



# At Last! Applying the National Hypertension Guidelines in Special Populations

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# Disclosures

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# Learning Objectives

- Describe the population at risk for developing hypertension (HTN) and current blood pressure control rates.
- Develop optimal blood pressure goals for a patient with HTN and co-morbid conditions according to practice guidelines and clinical trial evidence.
- Demonstrate appropriate drug selection for the treatment of HTN according to concomitant conditions and compelling indications.
- Devise an evidence-based treatment strategy for resistant HTN to achieve blood pressure goals.



## 2017 ACC/AHA Hypertension Guidelines General Updates

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults, *Journal of the American College of Cardiology* (2017), doi: 10.1016/j.jacc.2017.11.006.

# Major HTN Practice Guidelines

- JNC 7 (2002)
- **KDIGO, chronic kidney disease (2012)**
- Recommendations from former JNC 8 panel (2013; not sanctioned by NHLBI)
- ASH/ISH (2013)
- AHA/ASA Stroke guidelines (2014)
- AHA/ACC/ASH HTN and CAD guidelines (2015)
- **ADA Standards of Medical Care in diabetes (2018)**
- **ACC/AHA/HFSA Heart failure guidelines update (2017)**
- **ACC/AHA/APhA/ASH High Blood Pressure in Adults guideline (2017)**
- **ESC/ESH HTN guidelines (2018)**
- **AHA Scientific Statement on Resistant HTN (2018)**

# Show of Hands

How many of you are familiar with the 2017 ACC/AHA BP Guidelines?

- A** Very. I use them every single day
- B** Mostly, I treat HTN regularly
- C** Fairly, I've reviewed them
- D** Not, please teach me



## 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

# 2017 BP Guideline

### A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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# Hypertension

# Systematic Review Questions

1. Is there evidence that **self-directed monitoring of BP and/or ambulatory BP monitoring** are superior to office-based measurement of BP by a healthcare worker for
  - a. preventing adverse outcomes for which high BP is a risk factor
  - b. achieving better BP control?
2. What is the **optimal target for BP lowering** during antihypertensive therapy in adults?
3. In adults with hypertension, do various **antihypertensive drug classes differ** in their comparative benefits and harms?
4. In adults with hypertension, does initiating treatment with antihypertensive pharmacological **monotherapy versus initiating treatment with 2 drugs** (including fixed dose combination therapy), either of which may be followed by the addition of sequential drugs, differ in comparative benefits and/or harms on specific health outcomes?

# Hypertension

- Definition

COR	LOE	BP should be categorized as normal, elevated, or stage 1 or 2 hypertension to prevent and treat high BP
I	B-NR	

BP Category	SBP		DBP
Normal	< 120 mm Hg	And	< 80 mm Hg
Elevated	120-129 mm Hg	And	< 80 mm Hg
Hypertension			
Stage 1	130-139 mm Hg	Or	80-89 mm Hg
Stage 2	≥ 140 mm Hg	Or	≥ 90 mm Hg

# Prevalence of High BP

## ≥ 130/80 mm Hg or taking antihypertensive therapy

- Overall: 46%
  - Men: 48%, Women: 43%
- Prevalence increases with age

Age (y)	Men	Women
20-44	30%	19%
55-64	70%	63%
75+	79%	85%

- Prevalence highest in non-Hispanic black people
  - Men: 59%, Women: 56%

## ≥ 140/90 mm Hg or taking antihypertensive therapy

- Overall: 32%
  - Men: 31%, Women: 32%
- Prevalence increases with age

Age (y)	Men	Women
20-44	11%	10%
55-64	53%	52%
75+	71%	78%

- Prevalence highest in non-Hispanic black people
  - Men: 42%, Women: 46%

# BP Thresholds and Goals – General

Clinical Condition	BP Threshold, mm Hg	BP Goal, mm Hg
Clinical CVD or 10-year ASCVD risk $\geq 10\%$	$\geq 130/80$	$< 130/80$
No clinical CVD and 10-year ASCVD risk $< 10\%$	$\geq 140/90$	$< 130/80$
Older persons ( $\geq 65$ years; noninstitutionalized, ambulatory, community-living)	$\geq 130$ (SBP)	$< 130$ (SBP)

# Blood Pressure Goal Trials

- SPRINT trial (2015)
  - Cited in 2017 HF focused update and 2017 ACC/AHA HTN guidelines as justification for lower BP goals
- Meta-analysis comparing BP levels and CVD risk (2017)



# SPRINT Trial (2015)

- Randomized Trial of Intensive versus Standard Blood-Pressure Control
  - 9300 people aged 50 years or old without diabetes or previous TIA/stroke
  - Baseline SBP 130-180 mm Hg with increased CV risk
  - Randomized to either SBP goal <120 mm Hg or <140 mm Hg
  - Primary outcome: Composite MI, acute coronary syndrome, acute decompensated heart failure, death from CV causes

N Engl J Med. 2015 Nov 26;373(22):2103-16.  
doi: 10.1056/NEJMoa1511939



# SPRINT Trial (2015)

- Results
  - Intensive control reduced the primary outcome
    - 1.65% per year vs. 2.19% per year
    - Hazard ratio 0.75; 95% confidence interval [CI], 0.64–0.89;  $p < 0.001$ )
    - Number needed to treat = 61.
    - Benefits also occurred in patients older than 75.
  - Adverse reactions in intensive arm
    - Increased rates of hypotension, syncope, electrolyte abnormalities, and acute kidney injury/failure
    - Number needed to harm = 100 for hypotension.

