

Hypertension: Diagnosis and Management – Adult – Ambulatory Clinical Practice Guideline

Note: Active Table of Contents - Click each header below to jump to the section of interest

Table of Contents

| INTRODUCTION | 3 |
|----------------------------------------------------------------------------|----------|
| SCOPE | |
| DEFINITIONS | |
| Table 1. Categories of blood pressure | |
| RECOMMENDATIONS | |
| Blood Pressure Measurement | |
| Table 2. When to screen for white coat hypertension or masked hypertension | |
| Patient Hypertension Evaluation | |
| Treatment and Management | 6 |
| Treatment Goals | <i>6</i> |
| Non-pharmacologic Interventions | ε |
| Pharmacotherapy | 8 |
| Table 9. Select Antihypertensive medications | 11 |
| METHODOLOGY | 14 |
| COLLATERAL TOOLS & RESOURCES | 17 |
| APPENDIX A. BLOOD PRESSURE MEASUREMENT | 19 |
| REFERENCES | 20 |

Content Expert(s):

Name: Heather Johnson, MD - Cardiology

Phone Number: (608) 262-2075

Email Address: hm2@medicine.wisc.edu

Name: James Stein, MD - Cardiology Phone Number: (608) 262-2075

Email Address: jhs@medicine.wisc.edu

Name: Jeff Huebner, MD - Family Medicine/Population Health

Phone Number: (608) 274-1100

Email Address: jhuebner@uwhealth.org

Contact for Changes:

Center for Clinical Knowledge Management (CCKM)

Email Address: CCKM@uwhealth.org

Workgroup Members:

Matt Anderson, MD - Internal Medicine
Nancy Fuller, MD - Internal Medicine
James Bigham, MD - Family Medicine
Joel Buchanan, MD - Internal Medicine
Tim Flynn, MD - SwedishAmerican Family Medicine
James Bigham, MD - Family Medicine
Sara Shull, PharmD - Drug Policy Program
Kristina Yokes, PharmD - Ambulatory Pharmacy
Kayla McGowan, PharmD - Ambulatory Pharmacy
Karen Kopacek, R. Ph - UW-Madison School of Pharmacy
Vonda Shaw, MS, MPH - Preventive Cardiology
Diana Renken, PharmD - CCKM
Katherine Le, PharmD - CCKM

Committee Approval(s): Clinical Knowledge Management (CKM) Council (12/20/18)

Introduction

The global prevalence of hypertension was estimated to be 1.13 billion in 2015 (based on office blood pressures.)¹ Hypertension now affects over 40% of the U.S. adult population³ and is the most common diagnosis at outpatient office visits. Hypertension is also a leading risk factor that contributes to heart failure, heart attack, stroke, and chronic kidney disease. From 2005 to 2015, the death rates attributable to high blood pressure increased 10.5%, and the actual number of deaths attributable to high blood pressure rose 37.5%.² In 2015, it was the primary or contributing cause of death for more than 427,000 Americans ².

This guideline outlines the preferred hypertension management approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. Although guidelines in general may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests.

Hypertension management, in accordance with guideline recommendations, is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions based on individual values, preferences, and associated conditions and comorbidities.

Scope

Intended User(s): Physicians, Advanced Practice Providers, Registered Nurses, Pharmacists

Objective(s): To provide recommendations that reduce the incidence of stroke, myocardial infarction, congestive heart failure, and kidney failure by identifying and treating hypertension.

Target Population: Adults age 18 years or older

Clinical Questions Considered:

- What is the threshold for a new hypertension diagnosis?
- When is pharmacotherapy indicated for the treatment of hypertension?
- Which medications are considered first-line agents for treating hypertension?

Definitions

Blood pressure (BP) is categorized into 4 levels as outlined in **Table 1**.

Table 1. Categories of blood pressure³

| Tubic ii categorice of at | | |
|---------------------------|-------------------|--------------|
| BP Category | Systolic BP | Diastolic BP |
| Normal | <120 mm Hg and | < 80 mm Hg |
| Elevated | 120-129 mm Hg and | < 80 mm Hg |
| Hypertension | | |
| Stage 1 | 130-139 mm Hg or | 80-89 mm Hg |
| Stage 2 | ≥140 mm Hg or | ≥90 mm Hg |

Recommendations

Blood Pressure Measurement

Proper methods are recommended for accurate measurement and documentation of BP. (ACC-AHA Class I, Level C-EO)

Clinic blood pressure measurements obtained using proper technique with manual and/or validated automated devices are acceptable, however automated devices are preferable.⁴ (UW Health Moderate quality evidence, C recommendation)

Establishing the diagnosis

The diagnosis of hypertension requires the average of ≥2 blood pressure measurements on ≥2 office visits. (ACC-AHA Class I, Level A)

Clinic blood pressures can be highly variable. Out-of-office blood pressure measurements (home blood pressure monitoring [HBPM] with or without 24-hour ambulatory blood pressure monitoring [ABPM]) are recommended to confirm the diagnosis of hypertension. (ACC-AHA Class I, Level A) Out-of-office blood pressure measurements are also recommended for titration of blood pressure medication, in conjunction with telehealth counseling or other clinical interventions. (ACC-AHA Class I, Level A) For additional information on blood pressure measuring, refer to **Appendix A**.

Patients may also have white coat hypertension or masked hypertension (see **Table 2**).

