Reaching for the "New Normal" with the 2017 ACC/AHA Hypertension Guideline

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Disclosures

- The presenter has no conflicts of interest to disclose

Objectives for Pharmacists

- Identify blood pressure (BP) goals for various populations from the 2017 ACC/AHA hypertension (HTN) guideline
- State when pharmacologic treatment should be initiated for a given patient based on BP
- List primary agents for treating uncomplicated HTN
- Specify antihypertensive drug of choice in patients with concomitant conditions
- Describe the differences between previous HTN guideline (JNC 7) and the newer HTN guideline (2017 ACC/AHA)

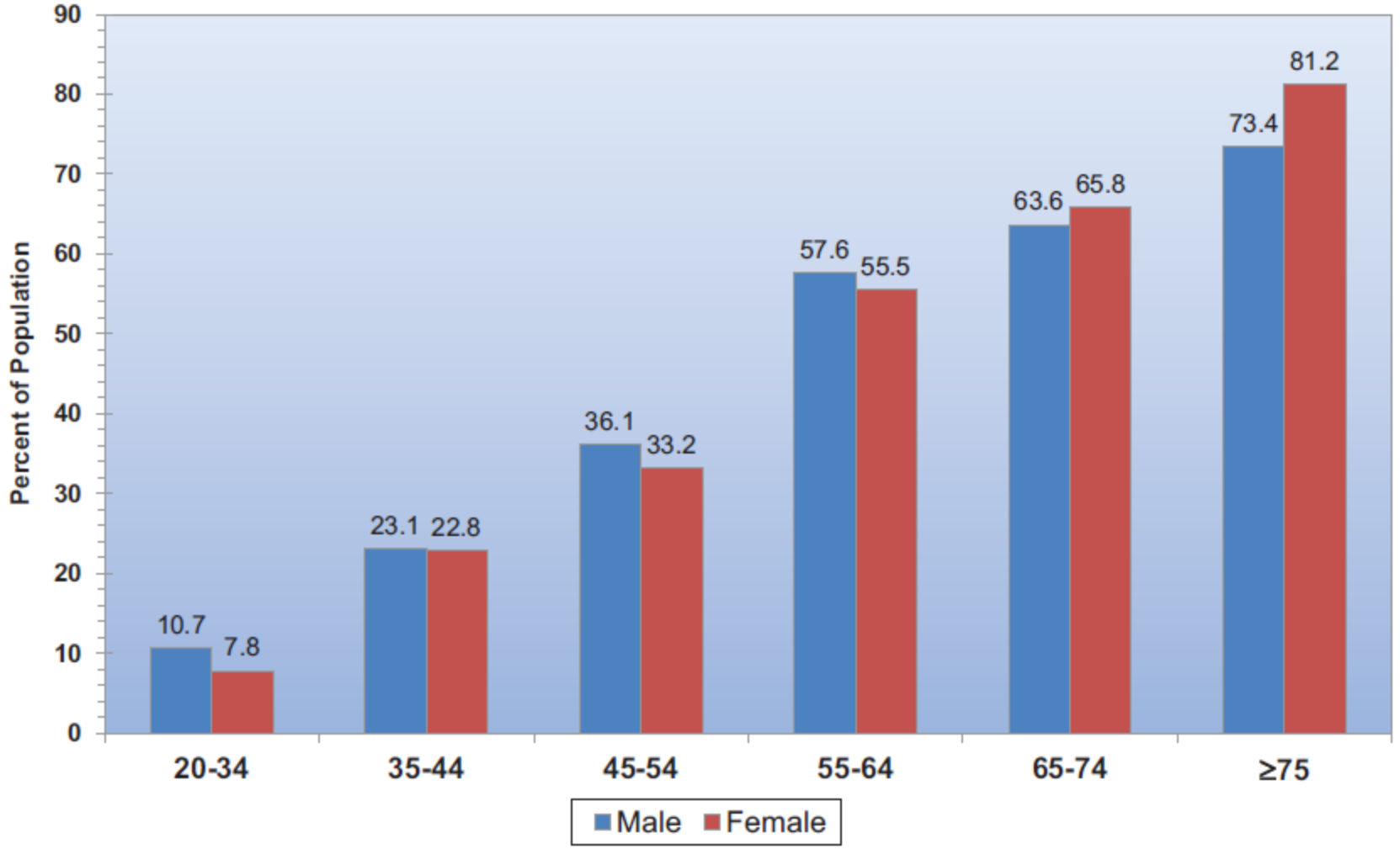
Objectives for Pharmacy Technicians

- Describe the various classes of medications used to treat HTN
- State specific agents from each class of antihypertensive medications
- Specify typical dosages of antihypertensive medications
- Identify common adverse effects of specific antihypertensive agents

