Resistant Hypertension: Evaluation and Management

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- No Disclosure
- No Conflict of interest

Objectives

- Define Resistant Hypertension
- Evaluation of patients with Resistant hypertension
- Explain why is it important
- Management of Resistant Hypertension

Which of the following is NOT a necessary part of the definition of resistant hypertension?

a. An elevated BP on an ambulatory blood pressure monitor.
b. Adherence to the medication regimen.
c. At least three appropriate drugs.
d. Appropriate doses of the appropriate drugs.

Definition

When properly measured blood pressure is above goal on three or more appropriately chosen anti-hypertensives agents administered at appropriate doses including one diuretic.

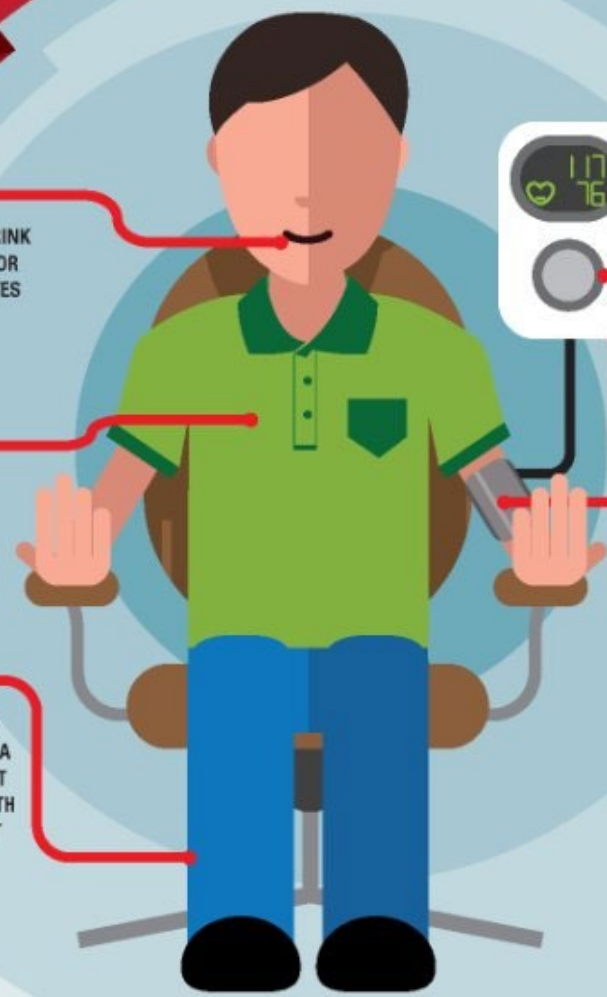
1. Properly measured blood pressure

Office vs ABPM vs at home

Validate Home BP readings by calibrating and checking with office BP monitor.

BLOOD PRESSURE MEASUREMENT INSTRUCTIONS

American Heart Association | American Stroke Association
life is why



DON'T SMOKE, EXERCISE, DRINK CAFFEINATED BEVERAGES OR ALCOHOL WITHIN 30 MINUTES OF MEASUREMENT.

REST IN A CHAIR FOR AT LEAST 5 MINUTES WITH YOUR LEFT ARM RESTING COMFORTABLY ON A FLAT SURFACE AT HEART LEVEL. SIT CALMLY AND DON'T TALK.

MAKE SURE YOU'RE RELAXED. SIT STILL IN A CHAIR WITH YOUR FEET FLAT ON THE FLOOR WITH YOUR BACK STRAIGHT AND SUPPORTED.

TAKE AT LEAST TWO READINGS 1 MIN. APART IN MORNING BEFORE TAKING MEDICATIONS, AND IN EVENING BEFORE DINNER. RECORD ALL RESULTS.

USE PROPERLY CALIBRATED AND VALIDATED INSTRUMENT. CHECK THE CUFF SIZE AND FIT.

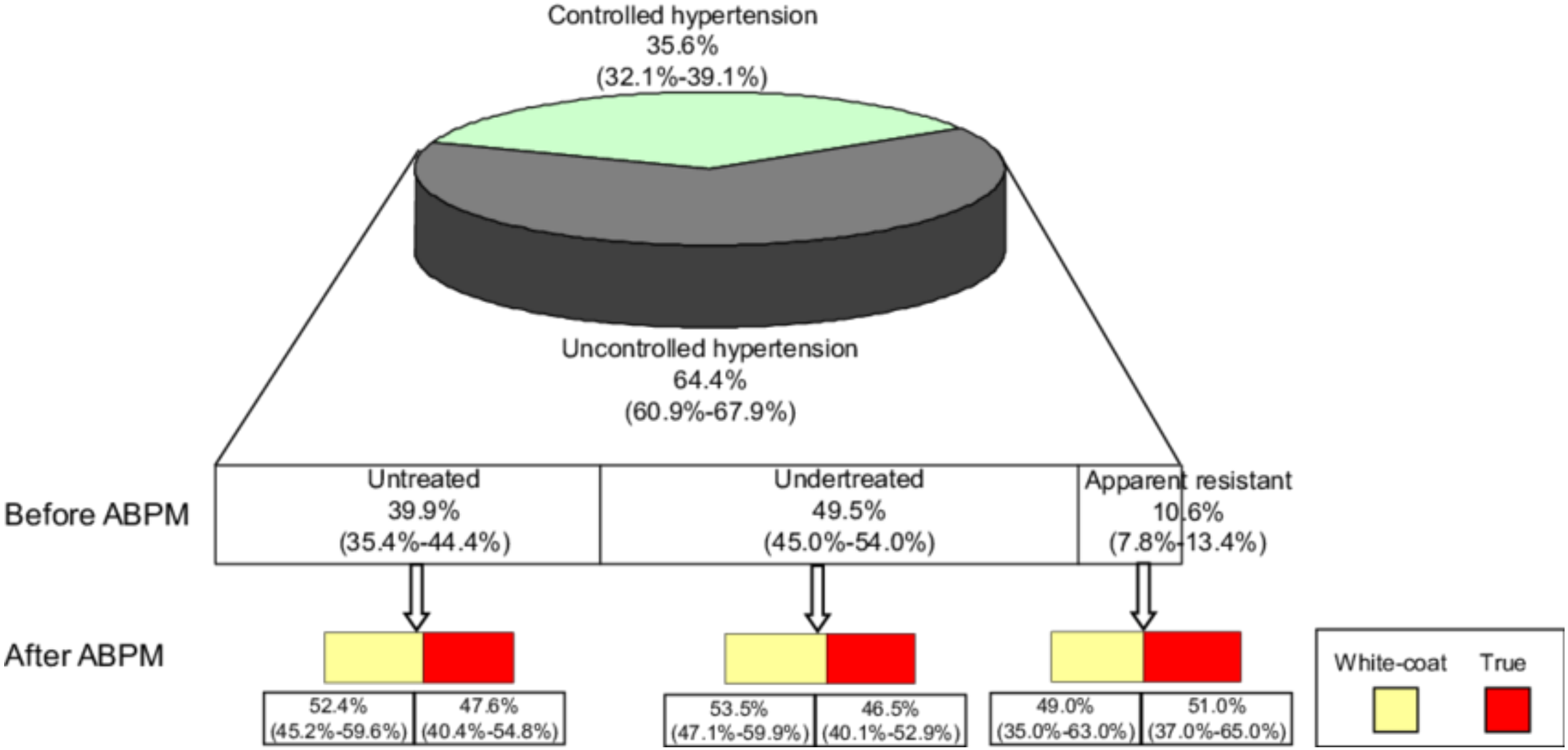
PLACE THE BOTTOM OF THE CUFF ABOVE THE BEND OF THE ELBOW.

Not All Refractory Hypertension is True Treatment-Resistant Hypertension

proposed in a retrospective analysis of patients referred to the University of Alabama at Birmingham Hypertension Clinic whose blood pressure could not be controlled on any antihypertensive regimen.[6] The analysis included 304 consecutive patients referred for uncontrolled resistant hypertension, of whom 29 were identified as having refractory hypertension.

Secondary Hypertension[1]	Pseudoresistance[1,2]	Masked Hypertension[2]	White coat hypertension[2]	True treatment-resistant hypertension*[3]
Hypertension elicited or exacerbated by other drugs or diseases	Apparent hypertension due to lack of adherence, poor BP measurement technique	Clinic BP <140/90 mm Hg; daytime BP >135 or >85 mm Hg	Clinic BP ≥140 or ≥90 mm Hg; daytime BP <135/85 mm Hg	BP ≥140/90 mm Hg despite adequate doses of ≥3 drugs (including diuretic) after exclusion of spurious hypertension

Calhoun et al. Hypertension. 2016;67:1085-1092



Banegas JR et al. Journal of the American Medical Directors Association 16(8) · April 2015

2. Goal BP- Information and guideline overload

- ABPM- average 24 hrs BP >135/85
- <140/90 or <150/90
- <130/80 or <120/80
- Patients with heart failure or coronary artery disease
- Patients with transplants
- African American populations?

3. Appropriately chosen anti-hypertensives agents (≥3) including one diuretic

RAAS blocker + CCB + diuretic

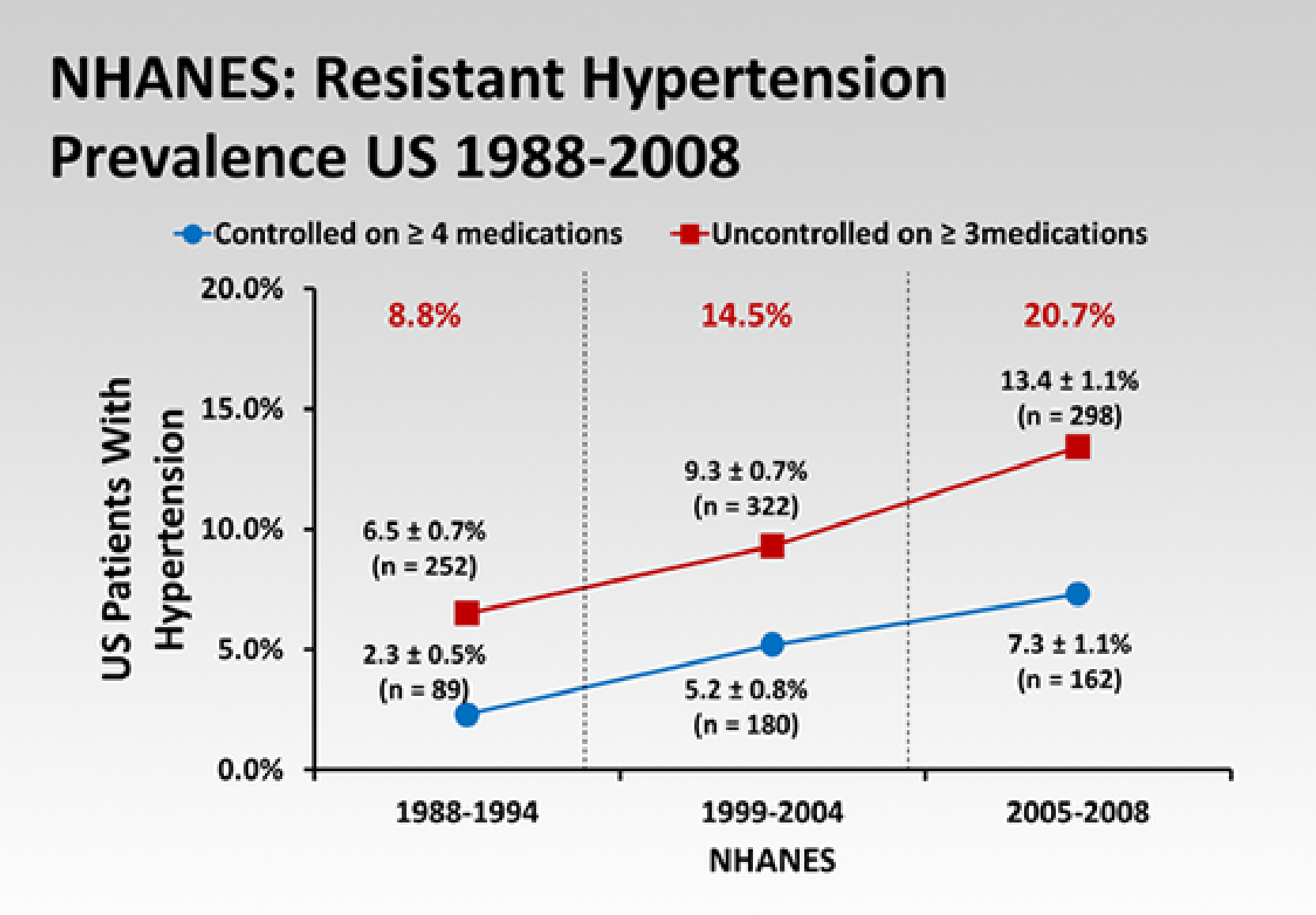
When to use Loop vs thiazide diuretics

Individualized for each patient.

4. Appropriate doses

Maximize to best tolerated doses before adding new agent

PREVALENCE



HYPERTENSION

Roberie DR, et al. *Curr Opin Cardiol*. 2012;27:386-391.[2]

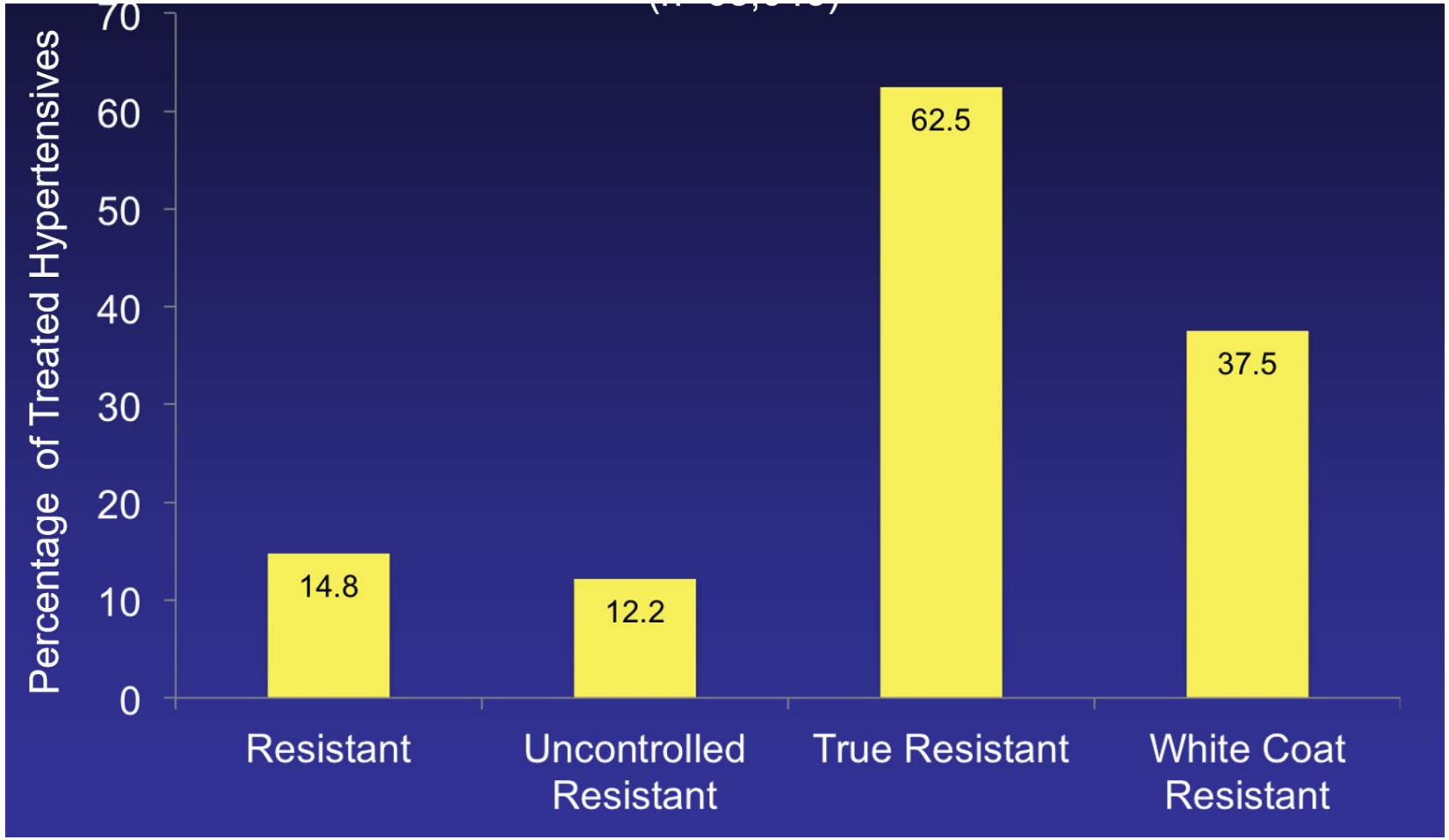
the heart.org

Medscape EDUCATION

Prevalence of Resistant Hypertension in Spain

Spanish APBM Registry 2009

(n=68,045)



De La Sierra, Hypertension 2011

Framingham Heart study – Only 48% controlled BP <140/90.

JNC7 reports higher proportion of uncontrolled patients is higher especially in patients with Diabetes mellitus (DM) or chronic Kidney disease (CKD)

Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) Hypertension. 2014;64:1012–1021

- Among the 14, 684 participants included, 12.7% had apparent Treatment resistant hypertension
- Compared to their counterparts they were more likely to be

  black,

  have less than a high school education

  chronic kidney disease (S Creatinine >1.5mg/dl)

  female

  higher body mass index,

  diabetic

  left ventricular hypertrophy,

  on antihypertensive medication before ALLHAT randomization.

Evaluation Objectives

- Confirm true treatment resistance
  - Patient adherent with 3 or more medications
  - Accurate BP measurement
  - Exclude white coat "resistant hypertension"
- Screen for secondary causes of hypertension
  - Primary aldosteronism
  - Renal artery stenosis
  - Obstructive sleep apnea
- Document degree of target-organ damage
  - LVH, retinopathy, CKD, proteinuria

The most common explanation for why a patient referred to a hypertension specialist for resistant hypertension is:

a. An undiagnosed identifiable cause

b. An incorrect regimen

c. Non–adherence

d. Alcohol excess

BMJ 2012;345:e7473 doi: 10.1136/bmj.e7473 (Published 20 November 2012)

When should patients be referred to a specialist?