White coat hypertension - characterized by elevated office BP but normal readings when measured outside the office with either 24-hour ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM).³

<u>Masked hypertension</u> - characterized by normal office BP readings but out-of-office (ABPM/HBPM) readings that are consistently above normal. ³

Table 2. When to screen for white coat hypertension or masked hypertension³

Screen for white coat hypertension Screen for masked hypertension • In adults with an untreated SBP greater • In adults with untreated office BPs that are than 130 mm Hg but less than 160 mm Hg consistently between 120 mm Hg and 129 mm or DBP greater than 80 mm Hg but less Hg for SBP or between 75 mm Hg and 79 mm than 100 mm Hg (ACC-AHA Class IIa, Level Hg for DBP (ACC-AHA Class IIa, Level B-NR) • It may be reasonable to screen for masked In adults on multiple-drug therapies for uncontrolled hypertension with HBPM in adults hypertension and office BPs within 10 mm being treated for hypertension and office Hg above goal (ACC-AHA Class IIb, Level Creadings at goal, in the presence of target organ LD) damage or increased overall CVD risk. (ACC-AHA Class IIb, Level C-EO)

Patient Hypertension Evaluation

Assess lifestyle, identify modifiable and non-modifiable risk factors for hypertension and other cardiovascular disease (CVD) risk factors, and evaluate for target organ damage using personal history, physical examination and selective testing (**Table 3**).^{3,5}

Table 3. Hypertensive Target Organ Damage^{3,6}

- Heart disease (left ventricular hypertrophy, heart failure, coronary artery disease, atrial fibrillation)
- · Chronic kidney disease
- Stroke/Transient Ischemic Attack
- · Peripheral arterial disease
- Retinopathy

For new onset or uncontrolled hypertension in adults, screening for specific form(s) of secondary hypertension is recommended when the clinical indications and physical examination findings are present (see **Tables 4** and **5**). (ACC-AHA Class I, Level C-EO) ³ It is also important to evaluate for the presence of target organ damage (see **Table 3**).

Table 4. When to Evaluate for Secondary Hypertension³

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

Table 5. Secondary Causes of Hypertension³

- Renovascular disease/renal artery stenosis
- Primary aldosteronism
- Obstructive sleep apnea
- Drug- or alcohol-induced
- Pheochromocytoma/paraganglioma
- Cushing's syndrome
- Aortic coarctation
- Thyroid or parathyroid disease
- Congenital adrenal hyperplasia

- Acromegaly
- Alcohol abuse
- Illicit stimulants (amphetamines, methamphetamines, cocaine)
- Chronic kidney disease (CKD)
- Medications (stimulants, estrogen, corticosteroids, erythropoietin alfa, mineralocorticosteroids, cyclosporine, tacrolimus, NSAIDS, herbals, OTC decongestants, triptans, bupropion, SNRIs, others)

Screening for Hypertension

The U.S. Preventive Services Task Force (USPSTF) recommends screening for high blood pressure in adults aged 18 years or older without known hypertension and to obtain measurements outside of the clinical setting for diagnostic confirmation. ⁷ (USPSTF Grade A)

Annual blood pressure screening is recommended for adults aged ≥40 years old and for all adults with an increased risk for high blood pressure (see risk factors above). (UW Health Moderate quality evidence, S recommendation) Patients aged 18-39 years with normal blood pressure (< 120/80 mmHg)³, and no other cardiovascular disease risk factors, should be rescreened every 3-5 years. (USPSTF Grade A)

Table 6. Time Interval for Blood Pressure Screening

| Table of Time Hiter fall of Blood 1 1000al 5 Colo | O9 |
|----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Patient | Interval |
| Patients 18-39 years with blood pressure <130/85 mm Hg and no other cardiovascular disease risk factors | Every 3-5 years |
| Patients ≥ 40 years | |
| Any adult age with increased risk for high blood pressure (see Table 3) | Annual blood pressure screening |

Treatment and Management

As the relationship between blood pressure and risk of CVD events is continuous and independent of other risk factors, the benefits of blood pressure treatment are highest at higher levels and diminish at lower blood pressures.^{8,9}

For patients with confirmed hypertension, assess the 10-year risk for heart disease and stroke using the atherosclerotic cardiovascular disease (ASCVD) risk calculator to guide patient discussions and treatment decisions. ASCVD is defined as first coronary heart disease death, non-fatal MI or fatal or non-fatal stroke. A patient's ASCVD Risk Estimate can be calculated with the ACC-AHA Pooled Cohort equation (http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/) or the HealthDecision tool found in UW HealthLink.

Treatment Goals

For adults with confirmed hypertension, without additional target organ damage or other CVD risk factors, a goal blood pressure target of less than 130/80 mmHg may be reasonable.³ (ACC-AHA Class I, Level B-NR for systolic BP; ACC-AHA Class I, Level C-EO for diastolic BP)

For adults with confirmed hypertension and known cardiovascular disease or a 10-year ASCVD event risk of ≥10%, a blood pressure goal of less than 130/80 is recommended.³ (ACC-AHA Class I, Level B-R for systolic BP; ACC-AHA Class I, Level C-EO for diastolic BP)

Less intensive target blood pressures may be considered in patients¹⁰ (UW Health High quality evidence, C recommendation):

- With a one-minute standing SBP <110 mmHg
- With a history of orthostatic hypotension
- Who are intolerant to their current medications
- With a history of falls and/or frailty
- Who have difficulty with medication adherence including alcohol abuse, psychiatric disease

Response to treatment (non-pharmacologic and/or pharmacologic) should be monitored using home blood pressure measurements. ^{3,11-14} (UW Health High quality evidence, S recommendation)

