Hypertension Pearls

For the Diagnosis and Management of Complex Hypertension

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Disclosures

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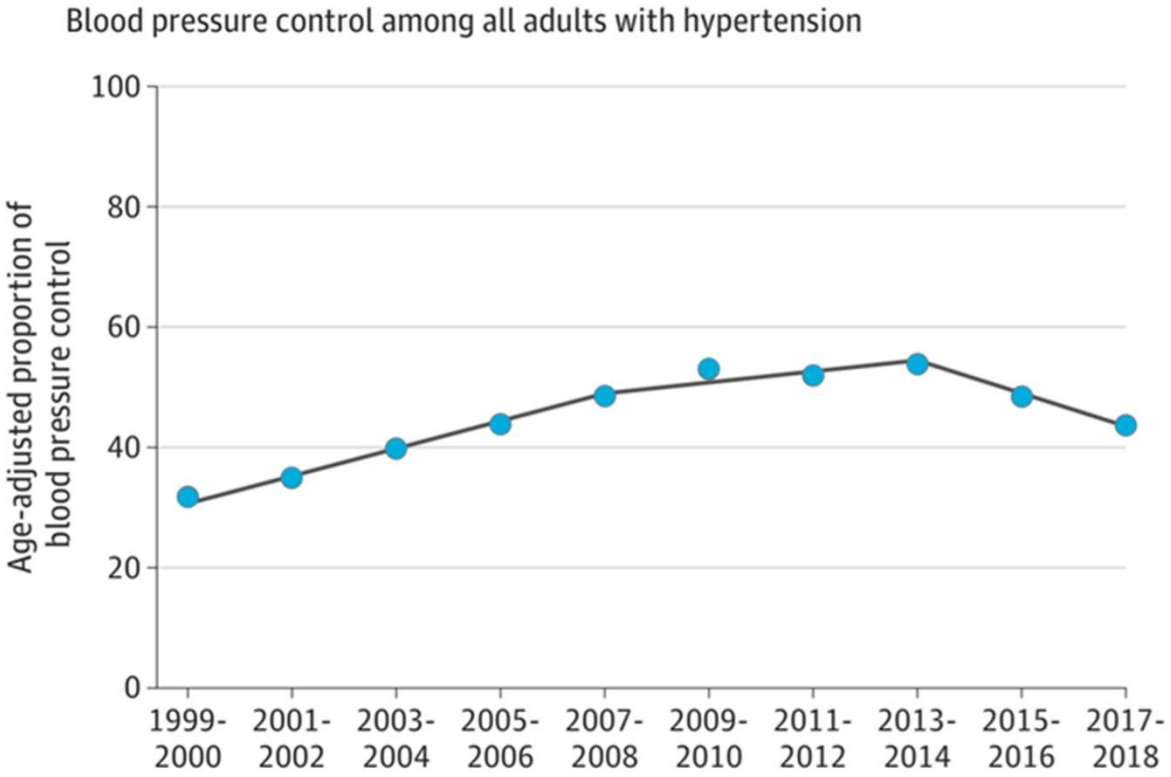
- Disclosures: UpToDate (royalties)
- Off-Label Use: None

Objectives

- Reinforce key competencies in hypertension diagnosis and management based on most the recent guidelines and evidence
- Develop a practical approach to the evaluation and management of resistant hypertension

The power of inertia

Muntner P, et al. *JAMA*. 2020;324(12):1190-1200



- Current hypertension **diagnostic** thresholds
  - ≥130/80 in all comers
  - *Except* ≥140/90 in those with ASCVD risk <10%
- Current hypertension **treatment** thresholds
  - <130/80 in all comers

TABLE 23 BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

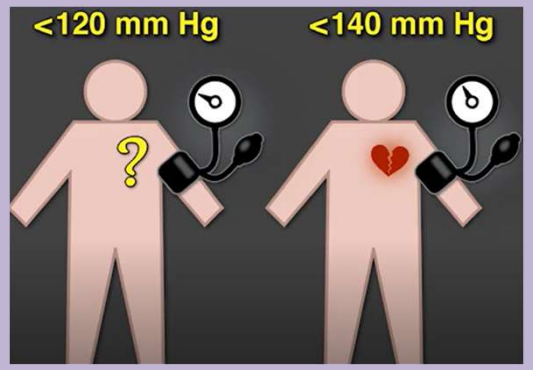
Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific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

2021 KDIGO Guidelines

• **Recommendation 3.1.1** We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement *(2B)*.