- Referral to the appropriate specialist is warranted when the history, examination, and initial screening tests suggest a secondary cause of resistant hypertension—refer to the clinical evaluation algorithm in the supplementary material on bmj.com
- Individuals under 40 years old,
- Difficulty in interpretation of office and ambulatory or home blood pressure measurements
- Difficulty in differentiating pseudo-resistant from true resistant hypertension
- Difficulty in controlling blood pressure despite an assessment of adherence to treatment, modification of lifestyle factors, and appropriate intensification of combination therapy over a six month period
- Difficulty in finding a well tolerated drug regimen
- Those who have evidence of target organ damage or clinical manifestations of cardiovascular disease
- For consideration of device therapy to control blood pressure when all drug interventions have been exhausted

PSEUDORESISTANCE HYPERTENSION

POOR BP MONITORING

POOR ADHERENCE

WHITE COAT EFFECT

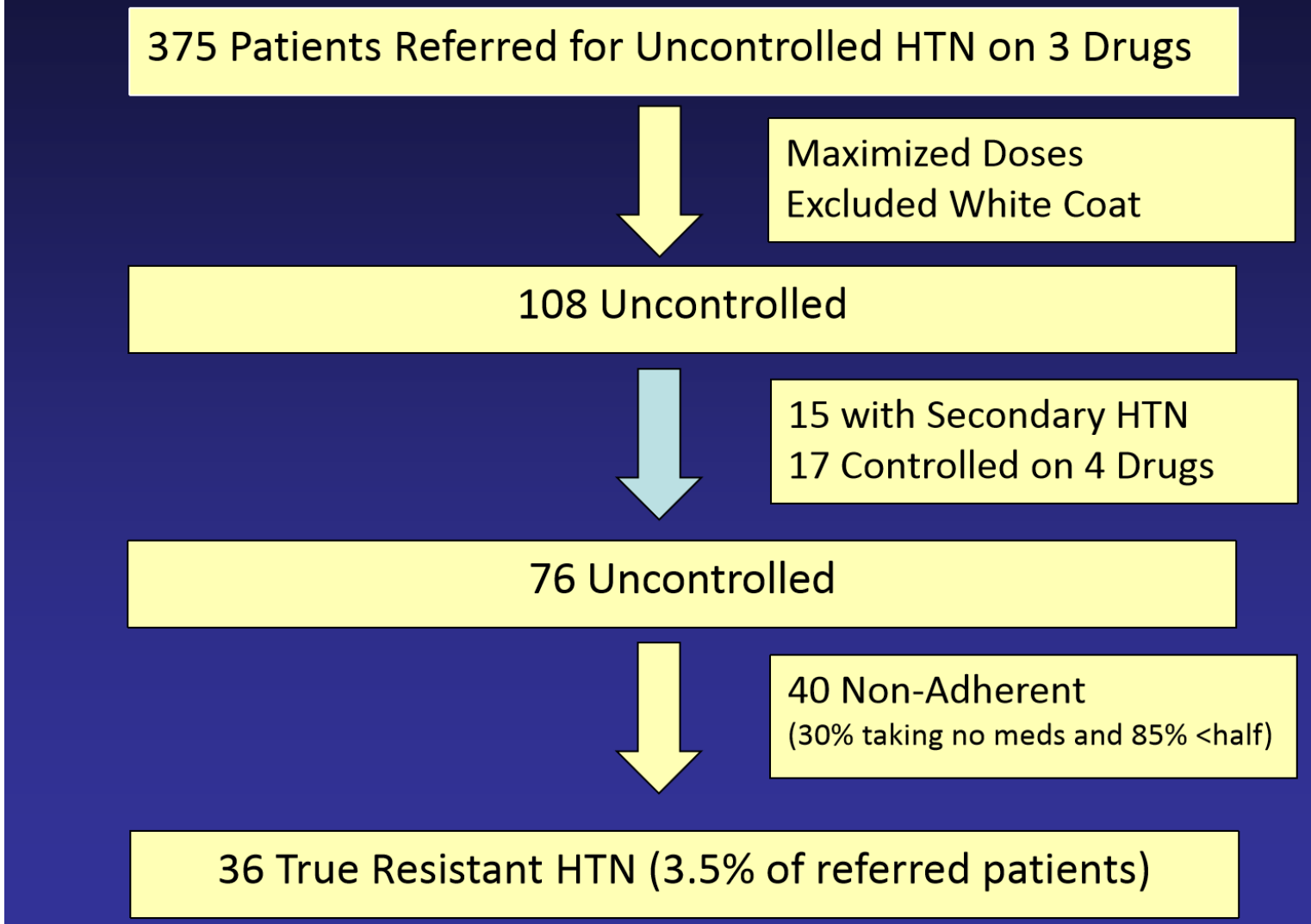
Most common reason for resistant hypertension

Non adherence

- Non compliance
- Doses too low
- Inappropriate combinations
- Other drugs/ herbal supplements
- Cost and access
- Fragmented care
- Complicated regimens

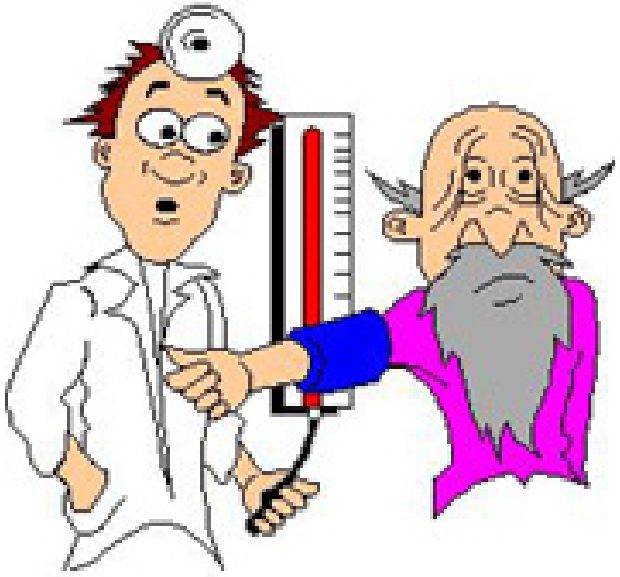
Resistant hypertension? Assessment of adherence by toxicological urine analysis

Oliver Jung[a], Janis L. Gechter[a], Cora Wunder[b], Alexander Paulke[b], Christine Bartel[a], Helmut Geiger[a], and Stefan W. Toennes[b]



J Hypertension 2013

White coat Hypertension



- 20-30% in general population with hypertension. *
- These patients manifest less severe target organ damage and are at less risk for cardiovascular risk compared to persistently hypertensive patients. #

*Brown et al, Am J Hypertens. 2001;14:1263-69 and Hermida et al. Hypertension 2005;46:1053-59
#Mezzeti et al Am J Hypertens2005;18:1422-28; Salles et al, Bloo Press Moni 2003;8:181-85

Life style factors

OBESITY

DIETARY SALT

ALCOHOL

ANXIETY/ STRESS

Which of the following are commonly used substances that can raise blood pressure and may explain why a patient is a resistant hypertensive?

a. Anti–inflammatory agents

b. Erythropoietin

c. Corticosteroids

d. All of the above

Interfering substances/ medications

Amphetamines
Anabolic steroids
Anti–inflammatory agents
Appetite suppressants
Caffeine
Cocaine
Corticosteroids
Cyclooxygenase–2 inhibitors
Cyclosporine
Erythropoietin
Ephedra (ma huang)
Ethanol
Ginseng
Guarana
Licorice (natural licorice, herbal remedies, and chewing tobacco)
Monoamine oxidase inhibitors
Neosynephrine
Nicotine
Oral contraceptives
Phenylephrine
Phenylpropanolamine
Pseudoephedrine
Sibutramine
Sodium chloride
Sympathomimetics
Tacrolimus
Venlafaxine
Yohimbine

NSAIDs Most common offending agents

- Avg increase in BP by approx. 5mmHg
- Blunts effect of other BP meds including diuretics, RAAS blockers and beta blockers. *
- Cox-2 inhibitors have similar effects. #

* Day et al, Ann Int Med 1994;121;289-300; Bloomfield et al Ann Int Med 1987;107;628-635; Conlin et al Hypertension 2000; 36;461-465;

Whelton et al Am J Cardiol 2002;90;959-963; White et al Hypertension. 2002;39; 929-34

Secondary Causes of Resistant Hypertension

Common

- Obstructive sleep apnea
- Renal parenchymal diseas
- Primary hyperaldosteronism
- Renal artery stenosis

Uncommon

- Pheochromocytoma
- Cushing’s disease
- Hyperthyroidism
- Aortic coarctation
- Intracranial Tumor

The most common cause for hypertension with an identifiable cause is:

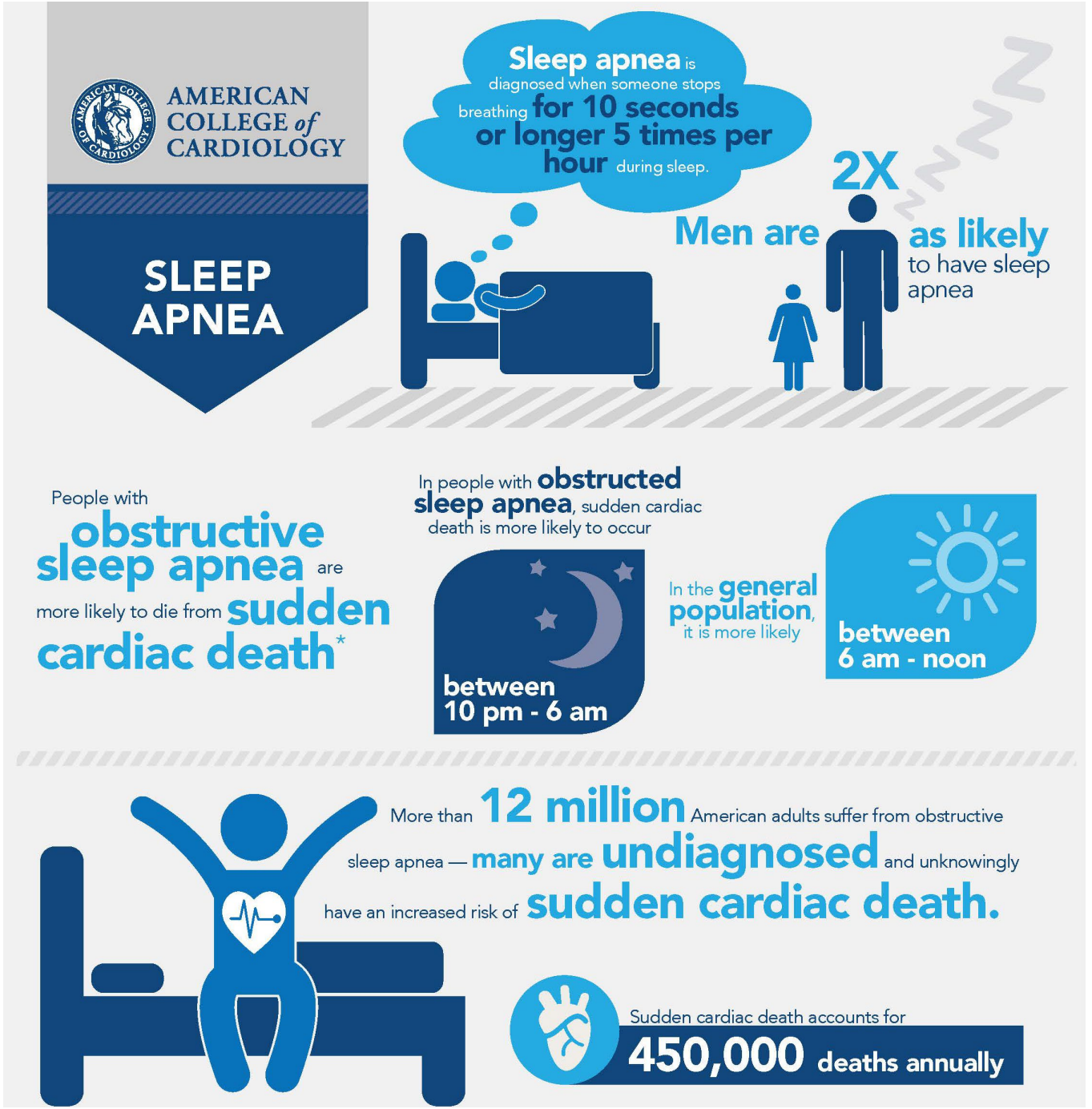
a. Pheochromocytoma

b. Renovascular hypertension

c. Chronic kidney disease

d. Mineralocorticoid excess syndromes

Obstructive Sleep Apnea



Obstructive Sleep Apnea: Mechanism

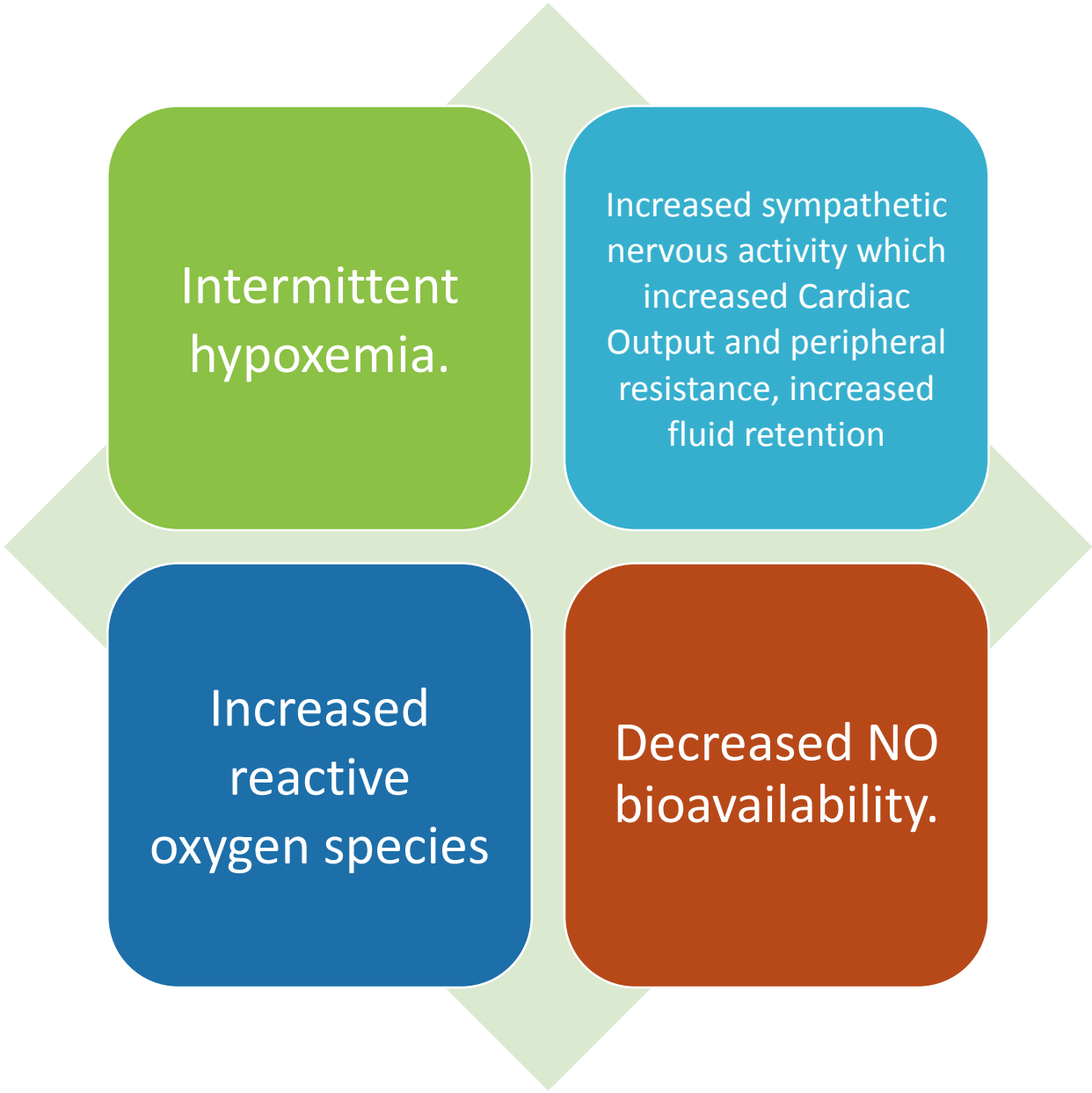


TABLE 3. ADJUSTED ODDS RATIOS FOR HYPERTENSION AT A FOLLOW-UP SLEEP STUDY, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

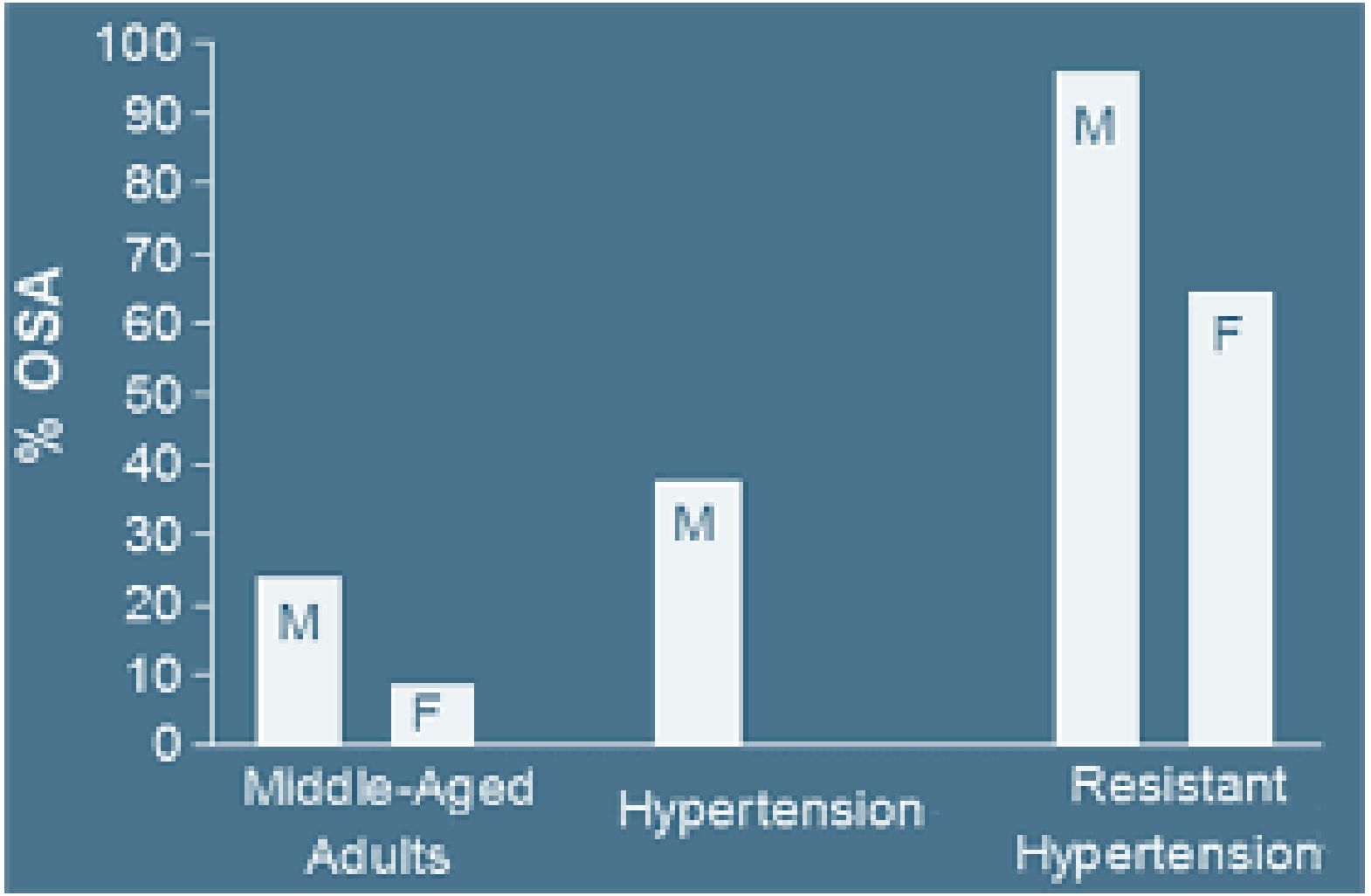
BASE-LINE APNEA–HYPOPNEA INDEX	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS AND NONMODIFIABLE RISK FACTORS (AGE AND SEX)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, AND HABITUS (BMI AND WAIST AND NECK CIRCUMFERENCE)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, HABITUS, AND WEEKLY ALCOHOL AND CIGARETTE USE
	odds ratio (95% confidence interval)			
0 events/hr†	1.0	1.0	1.0	1.0
0.1–4.9 events/hr	1.66 (1.35–2.03)	1.65 (1.33–2.04)	1.42 (1.14–1.78)	1.42 (1.13–1.78)
5.0–14.9 events/hr	2.74 (1.82–4.12)	2.71 (1.78–4.14)	2.03 (1.29–3.19)	2.03 (1.29–3.17)
≥15.0 events/hr	4.54 (2.46–8.36)	4.47 (2.37–8.43)	2.89 (1.47–5.69)	2.89 (1.46–5.64)
P for trend‡	<0.001	<0.001	0.002	0.002

*Hypertension was defined as a blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications. Data on 893 follow-up sleep studies from 709 participants were analyzed. The odds ratios and confidence intervals were adjusted for the fact that 184 participants completed two follow-up sleep studies. BMI denotes body-mass index.

