Hypertension Update

ACOI 2017

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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

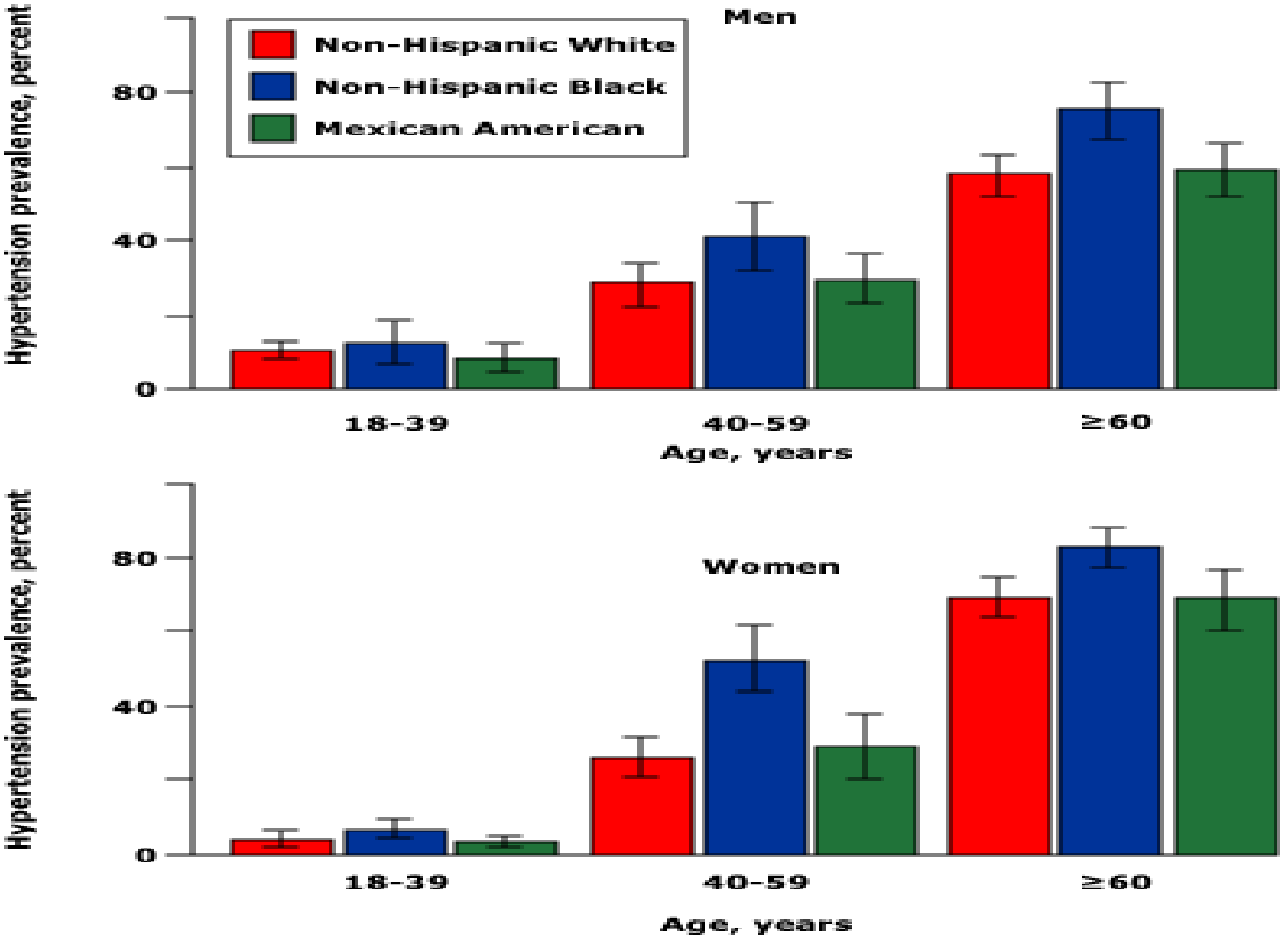
Most common risk for CVD

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

History

Report (JAMA, 1977)	6 pages
1980 Report (Archives)	6 pages
1984 Report (Archives)	13 pages
1988 Report (Archives)	16 pages
JNC V (Archives, ‘93)	30 pages
JNC VI (Archives ‘97)	34 pages
JNC 7 (Hypertension ‘03)	47 pages
NICE HTN 2011	36 pages
JNC 8 2013	14 pages


Men
Non-Hispanic White
Non-Hispanic Black
Mexican American
Hypertension prevalence, percent
80
40
0
18–39
40–59
≥60
Age, years
Women
Hypertension prevalence, percent
80
40
0
18–39
40–59
≥60
Age, years

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

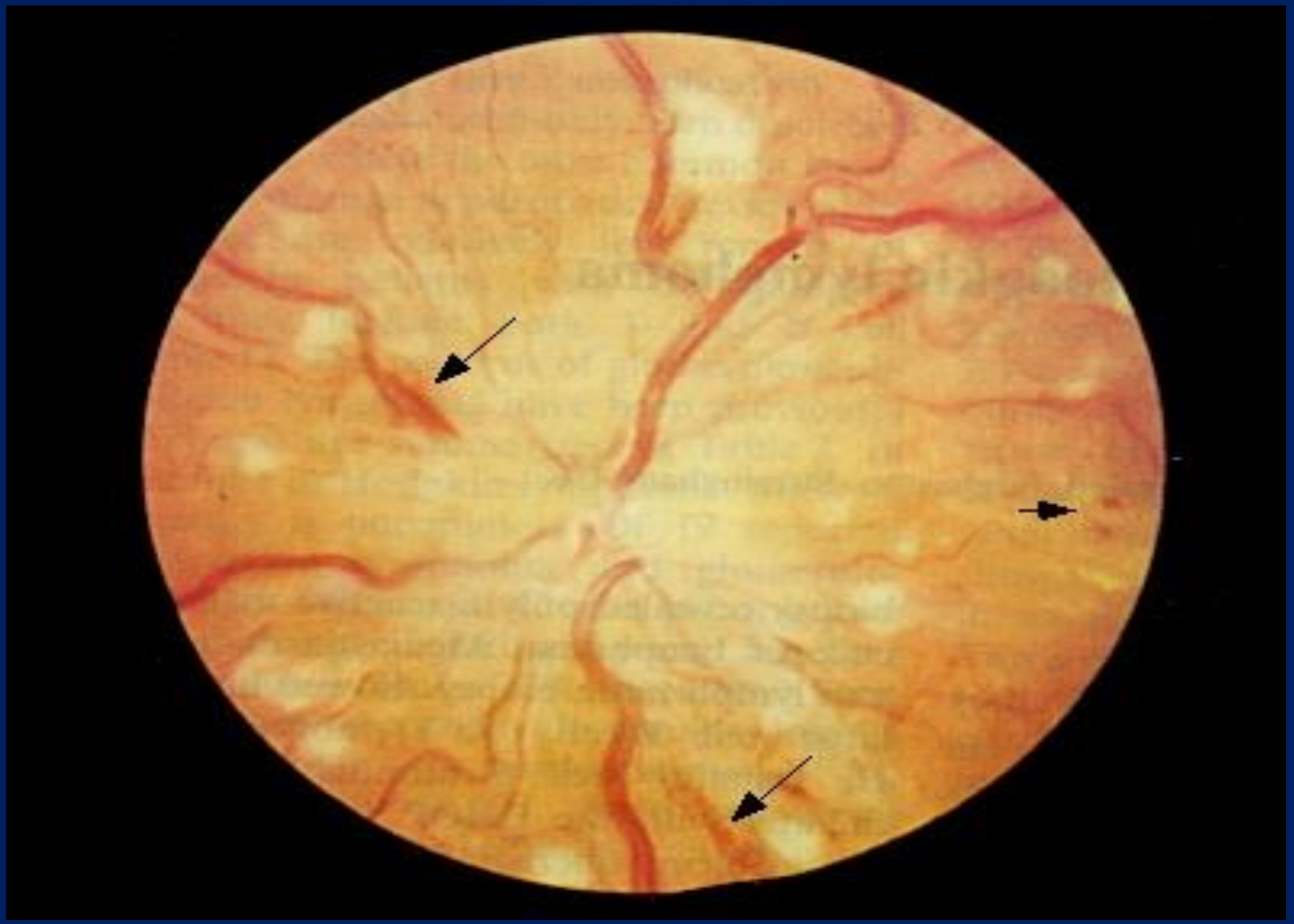
> 140/90 at home (end organ damage)

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)

BP Control Rates

Trends in awareness, treatment, and control of high blood pressure in adults ages 18–74

	National Health and Nutrition Examination Survey, Percent			
	II 1976–80	II (Phase 1) 1988–91	II (Phase 2) 1991–94	1999–2000
Awareness	51	73	68	70
Treatment	31	55	54	59
Control	10	29	27	34

Sources: Unpublished data for 1999–2000 computed by M. Wolz, National Heart, Lung, and Blood Institute; JNC 6.

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.

Laboratory Tests

Routine Tests

- Electrocardiogram
- Urinalysis
- Blood glucose, and hematocrit
- Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
- Lipid profile, after 9- to 12-hour fast, that includes high-density and low-density lipoprotein cholesterol, and triglycerides

Optional tests

- Measurement of urinary albumin/creatinine ratio

More extensive testing for identifiable causes is not generally indicated unless BP control is not achieved

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

Causes of Resistant Hypertension

Improper BP measurement

Excess sodium intake

Inadequate diuretic therapy

Medication

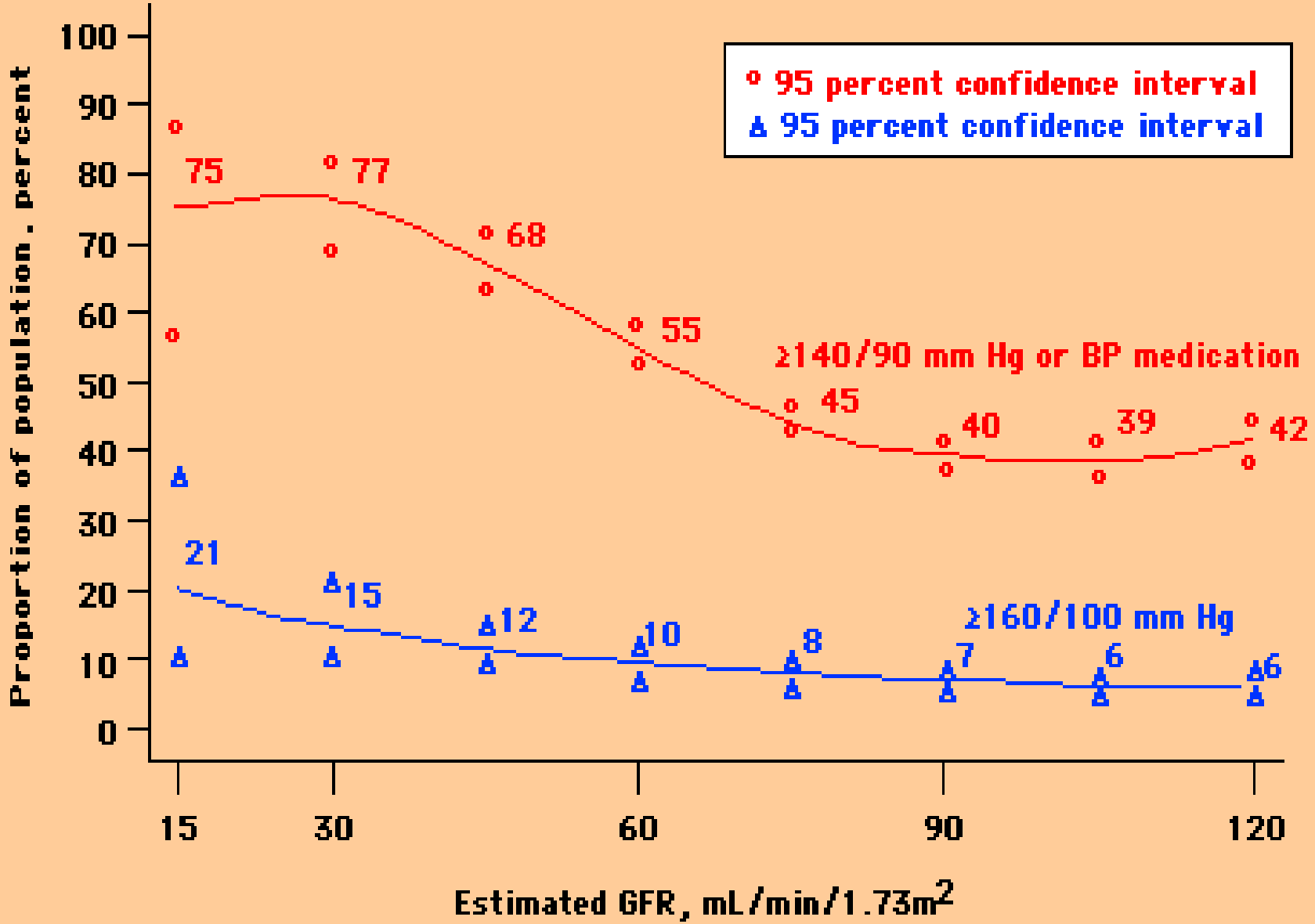
- Inadequate doses or timing
- Drug actions and interactions (e.g., NSAIDs, illicit drugs, sympathomimetics, oral contraceptives)
- Over-the-counter (OTC) drugs and herbal supplements

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

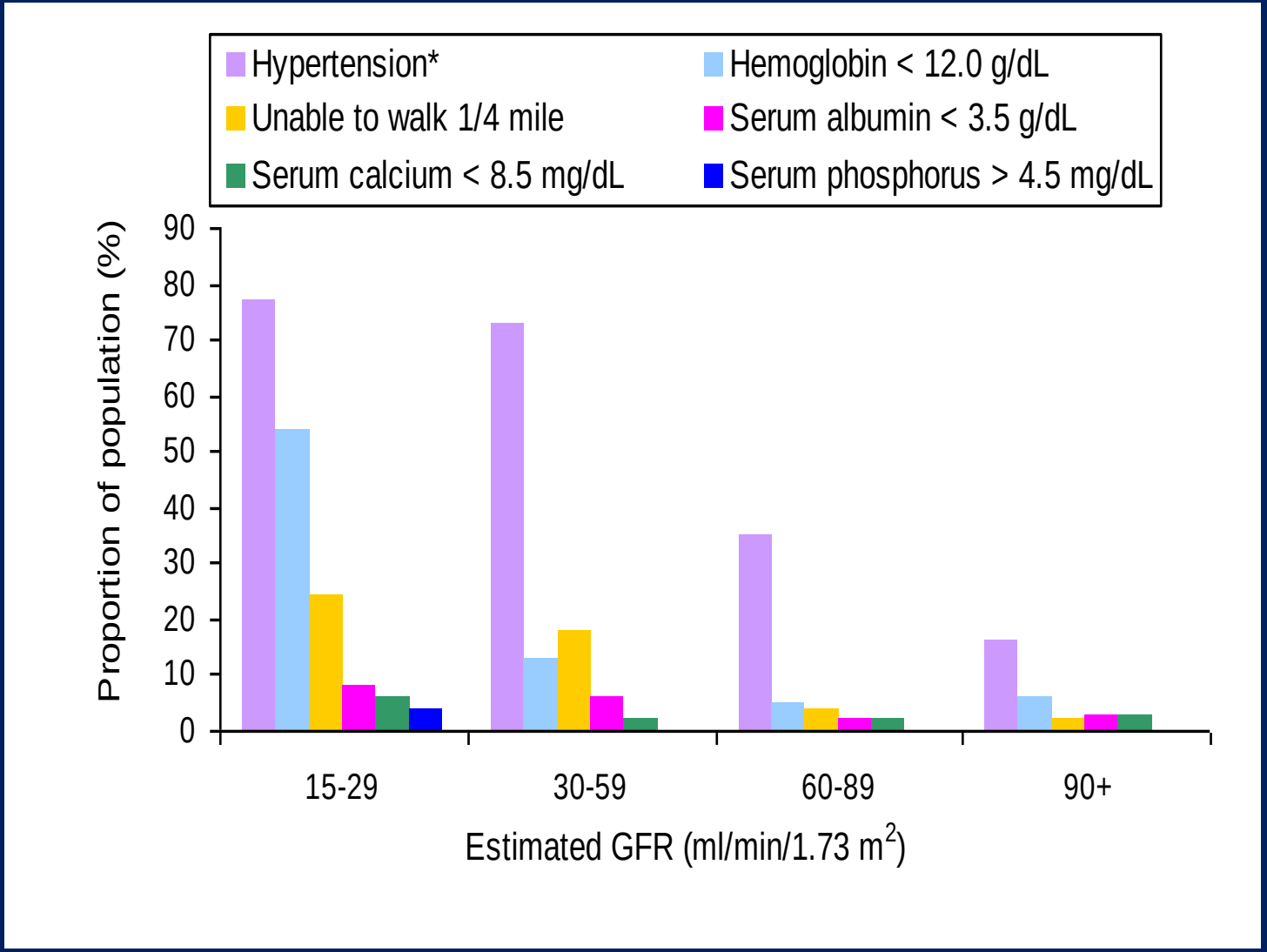
Identifiable causes of HTN – sleep apnea, RAS, primary aldosteronism etc