Significance

- About 46% (103 million people) US adults have HTN according to the 2017 ACC/AHA HTN guideline
- HTN is the most common chronic condition treated by PCP
- Approximately 79,000 deaths were primarily attributable to HTN in 2015
- Death rates due to HTN ↑ 10.5% from 2005 to 2015
- Direct costs of HTN could ↑ to an estimated $221 billion in 2035

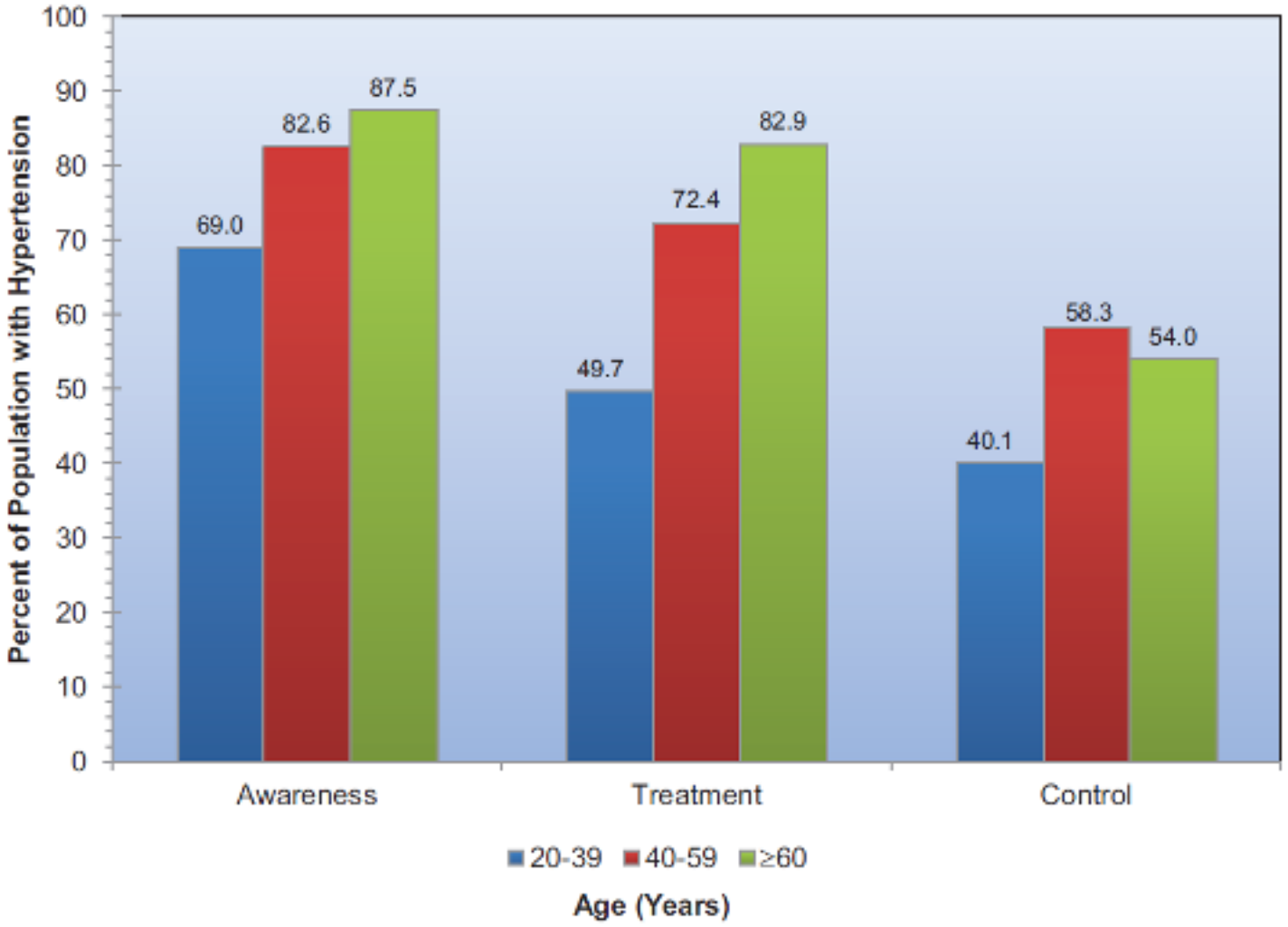
Prevalence of high blood pressure in adults ≥20 years of age by sex and age (National Health and Nutrition Examination Survey: 2011-2014)



