UPDATE IN HYPERTENSION

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Certified Hypertension Specialist
OBJECTIVES

• Epidemiology & Definition Of Hypertension
• Devise Evidence-based Treatment Plans For Managing Hypertension.
• Approach To Refractory Hypertension.
• Role of Ambulatory Blood Pressure Monitoring.
• Treating Hypertensive Urgency And Emergency.
• Current BP Goals And Controversies.
Hypertension affects 1 in 3 adults in the US and more than 1 billion people worldwide.
Prevalence is projected to increase by 60% by 2025.
Hypertension costed $46 billion in health care services and loss of work in 2011 in USA.
In 2010, high BP was the leading cause of death worldwide. Accounting for 1 out of 8 deaths worldwide.
In the United States, hypertension accounted for more CVD deaths than any other modifiable CVD risk factor.
Hypertension comes second only to cigarette smoking as a preventable cause of death for any reason.
PREVALENCE OF HYPERTENSION AMONG ADULTS AGED 18 AND OVER, BY SEX AND AGE: UNITED STATES, 2015–2016

National Health and Nutrition Examination Survey

32.1%
31.8%
32.4%

Men significantly different from women in the same age group.

NOTES: Estimates for age group 18 and over are age adjusted by the direct method to the 2000 U.S. Census population using age groups 18–39, 40–59, and 60 and over. Crude estimates for age group 18 and over are 32.1%, total; 31.8%, men; and 32.4%, women. Access data table for Figure 1 at: https://www.cdc.gov/nchs/data/databriefs/db289_table.pdf#1.

## Prevalence of Hypertension Based on 2 SBP/DBP Thresholds

**NHANES 2011–2014**

<table>
<thead>
<tr>
<th></th>
<th>SBP/DBP ≥130/80 mm Hg or Self-Reported Antihypertensive Medication†</th>
<th>SBP/DBP ≥140/90 mm Hg or Self-Reported Antihypertensive Medication‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall, crude</td>
<td>46%</td>
<td>32%</td>
</tr>
<tr>
<td>Men (n=4717)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women (n=4906)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, age-sex adjusted</td>
<td>48%</td>
<td>43%</td>
</tr>
<tr>
<td>Men (n=4717)</td>
<td></td>
<td>31%</td>
</tr>
<tr>
<td>Women (n=4906)</td>
<td></td>
<td>32%</td>
</tr>
<tr>
<td>Age group, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–44</td>
<td>30%</td>
<td>19%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>45–54</td>
<td>50%</td>
<td>44%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td>55–64</td>
<td>70%</td>
<td>63%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>52%</td>
</tr>
<tr>
<td>65–74</td>
<td>77%</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>63%</td>
</tr>
<tr>
<td>75+</td>
<td>79%</td>
<td>85%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>71%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>78%</td>
</tr>
<tr>
<td>Race-ethnicity §</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>47%</td>
<td>41%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30%</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>59%</td>
<td>56%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>46%</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
<td>45%</td>
<td>36%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>44%</td>
<td>42%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>32%</td>
</tr>
</tbody>
</table>
RISK OF DEVELOPING HYPERTENSION

- For an adult 45 years of age without hypertension, the 40-year risk for developing hypertension is 93% for African Americans, 92% for Hispanics, 86% for whites, and 84% for Chinese adults.

- In the Framingham Heart Study, approximately 90% of adults free of hypertension at age 55 or 65 years developed hypertension during their lifetimes.
Why do we need to control High BP?

• In a follow-up study of 23,272 U.S. NHANES (National Health and Nutrition Examination Survey) participants, >50% of deaths from CAD and stroke occurred among individuals with hypertension.

• Hypertension is the second leading cause of ESRD, behind diabetes mellitus.

• Hypertension results in an average loss of life of 5 years, and those living with hypertension are more often burdened with morbidities of CHF, CKD, stroke, and vision loss.
HYPERTENSION DEFINITION

**JNC 7: Guidelines for Hypertension**

- **Goal:** To reduce cardiovascular and renal morbidity and mortality through prevention and management of hypertension

**Classification of Blood Pressure**

<table>
<thead>
<tr>
<th>Category</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td>Hypertension, Stage 1</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Hypertension, Stage 2</td>
<td>≥160</td>
<td>≥100</td>
</tr>
</tbody>
</table>

JNC 7, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. SBP, systolic blood pressure; DBP, diastolic blood pressure.

Adapted from the JNC 7 Slide Deck. Available at: http://www.nhlbi.nih.gov.

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**JNC 8**

**Table 3. Classification of blood pressure for adults**

<table>
<thead>
<tr>
<th>Classification</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139</td>
<td>or 80-89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140-159</td>
<td>or 90-99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160</td>
<td>or ≥100</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure.
# EUCLIDEAN SOCIETY OF HYPERTENSION

2018

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>and</td>
</tr>
<tr>
<td>Normal</td>
<td>120–129</td>
<td>and/or</td>
</tr>
<tr>
<td>High normal</td>
<td>130–139</td>
<td>and/or</td>
</tr>
<tr>
<td>Grade 1 hypertension</td>
<td>140–159</td>
<td>and/or</td>
</tr>
<tr>
<td>Grade 2 hypertension</td>
<td>160–179</td>
<td>and/or</td>
</tr>
<tr>
<td>Grade 3 hypertension</td>
<td>≥180</td>
<td>and/or</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>≥140</td>
<td>and</td>
</tr>
</tbody>
</table>

*The blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic. Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.*
SCREENING AND DIAGNOSIS OF HYPERTENSION

2018 ESC/ESH GUIDELINES FOR THE MANAGEMENT OF ARTERIAL HYPERTENSION

- **Optimal BP**
  - <120/80
  - Repeat BP at least every 5 years

- **Normal BP**
  - 120-129/80-84
  - Repeat BP at least every 3 years

- **High-normal BP**
  - 130-139/85-89
  - Repeat BP at least annually
  - Consider masked hypertension

- **Hypertension**
  - ≥140/90
  - Use either to confirm diagnosis
  - Repeated visits for office BP measurement
  - Out-of-office BP measurement (ABPM or HBPM)
  - Indications for ABPM or HBPM see Table 11
Hypertension Canada’s 2018 Guidelines

Hypertension Diagnostic Algorithm for Adults

1. Elevated BP Reading (office, home or pharmacy)
   - Yes
     - Dedicated Office Visit
       - Mean Office BP ≥ 180/110
         - No
           - No Diabetes
             1. AOBP ≥ 135/85 (preferred)
               OR
             2. Non-AOBP ≥ 140/90 (if AOBP unavailable)
               - Yes
                 - Out-of-office Measurement
                   1. ABPM (preferred)
                      Daytime mean ≥ 135/85
                      24-hour mean ≥ 130/80
                      OR
                   2. Home BP Series
                      Mean ≥ 135/85
                     - Yes
                       - Hypertension
                     - No
                       - White Coat Hypertension
     - Yes
       - Hypertension
   - No
     - No Hypertension

Notes:
1. If AOBP is used, use the mean calculated and displayed by the device. If non-AOBP (see note 2) is used, take at least three readings, discard the first and calculate the mean of the remaining measurements. A history and physical exam should be performed and diagnostic tests ordered.
2. AOBP = Automated Office BP. This is performed with the patient unattended in a private area.
   Non-AOBP = Non-automated measurement performed using an electronic upper arm device with the provider in the room.
3. Diagnostic thresholds for AOBP, ABPM, and home BP in patients with diabetes have yet to be established (and may be lower than 130/80 mmHg).
4. Serial office measurements over 3-5 visits can be used if ABPM or home measurement not available.
5. Home BP Series: Two readings taken each morning and evening for 7 days (28 total). Discard first day readings and average the last 6 days.
6. Annual BP measurement is recommended to detect progression to hypertension.

