

Evaluation of the Resistant Hypertension Patient

Budapest Nephrology School

Debbie Cohen, MD

University of Pennsylvania



UNIVERSITY of PENNSYLVANIA

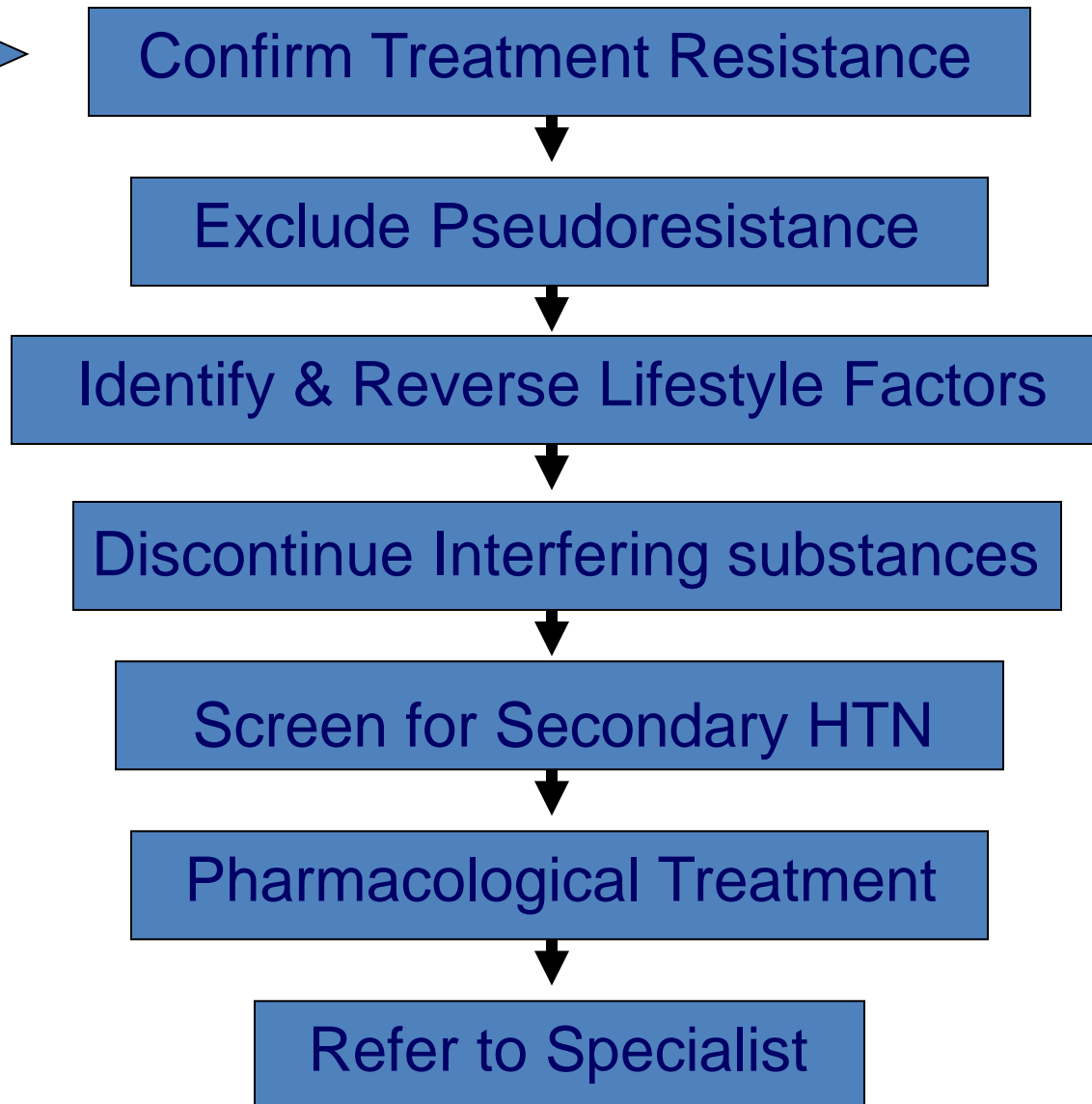
Case

- 51 year old man
- Hypertension x 12 years
- Diabetes x 5 years
- Tired, dry mouth
- MEDS: HCTZ & Valsartan, Diltiazem, Metoprolol, Clonidine, Metformin, Tricor, Statin
- 156-158/90 mm Hg (no orthostasis)

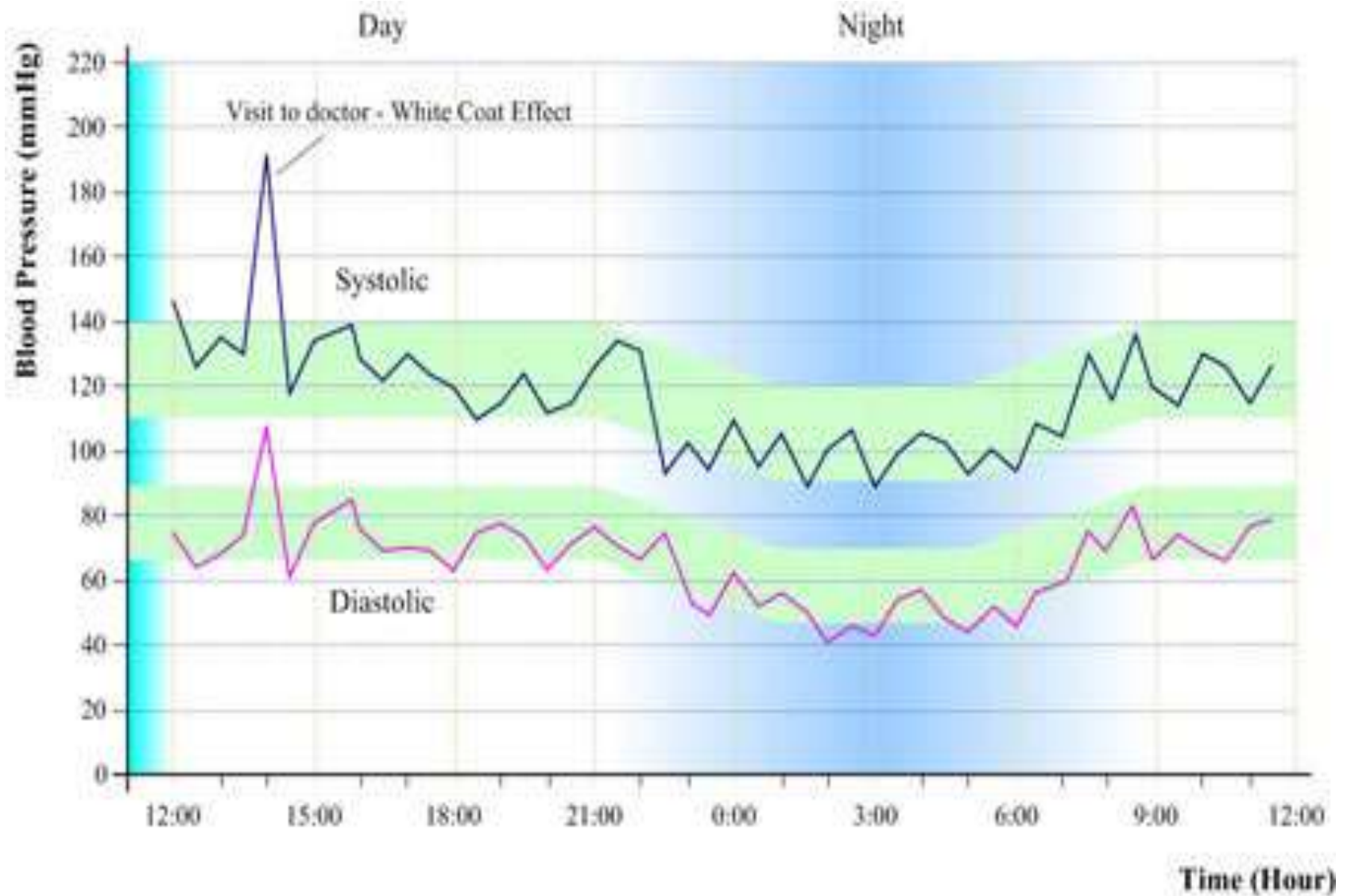
Definition of Resistant Hypertension

- Failure to achieve goal blood pressure in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic** (JNC 7)
 - < 140/90 mm Hg
 - < 130/80 mmHg in DM or CKD or CHD
- In large clinical trials 10-30% fail to reach DBP < 90 mmHg and 40-60% fail to reach SBP < 140 mmHg

Diagnostic and Treatment Recommendations



White Coat Hypertension

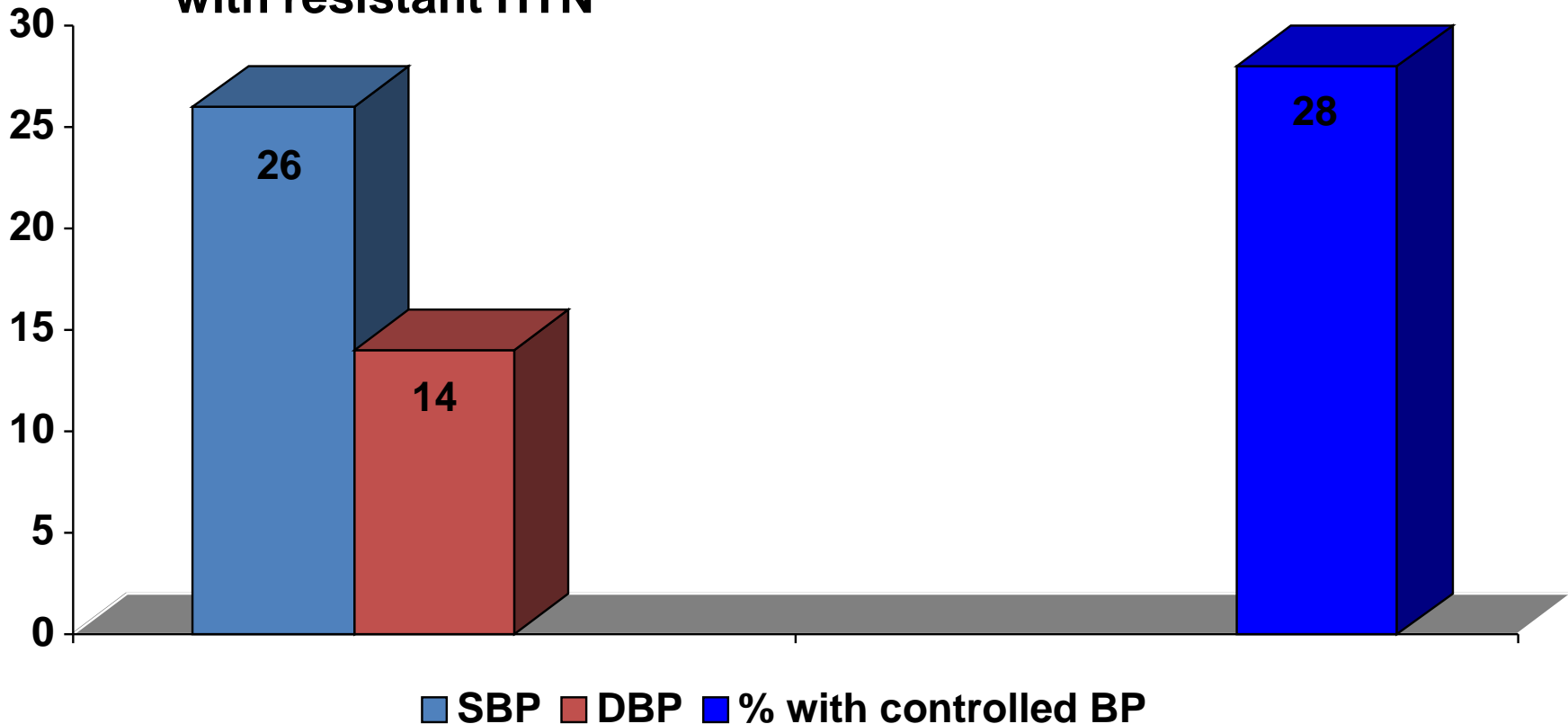


Is the Hypertension Real?