Secondary HTN

CKD and HTN


° 95 percent confidence interval
Δ 95 percent confidence interval
≥140/90 mm Hg or BP medication
≥160/100 mm Hg
75
77
68
55
45
40
39
42
21
15
12
10
8
7
6
6
100
90
80
70
60
50
40
30
20
10
0
15
30
60
90
120
Proportion of population, percent
Estimated GFR, mL/min/1.73m2

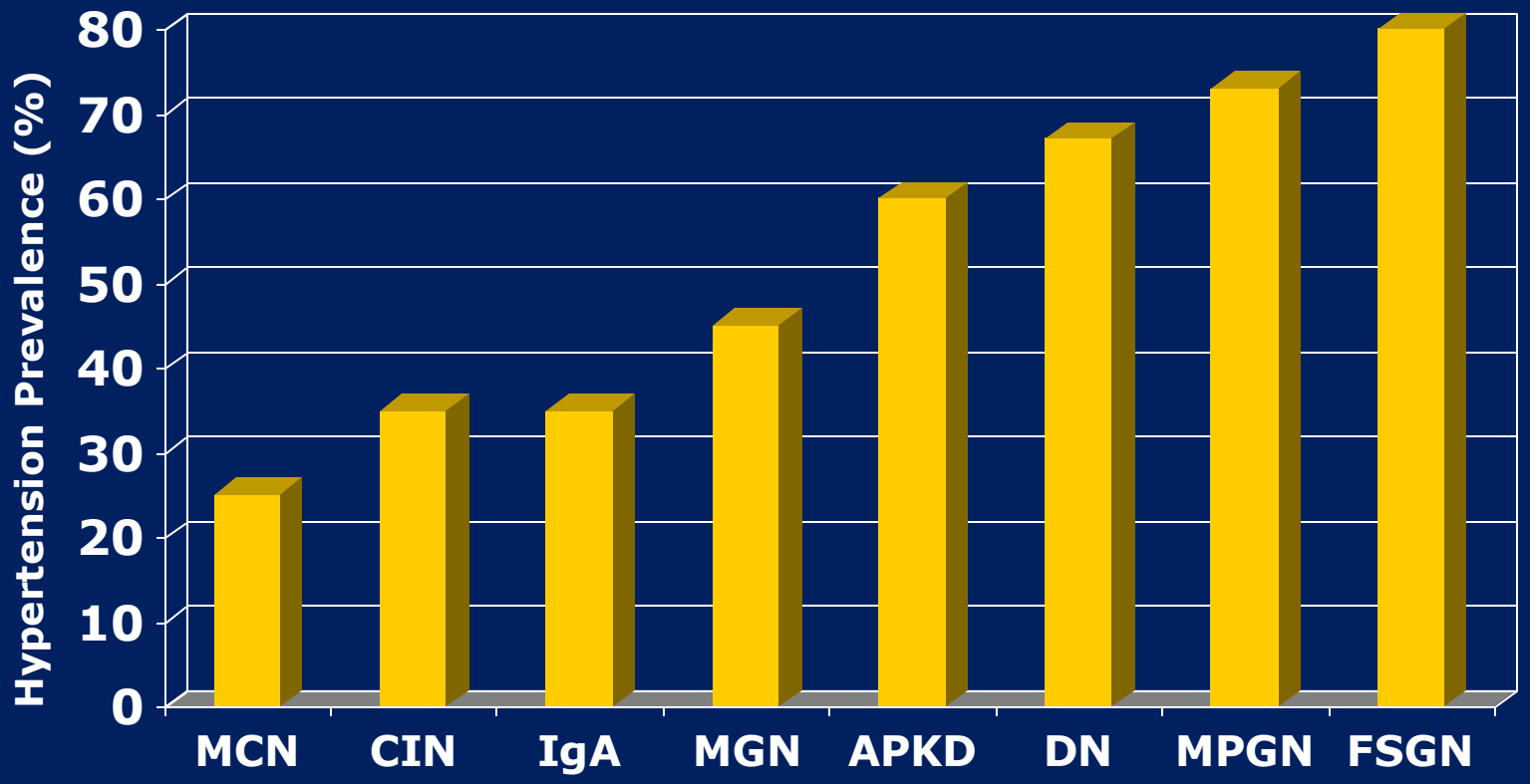
Prevalence of Abnormalities at each level of GFR



*>140/90 or antihypertensive medication

p-trend < 0.001 for each abnormality

Prevalence of Hypertension In Chronic Renal Diseases



MCN=minimal change nephropathy CIN=chronic interstitial nephritis IgA=IgA nephropathy
MGN=membranous glomerulonephritis APKD=adult-onset polycystic kidney disease DN=diabetic nephropathy
MPGN=membranoproliferative glomerulonephritis FSGN=focal segmental glomerulonephritis

Pathogenesis HTN - CKD

1. Volume Dependent : Salt sensitive HTN
2. Volume Independent :
   A. Activation of the RAS
   B. Activation of the Sympathetic NS
   C. Nitric oxide deficiency
   D. Endothelin
   F. Hyperuricemia
   G. Sleep Apnea
   H. Renal artery stenosis
   I. Nephron number

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)

Pathogenesis HTN – CKD
Uric Acid

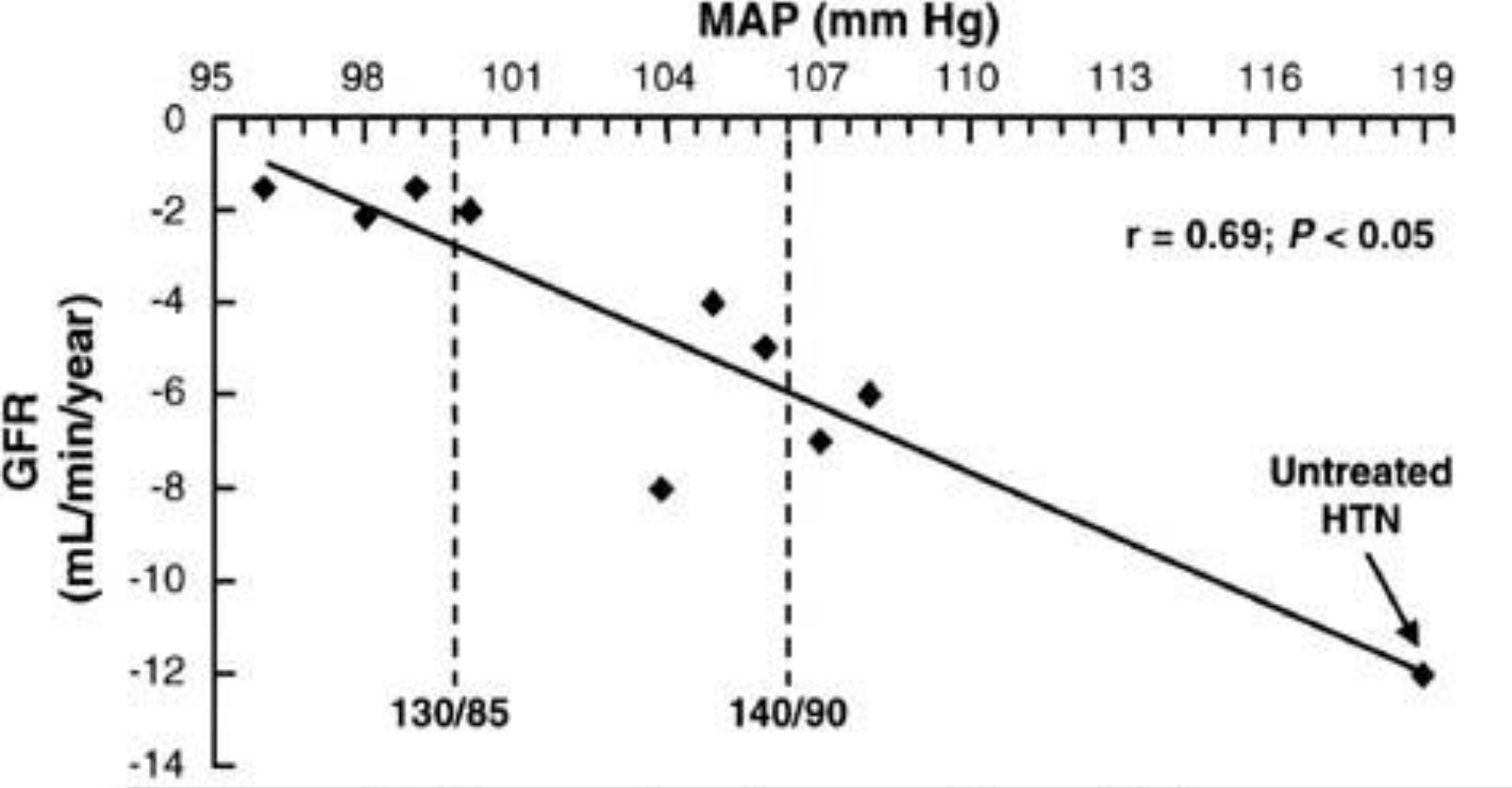
Uric acid acts as a renal vasoconstrictor by decreasing NO and activating RAS

Vasculopathic

Treatment will improve angina in adults and HTN in adults and adolescents

Pathogenesis HTN – CKD
Nephron Number

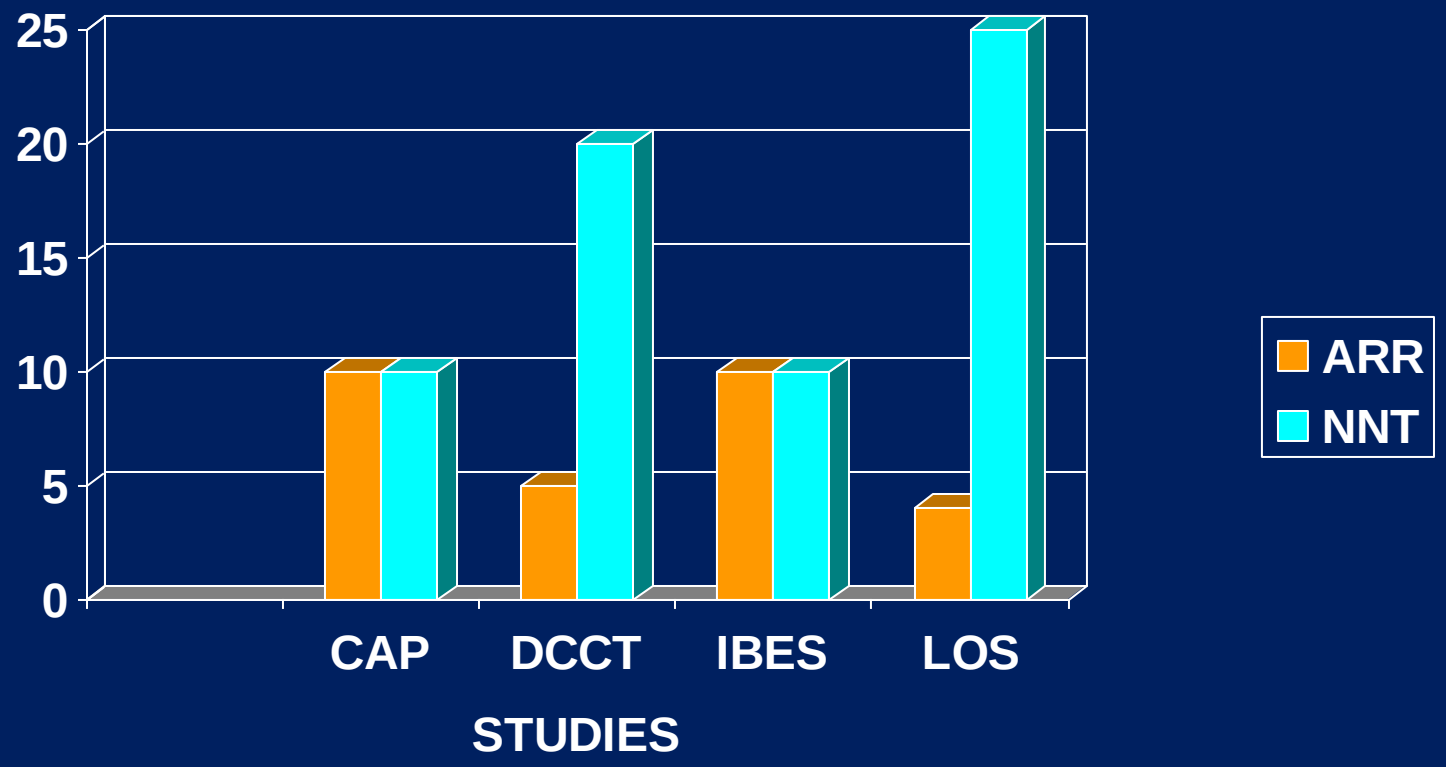
- Low nephron numbers in HTN
- This leads to HTN and progressive HTN by maladaption
- HTN mothers have small babies who have small kidneys (low nephrons) and develop HTN to have small babies and so on
- Genetic influences as well