Cheung AK, et al. *Kidney Int.* 2021; 99:559–569

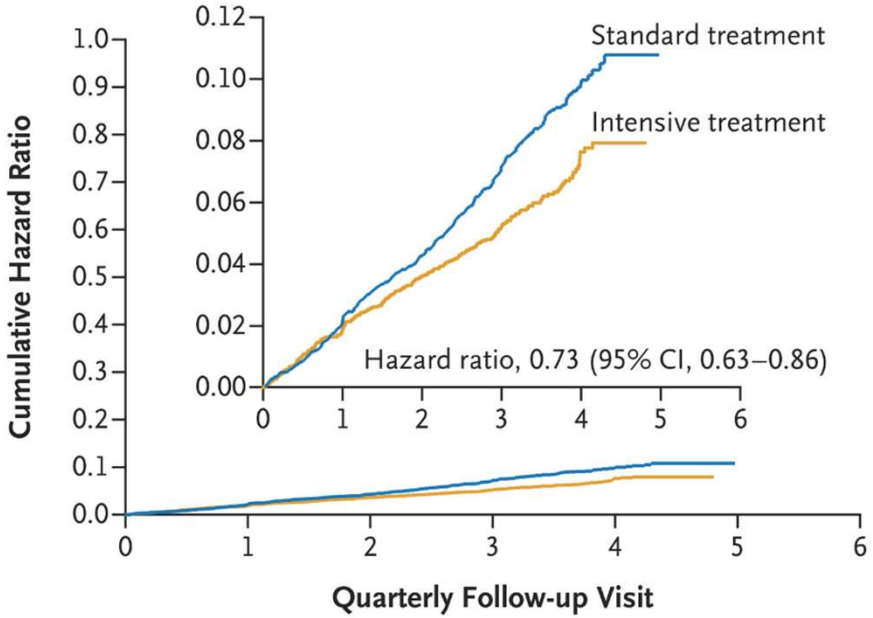
SPRINT Trial



Final Report of a Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

DOI: 10.1056/NEJMoa1901281



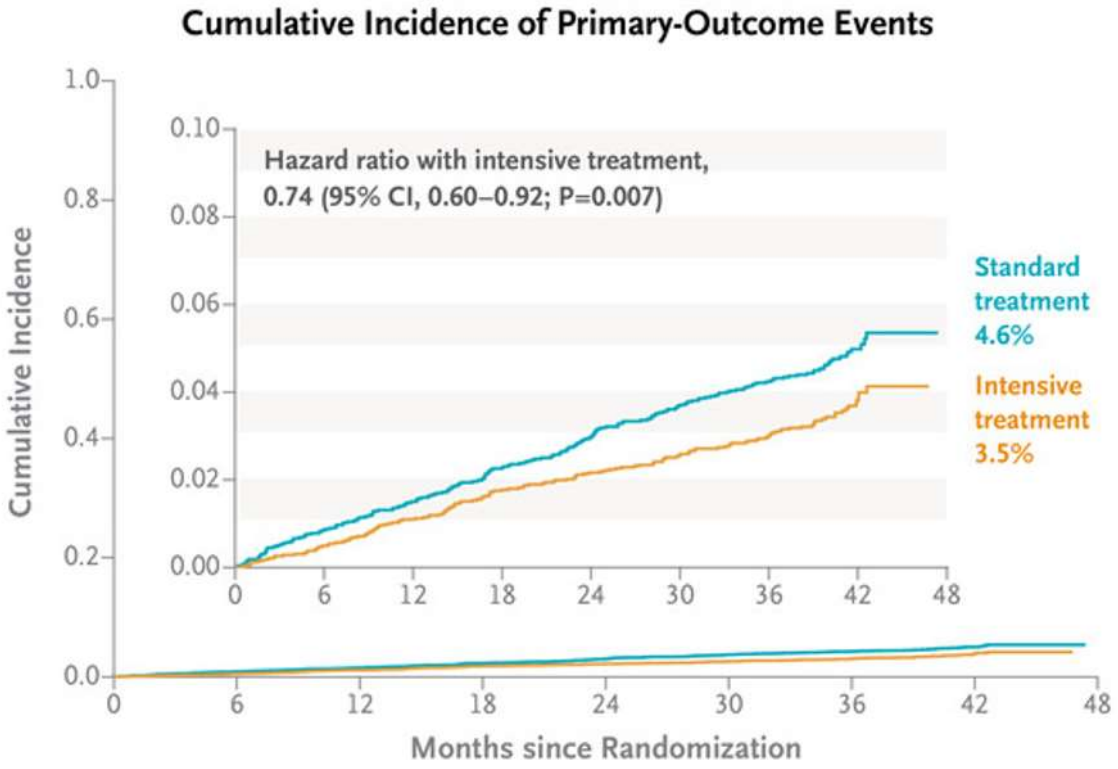
No. at Risk

Standard treatment	4683	4443	4247	2950	801	120
Intensive treatment	4678	4439	4275	3028	855	125