ABPM: Ambulatory Blood Pressure Measurement
AOBP: Automated Office Blood Pressure
<table>
<thead>
<tr>
<th>BP Category</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 mm Hg</td>
<td>and &lt;80 mm Hg</td>
</tr>
<tr>
<td>Elevated</td>
<td>120–129 mm Hg</td>
<td>and &lt;80 mm Hg</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>130–139 mm Hg</td>
<td>or 80–89 mm Hg</td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥140 mm Hg</td>
<td>or ≥90 mm Hg</td>
</tr>
</tbody>
</table>
HYPERTENSION DIAGNOSIS BASED ON 2017 AHA GUIDELINES

BP >130/80

NO END ORGAN DAMAGE

24 HR ABPM

HOME BP

OFFICE BP READINGS

HTN EMERGENCY /EVIDENCE OF TARGET ORGAN DAMAGE

HTN DIAGNOSED

HTN DIAGNOSED

BP <130/80

WHITE COAT HYPERTENSION

HTN DIAGNOSED
DEVISE EVIDENCE-BASED TREATMENT PLANS FOR MANAGING HYPERTENSION
<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure office BP accurately</td>
<td></td>
</tr>
<tr>
<td>Detect white coat hypertension or masked hypertension by using ABPM and HBPM</td>
<td></td>
</tr>
<tr>
<td>Evaluate for secondary hypertension</td>
<td></td>
</tr>
<tr>
<td>Identify target organ damage</td>
<td></td>
</tr>
<tr>
<td>Introduce lifestyle interventions</td>
<td></td>
</tr>
<tr>
<td>Use ASCVD risk estimation to guide BP threshold for drug therapy</td>
<td></td>
</tr>
<tr>
<td>Initiate antihypertensive pharmacological therapy &amp; Align treatment options with comorbidities</td>
<td></td>
</tr>
<tr>
<td>Detect and reverse nonadherence &amp; Account special circumstances in antihypertensive treatment</td>
<td></td>
</tr>
<tr>
<td>Use health information technology for remote monitoring and self-monitoring of BP</td>
<td></td>
</tr>
</tbody>
</table>
BLOOD PRESSURE THRESHOLDS AND RECOMMENDATIONS FOR TREATMENT AND FOLLOW-UP

BP thresholds and recommendations for treatment and follow-up

Normal BP (BP <120/80 mm Hg)

- Promote optimal lifestyle habits
- Reassess in 1 y (Class IIa)

Elevated BP (BP 120–129/<80 mm Hg)

- Nonpharmacologic therapy (Class I)
- Reassess in 3–6 mo (Class I)

Stage 1 hypertension (BP 130–139/80–89 mm Hg)

- Nonpharmacologic therapy (Class I)
- Reassess in 3–6 mo (Class I)

Stage 2 hypertension (BP ≥ 140/90 mm Hg)

Clinical ASCVD or estimated 10-yr CVD risk ≥10%

- No
- Yes

- Nonpharmacologic therapy and BP-lowering medication† (Class I)
- Nonpharmacologic therapy and BP-lowering medication† (Class I)

No

Yes
<table>
<thead>
<tr>
<th>Nonpharmacological Intervention</th>
<th>Dose</th>
<th>Approximate Impact on SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight loss</strong></td>
<td>Weight/body fat</td>
<td>Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.</td>
</tr>
<tr>
<td><strong>Healthy diet</strong></td>
<td>DASH dietary pattern</td>
<td>Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.</td>
</tr>
<tr>
<td><strong>Reduced intake of dietary sodium</strong></td>
<td>Dietary sodium</td>
<td>Optimal goal is &lt;1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.</td>
</tr>
<tr>
<td><strong>Enhanced intake of dietary potassium</strong></td>
<td>Dietary potassium</td>
<td>Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.</td>
</tr>
</tbody>
</table>
## BEST PROVEN NONPHARMACOLOGICAL INTERVENTIONS
### FOR PREVENTION AND TREATMENT OF HYPERTENSION*

<table>
<thead>
<tr>
<th>Nonpharmacological Intervention</th>
<th>Dose</th>
<th>Approximate Impact on SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Hypertension</strong></td>
</tr>
<tr>
<td>Physical activity</td>
<td>Aerobic</td>
<td>-5/8 mm Hg</td>
</tr>
<tr>
<td></td>
<td>● 90–150 min/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● 65%–75% heart rate reserve</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dynamic resistance</td>
<td>-4 mm Hg</td>
</tr>
<tr>
<td></td>
<td>● 90–150 min/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● 50%–80% 1 rep maximum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● 6 exercises, 3 sets/exercise, 10 repetitions/set</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isometric resistance</td>
<td>-5 mm Hg</td>
</tr>
<tr>
<td></td>
<td>● 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% max voluntary contraction, 3 sessions/wk</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● 8–10 wk</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>In individuals who drink alcohol† to:</td>
<td>-4 mm Hg</td>
</tr>
<tr>
<td></td>
<td>● Men: ≤2 drinks daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● Women: ≤1 drink daily</td>
<td></td>
</tr>
</tbody>
</table>

†Reduce alcohol intake to:

*Based on evidence from various studies.
A combination of 2 first line drugs may be considered as initial therapy if the blood pressure is ≥20 mmHg systolic or ≥10 mmHg diastolic above target.
CONSIDER RACE & COMORBIDITIES IN INITIAL DRUG SELECTION

<table>
<thead>
<tr>
<th>Initial monotherapy</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>General Population</strong></td>
<td></td>
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<tr>
<td>Nonblack</td>
<td>THZD, ACE inhibitor, ARB, or CCB</td>
</tr>
<tr>
<td>Black</td>
<td>THZD or CCB</td>
</tr>
<tr>
<td><strong>CKD</strong></td>
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<tr>
<td>Nonblack</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td>Black</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
</tr>
<tr>
<td>Nonblack</td>
<td>ACE inhibitor or ARB</td>
</tr>
<tr>
<td>Black</td>
<td>THZD or CCB (^a)</td>
</tr>
</tbody>
</table>
POSSIBLE COMBINATION OF CLASSES OF ANTIHYPERTENSIVE DRUGS

