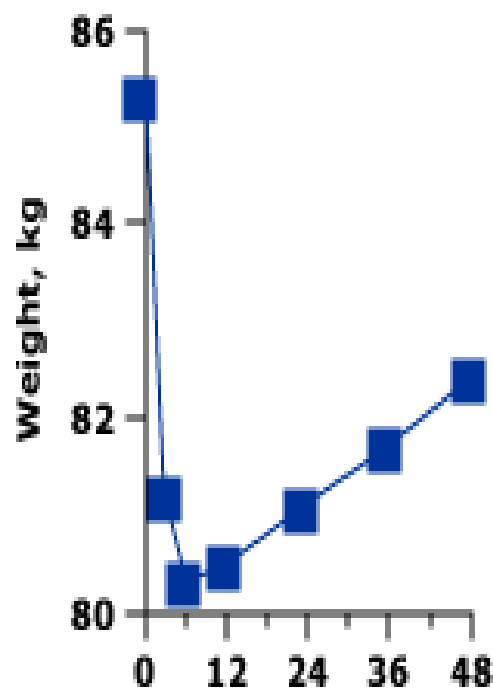


Table 107. Summary of Number of Antihypertensive Agents To Reach Target Blood Pressure*

Study, Year, Reference	Target SBP (mm Hg)	Achieved SBP (mm Hg)	Mean Number of Agents
IDNT, 2001 ¹³⁹	<135	138	2.6
RENAAL, 2001 ³³⁸	<140	141	2.7
ABCD, 2000 ⁴⁰⁷	<75 or 80-89*	128 and 137	2.4
CSG Captopril Trial, 1993 ³²⁹	<140	136	1-3 [#]

* Includes studies of progression of diabetic kidney disease randomized by DBP-[#] no data given on SBP in reference; there were approximately 25% normotensive participants.

HTN 2015-2017 Update

JNC 8

SPRINT

ACC 2017 Guidelines

JNC 8 Etal. Summary

JNC 8 published in close temporal proximity with
ASH/ISH and AHA/ACC/CDC guidelines

Confusion reigns supreme

All agree with:

1. Use of ACE/ARB, thiazides and CCB 1st
2. BB, aldactone etc used for pts who fail this
3. AA should use thiazides or CCB 1st
4. Avoid ACE/ARB combination
5. ACE for all CKD (JNC8)

JNC 8 Etal. Summary

BP Goals

1. Age > 80 – SBP $< 150/$
2. Age 60 – 80 – SBP $< 150/$ (JNC8);
SBP $< 140/$ (ASH)
3. Age < 60 – SBP $< 140/$ and DBP < 90
(JNC8)(ASH)
4. CKD/Albuminuria - $< 130/$ (ASH)

SPRINT Trial

High CV risk patients with HTN randomized to
SBP < 140/ or < 120/ (9361 participants)

Inclusion – HTN and increased CV risk

Exclusion =- DM , GFR < 20, ADPCKD, stroke

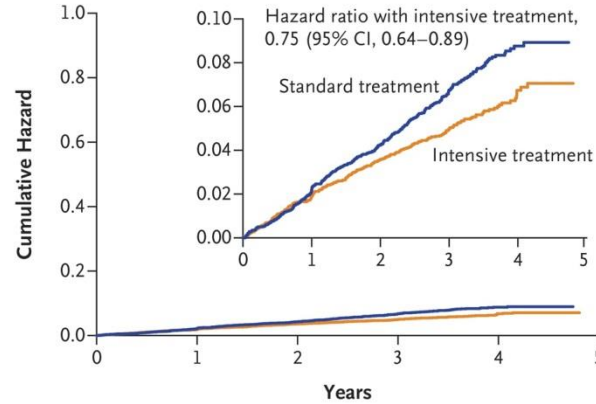
< 120/ resulted in a decrease in primary
outcome (MI, ACS, CVA, HF or CV death) NNT
61

< 120/ resulted in a decrease in all cause
mortality NNT 90

< 120/ resulted in decreased death from CV
cause NNT 172

Primary Outcome and Death from Any Cause.