MA Brown, et al. AJH 2001

**Mean difference
between referring
doctor BP and ABP
(mmHg) in patients
with resistant HTN**

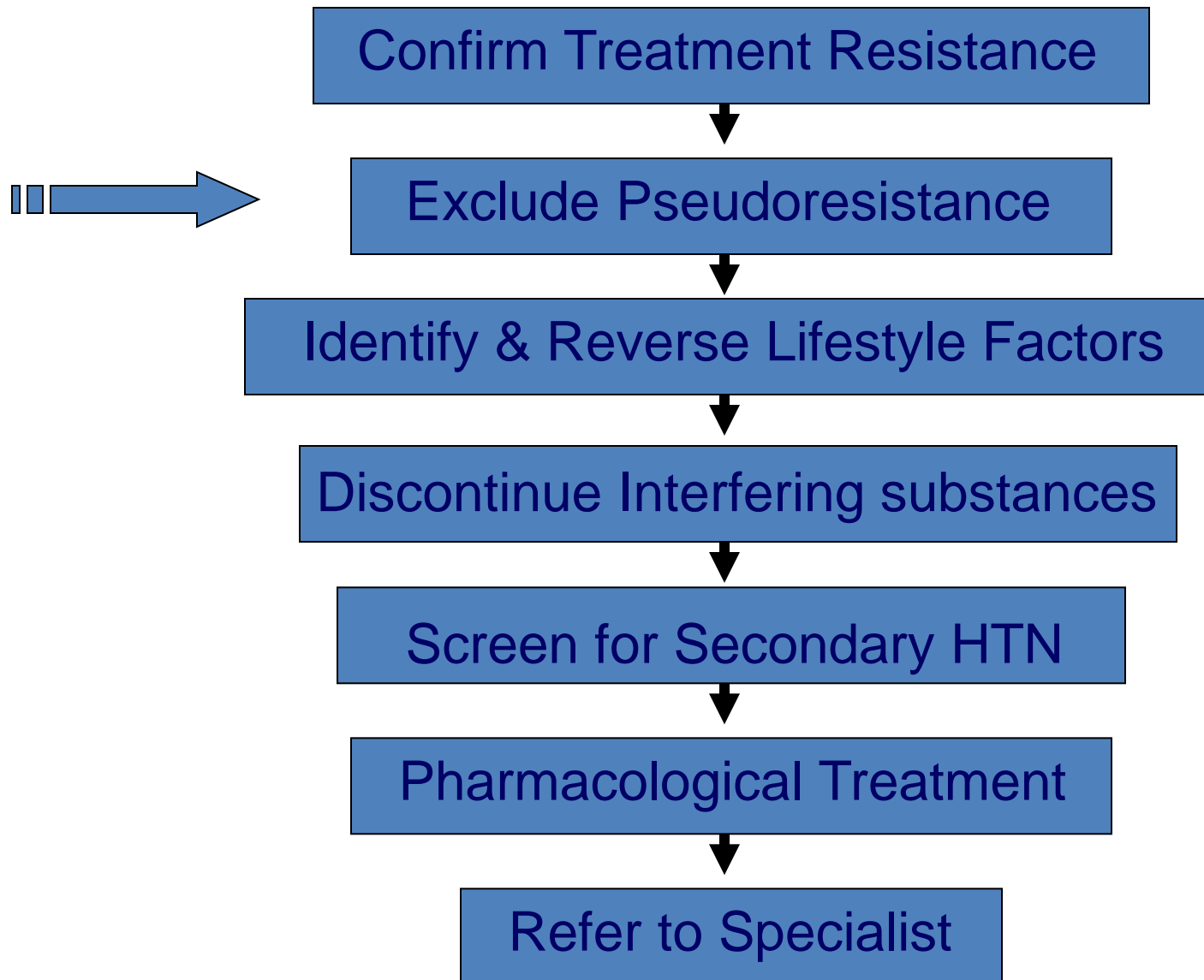
**Percent of patients
with resistant HTN
who had BP < 135/85
mmHg with ABP**



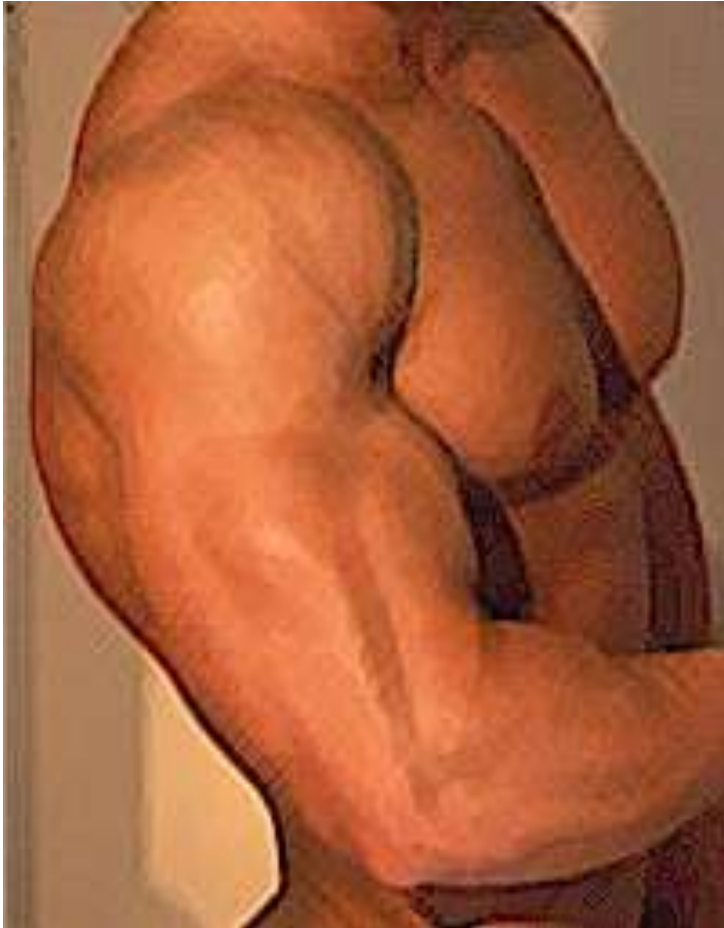
Case

- Home blood pressure checked with a home BP monitor
- They run systolic values of 150-160 mm Hg for the last 6+ months

Diagnostic and Treatment Recommendations



Big Arm + Small Cuff = High BP

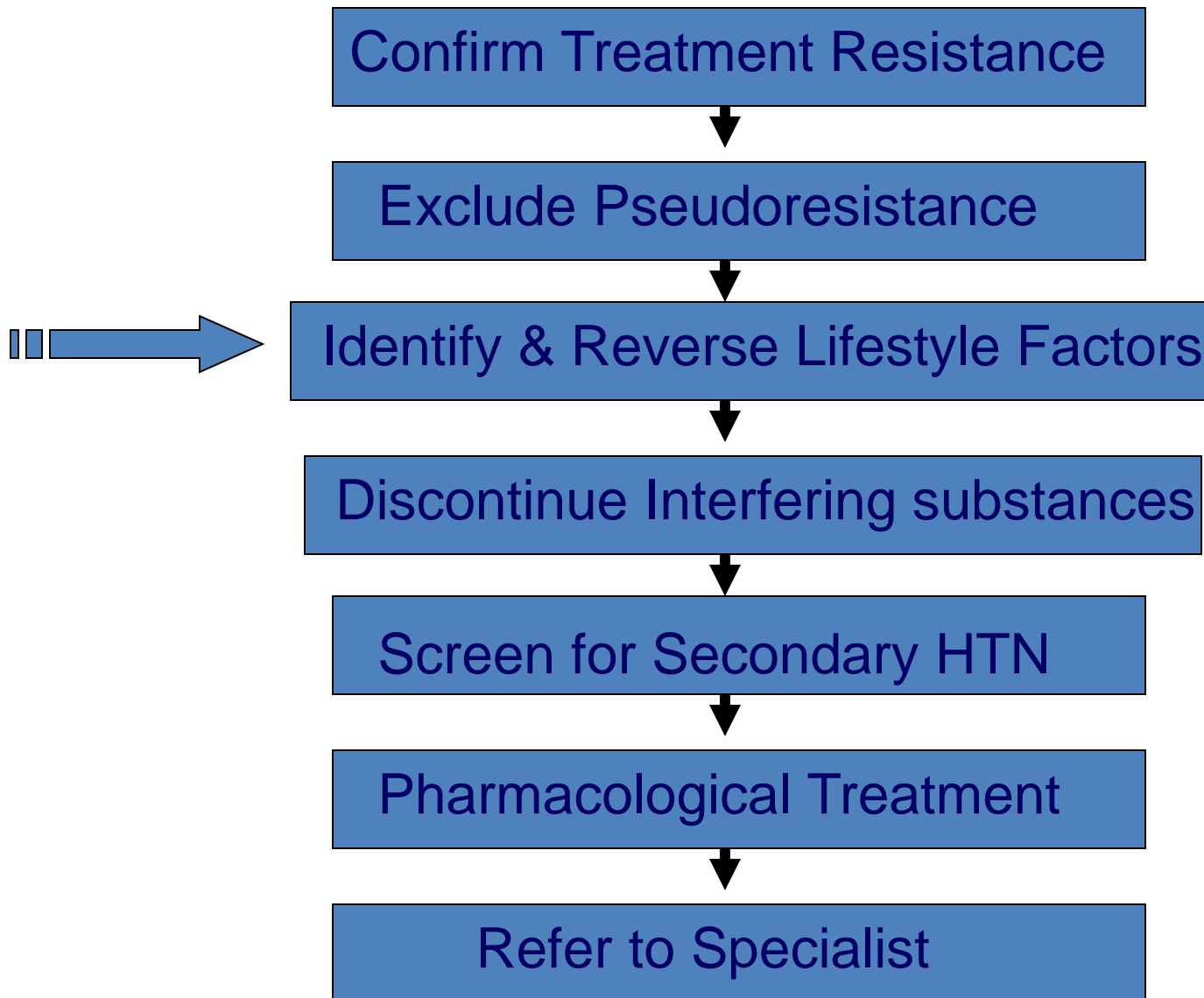




Case

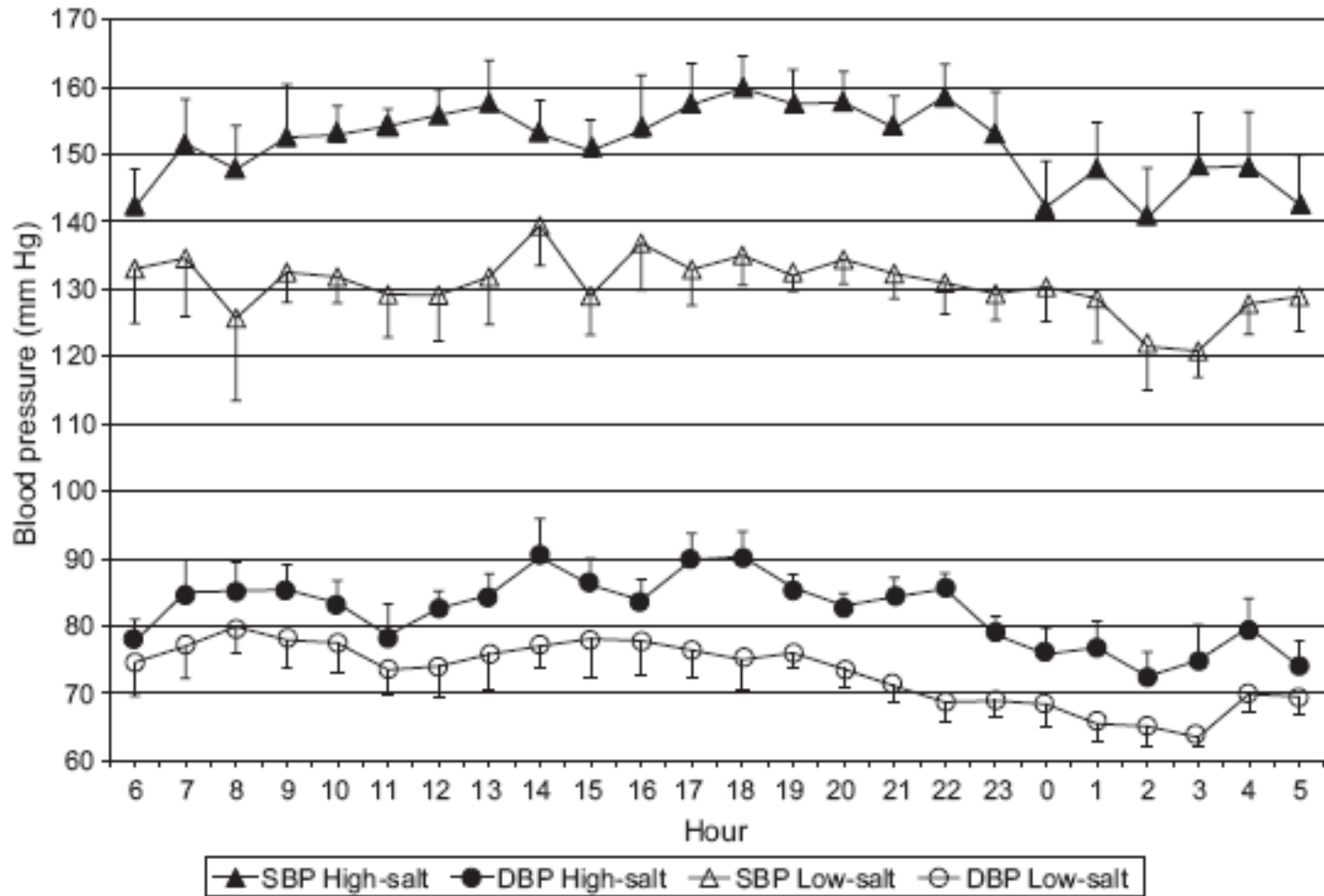
- Technique checked
- Monitor checked
 - $\sqrt{\quad}$ OK