- Thiazide diuretics: ALLHAT, CONVINCE, CAPP, LIFE, VALUE
- Beta-blockers
- Angiotensin-receptor blockers: COPE, COLM
- Other antihypertensives
- Calcium antagonists: ACCOMPLISH, ASCOT, NORDIL, INVEST
- ACE inhibitors

ACE = angiotensin-converting enzyme.
LANDMARK TRIALS

- ALLHAT
- ACCOMPLISH
THE ANTIHYPERTENSIVE AND LIPID-LOWERING TREATMENT TO PREVENT HEART ATTACK TRIAL 2002

Age ≥55 years
Stage 1 or 2 HTN with ≥1 additional CV risk factor:
- Previous (>6 months) MI or stroke
- LVH on EKG or echo
- T2DM
- Current cigarette smoking
- HDL <35 mg/dL
- Documentation of other atherosclerotic CVD

Mean age 66 yrs
Mean follow-up: 4.9 years

Goal BP <140/90 mmHg achieved by:
Step 1: titrating assigned study drug
- 12.5 to 25 mg/d for chlorthalidone
- 2.5 to 10 mg/d for amlodipine
- 10 to 40 mg/d for lisinopril

Step 2: adding open-label agents (atenolol, clonidine, or reserpine) or low doses of open-label step 1 drug classes
- 25 to 100 mg/d of atenolol
- 0.05 to 0.2 mg/d of reserpine
- 0.1 to 0.3 mg BID of clonidine

Step 3: adding 25 to 100 mg BID of hydralazine

42,418 - RANDOMIZED

15255-CTD
9048-AMLODIPINE
9054-LISINOPRIL
9061-DOXAZOSIN
MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE BY YEAR DURING FOLLOW-UP
Cumulative Event Rates for the Primary Outcome (Fatal Coronary Heart Disease or Nonfatal Myocardial Infarction) by Treatment Group

11.5% vs 11.3% vs 11.4% (p=NS)
Summary of Outcomes
Relative Risks and 95% CI

Amlodipine / Chlorthalidone  
CHD: 0.98 (0.91, 1.08)  
Death: 0.96 (0.89, 1.02)  
CCHD: 1.00 (0.94, 1.07)  
Stroke: 0.93 (0.82, 1.06)  
CCVD: 1.04 (0.99, 1.09)  
HF: 1.38 (1.25, 1.52)  

Lisinopril / Chlorthalidone  
CHD: 0.99 (0.91, 1.08)  
Death: 1.00 (0.94, 1.08)  
CCHD: 1.05 (0.98, 1.11)  
Stroke: 1.15 (1.02, 1.30)  
CCVD: 1.10 (1.05, 1.16)  
HF: 1.19 (1.07, 1.31)  

Amlodipine Better  
Chlorthalidone Better  
Lisinopril Better  
Chlorthalidone Better
AVOIDING CARDIOVASCULAR EVENTS THROUGH COMBINATION THERAPY IN PATIENTS LIVING WITH SYSTOLIC HYPERTENSION (ACCOMPLISH) TRIAL

- Randomized 11,506 patients to benazepril/amldipine or benazepril/HCTZ. With a mean follow-up of 2.5 years,
- Inclusion Criteria: SBP ≥160 mmHg or on antihypertensives
- Age 55-59 years and ≥2 of the following or ≥60 years and ≥1 of the following in their medical history:
  - Acute coronary syndrome, Coronary revascularization, CVA, CKD, PAD, LVH, DM
- Target BP <140/90 or <130/80 among patients with DM
EFFECTS OF TREATMENT ON SYSTOLIC AND DIASTOLIC BLOOD PRESSURE OVER TIME.

131.6/73.3

132.5/74.4
PRIMARY COMPOSITE END POINT
HAZARD RATIOS FOR THE PRIMARY OUTCOME AND THE INDIVIDUAL COMPONENTS.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite of death from cardiovascular causes and cardiovascular events</td>
<td>0.80 (0.72–0.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>0.80 (0.62–1.03)</td>
<td>0.08</td>
</tr>
<tr>
<td>Myocardial infarction (fatal or nonfatal)</td>
<td>0.78 (0.62–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>Stroke (fatal or nonfatal)</td>
<td>0.84 (0.65–1.08)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hospitalization for unstable angina</td>
<td>0.75 (0.50–1.10)</td>
<td>0.14</td>
</tr>
<tr>
<td>Coronary revascularization procedure</td>
<td>0.86 (0.74–1.00)</td>
<td>0.05</td>
</tr>
<tr>
<td>Resuscitation after sudden cardiac arrest</td>
<td>1.75 (0.73–4.17)</td>
<td>0.20</td>
</tr>
</tbody>
</table>
APPROACH TO REFRACTORY HYPERTENSION.

- Among adults taking antihypertensive medication in US:
- 53.4% had BP above the treatment goal according to the 2017 ACC/AHA guideline and are recommended more intensive antihypertensive treatment.
AGE-ADJUSTED TRENDS IN HYPERTENSION AND CONTROLLED HYPERTENSION AMONG ADULTS AGED 18 AND OVER: UNITED STATES, 1999–2016
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

*Significant increasing trend for 1999–2010, p < 0.001.
NOTES: Hypertension estimates are age adjusted by the direct method to the 2000 U.S. Census population using age groups 18–39, 40–59, and 60 and over. Estimates of controlled hypertension are age adjusted by the direct method using computed weights based on the subpopulation of persons with hypertension in the 2007–2008 National Health and Nutrition Examination Survey, using age groups 18–39, 40–59, and 60 and over. Access data table for Figure 5 at: https://www.cdc.gov/nchs/data/databriefs/db289_table.pdf.5
RESISTANT HYPERTENSION: DIAGNOSIS, EVALUATION, AND TREATMENT

RESISTANT HYPERTENSION

Confirm treatment resistance
Office SBP/DBP ≥130/80 mm Hg
and
Patient prescribed ≥3 antihypertensive medications at optimal doses, including a diuretic, if possible
or
Office SBP/DBP <130/80 mm Hg but patient requires ≥4 antihypertensive medications

Exclude pseudoresistance
Ensure accurate office BP measurements
Assess for nonadherence with prescribed regimen
Obtain home, work, or ambulatory BP readings to exclude white coat effect

Identify and reverse contributing lifestyle factors

Discontinue or minimize interfering substances

Screen for secondary causes of hypertension

Pharmacological treatment
Maximize diuretic therapy
Add a mineralocorticoid receptor antagonist
Add other agents with different mechanisms of actions
Use loop diuretics in patients with CKD
and/or patients receiving potent vasodilators (e.g., minoxidil)

Refer to specialist

BP indicates blood pressure; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; NSAIDs, nonsteroidal anti-inflammatory drugs; and SBP, systolic blood pressure.

