

Resistant Hypertension

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Conflicts of interest

- None

Objectives

- Definition of resistant hypertension
 - Distinguish true resistant hypertension from pseudoresistance
- Evaluation
- Treatment
 - How to optimize pre-existing treatment
 - What to add-on

Case

- 58 year old male patient

RC : Hypertension –suboptimal control with four meds.

- Past medical history :

- 1) HTA

- 2) Obesity – BMI 32

- 3) Osteoarthritis

- 4) Glucose intolerance A1c 6.3%

Case (continued)

Medications :

- HCTZ 25mg po die
- Amlodipine 5mg po die
- Perindopril 4mg po die
- Terazosin 2mg po HS
- Naproxen 250mg po bid

Case (continued)

Habits :

- Smokes 10 cig/day
- Drinks 24 beers on the weekend

History :

- Takes meds : « most of the time »
- Blood pressure readings at home : « machine broken »
- Eating habits : « terrible »

Case (continued)

Physical examination :

- Office measurement : 162/98
- Large neck
- Obese

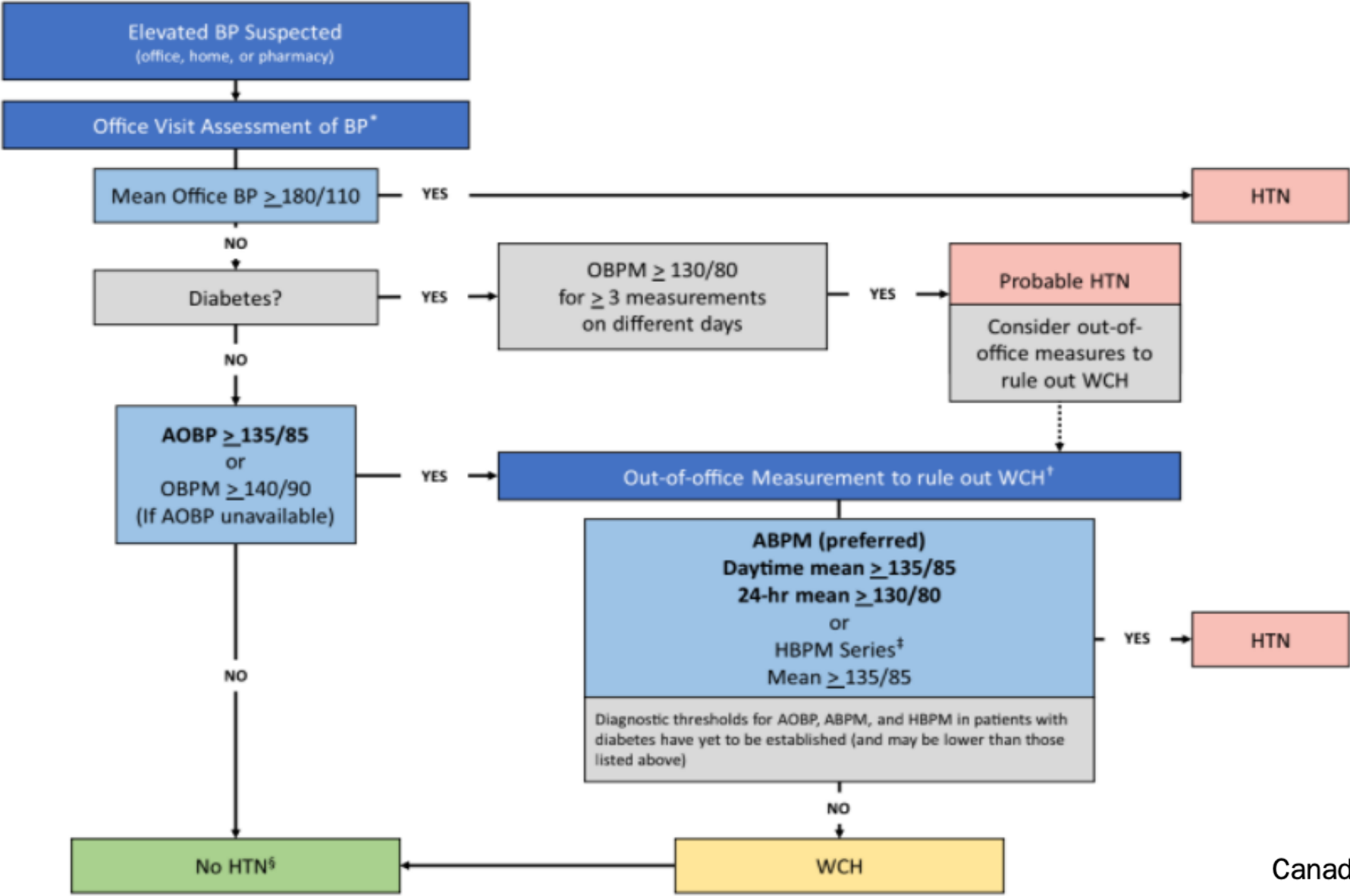
Tests :