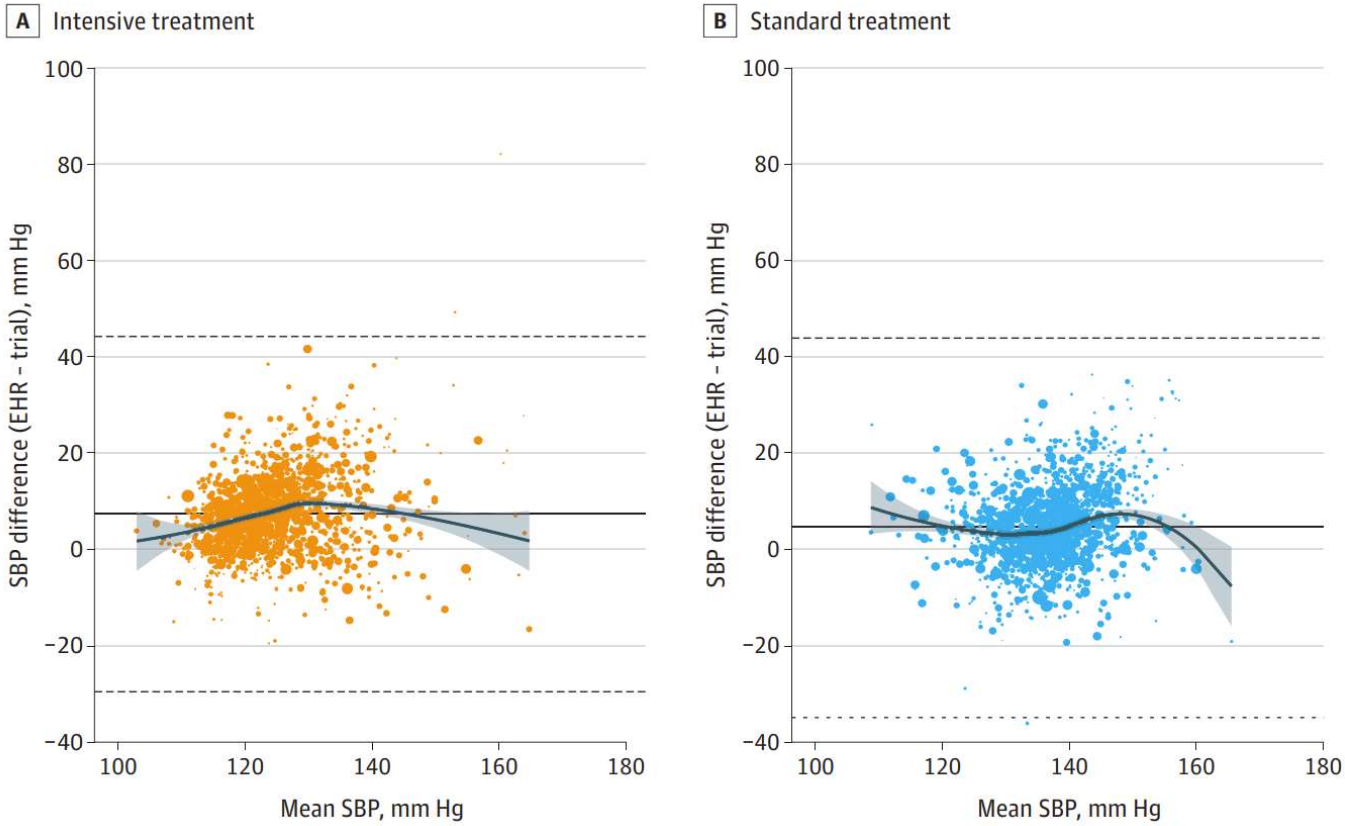
STEP Trial

Trial of Intensive Blood-Pressure Control in Older Patients with Hypertension

Zhang W et al. DOI:10.1056/NEJMoa2111437



Differences in clinic vs. research study blood pressure measurements: SPRINT



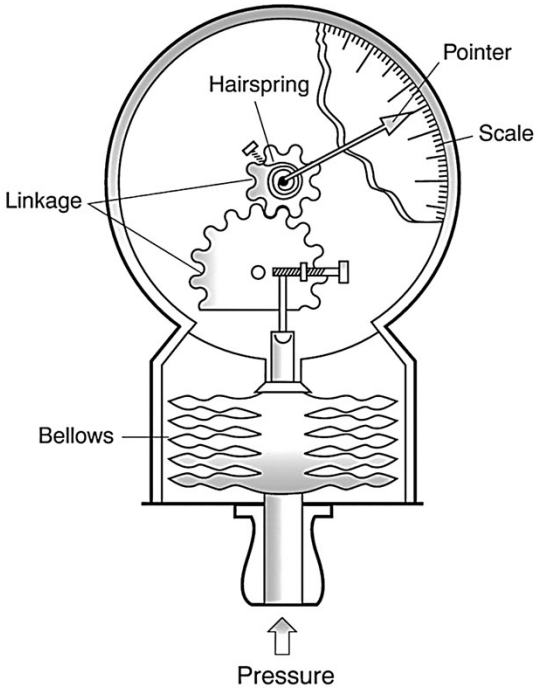
Drawz PE. *JAMA Intern Med.* 2020 Dec 1;180(12):1655-166

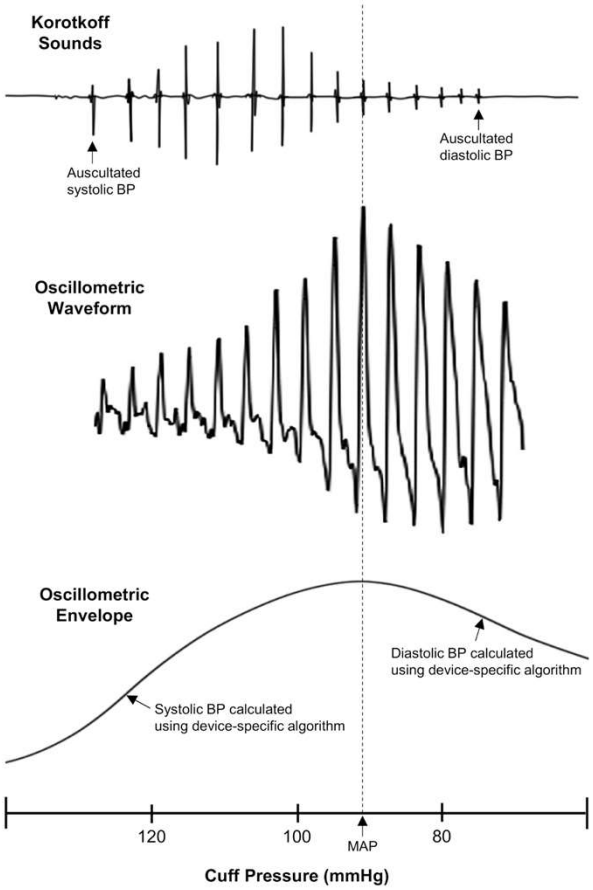
Table 9. Blood Pressure Variability[52]	
Factor	**Systolic (mmHg)**
Cuff too small	10–40 ↑
Cuff over clothing	10–40 ↑ or ↓
Back/feet unsupported	5–15 ↑
Legs crossed	5–8 ↑
Arm tense	15 ↑
Not resting 3 to 5 minutes	10–20 ↑
Anxiety/white coat hypertension	As much as 30 ↑
Patient talking	10–15 ↑
Labored breathing	5–8 ↑
Full bladder	10–15 ↑
Pain	10–30 ↑
Arm below or above heart level	10 ↑ or ↓ For every 1 cm above or below heart level, blood pressure varies by 0.8 mmHg.
Factor	**Diastolic (mmHg)**
Arm extended and unsupported	Diastolic ↑ 10%