N Engl J Med. 2015 Nov 26;373(22):2103-16.

doi: 10.1056/NEJMoa1511939

# Systematic Review and Meta-analysis (2017)

- Systolic Blood Pressure Reduction and Risk of Cardiovascular Disease and Mortality
  - Assessed the association of mean achieved SBP levels with the risk of CVD and all-cause mortality in adults with HTN treated with antihypertensive therapy
  - Over 144,000 patients from 42 trials were included
  - Linear association between mean achieved SBP and risk of CVD and mortality were seen
  - Authors concluded that reducing SBP to levels below currently recommended goals could **significantly reduce CVD and all-cause mortality**

JAMA Cardiol. 2017;2(7):775-81.

## Major CVD and All-Cause Mortality Associated with More Intensive Reductions in Systolic Blood Pressure

### Major CVD: Compared to 120-124 mm Hg

130 to 135 mm Hg: HR 0.71 (95% CI 0.60-0.83)

140 to 144 mm Hg: HR 0.58 (95% CI 0.48-0.72)

150 to 154 mm Hg: HR 0.46 (95% CI 0.34-0.63)

Greater than 160 mm Hg: HR 0.36 (95% CI 0.26-0.51)

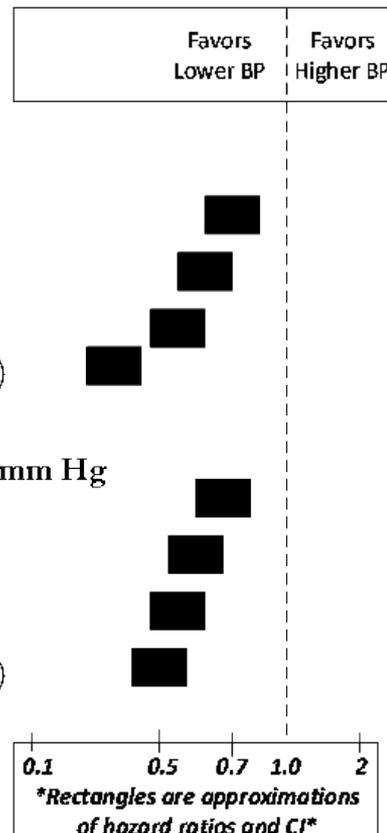
### All-cause mortality: Compared to 120-124 mm Hg

130 to 135 mm Hg: HR 0.73 (95% CI 0.58-0.93)

140 to 144 mm Hg: HR 0.59 (95% CI 0.45-0.77)

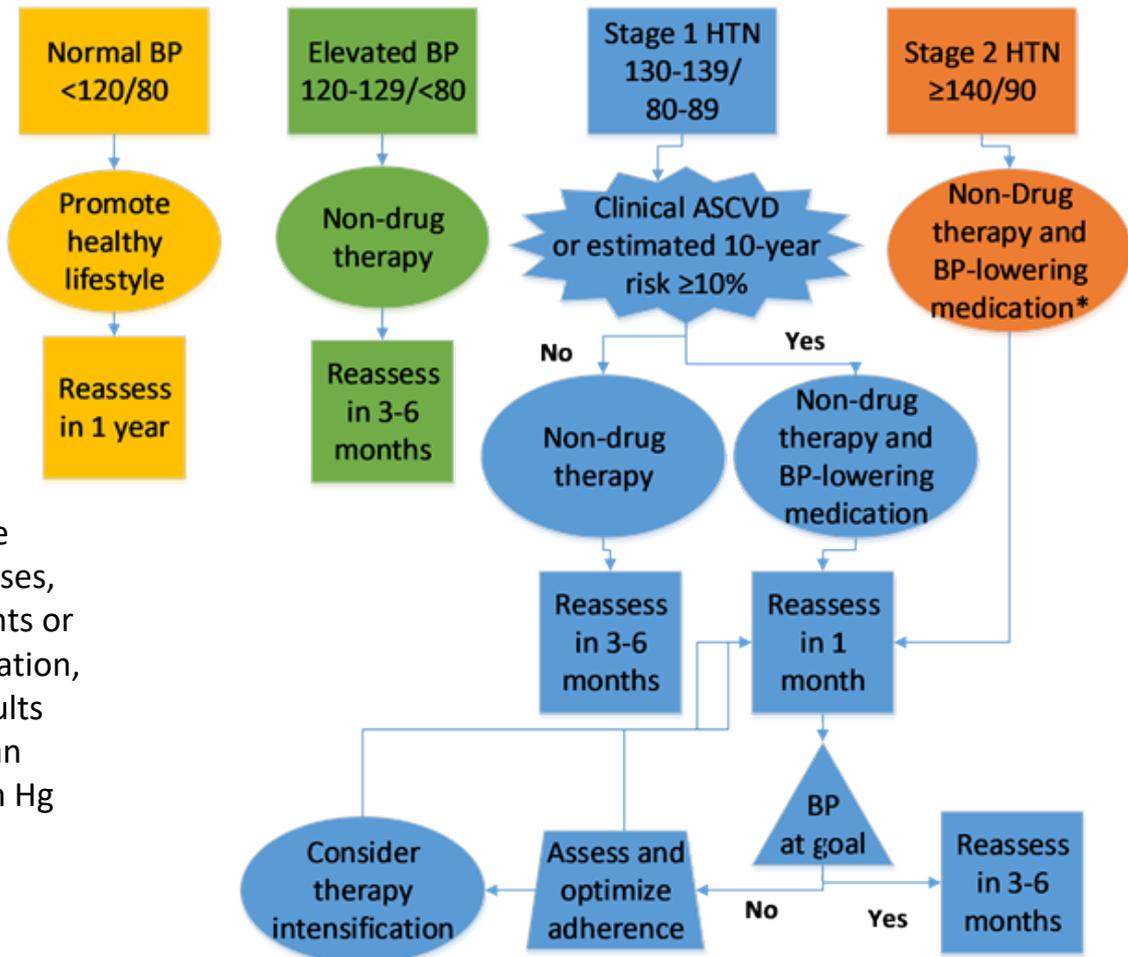
150 to 154 mm Hg: HR 0.51 (95% CI 0.36-0.71)