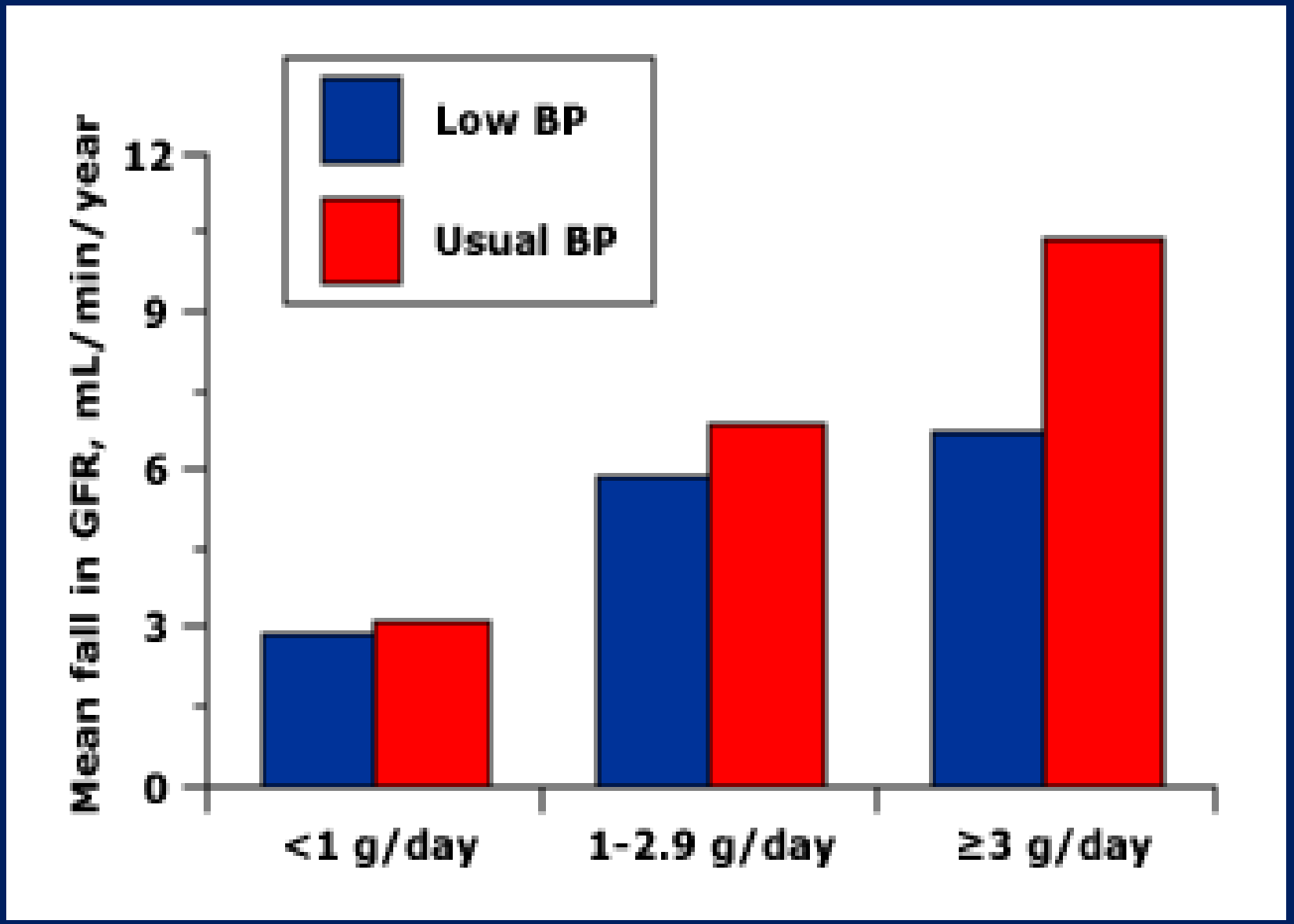


Summary of studies on nephropathy progression used in figure

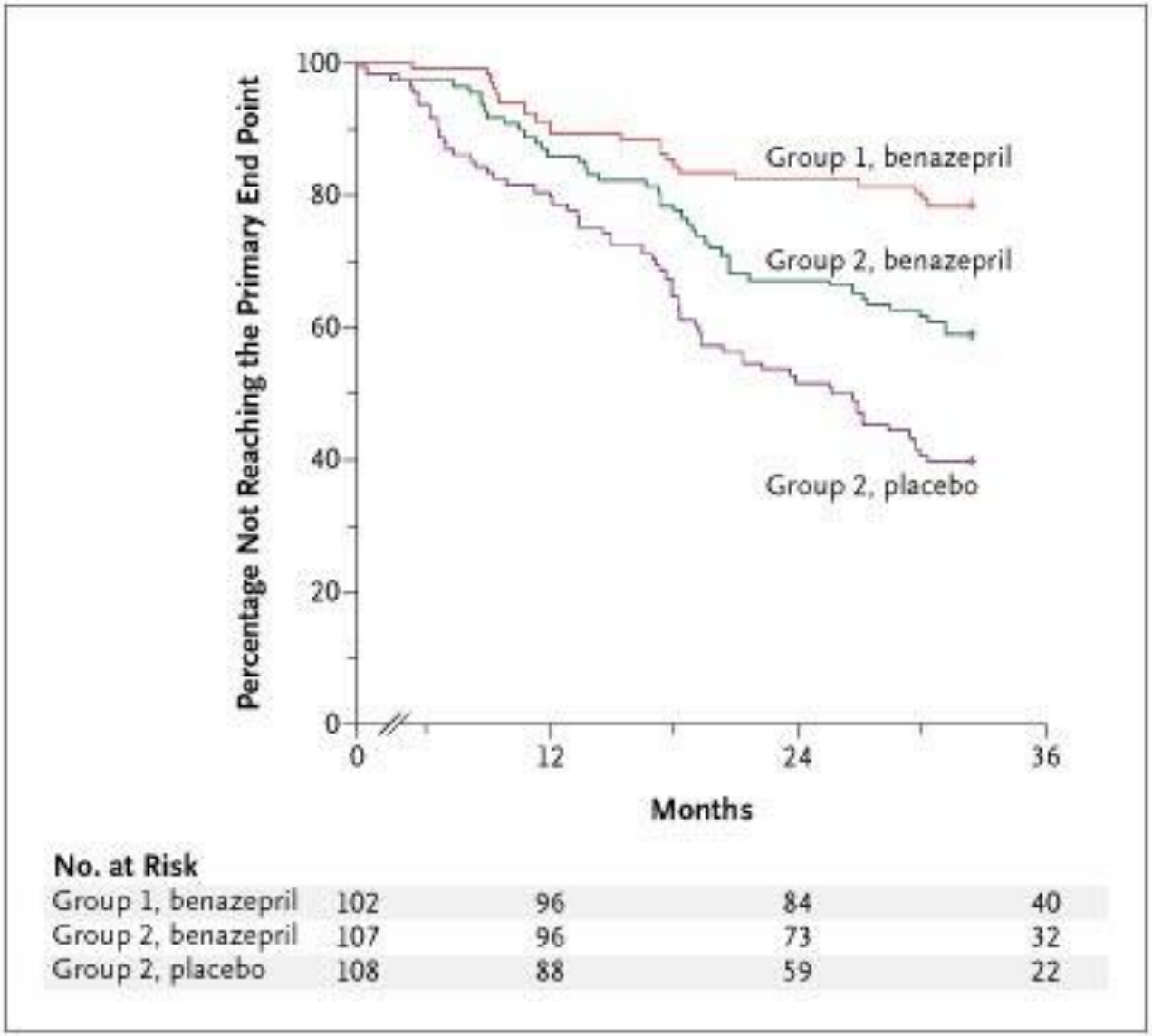
- Parving HH et al. *Br Med J*, 1989
- Viberti GC et al. *JAMA*, 1993
- Klaur S et al. *N Eng J Med*, 1993*
- Hebert L et al. *Kidney Int*, 1994
- Lebovitz H et al. *Kidney Int*, 1994
- Moschio G et al. *N Engl J Med*, 1996*
- Bakris GL et al. *Kidney Int*, 1996
- Bakris GL. *Hypertension*, 1997
- GISEN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

Summary of ACE or ARBs in Diabetic CKD




Low BP
Usual BP
Mean fall in GFR, mL/min/year
12
9
6
3
0
<1 g/day
1-2.9 g/day
≥3 g/day

Kaplan-Meier Estimates of the Percentage of Patients Not Reaching the Primary Composite End Point of a Doubling of the Serum Creatinine Level, End-Stage Renal Disease, or Death



No. at Risk				
Group 1, benazepril	102	96	84	40
Group 2, benazepril	107	96	73	32
Group 2, placebo	108	88	59	22

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)	≥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

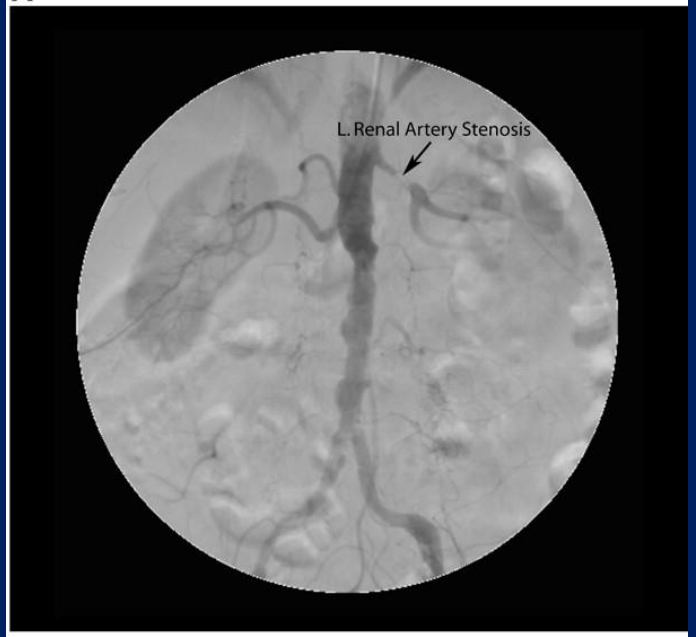
Anatomic Diagnosis not functional diagnosis

Renovascular Disease

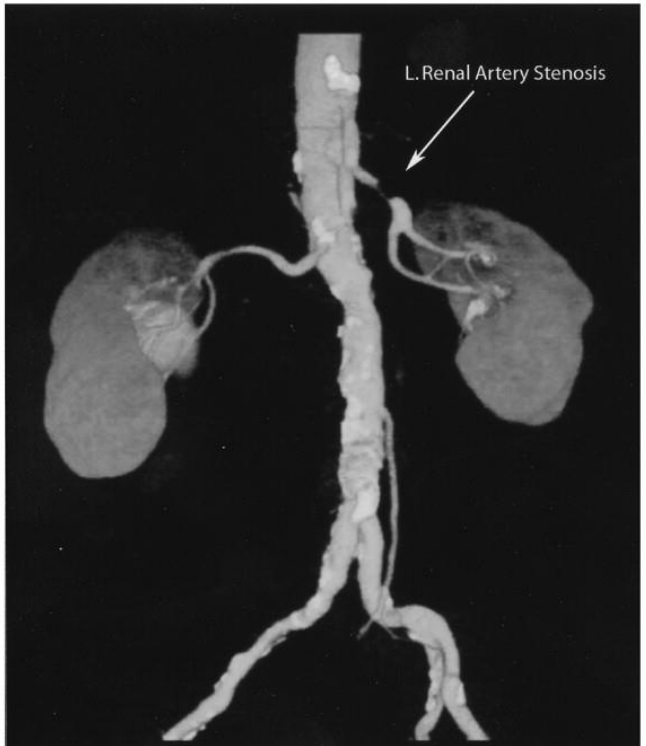
Angiography, with or without digital subtraction, is the "gold standard" for diagnosis for renovascular disease

Drive by angio

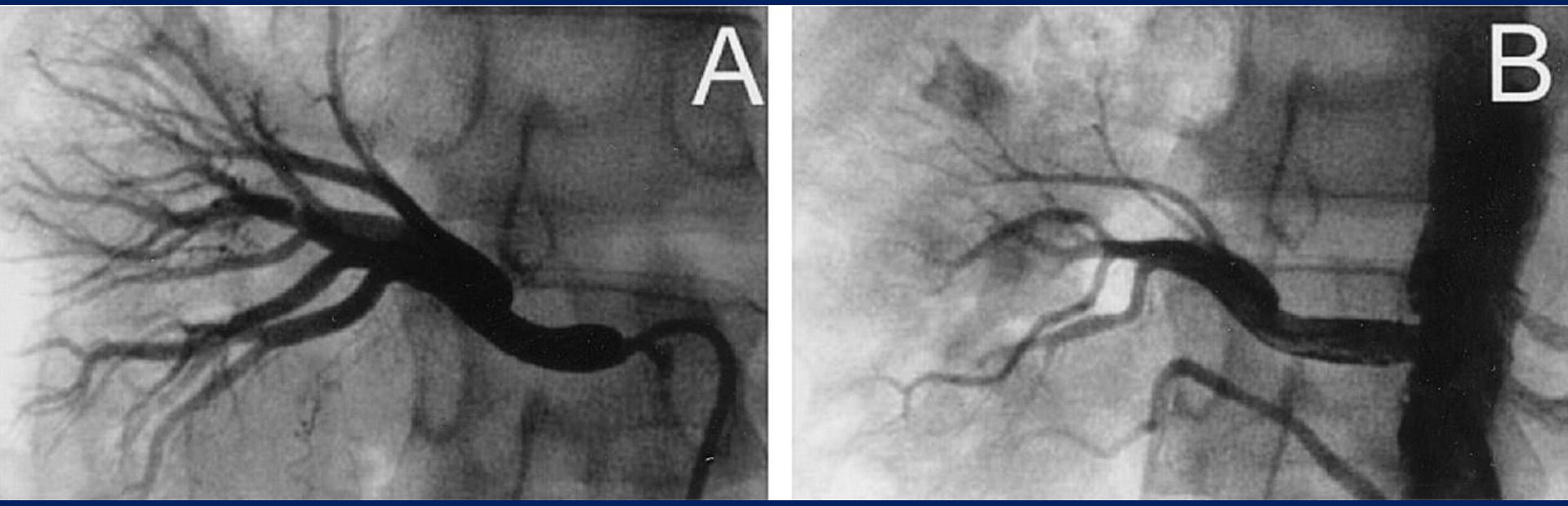
A

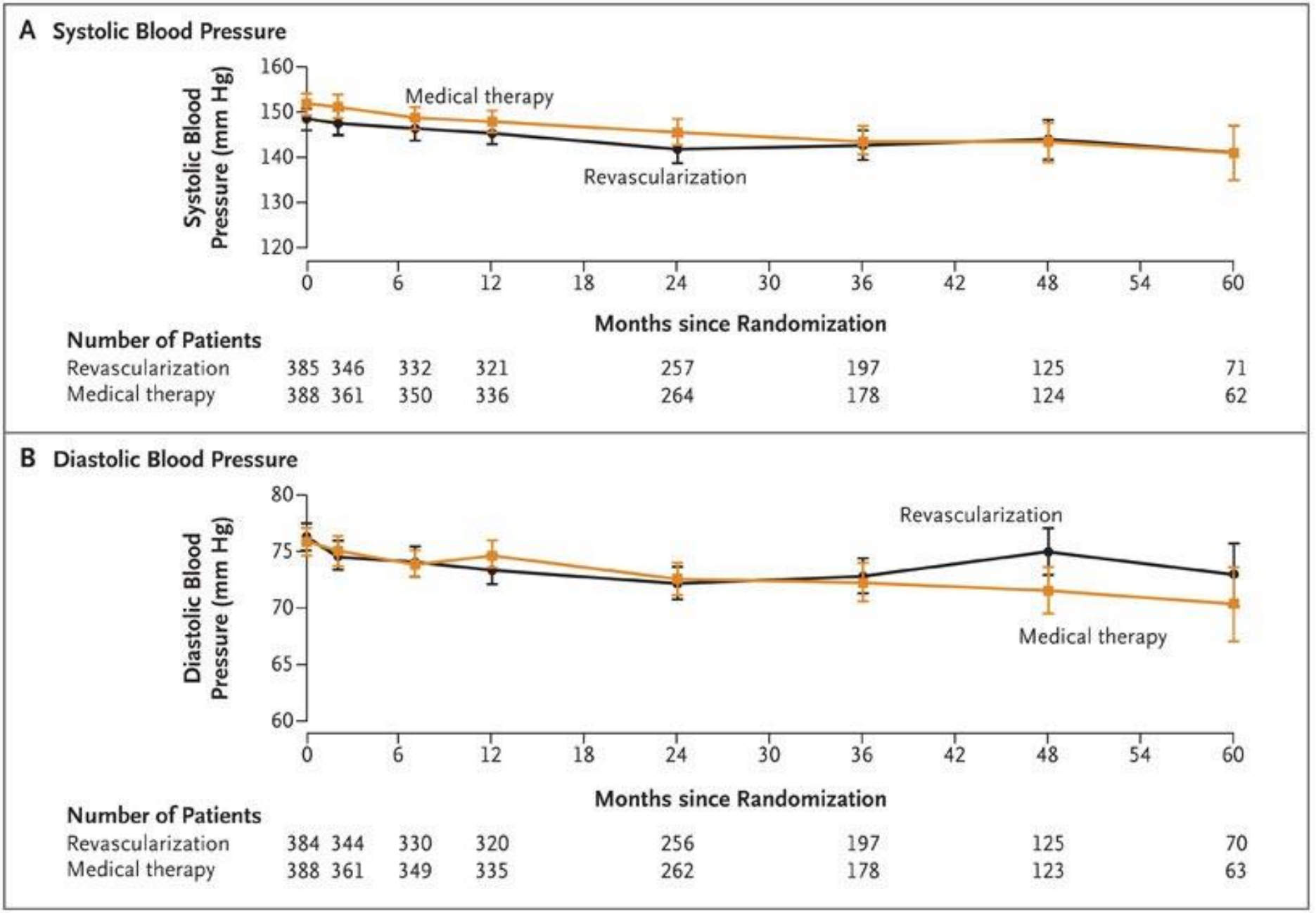


B

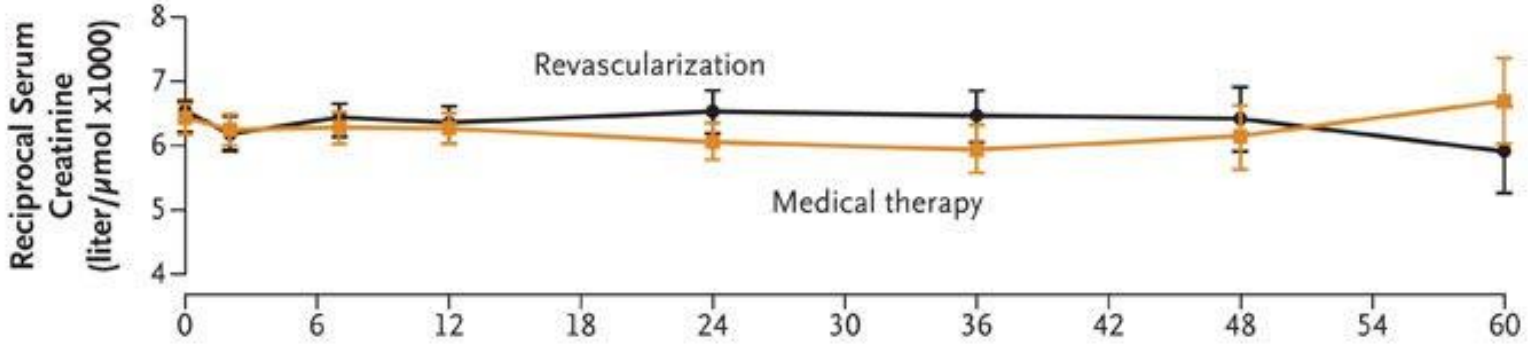


A, Baseline selective renal angiogram showing tight ostial stenosis with normal filling of the renal arteries to the cortex