†This category served as the reference group.

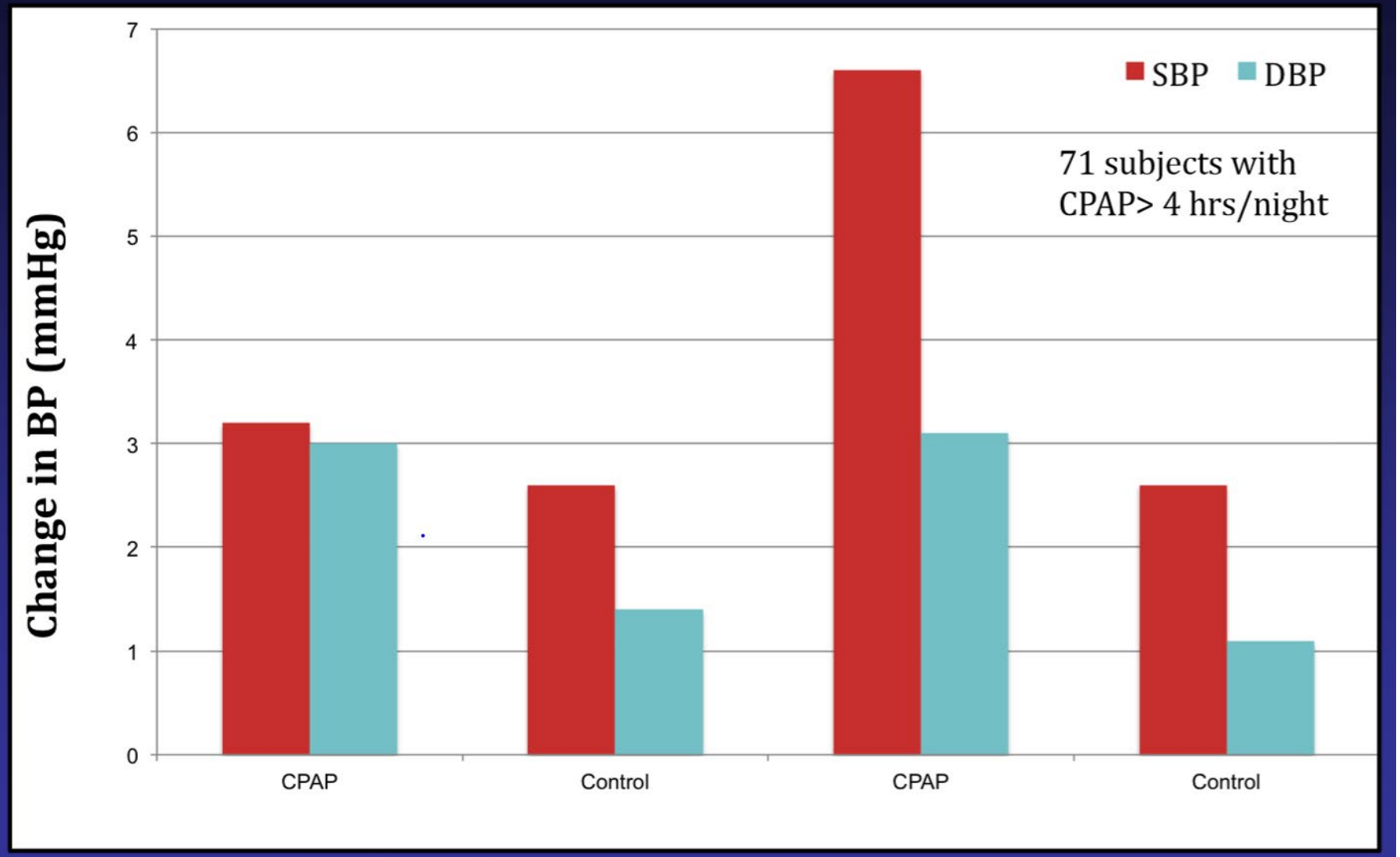
‡P values are for the linear trend of the logistic-regression coefficients ($\log_e$ of the odds ratios).

N Engl J Med 2000; 342:1378-1384



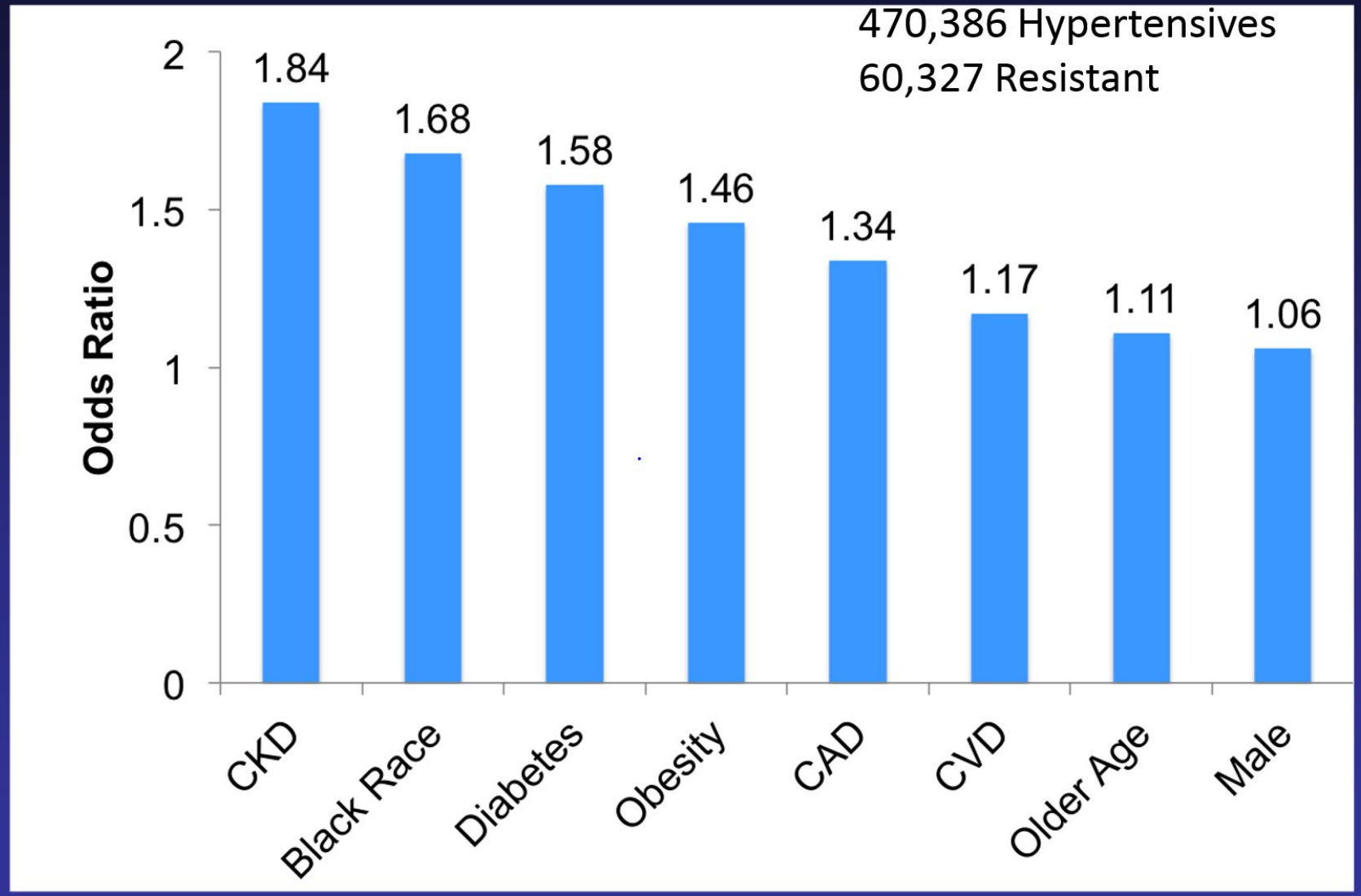
Logan et al J Hypertension 2001

Effect of CPAP on BP in Patients with OSA and Resistant HTN



Martinez-Garcia, JAMA 2013

Risk Factors for Having Resistant Hypertension
Kaiser-Permanente Southern California



Sim et al., Mayo Clinic Proceedings 2013

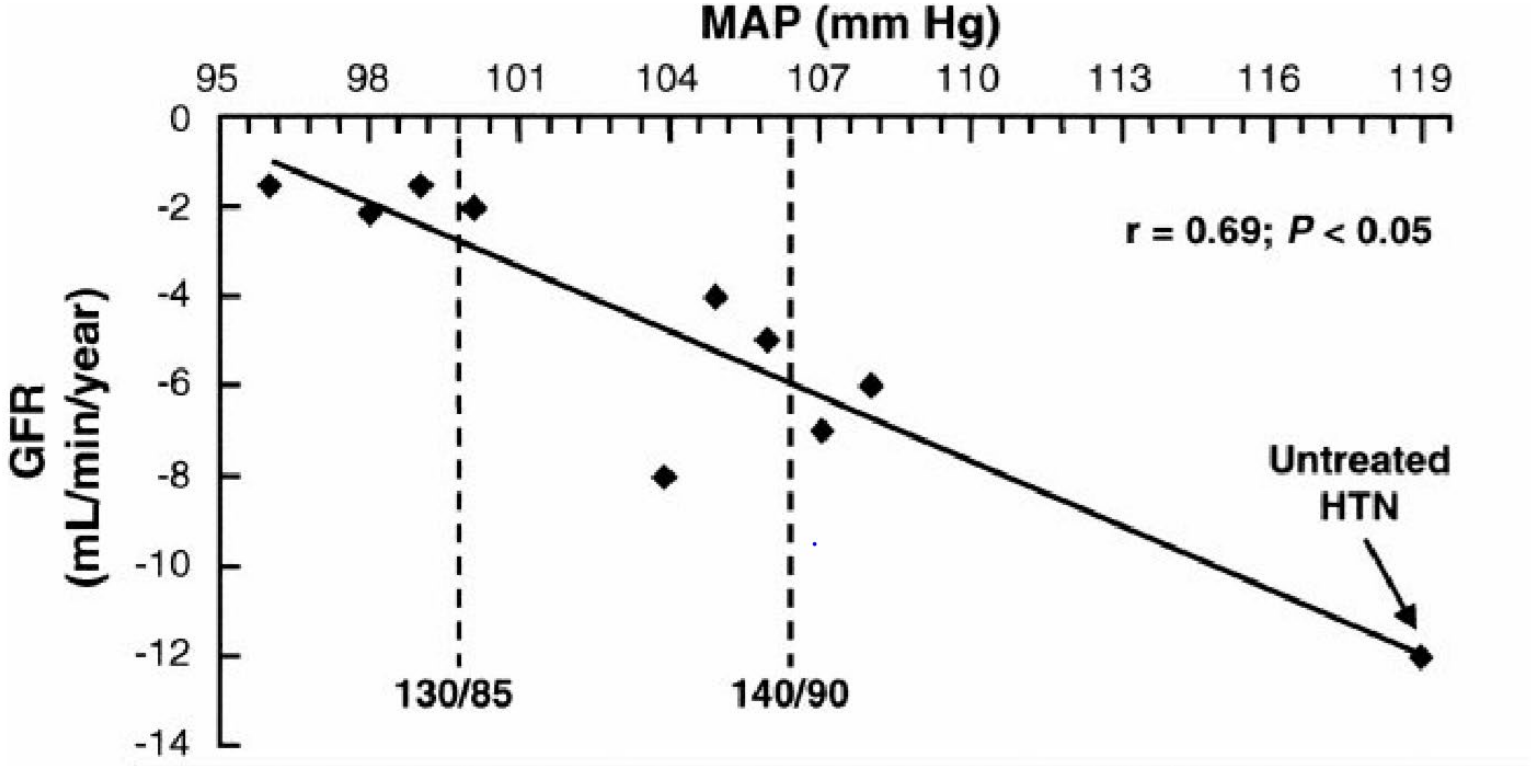
Renal Parenchymal Disease

Cause and effect

NHANES data- 3% have creatinine >1.6mg/dl making 5.6 million of gen population. 75% of these were on anti hypertensive medications. (*Coresh et al, Arch Internal Medicine. 2001; 161:1207-16*)

ALLHAT trial, CKD was strong predictor of failure to achieve goal blood pressure (*Cushman et al, J Clin Hypertens, 2002; 4:393-404*)

Lowering Blood pressure slows progression of chronic kidney disease



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*

Fig 3. Relationship between achieved blood pressure control and declines in GFR in clinical trials of diabetic and nondiabetic renal disease.[30] In the table, the trials marked by an asterisk are those in nondiabetic renal disease patients.

Primary Hyperaldosteronism

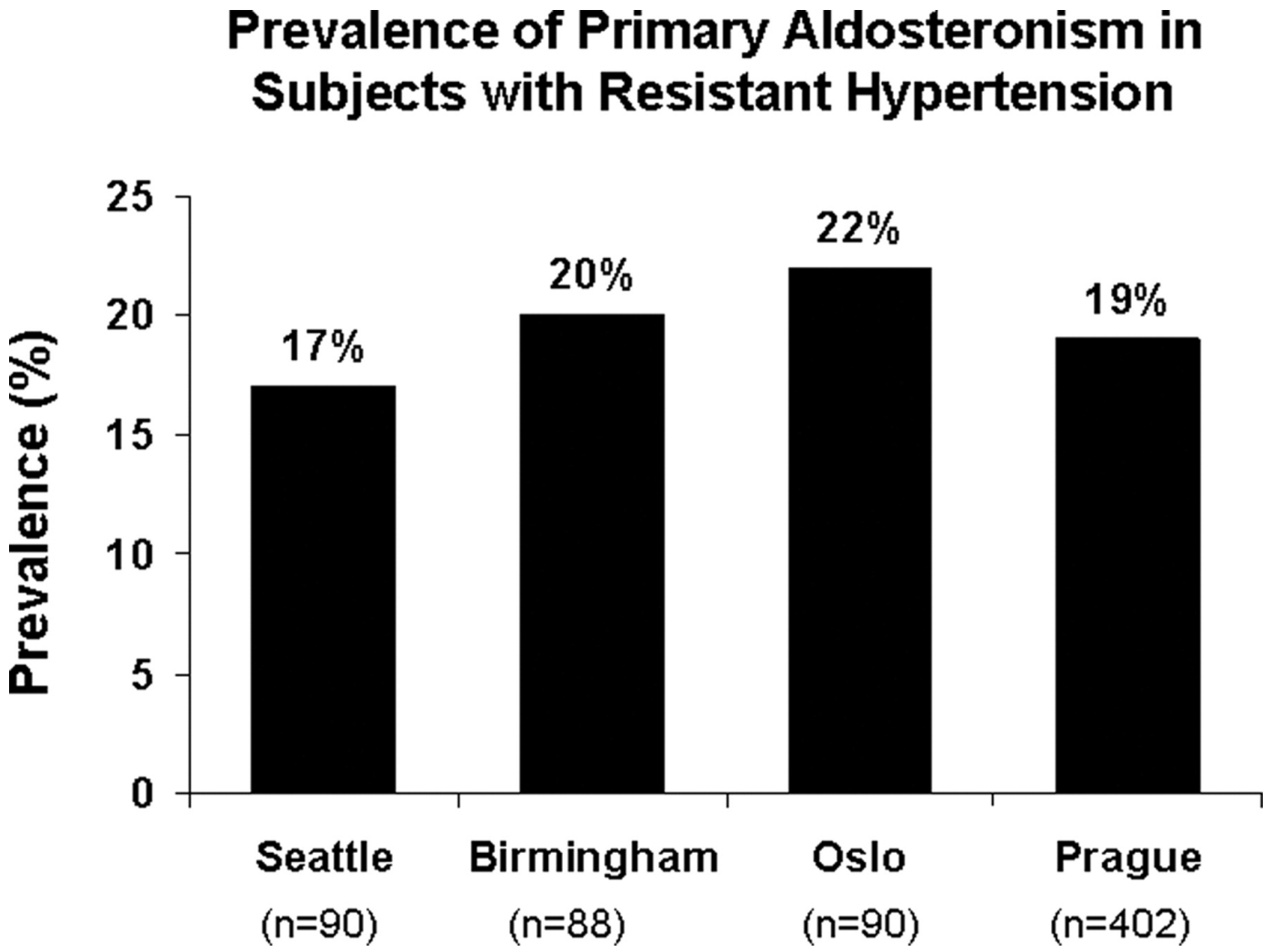
- At least 11.2% of consecutive patients with newly diagnosed hypertension who are referred to hypertension centers.