Greater than 160 mm Hg: HR 0.47 (95% CI 0.32-0.67)



JAMA Cardiol. 2017;2(7):775-781.

\*Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended in adults with stage 2 HTN and an average BP >20/10 mm Hg above their BP target.



# Principles of Drug Therapy

COR	LOE
I	A

For initiation of antihypertensive drug therapy, **first-line agents** include thiazide diuretics, CCBs, and ACE inhibitors or ARBs.

COR	LOE
I	B-R

In **black adults** with HTN but without HF or CKD, including those with DM, initial antihypertensive treatment should include a thiazide-type diuretic or CCB

COR	LOE
III: Harm	A

Simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended to treat adults with HTN



## Hypertension and Diabetes



# Patient Case: AS

- AS is a 67 year old white woman with diabetes. She has been told in the past that her blood pressure is “a little high,” but she has never been on BP medications or bought a home BP monitor.
- Social History: nonsmoker; no alcohol; walks for 30 minutes 3x/week; follows a low carb diet
- Medications:
  - Atorvastatin 40 mg daily
  - Metformin 1 g twice daily
  - Empagliflozin 25 mg daily
  - Omeprazole 40 mg daily

# Patient Case: AS

- Reports adherence with all medications
- Labs and vitals:
  - BP 138/88 mm Hg (138/84 repeat), HR 80 bpm
  - A1C 6.7%; SCr is 1.3 mg/dL (CrCl [adjusted BW] 46.8 ml/min), K 4.1 mEq/L, Na 135 mEq/L, no proteinuria, other labs are normal
  - BMI 33.4 kg/m<sup>2</sup>
- When discussing her BP, she said she was grateful that her BP is still at goal today

# What is AS's BP goal?

**A** < 120/80 mm Hg

**B** < 130/80 mm Hg

**C** < 140/90 mm Hg

**D** < 150/90 mm Hg

# How should her BP be addressed?

- A Start lisinopril 10 mg/day
- B Start chlorthalidone 12.5 mg/day
- C Start amlodipine 5 mg/day
- D Dealer's choice, all of the above are correct

# Diabetes Mellitus

- Most patients with diabetes are affected by HTN
  - Prevalence of HTN among adults with DM is approximately 80%
  - HTN is at least twice as common in persons with type 2 DM than in age-matched individuals without DM
- HTN is a risk factor for macro- and microvascular complications
  - Results in higher incidence of CHD, HF, PAD, stroke, CVD mortality
  - May increase risk of nephropathy and retinopathy
- Because CVD is the #1 killer of, and main source of morbidity in, patients with diabetes, controlling CV risk factors such as HTN in patients with diabetes is of utmost importance.

# ACCORD Trial (2010)

- Action to Control Cardiovascular Risk in Diabetes blood pressure trial
  - 4700 patients with Type 2 diabetes who had CVD or at least 2 additional CVD risk factors
  - Mean baseline BP was 139/76 mm Hg
  - Randomized to either SBP goal <120 mm Hg or <140 mm Hg
  - Primary composite outcome (nonfatal MI, nonfatal stroke, or death from CV causes)
- Results, after 4.7 year follow-up period
  - Mean SBP for intensive group: 119.3 mm Hg
  - Mean SBP for standard group: 133.5 mm Hg



# ACCORD Trial (2010)

- Results
  - No significant difference in rate of primary outcome for intensive vs. standard therapy
    - 1.87% vs. 2.09%; HR 0.88; 95% CI, 0.73–1.06
  - No difference in all-cause mortality or CV death
  - Intensive therapy was associated with less stroke (0.32% vs. 0.53%; HR 0.59; 95% CI, 0.39–0.89)
  - Serious adverse events from antihypertensive drugs occurred significantly more often in the intensive therapy group
    - For example, hypotension, syncope, bradycardia, electrolyte abnormalities, angioedema, and renal failure

# Guideline Response to ACCORD

- The ACCORD trial was underpowered to detect a statistically significant difference between the 2 treatment arms.
- The ACCORD trial demonstrated a small reduction in absolute risk (1.1%) for stroke, but there were few such events.
- More adverse events (2% increase in absolute risk) were identified in the lower BP group, especially self-reported hypotension and a reduction in estimated GFR, but these did not result in an excess of stroke or ESRD.
- The ACCORD trial was a factorial study
  - Secondary analysis demonstrated a significant outcome benefit in the intensive BP/standard glycemic group
  - Benefit in the intensive BP/intensive glycemic control group was no better than in the intensive BP/standard glycemic control group
  - Suggests a floor benefit beyond which the combined intensive interventions were ineffective
- An ACCORD secondary analysis suggested that an SBP <120 mm Hg is superior to standard BP control in reducing LVH