Non-pharmacologic Interventions

All patients should be encouraged to make lifestyle modifications (see **Table 7**).^{3,5,15} (*ACC-AHA Class I hypertension, Class IIa normotension; Level A*) Lifestyle modifications can be quite effective and may mitigate the need for antihypertensive pharmacotherapy. Lifestyle changes should be reinforced at every patient encounter, even after antihypertensive medication initiation.³

| Table 7. Non-pharmacologic Interventions to Lower Blood Pressure ³ | | | | |
|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|--|
| Lifestyle modification | Recommenda tion* | Comments | Approximate reduction in SBP (hypertensive, normotensive) | |
| Weight loss (ACC-AHA Class I, Level A) | Aim for ideal body weight; at least 1 kg reduction in body weight for overweight adults | Weight loss can lower BP, increase the efficacy of antihypertensive medications, and improve CVD risk factors such as diabetes mellitus and dyslipidemia. For every 1 kg of weight lost, BP may decrease by 1 mm Hg. | -5 mm Hg, -2/3 mmHg | |
| Healthy diet (ACC-AHA Class I, Level A) | DASH diet | A diet rich in fruits, vegetables, whole grains, low-fat dairy products with a reduced content of saturated and total fat. The DASH diet is not recommended in patients with end-stage kidney disease. | -11 mm Hg, -3 mmHg | |
| Reduced intake of dietary sodium (ACC-AHA Class I, Level A) | Optimal goal is < 1500 mg/day, but start with an initial goal of 1000 mg/day reduction and no more than 2300 mg sodium/day | More than 40% of sodium in American diet comes from only 10 types of food (i.e., breads and rolls, pizza, sandwiches, cold cuts and cured meats, canned soup, chips). Eat less processed foods and dine out less | -5/6 mm Hg, -2/3 mmHg | |
| Enhance intake of dietary potassium (ACC-AHA Class I, Level A) | 3500-5000 mg/day, preferably by diet rich in potassium | Foods high in potassium include certain fruits (i.e., bananas, oranges, cantaloupe, grapefruit), leafy green vegetables (e.g., broccoli, kale, spinach), sweet potatoes, mushrooms. Increased dietary potassium is not recommended in patients with endstage kidney disease. | -4/5 mm Hg, -2 mmHg | |
| Physical activity (ACC-AHA Class I, Level A) | 30-45 minutes of moderately intense physical activity most days of the week | Exercise contributes to weight loss and reduces the risks of CVD and overall mortality. Patients at high risk should have an exercise stress test prior to starting a new program. Medically supervised exercise programs should be advised if BP response to exercise is a concern (call UW Preventive Cardiology Program 263-7420 for information about monitored exercise sessions). | -5/8 mm Hg, -2/4 mmHg | |
| Moderate Alcohol consumption (ACC-AHA Class I, Level A) | Reduce or eliminate alcohol intake | Alcohol is a risk factor for hypertension, contributes excess calories, can reduce efficacy of antihypertensive medications, and increases the risk of stroke. Men should have no more than 2, and women no more than 1, alcoholic drink(s) daily. Examples of one drink are 12 oz. of beer, 4 oz. of wine, or 1 oz. of spirits. | -4 mm Hg, -3 mmHg | |
| Tobacco and secondhand smoke (ACC-AHA Class I, Level A) | Smoking cessation and avoidance of secondhand smoke | Tobacco and its by-products increase CVD risk³ and may make antihypertensive medications less effective. Each cigarette causes an increase in blood pressure. The CVD benefits of smoking cessation are evident in one year. | | |

Pharmacotherapy

Prior to initiating or if considering antihypertensive therapy for primary prevention of ASCVD, a patient-health care provider discussion should focus on the patient's estimated 10-year ASCVD risk, management of other ASCVD risk factors, expected ASCVD event reduction, potential drug interactions, adverse drug effects, and costs.

When to initiate antihypertensive medication

Antihypertensive medication is recommended for the following³ (see Figure 1):

- for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP ≥ 130 mmHg or an average DBP ≥ 80 mmHg (ACC-AHA Class I, Level A for systolic BP; ACC-AHA Class I, Level C-EO for diastolic BP)
- for primary prevention in adults with an estimated 10-year ASCVD risk ≥10% and an average SBP ≥130 mmHg or an average DBP ≥ 80 mmHg (ACC-AHA Class I, Level A for systolic BP; ACC-AHA Class I, Level C-EO for diastolic BP)
- for primary prevention of CVD in adults with no history of CVD, an estimated 10-year ASCVD risk <10% and an average SBP ≥140 mmHg or an average DBP ≥ 90 mmHg (ACC-AHA Class I, Level C-LD)

For patients with stage 2 hypertension and an average BP more than 20/10 mm Hg above their BP target, initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended. (ACC-AHA Class I, Level C-EO)

The choice of medication should be influenced by patient age, ethnicity/race, and other clinical characteristics such as comorbidities or pregnancy status. (Refer to <u>Tables 8</u> and <u>9</u>)

Monitoring for Side Effects

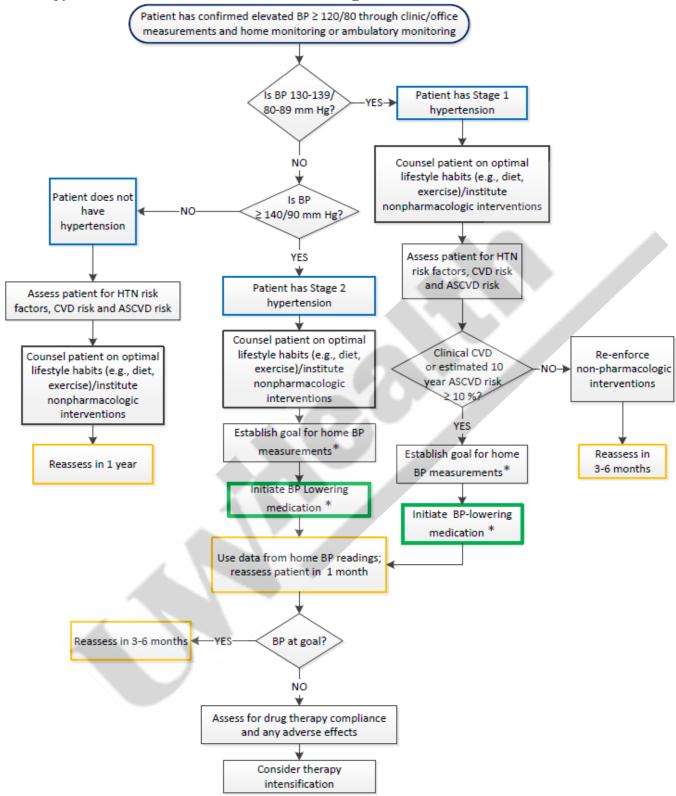
Patients on pharmacotherapy should be monitored for possible side effects of medication to help assure patient compliance.³

Creatinine and potassium levels should be checked (ACC-AHA Class I, Level B-R for renal/electrolyte monitoring) 1-2 weeks after medication initiation, at each dose change, and every 12 months thereafter in patients on diuretics, ACE-Is, ARBs, or spironolactone (UW Health Moderate quality evidence, strong recommendation for frequency).^{5,16,17} More frequent monitoring may be needed if symptoms suggest renal or electrolyte disorders.