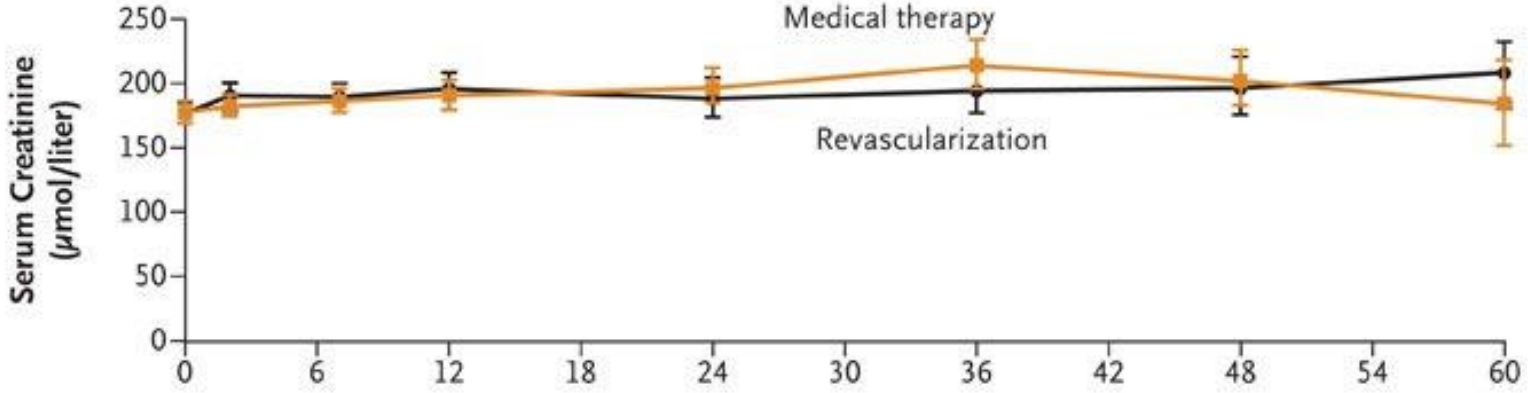

A Systolic Blood Pressure
Systolic Blood Pressure (mm Hg)
160
150
140
130
120
Medical therapy
Revascularization
0 6 12 18 24 30 36 42 48 54 60
Months since Randomization
Number of Patients
Revascularization 385 346 332 321 257 197 125 71
Medical therapy 388 361 350 336 264 178 124 62
B Diastolic Blood Pressure
Diastolic Blood Pressure (mm Hg)
80
75
70
65
60
Revascularization
Medical therapy
0 6 12 18 24 30 36 42 48 54 60
Months since Randomization
Number of Patients
Revascularization 384 344 330 320 256 197 125 70
Medical therapy 388 361 349 335 262 178 123 63

A Reciprocal of Serum Creatinine



No. of Patients								
Revascularization	403	349	336	329	263	191	127	72
Medical therapy	403	363	347	343	272	183	119	61

B Serum Creatinine



No. of Patients								
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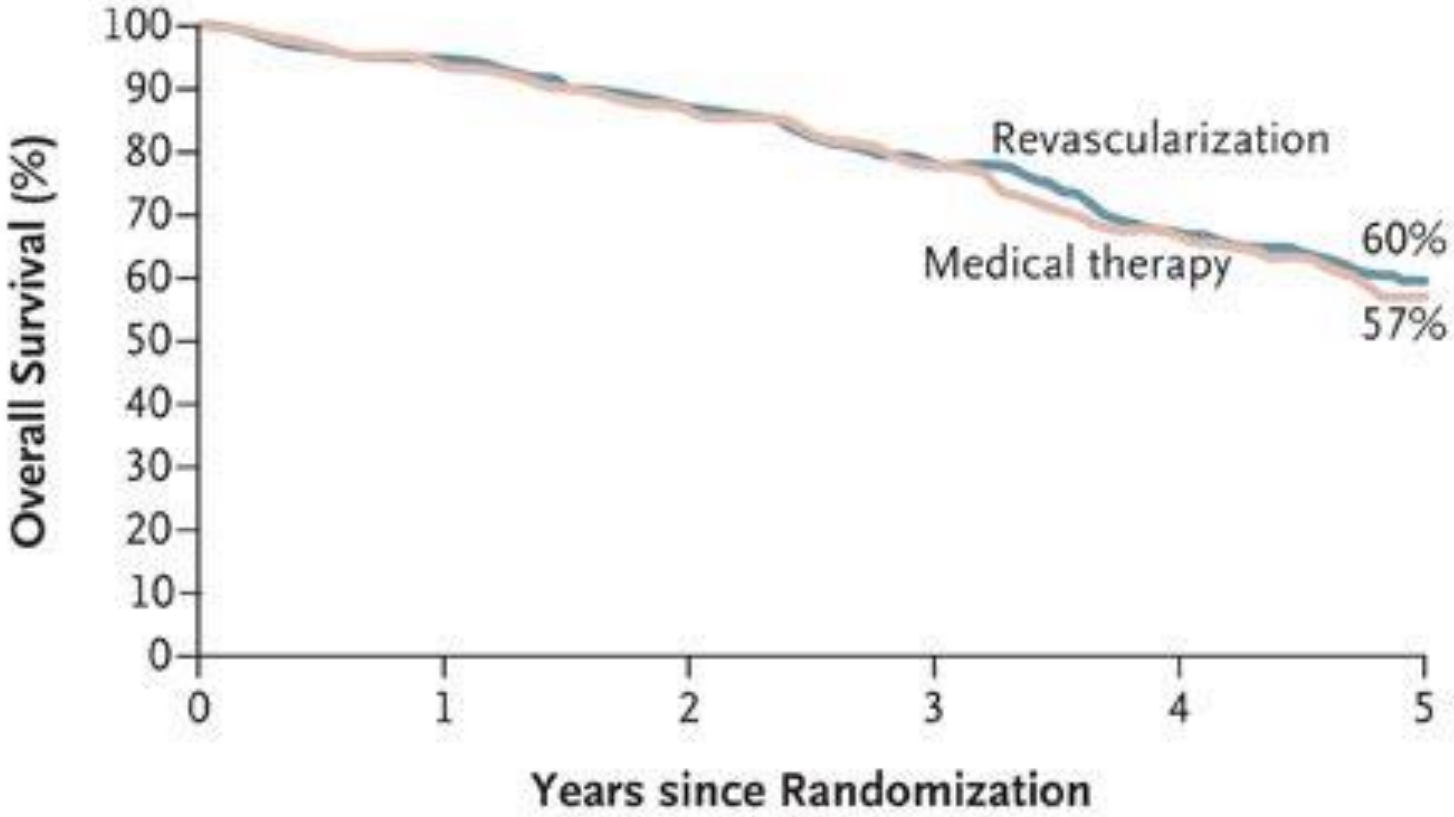


No. at Risk

Revascularization	403	337	257	178	109	46
Medical therapy	403	332	248	165	96	40

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

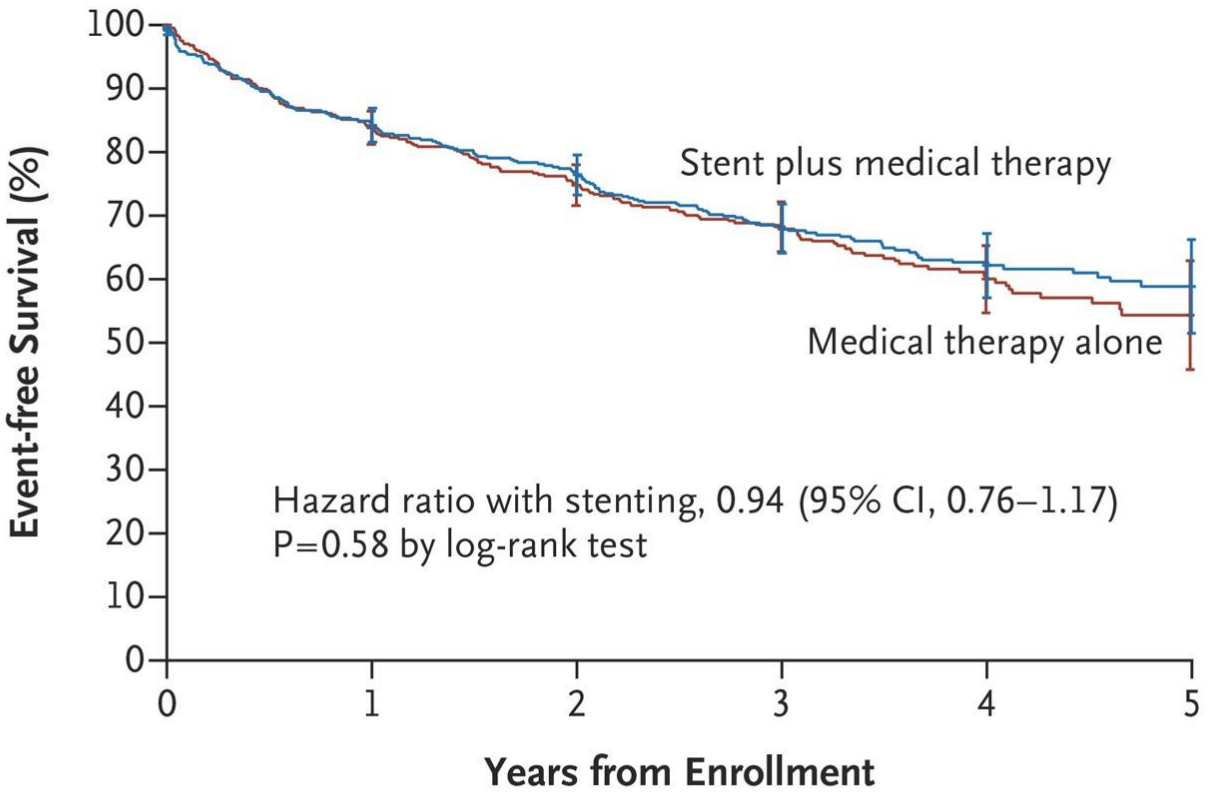
CORAL TRIAL

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.