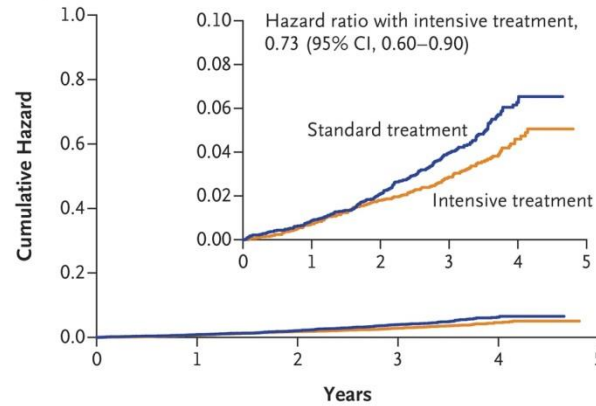
A Primary Outcome



No. at Risk

Standard treatment	4683	4437	4228	2829	721
Intensive treatment	4678	4436	4256	2900	779

B Death from Any Cause



No. at Risk

Standard treatment	4683	4528	4383	2998	789
Intensive treatment	4678	4516	4390	3016	807

Serious adverse event only

Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001

Emergency department visit or serious adverse event

Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001

**2017 ACC/AHA/AAPA/ABC/ACPM/AGS/
APhA/ASH/ASPC/NMA/PCNA
Guideline for the Prevention, Detection,
Evaluation, and Management of High Blood
Pressure in Adults**

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Categories of BP in Adults*

BP Category	SBP		DBP
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
Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in DBP, diastolic blood pressure; and SBP systolic blood pressure.

BP Treatment Threshold and the Use of CVD Risk Estimation to Guide Drug Treatment of Hypertension

COR	LOE	Recommendations for BP Treatment Threshold and Use of Risk Estimation* to Guide Drug Treatment of Hypertension
I	SBP: A	Use of BP-lowering medications is recommended for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher, and for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher.
	DBP: C-EO	
I	C-LD	Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher.

*ACC/AHA Pooled Cohort Equations (<http://tools.acc.org/ASCVD-Risk-Estimator/>) to estimate 10-year risk of atherosclerotic CVD.

BP Goal for Patients With Hypertension

COR	LOE	Recommendations for BP Goal for Patients With Hypertension
I	SBP: B-R ^{SR}	For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher a BP target of less than 130/80 mm Hg is recommended.
	DBP: C-EO	
IIb	SBP: B-NR	For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable.
	DBP: C-EO	

SR indicates systematic review.

BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk $\geq 10\%$	$\geq 130/80$	$< 130/80$
No clinical CVD and 10-year ASCVD risk $< 10\%$	$\geq 140/90$	$< 130/80$
Older persons (≥ 65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥ 130 (SBP)	< 130 (SBP)
Specific comorbidities		
Diabetes mellitus	$\geq 130/80$	$< 130/80$
Chronic kidney disease	$\geq 130/80$	$< 130/80$
Chronic kidney disease after renal transplantation	$\geq 130/80$	$< 130/80$
Heart failure	$\geq 130/80$	$< 130/80$
Stable ischemic heart disease	$\geq 130/80$	$< 130/80$
Secondary stroke prevention	$\geq 140/90$	$< 130/80$
Secondary stroke prevention (lacunar)	$\geq 130/80$	$< 130/80$
Peripheral arterial disease	$\geq 130/80$	$< 130/80$

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

HTN Treatment Summary

BP Goals - $<140/90$ in all but elderly ($<150/80$).