For patients using a diuretic antihypertensive medication (including aldosterone antagonists), serum sodium should be checked at initiation, 1-2 weeks after each dose change, and as needed to evaluate for hyponatremia (ACC-AHA Class I, Level B-R for hyponatremia monitoring).

Additional serial laboratory monitoring (e.g., BUN, fasting lipid panel, fasting glucose) can be considered for individual patients, but are no longer recommended based on a diagnosis of hypertension alone.

Figure 1. Hypertension Assessment and Treatment Algorithm³



^{*} Prior to initiating or if considering antihypertensive therapy for primary prevention of ASCVD, a patient-health care provider discussion should focus on the patient's estimated 10-year ASCVD risk, management of other ASCVD risk factors, expected ASCVD event reduction, potential drug interactions, adverse drug effects, and costs.

Table 8 - Treatment of Hypertension With and Without Co-Morbidities^{5,7,18,19}

| | Patient Type | First Drug | Add Second Drug if Needed to Achieve a BP < 140/90 mmHg | If Third Drug is Needed to Achieve a BP < 140/90 mmHg |
|------------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Hypertension is primary | Black patients (African ancestry): All ages | CCB ^a or thiazide-like diuretic | ARB ^b or ACE inhibitor (If ARB or ACE inhibitor unavailable, may use CCB or diuretic if not already using) | Combination of CCB + ACE inhibitor or ARB + thiazide-like diuretic |
| condition being treated and/or no co- morbidities | White and other non- black patients: < 60 years | ARB ^b or ACE inhibitor | CCB ^a or thiazide- like diuretic | Combination of CCB + ACE inhibitor or ARB + thiazide-like diuretic |
| morbidities | White and other non- black patients: ≥ 60 years | CCB ^a or thiazide-like diuretic (ACE inhibitors or ARBs also effective) | ARB ^b or ACE inhibitor (for CCB or thiazide-like diuretic if ACE inhibitor or ARB used first) | Combination of CCB + ACE inhibitor or ARB + thiazide-like diuretic |
| | Diabetes mellitus | ARB or ACE inhibitor Note: In black patients, it is acceptable to start with a CCB or thiazide/like | CCB or thiazide-like diuretic Note: In black patients, if starting with a CCB or thiazide-like diuretic, add an ARB or ACE inhibitor | The alternative second drug (thiazide-like diuretic or CCB) |
| Hypertension is associated with other comorbidities | Chronic kidney disease | ARB or ACE inhibitor | CCB or thiazide-like diuretic ^c | The alternative second drug (thiazide-like diuretic or CCB) |
| | Clinical coronary artery disease ^d | β-blocker plus ARB or ACE inhibitor | CCB or thiazide-like diuretic | The alternative second drug (thiazide-like diuretic or CCB) |
| | Stroke history | ARB or ACE inhibitor | Thiazide-like diuretic or CCB | The alternative second drug (CCB or thiazide-like diuretic) |
| | Heart failure | Refer to <u>UW Health Chro</u> <u>Management guideline</u> | onic Left Ventricular Sys | tolic Heart Failure: |

Abbreviations: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium channel blocker; eGFR = estimated glomerular filtration rate

^a CCBs are generally preferred, but thiazide/thiazide-like diuretics like chlorthalidone may cost less.

^b ARBs can be considered because ACE inhibitors can cause cough and angioedema, although ACE inhibitors may cost less.

[°] If eGFR < 40 mL/min, a loop diuretic (e.g., furosemide or torsemide) may be needed.

^d Note: If history of myocardial infarction, a β-blocker and ARB/or ACE inhibitor are indicated regardless of blood pressure.