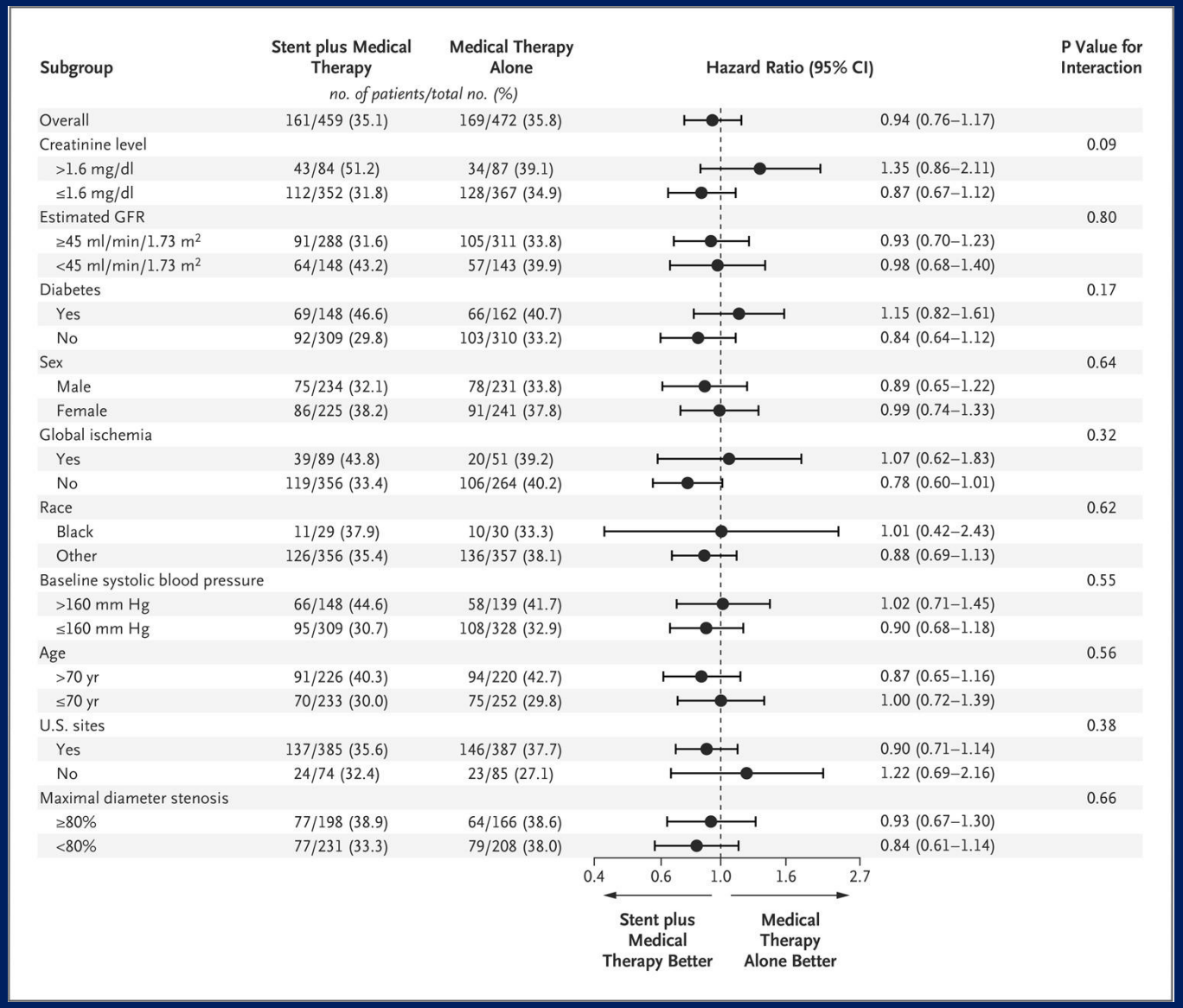


No. at Risk

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

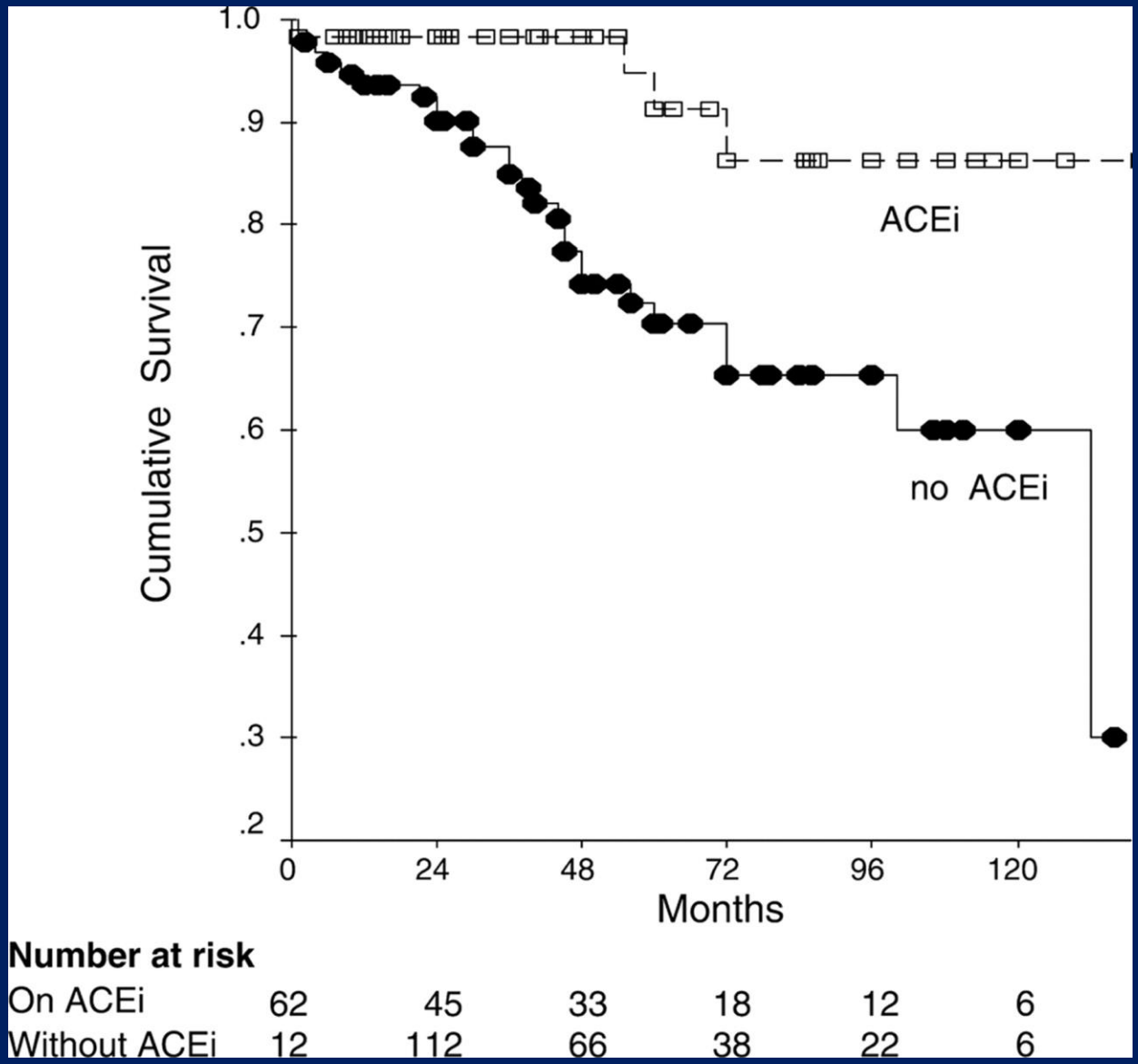
Cooper CJ et al. N Engl J Med 2014;370:13-22

CORAL Forest Plot of Treatment Effects within Subgroups.



Cooper CJ et al. N Engl J Med 2014;370:13-22

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



Hackam, D. G. et al. Hypertension 2007;50:998-1003

RAS – Principles of Treatment

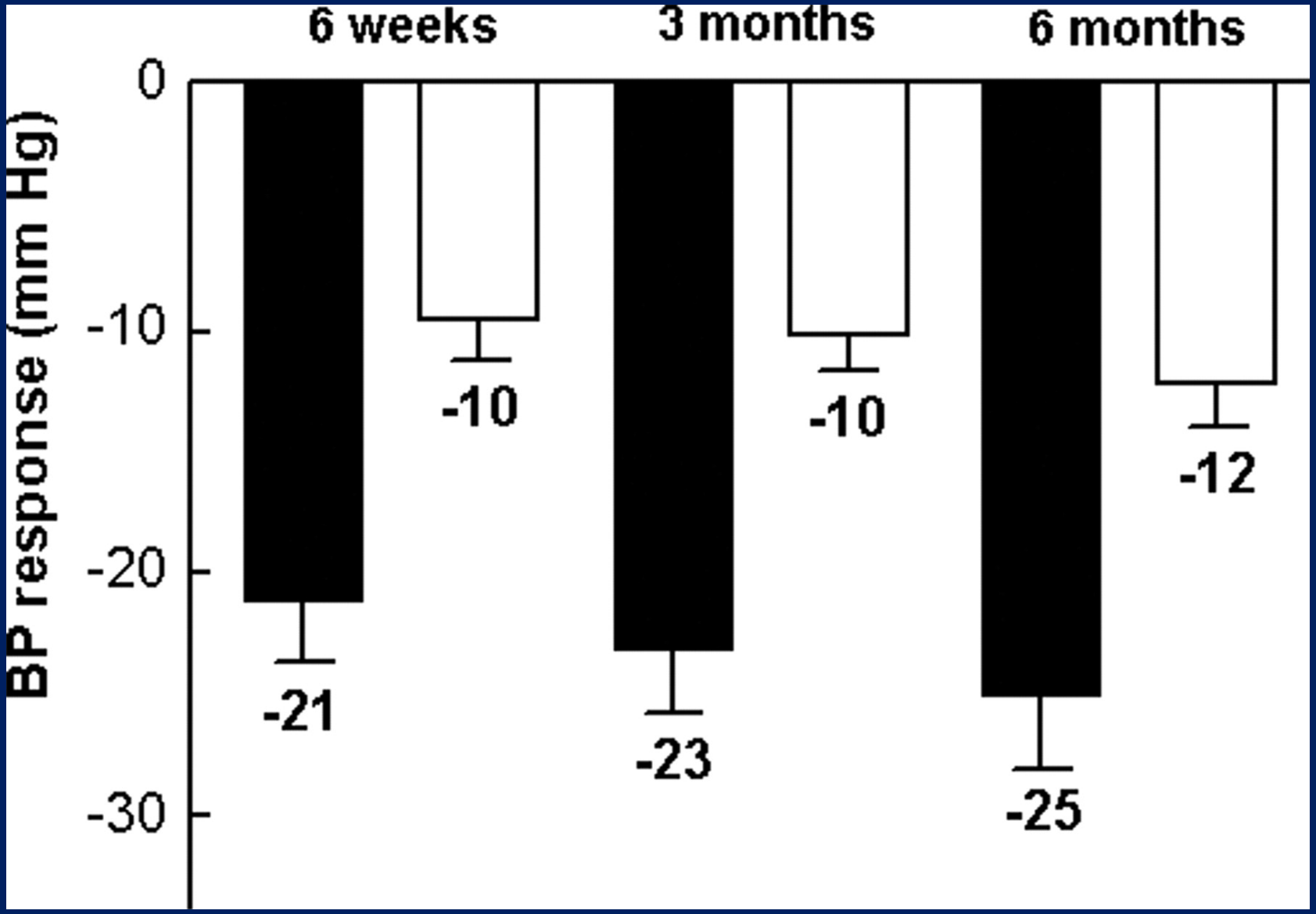
Don’t poke the skunk

Unless you’ve already been sprayed

USE ACEI or ARBs

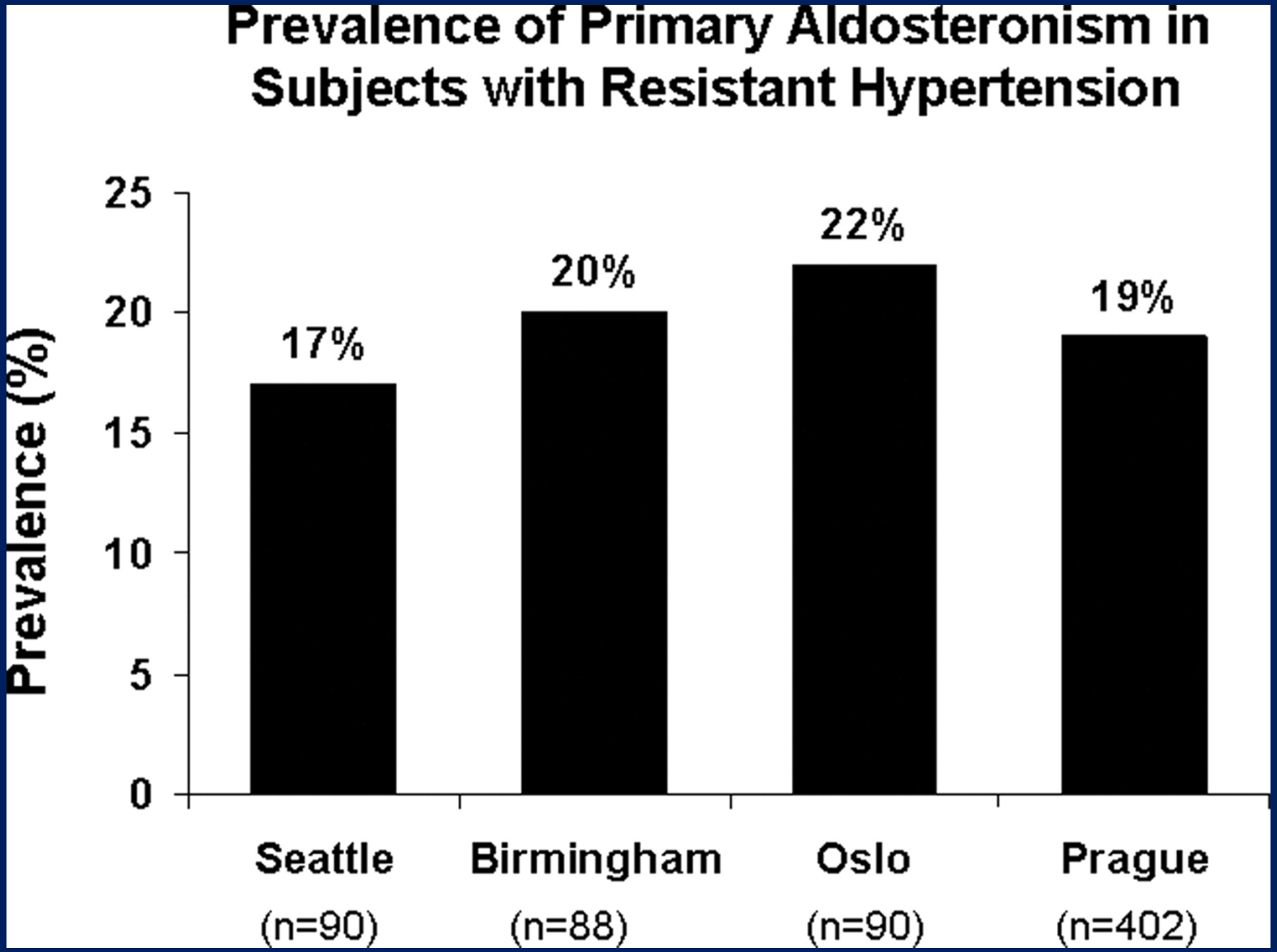
Primary Aldosteronism

Spironolactone-induced reduction in systolic ({blacksquare}) and diastolic BP ({square}) at 6-wk, 3-mo, and 6-mo follow-up in patients with resistant hypertension



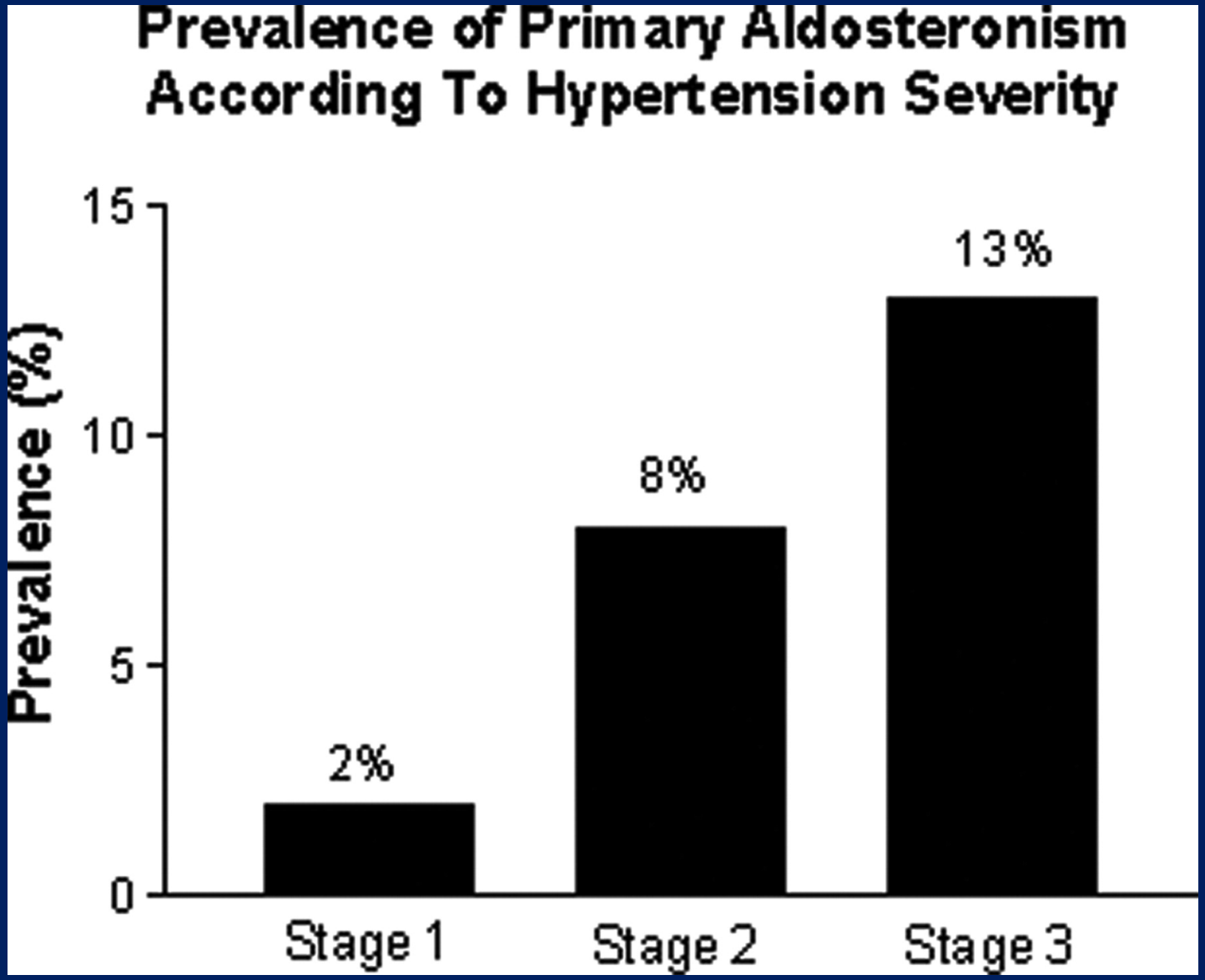
Calhoun, D. A. Clin J Am Soc Nephrol 2006;1:1039-1045