- Creat 96 (GFR 50 ml/min), urinalysis : prot 0.5 g/L
- Na 137, K 3.5

Question – How to optimize treatment?

1. Change HCTZ to indapamide 2.5 die
2. Increase perindopril to 8mg po die
3. Stop NSAIDs
4. Sleep studies to r/o sleep apnea
5. Refer to GIM
6. All of the above

Definition - Hypertension



Definition – resistant hypertension

- Hypertension resistant to ≥ 3 medications at optimal doses including a diuretic.

Diagnosis – resistant hypertension

Four things are essential for diagnosis:

1. Accurate measurements!
2. White coat syndrome should be ruled out.
3. Adherence should be assessed.
4. Patients should be receiving the right drugs at the right doses.

Resistant hypertension

Why is it important?

- Hypertension is the most prevalent risk of cardiovascular disease.
- Resistant hypertension is worse than hypertension.
- Increases further the risk of (x1.5-2):
 - Cardiovascular disease (CAD, PAD, stroke)
 - Heart failure
 - Renal insufficiency
 - All cause mortality

Muntner et al. 2014

Carey et al. 2018

Prevalence

- Relatively rare – 5% of all patients with hypertension
- Most patients have essential hypertension (>85%).
- Can be a result of secondary hypertension (5-10% - much more common than if non-resistant):
 - Hyperaldosteronism
 - Sleep apnea
 - Renal artery stenosis
 - Chronic kidney disease
 - Medications

Risk factors

- Age
- Obesity
- Ethnicity
- Chronic renal disease
- Lifestyle and diet
 - Alcohol
 - Salt!
 - Drugs

Evaluation

History:

- Adherence
- Values at home
- Habits (including salt!)
- Symptoms of organ damage
- Loud snoring/witnessed apnea
- Sudden onset or acute rise of hypertension

Evaluation

Physical exam:

- Take BP correctly
- Both arms
- Murmurs (neck, abdomen)
- Fundoscopy

Evaluation

Labs :

- Electrolytes
- Kidney function (watch for sudden deterioration) + albuminuria
- TSH
- Calcium
- Aldosterone/renin ratio
- 24h urinary catecholamine/metanephrine

Evaluation

Tests :

- ECG
- Renal ultrasound (with doppler)
- Look for incidental adrenal adenoma on old scans
- Sleep studies

Evaluation

ABPM – ambulatory blood pressure measurements

- Gold standard, but not always available rapidly
 - Consider if home measures impossible, inaccurate or fluctuate

Treatment

Two steps:

1. Optimize
2. Add-on

Treatment - optimize

Non-pharmacological

- Include patient in treatment plan
- Avoid clinician inertia
- Address non-adherence
- Salt (DASH)
- Exercise
- Lose weight
- Moderating alcohol intake
- Identify sleep apnea