Table 9. Select Antihypertensive medications 3,20-23

| Table 9. Select Antihypertensive medications 3,20-23 | | | | | |
|------------------------------------------------------|----------------------------|-----------------------|---------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| Drug class | Drug | Usual Dose (mg) | Doses per day | Max Daily Dose (mg) | Comments |
| | Chlorthalidone | 12.5-25 | 1 | 25 | Chlorthalidone is preferred over hydrochlorothiazide ^{22,23} because it is longer acting and more potent; |
| THIAZIDE AND THIAZIDE-LIKE | Hydrochlorothiazide (HCTZ) | 12.5-25 | 1 | 25 | however, more careful monitoring for electrolyte and renal disturbances is needed. • Monitor for electrolyte imbalances |
| DIURETICS | Indapamide | 1.25-2.5 | 1 | 5 | Use with caution in patients with history of acute gout Thiazides are sulfonamides and may |
| | Metolazone | 2.5-5 | 1 | 5 | share cross-reactivity with other members of this chemical group (low risk) |
| | Benazepril | 10-40 | 1-2 | 40 | DO NOT use in combination with ARBs or direct renin inhibitor |
| | Captopril | 12.5-50 | 2-3 | 150 | Avoid in pregnancy; counsel women of child-bearing potential on risks of |
| | Enalapril | 5-40 | 1-2 | 40 | pregnancy Dry cough can develop at any time during usage |
| ACE INHIBITORS (ACE-I) | Fosinopril | 10-40 | 1 | 80 | Monitor for hyperkalemia, especially |
| | Lisinopril | 10-40 | 1 | 40 | in patients with CKD, using K ⁺ supplements or K ⁺ sparing drugs |
| | Perindopril | 4-8 | 1 | 16 | Can cause acute renal failure, particularly in patients with bilateral renal artery stenosis |
| | Quinapril | 10-80 | 1-2 | 80 | Angioedema is rare but serious reaction; do not use if history of |
| | Ramipril | 2.5-10 | 1-2 | 20 | angioedema with ACE-IConsider lower starting dose when |
| | Trandolapril | 1-4 | 1 | 4 | receiving concomitant diuretics or in volume depleted state. |
| | Azilsartan | 40-80 | 1 | 80 | DO NOT use in combination with ACE-Is or direct renin inhibitor |
| | Candesartan | 8-32 | 1 | 32 | Avoid in pregnancy; counsel women of child-bearing potential on risks of pregnancy |
| ANGIOTENSIN II RECEPTOR BLOCKERS (ARB) | Irbesartan | 150-300 | 1 | 300 | Monitor for hyperkalemia, especially in patients with CKD, using K ⁺ |
| | Losartan | 50 | 1-2 | 100 | supplements or K⁺ sparing drugs Can cause acute renal failure, particularly in patients with bilateral |
| | Olmesartan | 20-40 | 1 | 40 | renal artery stenosis Can be used if history of angioedema |
| | Telmisartan | 20-80 | 1 | 80 | with ACE-I, starting 6 weeks after ACE-I is discontinued |
| | Valsartan | 80-320 | 1 | 320 | Consider lower starting dose when receiving concomitant diuretics or in volume depleted state |

Select Antihypertensive medications (continued) 3,20-23

| Class | tensive medicatio | Usual Dose (mg) | Doses per day | Max Daily Dose (mg) | Comments |
|----------------------------------------|-------------------|-----------------------|---------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| | Amlodipine | 2.5-10 | 1 | 10 | Do not use immediate-release/short acting nifedipine. More effective than non-dihydropyridines in controlling blood |
| CALCIUM CHANNEL BLOCKER – | Felodipine ER | 2.5-10 | 1 | 10 | pressure Associated with dose-related peripheral edema, which is more common in women than men |
| DIHYDROPYRIDINE | Nifedipine ER | 30-90 | 1 | 120 | Be aware of interaction between amlodipine and simvastatin Avoid use in patients with heart failure or heart failure w/reduced ejection fraction (HFrEF)amlodipine or felodipine may be used if required |
| | Diltiazem SR | 60-120 | 2 | 360 | Avoid use with beta-blockers due to increased risk for bradycardia and |
| CALCIUM | Diltiazem ER | 120-360 | 1 | 480 | heart block • Do not use in patients with HFrEF |
| CHANNEL BLOCKER - NON- | Verapamil IR | 40-80 | 3 | 480 | Be aware of many drug interactions (CYP3A4 major substrate and) |
| DIHYDROPYRIDINE | Verapamil SR | 120-240 | 1-2 | 480 | moderate inhibitor); avoid use with simvastatin |
| | Verapamil ER | 100-480 | 1 | 480 | May cause constipation |
| | Bumetanide | 0.25-2 | 2 | 4 | Monitor electrolytes (e.g., hypokalemia) |
| LOOP DIURETICS | Furosemide | 10-40 | 2 | 80 | Preferred over thiazides in patients with CKD (i.e., GFR <30 mL/min) |
| | Torsemide | 5-10 | 1 | 10 | Preferred diuretic in patients with symptomatic heart failure |
| | Spironolactone | 12.5-50 | 1-2 | 100 | Preferred agents in primary aldosteronism and resistant hypertension. Low dose spironolactone (12.5-25 mg daily) can be very effective as a 3 rd or 4 th line agent, especially in overweight patients and patients with hypokalemia |
| ALDOSTERONE ANTAGONIST DIURETICS | Eplerenone | 25-50 | 1-2 | 100 | Monitor electrolytes (e.g., hyperkalemia) especially with spironolactone Avoid use with K+ supplements, other K+ sparing diuretics, or significant renal dysfunction Spironolactone is associated with greater risk of gynecomastia and impotence compared to eplerenone Eplerenone often requires twice-daily dosing for adequate BP lowering |

Antihypertensive Medications (continued)

| Class | Drug | Usual Dose (mg) | Doses per | Max Daily | Comments |
|---------------------------|----------------------|--------------------|--------------|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| | | | day | Dose (mg) | |
| | Atenolol | 25-100 | 1 | 100 | Only recommended for hypertension if there is a compelling indication (e.g., |
| BETA BLOCKERS | Bisoprolol | 2.5-10 | 1 | 10 | coronary artery disease, LV systolic dysfunction, atrial fibrillation rate |
| CARDIOSELECTIVE | Metoprolol tartrate | 50-100 | 2 | 200 | control, etc.) • Combined alpha-beta-blockers (i.e., |
| | Metoprolol succinate | 50-200 | 1 | 200 | carvedilol, labetalol) are much more effective and less likely to cause metabolic disturbances than high dose |
| BETA-BLOCKERS- | Carvedilol | 6.25-25 | 2 | 50 | pure beta-blockers (e.g., atenolol and metoprolol) |
| β-RECEPTOR | Labetalol | 100-400 | 2 | 800 | Can worsen insulin resistance and dyslipidemia in susceptible individuals, |
| | Nadolol | 40-120 | 1 | 120 | such as those with diabetes mellitus or the metabolic syndrome |
| BETA-BLOCKERS | Propranolol IR | 40-80 | 2 | 640 | Use with caution in patients with diabetes mellitus because of potential |
| - NON- CARDIOSELECTIVE | Propranolol LA | 80-160 | 1 | 640 | to mask hypoglycemia Bisoprolol, metoprolol succinate, and carvedilol are preferred in patients with HFrEF Labetalol may be used in pregnancy |
| | | / | | | Avoid abrupt cessation |

Disclaimer

Clinical practice guidelines assist clinicians by providing a framework for the evaluation and treatment of patients. This guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment or to establish a protocol for all patients. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.