Diagnostic and Treatment Recommendations



Causes of Resistant Hypertension

- ***Volume, volume, volume***
- Drug-related issues
 - Drug interaction
 - Intolerance due to known side effect
 - Suboptimal regimen
 - Interfering substance
- Nonadherence
- Secondary forms



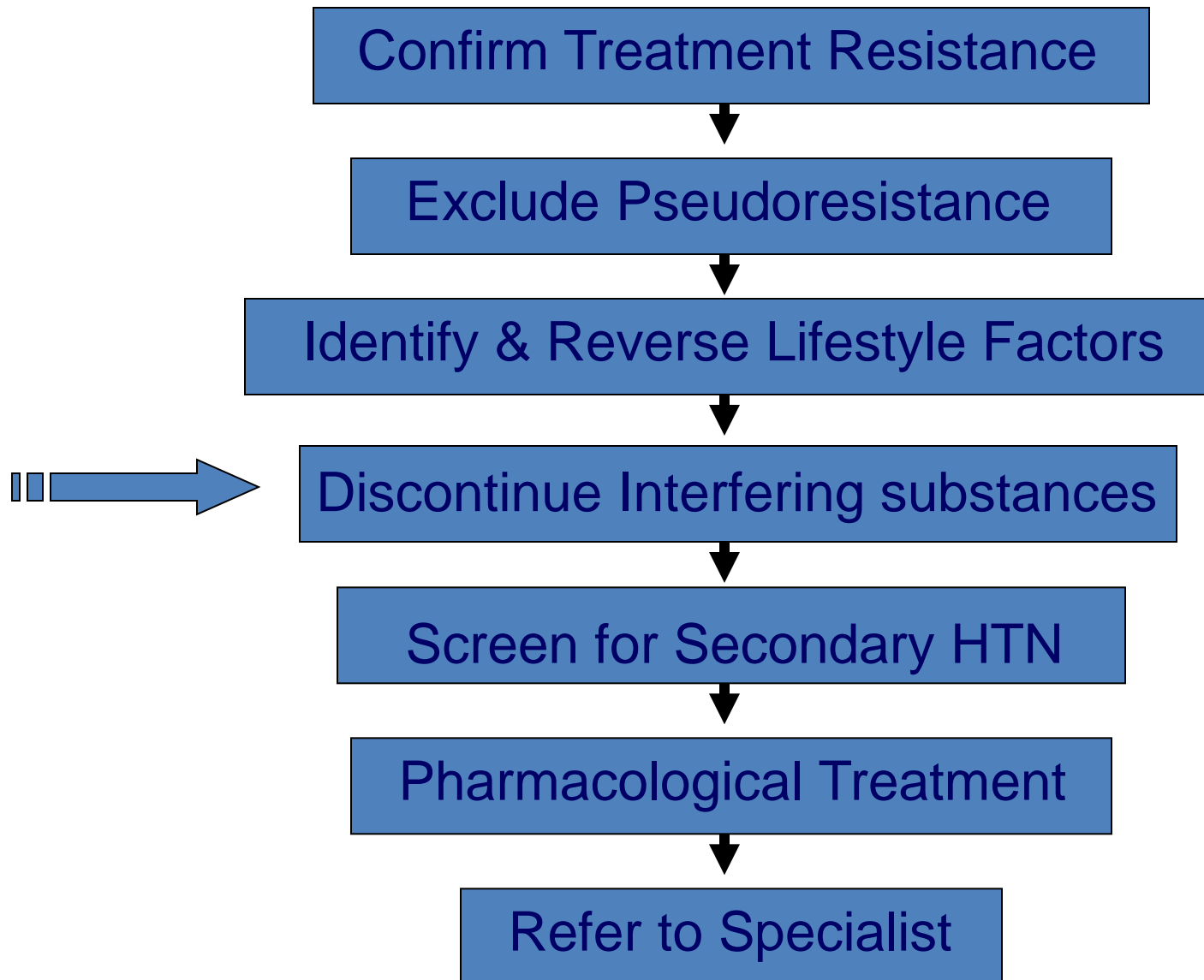
Pimenta Hypertension 2009;54:475-481

N=12

Case

- Very aware of salt and sodium
- Has been working on weight, has lost 7 pounds
- Currently 209 pounds (30.9 kg/m²)

Diagnostic and Treatment Recommendations



Interfering Substances

Table 2. Medications That Can Interfere With Blood Pressure Control

Nonnarcotic analgesics

Nonsteroidal antiinflammatory agents, including aspirin

Selective COX-2 inhibitors

Sympathomimetic agents (decongestants, diet pills, cocaine)

Stimulants (methylphenidate, dexamethylphenidate, dextroamphetamine, amphetamine, methamphetamine, modafinil)

Alcohol

Oral contraceptives

Cyclosporine

Erythropoietin

Natural licorice

Herbal compounds (ephedra or ma huang)

Apparent Mineralocorticoid Excess: Acquired

- 62 y/o woman with type 2 DM for 12 yrs and hypertension for 10 years
- Current Medication: Valsartan, Lasix, Verapamil, Vitamin E, Vitamin C, Ibuprofen, Herbal preparation
- Home BP: am 180/110, midday 110/80, evening 150/100 mmHg
- Lab
 - Today: Na 144, K 2.6 TCO₂ 35, Cl 95
 - 6 months ago: Na 138, K 4.5 TCO₂ 26, Cl 101

Resistant Hypertension 62 y.o. Woman

Plasma aldosterone = 2 ng/dl

Plasma renin activity = 0.2 ng/ml/hr



ECLECTIC INSTITUTE

HERBAL EXTRACT
A DIETARY SUPPLEMENT

Licorice

Glycyrrhiza glabra

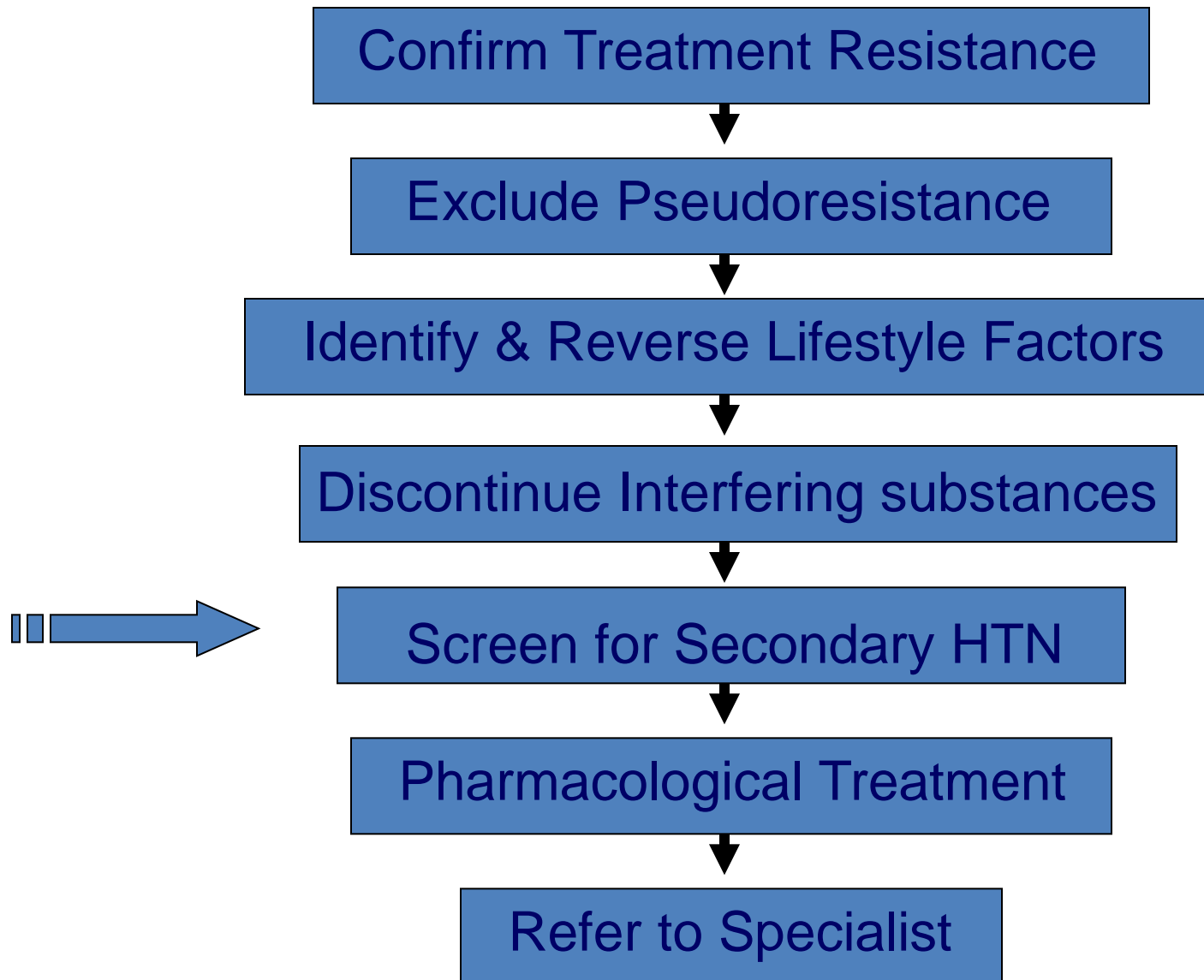
one fluid ounce

THE
HERBAL SOCIETY'S
CHOICE
ORGANIC
ORGANIC &...