Adapted with permission from Calhoun et al.
SCREENING FOR SECONDARY HYPERTENSION

New-onset or uncontrolled hypertension in adults

Conditions
- Drug-resistant/induced hypertension
- Abrupt onset of hypertension
- Onset of hypertension at <30 y
- Exacerbation of previously controlled hypertension
- Disproportionate TOD for degree of hypertension
- Accelerated/malignant hypertension
- Onset of diastolic hypertension in older adults (age ≥65 y)
- Unprovoked or excessive hypokalemia

Yes

Screen for secondary hypertension (Class I) (see Table 13)

Positive screening test

Yes

Refer to clinician with specific expertise (Class IIb)

No

Screening not indicated (No Benefit)

No

Yes

Referral not necessary (No Benefit)

Colors correspond to Class of Recommendation in Table 1.
TOD indicates target organ damage (e.g., cerebrovascular disease, hypertensive retinopathy, left ventricular hypertrophy, left ventricular dysfunction, heart failure, coronary artery disease, chronic kidney disease, albuminuria, peripheral artery disease).
HYDROCHLOROTHIAZIDE AS THE DIURETIC OF CHOICE FOR HYPERTENSION: IS IT TIME TO KICK THE HABIT?

VISIT-TO-VISIT MEAN OFFICE SBP
Diuretics for Hypertension: Hydrochlorothiazide or Chlorthalidone?

- Chlorthalidone has a longer duration of action and a longer half-life than hydrochlorothiazide.
- Chlorthalidone may be more potent than hydrochlorothiazide, but can be associated with more metabolic adverse effects.
- No study has conclusively shown either drug to be better in preventing adverse clinical outcomes.
- These differences should be considered when making choices about thiazide diuretic therapy for hypertension.
SPIRONOLACTONE FOR RESISTANT HYPERTENSION—HARD TO RESIST?

• Spironolactone is recommended as fourth-line therapy for resistant hypertension.
• PATHWAY-2 trial
• Spironolactone Versus Clonidine as a Fourth-Drug Therapy for Resistant Hypertension: The ReHOT Randomized Study (Resistant Hypertension Optimal Treatment)
**Trial Profile**

436 Screened

- 88 excluded
- 13 did not take study drug*

335 Randomized

- 21 no follow-up for any drug

314 with any follow-up (ITT analysis)

- 285 for spironolactone
- 282 for doxazosin
- 285 for bisoprolol
- 274 for placebo
- 230 completed all treatment cycles

---

*Randomised but instructed not to take any study drug after the result of directly observed therapy. Participants with any follow-up were included in the intent-to-treat analysis and the full analysis dataset consisted of all available data for these participants. Per-protocol analyses included participants who completed all follow-up visits without major deviation from the protocol. ITT=intention to treat.
Home Systolic And Diastolic Blood Pressures Comparing Spironolactone With Each Of The Other Cycles

- Systolic Blood Pressure
  - Baseline (n=314): 148 mm Hg
  - Placebo (n=274): 142 mm Hg
  - Spironolactone 25-50 mg: 12.8 mm Hg
  - Doxazosin 4-8 mg: 8.7 mm Hg
  - Bisoprolol 5-10 mg: 8.3 mm Hg

- Diastolic Blood Pressure
  - Baseline (n=314): 86 mm Hg
  - Placebo (n=274): 82 mm Hg
  - Spironolactone 25-50 mg: 12.8 mm Hg
  - Doxazosin 4-8 mg: 8.7 mm Hg
  - Bisoprolol 5-10 mg: 8.3 mm Hg

Significance:
- Baseline vs Placebo: p<0.0001
- Spironolactone vs Placebo: p<0.0001
RESISTANT HYPERTENSION OPTIMAL TREATMENT – REHOT

1893 patients assessed for eligibility

- 296 ineligible

1597 enrolled

1410 non-resistant:
- 1144 controlled with 3 drugs (good adherence)
- 215 controlled with 3 drugs (without good adherence)
- 51 uncontrolled but no good adherence

187 randomized

95 assigned to spironolactone
- 11 discontinued study
  - 2 external medical decision
  - 3 withdrew consent
  - 0 serious adverse events
  - 3 lost follow-up
  - 3 others

84 included in the modified intention-to-treat analysis

56 included in the per-protocol analysis

92 assigned to clonidine
- 14 discontinued study
  - 2 external medical decision
  - 2 withdrew consent
  - 1 serious adverse events
  - 5 lost follow-up
  - 4 others

78 included in the modified intention-to-treat analysis

57 included in the per-protocol analysis
ABPM DATA IN PATIENTS RANDOMIZED TO SPIRONOLACTONE OR CLONIDINE TREATMENT.
OFFICE BLOOD PRESSURE DATA IN PATIENTS RANDOMIZED TO SPIRONOLACTONE OR CLONIDINE TREATMENT
<table>
<thead>
<tr>
<th>End Point</th>
<th>Spironolactone (n=84)</th>
<th>Clonidine (n=78)</th>
<th>Relative Risk</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end point</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office BP and 24-h ABPM control, %</td>
<td>20.5</td>
<td>20.8</td>
<td>1.01 (0.55 to 1.88)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Secondary end points</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Office blood pressure &lt;140/90 mm Hg, %</td>
<td>33.3</td>
<td>29.9</td>
<td>0.9 (0.56 to 1.43)</td>
<td>0.771</td>
</tr>
<tr>
<td>24-h ABPM &lt;130/80 mm Hg, %</td>
<td>44</td>
<td>46.2</td>
<td>1.05 (0.75 to 1.47)</td>
<td>0.911</td>
</tr>
<tr>
<td>Office BP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>140.1±18.8</td>
<td>138±19</td>
<td>-2.08 (-7.95 to 3.8)</td>
<td>0.486*</td>
</tr>
<tr>
<td>Diastolic</td>
<td>85.9±11.1</td>
<td>85±13.2</td>
<td>-0.91 (-4.71 to 2.89)</td>
<td>0.635*</td>
</tr>
<tr>
<td>ABPM, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-h systolic</td>
<td>131.3±12.8</td>
<td>133.9±13.8</td>
<td>2.68 (-1.55 to 6.9)</td>
<td>0.212*</td>
</tr>
<tr>
<td>24-h diastolic</td>
<td>80.4±10.1</td>
<td>81.4±9.9</td>
<td>1 (-2.17 to 4.18)</td>
<td>0.533*</td>
</tr>
<tr>
<td>Daytime systolic</td>
<td>133.8±12.7</td>
<td>136.1±13.6</td>
<td>2.32 (-1.87 to 6.51)</td>
<td>0.275*</td>
</tr>
<tr>
<td>Daytime diastolic</td>
<td>83.1±10.3</td>
<td>83.9±10.3</td>
<td>0.91 (-2.35 to 4.17)</td>
<td>0.583*</td>
</tr>
<tr>
<td>Night-time systolic</td>
<td>125.9±15.2</td>
<td>128.4±17.1</td>
<td>2.52 (-2.62 to 7.66)</td>
<td>0.334*</td>
</tr>
<tr>
<td>Night-time diastolic</td>
<td>74.1±10.8</td>
<td>75.3±11</td>
<td>1.17 (-2.29 to 4.63)</td>
<td>0.505*</td>
</tr>
</tbody>
</table>

ABPM indicates ambulatory blood pressure monitoring; and BP, blood pressure.