Treatment - optimize

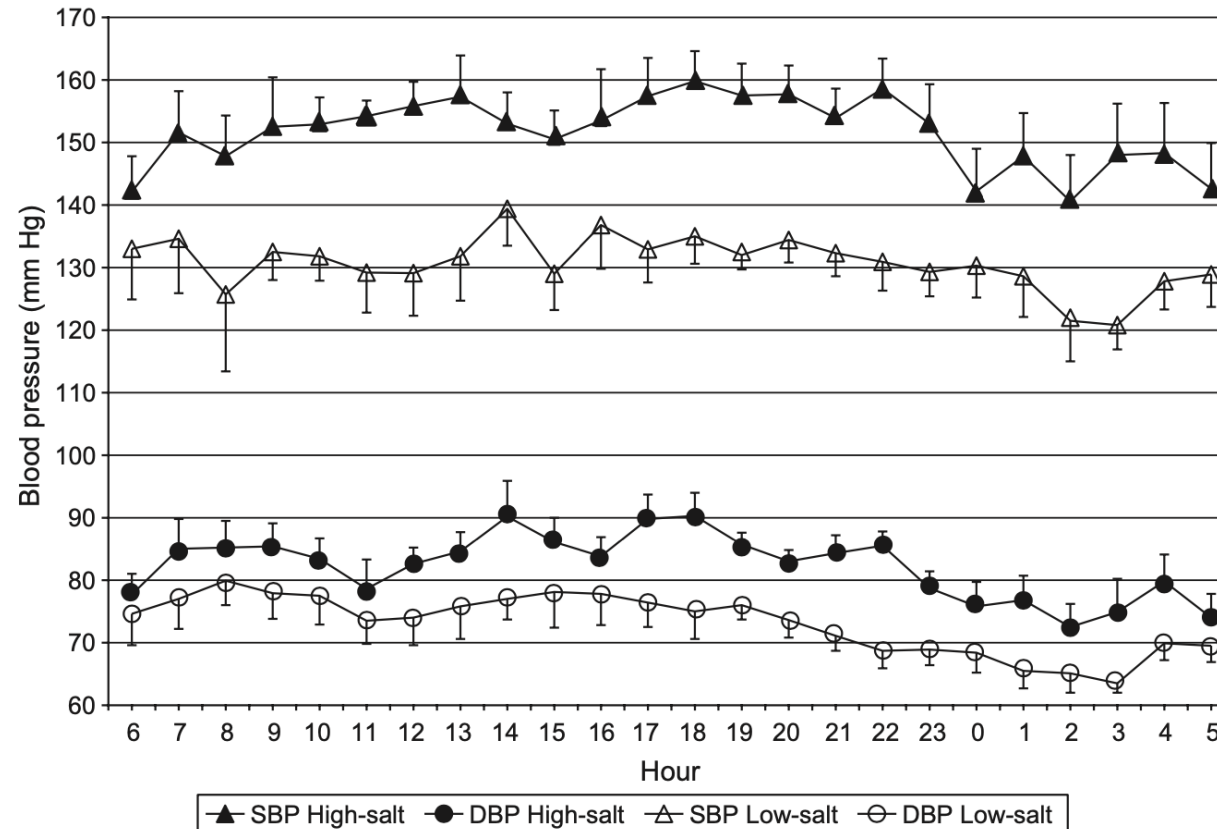


Figure. Comparison of 24-hour ambulatory blood pressure values during low- and high-salt diet. Data presented as mean \pm SE.

Table 12. Strategies to improve patient adherence

Assist your patient by:

- Tailoring pill-taking to fit patient's daily habits (Grade D)
- Simplifying medication regimens to once-daily dosing (Grade D)
- Replacing multiple pill antihypertensive combinations with single-pill combinations (Grade C)
- Using unit-of-use packaging (of several medications to be taken together) (Grade D)
- Using a multidisciplinary team approach to improve adherence to an antihypertensive prescription (Grade B)

Assist your patient in getting more involved in their treatment by:

- Encouraging greater patient responsibility/autonomy in monitoring their blood pressure and adjusting their prescriptions (Grade C)
- Educating patients and their families about their disease and treatment regimens (Grade C)

Improve your management in the office and beyond by:

- In patients with hypertension who are not at target, adherence to all health behaviour recommendations (including use of prescription medications) should be reviewed before adjustment in therapy is considered (Grade D; **revised recommendation**)
 - Encouraging adherence with therapy using out-of-office contact (either phone or mail), particularly during the first 3 months of therapy (Grade D)
 - Coordinating with pharmacists and work-site health caregivers to improve monitoring of adherence with pharmacological and health behaviour modification prescriptions (Grade D)
 - Using electronic medication compliance aids (Grade D)
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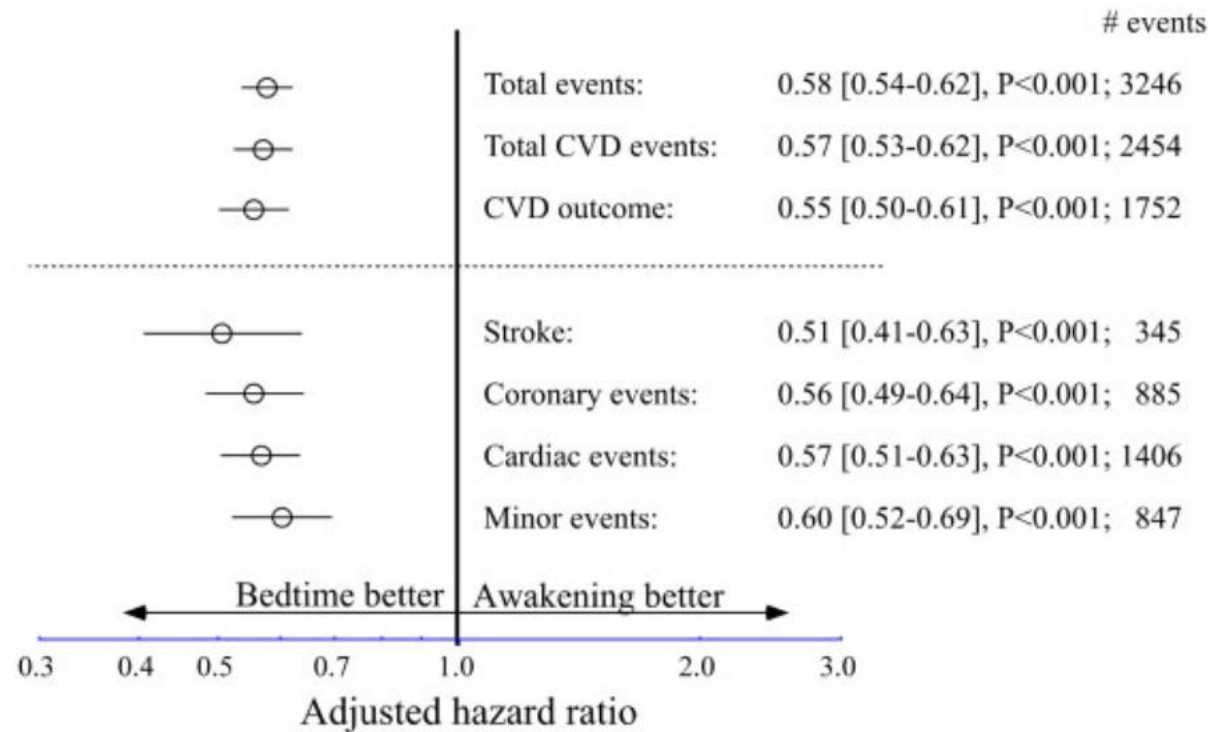
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Treatment - optimize

Chronotherapy of medication:

- Restores natural homeostasis (dipping)
- Intervention without cost
- Less side effects, no increase in harm
- Decreases BP
- Cardiovascular benefit!

Treatment - optimize



Treatment - optimize

Stop medications that increase BP (if possible):

- NSAIDs including COX 2
- Oral contraceptives
- Amphetamines
- Licorice or other natural products
- Certain antidepressants (venlafaxine, MAOIs)

Treatment - optimize

Three medication that should be on-board (unless contraindicated):

- ACEI or ARB
- CCB
- Diuretic (with preference thiazide-like)

Treatment - optimize

Combine medications:

- ACEI or ARB + thiazide/thiazide-like
- ACEI + CCB
- Can be considered initially if target $>20/10$ mmHg

Treatment - optimize

Increase medication to standard doses:

- All first-line agents have similar potency.
- Half-standard to standard doses – gain of a few mmHg of effect.
- More side effects when higher than standard doses.