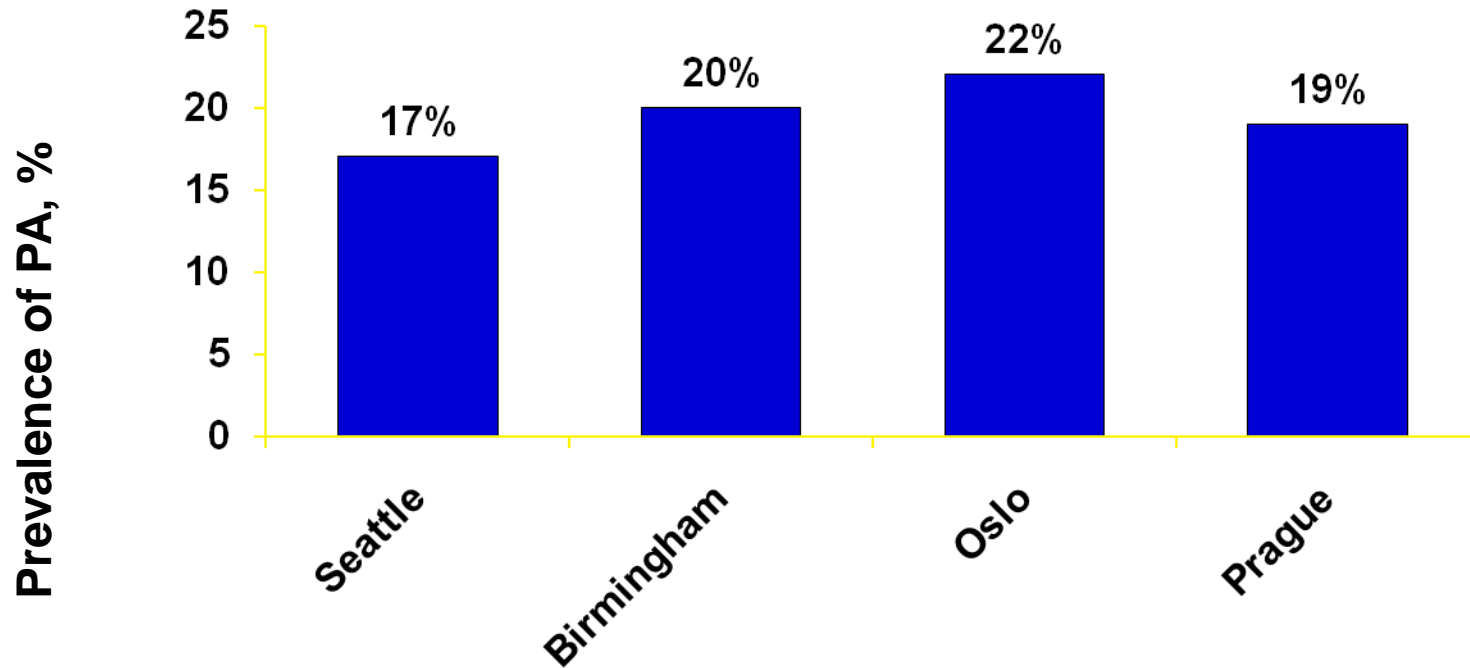
Case

- Patient was not taking any interfering substances

Diagnostic and Treatment Recommendations



Prevalence of Primary Aldosteronism in Subjects With Resistant Hypertension



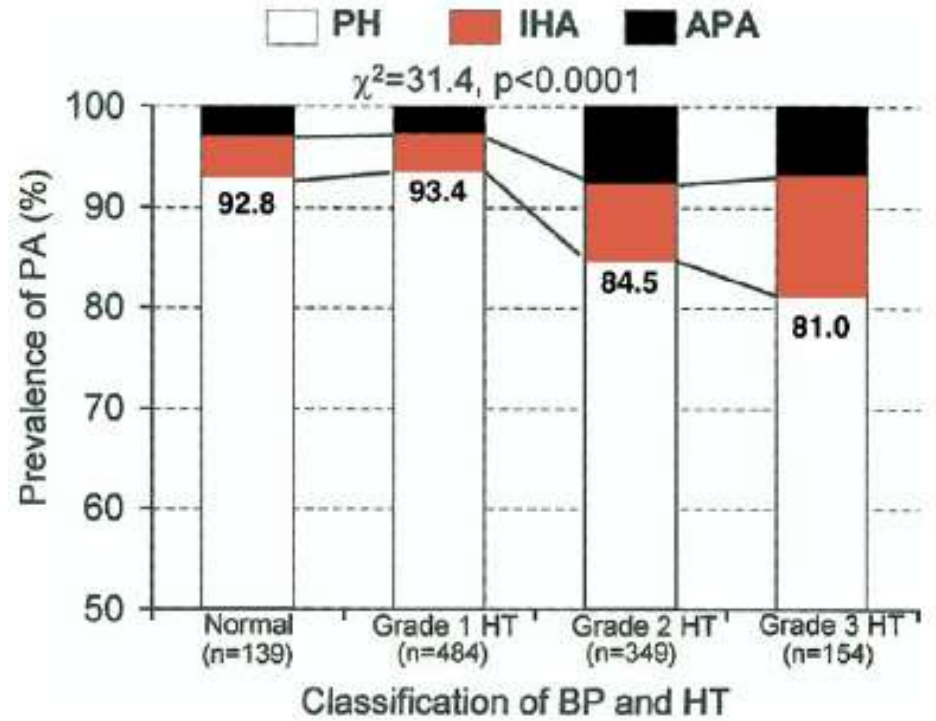
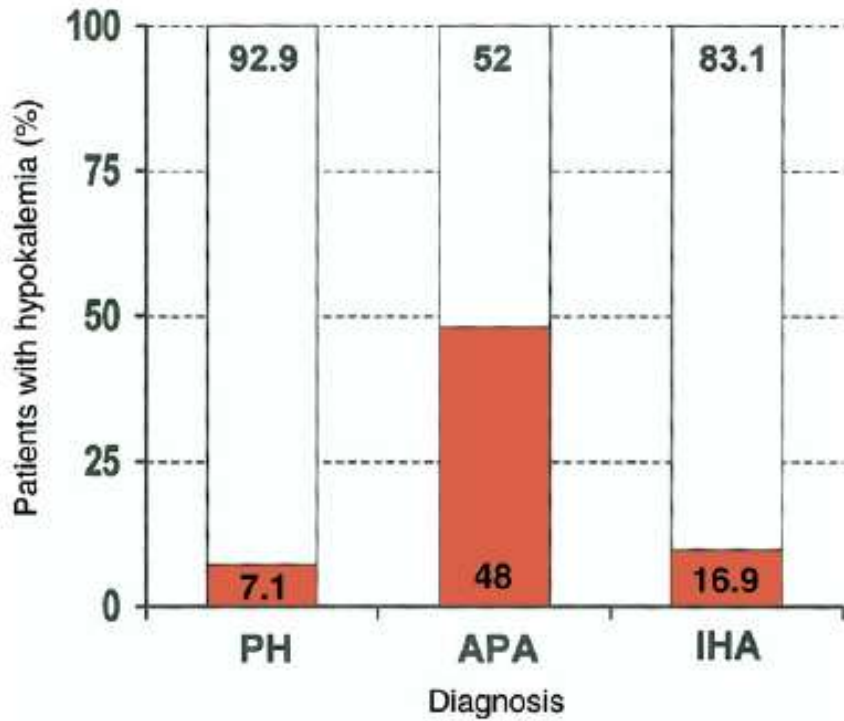
PA = Primary aldosteronism

1. Gallay BJ, et al. *Am J Kidney Dis.* 2001;37:699-705.
2. Calhoun DA, et al. *Hypertension.* 2002;40:892-896.
3. Eide IK, et al. *J Hypertens.* 2004;22:2217-2226.
4. Strauch B, et al. *J Hum Hypertens.* 2003;17

Whom to suspect?

- Low K⁺
- Drug Resistance
- Negative Family History of Hypertension
- Obesity and sleep apnea
- Serendipitous occasions
 - The unexpected adenoma

PAPY Study

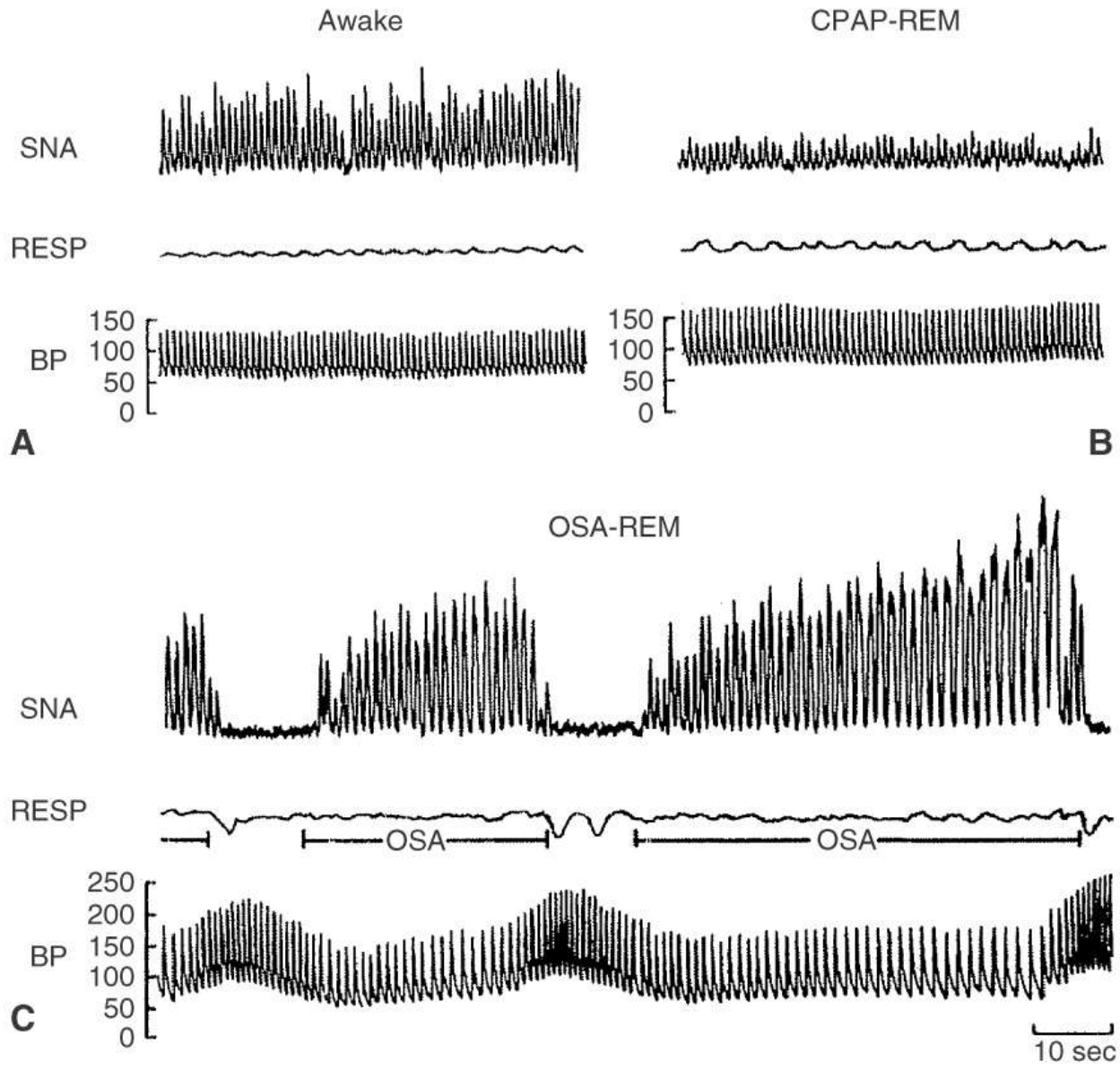


Sleep Apnea

Table. Obstructive Sleep Apnea (OSA) Effects on Blood Pressure (BP)

STUDY	SUBJECTS	BP METHOD	FINDINGS, SBP/DBP, MM HG
Coughlin et al ²⁷	N=104: 61 obese OSA, 43 obese control	Clinic	BP ↑ 11.4/5.2 in OSA vs control ($P<.004$)
Moller et al ¹⁹	N=42: 24 overweight OSA, 18 overweight control	24 hour	Daytime BP ↑ 20/12 in OSA vs control; nighttime BP ↑ 22/22 in OSA vs control ($P<.001$)
Davies et al ²⁸	N=90: 45 obese OSA, 45 obese control	24 hour	Daytime and nighttime DBP ↑ 4.6 and 7.2 in OSA vs control ($P<.001$ and 0.04, respectively); nighttime SBP ↑ 9.2 in OSA vs control ($P=.01$)
Pankow et al ²⁹	N=93: 38 overweight severe OSA, 35 overweight moderate OSA, 20 overweight control	24 hour	Daytime BP ↑ 13/10 and 8/7 for severe OSA and moderate OSA respectively vs control ($P<.005$); nighttime BP ↑; 21/15 and 7/6 for severe OSA and moderate OSA respectively vs control ($P<.001$)
Pankow et al ³⁰	N=50: 25 overweight OSA, 25 overweight control	24 hour	Daytime BP ↑ 7.9/6.9 in OSA vs control ($P<.05$); nighttime BP ↑ 14.3/9.1 in OSA vs control ($P<.01$)

SBP indicates systolic BP; DBP, diastolic BP; and control, study group free from OSA.



Somers VK JCI 1995;96:1897-1904

Potential mechanisms by which OSA contributes to the development of resistant hypertension

- Calhoun et al have demonstrated increased aldosterone excretion in subjects with resistant hypertension and symptoms of sleep apnea.
- Stimulation of the catecholamine axis through repeated exposure to hypoxia

BP responses to CPAP

- Usually in the range of 10/5 mm Hg

Atherosclerotic Renal Artery Stenosis (ARAS): Clinical Characteristics

- Older, men > women
- Generalized atherosclerosis
- Correlates:
 - HTN
 - Chronic kidney disease (ischemic nephropathy)
 - Usually have a cigarette history
 - Volume overload
 - “Flash” pulmonary edema