Methodology

Development Process

Each guideline is reviewed and updated a minimum of every 3 years. All guidelines are developed using the guiding principles, standard processes, and styling outlined in the UW Health Clinical Practice Guideline Resource Guide. This includes expectations for workgroup composition and recruitment strategies, disclosure and management of conflict of interest for participating workgroup members, literature review techniques, evidence grading resources, required approval bodies, and suggestions for communication and implementation.

Methods Used to Collect the Evidence:

The following criteria were used by the guideline author(s) and workgroup members to conduct electronic database searches in the collection of evidence for review.

Literature Sources:

- Electronic database search (e.g., PubMed)
- Databases of systematic reviews (e.g., Cochrane Library)
- Hand-searching journals, external guidelines, and conference publications

Time Period: July 2018 to December 2018

The following is a list of various search terms that were used individually or in combination with each other for literature searches on PubMed: hypertension, SPRINT, ACC, AHA

Methods to Select the Evidence:

Literary sources were selected with the following criteria in thought: English language, subject age (i.e., >18 years), publication in a MEDLINE core clinical journal and strength of expert opinion (e.g., international or national guideline).

Methods Used to Formulate the Recommendations:

The workgroup members agreed to adopt recommendations developed by external organizations and/or created recommendations internally via a consensus process using discussion of the literature and expert experience/opinion. If issues or controversies arose where consensus could not be reached, the topic was escalated appropriately per the guiding principles outlined in the UW Health Clinical Practice Guideline Resource Guide.

Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:

Recommendations developed by external organizations maintained the evidence grade assigned within the original source document and were adopted for use at UW Health.

Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see **Figure 1**).

Step 2: Consider Downgrade or Upgrade Step 1: Identify Risk of bias Type of Evidence Step 4: Consider Inconsistency Step 3: Assign Quality Step 5: Assign Randomized **External Factors** Indirectness of Evidence Strength of controlled trial Balance of Imprecision High Recommendation (HIGH) benefits/harms Publication bias Moderate Strong Observational Patient preferences study (LOW) • Low Weak/Conditional Large consistent Cost-effectiveness Very Low • Expert consensus effect (VERY LOW) Dose response Confounders only reducing size of effect

Figure 1. GRADE Methodology adapted by UW Health

Rating Scheme for the Strength of the Evidence/Recommendations:

GRADE Ranking of Evidence

| High | We are confident that the effect in the study reflects the actual effect. |
|----------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Moderate | We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different. |
| Low | The true effect may differ significantly from the estimate. |
| Very Low | The true effect is likely to be substantially different from the estimated effect. |

GRADE Ratings for Recommendations For or Against Practice

| Strong (S) | Generally should be performed (i.e., the net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Conditional (C) | May be reasonable to perform (i.e., may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.) |

ACC/AHA Grading Scheme

SIZE OF TREATMENT EFFECT

| | CLASS I Benefit >>> Risk Procedure/Treatment SHOULD be performed/ administered | CLASS IIa Benefit >> Risk Additional studies with focused objectives needed IT IS REASONABLE to perform procedure/administer treatment | CLASS IIb Benefit ≥ Risk Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED | CLASS III No Benefit or CLASS III Harm Procedure/ Test Treatment COR III: No benefit Helpful COR III: W/o Benefit Or Harmful To Patients Or Harmful |
|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses | ■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses | ■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses | ■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses | ■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses |
| LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies | ■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies | Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies | ■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies | ■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies |
| Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care | ■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care | ■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care | ■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care | Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care |
| Suggested phrases for writing recommendations | should is recommended is indicated is useful/effective/beneficial | is reasonable can be useful/effective/beneficial is probably recommended or indicated | may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established | COR III: COR III: No Benefit Harm is not potentially recommended harmful is not indicated causes harm should not be associated with |
| Comparative effectiveness phrases† | treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B | treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B | | performed/ excess morbid ity/mortality other should not be is not useful/ beneficial/ effective associated with associated with access morbid ity/mortality should not be performed/ administered/ other |

Recognition of Potential Health Care Disparities: Hypertension is more prevalent in certain race/ethnicities, especially non-Hispanic blacks, who have the highest age-adjusted prevalence not only in the US but the world. Certain racial groups/ethnicities (non-Hispanic blacks and Hispanic adults) are also known to have poorer control of their hypertension compared to non-Hispanic whites.²⁴⁻²⁶

Collateral Tools & Resources

The following collateral tools and resources support staff execution and performance of the evidence-based guideline recommendations in everyday clinical practice.

Metrics

WCHQ (2015)

- 1. CKD Screening- % of patients age 18-85 years with either diabetes or hypertension (excluding those with CKD and ESRD) who had an eGFR test during the last year.
- 2. Blood Pressure Control in CKD Stages I, II, III- % age 18-85 years with a diagnosis of CKD in stage I, II, or III (excluding those with CKD in stages IV or V or with ESRD) whose most recent blood pressure reading within the last year is controlled to a rate of < 140/90 mmgHg.
- 3. Blood Pressure Control in CKD Stages IV, V- % age 18-85 years with a diagnosis of CKD in stage IV or V (excluding ESRD) whose most recent blood pressure reading within the last year is controlled to a rate of < 140/90 mmHg.
- 4. Blood Pressure Control in Diabetes- % age 18-75 years whose most recent blood pressure reading within the last year is controlled to a rate of < 140/90 mmHg.
- 5. Blood Pressure Control in IVD- % age 18-75 years with a diagnosis of IVD whose most recent blood pressure reading within the last year is controlled to a rate of < 140/90 mmHg.
- 6. High Blood Pressure- % age 18-85 years who have a diagnosis of essential hypertension and whose blood pressure was adequately controlled based on JNC 8 goals: < 140/90 mmHg for patients less than 60 years of age or patients of any age with a diagnosis of diabetes and/or chronic kidney disease; < 150/90 for patients 60 years of age and older without diabetes or chronic kidney disease.