GFR < 60 ml + proteinuria goals $< 130/80$

JNC 8 Lifestyle modification effective but not durable

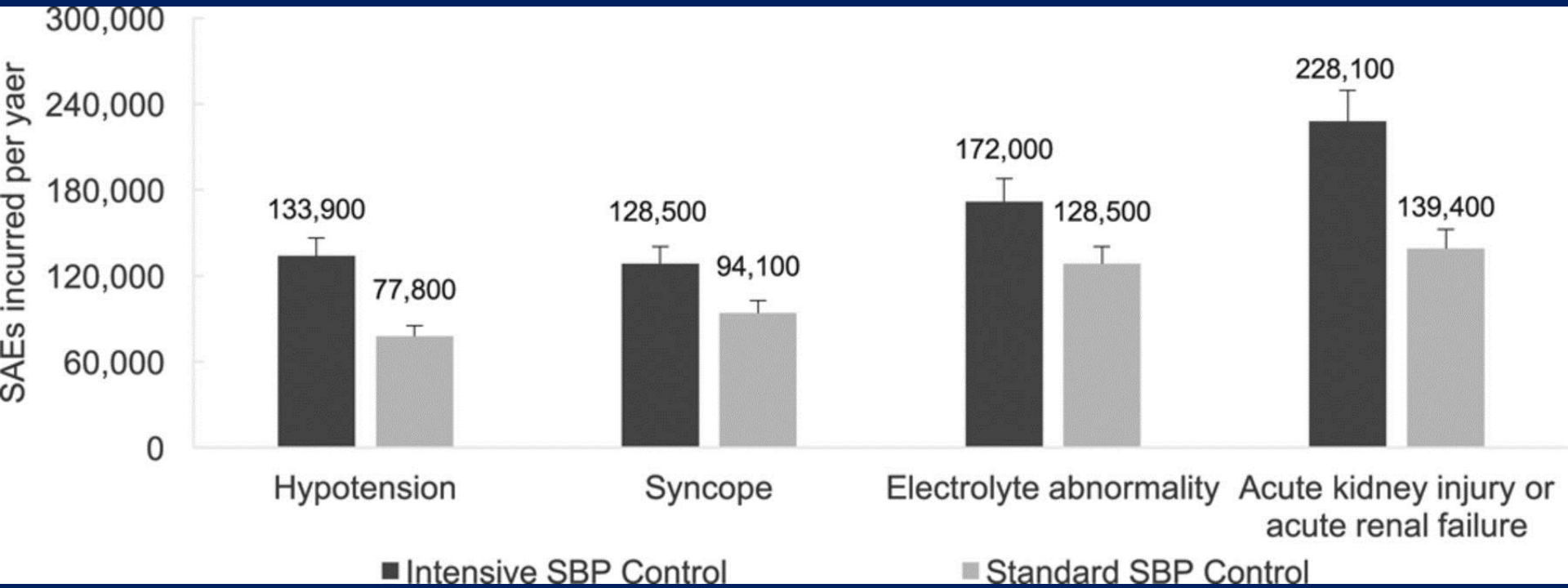
Expect to use 2-3 drugs to achieve goals

Nocturnal dosing better than AM dosing

ACE/ARB combination should not be used

Spironolactone effective for resistant HTN

ACC Guideline - more aggressive based on CV Risk (high risk only)



**People who don't think too good
should not think too much**

Ted Williams

Nephrolithiasis - Facts

The lifetime incidence of kidney stones is approximately 13 percent for men and 7 percent for women.

Among adults with kidney stones, approximately 80 percent consist predominately of calcium oxalate and/or calcium phosphate stones.

Following an initial stone event, the 5-year recurrence rate in the absence of specific treatment is 35 to 50 percent.

Nephrolithiasis - Facts

Genetic factors are thought to account for about half the risk of developing kidney stones.

Environmental risk factors include low fluid intake, low calcium intake, and high fructose intake.

The evidence for a role for increased animal protein intake, high sodium intake, increased sucrose intake, and low magnesium intake as risk factors for kidney stones is mixed.

Risk of kidney stones may be increased by medical conditions such as obesity, diabetes, primary hyperparathyroidism, gout, paralysis, and anatomic abnormalities of the kidney and bowel

Nephrolithiasis - Workup

Standard workup for stones is comprehensive metabolic panel, UA, PTH, and Vitamin D

24 HR urine for volume, Na, UA, Ca, PO₄, oxalate, citrate, and Mg

Limited evidence to support that therapy directed by workup is better than empiric tx alone (exception serum and urine uric acid)

Nephrolithiasis - Treatment

Fluid intake to maintain urine excretion of > 2 liters per day may provide a clinically significant reduction in risk of stone recurrence.

Abstaining from soft drinks or eliminating soft drinks acidified solely with phosphoric acid but not by citric acid (based on a single study in men) reduces risk of stone recurrence in frequent consumers.

A normal-calcium, low-sodium, low-animal protein diet may reduce the risk for stone recurrence, but the independent effect of increasing dietary calcium has not been determined.

High-fiber and reduced-animal protein diets may or may not help prevent stone recurrence.

The effectiveness of other dietary interventions is not clear.

Nephrolithiasis - Treatment

Thiazide diuretics (any) reduce the risk of calcium stone recurrence (ARR = 29 percent; (NNT) = 3

Citrate reduces the risk of calcium stone recurrence ARR = 41 percent; NNT = 3

Allopurinol reduces the risk of calcium stone recurrence in patients with elevated blood and urine UA levels ARR = 22 percent; NNT = 5

Treatment with magnesium did not reduce the risk of stone recurrence