Table 2 Conditions that should trigger the search for primary aldosteronism in a hypertensive patient

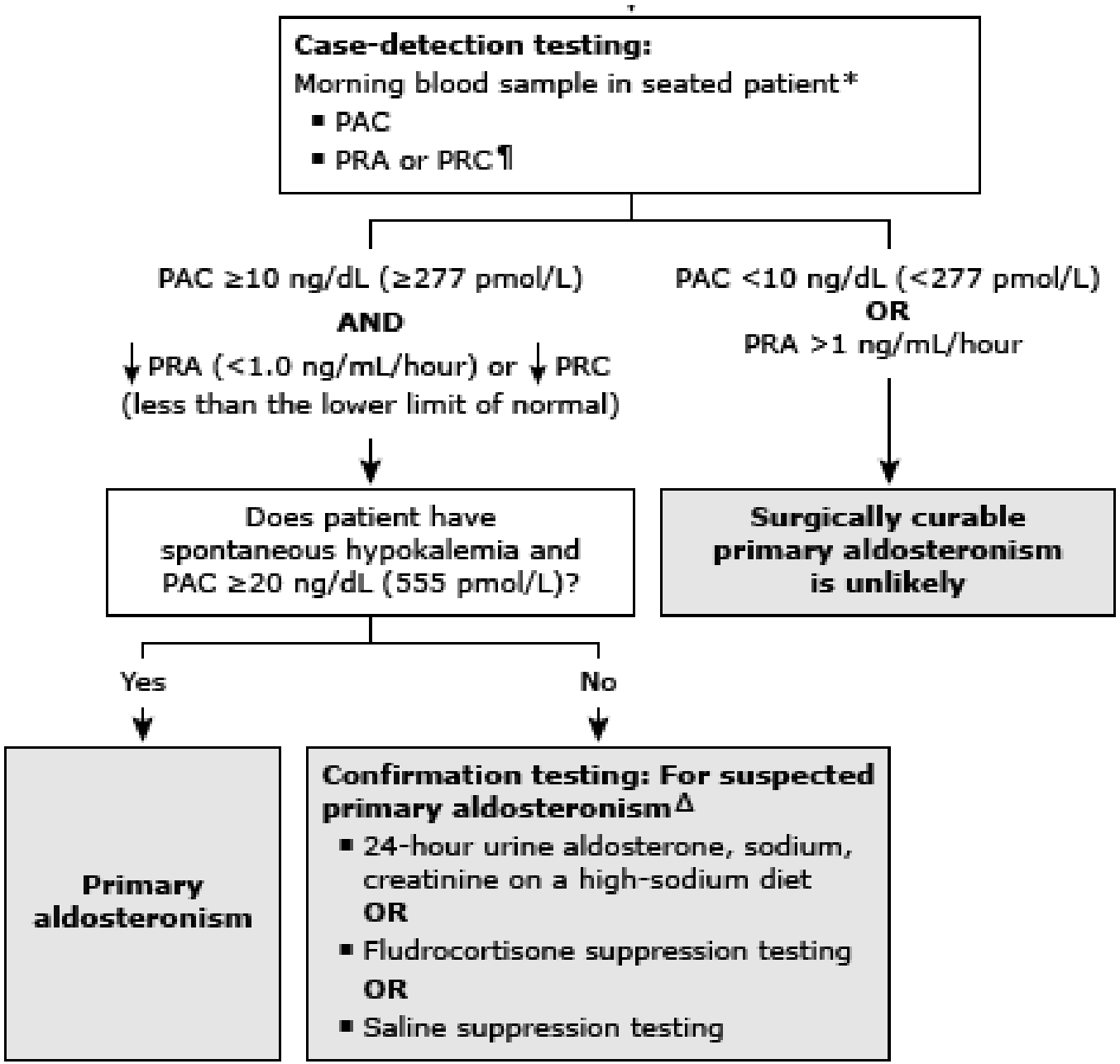
- Hypokalemia (spontaneous or diuretic-induced)
- Resistant hypertension; grade 2 or 3 hypertension
- Early-onset (juvenile) hypertension and/or stroke (<50 years)
- First-degree relatives of patients with primary aldosteronism
- Incidentally discovered, apparently nonfunctioning adrenal mass ("incidentaloma")
- Evidence of organ damage (left ventricular hypertrophy, diastolic dysfunction, AV block, carotid atherosclerosis, microalbuminuria, endothelial dysfunction), particularly if disproportionate for the severity of hypertension
- Obstructive sleep apnea syndrome
- Overweight/obesity

Rossi, G.P. Curr Hypertens Rep (2010) 12: 342

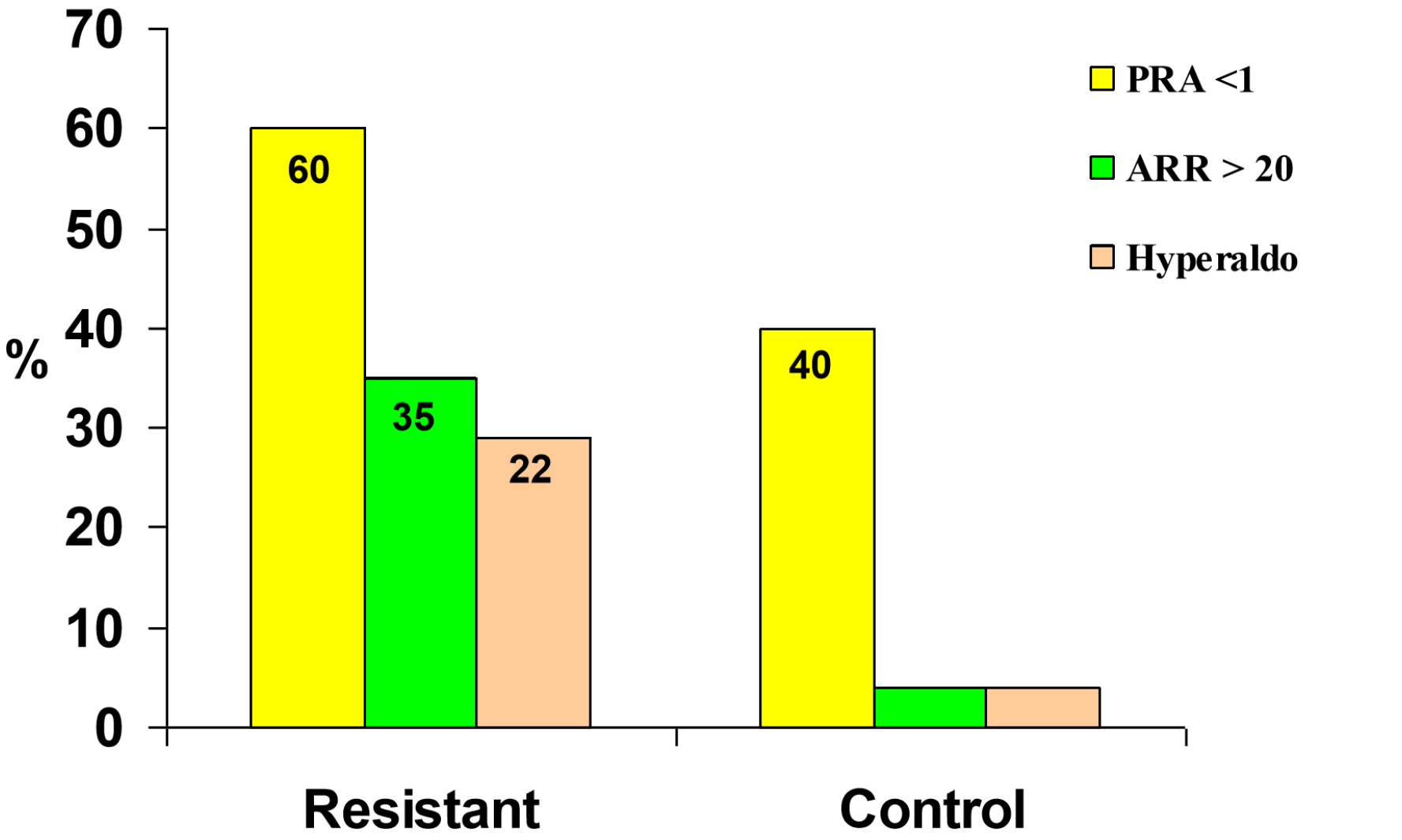
Prevalence of primary aldosteronism in patients with resistant hypertension from multiple clinics worldwide (25–28).



David A. Calhoun CJASN 2006;1:1039-1045


Case-detection testing:
Morning blood sample in seated patient*
PAC
PRA or PRC¶
PAC ≥10 ng/dL (≥277 pmol/L)
AND
↓ PRA (<1.0 ng/mL/hour) or ↓ PRC
(less than the lower limit of normal)
PAC <10 ng/dL (<277 pmol/L)
OR
PRA >1 ng/mL/hour
Does patient have spontaneous hypokalemia and PAC ≥20 ng/dL (555 pmol/L)?
Surgically curable primary aldosteronism is unlikely
Yes
No
Primary aldosteronism
Confirmation testing: For suspected primary aldosteronism△
24-hour urine aldosterone, sodium, creatinine on a high-sodium diet
OR
Fludrocortisone suppression testing
OR
Saline suppression testing

Percent suppressed PRA, high ARR, and High Aldo in Resistant Hypertension vs. Controls



Gaddam et al., Arch Intern Med 2008

24-hr Urinary Aldosterone and BMI in Patients with Resistant Hypertension

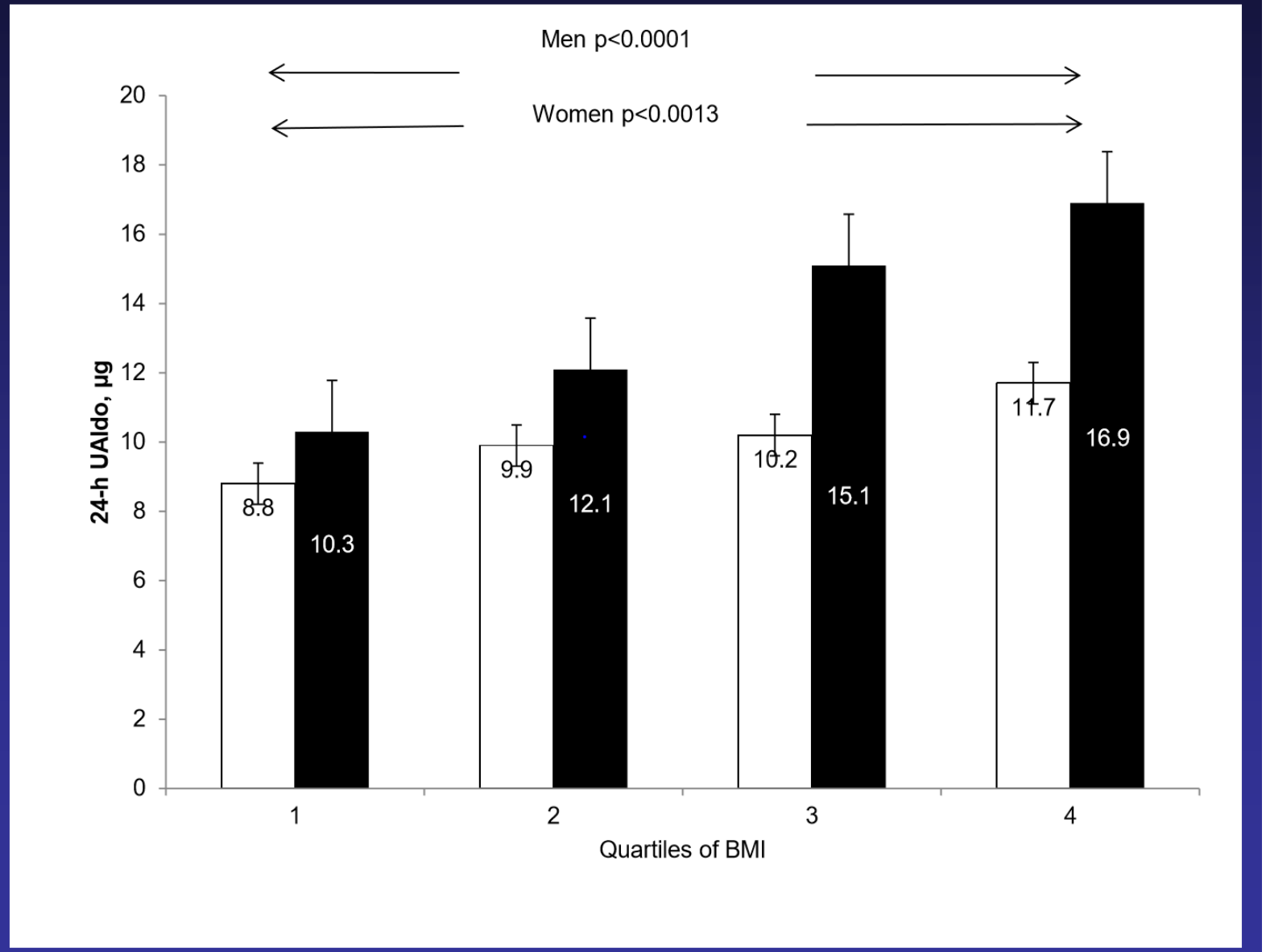


Table 1 Causes of primary aldosteronism (PA): surgically curable and not curable

Surgically curable

- Aldosterone-producing adenoma (aldosteronoma, APA)
  - Unilateral
  - Bilateral
- Primary unilateral adrenal hyperplasia (PAH)
- Multinodular unilateral adrenocortical hyperplasia (MUAN)
- Ovary aldosterone-secreting tumor
- APA or bilateral adrenal hyperplasia (BAH) with concomitant pheochromocytoma
- Aldosterone-producing carcinoma (APC)

Not surgically curable

- Bilateral adrenal hyperplasia (BAH)
- Unilateral APA with BAH
- Familial type I (FHI) hyperaldosteronism, also known as glucocorticoid-remediable aldosteronism (GRA)
- Familial type II hyperaldosteronism (FHII)
- Apparent mineralocorticoid excess (AME)
  - Chronic licorice intake
  - Carbenoxolone (antacid) use

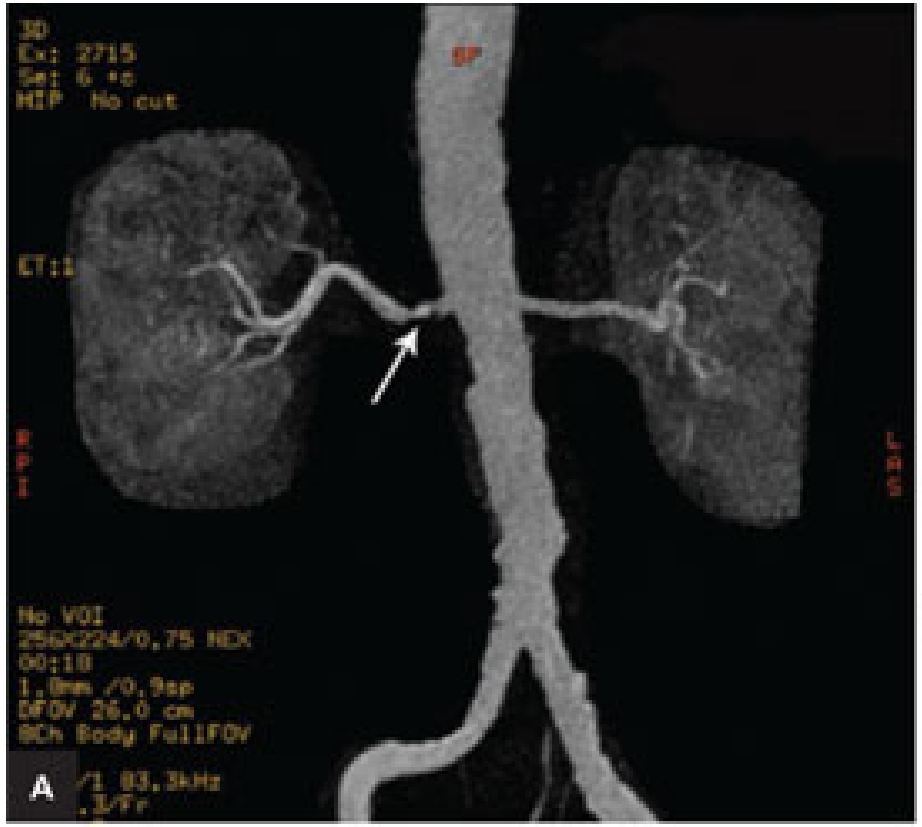
Rossi, G.P. Curr Hypertens Rep (2010) 12: 342

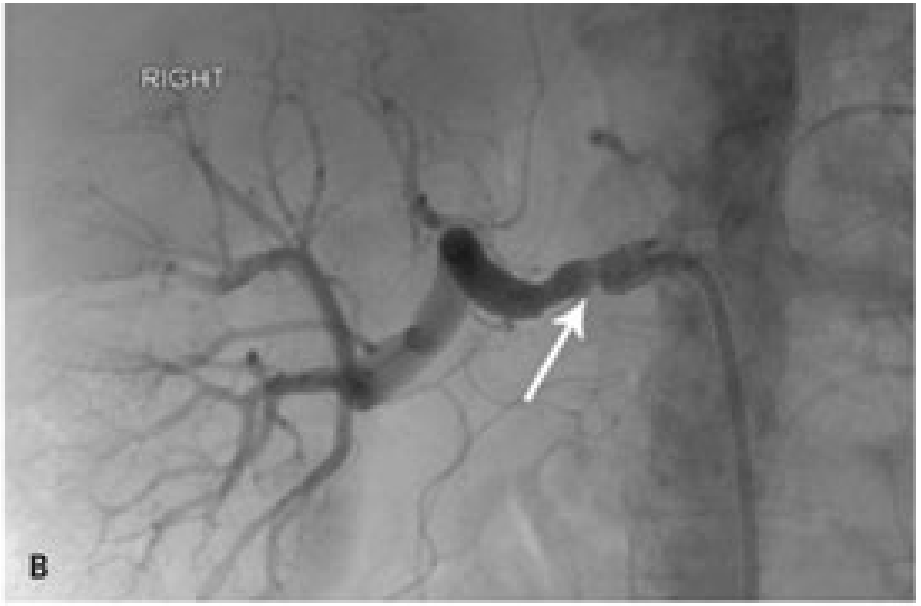
Renovascular Hypertension

- Renal Artery stenosis
- Fibromuscular dysplasia
- Atherosclerotic disease

When to suspect

- Diastolic blood pressure > 120
- Sudden acceleration blood pressure
- Blood pressure which is resistant to control with three or 4 drugs ,that shall typically include a diuretic.
- flash pulmonary edema
- Presence of Hypertensive retinopathy
- Para umbilical bruit
- HTN associated with significant CAD/ atherosclerotic disease
- Marked LVH in echocardiography
- Worsening of renal function with ACE inhibitor is a strong clue.