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



Calhoun, D. A. Clin J Am Soc Nephrol 2006;1:1039-1045

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



Calhoun, D. A. Clin J Am Soc Nephrol 2006;1:1039-1045

Diagnosis of Primary Aldosterone Excess

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

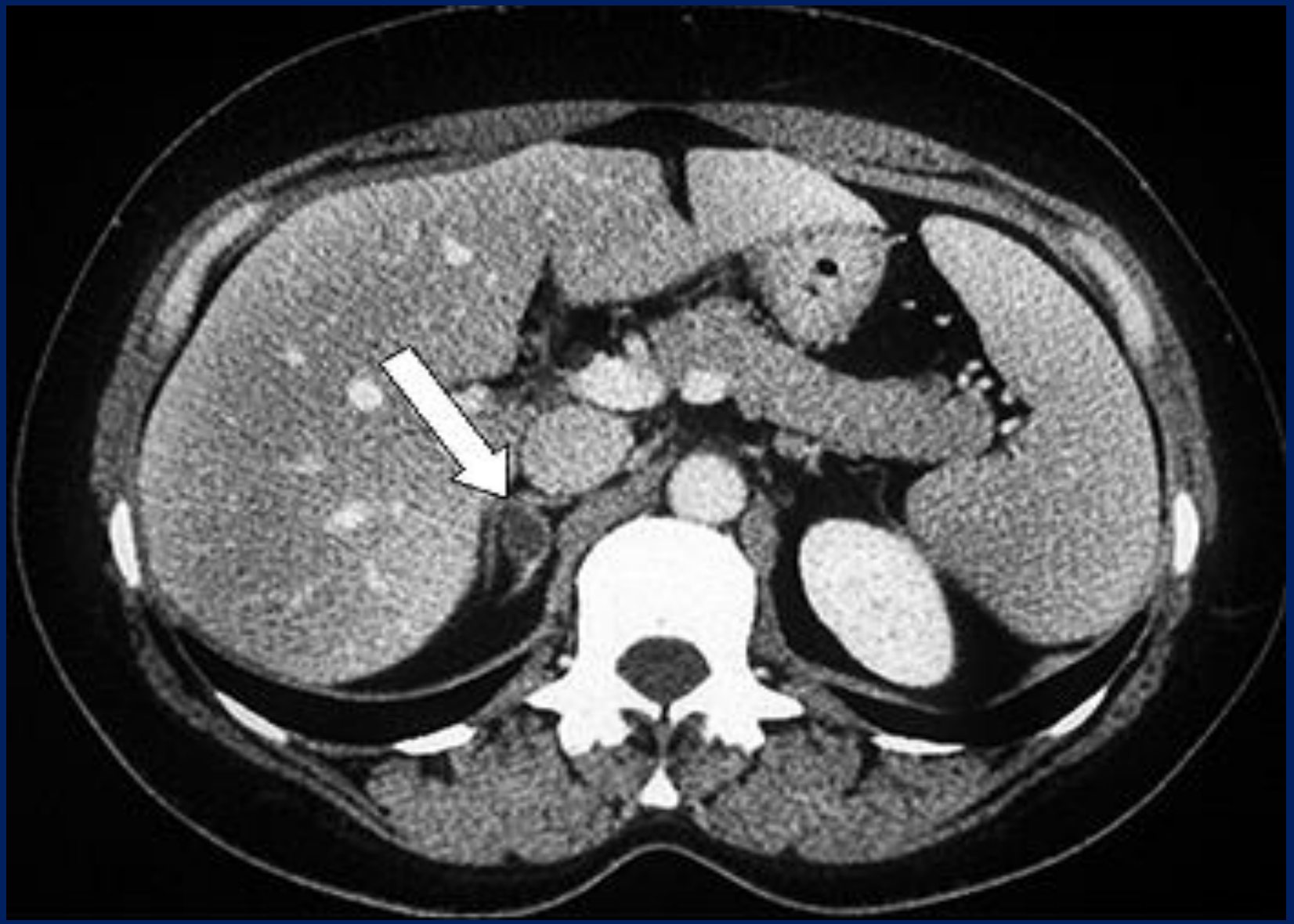
Confirmation

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

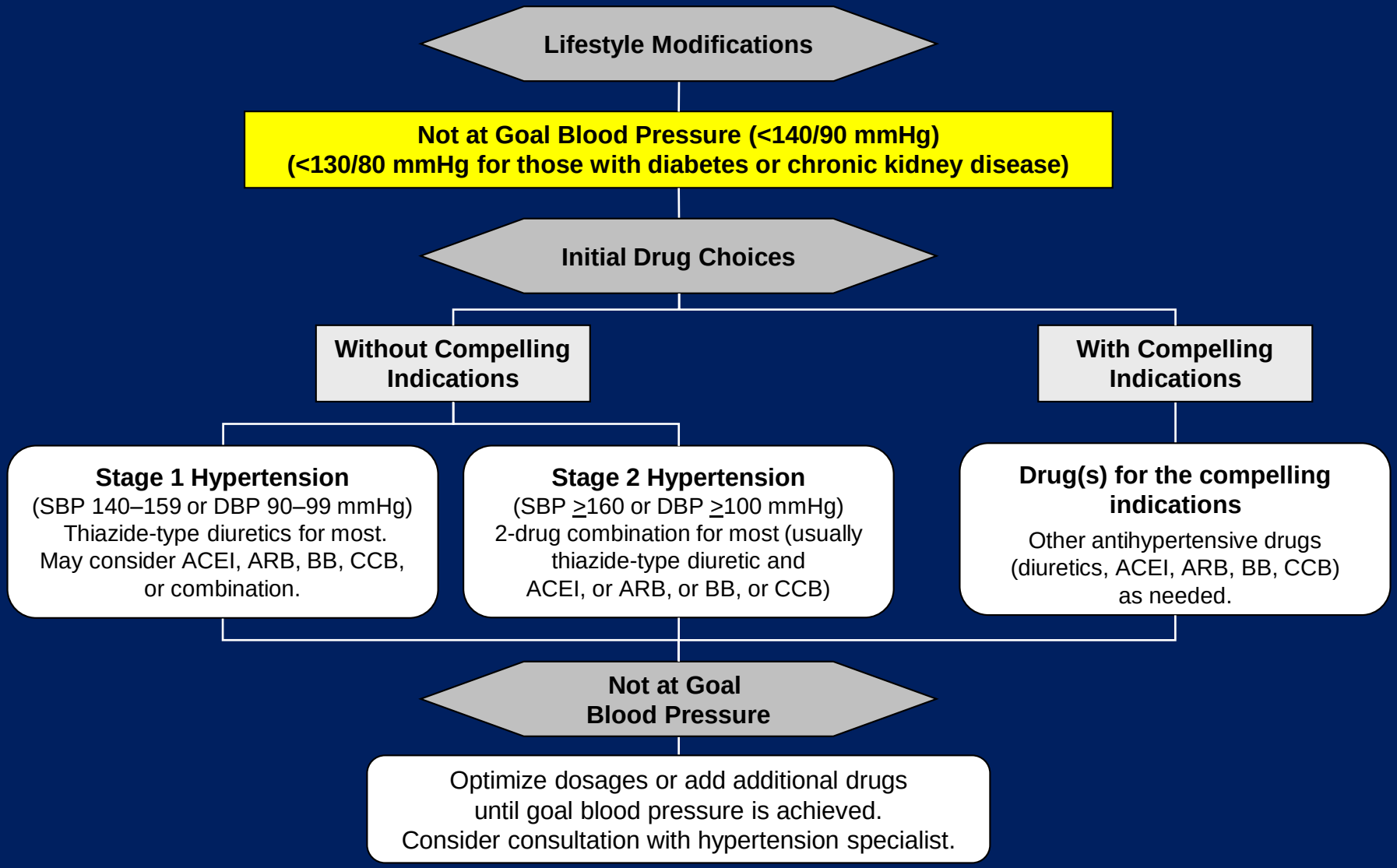
plasma aldosterone after 2000 cc NSS

(<6 nl, > 10 primary aldo)

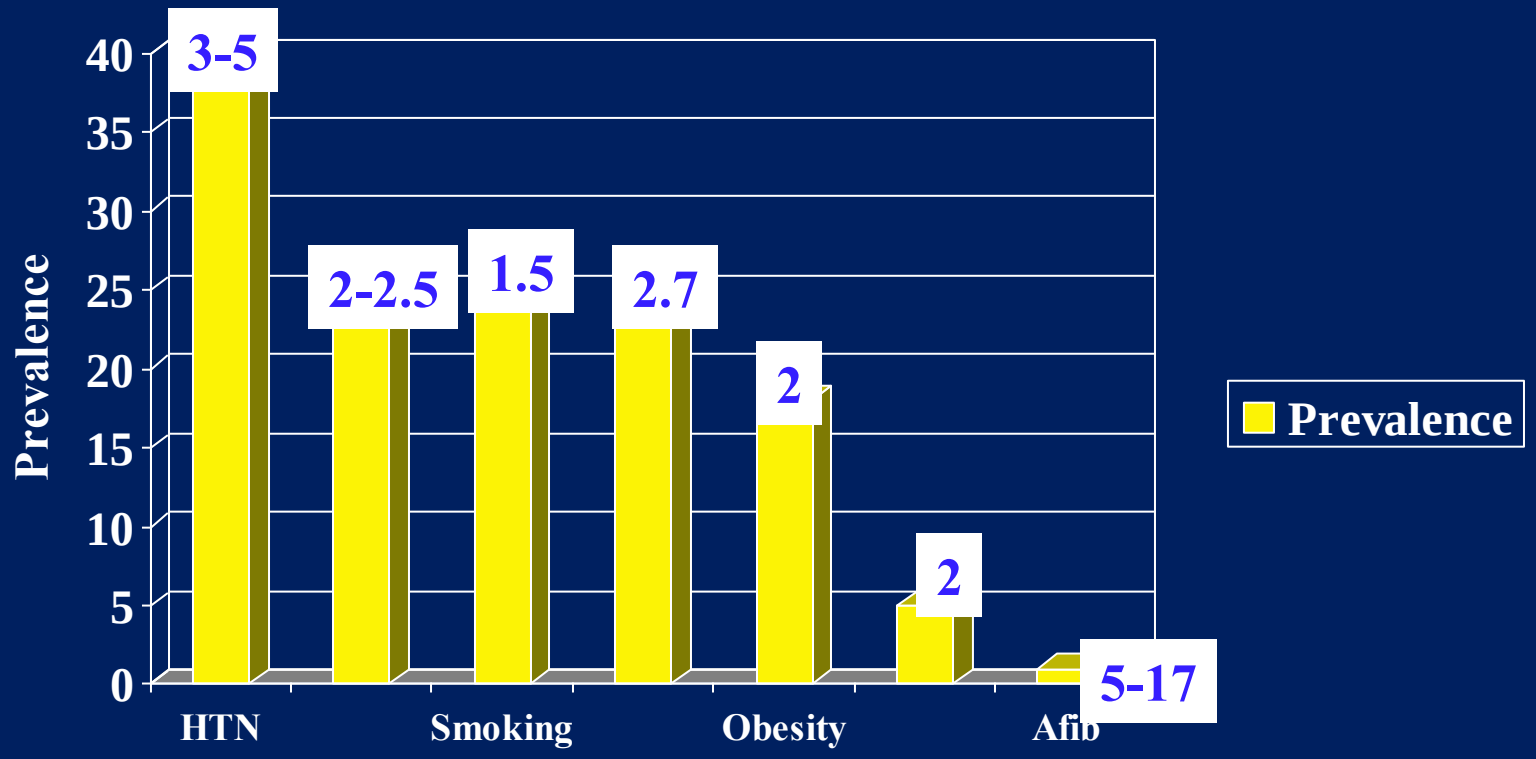
CT – hyperplasia more common than adenoma



Algorithm for Treatment of Hypertension



Importance of Stroke Risk Factors



Primary Prevention

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

Straus et al, JAMA, 2002

Secondary Prevention

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

Lifestyle Modifications

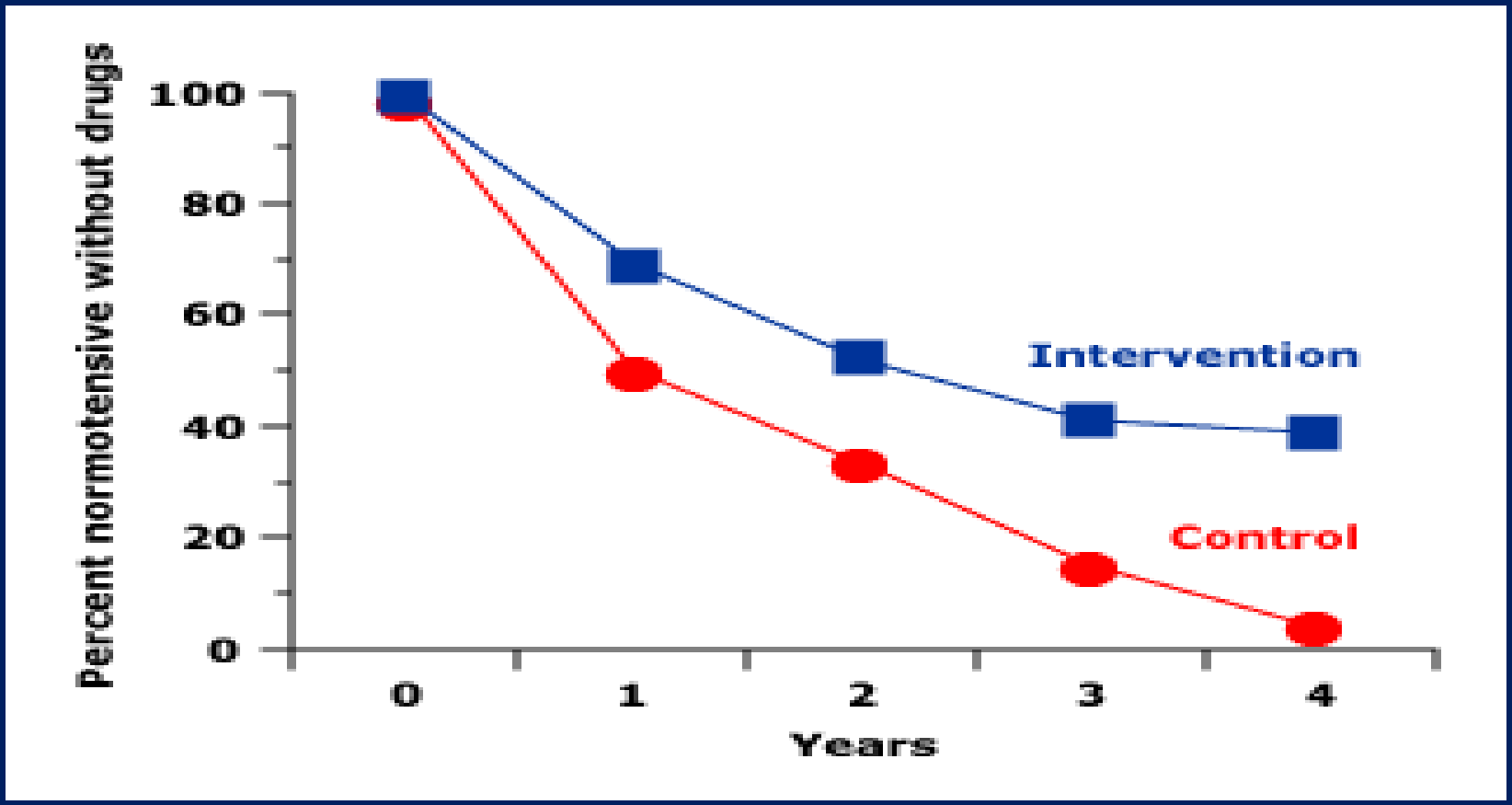
Table 3. Lifestyle Modifications to Manage Hypertension*

Modification	Recommendation	Approximate Systolic BP Reduction, Range
Weight reduction	Maintain normal body weight (BMI, 18.5-24.9)	5-20 mm Hg/10-kg weight loss[2,23]
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8-14 mm Hg[2,19]
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)	2-8 mm Hg[2,24]
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mm Hg[2,8,25]
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter weight persons	2-4 mm Hg[2]

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension.

*For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals.