# Diabetes Mellitus

- Limited quality evidence to determine a precise BP target in adults with DM
- No RCTs have explicitly
  - Documented whether treatment to an SBP goal <140 mm Hg versus a higher goal improves clinical outcomes in adults with hypertension and DM or
  - Directly evaluated clinical outcomes associated with SBP <130 mm Hg
- Two high-quality systematic reviews of RCTs support an SBP target of <140 mm Hg (Lancet. 2016;387:435-43; CMAJ. 2013;185:949-57)
- A meta-analysis of almost 74,000 patients with DM reported that an SBP <130 mm Hg reduced stroke by 39%, but there was no significant risk reduction for MI (J Hypertens. 2011;29:1253-69)
- SPRINT trial did not include patients with DM

## BP Thresholds and Goals – Comorbidities

Clinical Condition	BP Threshold, mm Hg	BP Goal, mm Hg
Diabetes mellitus*	≥130/80	<130/80

\*Not supported by 2018 ADA guidelines

The vast majority of adults with DM have a 10-year ASCVD risk  $\geq 10\%$ , the high risk category that requires antihypertensive drug therapy at BP  $\geq 130/80$  mm Hg

# Diabetes Mellitus

COR	LOE
I	SBP: B-R
	DBP: C-EO

In adults with DM and HTN, antihypertensives should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of <130/80 mm Hg

COR	LOE
I	A <sup>SR</sup>

In adults with DM and HTN, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective

COR	LOE
IIb	B-NR

In adults with DM and HTN, ACE inhibitors or ARBs may be considered in the presence of albuminuria

# Diabetes Mellitus

- BP control is more difficult to achieve in patients with DM than in those without DM, necessitating use of combination therapy in the majority of patients
  - ACE inhibitors and ARBs have the best efficacy among the drug classes on urinary albumin excretion and may be considered as part of the combination for patients with DM



# 2018 ADA Standards of Medical Care in Diabetes



- Goal blood pressure <140/90 mm Hg
- Lower SBP and DBP targets, such as 130/80 mm Hg, may be appropriate for individuals at high risk of CVD if targets can be achieved without undue treatment burden
- For patients with diabetes but without albuminuria, any of the four classes of BP medications with beneficial CV outcomes may be used.
  - ACEIs
  - ARBs
  - Thiazide-like diuretics
  - Dihydropyridine CCBs

Diabetes Care 2018;41(suppl 1):S1-159.

## 2018 ADA Standards of Medical Care in Diabetes

- An ACEI or ARB, at max tolerated dose, is first-line for HTN in patients with diabetes and a urinary **albumin/creatinine ratio**:
  - 300 mg/g of creatinine or greater (level A) or
  - 30–299 mg/g of creatinine (level B).
- If one class is not tolerated, the other should be substituted.
- Combinations of 2 or more drugs (ACEI and ARB should not be combined) are usually needed to achieve a goal of <140/90 mm Hg.
- For patients treated with an ACE inhibitor, ARB, or diuretic, serum creatinine/ estimated GFR and serum K levels should be monitored at least annually

# Show of Hands

Do you struggle controlling the blood pressure for your patients with diabetes?

- A** Yes, every day
- B** Some, depending on the patient
- C** No, most of my patients have controlled BP





# Hypertension and Chronic Kidney Disease

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# Case: TN

- TN is a 50-year-old African-American man with a history of hypertension, hypercholesterolemia and gout
- Social History: nonsmoker; alcohol 2 to 3 drinks per week; minimal exercise; follows no specific diet
- Medications:
  - Atorvastatin 10 mg daily
  - Lisinopril 40 mg daily
  - Amlodipine 10 mg daily
  - Aspirin 81 mg daily
  - Allopurinol 200 mg daily

## Case: TN, continued

- Reports adherence with all medications
- Laboratory values:
  - TC 200 mg/dL, LDL-C 134 mg/dL, HDL 30 mg/dL, TG 180 mg/dL
- Other values:
  - BP 136/84 mm Hg (134/82 when repeated), HR 80 bpm, A1C 5.6%, BMI 29.2 kg/m<sup>2</sup>; SCr is 1.6 mg/dL (eGFR is 59 mL/min/1.73m<sup>2</sup>), potassium is 4.9 mEq/L, urinalysis shows albuminuria (150 mg/g)
  - All other labs are normal
  - BP was “high” prior to starting antihypertensive medications

# What would you say TN's BP goal is?

- A < 120/80 mm Hg
- B < 125/85 mm Hg
- C < 130/80 mm Hg
- D < 140/90 mm Hg

# Which of the following is the most appropriate change to TN's regimen?

- A Re-evaluate 1 month after additional healthy lifestyle changes
- B Start HCTZ or chlorthalidone
- C Start labetalol
- D Start spironolactone

# Hypertension – Guidelines

- 2012: KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease
- 2014: Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report from the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)
- 2014: ASH/ISH Clinical practice guidelines for the management of hypertension in the community
- 2017: 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
- 2018: AHA Scientific Statement on Resistant Hypertension