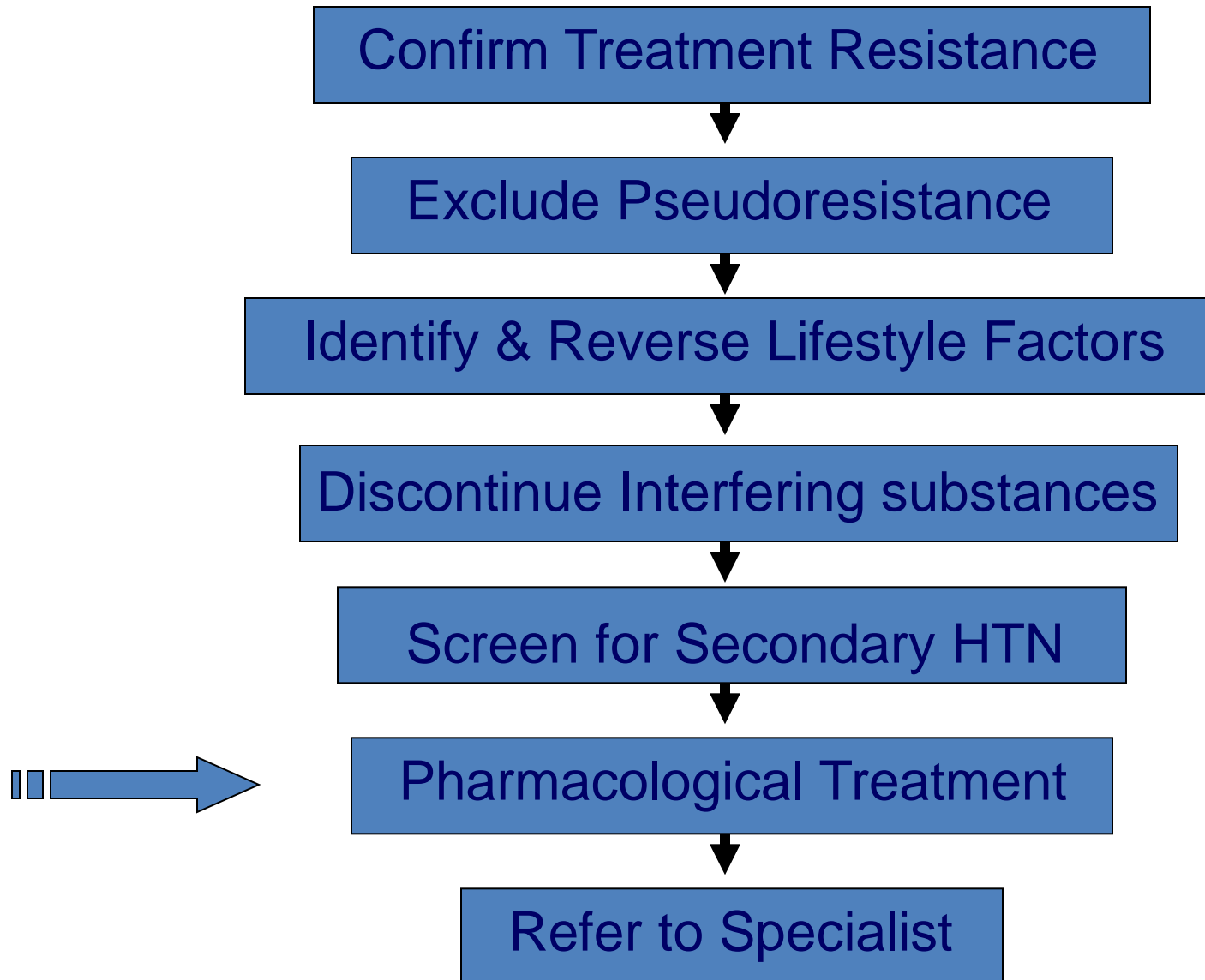
ARAS: Treatment options

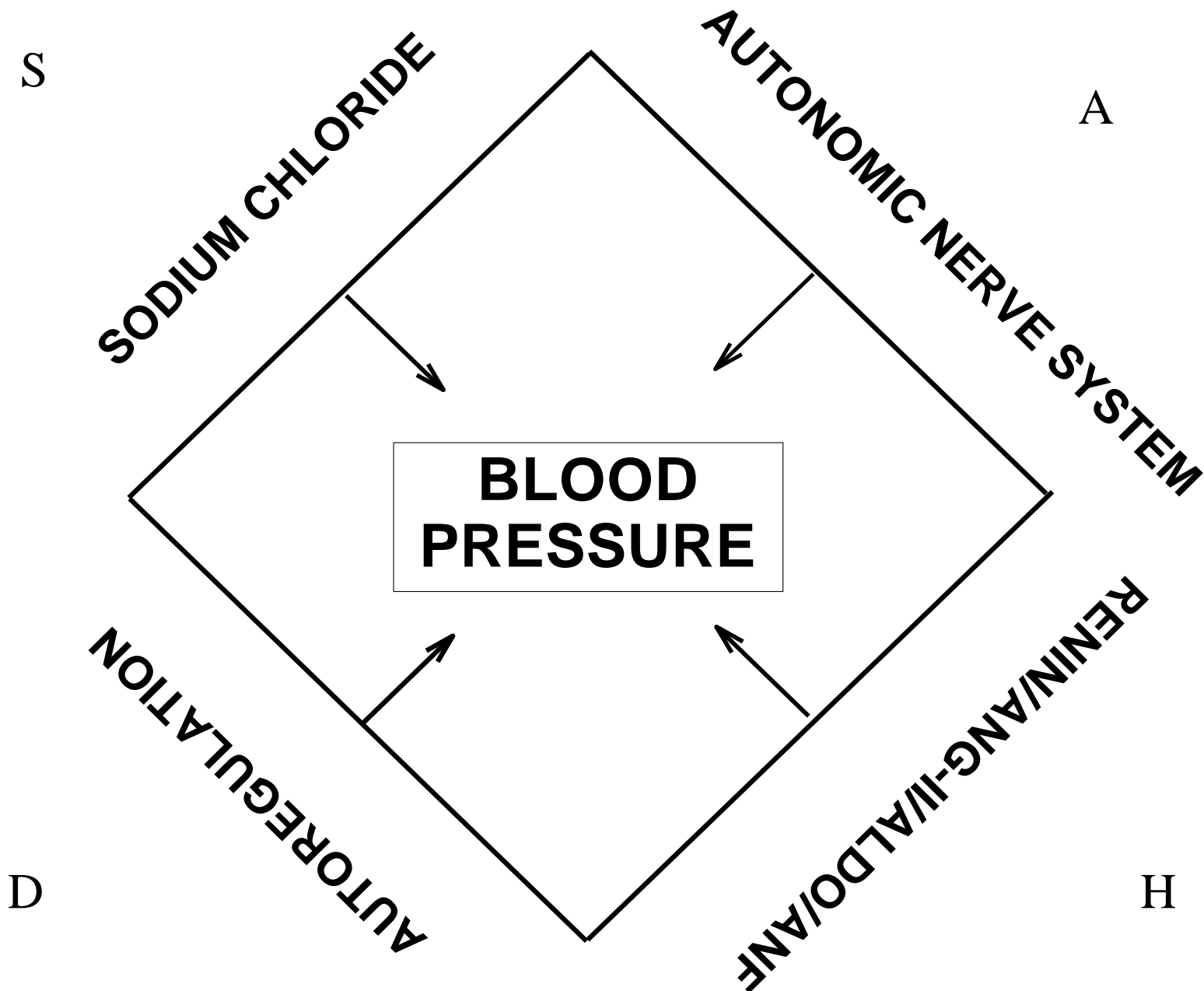
- Medical therapy
- Revascularization
 - Surgical
 - Percutaneous
- Best therapy, particularly for bilateral disease with some renal function impairment, is still debated

Case

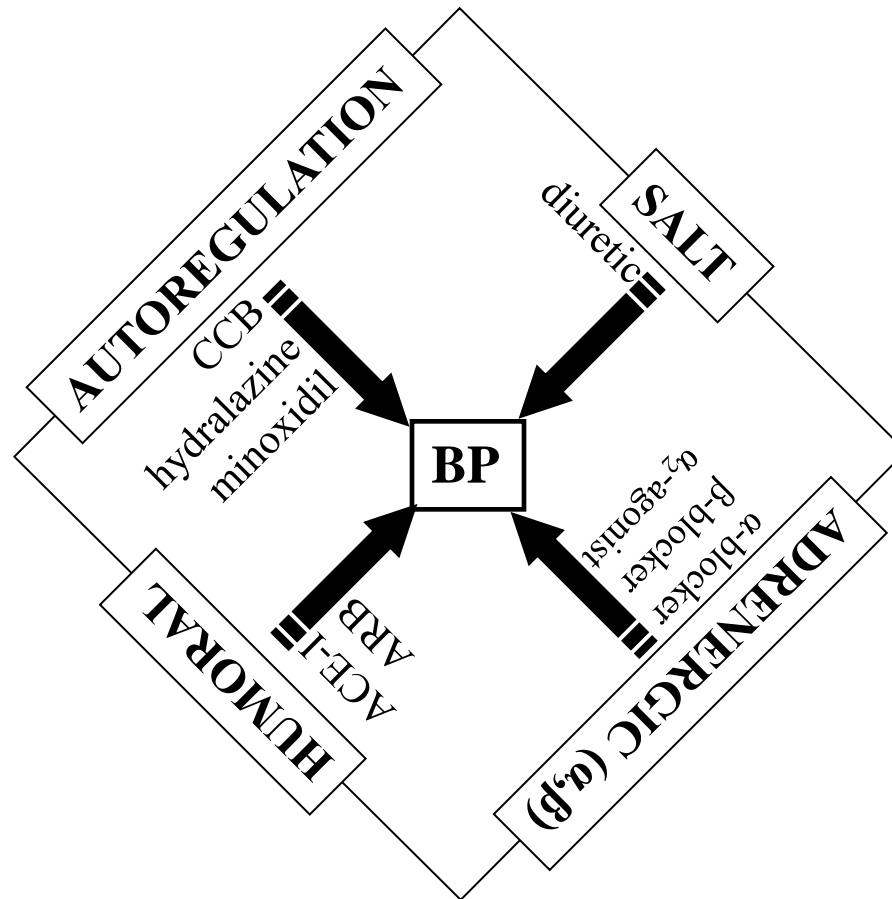
- Non-smoker
- No bruits
- Renal CT angio was not done
- Plasma metanephrines were normal (and an MRI was also done, adrenal glands appeared normal)
- There are no symptoms of snoring, no daytime somnolence, but NO sleep study was done

Diagnostic and Treatment Recommendations

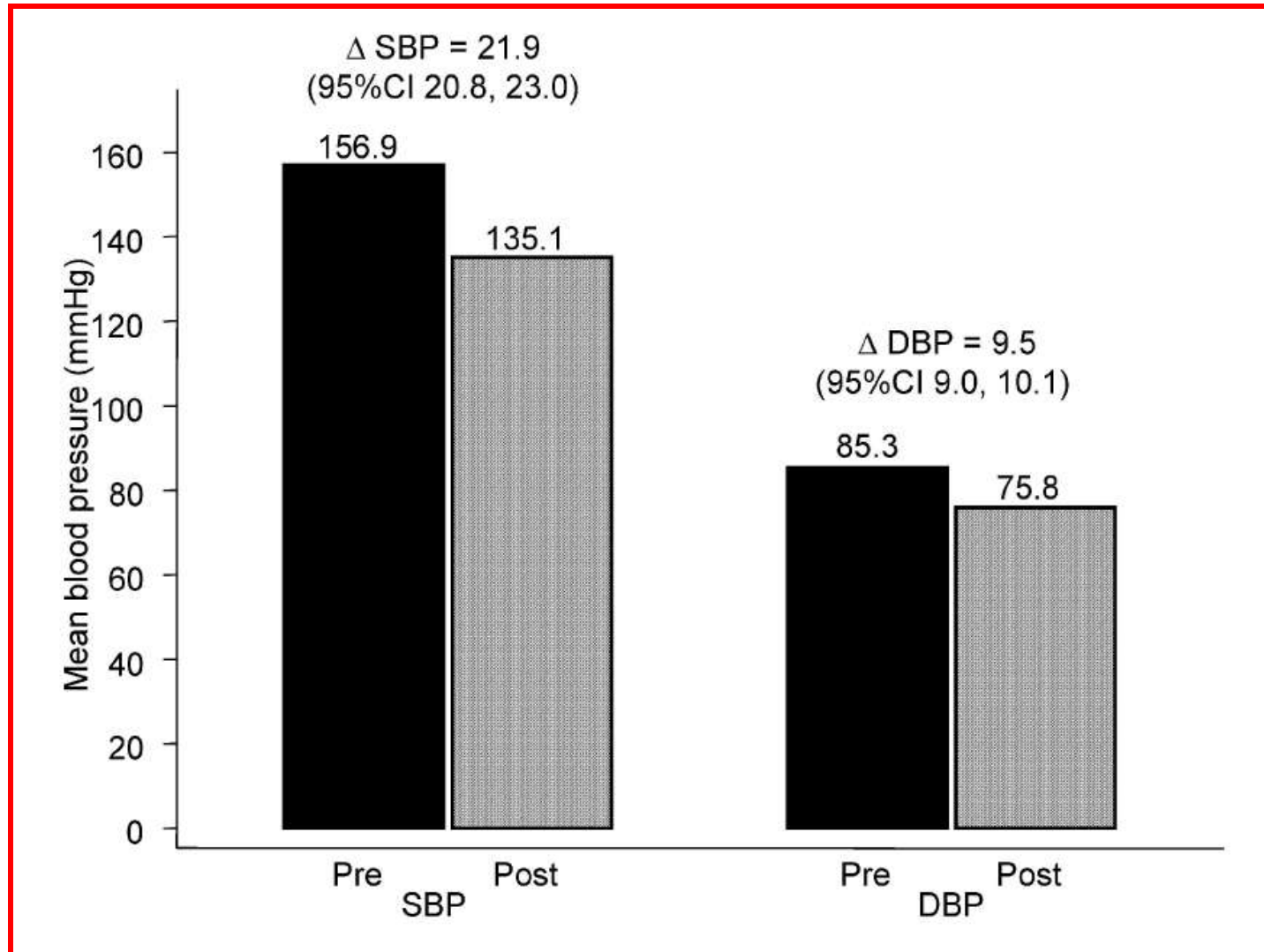




BASICS of BLOOD PRESSURE



ASCOT: BP Response to Spironolactone



Diagnostic and Treatment Recommendations

Confirm Treatment Resistance



Exclude Pseudoresistance



Identify & Reverse Lifestyle Factors



Discontinue Interfering substances



Screen for Secondary HTN



Pharmacological Treatment



Refer to Specialist



Resistant or Difficult-to-Control Hypertension

Marvin Moser, M.D., and John F. Setaro, M.D.