Kallioinen N et al, *J Hypertens* 2017; 35:421-41

Evolution of blood pressure measurement

History and Justification of a National Blood Pressure Measurement Validated Device Listing





Cohen JB, Brady TM. *Circulation* 2022;145(2):94-96

One solution to issues with in-office blood pressure measurement: *Automated office blood pressure*

- Considered “standardized blood pressure measurement” by multiple guidelines
- Oscillometric device
- Records multiple blood pressure readings (observed or unobserved) after a rest period with a single activation
  - Pre-programmed 5-minute rest, then 3 readings at 1-minute intervals
  - Can calculate an average of these readings

Cohen JB et al. *Hypertension* 2019; 73:258-264

Images:
https://omronhealthcare.com/products/intellisense-professional-digital-blood-pressure-monitor-hem907xl/
https://www.microlife.com/professional-products/watchbp-office/watchbp-office-2g

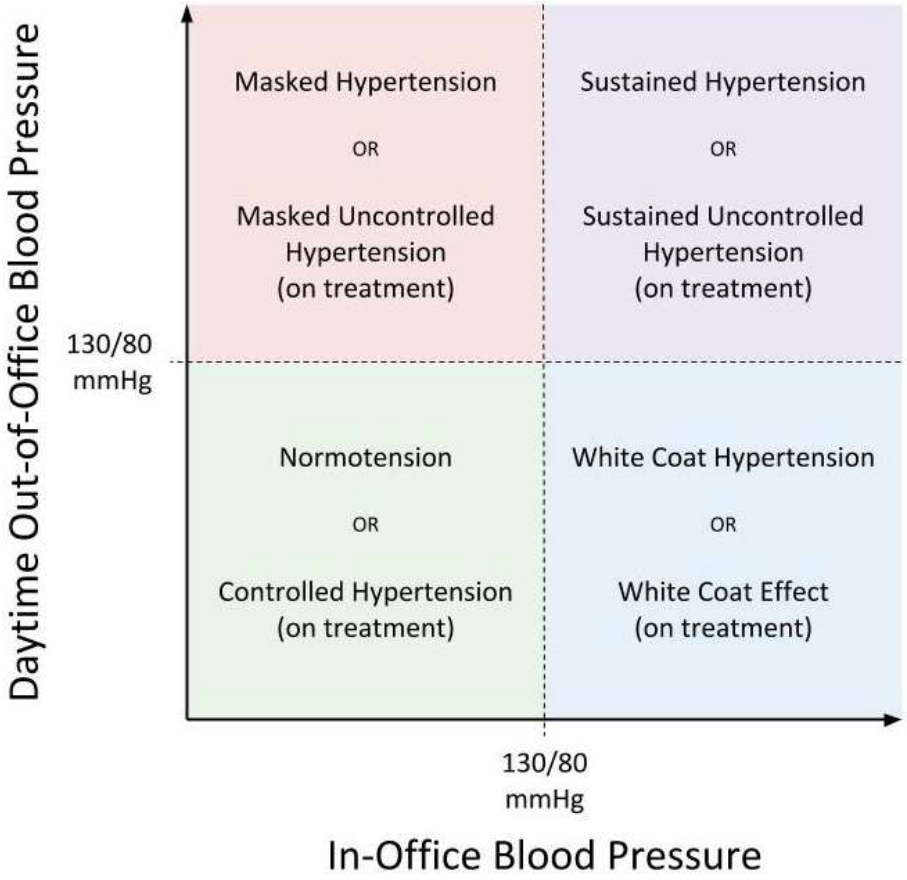
Out-of-office Blood pressure screening

Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

Population	Adults aged ≥18 y without known hypertension
Recommendation	Screen for high blood pressure; obtain measurements outside of the clinical setting for diagnostic confirmation. Grade: A