3D
Ex: 2715
Se: 6 *6
MIP No cut
SP
ET:1
R P I
S A S
No VOI
256X224/0.75 NEX
00:10
1.0mm /0.9sp
DFOV 26.0 cm
8Ch Body FullFOV
A
/1 83.3kHz
.1/Tr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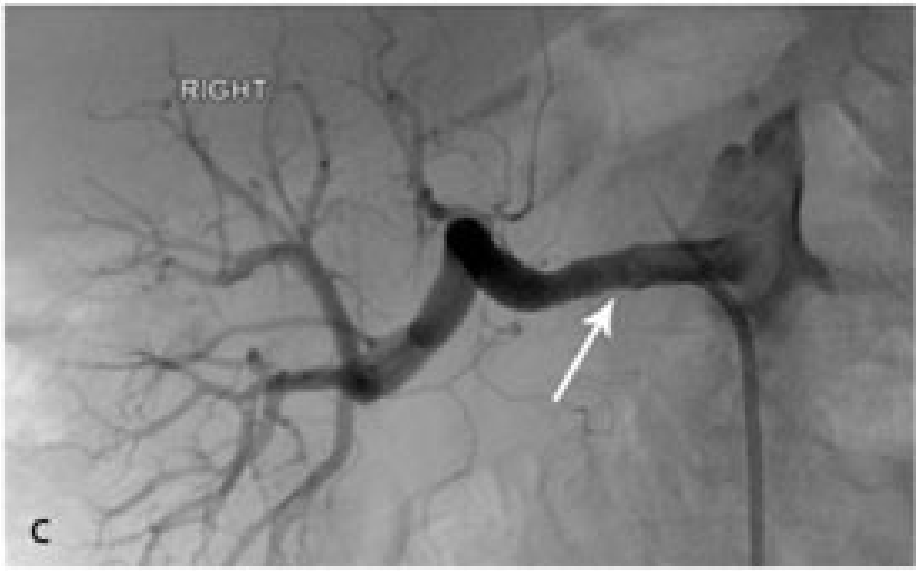
B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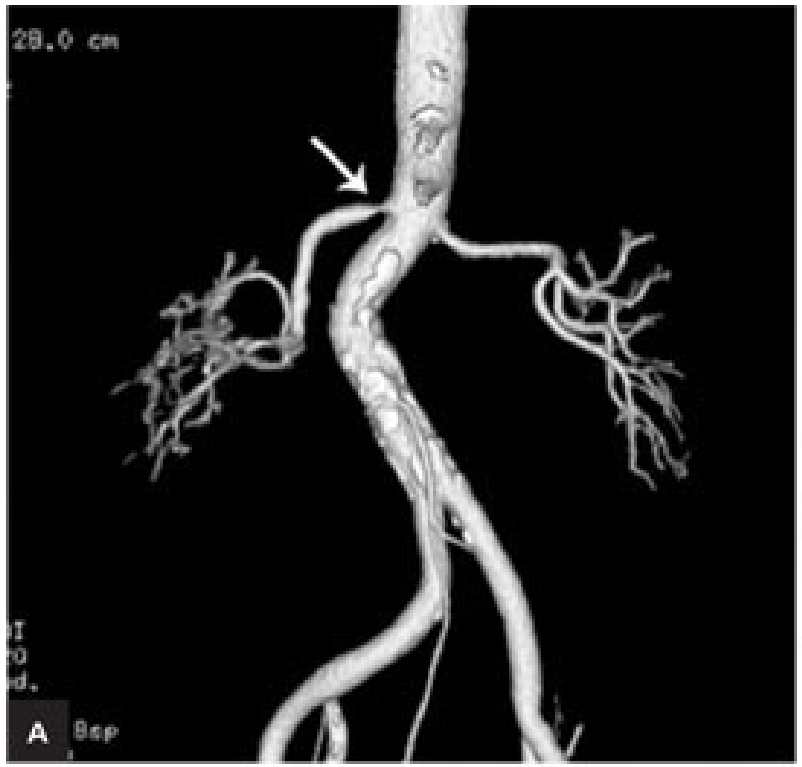
28.0 cm
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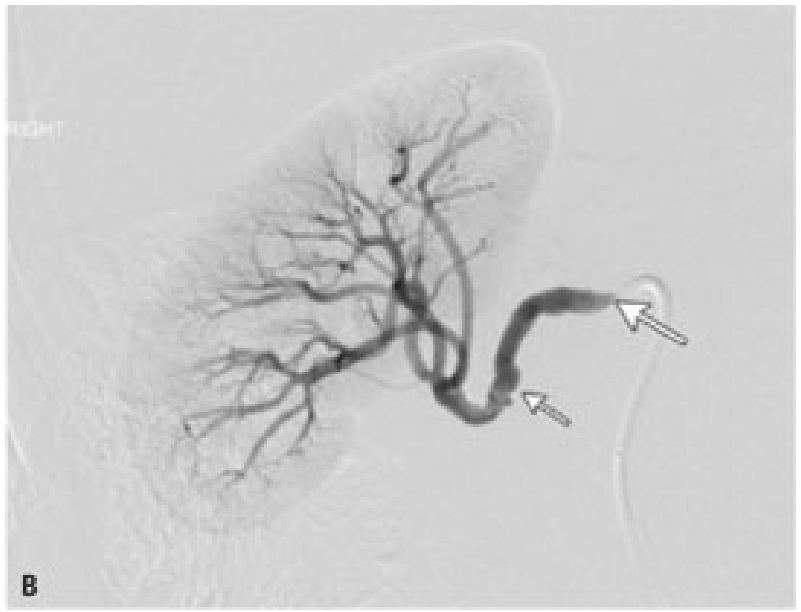
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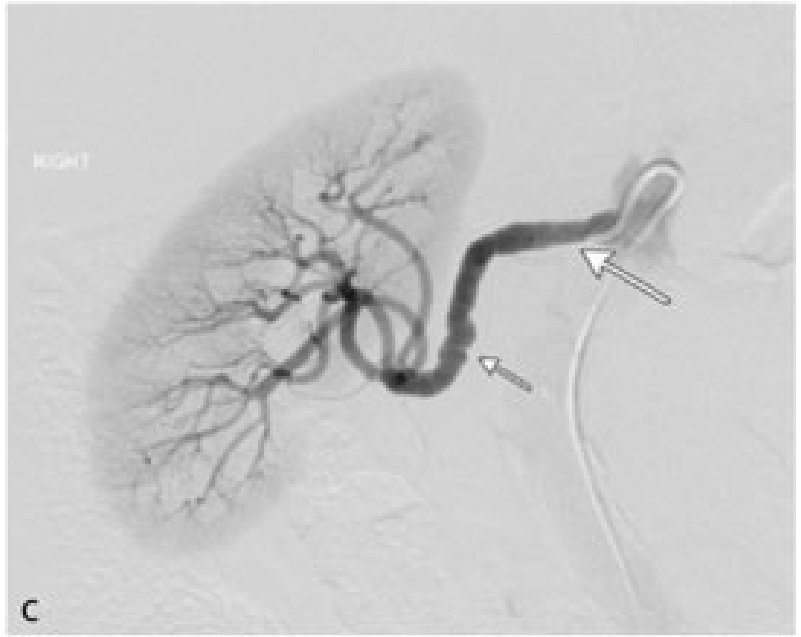
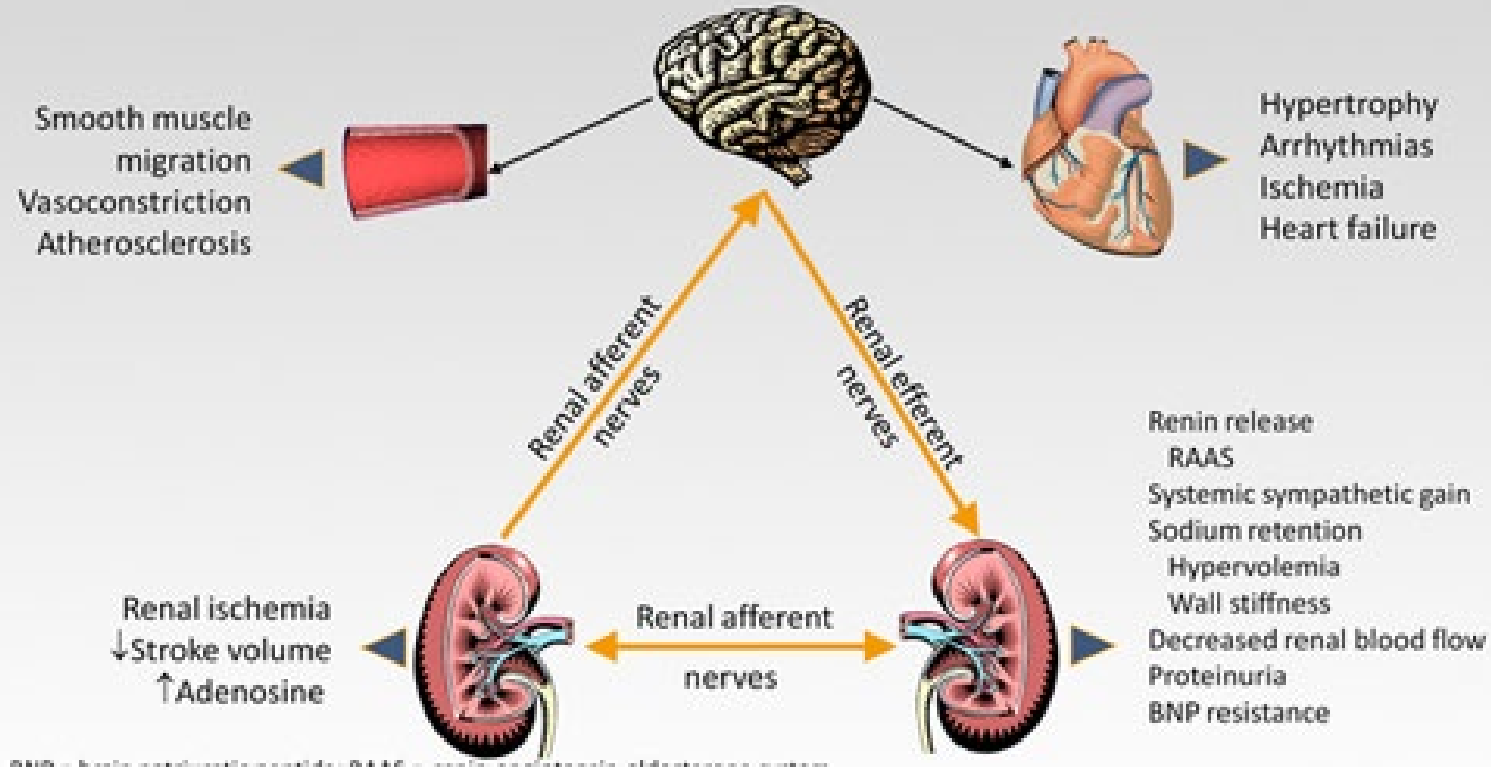

C

Renal Sympathetic Activation in Hypertension



BNP = brain natriuretic peptide; RAAS = renin-angiotensin-aldosterone system

HYPERTENSION

From Krum H, et al. *Circulation*. 2011;123;209-215.
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theheart.org Medscape EDUCATION

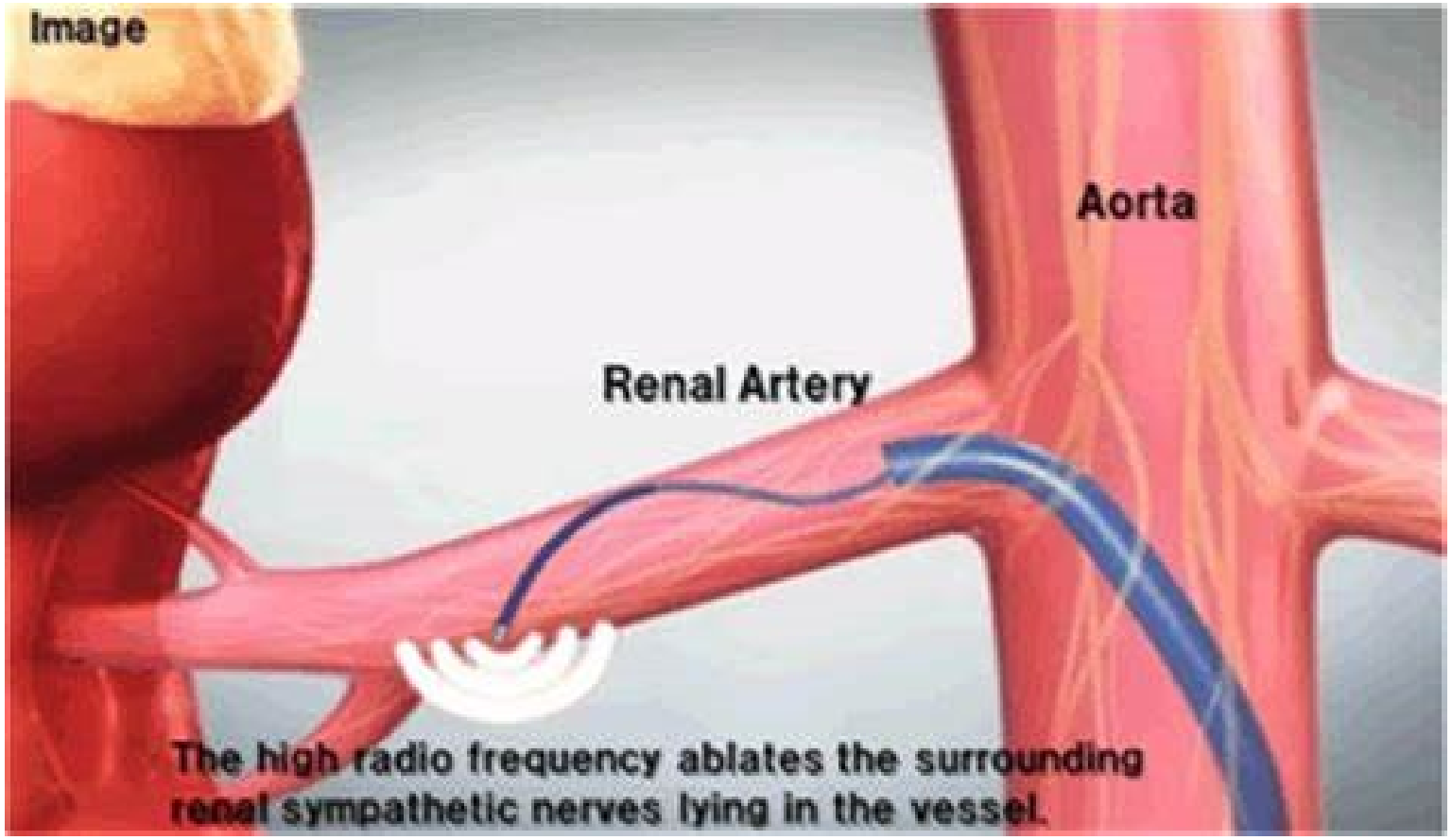


Image
Aorta
Renal Artery
The high radio frequency ablates the surrounding renal sympathetic nerves lying in the vessel.

Table 1

Participant entry criteria used recently in clinical trials of renal denervation

Inclusion Criteria
Office-based systolic BP ≥ 160mmHg (≥ 150mmHg in diabetes type 2) on ≥ 3 antihypertensive drugs in adequate dosage and combination (including diuretic)
Exclusion Criteria
Known cause of secondary hypertension
Pseudo-resistance determined using ABPM (average BP > 130 mmHg or mean daytime BP > 135 mmHg)
Poor renal function (GFR ≤ 45 ml/min/1.73 m^2)
Presence of renovascular abnormalities: polar or accessory arteries, renal artery stenosis, prior revascularization
Pregnancy
Type 1 Diabetes
Existing permanent pacemaker or implantable cardioverter-defibrillator
Myocardial infarction, unstable angina or cerebrovascular accident in previous 6 months

BP: blood pressure; ABPM: Ambulatory blood pressure monitoring; GFR: glomerular filtration rate

Journal of the American Society of Hypertension : JASH [15 Aug 2013, 7(6):484-493]

Renal denervation- SIMPLICTY HTN-1 trial

- Proof of concept, uncontrolled, n=153.
- Office BP ~ -30mmHg.
- Reported in Lancet 2009/2014

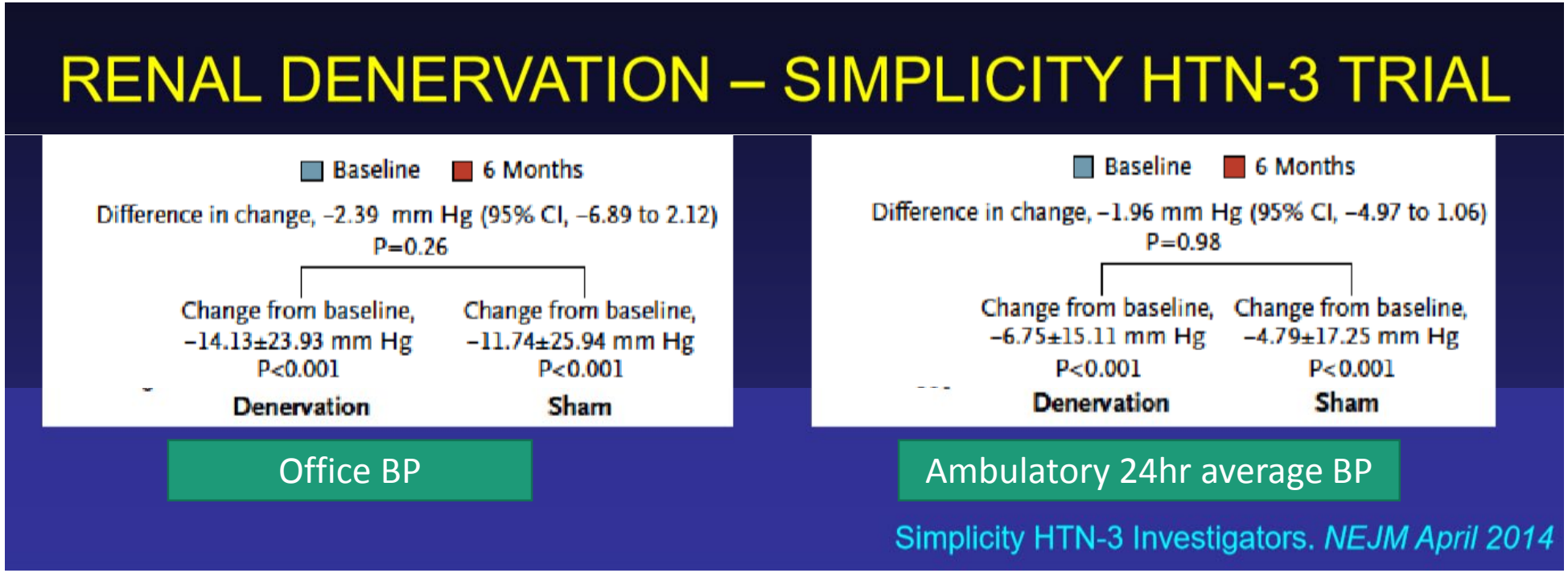
RENAL DENERVATION – SIMPLICITY HTN-2 TRIAL

Simplicity HTN-2 Investigators. *Lancet* 2010;376:1903-9.

Open label nonblinded RCT n=106

Home BP -20/12mmHg

24-hr ABPM -11/7 mmHg



Single blind randomized sham controlled 2:1 randomization. N=535.

At 12 months same number of anti HTN

Helped mostly in- non blacks, eGFR>60ml/min; age <65

Pheochromocytoma

Most commonly suspected and least diagnosed entity.