HTN is defined as BP ≥140/90 mmHg

Heart Disease and Stroke Statistics – 2018 Update.
Circulation. 2018; 137:XX-XX. DOI: 10.1161/CIR.0000000000000558

Extent of awareness, treatment, and control of high blood pressure by age (National Health and Nutrition Examination Survey: 2011–2014)



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Consequences of High Blood Pressure

American Heart Association | American Stroke Association

High blood pressure (HBP) can injure or kill you. when high blood pressure is uncontrolled, it can lead to:

STROKE

HBP damages arteries that burst or clog more easily.

77% of people who have a first stroke have HBP.

HBP increases your stroke risk by four to six times.

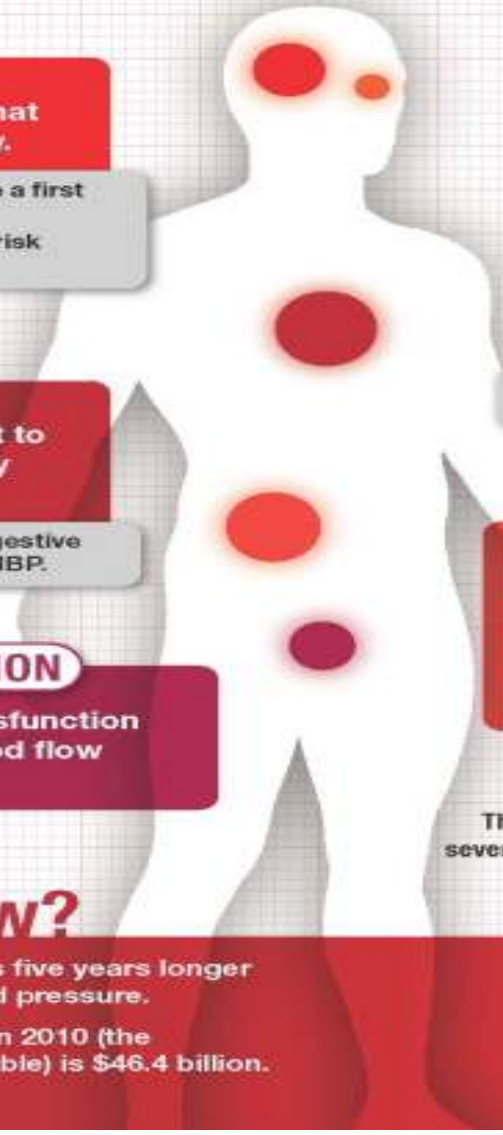
HEART FAILURE

HBP can cause the heart to enlarge and fail to supply blood to the body.

75% of people with congestive heart failure have HBP.

ERECTILE DYSFUNCTION

HBP leads to erectile dysfunction because of reduced blood flow throughout the body.



VISION LOSS

HBP can strain the vessels in the eyes.

HEART ATTACK

HBP damages arteries that can become blocked.

69% of people who have a first heart attack have HBP.

KIDNEY DISEASE/FAILURE

HBP can cause arteries around the kidneys to narrow, weaken or harden so the kidneys lose their ability to filter blood.

HBP is the second-leading cause of kidney failure

These conditions can happen over several years, but they can be prevented by controlling blood pressure.

Did You Know?

- At 50, total life expectancy is five years longer for people with normal blood pressure.
- The estimated cost of HBP in 2010 (the most-recent statistics available) is $46.4 billion.