*Mean difference (spironolactone vs clonidine).
DEVICE-BASED HYPERTENSION TREATMENT

• Renal Nerve Denervation

• Baroreflex Activation Therapy (Bat)/Carotid Baroreceptor Stimulation

• Central Arteriovenous Anastomosis/Creation Of An Arteriovenous Fistula
In summary, device-based therapy for hypertension is a fast-moving field. Further sham-controlled studies are needed before device-based therapies can be recommended for the routine treatment of hypertension outside of the framework of clinical trials.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

\(^{367,368}\)
ROLE OF AMBULATORY BLOOD PRESSURE MONITORING

• Can identify white-coat and masked hypertension
• Night-time readings/Dipping status
• Measurement in real-life settings
• Additional prognostic BP phenotypes and BP variability
• Consistently shown to have a closer relationship with morbid or fatal events, and is a more sensitive risk predictor than office BP of CV outcomes.
RELATIONSHIP BETWEEN OFFICE BP OR 24-HOUR AVERAGE SYSTOLIC BP WITH CARDIOVASCULAR EVENTS OR MORTALITY IN 3 STUDIES
CUMULATIVE INCIDENCE OF CARDIOVASCULAR EVENTS

Cumulative Incidence of Cardiovascular Events, %

Years of follow-up

Reverse Dippers

Non dippers

Dippers

Extreme Dippers

Clinical Value of Ambulatory Blood Pressure, Volume: 116, Issue: 6, Pages: 1034-1045, DOI: (10.1161/CIRCRESAHA.116.303755)
Increase in CV death for every 10 mm Hg rise in SBP

Probability of microalbuminuria during a 2-year follow-up in DM-1
CORRESPONDING VALUES OF SBP/DBP FOR CLINIC, HBPM, DAYTIME, NIGHTTIME, AND 24-HOUR ABPM MEASUREMENTS

<table>
<thead>
<tr>
<th>Clinic</th>
<th>HBPM</th>
<th>Daytime ABPM</th>
<th>Nighttime ABPM</th>
<th>24-Hour ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>120/80</td>
<td>120/80</td>
<td>100/65</td>
<td>115/75</td>
</tr>
<tr>
<td>130/80</td>
<td>130/80</td>
<td>130/80</td>
<td>110/65</td>
<td><strong>125/75</strong></td>
</tr>
<tr>
<td>140/90</td>
<td>135/85</td>
<td>135/85</td>
<td>120/70</td>
<td><strong>130/80</strong></td>
</tr>
<tr>
<td>160/100</td>
<td>145/90</td>
<td>145/90</td>
<td>140/85</td>
<td>145/90</td>
</tr>
</tbody>
</table>

ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; HBPM, home blood pressure monitoring; and SBP, systolic blood pressure.
The prevalence of WCH varies widely. In the PAMELA population, prevalence ranged from 9% - 12%, respectively and can be up to 30-40% in hypertensives.

WCH is by no means clinically innocent because of its frequent association with metabolic abnormalities, subclinical organ damage, and a risk of CV events that, although less than in sustained hypertensives, is higher than that of truly normotensive individuals.

In 2002, Pickering et al first proposed the concept of masked hypertension. Since this condition is “masked” for physicians & patients, such patients gradually develop TOD.

Prevalence 9% in SHEAF study and 15% in International database.

The risk of CVD events in masked hypertension is 1.5- to 3-fold increased compared with normotensive or well-controlled BP cases, and the risk is comparable to the risk of sustained hypertension.
DETECTION OF WHITE COAT HYPERTENSION OR MASKED HYPERTENSION IN PATIENTS NOT ON DRUG THERAPY

**Office BP:** ≥130/80 mm Hg but <160/100 mm Hg after 3 mo trial of lifestyle modification and suspected white coat hypertension

- **Daytime ABPM or HBPM**
  - BP <130/80 mm Hg

**Yes**
- **White Coat Hypertension**
  - Lifestyle modification
  - Annual ABPM or HBPM to detect progression (Class IIa)

**No**
- Continue lifestyle modification
- **Annual ABPM or HBPM**

**Office BP:** 120–129/<80 mm Hg after 3 mo trial of lifestyle modification and suspected masked hypertension

- **Daytime ABPM or HBPM**
  - BP ≥130/80 mm Hg

**Yes**
- **Masked Hypertension**
  - Continue lifestyle modification and start antihypertensive drug therapy (Class IIa)

**Elevated BP**
- Lifestyle modification
- Annual ABPM or ABPM to detect masked hypertension or progression (Class IIa)

**No**
- **Hypertension**
  - Continue lifestyle modification and start antihypertensive drug therapy (Class IIa)
DETECTION OF WHITE COAT EFFECT OR MASKED UNCONTROLLED HYPERTENSION IN PATIENTS ON DRUG THERAPY

Detection of white coat effect or masked uncontrolled hypertension in patients on drug therapy

Office BP at goal

Yes

Increased CVD risk or target organ damage

Yes

Screen for masked uncontrolled hypertension with HBPM (Class IIb)

HBPM BP above goal

Yes

ABPM BP above goal

Yes

Masked uncontrolled hypertension: Intensify therapy (Class IIb)

No

Continue current therapy

No

Screening not necessary (No Benefit)

Screen for white coat effect with HBPM (Class IIb)

HBPM BP above goal

Yes

White coat effect: Confirm with ABPMM (Class IIa)

No

Continue titrating therapy

No

Office BP ≥5–10 mm Hg above goal on ≥3 agents

Screening not necessary (No Benefit)
HYPERTENSIVE EMERGENCY & URGENCY

• Hypertensive crisis is an abrupt increase in BP > 180 / 120 mmHg. Based on the presence or absence of end-organ damage, it is classified as hypertensive emergency or urgency.

• Despite the differences, 4% of all inpatients were ordered a 1-time IV antihypertensive for HTN urgency. Guidelines recommend managing HTN urgency with oral agents, gradually lowering BP.

• HTN emergency, on the other hand, requires immediate Hospitalization.

• A retrospective cohort study of over 58 000 patients in the office with HTN urgency, showed no difference in the rate of major adverse cardiovascular events in those patients referred to the ER vs treated in the ambulatory setting.