Siu AL et al. *Ann Intern Med.* 2015;163:778-786

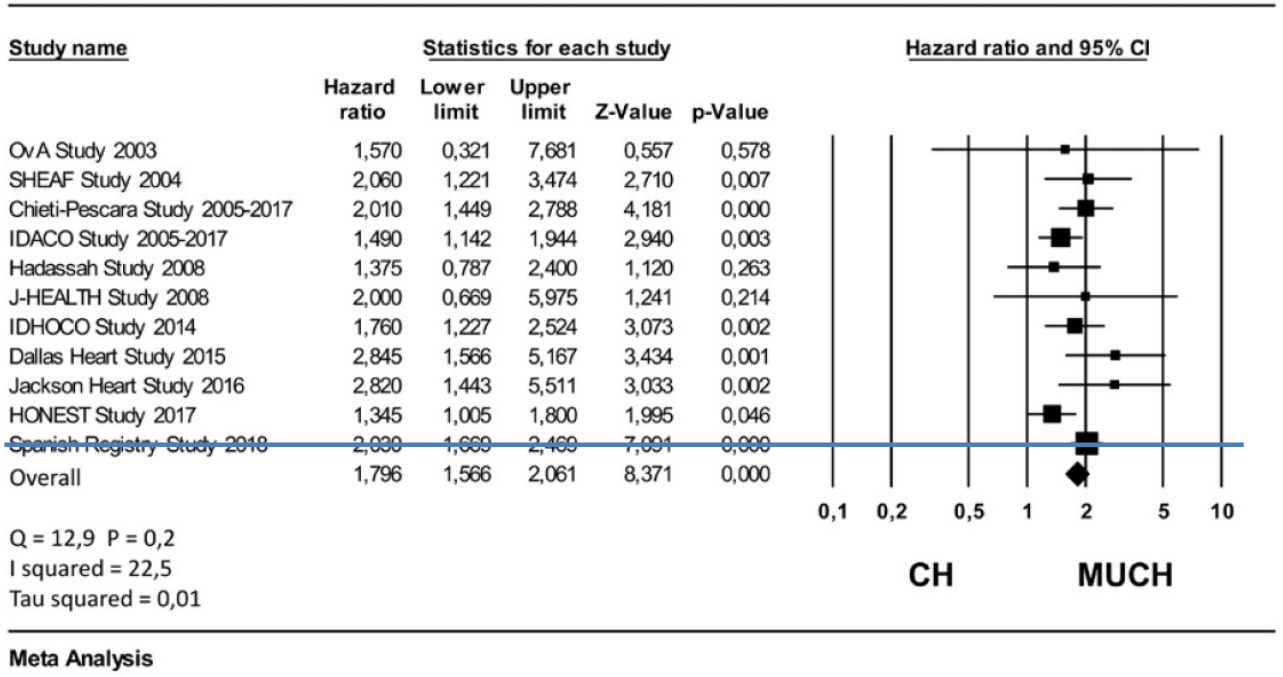


Many of the limitations of in-office BP are mitigated by out-of-office BP measurement

Clinic	HBPM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

Cohen JB and Townsend RR. *UpToDate*

Cardiovascular risk of masked hypertension



Study name	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
OvA Study 2003	1,570	0,321	7,681	0,557	0,578
SHEAF Study 2004	2,060	1,221	3,474	2,710	0,007
Chieti-Pescara Study 2005-2017	2,010	1,449	2,788	4,181	0,000
IDACO Study 2005-2017	1,490	1,142	1,944	2,940	0,003
Hadassah Study 2008	1,375	0,787	2,400	1,120	0,263
J-HEALTH Study 2008	2,000	0,669	5,975	1,241	0,214
IDHOCO Study 2014	1,760	1,227	2,524	3,073	0,002
Dallas Heart Study 2015	2,845	1,566	5,167	3,434	0,001
Jackson Heart Study 2016	2,820	1,443	5,511	3,033	0,002
HONEST Study 2017	1,345	1,005	1,800	1,995	0,046
~~Spanish Registry Study 2018~~	~~2,030~~	~~1,660~~	~~2,460~~	~~7,091~~	~~0,000~~
Overall	1,796	1,566	2,061	8,371	0,000

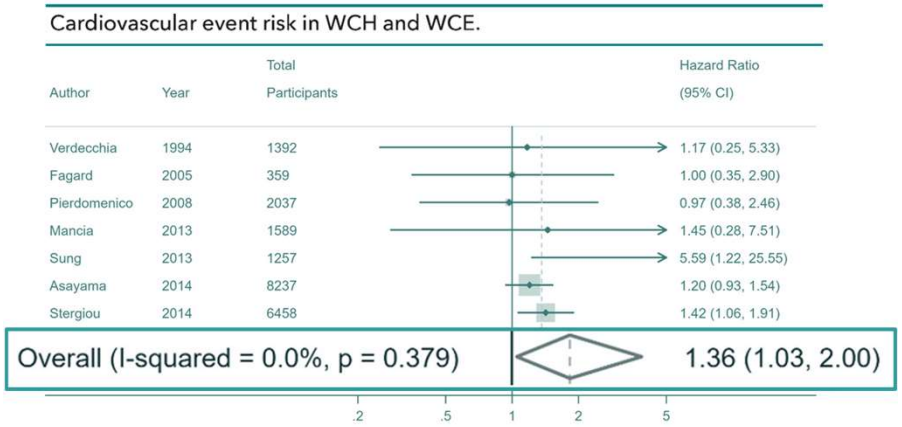
Q = 12,9 P = 0,2
I squared = 22,5
Tau squared = 0,01

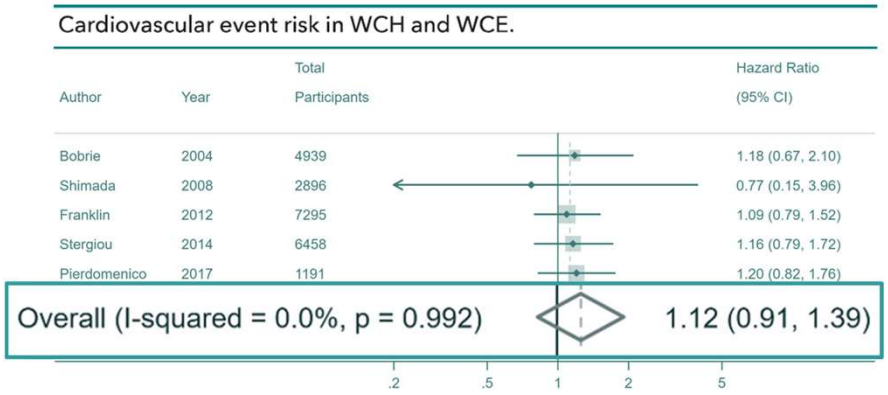
Meta Analysis

Pierdomenico SD et al. *Hypertension*. 2018;72(4):862-869

Cardiovascular risk of white coat hypertension

- Risk is only present among untreated patients
- Risk is substantially lower than sustained or masked hypertension
- **Patients with white coat hypertension**
  - **Should be treated based on their out-of-office BP readings**
  - **Should be monitored closely with out-of-office BP monitoring due to a high risk of transitioning to sustained hypertension**





Cohen JB et al. *Ann Intern Med.* 2019; 170:853-862

FDA 510(k) device clearance

- The FDA does not "approve" most devices for patient use, they "clear" them
- Clearance requires demonstrating "equivalence" to an existing device
  - There are no enforced guidelines on what "equivalence" means
  - Up to the manufacturer to determine
- **The 510(k) process does not require demonstration of accuracy**
- The FDA has no enforcement division to prohibit selling invalid devices

Cohen JB et al. *Hypertension* 2019; 73:258-264

"From about 3000 cuff-based BP measuring devices on the market today, less than 15% have published evidence on accuracy performance."