0.1-0.6% of hypertensives patients. [1,2]

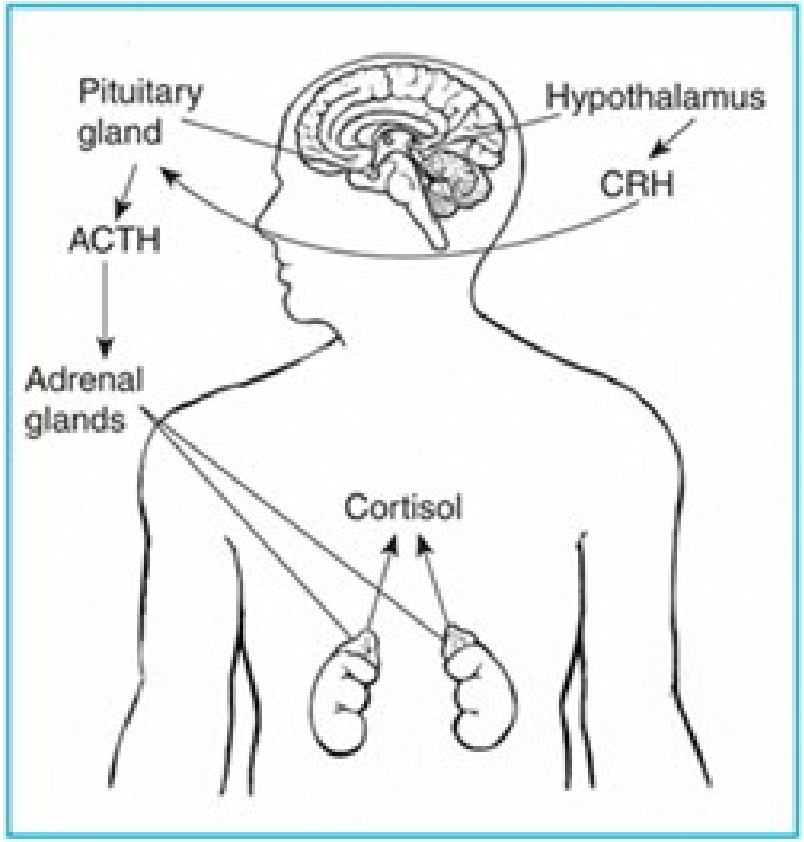
Increased BP variability which is an independent risk factor for cardiovascular morbidity and mortality. [3,4]

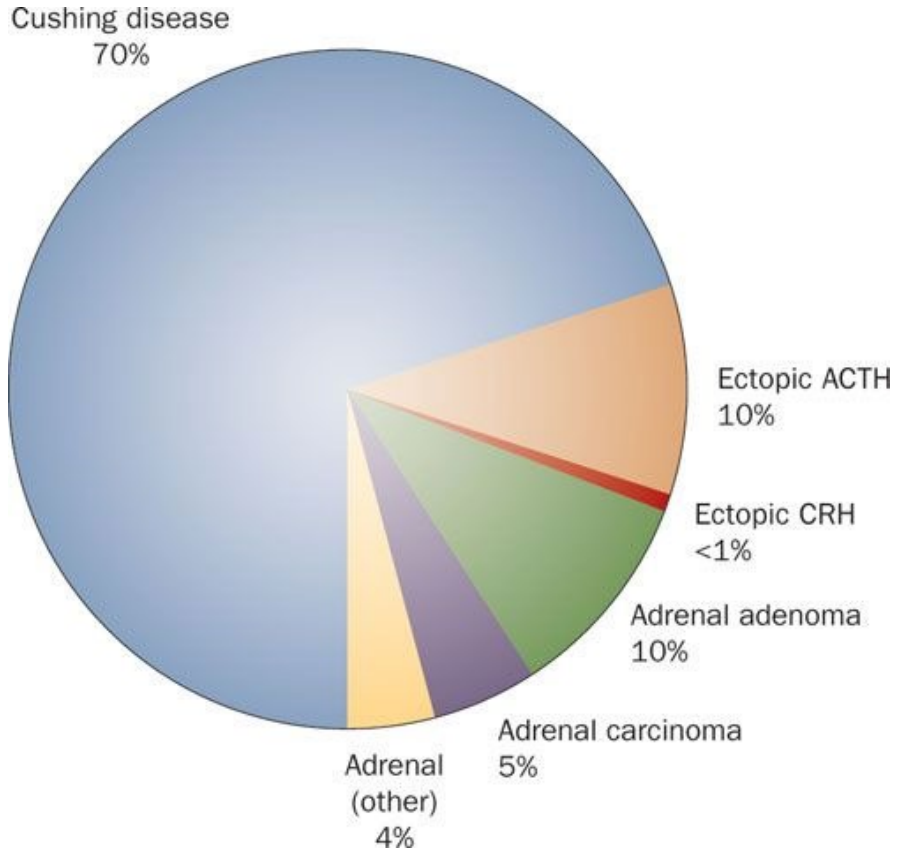
Entertain diagnosis in hypertensive patients with headaches, palpitations, sweating occurring in episodic fashion, with a diagnostic accuracy of 90%.

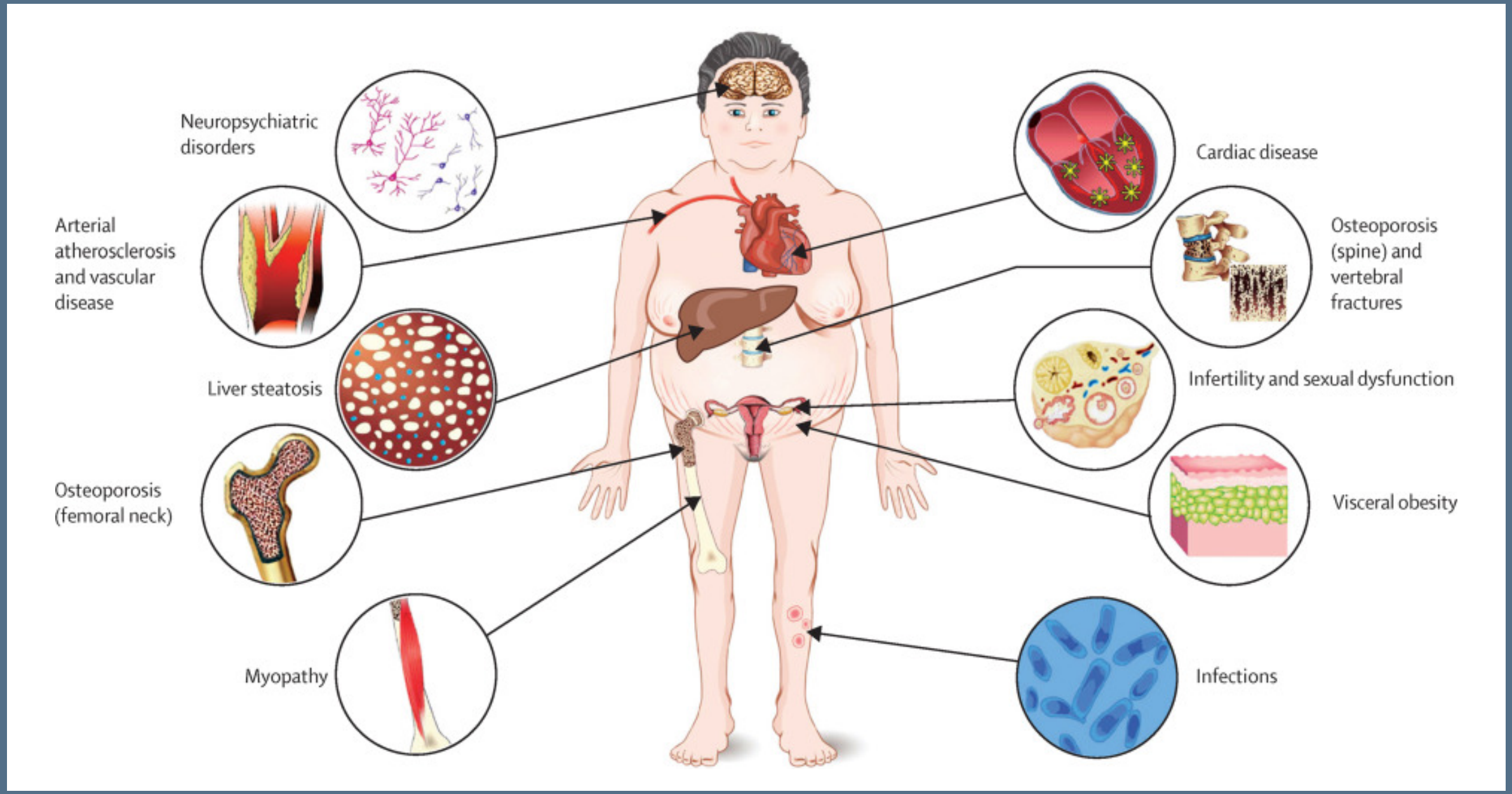
Best test- Plasma free metanephrines (fractionated-metanephrine and normetanephrine). [5]

- *1.Omura et al, Hyperten Res, 2004; 27:193-202*
- *2. Sinclair et al. Arch Intern Med. 1987; 147:1289-93*
- *3. Bjorklund et al. J Hypertens. 2004; 22:1691-1697*
- *4. Kikuya et al. Hypertension. 2000; 36:901-6*
- *5. Lenders et al. Lancet. 2005;366:665-75*

Cushing's Syndrome

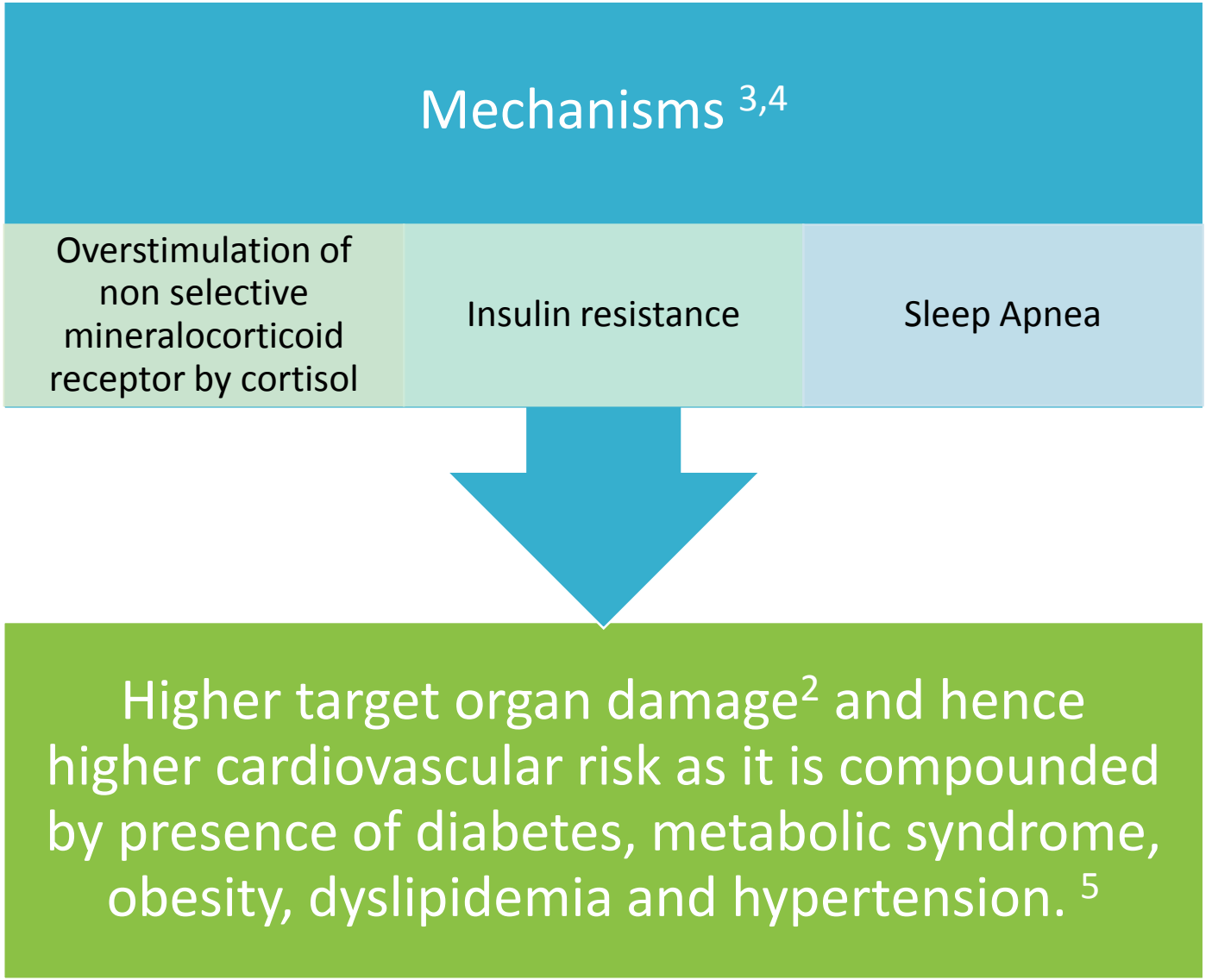




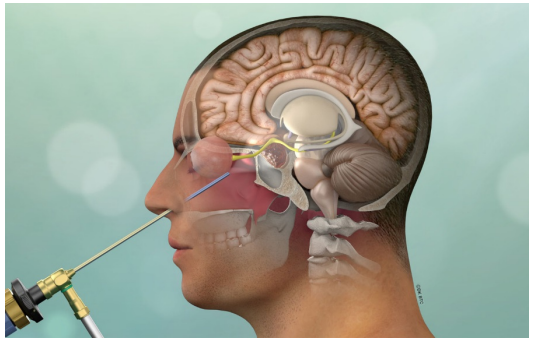

Neuropsychiatric disorders
Arterial atherosclerosis and vascular disease
Liver steatosis
Osteoporosis (femoral neck)
Myopathy
Cardiac disease
Osteoporosis (spine) and vertebral fractures
Infertility and sexual dysfunction
Visceral obesity
Infections

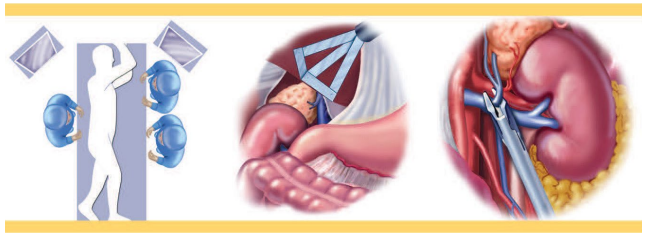
Cushing's Syndrome

70-90% of patients have Hypertension. [1]
17% with severe hypertension. [2]



1. *Moneva et al. Semin Nephrol 2002;22:44-53*
2. *Muiesan et al. J Am Coll Cardiol.2003;41;2275-79*
3. *Mcfarlane et al. J Clin Endocrinol Metab. 2001;86;713-18*
4. *Sacerdote et al. Curr Hyperten Rep. 2004; 7:253-56.*
5. *Faggiano et al. J Clinc Endocrin Metab. 2003; 88:2527-33*



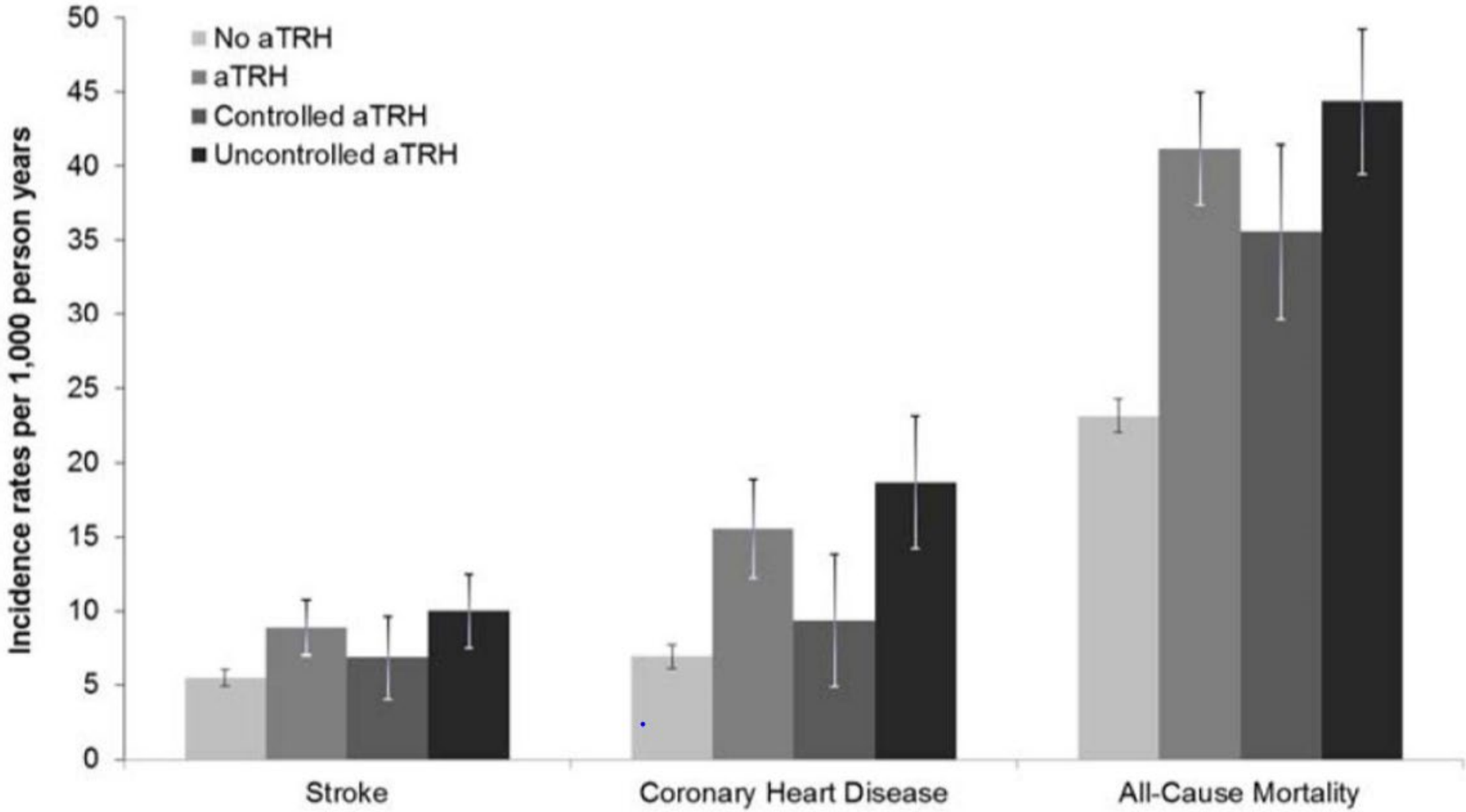


Cushing's Syndrome: Management

- Usual medications are not effective.
- Surgical intervention is often necessary to excise ACTH or cortisol producing tumor
- Most effective pharmacological management- Mineralocorticoid receptor antagonist
- SPIRONOLACTONE or EPLERENONE

Objectives

- Define Resistant Hypertension
- Evaluation of patients with Resistant hypertension
- Explain why is it important
- Management of Resistant Hypertension


No aTRH
aTRH
Controlled aTRH
Uncontrolled aTRH
Incidence rates per 1,000 person years
50
45
40
35
30
25
20
15
10
5
0
Stroke
Coronary Heart Disease
All-Cause Mortality

Results From the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

Increased risk of

- Coronary artery disease,
- Stroke,
- Peripheral artery disease,
- End stage renal disease
- Congestive heart failure
- All cause mortality,

Treatment-Resistant Hypertension and the Incidence of Cardiovascular Disease and End-Stage Renal Disease, Volume: 64, Issue: 5, Pages: 1012-1021, DOI: (10.1161/HYPERTENSIONAHA.114.03850)

Objectives

- Define Resistant Hypertension
- Evaluation of patients with Resistant hypertension
- Explain why is it important
- Management of Resistant Hypertension

Diuretic use: practical Considerations

Chlorthalidone

- 12.5-25mg daily
- Metabolic complications like hypokalemia

Loop diuretics

- Not needed until eGFR<30ml/min.
- Use with minoxidil or hydralazine
- Long acting or twice daily dose

Spironolactone

- 12.5mg-100mg daily
- Hyperkalemia uncommon if renal function is good
- Risk of hyperkalemia higher if used in CKD, with NSAIDs, ACE-I or ARBs
- Side effect dose dependent.