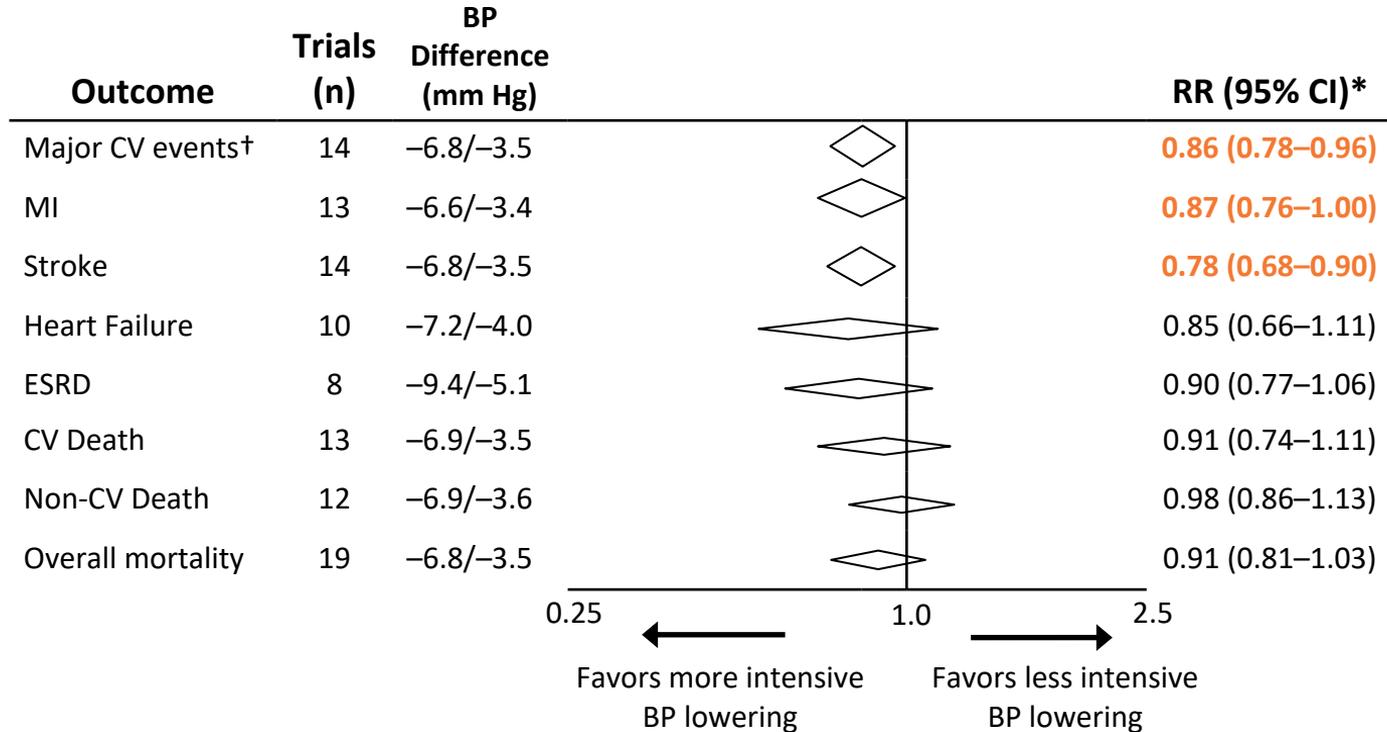
# BP Thresholds and BP Goals for CKD Patients

Clinical Condition	BP Threshold, mm Hg	BP Goal, mm Hg
<b>Specific Co-morbidities</b>		
Chronic kidney disease	$\geq 130/80$	$< 130/80$
Chronic kidneys disease post renal transplant	$\geq 130/80$	$< 130/80$

# Effects of Intensive BP lowering on CV and renal outcomes

- Objective: Assess safety and efficacy of intensive BP-lowering
- Methods:
  - Updated systematic review and meta-analysis
  - More intensive vs. less intensive BP lowering compared
- Trials and Patients:
  - 19 trials including 44,989 participants; no age restrictions
  - 2,496 CV events recorded during mean follow-up of 3.8 yr.
  - Studies  $\geq 6$  mos. follow-up
- Outcomes:
- Major CV events, non-vascular and all-cause mortality, stroke, HF, end-stage renal disease (ESRD), adverse events, albuminuria, progression of retinopathy

# Effects of Intensive vs. Less Intensive BP Lowering



# Antihypertensive Therapy Recommendations: Compelling Indications

Clinical Condition	1 <sup>st</sup> Line Drug
Specific Co-morbidities	
Chronic kidney disease	ACE-I or ARB

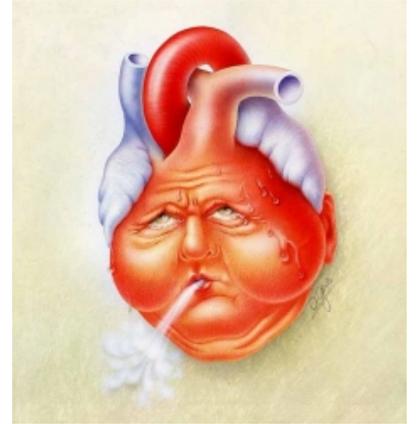
# KDIGO\*: Albuminuria Influences Treatment

- Chronic kidney disease, non-dialysis patients

Urine Albumin Excretion per 24 hr	BP Goal (mm Hg)	Treatment
< 30 mg	≤140/90	Not specified
30 to 300 mg	≤130/80	ACE-I or ARB
> 300 mg	≤130/80	ACE-I or ARB