Sharman JE et al, *J Hypertens* 2020 2020;38(1):21-29

Cuffless Technology

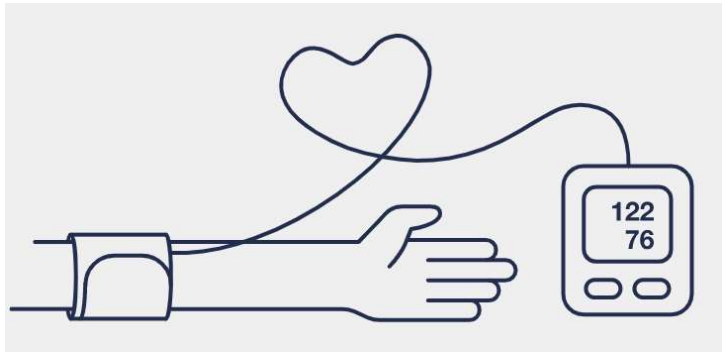
Caution : FDA 510(k) cleared, NOT recommended for clinical use

Cohen JB, Brady TM. *Circulation* 2022;145(2):94-96

Validated device listings

www.validatebp.org

www.stridebp.org



Cohen JB et al. *Hypertension* 2019; 73:258-264
Cohen JB, Brady TM. *Circulation* 2022;145(2):94-96

Evaluation and Management of Patients with Difficult to Control Hypertension

Treatment Resistant Hypertension

- Hypertension affects 46% of the adult population in the United States
- Approximately 20% of patients taking antihypertensive medications appear to have treatment-resistant hypertension
  - BP not adequately controlled with 3 antihypertensive medications including a diuretic or requires a minimum of 4 antihypertensive medications to achieve adequate control
- Apparent treatment-resistant hypertension is associated with a markedly higher risk of cardiovascular mortality and all-cause mortality, independent of BP control

Whelton PK, et al. *Hypertension.* 2018;71(6):e13-e115
Carey RM, et al. *Hypertension.* 2019;73(2):424-31