Check. Change. *Control.*™

Perspectives from early 1900s

The greatest danger to a man with high blood pressure lies in its discovery, because then some fool is certain to try and reduce it.
—J.H. Hay, 1931

Hypertension may be an important compensatory mechanism which should not be tampered with, even were it certain that we could control it.
—Paul Dudley White, 1937

FDR's Journey with HTN

- In 1937, at age 54, BP = 162/98 mmHg
- By 1940, BP reached 180/88 mmHg
- In 1941, BP = 188/105 mmHg (phenobarbital and massages were prescribed)
- In 1943 and 1944, his failing health led to speculation regarding his competence
- He developed SOB, orthopnea, lethargy (evidence of HF); digitalis was added

Moser M. J Clin Hypertens. 2006; 8(8 suppl 2):15-20

FDR's Journey with HTN

- In 1944, BP = 180-230/110-140 mmHg, the 62 yo president had a series of CVAs
- In 1945, he suddenly lost consciousness and died of a cerebral hemorrhage at age of 63 (BP > 300/190 mmHg!)
- Roosevelt represents a textbook case of untreated HTN progressing to target organ failure and death from stroke

Moser M. J Clin Hypertens. 2006; 8(8 suppl 2):15-20

Search continued for more effective medications for HTN

- In 1957, chlorothiazide was studied
- In 1960s, propranolol was discovered by Sir James Black
- In 1975, captopril was developed and gained FDA approval in 1981

History of HTN Guidelines

- The First Report of the Joint National Committee on Prevention, Detection, Evaluation, an Treatment of High Blood Pressure (JNC) – 1977
- JNC 7 – 2003
- JNC 8 Committee appointed by the NHLBI – 2008
- ACC/AHA are now responsible for HTN guidelines – 2013
- Recommendations by the JNC 8 panel – 2014
- ASH/ISH guideline – 2014
- ACC/AHA HTN guideline – 2017

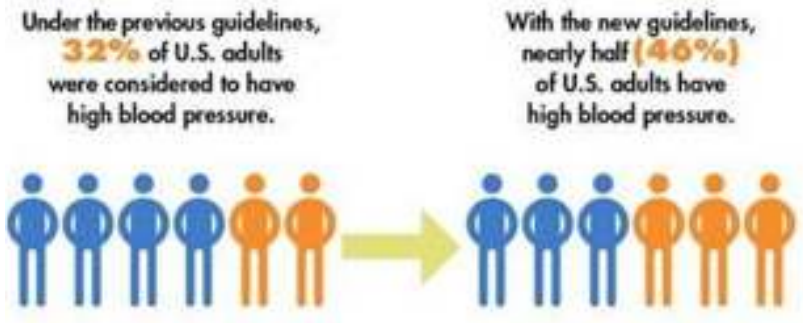
Key Updates in Classification of HTN

2003 Guideline (JNC 7)

BP Category	SBP (mmHg)		DBP (mmHg)
Normal	<120	and	<80
Pre-HTN	120-139	or	80-89
Stage 1 HTN	140-159	or	90-99
Stage 2 HTN	≥160	or	≥100

2017 ACC/AHA Guideline

BP Category	SBP (mmHg)		DBP (mmHg)
Normal	<120	and	<80
Elevated	120-129	and	<80
Stage 1 HTN	130-139	or	80-89
Stage 2 HTN	≥140	or	≥90



SBP = Systolic blood pressure
DBP = Diastolic blood pressure

Blood Pressure Goals (No comorbidities)

