Hypertension
Matthew Parker, MD

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SESSION OBJECTIVES

• State the JNC-8 definition of hypertension and state the target of therapy in patients under age 60 without comorbid illness, patients with diabetes, patients with chronic kidney disease, and patients over age 60.

• Discuss initial lifestyle and specific pharmacologic therapy for hypertension.

• Recognize common reasons for failure of initial therapy and options for add-on therapy as well as indications for further evaluation of hypertension.
Hypertension in 2015

Matthew W Parker, MD, FACC
Hypertension: Scope of the Problem

Current Hypertension “Guidelines”: JNC 8, ACC/AHA, ESC

Resistant and Secondary Hypertension
1 in 3 Americans

70 million people with HTN
A SNAPSHOT: BLOOD PRESSURE IN THE U.S.
Make Control Your Goal

High blood pressure is a major risk factor for heart disease and stroke, the first and fourth leading causes of death for all Americans.

When your blood pressure is high:

- You are 4x more likely to die from a stroke
- You are 3x more likely to die from heart disease
- 69% of people who have a first heart attack...
- 77% of people who have a first stroke...
- 74% of people with chronic heart failure...

HAVE HIGH BLOOD PRESSURE

Annual estimated costs associated with high blood pressure:

$51 BILLION

$47.5 BILLION in direct medical expenses

millionhearts.hhs.gov/aboutdhs/blood_pressure.html

This infographic was developed by the Centers for Disease Control and Prevention's Division for Heart Disease and Stroke Prevention in support of achieving the Million Hearts® initiative goal to prevent 1 million heart attacks and strokes by 2017.
36 million Americans with Uncontrolled Hypertension
55M presents to your office to establish primary care. He feels well and has no complaints. He does not smoke. He drinks 1-2 alcoholic beverages per week. He tries to go to the gym 3 times a week. He takes no medicines and reports no chronic medical problems.
BP 148/88 mm Hg (R arm), 144/86 mm Hg (L arm)
P 76/min  RR 12/min  Temp 98.4

Weight 205 lbs  Height 5’11”  BMI 28  Waist circumference 40”

Physical Exam otherwise unremarkable
You recheck the blood pressure after he has been sitting with feet on the floor for 10 minutes. Right arm blood pressure is now 146/84 mm Hg

How would you characterize this man’s blood pressure?
A. Need to recheck in a month before deciding
B. Normal for age
C. Pre-hypertension
D. Stage 1 Hypertension
E. Grade 1 Hypertension
What IS the right answer?
National High Blood Pressure Education Program

JNC 7 Express
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

American Heart Association
American Stroke Association
Check. Change. Control.

National Heart Lung and Blood Institute
“Refocus our health education agenda on our mission of knowledge generation and synthesis by supporting and producing rigorous systematic reviews to inform practice guidelines” (Circulation 2013)

i.e., NHLBI will no longer produce clinical practice guidelines focused on risk factor management for cardiovascular disease
Enter the AHA, ACC, ESC, and CDC

An Effective Approach to High Blood Pressure Control

A Science Advisory From the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention

Alan S. Go, MD; Mary Ann Bauman, MD; Sallyann M. Coleman King, MD, MSc; Gregg C. Fonarow, MD, FAHA, FACC; Willie Lawrence, MD, FAHA, FACC; Kim A. Williams, MD, FAHA, FACC; Eduardo Sanchez, MD, MPH
JNC-8 Went Rogue!
No sponsorship or endorsement – Just published in JAMA like any other review
9 RECOMMENDATIONS FOR TREATING HIGH BLOOD PRESSURE
Recommendation 1

In the general population aged ≥60 years, initiate pharmacologic treatment to lower blood pressure (BP) at systolic blood pressure (SBP) ≤150 mm Hg or diastolic blood pressure (DBP) ≤90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

(Strong Recommendation – Grade A)
Corollary

In the general population aged ≥60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg, <140 mm Hg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted.