- Same suggestions and recommendations provided for patients with diabetes and without, but different cited level of evidence

**\*KDIGO has noted the publication of the Systolic Blood Pressure Intervention Trial (SPRINT) results and has launched a process to review these and other new data to determine if revisions to its Blood Pressure Guideline are required.**



## Hypertension and Heart Failure



# Patient Case Continued: AS

- AS is now a 71 year old white woman with diabetes, 4 years since the last time we saw her. About 2 years ago, she developed HFrEF.
- Current Medications:
  - Atorvastatin 80 mg daily
  - Metformin 1 g twice daily
  - Insulin as directed
  - Empagliflozin 25 mg daily
  - Omeprazole 40 mg daily
  - Lisinopril 20 mg/day
  - Furosemide 40 mg twice daily

# Patient Case: AS

- Reports adherence with all medications
- Labs and vitals:
  - BP 142/80 mm Hg (138/80 repeat), HR 90 bpm
  - A1C 7.5%; SCr is 1.5 mg/dL (CrCl [adjusted BW] 40.3 ml/min), K 4.3 mEq/L, Na 134 mEq/L, no proteinuria, other labs are normal
  - EF 30%
  - BMI 36.7 kg/m<sup>2</sup>

# What is AS's BP goal?

**A** < 120/80 mm Hg

**B** < 130/80 mm Hg

**C** < 140/90 mm Hg

**D** < 150/90 mm Hg

## How should her BP be addressed?

- A** Titrate lisinopril to 40 mg/day
- B** Start chlorthalidone 12.5 mg/day
- C** Start carvedilol 3.125 mg twice daily
- D** Start spironolactone 12.5 mg/day

# Heart Failure (HF<sub>r</sub>EF & HF<sub>p</sub>EF)

- HTN is one of the most important modifiable risk factors
  - Present in 75% of patients with chronic HF
- Patient with HTN have a much higher risk of developing HF than normotensive people
  - Compared with those with an average SBP <120 mm Hg, the adjusted incidence of HF was increased
    - 1.6 times → average SBPs between 120 and 139 mm Hg
    - 2.2 times → average SBPs between 140 and 159 mm Hg
    - 2.6 times → average SBPs ≥160 mm Hg
- Long-term treatment of both systolic and diastolic HTN reduces the risk of HF by around 50%.
- HTN is an important contributor to acute decompensated HF.

# BP Thresholds and Goals

Clinical Condition	BP Threshold, mm Hg	BP Goal, mm Hg
Heart failure	≥130/80	<130/80

COR	LOE
I	SBP: B-R
	DBP: C-EO

In adults at increased risk of HF, the optimal BP in those with HTN should be <130/80 mm Hg

- In SPRINT, the incidence of HF, a component of the primary outcome, was substantially decreased (hazard ratio: 0.62; 95% confidence interval: 0.45–0.84).
- Meta-analyses of clinical trials have identified a similar beneficial effect of more-intensive BP reduction on the incidence of HF (Hypertens. 2016; 34:613-22; Lancet. 2016;387:957-67), but information from randomized studies to different BP targets is more limited and less compelling (Lancet. 2016;387:435-43)

# Heart Failure With Reduced Ejection Fraction

- Approximately 50% of patients with HF have HFrEF
- No RCT evidence is available to support the superiority of one BP-lowering medication for treatment of HFrEF over another.
- Medications with compelling indications for HF that may be used as first-line therapy to treat high BP include
  - ACE inhibitors
  - ARBs
  - Angiotensin receptor–neprilysin inhibitors
  - Mineralocorticoid receptor antagonists
  - Diuretics
  - GDMT beta blockers (carvedilol, metoprolol succinate, or bisoprolol)

# HFrEF

COR	LOE
I	C-EO

Adults with **HFrEF** and HTN should be prescribed GDMT titrated to attain a BP of <130/80 mm Hg

COR	LOE
III: No benefit	B-R

Nondihydropyridine CCBs are not recommended in the treatment of HTN in adults with **HFrEF**

# Heart Failure With Preserved Ejection Fraction

- Patients with HFpEF (EF from >40% to  $\geq 55\%$ ) are usually older women with a history of hypertension.
- Hypertension is the most important cause of HFpEF, with a prevalence of 60% to 89% in large RCTs, epidemiological studies, and HF registries
- Patients with HFpEF also have an exaggerated hypertensive response to exercise
- Diuretics are the only drugs used for the treatment of hypertension and HF that can adequately control the fluid retention of HF: must balance hyper- and hypovolemia
- Renin-angiotensin-aldosterone system inhibition, however, with ACE inhibitor or ARB and especially MRA would represent the preferred choice

# HFpEF

COR	LOE
I	C-EO

In adults with **HFpEF** with symptoms of volume overload, diuretics should be prescribed to control HTN

COR	LOE
I	C-EO

Adults with **HFpEF** and persistent HTN after managing volume overload, ACE inhibitors or ARBs and beta blockers should be titrated to attain SBP of <130 mm Hg

# 2017 ACC/AHA/HFSA Focused Update for the Management of HF



- For patients at increased risk of developing HF (stage A HF), the optimal blood pressure in those with HTN should be less than **130/80 mm Hg**.