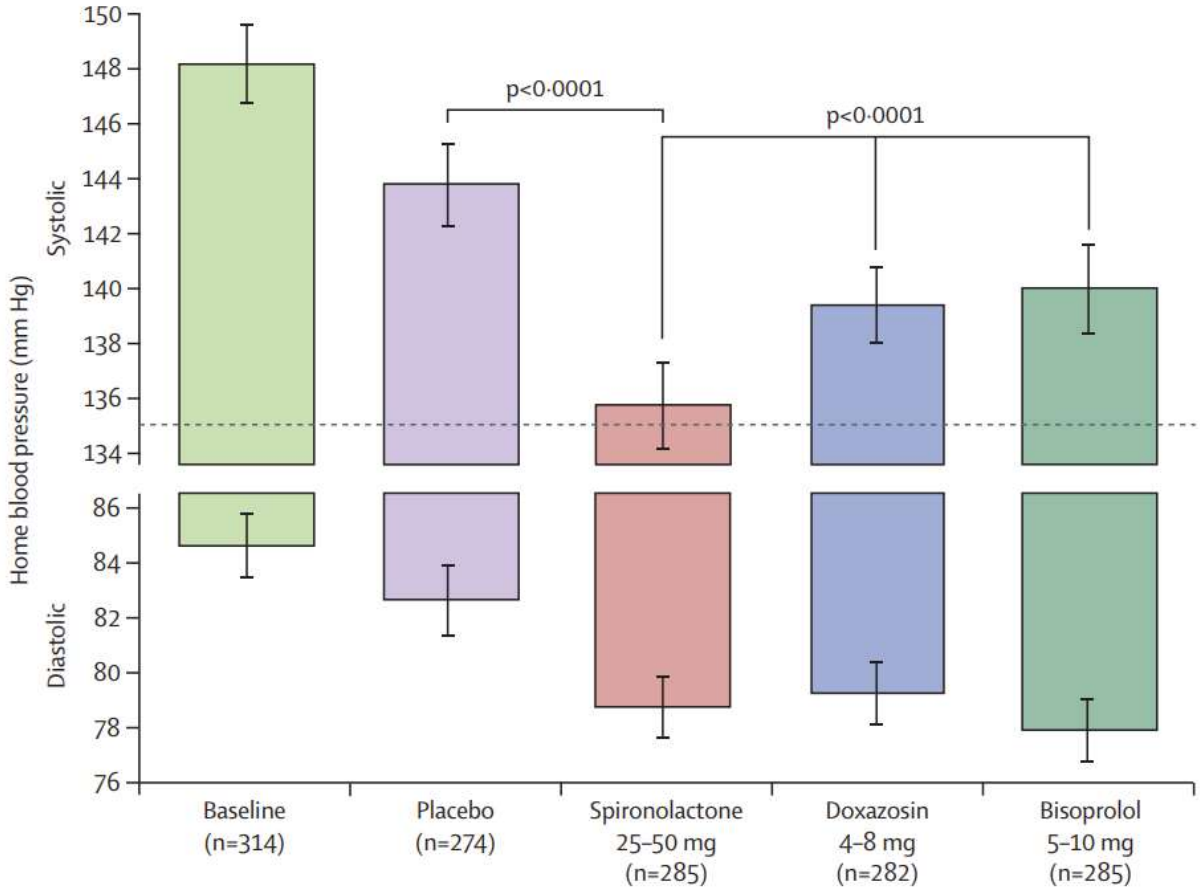
Management of resistant hypertension

1) Highest tolerated dose of first line agents
   a) ACEIs/ARBs, CCBs, thiazide/thiazide-like diuretics
2) Maximize diuretic therapy
3) Add a mineralocorticoid receptor antagonist or potassium-sparing diuretic
   a) Do this BEFORE adding a beta-blocker unless there is a specific indication
4) Add other agents with different/complimentary mechanisms of action

Whelton PK, et al. *Hypertension.* 2018;71(6):e13-e115
Carey RM, et al. *Hypertension.* 2019;73(2):424-31

Management of Treatment Resistant Hypertension

High quality evidence supports the use of mineralocorticoid receptor antagonist (MRA) therapy for the management of treatment-resistant hypertension



Williams B, et al. *Lancet* 2015; 386(10008): 2059–68
Chen C, et al. *Medicine* 2020; 99(34):e21694

Adding fourth through n_{th} line therapy

- Beta-blockers should NOT be used as first- (or even 4th) line antihypertensive therapy unless there is a specific indication for their use

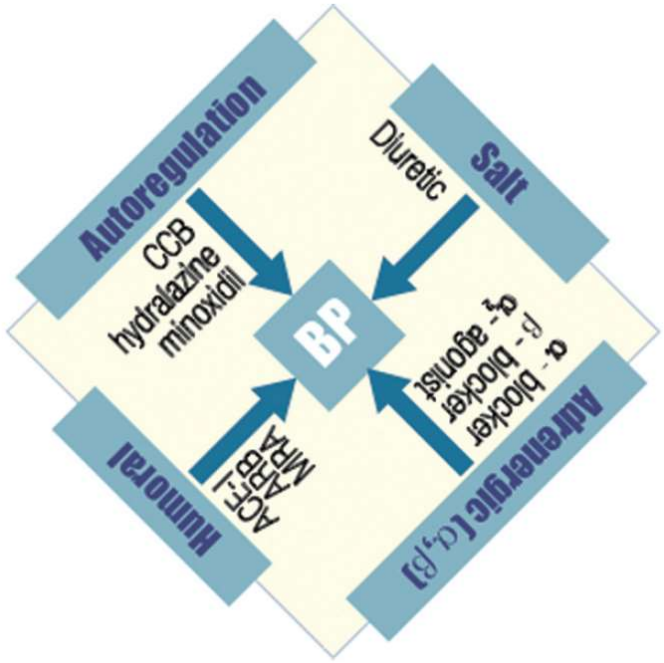
Table 3. Hazard Ratios of Incident CVD by Time-Updated Antihypertensive Class

Outcome	ACE inhibitor/ARB	β-Blocker	CCB*
		HR (95% CI)	HR (95% CI)
Incident CVD or death	Ref	1.71 (1.42–2.05)	0.88 (0.72–1.08)
Incident CVD	Ref	1.76 (1.45–2.14)	0.85 (0.67–1.08)
Incident HF	Ref	1.47 (1.12–1.92)	0.73 (0.52–1.03)

Rethy LB… Cohen JB. *Hypertension* 2021; 77(6)
Carey RM et al. *Hypertension* 2018; 72(5):e53–e90

Adding fourth through n_{th} line therapy

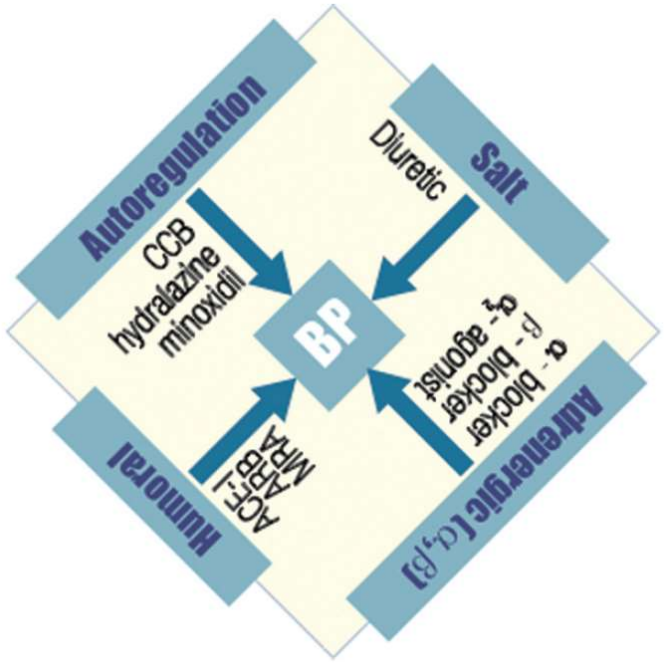
- Aim for simplicity
  - Things to consider:
    - Fixed-dose combinations
    - Long-acting medications (e.g., chlorthalidone, torsemide; if absolutely needed, consider clonidine patch or guanfacine over clonidine PO)
  - Only use minoxidil as a last resort; must be given with a loop diuretic