Diet and HTN


Percent normotensive without drugs
100
80
60
40
20
0
0
1
2
3
4
Years
Intervention
Control

Diet Durability

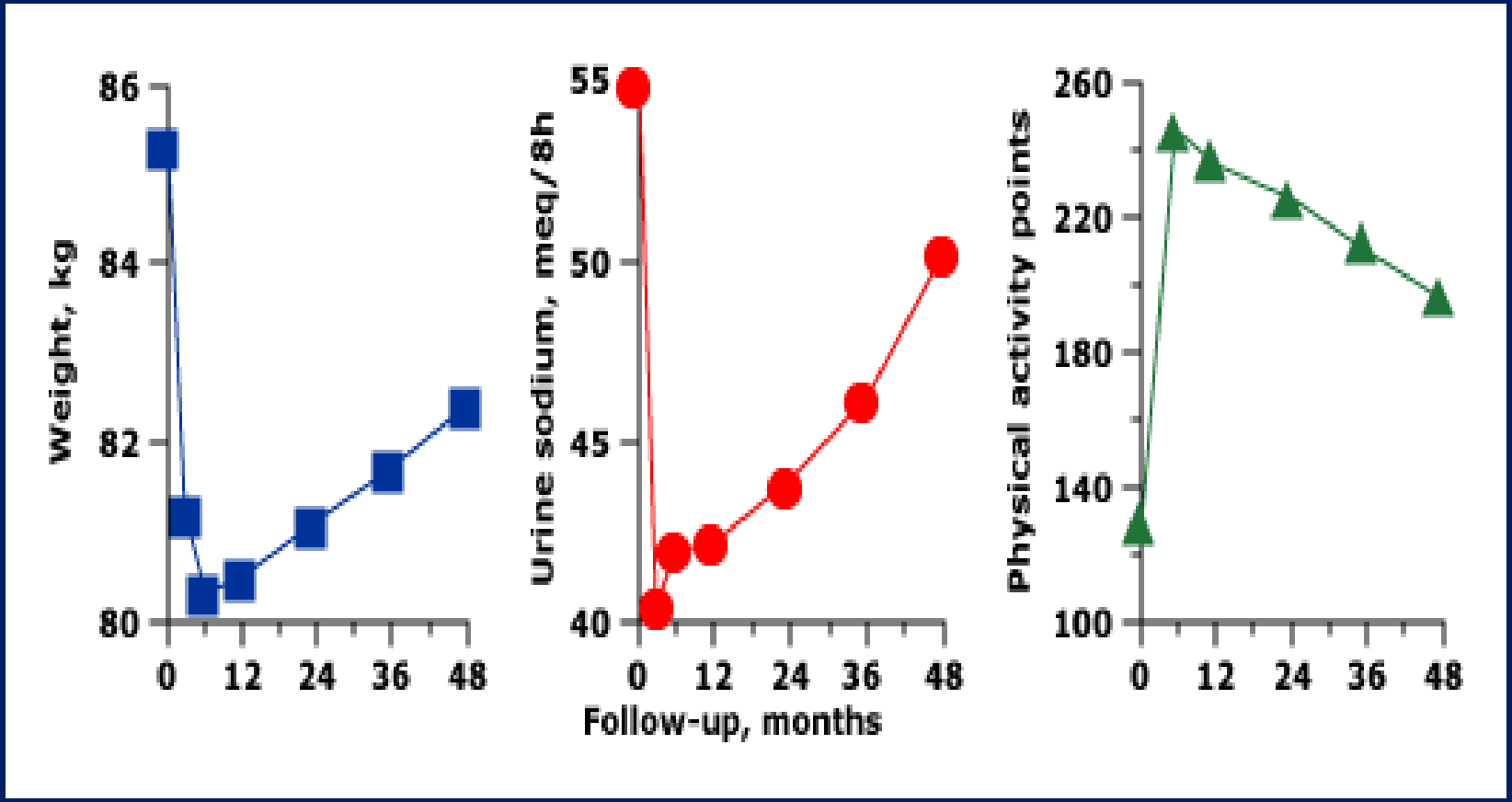


Table 107. Summary of Number of Antihypertensive Agents To Reach Target Blood Pressure*

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.

Antihypertensive Medicine and Risk of Diabetes

Beta blockers and thiazides diuretics increase risk for DMII

ARBs and ACEI decrease risk for DMII

HTN 2010-2016 Update

ONTARGET

SIMPLICITY

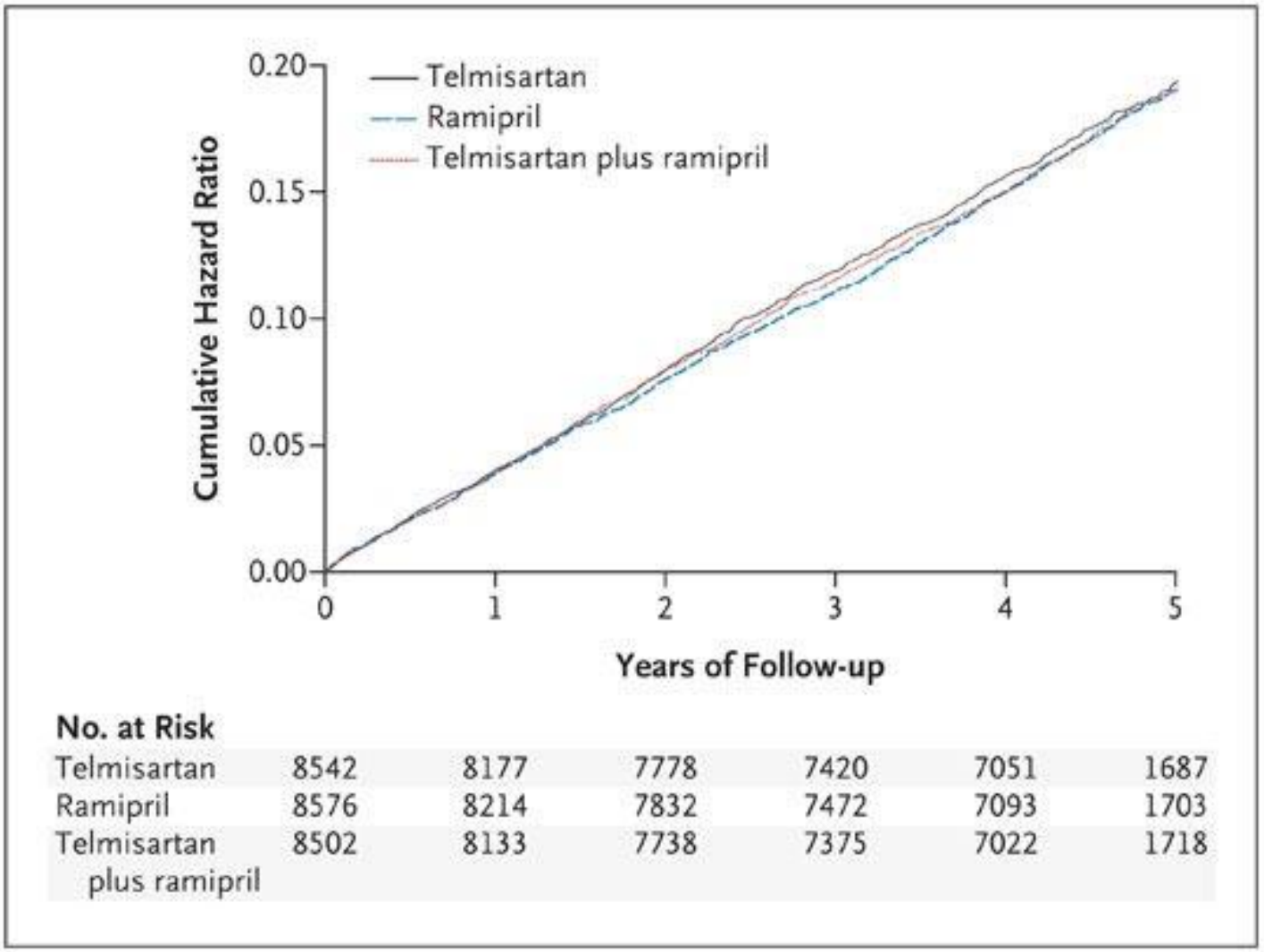
JNC 8

AASK

ACCORD

SPRINT

Kaplan-Meier Curves for the Primary Outcome in the Three Study Groups



No. at Risk						
Telmisartan	8542	8177	7778	7420	7051	1687
Ramipril	8576	8214	7832	7472	7093	1703
Telmisartan plus ramipril	8502	8133	7738	7375	7022	1718

The ONTARGET Investigators. N Engl J Med 2008;358:1547-1559

Conclusion

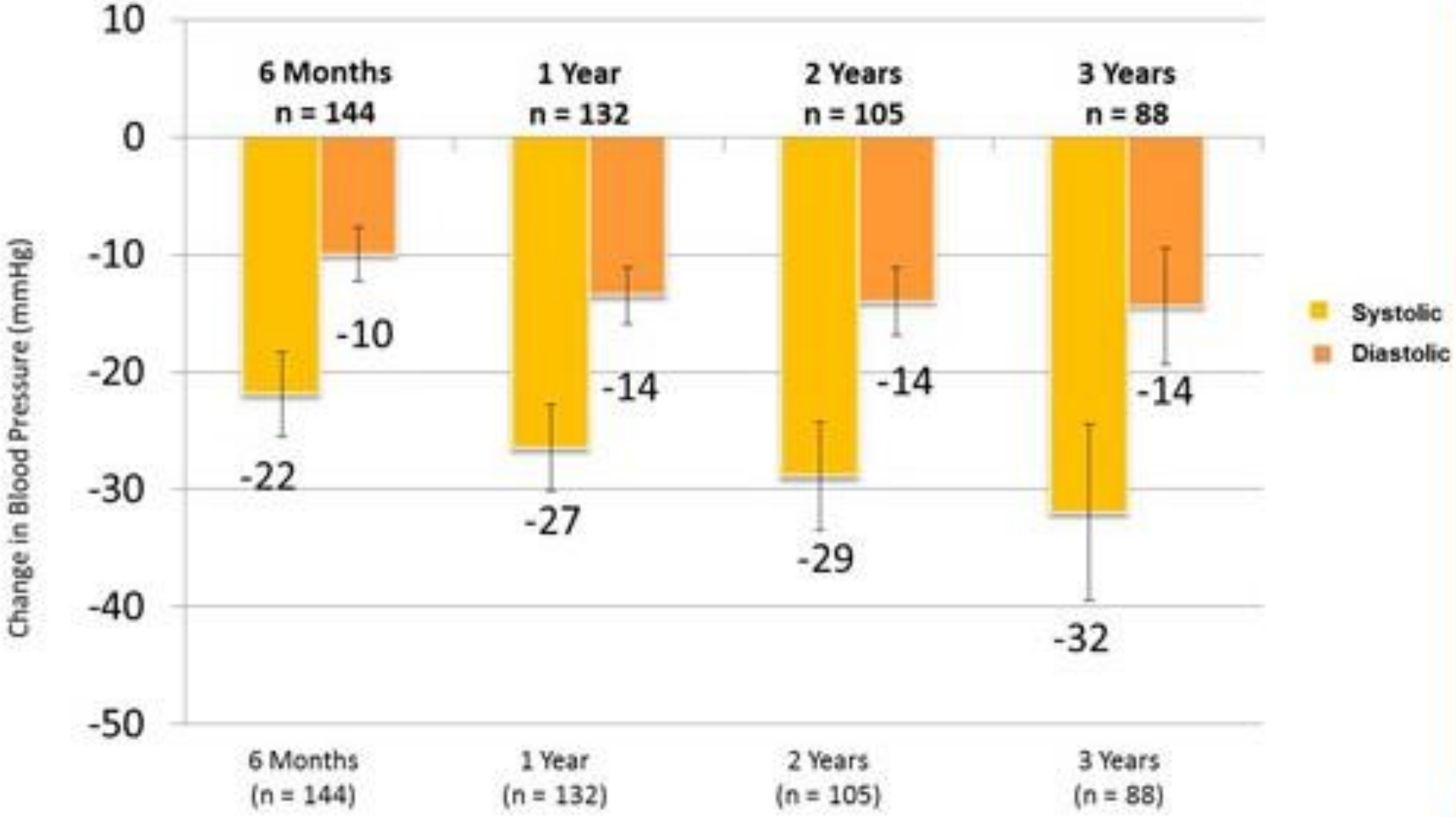
Telmisartan was equivalent to Ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema

The combination of the two drugs was associated with more adverse events without an increase in benefit

SIMPLICITY HTN

- Use of catheter based renal sympathetic nerve ablation
- Already widely used in Europe

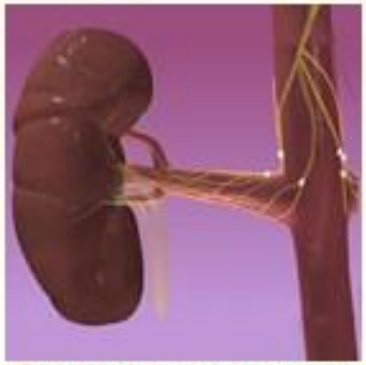
SYMPLICITY HTN-1



p <0.01 for Δ from baseline for all time points.
Data is reported only on the patients available at each time point.

Medtronic's U.S. Renal Denervation Trial Fails to Meet Efficacy Endpoint

Safety Endpoint is Met; All Symplicity Trials Suspended, Pending Review



Renal sympathetic nerves and the kidney

January 9, 2014 -- In a definite blow to the entire field of renal denervation, Medtronic reported this morning that its pivotal U.S. clinical trial for the Symplicity™ Renal Denervation System has failed to meet its endpoint for efficacy.

Pending review by a panel of invited experts, the company has suspended enrollment in all of its renal denervation clinical studies worldwide.

The negative results were posted by Medtronic, prior to presentation at a scientific symposium or publication in a peer-reviewed journal. In a press release, Dr. Rick Kuntz, chief medical officer for Medtronic, stated: "We believe this course of action is the most prudent and will help us thoroughly evaluate these findings and determine the appropriate next steps for renal denervation therapy."

Positive Results and a Hoped-for "Fix" for Treatment-Resistant Hypertension

Renal denervation has been considered to be one of the most highly-anticipated advances for treatment-resistant hypertension: high systolic blood pressure ≥ 160mm Hg that is not reduced, even when three anti-hypertensive drugs are used. The procedure involves threading a special catheter to the renal arteries and utilizing a controlled "burn" to disable the sympathetic nerves that control blood pressure.

A number of worldwide trials have shown positive results for this technology over the past two years. The European Society of Cardiology even authored *a consensus statement* on renal denervation in April 2013.