- Rationale:

- The SPRINT trial showed that patients with increased CV risk (older than 75 years, established vascular disease, chronic renal disease, or a Framingham Risk greater than 15%), controlling their BP to a goal SBP of <120 mm Hg was associated with a **significantly reduced incidence of HF and CV death**.
- Because BP measurements taken in the office are about 5–10 mm Hg higher than research measurements, the goal of <130/80 mm Hg is recommended.
- Note: Targeting a significant reduction in SBP is a **novel strategy** to prevent HF.

# 2017 ACC/AHA/HFSA Focused Update for the Management of HF

- HFrEF and HTN
  - SBP goal less than 130 mm Hg
  - Guideline-directed management and titrate dose
    - ACEIs or ARBs or angiotensin receptor-neprilysin inhibitors
    - $\beta$ -blockers for HF (metoprolol succinate, carvedilol, bisoprolol)
    - Diuretics as needed
    - Aldosterone antagonists when indicated
- HFpEF and HTN
  - SBP goal less than 130 mm Hg
  - First, manage volume overload,
  - Then, titrate ACEI or ARB and/or an aldosterone antagonist to goal.

# Show of Hands

Do you struggle controlling the blood pressure for your patients with heart failure?

- A** Yes, every day
- B** Some, depending on the patient
- C** No, most of my patients have controlled BP





## Resistant Hypertension

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# Case: TN

## back in clinic (2 years since previous encounter)

- TN is a 52-year-old African-American man with a history of hypertension, hypercholesterolemia, type 2 diabetes mellitus, gout, chronic kidney disease (Stage 3)
- Social History: nonsmoker; alcohol 2 to 3 drinks per week; minimal exercise; follows no specific diet
- Medications:
  - Metformin 1000 mg twice daily
  - Insulin glargine 30 units subcutaneous daily
  - Atorvastatin 40 mg daily
  - Lisinopril 40 mg daily
  - HCTZ 25 mg daily
  - Amlodipine 10 mg daily
  - Aspirin 81 mg daily
  - Allopurinol 200 mg daily

## Case: TN, continued

- Reports adherence with all medications
- Laboratory values:
  - TC 170 mg/dL, LDL-C 105 mg/dL, HDL 33 mg/dL, TG 160 mg/dL
- Other values:
  - BP 138/80 mm Hg (136/80 when repeated), A1C 7.5%, BMI 28.2 kg/m<sup>2</sup>; SCr is 1.8 mg/dL (eGFR is 52 mL/min/1.73m<sup>2</sup>), potassium is 4.7 mEq/L, urinalysis shows albuminuria (200 mg/g)
  - All other labs are normal

# Does this patient meet the 2018 American Heart Association (AHA) criteria for resistant hypertension?

- A Yes
- B No
- C Unsure

# What would you say TN's BP goal is?

- A < 120/80 mm Hg
- B < 125/85 mm Hg
- C < 130/80 mm Hg
- D < 140/90 mm Hg

# Which of the following is the most appropriate change to TN's regimen?

- A Add hydralazine
- B Change HCTZ to chlorthalidone
- C Add carvedilol or labetalol
- D Add spironolactone

# Hot off the Press....

## AHA Scientific Statement

### **Resistant Hypertension: Detection, Evaluation, and Management** **A Scientific Statement From the American Heart Association**

Robert M. Carey, MD, FAHA, Chair; David A. Calhoun, MD, FAHA, Vice Chair;  
George L. Bakris, MD, FAHA; Robert D. Brook, MD, FAHA; Stacie L. Daugherty, MD, MSPH;  
Cheryl R. Dennison-Himmelfarb, PhD, MSN, FAHA; Brent M. Egan, MD;  
John M. Flack, MD, MPH, FAHA; Samuel S. Gidding, MD, FAHA; Eric Judd, MD, MS;  
Daniel T. Lackland, DrPH, FAHA; Cheryl L. Laffer, MD, PhD, FAHA;  
Christopher Newton-Cheh, MD, MPH, FAHA; Steven M. Smith, PharmD, MPH, BCPS;  
Sandra J. Taler, MD, FAHA; Stephen C. Textor, MD, FAHA; Tanya N. Turan, MD, FAHA;  
William B. White, MD, FAHA; on behalf of the American Heart Association Professional/Public  
Education and Publications Committee of the Council on Hypertension; Council on Cardiovascular  
and Stroke Nursing; Council on Clinical Cardiology; Council on Genomic and  
Precision Medicine; Council on Peripheral Vascular Disease; Council on Quality of Care  
and Outcomes Research; and Stroke Council

# Resistant Hypertension

- American Heart Association (AHA) Definition:
  - “Clinic BP > 130/80 mm Hg and patient taking **3 or more antihypertensive agents** (including a long-acting CCB, RAS blocker [ACE -I or ARB] and a diuretic) at **maximally tolerated doses.**”
  - Also refers to **BP controlled with  $\geq 4$  medications**
- Secondary Hypertension
  - Elevated blood pressure as a result from either a co-morbid condition or drug
  - < 10% of overall hypertension

# Key Changes in Resistant Hypertension Definition (2008 to 2018)

- BP should be measured and the BP threshold for diagnosis and treatment goals should be in accord with current clinical practice guidelines
- Patients should be taking  $\geq 3$  antihypertensive agents
  - Commonly including a long-acting CCB, RAS blocker (ACE-I or ARB), and a diuretic at maximally tolerated doses
- Patients with the white-coat effect should not be included in the definition of resistant HTN
- Diagnosis of resistant HTN requires the exclusion of antihypertensive medication nonadherence