https://doi.org/10.2215/CJN.04120511

Adding fourth through n_{th} line therapy

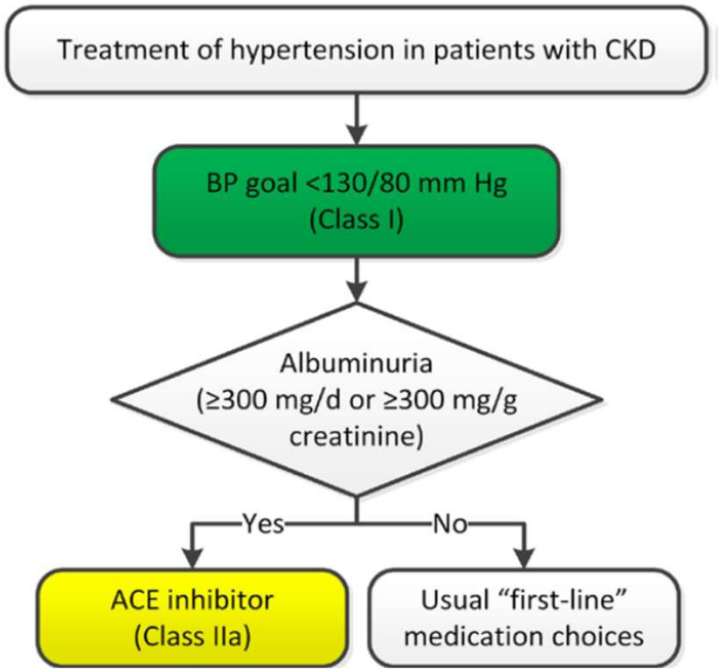
- Aim for simplicity
  - Things to avoid:
    - Short-acting medications like hydralazine and PO clonidine
    - Less frequent dosing of short-acting medications (e.g. QD furosemide, BID hydralazine)
      - Once-daily short-acting diuretics can increase sodium avidity later in the day
      - Even “appropriate” dosing of and adherence to hydralazine and clonidine can exacerbate labile hypertension due to short duration of action and rebound effects



https://doi.org/10.2215/CJN.04120511

Additional considerations in CKD

- Optimize diuretic therapy
  - Hypertension is often more volume-mediated in CKD than in the general population
  - Long-acting diuretics like chlorthalidone and torsemide
  - Loop AND thiazide/thiazide-like diuretic or MRA
    - Kaliuresis is a great way to help patients better-tolerate ACE-Is/ARBs
- MRAs and SGLT-2 inhibitors have anti-proteinuric properties



Whelton PK, et al. Hypertension. 2018;71(6):e13-e115
Agarwal R et al. *N Engl J Med* 2021; 385:2507-2519

Summary of challenges in hypertension management

- Therapeutic inertia is a major driver of inadequate management of hypertension and low (and declining) rates of blood pressure control in the US
- Greater trust in the accuracy of our blood pressure readings and use of out-of-office blood pressure monitoring can help to overcome inertia
  - **Accurate blood pressure measurement with validated devices is critical**
- We as clinicians need to do a better job of implementing best evidence
  - β-blockers should be considered 5th-line therapy for hypertension unless there is another indication
  - Avoid short-acting PO medications whenever possible

Thank you!

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Cardiometabolic teleECHO™ Clinic

Patient Recommendation Form

Presentation Date: Oct 5, 2022 **Presenter name:** Peter Berberian

Presenter Facility SeaMar

- 55yo Latino with originally uncontrolled DM (11 then 9 a1c), BMI 42 now 38 and wt was 135 kg now 126kg in setting of +microalbuminuria (300 then 80 and now 20) with normal creatinine. Also complicated by hypertensive heart disease and HLD on high dose statin with hypertriglyceridemia (241 and now 161). Activity diminished 2/2 pulmonary fibrosis post COVID. A1c now 7.1 on current medication management

Current Medication(s) (including dose frequency):

Medication	Dose	Frequency
Lantus	<100 up to 30 >100 up to 34	At bedtime
Metformin	1000mg	Daily
Atorvastatin	80 mg	Daily
Furosemide	80 mg	Daily
Albuterol inhaler	2 puffs	pm (2-4 times/ week)
Aspirin	81 mg	Daily
Gabapentin	300 mg	q8h
Bisoprolol Fumarate	5 mg	Daily
Jardiance	10 mg	Daily
Victoza	1.8 mg	Daily
Novolog	10 u	TID w/ meals

Case Recommendations:

In general, in our experience we have managed patients who have similar problems with the approach of:

1. Review resources for home PT available for patient to increase activity
2. ADD CGM as on intensive insulin therapy
3. Assess patient current goals. Is more weight loss desired? Is less shot burden desired?
4. Consider making no change in therapy except to increase empagliflozin to 25mg and reduction of lantus to 28 units and novolog at last meal to 8-9 units from 10 (based on bedtime sugars)
5. VS if weight loss and decrease in shot burden desired:

- Brief trial of exenatide twice a day 30 minutes prior to first and last meal 10mcg- with above changes to insulin (stop liraglutide).
- Then pre-auth for Tirzepatide 7.5mg weekly with increase monthly to goal 15mg
- Try Novolog 70/30 mix at 25 units twice a day (for breakfast and late lunch) and keep novolog 7 units for dinner "as needed" (this also keep requirement for CGM).
- Continue to either reduce lantus by 2-3 units and novolog by 1-2 with weight loss and dose increase of Tirzepatide or if using the mixed insulin by 5 units twice a day.

6. Repeat Lipid panel when weight loss is stable likely in 6-9 months
7. Consider Icosapent ethyl (vascepa) for triglycerides fasting > 135 after weight loss

Nicole Ehrhardt, MD

Physician Signature: *Nicole Ehrhasrdt*
Please Re-present case: dec 2022