(Expert Opinion – Grade E)
Treating High Blood Pressure is Good

High-quality evidence that treating high blood pressure reduces strokes, heart attacks, and heart failure

*Less evidence—mostly subgroup analyses—suggests that <140/80 is better than <150/90*

Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS
Recommendation 2

In the general population <60 years, initiate pharmacologic treatment to lower BP at DBP ≥ 90 mm Hg and treat to a goal DBP <90 mm Hg.

(For ages 30-59 years, Strong Recommendation – Grade A; For ages 18-29 years, Expert Opinion – Grade E)
Diastolic Hypertension Before Age 60

5 High-Quality Trials in people 30-65:
  HDFP, Hypertension-Stroke Cooperative, MRC, ANBP, and VA Cooperative
demonstrated lower rates of stroke, heart failure, and mortality when DBP >90 was treated

HOT randomized people to DBP <90, <85, <80 and found no statistically significant difference in primary or secondary outcomes
Recommendation 3

In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP ≥ 140 mm Hg and treat to a goal SBP <140 mm Hg.

(Expert Opinion – Grade E)
Systolic Hypertension Before Age 60

- No high-quality randomized controlled trials to discuss here

- In all of the DBP trials (Recommendation 2) those subjects reaching the DBP target were often SBP <140

- And the SBP 140 is easy to remember
Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.

(Expert Opinion – Grade E)
Chronic Kidney Disease

- eGFR or GFR <60ml/min or
- albuminuria >30 mg albumin/g creatinine

- AASK and MDRD used age-driven MAP targets and analyses of other trials did not prove that any target is better than 140/90
Recommendation 5

In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg and treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg.

(Expert Opinion – Grade E)
Don’t Diabetics Need Tighter BP Control?

In ACCORD-BP, control group was SBP 140 and intervention group was SBP 120... and no difference in primary or secondary endpoints
Recommendation 6

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).

(Moderate Recommendation – Grade B)
Thiazide-type diuretic

- chlorthalidone
- indapamide

Best at preventing HF

ACE-I

2nd Best at preventing HF

Wow—that’s it?

CCB

dihydropyridines:
*drugs that rhyme with -dipine*

ARB
Recommendation 7

In the general black population, including those with diabetes, initial anti-hypertensive treatment should include a thiazide-type diuretic or CCB.

(For general black population: Moderate Recommendation – Grade B; for black patients with diabetes: Weak Recommendation – Grade C)
ALLHAT

• Diuretics better than ACEI for preventing stroke, HF, and overall mortality in blacks

• CCB less effective for preventing HF but otherwise similar to the diuretic (ie, better than ACEI) in blacks

• Non-trivial: RR of stroke 1.51 (1.22-1.81) in blacks treated with ACEI
Recommendation 8

In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status.

(Moderate Recommendation – Grade B)
All About the Beans

• ACEI or ARB reduces kidney outcomes (proteinuria, dialysis), not cardiovascular outcomes

• What if you are black with CKD?
  – Use two drugs
Recommendation 9

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed.

(Expert Opinion – Grade E)
Whoa! Thought you could slip that by me?

1. Pick a goal for blood pressure
2. Start a drug
3. Recheck blood pressure in 2-4 weeks
4. Uptitrate and add drugs until target reached
5. Ask for help when 3 drugs don’t achieve goal
ACC/AHA/CDC:
The Pragmatic Approach

Systolic 140–159 or diastolic 90–99 (Stage 1 hypertension)
- Lifestyle modifications as a trial
- Consider adding thiazide

Recheck and review readings in 3 months*

Systolic >160 or diastolic >100 (Stage 2 hypertension)
Two drugs preferred:
- Lifestyle modifications and
- Thiazide and ACEI, ARB, or CCB
- Or consider ACEI and CCB

Recheck and review readings in 2–4 weeks*²
BP at goal?

- Thiazide for most patients or ACEI, ARB, CCB, or combo
- If currently on BP med(s), titrate and/or add drug from different class

Recheck and review readings in 2–4 weeks*²

BP at goal?