Treatment - optimize

Use a better diuretic:

- Use thiazide-like diuretic instead of thiazide diuretic
 - Chlorthalidone or indapamide
- Longer half-life (>24h vs. <12h) – better night coverage
- More potent (reduces BP +3-5 mmHg) at equivalent doses

- If GFR <30, consider the use of loop diuretic.

George et al. 2015

Engberink et al. 2020

Treatment - optimize

Some medication are better/more potent than others:

- ACEI : perindopril, trandolapril
- BB : labetalol, carvedilol
 - Vasodilating properties (alpha blocking activity)
- ARB : Olmesartan

Treatment – Add on

Use mineralocorticoid antagonist as 4th line treatment:

- This is the best medication for resistant hypertension.
- Spironolactone (or eplerenone, amiloride).
 - Add-on effect (patients already on triple-drug therapy): -10mmHg systolic/-5mmHg diastolic, but some patients are super responders (>20/10 mmHg).
- Elevation of potassium with normal kidney function : + 0.5 mmol/L

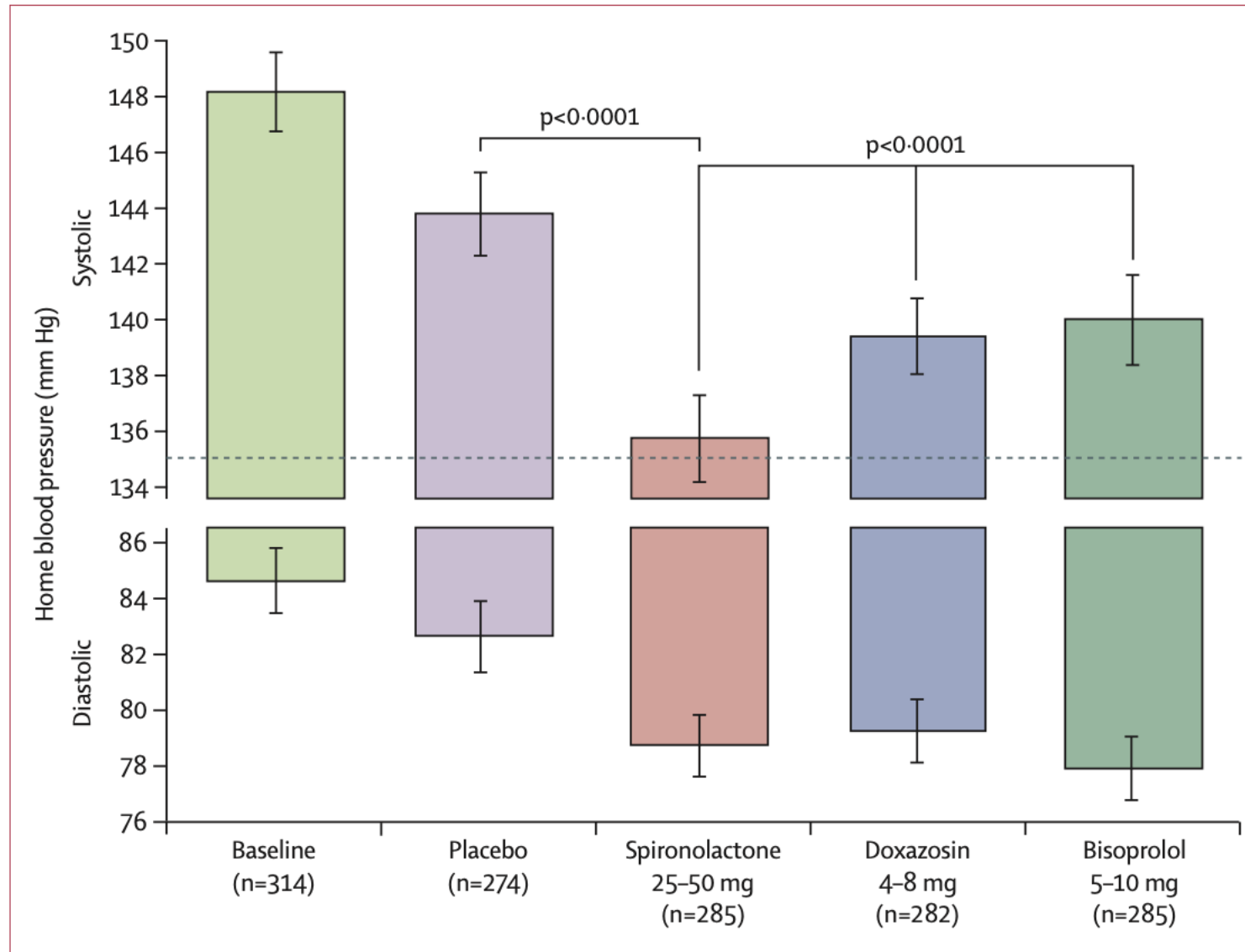


Figure 2: Home systolic and diastolic blood pressures comparing spironolactone with each of the other cycles