• While a less aggressive approach to treating HTN urgency appears safe, aggressive BP lowering with IV medications can lead to hypotension, stroke, and organ injury.
Diagnosis and Management of a Hypertensive Crisis

SBP >180 mm Hg and/or DBP >120 mm Hg

Target organ damage new/progressive/worsening

Hypertensive emergency

Admit to ICU (Class I)

Markedly elevated BP

Reinstitute/intensify oral antihypertensive drug therapy and arrange follow-up

Conditions:
- Aortic dissection
- Severe preeclampsia or eclampsia
- Pheochromocytoma crisis

Reduce SBP to <140 mm Hg during first h* and to <120 mm Hg in aortic dissection† (Class I)

Reduce BP by max 25% over first h†, then to 160/100–110 mm Hg over next 2–6 h, then to normal over next 24–48 h (Class I)

Colors correspond to Class of Recommendation in Table 1.
*Use drug(s) specified in Table 19.
†If other comorbidities are present, select a drug specified in Table 20.
BP indicates blood pressure; DBP, diastolic blood pressure; ICU, intensive care unit; and SBP, systolic blood pressure.
Acute (<6 h from symptom onset) spontaneous ICH

- SBP 150–220 mm Hg
  - SBP lowering to <140 mm Hg (Class III:Harm)

- SBP >220 mm Hg
  - SBP lowering with continuous IV infusion and close BP monitoring (Class IIa)
MANAGEMENT OF HYPERTENSION IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Acute (<72 h from symptom onset) ischemic stroke and elevated BP

Patient qualifies for IV thrombolysis therapy

Yes

Lower SBP to <185 mm Hg and DBP <110 mm Hg before initiation of IV thrombolysis (Class I)

And

Maintain BP <180/105 mm Hg for first 24 h after IV thrombosis (Class I)

No

BP ≤220/110 mm Hg

Initiating or reinitiating treatment of hypertension within the first 48-72 hours after an acute ischemic stroke is ineffective to prevent death or dependency (Class III: No Benefit)

BP >220/110 mm Hg

Lower BP 15% during first 24 h (Class IIb)

For preexisting hypertension, reinitiate antihypertensive drugs after neurological stability (Class IIa)

BP indicates blood pressure; DBP, diastolic blood pressure; IV, intravenous; and SBP, systolic blood pressure.
<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>PREFERRED DRUGS</th>
<th>PREFERRED INDICATION</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCB—dihydropyridines</td>
<td>Nicardipine</td>
<td>Acute coronary syndromes, AKI, Eclampsia, perioperative hypertension</td>
<td>Contraindicated in advanced aortic stenosis</td>
</tr>
<tr>
<td></td>
<td>Clevidipine</td>
<td>Acute pulmonary edema, AKI, perioperative hypertension</td>
<td>Contraindicated in patients with soybean, soy product, egg, and egg product allergy and in patients with defective lipid metabolism</td>
</tr>
<tr>
<td>Vasodilators—Nitric-oxide</td>
<td>Sodium nitroprusside</td>
<td>Acute pulmonary edema</td>
<td>Cyanide toxicity with prolonged use can result in irreversible neurological changes and cardiac arrest. Use only in patients with acute coronary syndrome and/or acute pulmonary edema. Do not use in volume-depleted patients.</td>
</tr>
<tr>
<td>dependent</td>
<td>Nitroglycerin</td>
<td>Acute coronary syndromes &amp; pulmonary edema, perioperative hypertension</td>
<td></td>
</tr>
<tr>
<td>Vasodilators—direct</td>
<td>Hydralazine</td>
<td>Eclampsia or preeclampsia</td>
<td>Unpredictability of response and prolonged duration of action do not make hydralazine a desirable first-line agent for acute treatment in most patients.</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>Enalaprilat</td>
<td>Mainly useful in hypertensive emergencies associated with high plasma renin activity</td>
<td>Contraindicated in pregnancy and should not be used in acute MI or bilateral renal artery stenosis</td>
</tr>
<tr>
<td>DRUG CLASS</td>
<td>PREFERRED DRUGS</td>
<td>PREFERRED INDICATION</td>
<td>REMARKS</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------------</td>
<td>---------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Adrenergic blockers—combined alpha(_1) and nonselective beta receptor antagonist</td>
<td><strong>Labetalol</strong></td>
<td>Acute aortic dissection&lt;br&gt;Acute coronary syndromes</td>
<td>Contraindicated in reactive airways disease or chronic obstructive pulmonary disease. Especially useful in hyperadrenergic syndromes</td>
</tr>
<tr>
<td>Adrenergic blockers—nonselective alpha receptor antagonist</td>
<td><strong>Phentolamine</strong></td>
<td>Pheochromocytoma&lt;br&gt;post-carotid endarterectomy status</td>
<td>interactions between monamine oxidase inhibitors and other drugs or food, cocaine toxicity, amphetamine overdose, or clonidine withdrawal</td>
</tr>
<tr>
<td>Adrenergic blockers—beta(_1) receptor selective antagonist</td>
<td><strong>Esmolol</strong></td>
<td>Acute aortic dissection&lt;br&gt;Acute coronary syndromes&lt;br&gt;perioperative hypertension</td>
<td>Contraindicated in patients with concurrent beta-blocker therapy, bradycardia, or decompensated HF. Monitor for bradycardia.</td>
</tr>
<tr>
<td>Dopamine(_1)-receptor selective agonist</td>
<td><strong>Fenoldopam</strong></td>
<td>Acute renal failure</td>
<td>Contraindicated in patients at risk of increased intraocular pressure (glaucoma) or intracranial pressure and those with sulfite allergy.</td>
</tr>
</tbody>
</table>
WHAT IS THE GOAL BP? DOWN THE RABBIT HOLE
<table>
<thead>
<tr>
<th>STUDY</th>
<th>DESIGN</th>
<th>CRITERIA</th>
<th>RESULTS</th>
<th>CONCLUSIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic HTN in the Elderly Program (SHEP), 2000</td>
<td>4736 older Pts randomized to chlorthalidone (atenolol and reserpine if necessary to achieve goal SBP &lt; 160 mm Hg) or placebo.</td>
<td>SBP ≥160 mm Hg and DBP ≤90 mm Hg; age ≥60 years</td>
<td>36% reduction in fatal and nonfatal stroke, 25% reduction in CAD, 32% reduction in all CV disease, 13% reduction in total mortality, reduction in TIAs and CHF.</td>
<td>Indicated treating isolated systolic HTN in older patients with diuretics reduces stroke and cardiac endpoints.</td>
</tr>
<tr>
<td>Hypertension Optimization Treatment Study (HOT), 1998</td>
<td>18,790 patients randomized to 3 different target DBP: ≤80, ≤85, or ≤90. Felodipine plus other agents to achieve DBP goal.</td>
<td>DBP 100–115 mm Hg, age 50–80 years</td>
<td>Lowest incidence of major CV events at average DBP of 82.6 mm Hg; lowest risk of CV mortality at 86.5 mm Hg; further reductions did not result in further benefit but were not harmful.</td>
<td>Indicated optimal DBP not established but worthwhile to maintain DBP &lt;90 mm Hg.</td>
</tr>
<tr>
<td>STUDY</td>
<td>DESIGN</td>
<td>CRITERIA</td>
<td>RESULTS</td>
<td>CONCLUSION</td>
</tr>
<tr>
<td>------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Modification of Diet in Renal Disease Study Group (MDRD), 1994</td>
<td>840 CKD subjects randomized to usual BP (MAP 107 mm Hg) or low BP (MAP 92 mm Hg). ACEI with or without diuretic encouraged as first-line agent</td>
<td>585 patients with CKD stage III/IV and 255 subjects with CKD stage IV/V</td>
<td>No benefit of low BP-no difference in death or decline in renal function or ESRD. Except proteinuric pts had a significantly slower rate of decline in the GFR.</td>
<td>No benefit in pts without proteinuria but may benefit proteinuric pts.</td>
</tr>
<tr>
<td>African American Study of Kidney Disease and Hypertension Trial (AASK), 2010</td>
<td>1094 black patients randomized to low (MAP &lt;92 mm Hg) or usual (MAP 102–107 mm Hg. 128/78 vs 141/85. )</td>
<td>Hypertensive nephrosclerosis, excluded diabetics</td>
<td>No difference in average rate of change in GFR.</td>
<td>No benefit in pts without proteinuria but may benefit proteinuric pts.</td>
</tr>
</tbody>
</table>
JNC-7 Treatment Algorithm