- Encourage self-monitoring and adherence to meds
- Advise patient to alert office if he/she notes BP elevation or side effects
- Continue office visits as clinically appropriate

No

- Optimize dosage(s) or add medications
- Address adherence, advise on self-monitoring, and request readings from home and other settings
- Consider secondary causes

Consider referral to HTN specialist

*Recheck interval should be based on patient’s risk of adverse outcomes

This algorithm should not be used to counter the treating healthcare provider’s best clinical judgment.
## Key Differences

<table>
<thead>
<tr>
<th>JNC-8</th>
<th>ACC/AHA/CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Separate considerations for age above/below age 60, black or nonblack, kidney disease</td>
<td>“One size fits all”</td>
</tr>
<tr>
<td>Start pharmacologic therapy for one BP reading</td>
<td>Stage 1 (SBP 140-159) trial of lifestyle modifications first</td>
</tr>
</tbody>
</table>
Common Ground

Blood pressure greater than 140/90 needs intervention, whether lifestyle or pharmacologic.

Diuretics, ACEI or ARB, and calcium channel blockers WORK and should be used liberally and often in combination.
What do the Europeans have to say?
2013 ESH/ESC Guidelines for Hypertension

<table>
<thead>
<tr>
<th>Other risk factors, asymptomatic organ damage or disease</th>
<th>Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High normal SBP 130–139 or DBP 85–89</td>
</tr>
<tr>
<td>No other RF</td>
<td>• No BP intervention</td>
</tr>
<tr>
<td>1–2 RF</td>
<td>• Lifestyle changes No BP intervention</td>
</tr>
<tr>
<td>≥3 RF</td>
<td>• Lifestyle changes No BP intervention</td>
</tr>
<tr>
<td>OD, CKD stage 3 or diabetes</td>
<td>• Lifestyle changes No BP intervention</td>
</tr>
<tr>
<td>Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs</td>
<td>• Lifestyle changes No BP intervention</td>
</tr>
</tbody>
</table>
# Lifestyle Interventions to Reduce Blood Pressure

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate Systolic BP Reduction, Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5–24.9 kg/m²)</td>
<td>5–20 mm Hg/10-kg weight loss&lt;sup&gt;160,514,515&lt;/sup&gt;</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8–14 mm Hg&lt;sup&gt;516,517&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride)</td>
<td>2–8 mm Hg&lt;sup&gt;160,516–518&lt;/sup&gt;</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 min/d, most days of the week)</td>
<td>4–9 mm Hg&lt;sup&gt;477,511,519&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks/d (1 oz or 30 mL ethanol [eg, 24-oz beer, 10-oz wine, or 3-oz 80-proof whiskey]) in most men and no more than 1 drink/d in women and lighter-weight persons</td>
<td>2–4 mm Hg&lt;sup&gt;478&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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**From this...**

![Fat Body](image1.png)

**...to this!**

![Fit Body](image2.png)

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**A little DASH will do you.**

The American Heart Association estimates that more than 82,100,000 people in the United States have at least one form of cardiovascular disease — and this number is still on the rise. It's time to take control of your health. Your first step? Put a little DASH in your life with Spirit of Women!

**DASH, or Dietary Approaches to Stop Hypertension, is a healthy lifestyle plan developed by the National Institutes of Health (NIH) to aid in lowering blood pressure and cholesterol levels without the need for medication. This invigorating program focuses on reducing and maintaining a healthy weight by:**

- Reducing sodium
- Regular exercise
- Smoking cessation
- Moderation of alcohol

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Case: Selecting a Second Agent

A 62F whom you recently diagnosed with hypertension presents for follow-up. At the last visit, her blood pressure was 168/92. You encouraged her to start an exercise routine and gave her a brochure on the DASH diet. You also started chlorthalidone 12.5 mg daily.

She shows you a log of blood pressure recordings taken at her neighborhood pharmacy weekly since her last visit. The range is between 146-160/80-90.
Blood pressure today in your office is 160/88.

Serum chemistries obtained since starting chlorthalidone are normal; K = 3.4 and Cr = 0.9.