# Prevalence of Resistant Hypertension

- American Heart Association (AHA) Definition:
  - “Clinic BP > 130/80 mm Hg and patient taking **3 or more antihypertensive agents** (including a long-acting CCB, RAS blocker [ACE -I or ARB] and a diuretic) at **maximally tolerated doses**.
  - Also refers to **BP controlled with  $\geq 4$  medications**
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  - Elevated blood pressure as a result from either a co-morbid condition or drug
  - < 10% of overall hypertension

# Prevalence of Resistant HTN in US

Population	Time Period	N	Uncontrolled with $\geq 3$ meds (%)	Controlled with $\geq 4$ meds (%)	aTRH (%)
NHANES	1988-1994	2755	8.3	1.1	9.4
NHANES	1999-2004	3031	8.8	2.9	11.7
NHANES	2003-2008	3710	----	----	12.8
NHANES	2005-2008	2586	9.7	4.8	14.5

aTRH = apparent treatment resistant hypertension

Do you utilize home blood pressure monitoring to screen for white coat HTN in your practice?

A Yes

B No

# Do you utilize 24hr Ambulatory BP monitoring to screen for white coat HTN in your practice?

**A** Yes

**B** No

# Resistant Hypertension

## Confirm Treatment Resistance

Clinic BP > 130/80 mm Hg

And

Patient prescribed  $\geq 3$  BP medications at optimal doses including a diuretic

Or

Clinic BP < 130/80 mm Hg receiving > 4 BP medications

## Exclude Pseudoresistance

Ensure accurate clinic BP measurement

Confirm adherence to antihypertensive therapy

Perform 24 hour ambulatory BP monitoring to exclude white-coat effect

# Resistant Hypertension

## Assess for Secondary Causes

Primary aldosteronism  
Renal Parenchymal disease  
Renal artery stenosis  
Pheochromocytoma/paraganglioma  
Cushing syndrome  
Other endocrine causes (Table 3)

## Assess for Target Organ Damage

Ocular: fundoscopic exam  
Cardiac: LVH, CAD  
Renal: proteinuria, reduced GFR  
Peripheral artery disease: Ankle/brachial index

# Management of Resistant Hypertension

## Step 1

### Exclude other causes of

### HTN

Secondary causes

White-coat effect

Medication nonadherence

+

### Ensure low sodium diet

### Maximize lifestyle interventions

≥ 6 hours uninterrupted sleep

Overall dietary pattern

Weight loss

Exercise

+

### Optimize 3-drug regimen

Ensure adherence to 3 drug regimen

**Different drug classes (RAS blocker, CCB, diuretic)**

Maximum tolerated dose

Diuretic type appropriate for renal function

**BP not at target** → **Step 2**

### Substitute optimally doses thiazide-like diuretic

Change to chlorthalidone or indapamide\*

**BP not at target** → **Step 3**

### Add mineralocorticoid receptor antagonist (MRA)

Spironolactone or eplerenone\*\*

\*Efficacy down to eGFR of 30 mL/min/1.73m<sup>2</sup>

\*\*Use caution if eGFR < 30 mL/min/1.73m<sup>2</sup>

# Management of Resistant Hypertension

**BP not at target** → **Step 4** (*Expert opinion*)

## Check heart rate

**Add Beta Blocker (eg, metoprolol succinate, bisoprolol) or combined Alpha/Beta Blocker (eg, labetalol, carvedilol)**

If contraindicated consider Central Alpha Agonist (ie, clonidine patch, guanfacine at bedtime)

If these options not tolerated consider once daily diltiazem

**BP not at target** → **Step 5** (*Expert opinion*)

## Add hydralazine\*

Dose of 25 mg TID and titrate to maximum dose

If known HF<sub>r</sub>EF should be given with isosorbide mononitrate 30 mg daily

**BP not at target** → **Step 6** (*Expert opinion*)

## Substitute minoxidil for hydralazine\*\*

Dose of 2.5 mg BID to TID and titrate to maximum dose

**If BP still not at target consider referral to hypertension specialist and/or for ongoing experimental studies/trials**

**\*Requires concomitant use of Beta Blocker and diuretic**    **\*\*Requires concomitant use of Beta Blocker and loop diuretic**

Hypertension. 2018;72:e000–e000. DOI: 10.1161/HYP.000000000000084.

# Case: TN

## back to the patient case

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- A Add hydralazine
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- C Add carvedilol or labetalol
- D Add spironolactone

# KEY TAKEAWAYS

- 1) *The goal BP for patients with diabetes is <130/80 mm Hg. All first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective. ACE inhibitors or ARBs may be considered in the presence of albuminuria.*
- 2) *BP goal for patients with CKD is less than 130/80 mm Hg with a compelling indication to initiate an ACE Inhibitor or ARB first line.*
- 3) *The goal BP for patients with heart failure is <130/80 mm Hg. Antihypertensive therapy should be based on type of heart failure and guideline-directed medical therapy.*
- 4) *Resistant Hypertension is defined as clinic BP > 130/80 mm Hg and patient taking 3 or more antihypertensive agents (including a long-acting CCB, RAS blocker and a diuretic) at maximally tolerated doses.*



# At Last! Applying the National Hypertension Guidelines in Special Populations

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