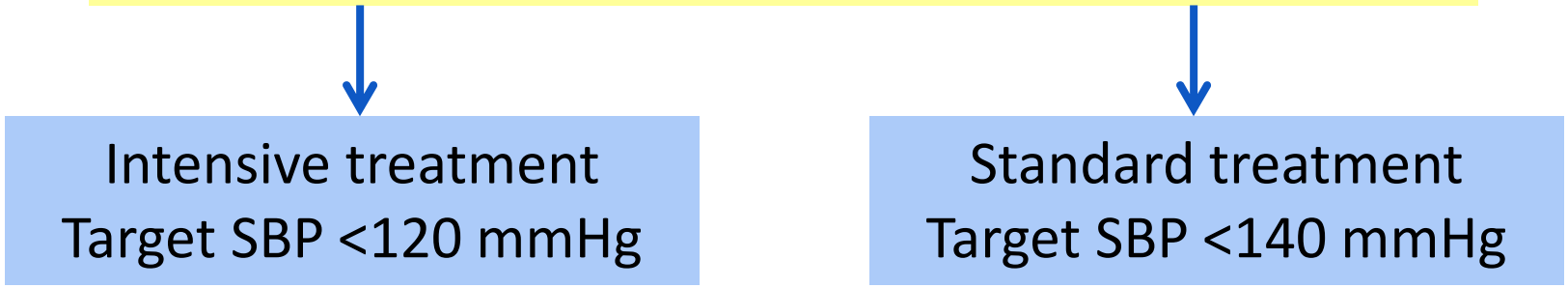
	ACC/AHA (2017)	JNC-8 Panel (2014)	ASH/ISH (2014)	JNC-7 (2003)
<60 years old	**<130/80 mmHg**	<140/90 mmHg	<140/90 mmHg	<140/90 mmHg
60-64 years old	**<130/80 mmHg**	<150/90 mmHg	<140/90 mmHg	<140/90 mmHg
65-79 years old	**SBP <130 mmHg**	<150/90 mmHg	<140/90 mmHg	<140/90 mmHg
≥80 years old	**SBP <130 mmHg**	<150/90 mmHg	<150/90 mmHg	<140/90 mmHg

SBP = Systolic blood pressure

SPRINT: Study Design

- Age ≥50 years
- SBP 130-180 mmHg (treated or untreated)
- Additional CV risk (≥1)
  - Clinical or subclinical CVD (excluding stroke)
  - CKD (eGFR 20 to <60 mL/min/1.73 m^2
  - Framingham Risk Score for 10-year risk ≥15%
  - Age ≥75 years

Patients with DM, prior stroke, polycystic kidney disease, eGFR<20 mL/min/1.73 m^2 and proteinuria were excluded



The SPRINT Research Group. N Engl J Med 2015:373:2103-16

SPRINT: Study Design

- All major antihypertensive classes can be used
- Chlorthalidone encouraged as primary thiazide
- Amlodipine encouraged as preferred CCB
- Doses of medications were adjusted based on an average of 3 seated office BP measurements, taken with an automated monitor

Primary outcome: Composite of MI, ACS not resulting in MI, stroke, acute decompensated HF, and CV mortality

Secondary outcomes: Individual components of the primary composite outcome and all-cause mortality

SPRINT: Study Results

Study Population

9,361 (4,678 intensive treatment; 4,683 standard treatment) participants were enrolled in the study between 2010 to 2013.
Baseline characteristics were comparable between both groups

- Mean age = 67.9 (~28% were 75 years or older)
- Mean Framingham 10-yr CVD risk score was ~25% (~76% had a risk score ≥15%, 20% already had CVD)
- Average baseline SBP was 139.7 mmHg
- Mean serum creatinine was ~1.1 mg/dL

Blood Pressure During Treatment

Throughout the 3.26 years of follow-up:
Mean SBP = 121.5 mmHg in the intensive treatment group (2.8 meds)
Mean SBP = 134.6 mmHg in the standard treatment group (1.8 meds)

SPRINT: Study Results

Outcome	Percent per year		
	Intensive therapy	Standard therapy	Hazard ratio
Primary outcome[a]	1.65	2.19	0.75[b]
Secondary outcomes			
Myocardial infarction	0.65	0.78	0.83
Other acute coronary syndromes	0.27	0.27	1.00
Stroke	0.41	0.47	0.89
Heart failure	0.41	0.67	0.62[b]
Cardiovascular mortality	0.25	0.43	0.57[b]
All-cause mortality	1.03	1.40	0.73[b]

[a]The composite of MI, ACS, stroke, HF, or death from CV causes

[b]$P<0.05$

The SPRINT Research Group. N Engl J Med 2015:373:2103-16

Thomas G, et al. Cleveland Clinic Journal of Medicine. 2016;83:187-195

SPRINT: Study Results

Adverse events	Percent of patients		
	Intensive therapy	Standard therapy	Hazard ratio
Hypotension	3.4	2.0	1.70[b]
Syncope	3.5	2.4	1.44[b]
Hyponatremia	3.8	2.1	1.76[b]
Hypokalemia	2.4	1.6	1.50[b]
Injurious fall	7.1	7.1	1.00
Orthostatic hypotension without dizziness	16.6	18.3	0.88[b]
Orthostatic hypotension with dizziness	1.3	1.5	0.85
Acute kidney injury	4.4	2.6	1.71[b]