Which of the following would you prescribe?
A. Increase chlorthalidone to 25 mg daily
B. Switch chlorthalidone to furosemide 20 mg daily
C. Switch chlorthalidone to amlodipine 10 mg daily
D. Add lisinopril 10 mg daily
E. Add labetolol 200 mg tid
Combination Therapy

Most patients with hypertension will need more than one drug.
Suggested Combinations

- Thiazide diuretics
- Angiotensin-receptor blockers
- Calcium antagonists
- ACE inhibitors
- Beta-blockers
- Other Antihypertensives
Case: Elderly HTN

An 84M you have been following for several years is seeing you in the office for his annual physical exam. He and his wife (age 82) live in assisted living and enjoy being around their extended family. His daughter is with him today and asks you if any of his medications can be stopped to prevent falls.
He currently takes **bimatoprost** and **timolol** eye drops for glaucoma, **simvastatin** for hypercholesterolemia, **glucosamine** and **naproxen** prn for osteoarthritis, **tamsulosin** for prostatism, **omeprazole** for GERD, **hydrochlorothiazide** and **atenolol** for blood pressure, low dose **aspirin**, and a daily **multivitamin**

He has no known drug allergies
You check his blood pressure:
- 162/88 while seated with feet supported
- 164/84 after standing for 2 minutes

What would you recommend for his blood pressure management?

A. Stop hydrochlorothiazide and atenolol
B. Add lisinopril
C. Replace atenolol with lisinopril
D. Replace hydrochlorothiazide with lisinopril
E. No changes
Blood Pressure and Age
Blood Pressure and Arterial Stiffness

A Normal

- Systolic BP
- Forward Traveling Wave
- Reflected Wave
- Pulse Pressure
- Diastolic BP

B Arterial Stiffness

- Systolic BP
- Augmentation

Diagram shows the comparison between normal blood pressure waveforms and those affected by arterial stiffness.
Hypertension in the Elderly

Age (years) | BP Nadirs
SBP  | DBP
---|---
<60 | 110 | 75
60-<70 | 115 | 75
70-<80 | 135 | 75
≥80 | 140 | 70

Hazard Ratio (adjusted)

Blood Pressure (mmHg)

- Diastolic
- Systolic
3845 patients over age 80 with SBP>160 mm Hg randomized to drug therapy (indapamide +/- perindopril) or placebo, titrated to SBP<150

Compared to placebo, 2 years of drug therapy:
- Decreased stroke by 30%
- Decreased heart failure by 64%
- Decreased heart attacks by 23%
- Decreased all-cause mortality by 21%
• Watch for orthostasis
  – Check blood pressure after 2-3 minutes of standing in octogenarians on blood pressure medications
• 150/90 is evidence-based target in octogenarians
Case: Resistant HTN

You are seeing a 56 year old woman with hypertension in follow-up. Her blood pressure is 162/94 today in your office.

Her current medications are **hydrochlorothiazide** 25 mg daily, **lisinopril** 40 mg daily, **nifedipine** sustained release 60 mg daily, and **sertraline** 50 mg daily
You suspect she has resistant hypertension.

Which of the following is the best next step?
A. Ambulatory blood pressure monitor
B. Measure plasma and urine metanephrines
C. Polysomnogram
D. Measure renin and aldosterone levels
E. Sodium restriction
Resistant Hypertension

JNC-7 defined as uncontrolled hypertension despite adequate doses of 3 meds including a diuretic

AHA defines it as uncontrolled hypertension with 3 meds or hypertension controlled only with a 4th med

NHANES estimates 13-21% of people with HTN meet these definitions
DDx: White-Coat HTN

BP >140/90 in your office, <130/80 on 24-hr ambulatory monitor

As many as 30% of adults with Resistant HTN

White Coat HTN associated with lower CV event rates than “real” HTN...