ACO-MSSP (2016)

1. %of patients age 18-85 years who had a diagnosis of hypertension and whose blood pressure was adequately controlled (< 140/90 mmHg) during the measurement period.

Best Practice Alerts (BPA)

Name [####]

eConsults

UWOP ECONSULT TO CARDIOLOGY- HYPERTENSION [5626]

Order Sets & Smart Sets

Advanced Hypertension [5068]; Blood Pressure (Allied Health Visit) [5055]; HTN [5094]; Kidney- Hypertension Clinic [3285

Patient Resources

- 1. Health Facts For You #379- Heart Health: The DASH Diet
- 2. Health Facts For You #4462- High Blood Pressure
- 3. Health Facts For You #7761- Hypertension Medicines- ACE Inhibitors
- 4. Health Facts For You #7762- Hypertension Medicines- ARBs (Angiotensin Receptor Blockers)
- 5. Health Facts For You #7765- Hypertension Medicines- Beta-Blockers
- 6. Health Facts For You #7764- Hypertension Medicines- Calcium Channel Blockers
- 7. Health Facts For You #7763- Hypertension Medicines- Diuretics
- 8. Health Facts For You #7684- Taking Your Blood Pressure at Home
- 9. Health Facts For You #523- Heart Health: Resources for Heart- Healthy Living
- 10. Health Facts For You #6246- The Benefits of Exercise
- 11. Health Facts For You #5117- Potassium Sparing Diuretics
- 12. Health Facts For You #4678- Loop Diuretics (oral)
- 13. Health Facts For You #5041- Thiazide Diuretics (oral)
- 14. Health Facts For You #5817- Your Risk of Heart and Vascular Disease
- 15. Healthwise- Blood Pressure Test: Home
- 16. Healthwise- Blood Pressure: Elevated

17

- 17. Healthwise- Diet: DASH
- 18. Healthwise- Hypertension
- 19. Healthwise- Hypertension: General Info
- 20. Healthwise- Hypertension: Acute
- 21. Health Information- Angiotensin II Receptor Blockers (ARBs) for High Blood Pressure
- 22. Health Information- Angiotensin-Converting Enzyme (ACE) Inhibitors for High Blood Pressure
- 23. Health Information- Antihypertensive Medications, Deciding About
- 24. Health Information- Automated Ambulatory Blood Pressure Monitoring
- 25. Health Information- Beta-Blockers for High Blood Pressure
- 26. Health Information- Blood Pressure Screening
- 27. Health Information- Blood Pressure Monitoring at Home
- 28. Health Information- Blood Pressure Numbers: When to Get Help
- 29. Health Information- Calcium Channel Blockers for High Blood Pressure
- 30. Health Information- DASH Diet Sample Menu
- 31. Health Information- Direct Renin Inhibitors for High Blood Pressure
- 32. Health Information- Diuretics for High Blood Pressure
- 33. <u>Health Information- High Blood Pressure: Should I Take Medicine?</u>
- 34. Health Information- High Blood Pressure in African Americans
- 35. Health Information- High Blood Pressure Treatment Guidelines
- 36. Health Information- Home Blood Pressure Test
- 37. Health Information- Hypertension (High Blood Pressure)
- 38. Health Information- Hypertension: Checking your blood pressure at home
- 39. Health Information- Hypertension: Taking medicines properly
- 40. Health Information- Hypertension: Using the DASH diet
- 41. Health Information- Other Medicines for High Blood Pressure
- 42. Health Information- Prehypertension
- 43. Health Information- Secondary High Blood Pressure

Protocols

Hypertension Lab Ordering – Adult [78]; Antihypertensive Medication Titration [99]
Primary Care Expanded Antihypertensive Medication Management - Adult - Ambulatory [164]
Prescription Renewal Delegation Protocol- UW Health - Adult/Pediatric - Ambulatory [186]

Reporting Workbench Reports

Multi-condition Report

Smart Texts

Home BP Monitoring [34557]; Goal BP [34550]; Buy Home BP Cuff [34555]; BP Check [34546]

Appendix A. Blood Pressure Measurement

It is important to consider all blood pressure measurements in the clinical context of the patient to avoid over- or under-diagnosis of hypertension (e.g., elevated measurement expected during acute injury such as a broken wrist or low blood pressure in the setting of dehydration).

Blood Pressure Measurement in the Office/Clinic Setting^{1,3}

| bioou Fressure Measurement in the | Omecronine octung |
|----------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Step 1: Properly prepare the patient | Have the patient relaxed, seated comfortably in a quiet environment for 5 minutes before beginning BP measurements Make sure patient avoids caffeine, exercise and smoking for at least 30 minutes before the measurement |
| Step 2: Use the proper technique for BP measurements | Support the patient's arm (e.g., resting on a desk) Use correct cuff size and position cuff at level of the heart |
| Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP | At first visit, record BP in both arms. Use the arm with higher value as the reference. If using auscultatory methods, deflate cuff pressure 2 mm Hg per second and listen for Korotkoff sounds to identify SBP and DBP respectively. Consider measuring BP 1 minute and 3 minutes after standing from a seated position in all patients at the first measurement to exclude orthostatic hypotension. |
| Step 4: Properly document acute BP readings | Record SBP and DBP. If using auscultatory technique, record SBP and DBP as onset of first and disappearance of all Korotkoff sounds, respectively, and with the nearest even number. |
| Step 5: Average the readings | Use an average of ≥2 readings obtained on ≥2 occasions to estimate an individual's level of BP |
| Step 6: Provide BP readings to patient | Provide patients the systolic/diastolic BP readings both verbally and in writing |

Out-of-clinic blood pressure readings may be obtained via ambulatory blood pressure monitoring (ABPM) or extended home blood pressure monitoring (HBPM).^{7,27,28}

ABPM provides the average of BP readings over a defined period, usually 24 hours. The USPSTF found convincing evidence that ABPM is the best method for diagnosing hypertension, and considers it to be the reference standard for confirming the diagnosis. Alternatively, good quality evidence suggests that confirmation of hypertension with HBPM may be acceptable.