[b] $P<0.05$

The SPRINT Research Group. N Engl J Med 2015:373:2103-16
Thomas G, et al. Cleveland Clinic Journal of Medicine. 2016;83:187-195

SPRINT: Discussion

- First large, adequately powered randomized trial to demonstrate CV and mortality benefit from lowering SBP (goal <120 mmHg) in older patients at CV risk but without a history of DM or stroke
- Trial excluded patients with DM or previous stroke, so it is uncertain if these subgroups would also benefit from intensive lowering of SBP
- Benefits came at a price of more adverse events
- Risks and benefits of intensive control of SBP will need to be balanced in individual patients

BP Thresholds and Goals for Pharmacological Therapy

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

ASCVD = atherosclerotic cardiovascular disease; BP = blood pressure; CVD = cardiovascular disease and SBP = systolic blood pressure

Whelton PK, et al. 2017 ACC/AHA High Blood Pressure Clinical Practice Guideline. Hypertension; Nov. 13, 2017

Non-Pharmacologic Treatment

- Reduce weight (↓ SBP 5 mmHg)
- Adopt DASH eating plan (↓ SBP 11 mmHg)
- Lower sodium intake (↓ SBP 5-6 mmHg)
- Enhance intake of dietary potassium (↓ SBP 4-5 mmHg)
- Physical activity, aerobic (↓ SBP 5-8 mmHg)
- Moderation of alcohol intake(↓ SBP 4 mmHg)

DASH = dietary approaches to stop HTN

Pharmacologic Treatment

- First-line agents for management of uncomplicated HTN:
  - Thiazide diuretics
  - Calcium channel blockers (CCBs)
  - Angiotensin converting enzyme (ACE) inhibitors
  - Angiotensin receptor blockers (ARBs)
- Initiation of therapy with 2 first-line agents of different classes is recommended for stage 2 HTN and an average BP >20/10 mmHg above BP goal

Thiazide Diuretics

- Work by inhibiting sodium reabsorption in the distal tubule
- Diuretics are most effective in reducing blood pressure when combined with ACE-I or ARB
- Monitor for hyponatremia and hypokalemia, uric acid and calcium levels
- Use with caution in patients with history of acute gout

Dosages of Thiazides

Drug Name	Usual Dose Range (mg/d)
Chlorthalidone	12.5-25
Hydrochlorothiazide	12.5-50
Indapamide	1.25-5

CCBs

- Blocks the inward flow of calcium ions through the L-type calcium channels of arterial smooth muscle cells
- Two main types of calcium channel blockers:
  - Dihydropyridines: work by dilating arteries
  - Nondihydropyridines: Reduce heart rate and contractility
- Work equally efficacious across all ethnic groups
- Avoid non-dihydropyridine use in patients with HFrEF
- Side effects include: Flushing, peripheral edema, palpitations, atrioventricular block, bradycardia and constipation

Dosages of CCBs

Drug Name	Usual Dose Range (mg/d)
<u>Nondihydropyridnes</u>	
Diltiazem (Cardizem CD)	120-480
Verapamil (Calan SR)	120-480 (may give TDD 1-2x/d)
<u>Dihydropyridines</u>	
Amlodipine (Norvasc)	2.5-10
Felodipine (Plendil)	5-10
Nifedipine (Procardia XL)	60-120

TDD = Total daily dose

ACE Inhibitors

- ↓ BP by blocking the renin-angiotensin system
- More effective as monotherapy in white versus black patients
- Benefits in patients with HF, post-MI, LV systolic dysfunction, diabetic and nondiabetic CKD
- Contraindicated in pregnant women
- Sides effects include cough, ↑ SCr, hyperkalemia and angioedema
- Do not use in combination with ARBs or direct renin inhibitor