N Engl J Med 2006;355:385-92.

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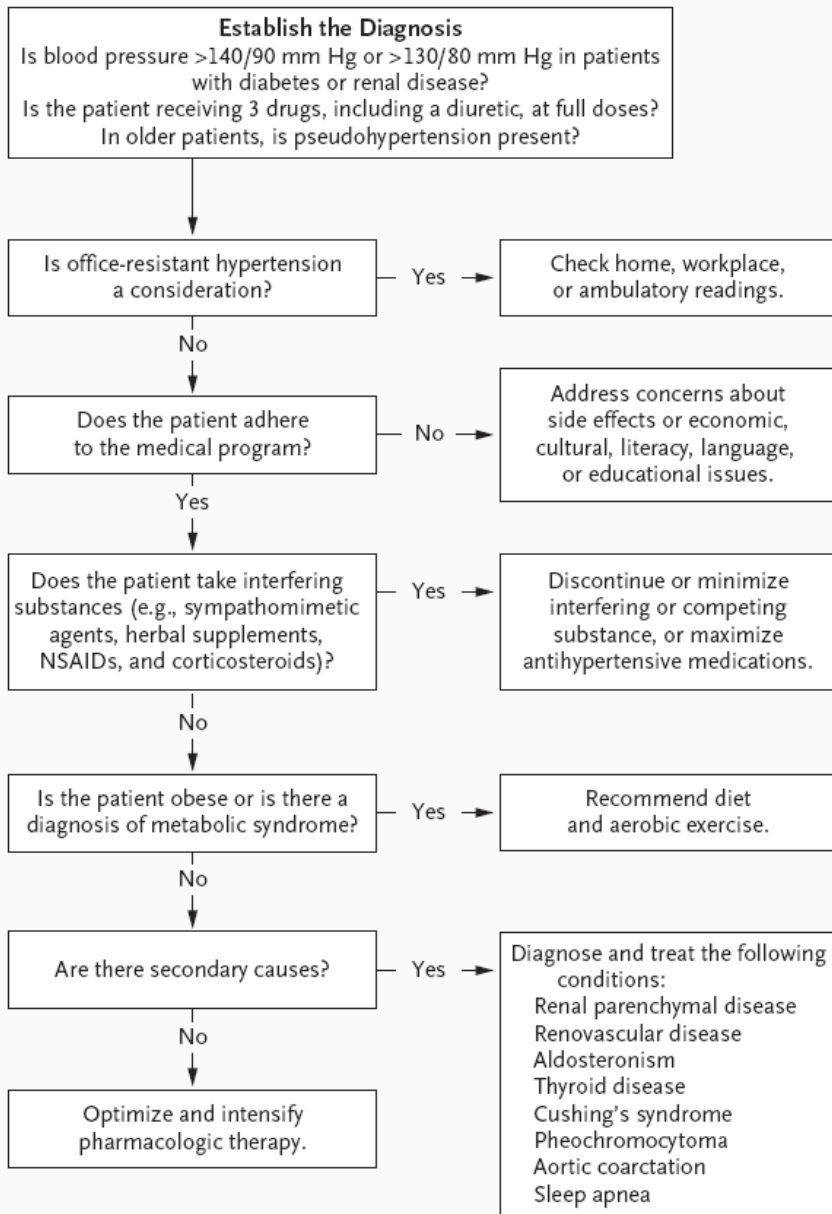


Figure 1. Treatment of Resistant Hypertension.

NSAIDs denotes nonsteroidal antiinflammatory drugs.

Diagnostic and Treatment

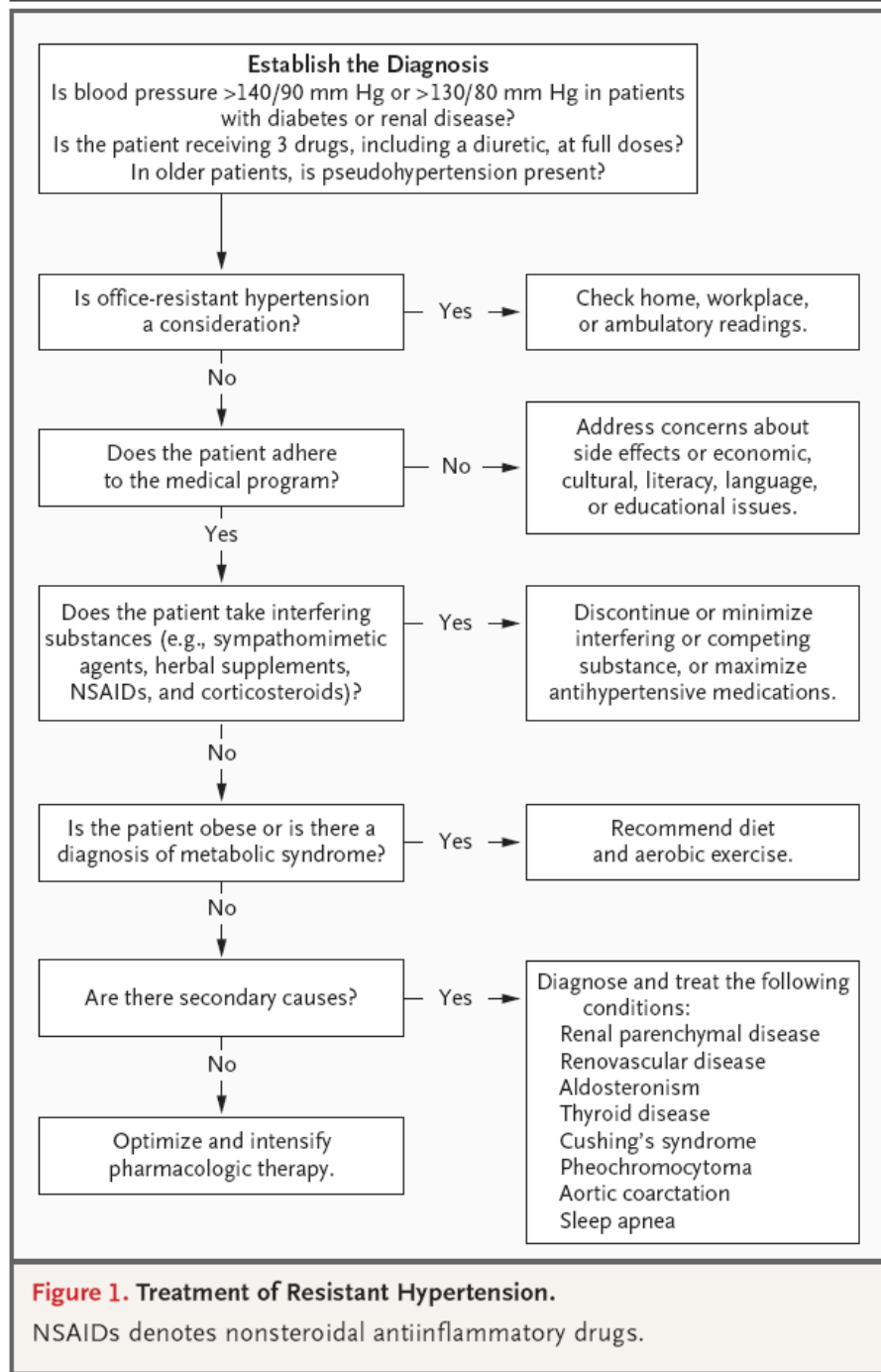
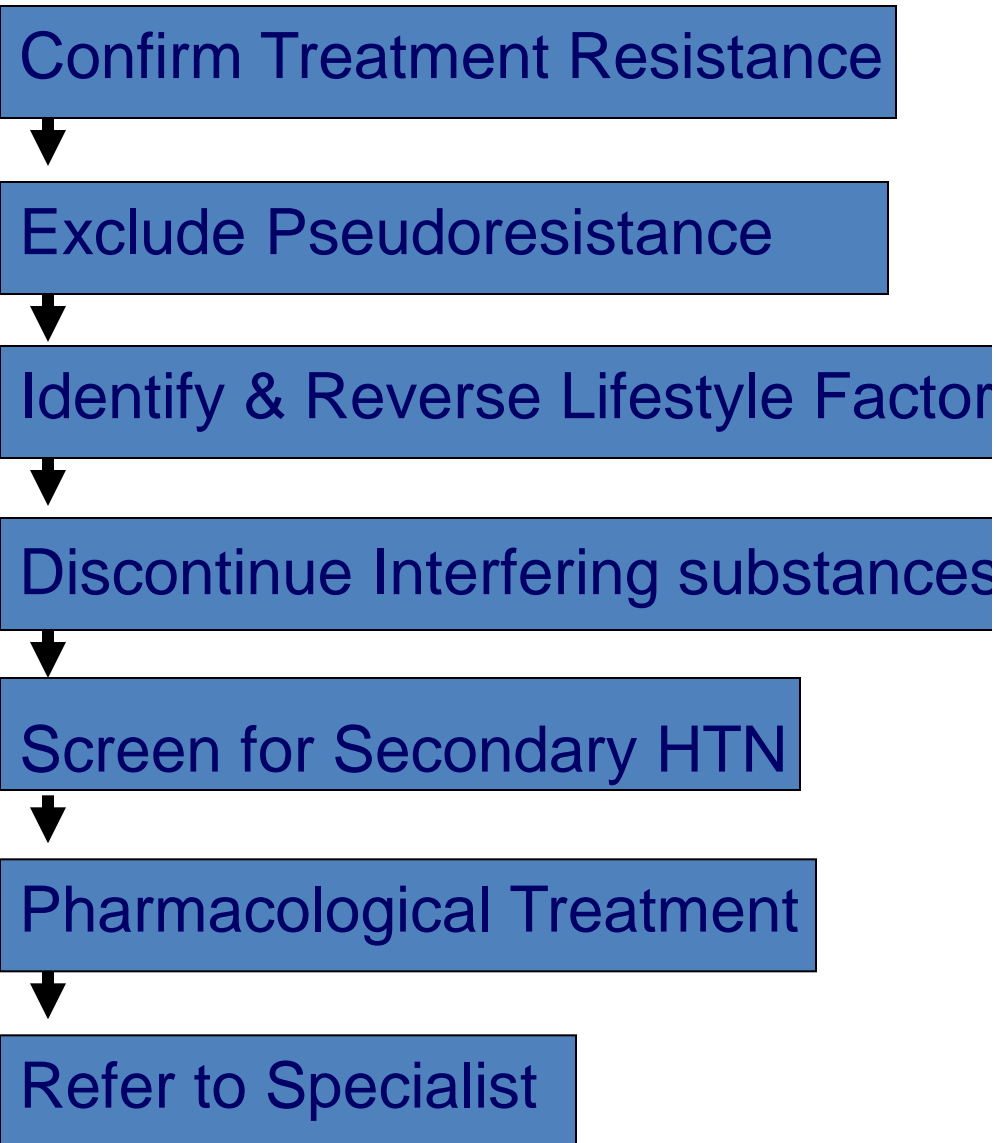
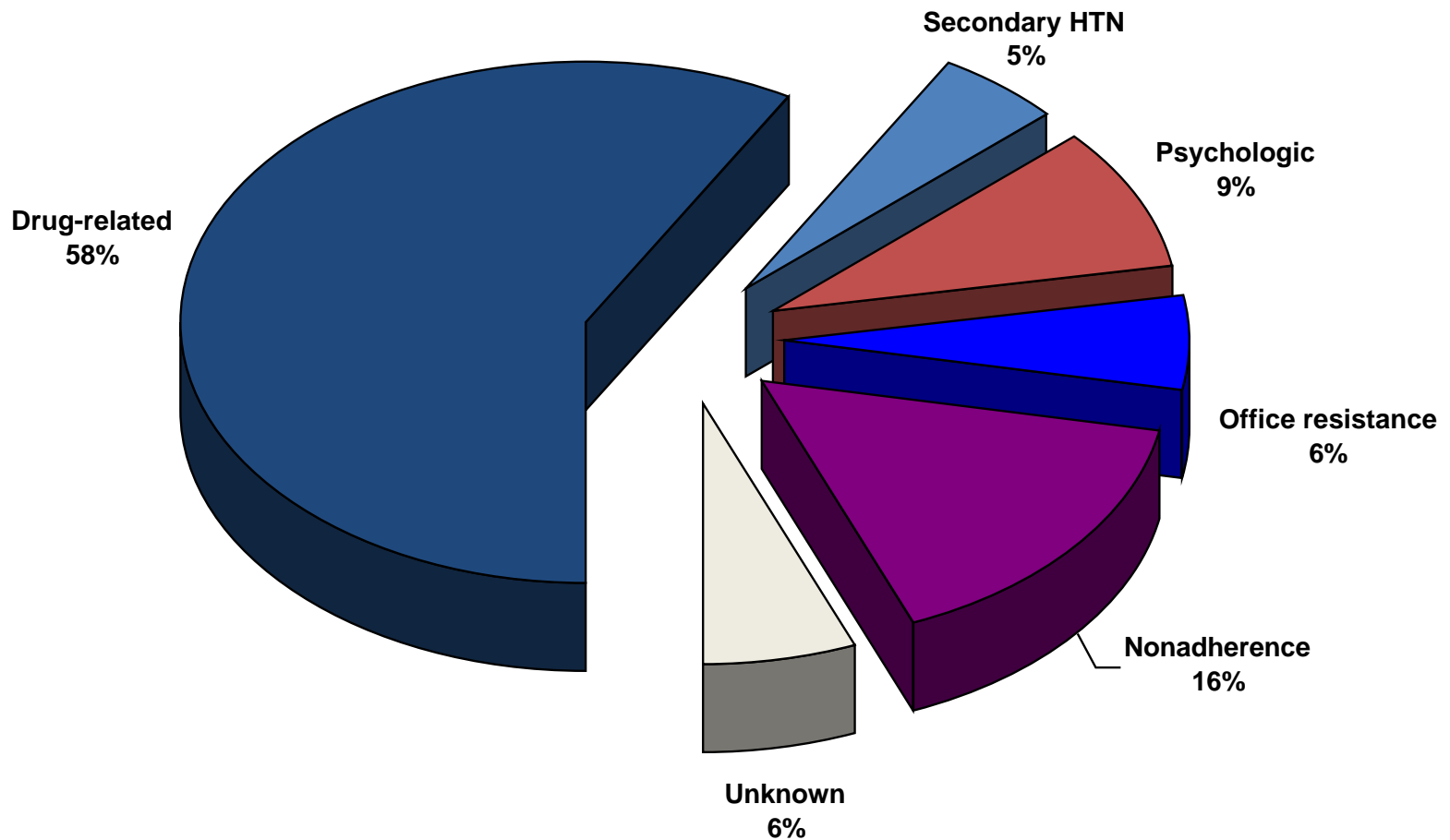