HCTZ vs Chlorthalidone

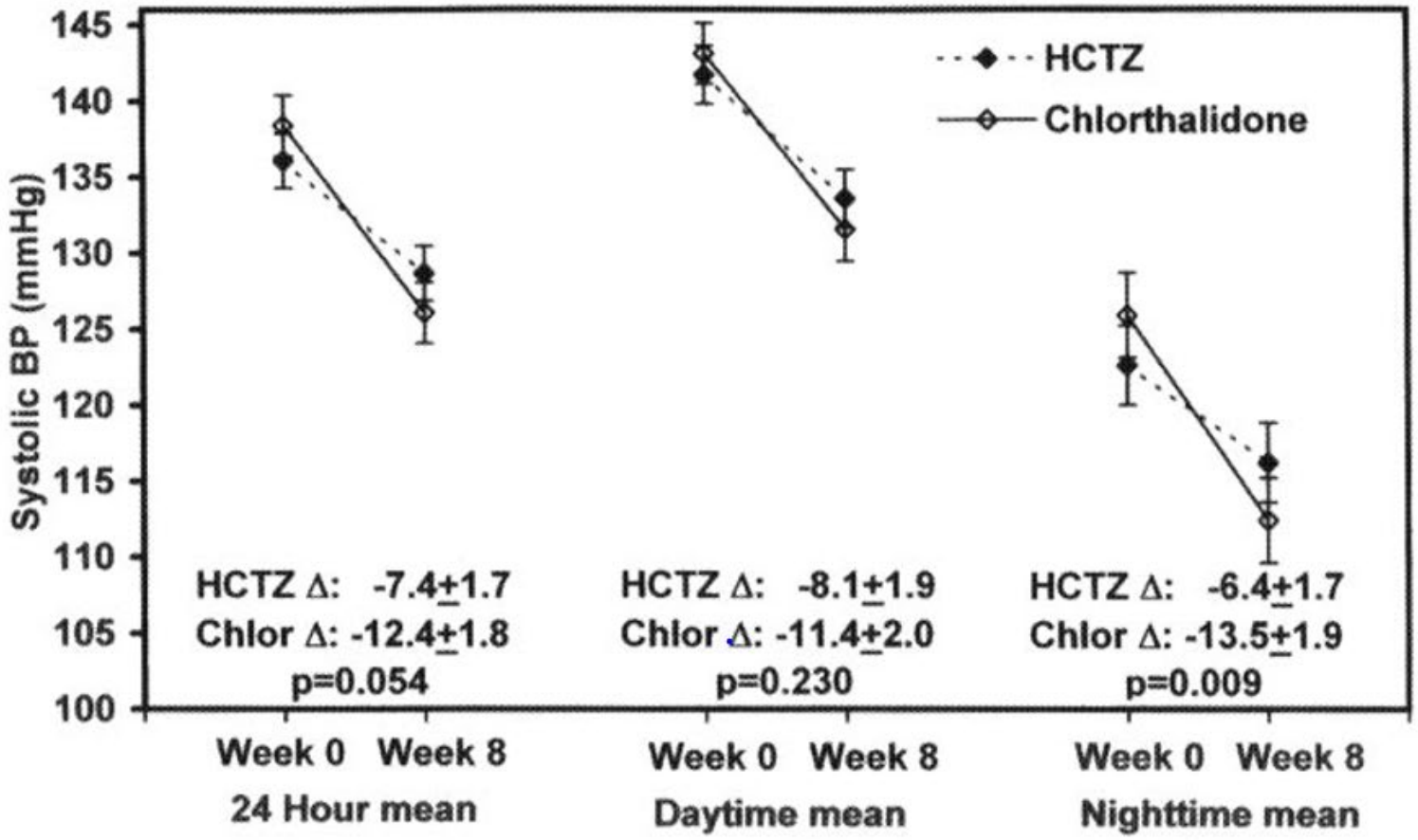


Figure 2. Mean 24-hour, daytime, and nighttime ambulatory SBP with change from baseline.

Ernst et al. Hypertension 2006;47:352

Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial

www.thelancet.com Vol 386 November 21, 2015

*Bryan Williams, Thomas M MacDonald, Steve Morant, David J Webb, Peter Sever, Gordon McInnes, Ian Ford, J Kennedy Cruickshank, Mark J Caulfield, Jackie Salsbury, Isla Mackenzie, Sandosh Padmanabhan, Morris J Brown, for The British Hypertension Society's PATHWAY Studies Group**

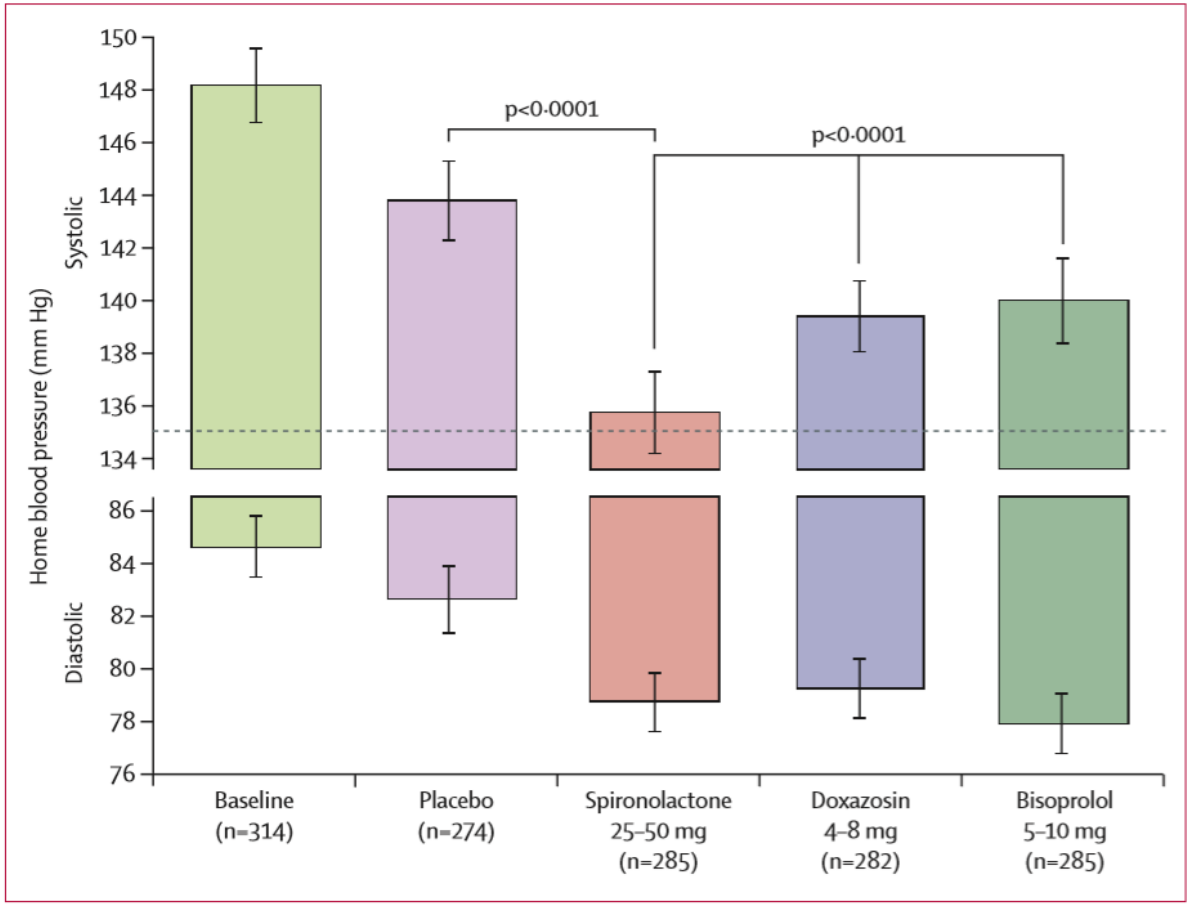


Figure 2: **Home systolic and diastolic blood pressures comparing spironolactone with each of the other cycles**

Resistant hypertension

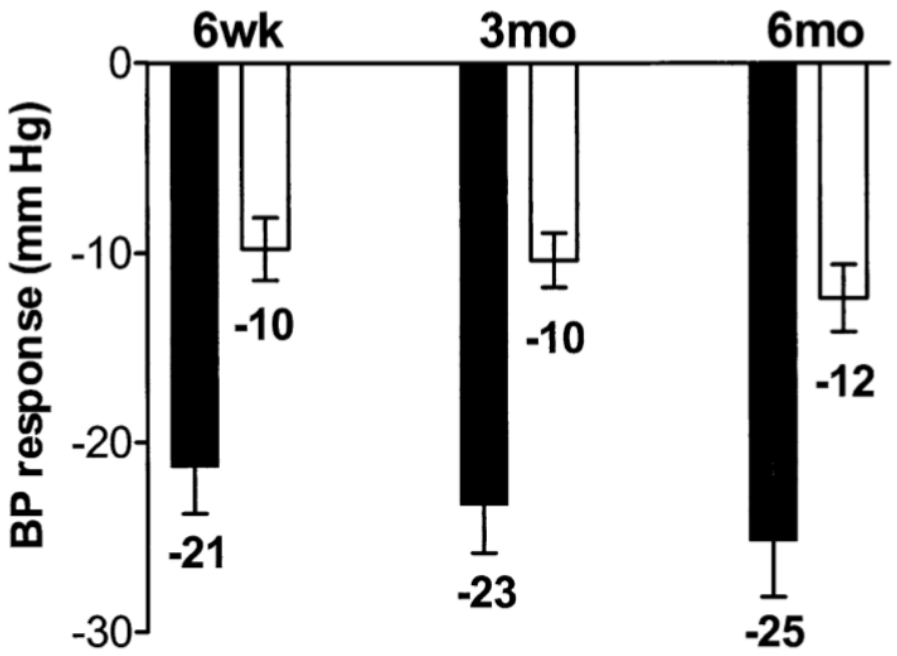


FIG. 1. Spironolactone-induced reduction in systolic blood pressure (BP) (**filled bars**) and diastolic BP (**open bars**) at 6 weeks, 3 months, and 6 months follow-up in subjects with resistant hypertension (n = 76). BP reduction was significant at all time points compared to baseline.

Primary aldosteronism

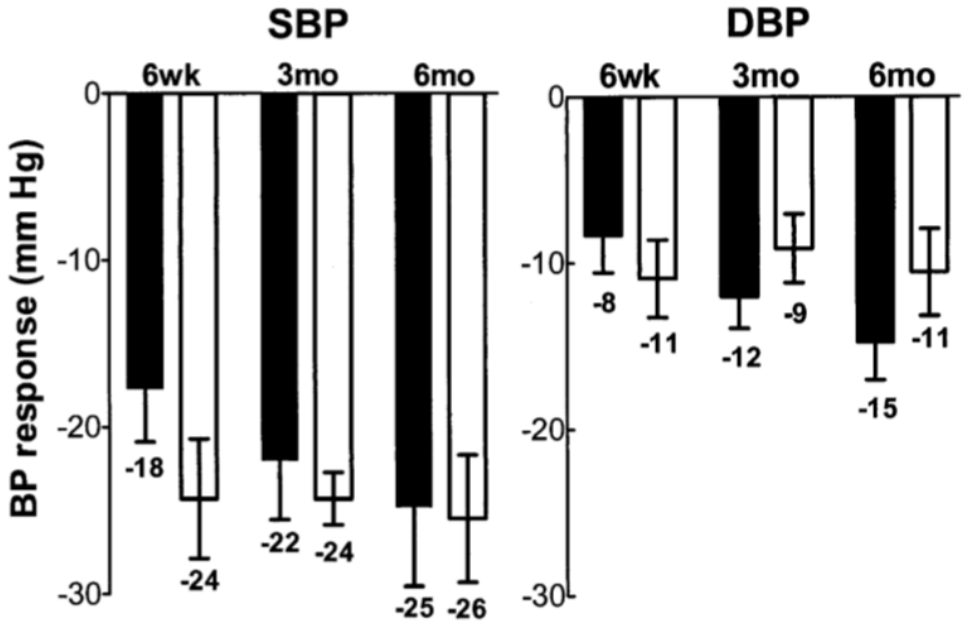


FIG. 2. Spironolactone-induced reduction in systolic blood pressure (SBP) and diastolic BP (DBP) at 6 weeks, 3 months, and 6 months follow-up in subjects with primary aldosteronism (**filled bars**, n = 34) and without primary aldosteronism (**open bars**, n = 42). BP reduction was not significantly different between primary aldosteronism and non-primary aldosteronism subjects at any time point.

Nishizaka MK et al. Am J Hypertens 2003;16:925-930

Resistant hypertension in African American population

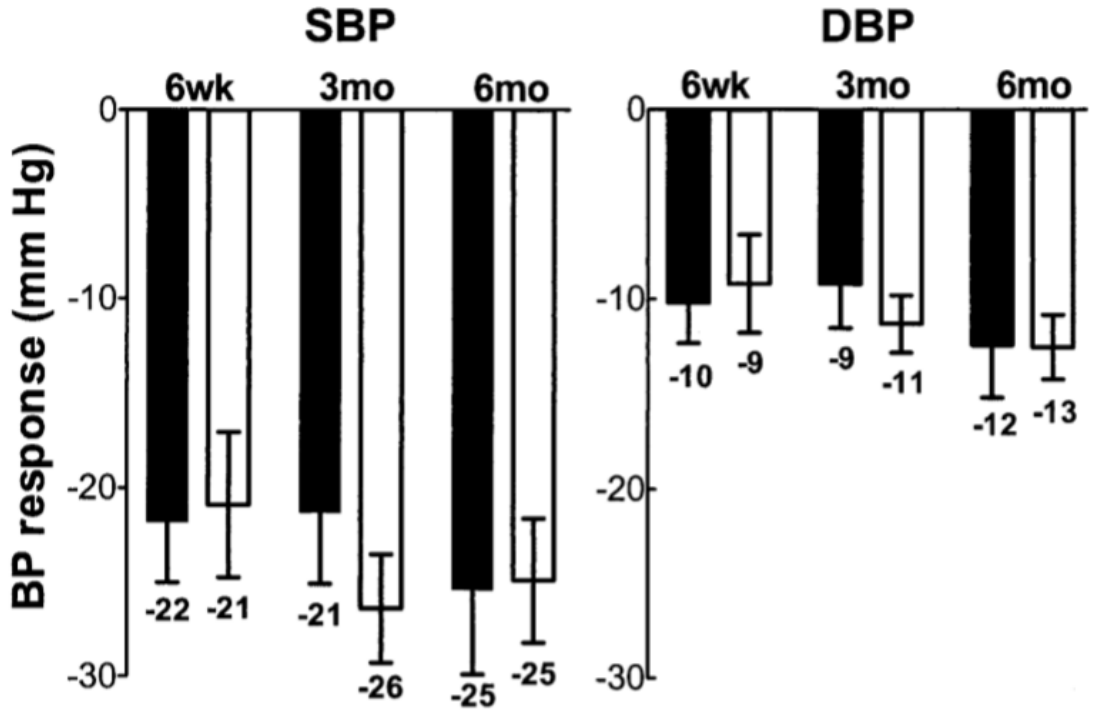


FIG. 3. Spironolactone-induced reduction in systolic blood pressure (SBP) and diastolic BP (DBP) at 6 weeks, 3 months, and 6 months follow-up in African American (**filled bars**, $n = 45$) and white (**open bars**, $n = 31$) subjects with resistant hypertension. BP reduction was not significantly different between African American and white subjects at any time point.

Nishizaka MK et al. Am J Hypertens 2003;16:925-930

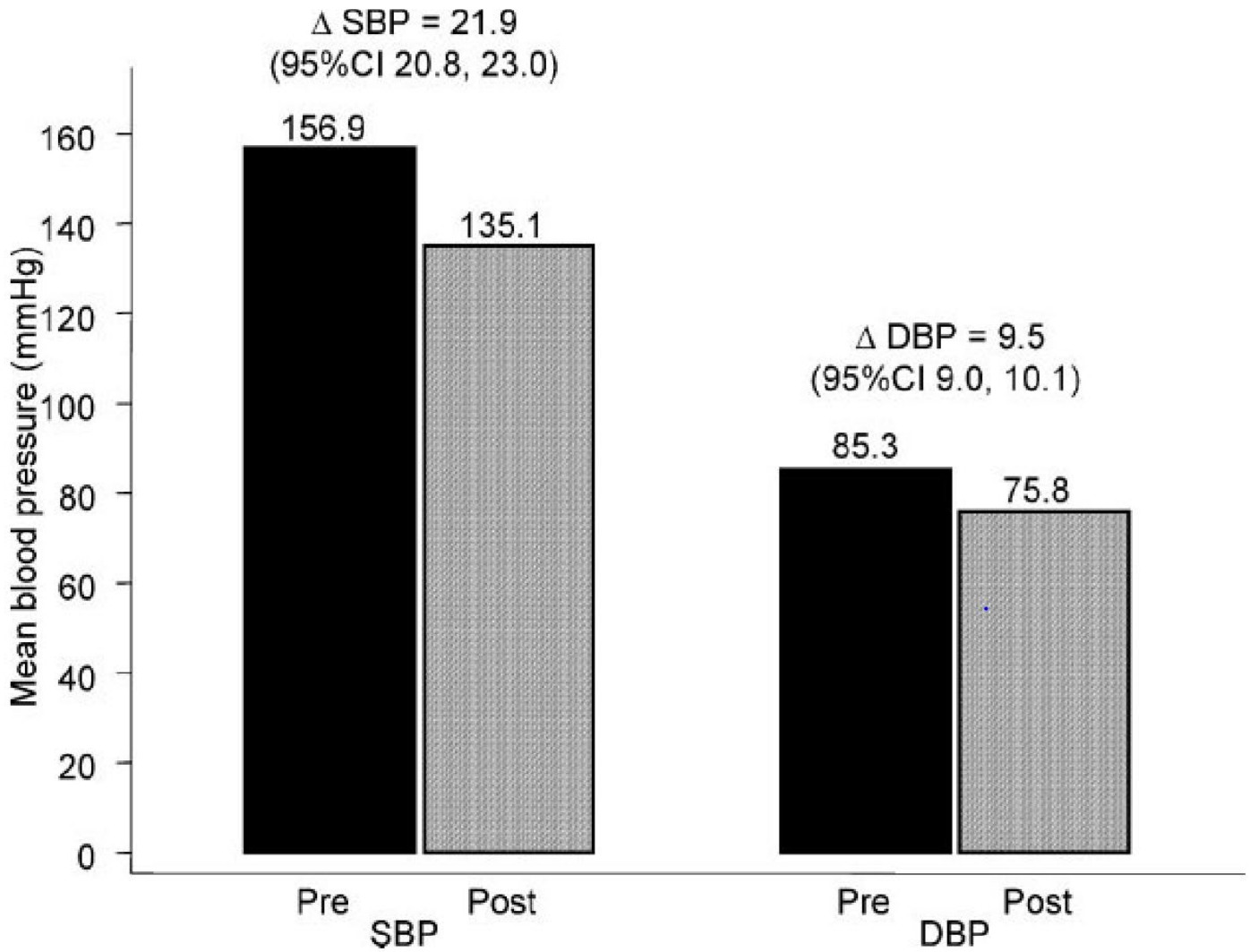
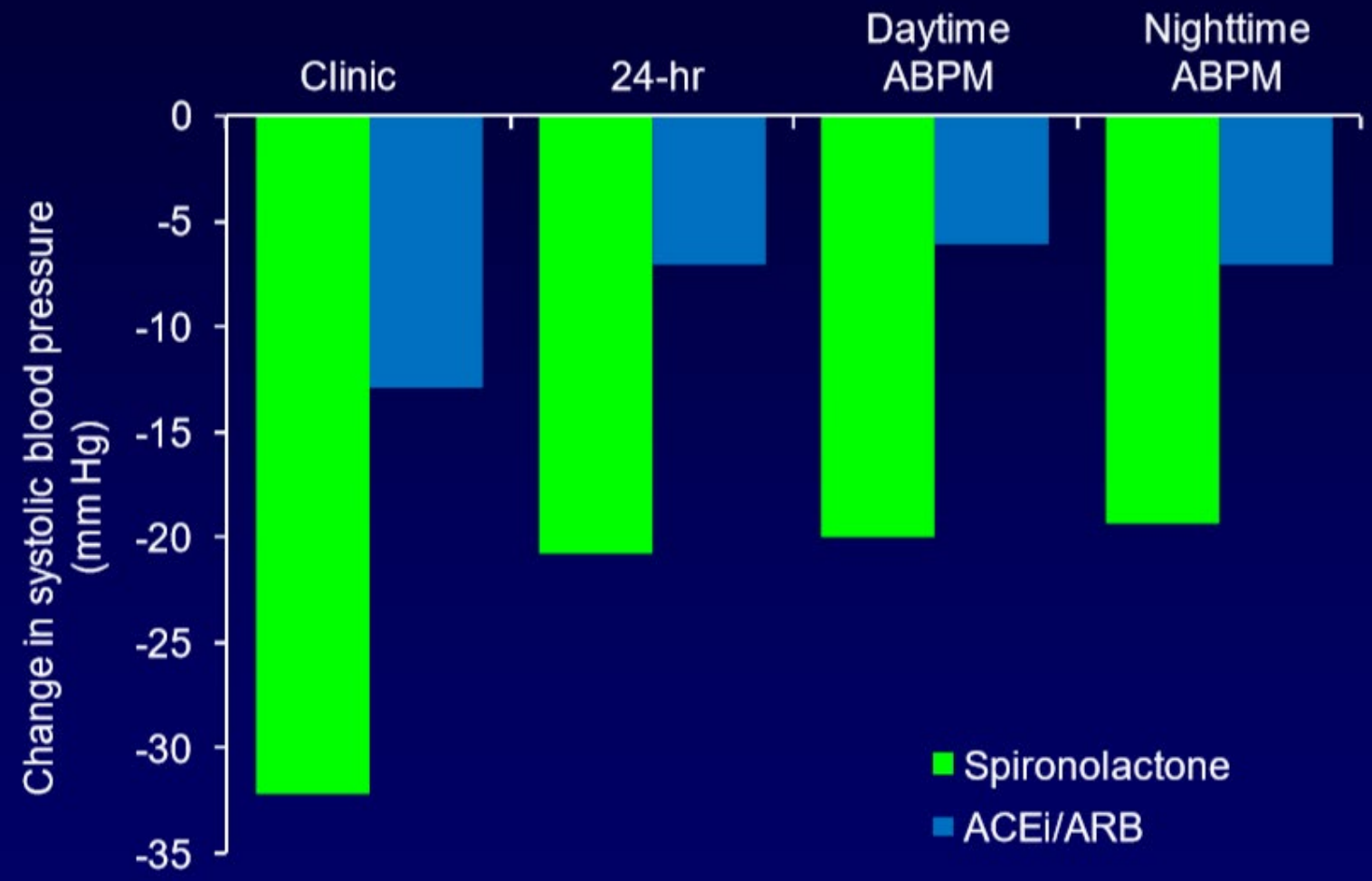


Figure 2. Mean BP before and during spironolactone treatment. Effect in 1411 ASCOT participants who received spironolactone for treatment of high BP with available BP measurements before (pre-), and during (post-), spironolactone treatment.