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

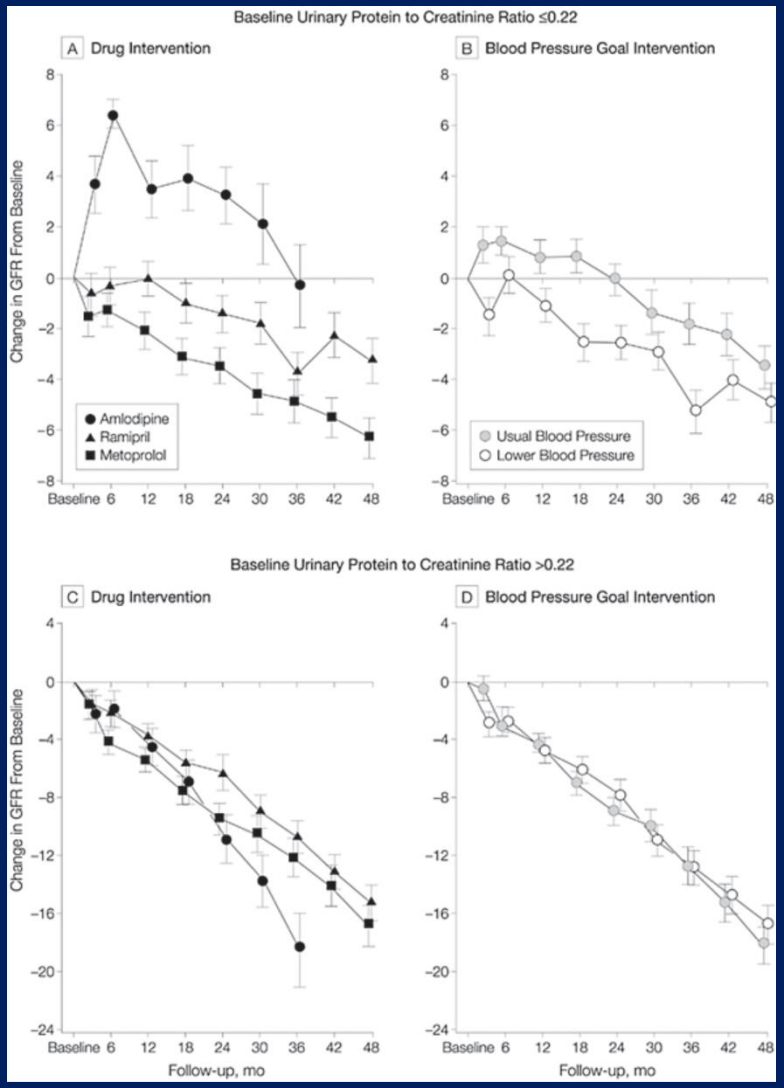
BP Goals

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)

AASK Trial

- Regardless of intervention, CKD progressed in African-American patients
- This was despite good BP control
- Genetic differences – APOL-1 Gene (MYH9 gene (nonmuscle myosin heavy chain)

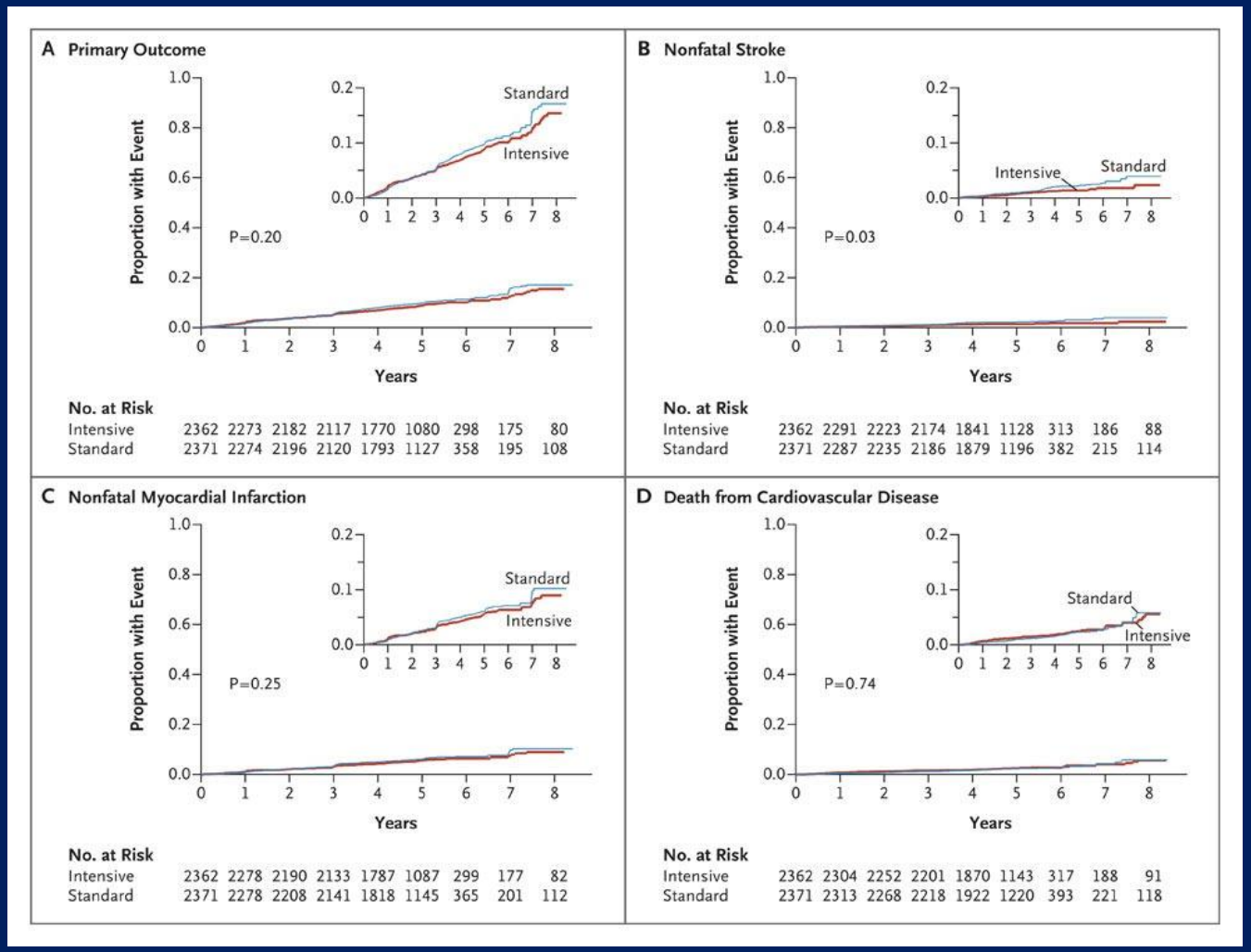
Effect of Blood Pressure Lowering and Antihypertensive Drug Class on Progression of Hypertensive Kidney Disease: Results From the AASK Trial



ACCORD Trial

- DM II patients with HTN and normal GFR and normal albuminuria randomized to SBP control of < 140/ and < 120/ (4733 participants)
- High risk for CV events
- Lower BP did not decrease the risk of fatal and non-fatal CV events
- Lower BP did decrease the incidence of stroke (p 0.001)

Kaplan–Meier Analyses of Selected Outcomes.



The ACCORD Study Group. N Engl J Med 2010;362:1575-1585.

SPRINT Trial

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

Inclusion – HTN and increased CV risk

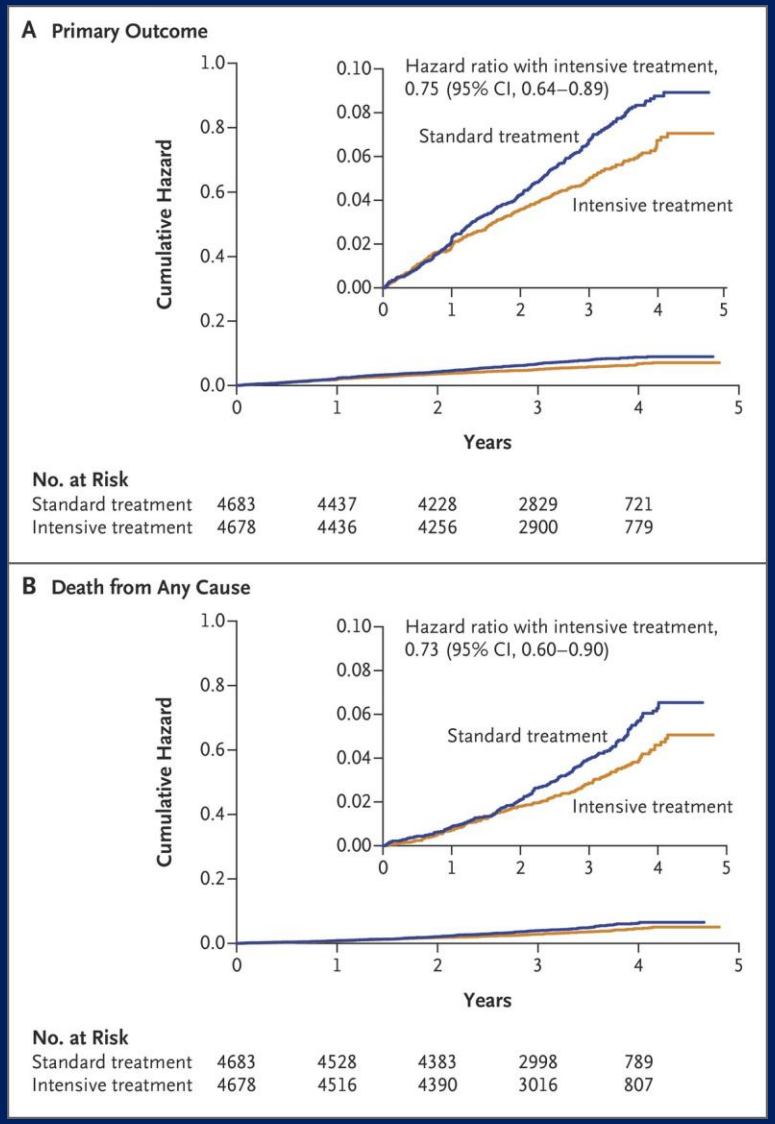
Exclusion =- DM , GFR < 20, ADPCKD, stroke

< 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

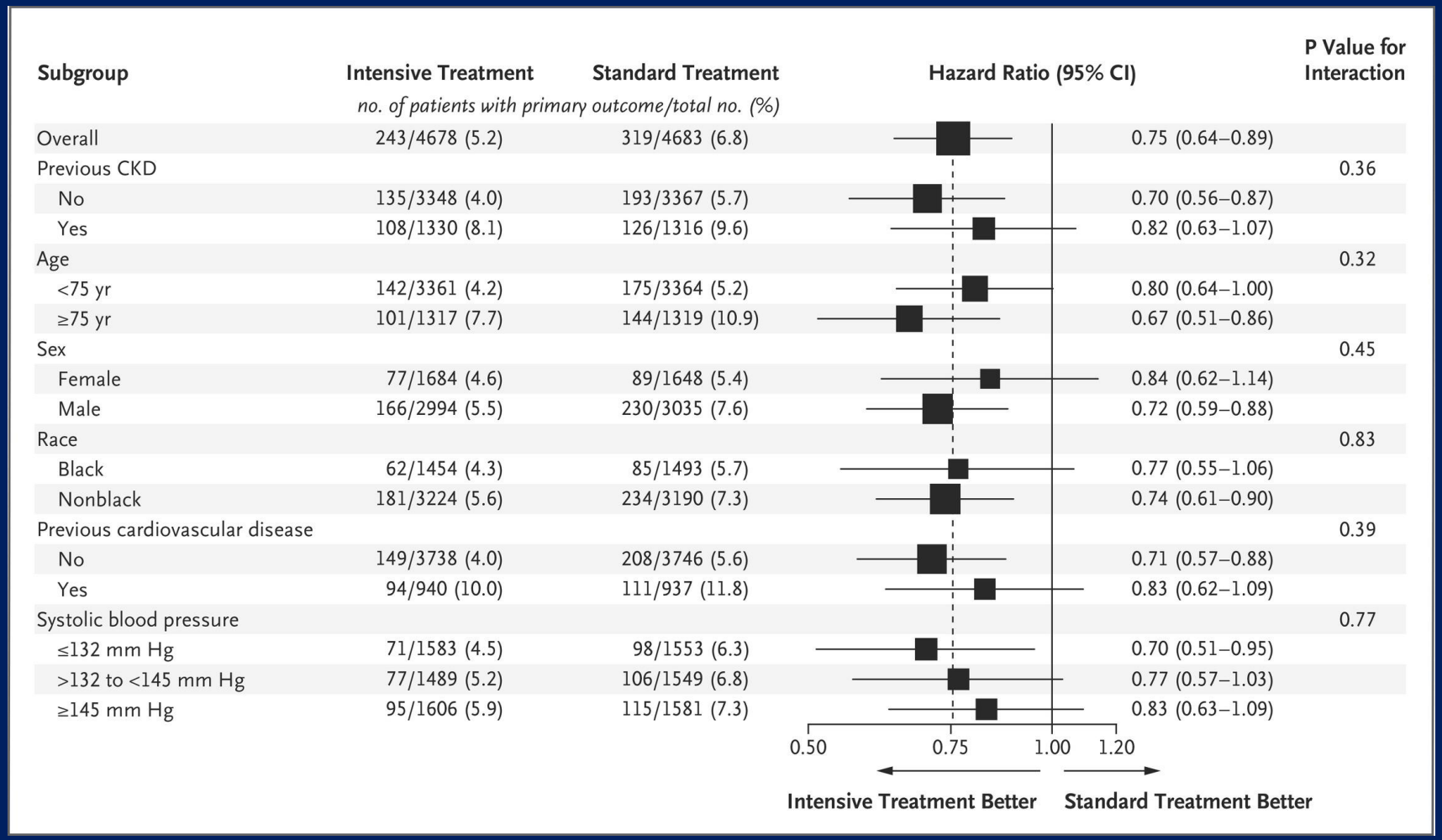
< 120/ resulted in decreased death from CV cause NNT 172

Primary Outcome and Death from Any Cause.



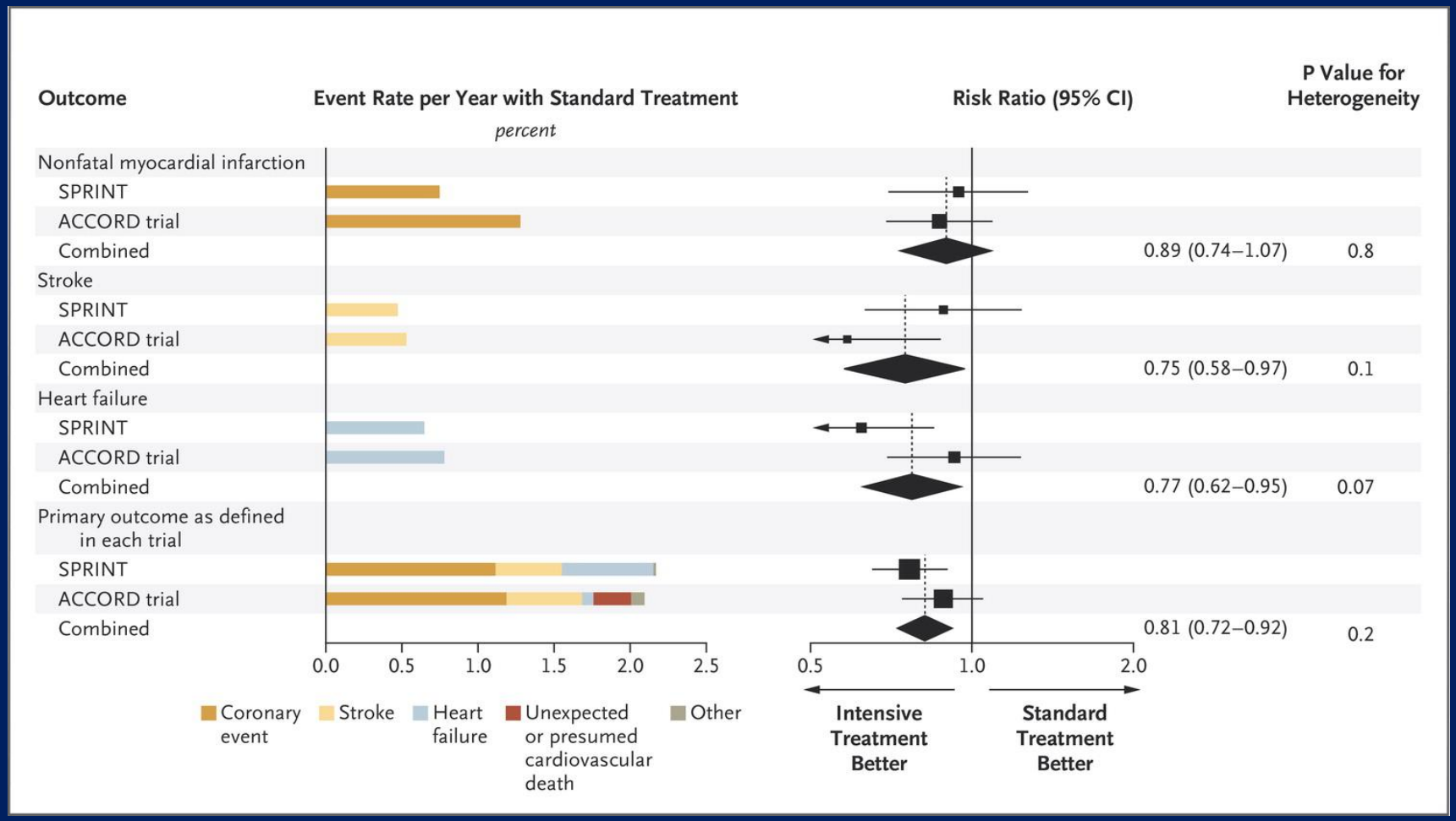
The SPRINT Research Group. N Engl J Med 2015;373:2103-2116

Forest Plot of Primary Outcome According to Subgroups.



The SPRINT Research Group. N Engl J Med 2015;373:2103-2116

Outcomes Data from SPRINT and the ACCORD Trial and Combined Data from Both Trials.



Perkovic V, Rodgers A. N Engl J Med 2015;373:2175-2178.

HTN Treatment Summary

BP Goals - <140/90 in all but elderly (<150/80).
GFR < 60 ml + proteinuria goals < 130/80

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

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