Figure 1. Treatment of Resistant Hypertension.

NSAIDs denotes nonsteroidal antiinflammatory drugs.

Causes of Resistant HTN

Garg et al AJH 2005



Reasons for Inadequate BP Control

- Acceptance of inadequate control by physician
- Difficulty achieving BP control with one agent/suboptimal regimens
- BP goals are more aggressive than in previous years
- Lack of compliance due to:
 - perceived side effects of antihypertensive medication(s)
 - frequency of dosing/multiple agents to attain control

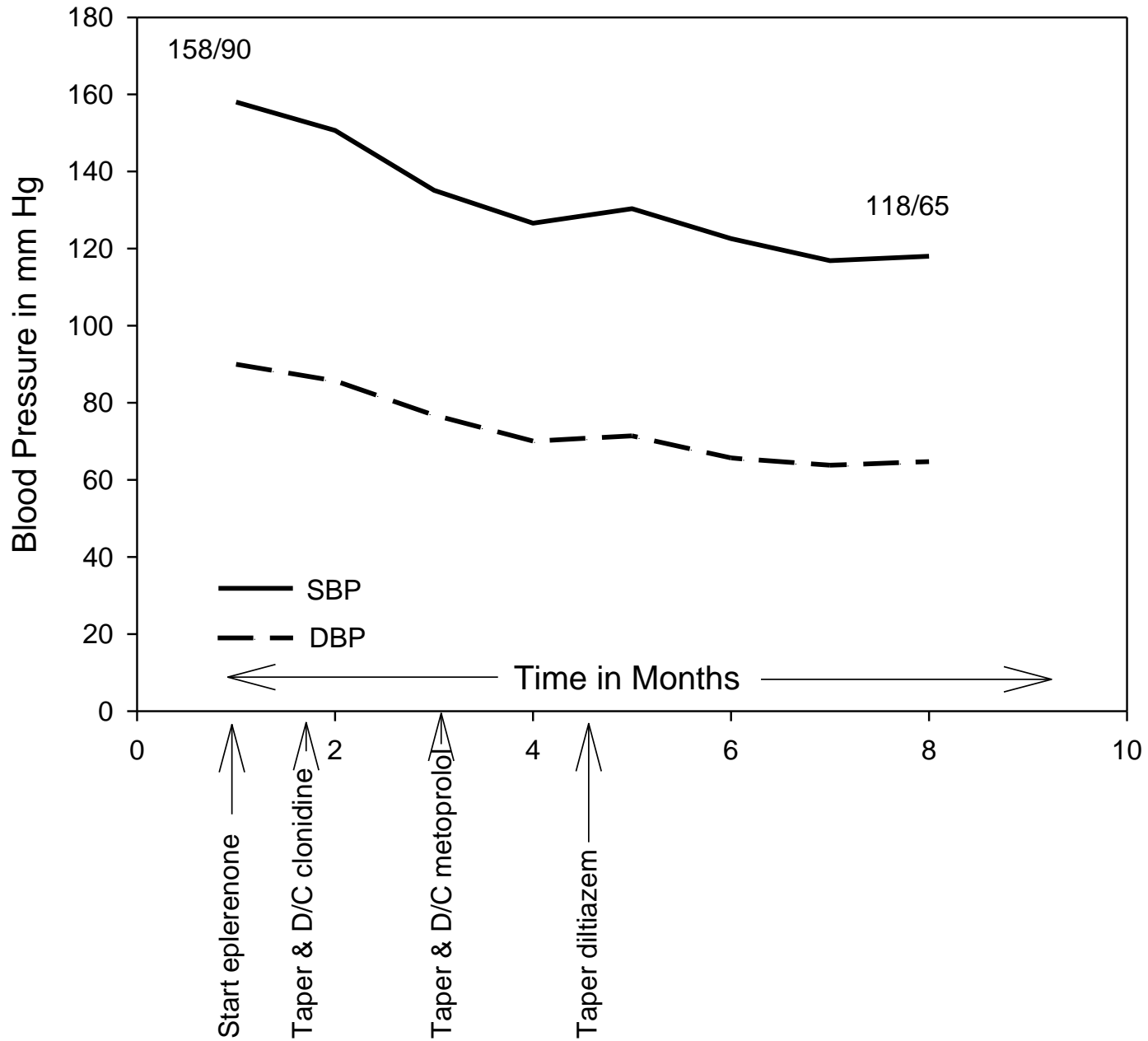
Strategies for Improving Adherence to Regimens

- Clinician empathy increases patient trust, motivation, and adherence to therapy
- Once daily dosing, combination therapies
- Physicians should consider their patients' cultural beliefs and individual attitudes in formulating therapy