**Lifestyle Modifications**

Not at Goal Blood Pressure (<140/90 mmHg)
(<130/80 mmHg for patients with diabetes or chronic kidney disease)

See Strategies for Improving Adherence to Therapy

**Initial Drug Choices**

Without Compelling Indications

- **Stage 1 Hypertension**
  - SBP 140-159 or DBP 90-99 mmHg
  - Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

With Compelling Indications

- **Stage 2 Hypertension**
  - SBP ≥160 or DBP ≥100 mmHg
  - 2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB).

- **Drug(s) for the compelling indications**
  - See Compelling Indications for Individual Drug Classes
  - Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

**Not at Goal Blood Pressure**

Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.

See Strategies for Improving Adherence to Therapy

<table>
<thead>
<tr>
<th>STUDY</th>
<th>DESIGN</th>
<th>CRITERIA</th>
<th>RESULTS</th>
<th>CONCLUSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>REIN-2</td>
<td>338 with ramipril: conventional (diastolic</td>
<td>Non-diabetic proteinuric nephropathies</td>
<td>Over a median follow-up of 19 months (23%) patients assigned to intensified BP and (20%) conventional progressed to ESRD p=0.99.</td>
<td>no additional benefit from further blood-pressure reduction by felodipine could be shown.</td>
</tr>
<tr>
<td>2005</td>
<td>&lt;90 mm Hg; n=169) or intensified (systolic/diastolic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;130/80 mm Hg; n=169)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAMELOT</td>
<td>1991 CAD pts : compare the effects of amloidine or enalapril vs placebo on cardiovascular events in patients with CAD. Baseline BP averaged 129/78</td>
<td>Angiographically documented CAD and diastolic blood pressure &lt;100 mm Hg</td>
<td>CV events occurred in 151 (23.1%) placebo-treated pts, in 110 (16.6%) amloidine-pts [P = .003]), and in 136 (20.2%) enalapril-treated pts [P = .16]</td>
<td>Administration of amloidine to CAD pts with normal BP reduced CV events. Directionally similar, but smaller and nonsignificant, treatment effects were observed with enalapril.</td>
</tr>
<tr>
<td>2004</td>
<td></td>
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</tr>
</tbody>
</table>
Hypertension In The Very Elderly Trial

HYVET-2008

4761 pts-Age > 80-yrs

Median follow-up -1.8 years
Fatal or non fatal stroke - 30%

Death from CV cause - 23%

Death from any cause - 21% REDUCTION

Death from CVA - 39%

Heart Failure - 74% Reduction
Action To Control Cardiovascular Risk In Diabetes-Blood Pressure

ACCORD 2010

Age-62-yrs

Median follow-up 4.7 years
Primary Outcome

Non Fatal Stroke

NNT 476

Nonfatal MI

Death from CV cause

No. at Risk
Intensive Standard
2362 2273 2182 2117 1770 1080 298 175 80
2371 2274 2196 2120 1793 1127 358 195 108

No. at Risk
Intensive Standard
2362 2291 2223 2174 1841 1128 313 186 88
2371 2287 2235 2186 1879 1196 382 215 114

No. at Risk
Intensive Standard
2362 2278 2190 2133 1787 1087 299 177 82
2371 2278 2208 2141 1818 1145 365 201 112

No. at Risk
Intensive Standard
2362 2304 2252 2201 1870 1143 317 188 91
2371 2313 2268 2218 1922 1220 393 221 118
Figure. 2014 Hypertension Guideline Management Algorithm

Adult aged ≥18 years with hypertension

Implement lifestyle interventions (continue throughout management).

Set blood pressure goal and initiate blood pressure lowering medication based on age, diabetes, and chronic kidney disease (CKD).

**General population (no diabetes or CKD)**

- **Age ≥60 years**
  - Blood pressure goal
    - SBP < 150 mm Hg
    - DBP < 90 mm Hg
  - Nonblack
    - Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.
  - Black
    - Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.

- **Age <60 years**
  - Blood pressure goal
    - SBP < 140 mm Hg
    - DBP < 90 mm Hg
  - All ages
    - All races
      - Initiate ACEI or ARB, alone or in combination with other drug class.

**Diabetes or CKD present**

- **All ages**
  - Diabetes present
    - No CKD
      - Blood pressure goal
        - SBP < 140 mm Hg
        - DBP < 90 mm Hg
        - Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.
  - CKD present with or without diabetes
    - Blood pressure goal
      - SBP < 140 mm Hg
      - DBP < 90 mm Hg
      - Initiate ACEI or ARB, alone or in combination with other drug class.
Exclusion Criteria

DM, Stroke
Not on disease-appropriate antihypertensives (e.g., beta blocker and recent MI)
Secondary cause of hypertension
Proteinuria ≥1 g/day, PKD
Glomerulonephritis
eGFR < 30 mL/min/1.73 m²
CV event, procedure, or UA hospitalization in prior 3 months
Symptomatic HF in prior 6 mo, LVEF < 35%, Life-limiting illness
Organ transplant
Unintentional weight loss > 10% in prior 6 months
Pregnancy

5331 Were ineligible or declined to participate
34 Were < 50 yr of age
352 Had low systolic blood pressure at 1 min after standing

2284 Were taking too many medications or had systolic blood pressure that was out of range
718 Were not at increased cardiovascular risk
703 Had miscellaneous reasons
587 Did not give consent
653 Did not complete screening

4678 TO INTENSIVE

224 Discontinued intervention
111 Were lost to follow-up
154 Withdraw consent

4683 TO STANDARD

242 Discontinued intervention
134 Were lost to follow-up
121 Withdraw consent

4678 Were included in the analysis

14,692

9361

4678 TO INTENSIVE

4683 TO STANDARD

4683 TO STANDARD

4683 TO STANDARD
SYSTOLIC BLOOD PRESSURE IN THE TWO TREATMENT GROUPS OVER THE COURSE OF THE TRIAL.

At randomization start with 2 or 3 drugs i.e. Thiazide/ACE-I or ARB/CCB

Age 67-yrs

Median follow-up of 3.26 years

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<thead>
<tr>
<th>Years</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
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<td>136/76</td>
<td>121/69</td>
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**No. with Data**