...but higher event rates than normotension
Or Use a Blood Pressure Journal

- Home Blood Pressure Cuff
- Check Blood Pressure Same Time Every Day
- Keep Log
- Bring to Office Appointment
## ESC Suggested Definitions of Hypertension Based on Setting Where Measured

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td>≥140</td>
<td>and/or</td>
</tr>
<tr>
<td>Ambulatory BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daytime (or awake)</td>
<td>≥135</td>
<td>≥85</td>
</tr>
<tr>
<td>Nighttime (or asleep)</td>
<td>≥120</td>
<td>≥70</td>
</tr>
<tr>
<td>24-h</td>
<td>≥130</td>
<td>≥80</td>
</tr>
<tr>
<td>Home BP</td>
<td>≥135</td>
<td>≥85</td>
</tr>
</tbody>
</table>

BP, blood pressure.
DDx: Pseudoresistant Hypertension

“Resistant Hypertension” based on his med list

“Untreated Hypertension” based on his pharmacy refill records

“Symptomatic Hypotension” if he ever took everything you prescribed
Pharmacy Refill Data:

40% of people are not taking all of their medications, all of the time

That number rises to more than half if you check serum levels of antihypertensives!
Resistant HTN is not Secondary HTN

Uncomplicated HTN
What percentage have secondary HTN?
10%

Resistant HTN
What percentage have secondary HTN?
33%
So what IS it?
1. The average American eats 8.6 grams of sodium per day

2. In uncomplicated HTN patients, restriction to <2 g per day will lower BP 5/3 mm Hg

3. In resistant HTN patients, restriction to <2 g per day will lower BP up to 20 mm Hg!
Urinary Sodium Excretion and Risk of Cardiovascular Events. JAMA 2011;306(20)
Sleep Apnea

Uncomplicated HTN
• 30% have OSA

Resistant HTN
• 60% have OSA
Primary Aldosteronism

Uncomplicated HTN
- 5-10%

Resistant HTN
- 20%
Other Secondary Hypertension

Cushings
Aortic coarctation
Pheochromocytoma (paraganglioma)
Renal artery stenosis
Hyper- or hypo-thyroidism
Hypokalemia
Polycystic kidney disease
Patient with clinic blood pressure $\geq 140/90$ mm Hg despite angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker plus calcium channel blocker plus diuretics at maximum or near maximal doses

- Average home blood pressure $\leq 135/85$ mm Hg?
  - Yes
    - Perform ambulatory blood pressure monitoring
  - No
    - Assess sodium intake and possible interference from substances or prescription or nonprescription drugs (e.g., nonsteroidal anti-inflammatory drugs, heavy alcohol use, pseudoephedrine, methylphenidate, corticosteroids, licorice, oral contraceptives)
    - Assess adherence to medications
      - Yes
        - Continue home blood pressure monitoring (early morning and evening daily)
      - No
        - Investigate for secondary hypertension as clinically indicated (plasma renin activity, serum aldosterone, polysomnography, renal duplex Doppler ultrasonograph, computed tomographic angiograph of renal artery, thyroid stimulating hormone, serum free thyroxin, 24-h urinary free cortisol)
          - Yes
            - Continue home blood pressure monitoring (early morning and evening daily)
          - No
            - Continue home blood pressure monitoring (early morning and evening daily)

- Ambulatory blood pressure $< 130/80$ mm Hg?
  - Yes
    - Continue home blood pressure monitoring (early morning and evening daily)
  - No
    - Continue home blood pressure monitoring (early morning and evening daily)

- Clinic blood pressure $< 140/90$ mm Hg?
  - Yes
    - Add spironolactone or eplerenone if eGFR $> 30$ mL/min per 1.73 m$^2$
  - No
    - Add fifth-line drug therapy
      - If heart rate $\geq 60$/min to $\leq 80$/min, add any drugs from different classes listed below.
      - If heart rate $< 60$/min, add $\alpha$-adrenergic receptor blockers. Avoid $\beta$-adrenergic receptor blockers, clonidine, or nondihydropyridine calcium channel blocker.
      - If heart rate $> 80$/min, add $\beta$-blocker, nondihydropyridine calcium channel blocker, or central sympatholytic drugs.
      - Or
      - Refer to hypertension specialist.
• LOTS of untreated HTN out there!
• HTN = >150/90 for those over age 60 and >140/90 for those under age 60, or with DM, or with CKD
• Diuretics, CCB, ACEI, ARB
• If resistant, think compliance, sodium, sleep apnea, primary aldo