Case

- Plasma renin activity = 0.1 ng/mL/hr
- Serum aldosterone = 8.0 ng/dL

Time Course for 51 y.o. Man

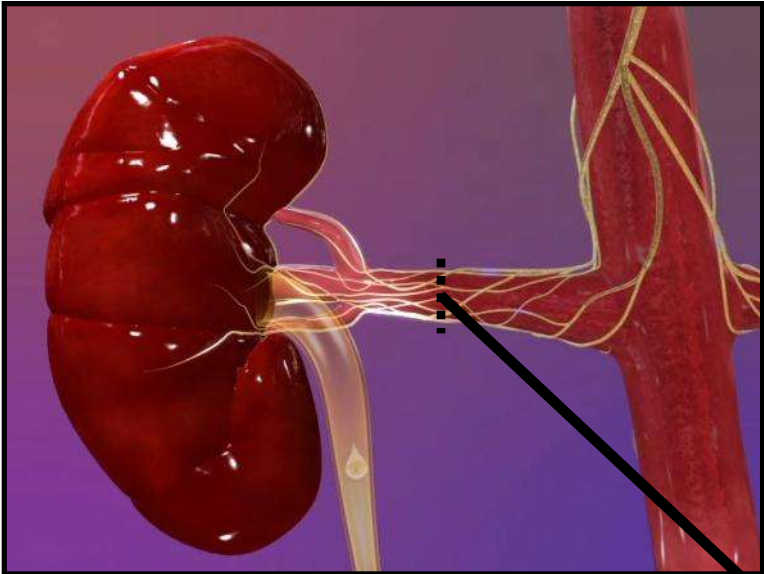


Novel Therapies

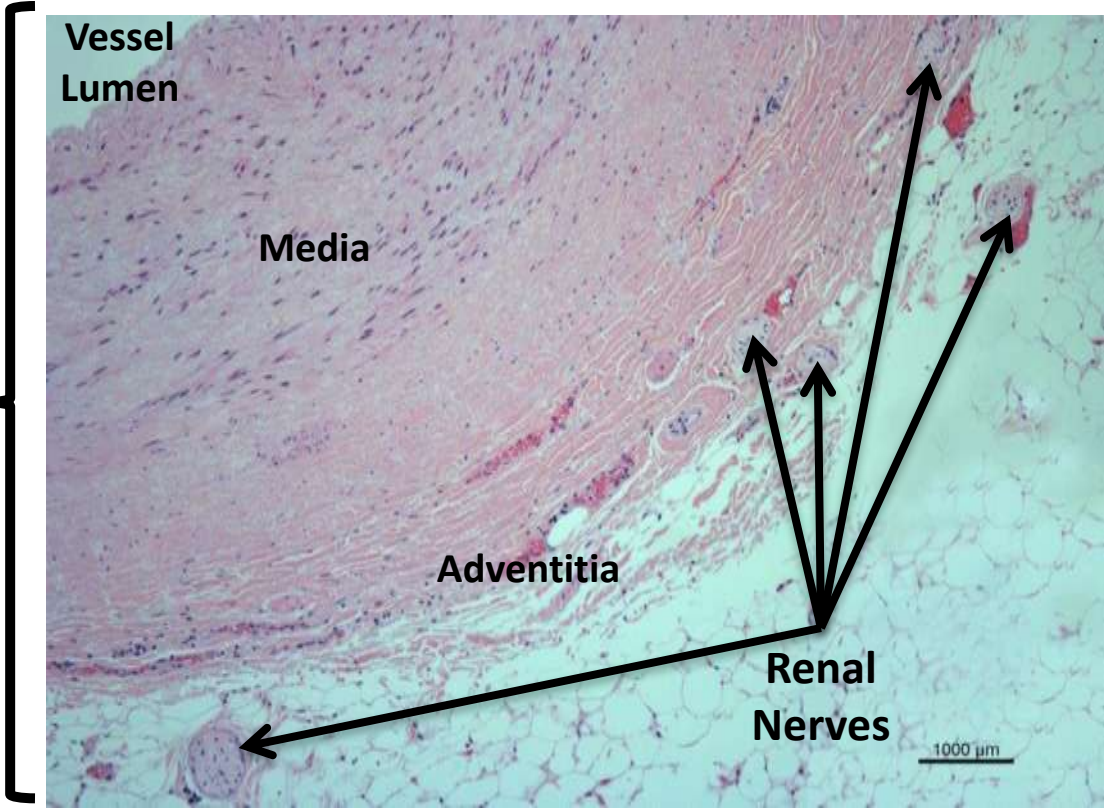
Symplivity Renal Denervation

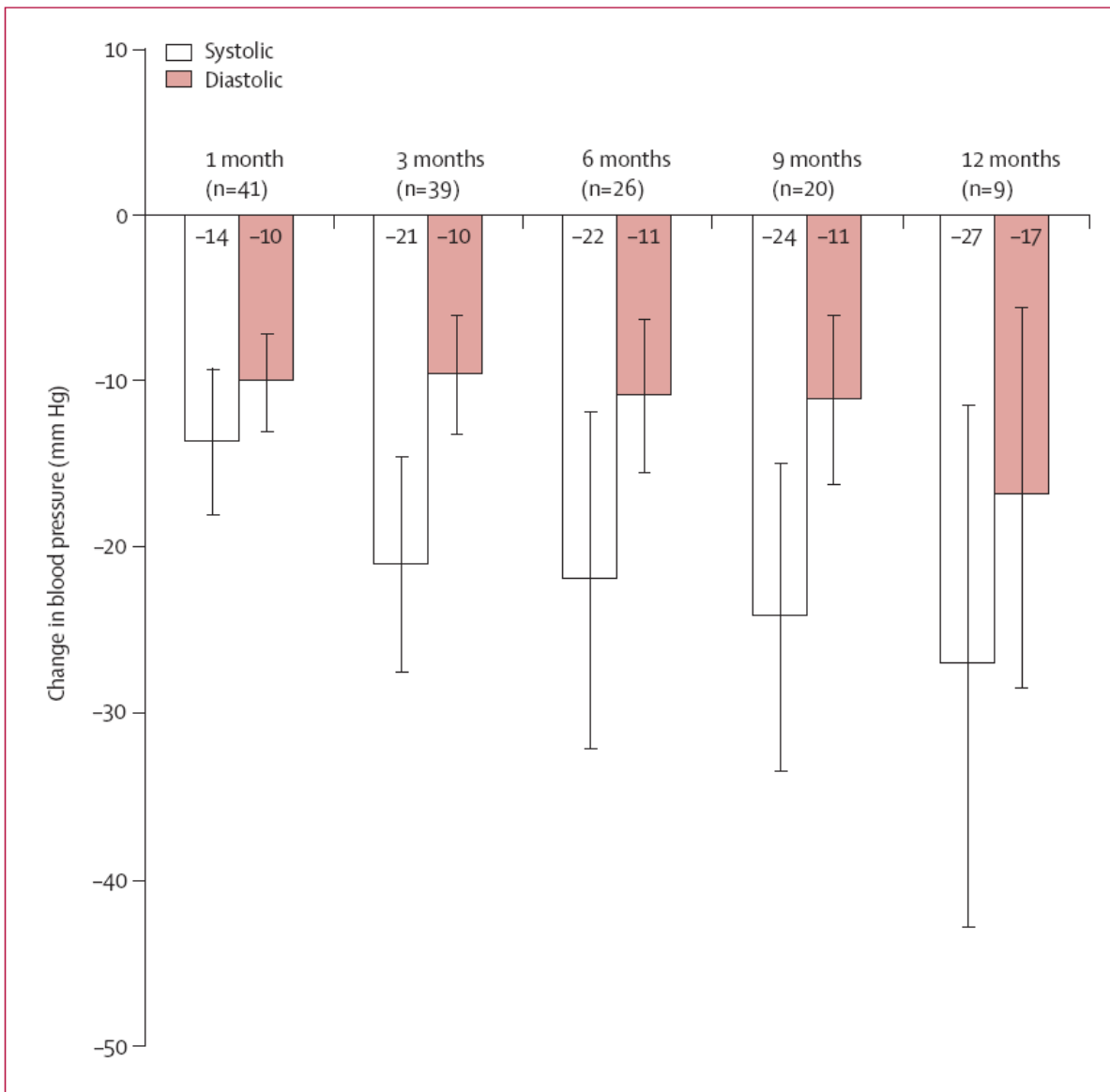
- Symplivity[®] System (Medtronic) uses radiofrequency ablation delivered by a catheter directly applied to the lumen of both renal arteries (sequentially) through a femoral access procedure that usually takes less than hour to complete.
- This procedure reduces sympathetic inflow into [efferent], and out from [afferent], the kidneys.
- The recent report of the Simplicity HTN-2 trial indicates sustained BP reduction in most patients at 6 months

Renal Nerves as a Therapeutic Target



Arise from ~ T10-L2
Follow the renal artery to the kidney
Primarily lie within the adventitia



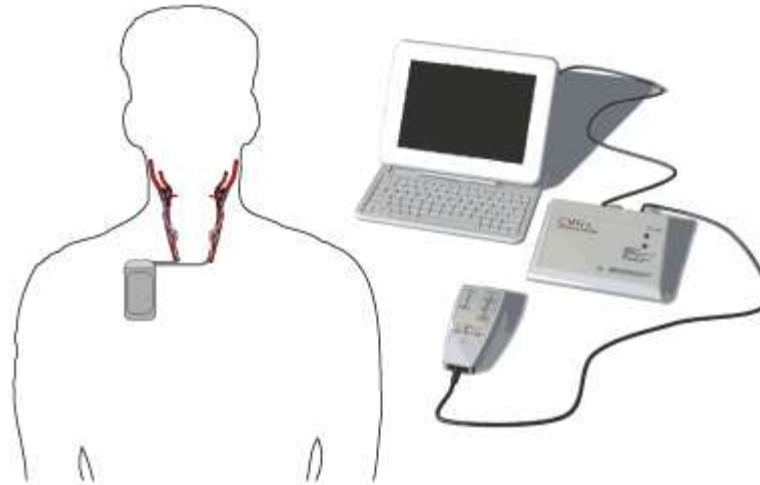


Krum: Lancet 2009;373:1275-1281

Rheos Device

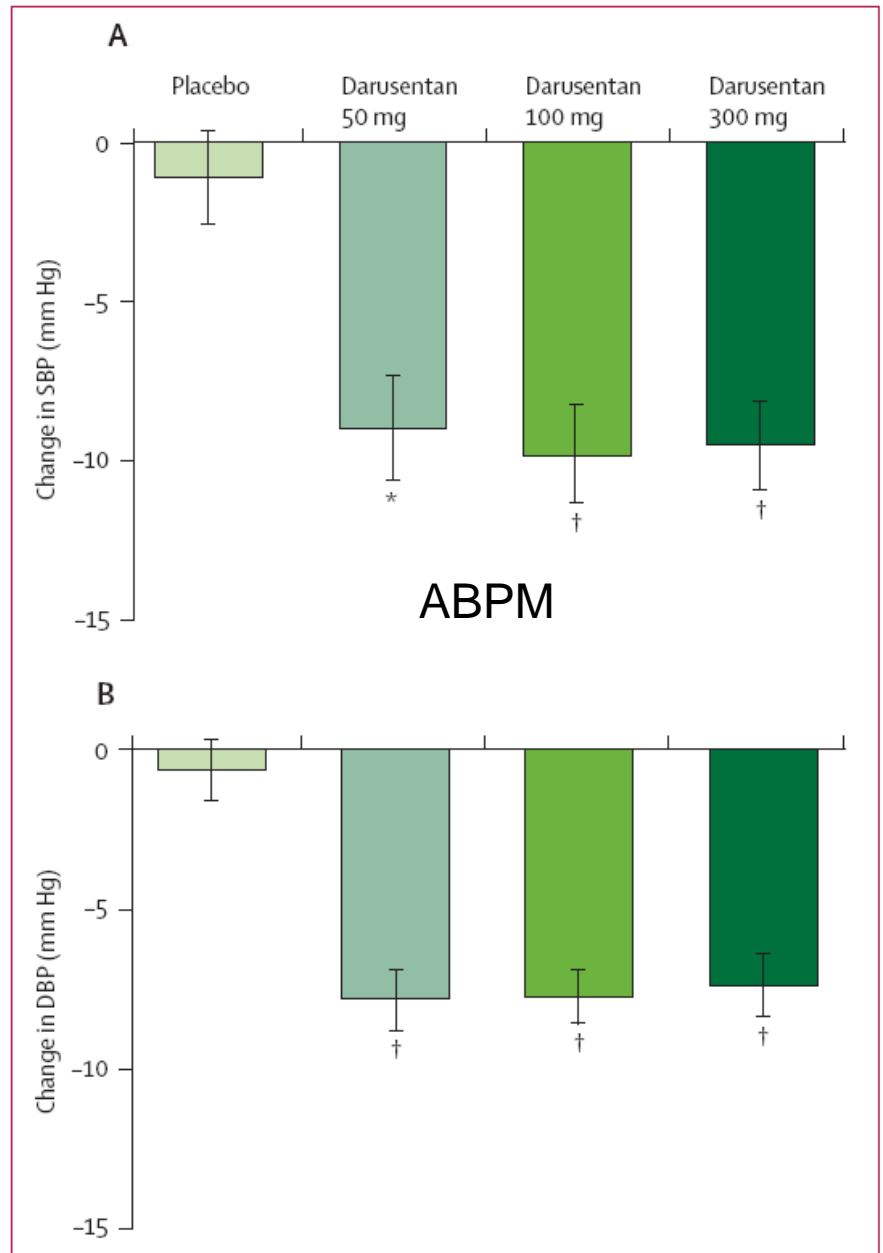
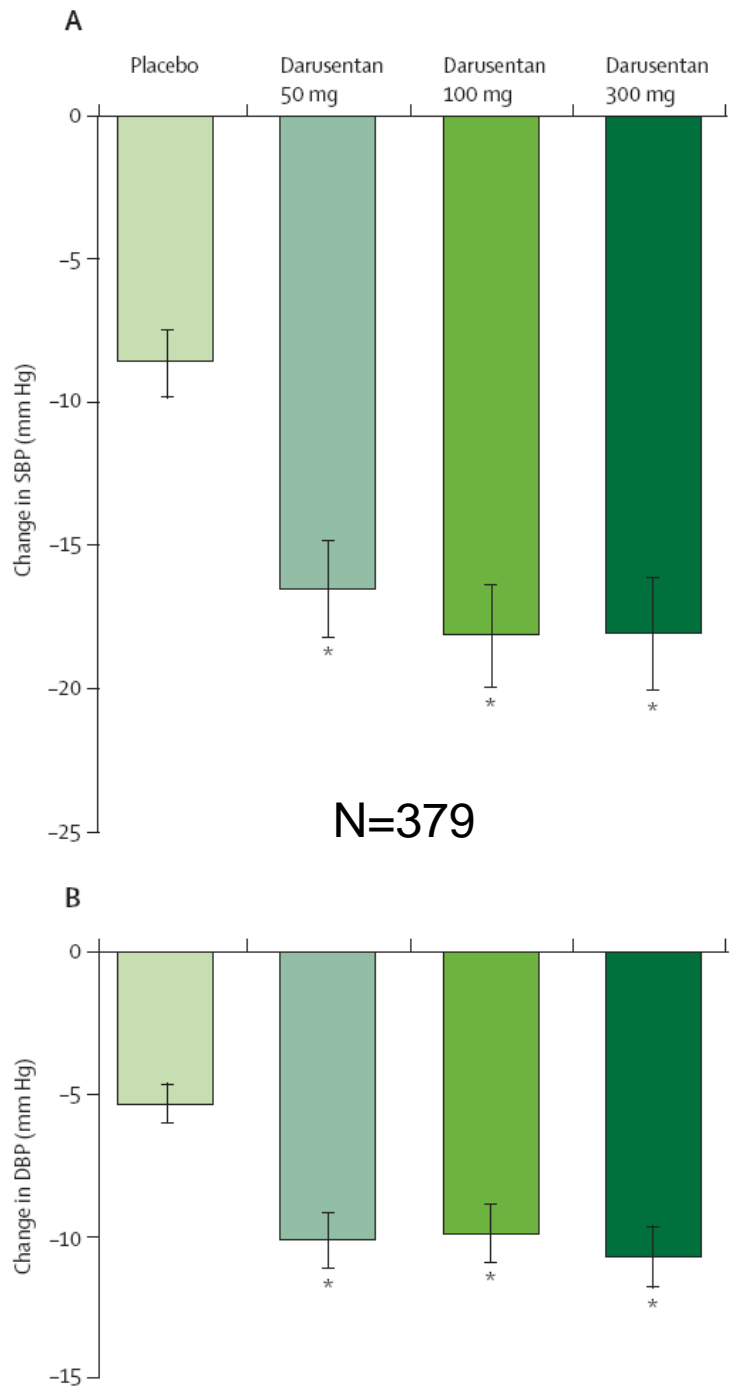
- Rheos[®] System (CVRx), utilizes the known effects of baroreceptor stimulation to reduce sympathetic output and lower BP
- Requires surgical implantation of a pacemaker-like device that has an electrode tunneled from its subclavicular location to the carotid body on each side of the neck
- When the pacemaker is turned on it activates baroreceptor input into the brainstem resulting in BP reduction that appears to be sustained for several years

Rheos System



Office-based baseline (mean±SD) and Annual Changes (mean±SE)

N=16	Baseline	Δ 1 year	Δ 2 year	Δ 3 year
Systolic BP (mmHg)	190 ± 30	-38 ± 8 (p<0.001)	-34 ± 8 (p<0.001)	-37 ± 10 (p=0.003)
Diastolic BP (mmHg)	111 ± 22	-25 ± 5 (p<0.001)	-20 ± 6 (p=0.005)	-23 ± 7 (p=0.005)
Heart rate (bpm)	79 ± 9	-12 ± 3 (p<0.001)	-11 ± 4 (p=0.008)	-6 ± 4 (p=0.14)



Weber Lancet 2009;372:1423-1431

Conclusion

- Most resistant hypertension is due to drug management issues (lack of adequate regimen, non-compliance, side effects, physician apathy)
- Secondary hypertension only accounts for 5-10 % of hypertension
- Hyperaldosteronism is present in approx 20 % of patients with resistant hypertension