Treatment – Add on

5th, 6th, 7th line:

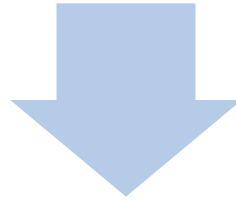
- Beta-blockers (labetalol or carvedilol)
- Alpha-blockers
- Vasodilators (hydralazine, nitroglycerin)
- Alpha-2-agonists

Treatment – Add on

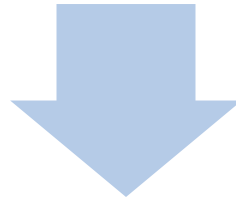
Refer to specialist:

- GIM, nephrologist, cardiologist
- Recommended by 2020 Canadian guidelines

Validate correct HTA measurements, rule out non-adherence, rule out secondary causes, optimize habits (alcohol, salt, etc).



Combine medication, optimize dosing, chronotherapy, thiazide-like diuretic, stop interfering medications



Add-on 4th line : spironolactone

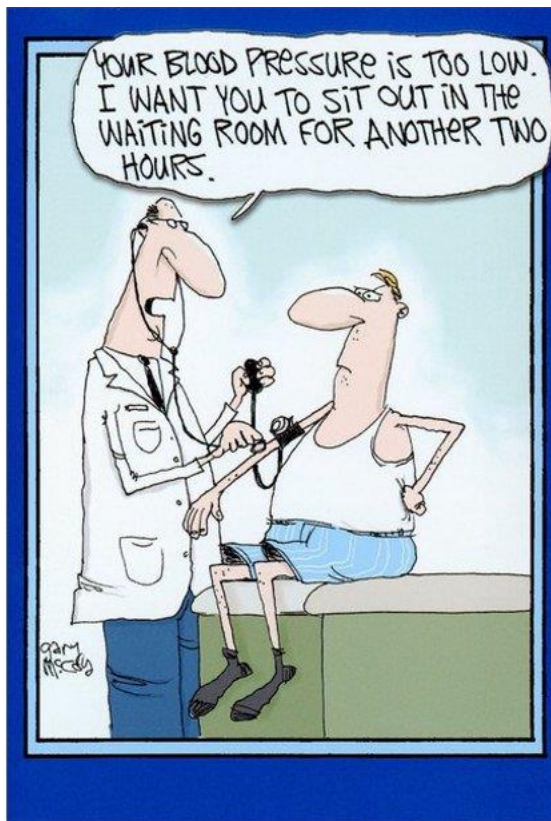
Add-on 5th line+ :

Beta-blockers (labetalol or carvedilol),
alpha blockers, hydralazine, etc

Take home messages

- Accurate BP measurements are essential for diagnosis
- Validate adherence
- Salt!
- Use medication judiciously (maximise doses, combine, bedtime dosing, use thiazide-like, etc.)
- Add a mineralocorticoid receptor antagonist

Thank you for your attention!



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