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<td></td>
<td>3115</td>
<td>3204</td>
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<td></td>
<td>1974</td>
<td>2035</td>
</tr>
<tr>
<td></td>
<td>1000</td>
<td>1048</td>
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<td>274</td>
<td>286</td>
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**Mean No. of Medications**

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<th>Standard treatment</th>
<th>Intensive treatment</th>
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</thead>
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<td>1.9</td>
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<tr>
<td></td>
<td>1.8</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>1.9</td>
<td>3.0</td>
</tr>
</tbody>
</table>
A Primary Outcome

5.2% vs. 6.8%
P<0.001; NNT 63

B Death from Any Cause

3.3% vs 4.5%
(P=0.003; NNT 83)
## OUTCOMES

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>(N = 4678)</td>
<td>(N = 4683)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome†</td>
<td>243 (5.2)</td>
<td>319 (6.8)</td>
<td>0.75 (0.64–0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>(N = 1330)</td>
<td>(N = 1316)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>116 (2.5)</td>
<td>0.83 (0.64–1.09)</td>
<td>0.19</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>40 (0.9)</td>
<td>1.00 (0.64–1.55)</td>
<td>0.99</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>70 (1.5)</td>
<td>0.89 (0.63–1.25)</td>
<td>0.50</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.62 (0.45–0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.57 (0.38–0.85)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>0.73 (0.60–0.90)</td>
<td>0.003</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>423 (9.0)</td>
<td>0.78 (0.67–0.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Participants with CKD at baseline</td>
<td>(N = 1330)</td>
<td>(N = 1316)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite renal outcome‡</td>
<td>14 (1.1)</td>
<td>15 (1.1)</td>
<td>0.36</td>
<td>0.89</td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR§</td>
<td>10 (0.8)</td>
<td>11 (0.8)</td>
<td>0.26</td>
<td>0.87</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>6 (0.5)</td>
<td>10 (0.8)</td>
<td>0.24</td>
<td>0.57</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>49/526 (9.3)</td>
<td>59/500 (11.8)</td>
<td>3.90</td>
<td>0.72</td>
</tr>
<tr>
<td>Participants without CKD at baseline</td>
<td>(N = 3332)</td>
<td>(N = 3345)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30% reduction in estimated GFR to &lt;60 ml/min/1.73 m²§</td>
<td>127 (3.8)</td>
<td>37 (1.1)</td>
<td>0.35</td>
<td>3.49</td>
</tr>
<tr>
<td>Incident albuminuria¶</td>
<td>110/1769 (6.2)</td>
<td>135/1831 (7.4)</td>
<td>2.41</td>
<td>0.81</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, and CKD chronic kidney disease.
† The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
‡ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
§ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
¶ Incident albuminuria was defined by a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
|| No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.
<table>
<thead>
<tr>
<th>Clinical Condition(s)</th>
<th>BP Threshold, mm Hg</th>
<th>BP Goal, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical CVD or 10-year ASCVD risk ≥10%</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>No clinical CVD and 10-year ASCVD risk &lt;10%</td>
<td>≥140/90</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)</td>
<td>≥130 (SBP)</td>
<td>&lt;130 (SBP)</td>
</tr>
<tr>
<td><strong>Specific comorbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Chronic kidney disease after renal transplantation</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Heart failure</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Stable ischemic heart disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Secondary stroke prevention</td>
<td>≥140/90</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Secondary stroke prevention (lacunar)</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>≥130/80</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>----------------------</td>
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<td>-----------------------------------</td>
</tr>
<tr>
<td><strong>CKD No DM No proteinuria</strong></td>
<td>sBP &lt;140 to 130 if tolerated dBP &lt; 80 to 70</td>
<td>140/90 sBP &lt; 120 if high CV risk*</td>
</tr>
<tr>
<td><strong>CKD No DM Proteinuria</strong></td>
<td>sBP &lt;140 to 130 if tolerated dBP &lt; 80 to 70</td>
<td>140/90 sBP &lt; 120 if high CV risk*</td>
</tr>
<tr>
<td><strong>CKD DM No proteinuria</strong></td>
<td>sBP 130 or lower if tolerated NOT &lt; 120 dBP &lt; 80 to 70</td>
<td>130/80</td>
</tr>
<tr>
<td><strong>CKD DM Proteinuria</strong></td>
<td>sBP 130 or lower if tolerated NOT &lt; 120 dBP &lt; 80 to 70</td>
<td>130/80</td>
</tr>
<tr>
<td><strong>Renal transplant</strong></td>
<td>No separate recommendation</td>
<td>140/90 sBP &lt; 120 if high CV risk*</td>
</tr>
<tr>
<td><strong>Elderly</strong></td>
<td>Age &gt; 65 sBP &lt;140 to 130 if tolerated dBP &lt; 80 to 70</td>
<td>140/90 sBP &lt; 120 if high CV risk*</td>
</tr>
</tbody>
</table>

**Notes:**
Proteinuria = 30 mg/day for KDIGO; > 300 mg/day for ACC/AHA
*See details at guidelines.hypertension.ca for definitions/cautionary statements; eg CKD with GFR 20-60 qualifies as high CV risk.
TAKE HOME MESSAGE

• **Hypertension is a silent killer**. Globally, over 1 billion people have hypertension and will rise towards 1.5 billion by 2025.

• **Definition of hypertension per AHA 2017**: Office BP ≥130 / ≥80 mmHg, which is equivalent to a 24 h ABPM average of ≥125/75 mmHg, or a HBPM average ≥130/80 mmHg.

• **Emphasize cardiovascular risk assessment and detection of target organ damage**.

• **Stress the importance of lifestyle interventions**.

• **We need to do better on BP control**: as less than 50% of patients with treated hypertension achieve an SBP target of <140 mmHg.

• **Physician inertia and poor patient adherence**: major factors contributing to poor BP control.
TAKE HOME MESSAGE

• **The benefit of pharmacologic treatment for BP reduction** is related to atherosclerotic CVD (ASCVD) risk. If risk > 10%, a BP target of <130/80 mm Hg is recommended.

• **Initial first-line therapy for stage 1 hypertension**: thiazide diuretics, CCBs, and ACE inhibitors or ARBs.

• **Principles of drug therapy**: Chlorthalidone is the preferred diuretic, especially in resistant HTN. Loop diuretics are preferred in HF and CKD-4. Beta-blockers are not first-line therapy except in CAD and CHF. Spironolactone is preferred for resistant HTN.

• **How low should BP be lowered?** - A hotly debated topic. A key point is the balance of potential benefits vs. potential harm. The evidence strongly suggests that lowering office BP to <140/90 mmHg for all patient groups. There is also evidence to support targeting BP to 130 mmHg for most patients, if tolerated.

• **Special considerations in frail and elderly patients**: Biological rather than chronological age, & frailty and independence, are important determinants of the tolerability of and likely benefit from BP-lowering medications. It is important to note that even in the very old (i.e. >80 years), BP-lowering therapy reduces mortality, stroke, and HF.

• **Manage cardiovascular disease risk in hypertensive patients beyond BP**
END

THANK YOU

QUESTIONS ?