Dosages of ACE inhibitors

Drug Name	Usual Dose Range (mg/d)
Benazepril (Lotensin)	10-40 (may give TDD 1-2x/d)
Captopril (Capoten)	25-150 (may give TDD 2-3x/d)
Enalapril (Vasotec)	2.5-40 (may give TDD 1-2x/d)
Fosinopril (Monopril)	10-40
Lisinopril (Prinivil, Zestril)	10-40
Moexipril (Univasc)	7.5-30 (may give TDD 1-2x/d)
Perindopril (Aceon)	4-16 (may give TDD 1-2x/d)
Quniapril (Accupril)	10-80 (may give TDD 1-2x/d)
Ramipril (Altace)	2.5-10 (may give TDD 1-2x/d)
Trandolapril (Mavik)	1-4

TDD = Total daily dose

ARBs

- ↓ BP by blocking the renin-angiotensin system
- More effective as monotherapy in white versus black patients
- Benefits in patients with HF, post-MI, LV systolic dysfunction, diabetic and nondiabetic CKD
- Contraindicated in pregnant women
- Lower incidence of cough compared to ACE inhibitors
- Side effects include ↑ SCr, hyperkalemia and angioedema
- Do not use in combination with ACE inhibitors or direct renin inhibitor

Dosages of ARBs

Drug Name	Usual Dose Range (mg/d)
Azilsartan (Edarbi)	40-80
Candesartan (Atacand)	8-32
Eprosartan (Teveten)	600-800 (may give TDD 1-2x/d)
Irbesartan (Avapro)	150-300
Losartan (Cozaar)	50-100 (may give TDD 1-2x/d)
Olmesartan (Benicar)	20-40
Telmisartan (Micardis)	20-80
Valsartan (Diovan)	80-320

TDD = Total daily dose

Drug of Choice in Patients with Concomitant Conditions

Comorbidity	Preferred Pharmacotherapy
HF with *reduced* EF	Beta-blockers, ACE inhibitors/ARBs and aldosterone antagonists
HF with *preserved* EF	Loop diuretics (if symptoms of volume overload)
Stable ischemic heart disease	Beta-blockers, ACE inhibitors/ARBs
CKD (Stage 3 or higher or stage 1-2 with albuminuria)	ACE inhibitors
Diabetes, no albuminuria	Thiazide diuretics, ACE inhibitors/ARBs, CCBs
Diabetes with albuminuria	ACE inhibitors/ARBs

Whelton PK, et al. 2017 ACC/AHA High Blood Pressure Clinical Practice Guideline. Hypertension; Nov. 13, 2017

Other Notable Recommendations by 2017 ACC/AHA HTN Guideline

- Measurement of BP
  - Accurate assessment in the office
  - Out-of-office and self-monitoring
  - Masked and white coat HTN
- Lifestyle modification promotion
- Antihypertensive medication adherence strategies
- Hypertensive crises management
- Resistant HTN diagnosis, evaluation and treatment
- Collaborative approach to patient care

Assessment Question 1

R.M. is a 48-year-old African-American man with no other chronic medical conditions. His 10-year ASCVD risk is 8.5%. At a medical appointment he is noted to have an average BP of 138/88 mmHg. Two weeks later, his average BP was 134/86 mmHg. Which one of the following is the preferred management for R.M.?

A. Lisinopril
B. Chlorothiazide
C. Amlodipine
D. Lifestyle modification

Assessment Question 2

Ten years later, R.M., is 58 years old and had a NSTEMI. He underwent PCI and had 2 DES placed. His BPs were 130/82 mmHg and 134/86 mmHg during hospitalization. HR = 80 bpm. LVEF = 50%. Which of the following should be initiated in addition to aspirin, clopidogrel and atorvastatin?

A. Amlodipine
B. Metoprolol
C. Chlorothiazide & lifestyle modification
D. Metoprolol & lifestyle modification

Summary

- The 2017 ACC/AHA guideline provides a new system for classification of BP
- In contrast to JNC 7, the new ACC/AHA HTN guideline recommends estimation of underlying ASCVD risk and use of this information to guide treatment
- This new guideline advocates treatment of HTN to a goal <130/80 mmHg in most patients
- Thiazide diuretics, CCBs, ACE inhibitors and ARBs are recommended as first-line agents
- Risks and benefits of intensive control of BP need to be balanced in each patient

Selected References

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