Following a medication change, patients should obtain blood pressure readings twice a day for 1-2 weeks and report back to provider. Patients who are at goal BP should check BP 1-2 weeks prior to their clinic visit and bring readings/log to clinic for review.³

To accurately record BP at home, patients should avoid smoking, caffeine or exercise within 30 minutes before BP measurement. In addition, patients should have at least 5 minutes of quiet rest before BP measurement. Patient should measure blood pressure twice a day (in the morning before medication and in the evening before supper), taking at least 2 readings that are 1 minute apart.

References

- 1. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens*. 2018;36(10):1953-2041.
- 2. Benjamin EJ, Virani SS, Callaway CW, et al. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. *Circulation*. 2018;137(12):e67-e492.
- Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71(6):1269-1324.
- 4. Myers MG, Kaczorowski J, Dawes M, Godwin M. Automated office blood pressure measurement in primary care. *Canadian family physician Medecin de famille canadien*. 2014;60(2):127-132.
- 5. Weber MA, Schiffrin EL, White WB, et al. Clinical practice guidelines for the management of hypertension in the community: a statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens (Greenwich)*. 2014;16(1):14-26.
- 6. Fitch A, Everling L, Fox C, et al. Prevention and Management of Obesity in Adults. In: Institute for Clinical Systems Improvement; 2013.
- 7. Siu AL, Force USPST. Screening for high blood pressure in adults: U.S. Preventive Services Task Force recommendation statement. *Annals of internal medicine*. 2015;163(10):778-786.
- 8. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. *Lancet (London, England)*. 2016;387(10017):435-443.
- 9. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels updated overview and meta-analyses of randomized trials. *J Hypertens.* 2016;34(4):613-622.
- 10. Wright JT, Williamson JD, Whelton PK, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *The New England journal of medicine*. 2015;373(22):2103-2116.
- 11. Ohkubo T, Asayama K, Kikuya M, et al. How many times should blood pressure be measured at home for better prediction of stroke risk? Ten-year follow-up results from the Ohasama study. *J Hypertens*. 2004;22(6):1099-1104.
- 12. Staessen JA, Den Hond E, Celis H, et al. Antihypertensive treatment based on blood pressure measurement at home or in the physician's office: a randomized controlled trial. *Jama*. 2004;291(8):955-964.
- 13. Celis H, Den Hond E, Staessen JA. Self-measurement of blood pressure at home in the management of hypertension. *Clinical medicine & research.* 2005;3(1):19-26.
- 14. Pickering TG, Miller NH, Ogedegbe G, Krakoff LR, Artinian NT, Goff D. Call to action on use and reimbursement for home blood pressure monitoring: Executive Summary. A joint scientific statement from the American Heart Association, American Society of Hypertension, and Preventive Cardiovascular Nurses Association. *J Clin Hypertens (Greenwich)*. 2008;10(6):467-476.
- 15. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(25 Suppl 2):S76-99.
- 16. Association AD. Professional Practice Committee for the Standards of Medical Care in Diabetes-2016. *Diabetes Care*. 2016;39 Suppl 1:S107-108.
- 17. Martin U, Coleman JJ. Monitoring renal function in hypertension. *BMJ (Clinical research ed)*. 2006;333(7574):896-899.
- 18. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *The New England journal of medicine*. 2001;345(12):861-869.

- 19. Group PC. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet (London, England)*. 2001;358(9287):1033-1041.
- 20. Katzung BG. Basic & clinical pharmacology. 2018.
- 21. Lexi-Drugs Online. Wolters Kluwer Clinical Drug Information, Inc. Accessed 12/10/18.
- 22. Pareek AK, Messerli FH, Chandurkar NB, et al. Efficacy of Low-Dose Chlorthalidone and Hydrochlorothiazide as Assessed by 24-h Ambulatory Blood Pressure Monitoring. *Journal of the American College of Cardiology*. 2016;67(4):379-389.
- 23. Lonn EM, Bosch J, López-Jaramillo P, et al. Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *The New England journal of medicine*. 2016.
- 24. Balfour PC, Jr., Rodriguez CJ, Ferdinand KC. The Role of Hypertension in Race-Ethnic Disparities in Cardiovascular Disease. *Current cardiovascular risk reports*. 2015;9(4):18.
- 25. Ferdinand KC, Yadav K, Nasser SA, et al. Disparities in hypertension and cardiovascular disease in blacks: The critical role of medication adherence. *Journal of clinical hypertension (Greenwich, Conn)*. 2017;19(10):1015-1024.
- 26. Thorpe RJ, Jr., Bowie JV, Smolen JR, et al. Racial disparities in hypertension awareness and management: are there differences among African Americans and Whites living under similar social conditions? *Ethnicity & disease*. 2014;24(3):269-275.
- 27. Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. *The New England journal of medicine*. 2006;354(22):2368-2374.
- 28. Shimbo D, Abdalla M, Falzon L, Townsend RR, Muntner P. Role of Ambulatory and Home Blood Pressure Monitoring in Clinical Practice: A Narrative Review. *Annals of internal medicine*. 2015;163(9):691-700.