Chapman et al. Hypertension 2007;49:839

Change in SBP with Spironolactone vs ACEi/ARB in Patients with True Resistant Hypertension



Alvarez-Alvarez et al, J Hypertens 2010

Eplerenone

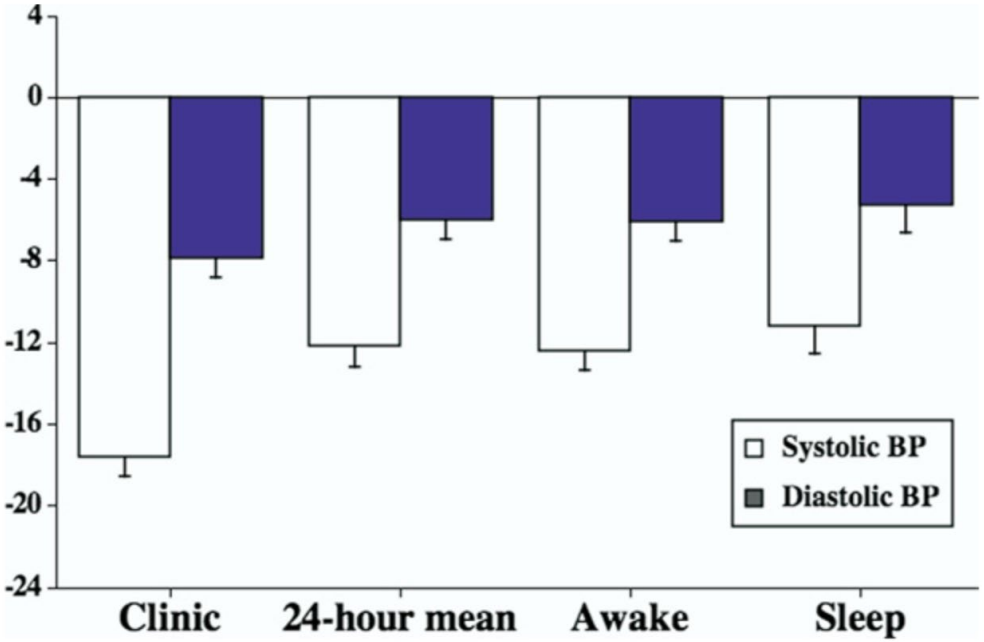


Figure 1. Changes from baseline in clinic, 24-hour, awake, and sleep BP after 12 weeks of therapy with eplerenone (50 to 100 mg daily) in patients with resistant hypertension. All reductions for both systolic and diastolic BP are statistically significant (P . .001). BP, blood pressure.

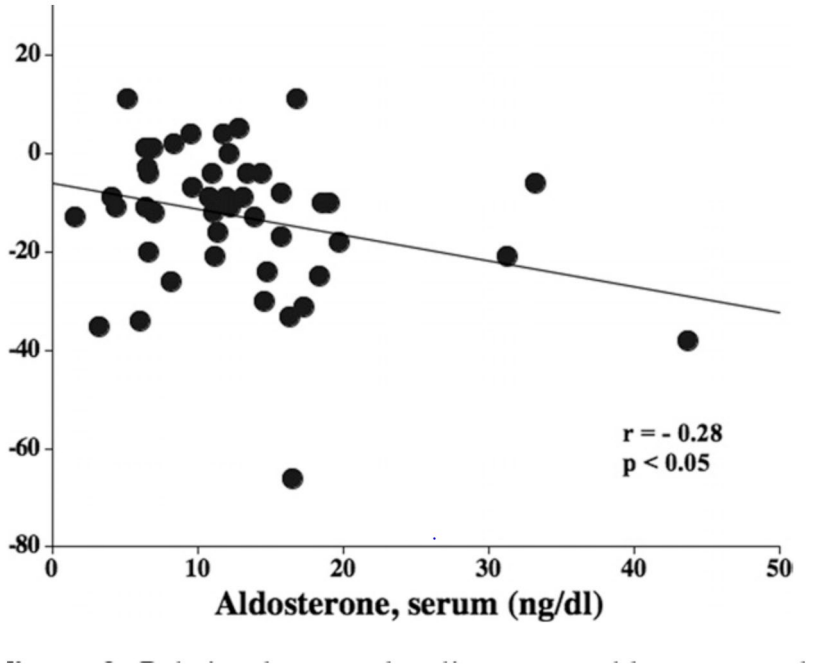


Figure 3. Relation between baseline serum aldosterone and changes from baseline in 24-hour SBP after eplerenone treatment (r 0.29; P .049). SBP, systolic blood pressure.


SALT

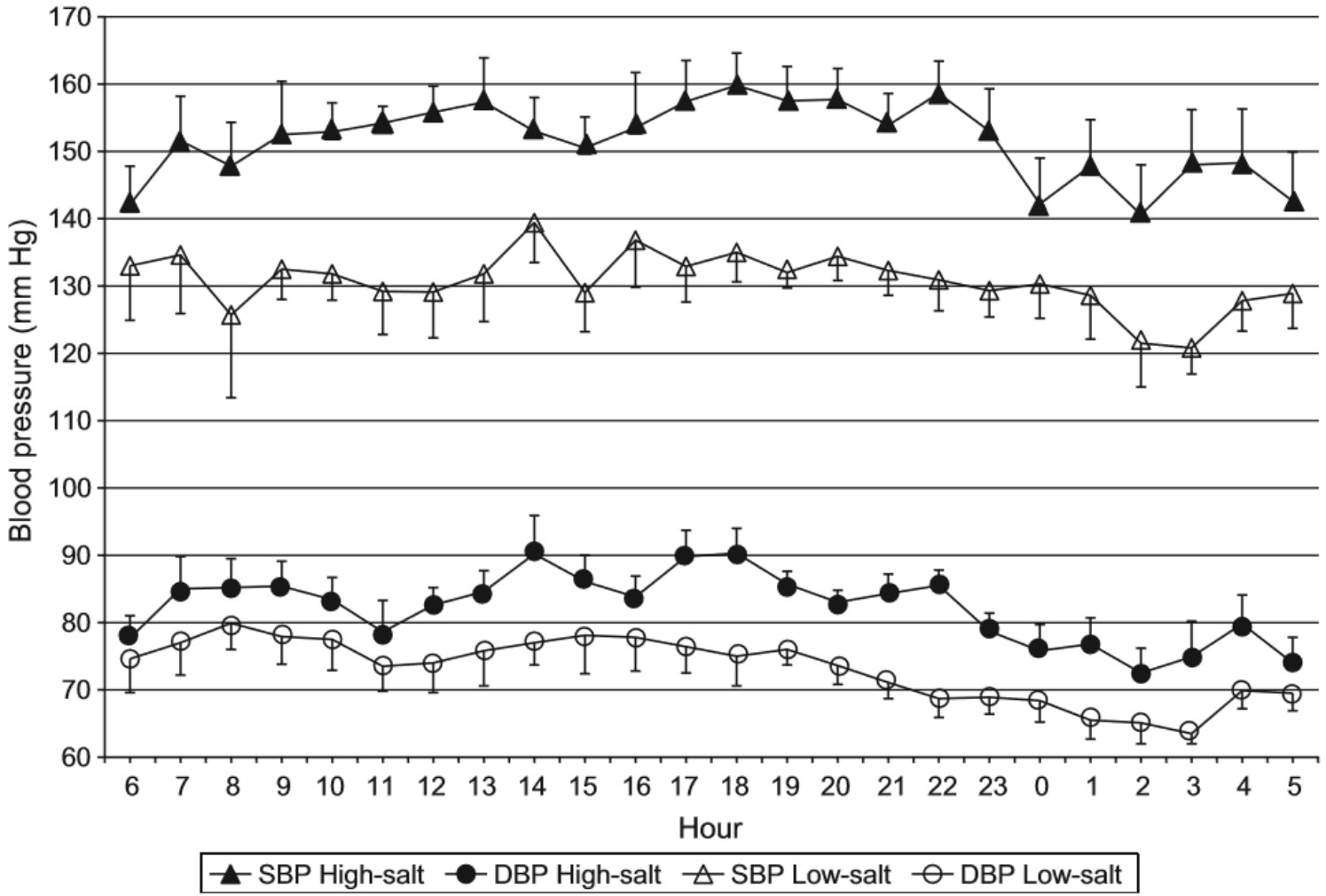
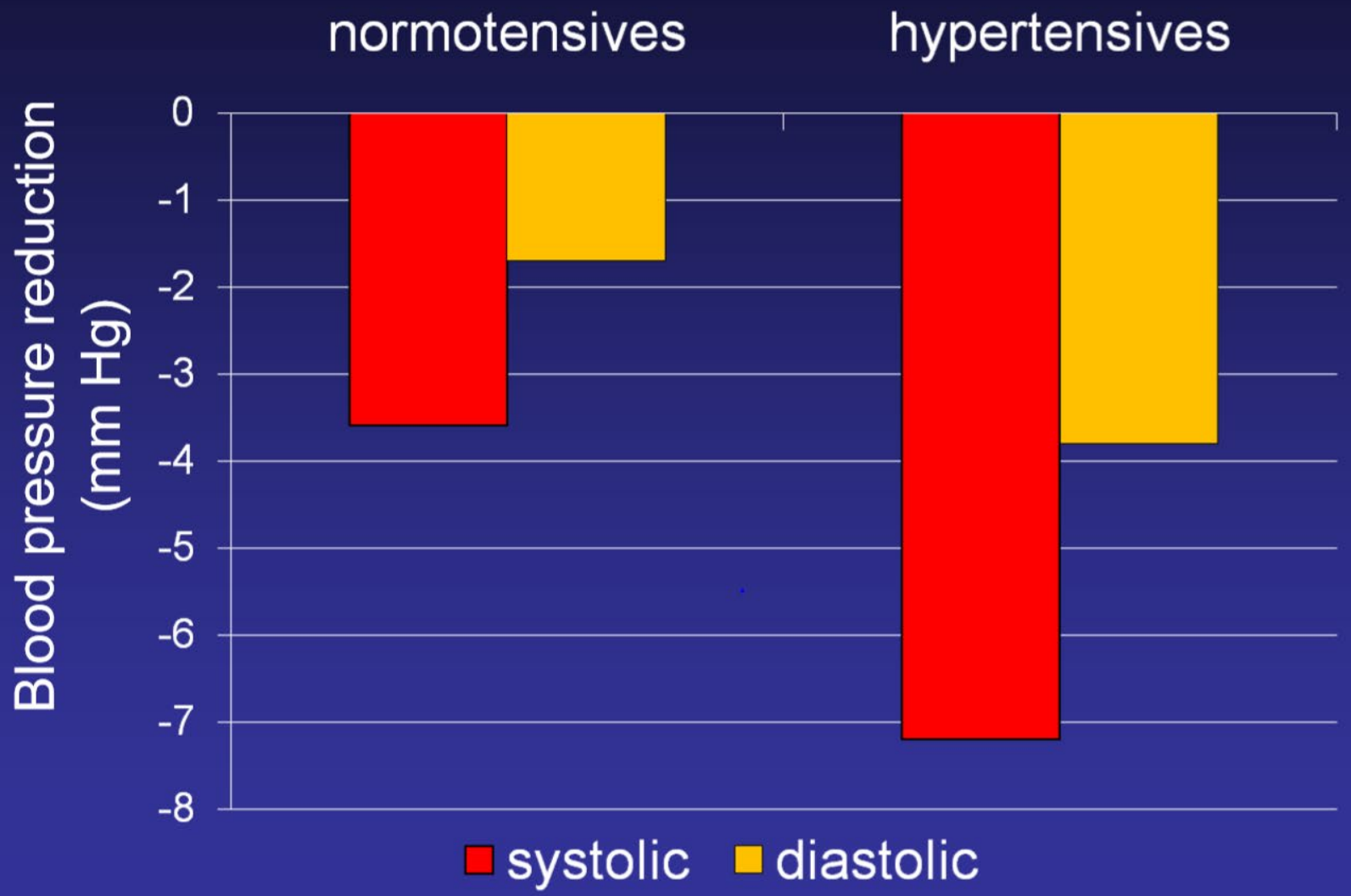


Figure. Comparison of 24-hour ambulatory blood pressure values during low- and high-salt diet. Data presented as mean±SE.

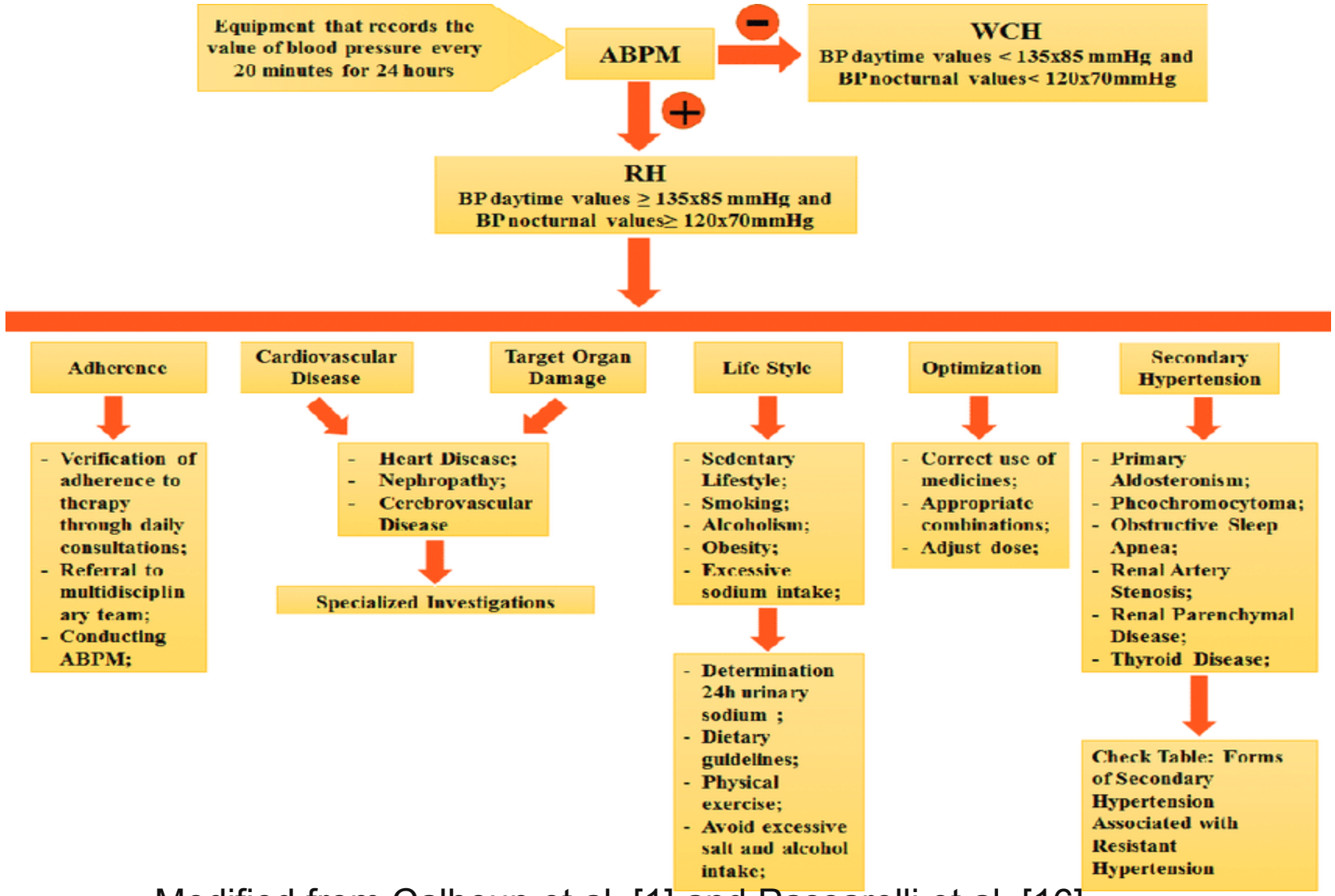
Pimenta et al. Hypertension 2009

EFFECTS OF SALT REDUCTION

(6 g/day)



He and MacGregor. *Cochrane Database of Systematic Reviews* 2004



Modified from Calhoun et al. [1] and Passarelli et al. [16].
Abbreviation: WCH, white coat hypertension.

Generalized Treatment Recommendations

- Life style modifications (weight loss, exercise, low-salt/high fiber diet)
- Standard triple regimen of ACE inhibitor or ARB, thiazide diuretic, and long-acting calcium channel blocker
- Preferential use of chlorthalidone
- Consider use of aldosterone antagonist (spironolactone, eplerenone, amiloride) as fourth drug
- Vasodilating beta-blocker as fifth drug
- Centrally-acting agent as fifth drug (clonidine, guanfacine)
- Vasodilating agents (hydralizine, minoxidil) as last resort

Calhoun DA, et al. *Hypertension*. 2008;51(6):1403-1419

Thank you!!

Questions??