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Last Revised

Area Ambulatory
Patient Care

Applicability UMHS-Clinical

**Public** 

References Guideline

### **Ambulatory Adult Hypertension Guideline**

### **Patient population:**

Adults age 18 and older.

### **Objectives:**

(1) Accurately diagnose hypertension. (2) Improve blood pressure (BP) control. (3) Decrease hypertension-related morbidity and mortality (4) Encourage patient's self-involvement. (5) Provide appropriate education and follow-up. (6) Provide cost-effective care.

### Key aspects and recommendations:

#### · Diagnosis

- Although a single, carefully taken blood pressure (BP) reading may predict future cardiovascular risk, for clinical purposes this risk is better identified by taking the mean BP level from recordings over several visits.
- Home and ambulatory blood pressure monitoring helps improve BP control, and identifies "white coat" and "masked" hypertension [IIA]\*.
- If home BP monitoring is used, careful calibration of the BP monitor and thorough patient education are essential.
- Individuals with mean BP > 135/80 should be screened for diabetes [IB].

#### Treatment

- For patients without diabetes or end organ damage, target of BP for
  - Age < 60 years is < 140/90 mm Hg [IA].</li>
  - Age ≥ 60 years is <150/90 mmHg [IB].</li>
- For patients with diabetes or end organ damage (e.g. renal insufficiency, retinopathy, CHF, CAD, PVOD, cerebrovascular disease), appropriate treatment of hypertension

(HTN) provides significant improvements in clinical outcomes [IA]. Recommended BP targets are systolic blood pressure of < 140 mmHg ([IB] for CHF and CAD; [ID] for diabetes and other end organ damage) and diastolic BP goal of < 90 mmHg [IB].

- Treatment of SBP over 160 mmHg is important in reducing CVA and CHF risk [IA].
- Lifestyle modifications to lower BP are important adjuncts to drug therapy [IA].
- Begin therapy with a thiazide diuretic, ACE inhibitor, or long-acting dihydropyridine calcium channel blocker for almost all patients. Add second and third agents as needed to achieve effective BP reduction goals [IA].
  - Specific illnesses may guide the initial and subsequent choice of agents, e.g.:
    - ACE inhibitors (ARB for those unable to tolerate ACE inhibitors) for patients with renal disease, diabetes with either micro- or macroalbuminuria, or LV dysfunction
    - Beta-blockers for those with CAD or CHF.
  - Over 70% of individuals require two or more drugs to achieve BP goals. A fixed combination therapy may be cost-effective. Once a day medications increase compliance and are preferred.

#### \* Strength of recommendation:

I= generally should be performed; II = may be reasonable to perform; III = generally should not be performed.

#### Levels of evidence for the most significant recommendations

A = randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel

### **Clinical Background**

### **Clinical Problem and Management Issues**

#### Incidence

Forty-three million United States adults have hypertension, representing 24% of the U.S. adult population; 20 million have no medication prescribed, and 12 million are on medication but not controlled. Thus, about one out of four hypertensive patients are adequately controlled. Uncontrolled hypertension results in end stage organ damage, which leads to significant mortality and morbidity.

Table 1. Selection of Initial and Subsequent Antihypertensive Drug(s) Based on Concurrent Disease States

| Coexisting<br>Condition                | Disease Specific Agent*   | Relatively<br>Contra-<br>indicated<br>Agents**     | Comments  |
|--|---|--|---|
| Cardiovascular                         |   |  |   |
| Angina                                 | β blocker; ACEI if LV dysfunction                                       |  | Short-acting DHP CCBs are relatively contraindicated for all coronary artery disease.   |
| MI History                             | β blocker, ACEI   |  |   |
| CHF - Systolic                         | ACEI, $\beta$ blocker; ARB if ACEI not tolerated, aldosterone inhibitor | Non-DHP<br>CCB, alpha<br>blocker                   | HYD and nitrate if ACEI and ARB not tolerated β blockers should be used in very low dosages and slowly titrated.  |
| Cardiomyopathy<br>(Hypertrophic)       | β blocker, non-DHP CCB  | diuretic,<br>ACEI & ARB,<br>α1 blocker,<br>DHP CCB | Effects may be less with cardioselective β blockers   |
| Tachycardia<br>(Supra-<br>ventricular) | β blocker, non-DHP CCB  |  |   |
| Bradycardia/<br>heart block            |   | β blocker,<br>Non-DHP<br>CCB, α2<br>agonist        |   |
| Aortic/Mitral<br>Regurgitation         | ACEI, DHP CCB, ARB if ACEI not tolerated                                |  |   |
| Metabolic                              |   |  |   |
| Diabetes                               | ACEI, ARB   |  | Concerns that thiazide diuretics and $\beta$ blockers may worsen glucose control and $\beta$ blockers may mask hypoglycemia have largely been refuted as clinically insignificant                   |
| Gout                                   | losartan is uricosuric  |  | Diuretic-induced hyperuricemia does not require treatment in absence of gout or kidney stones. Even with these, diuretics may be restarted if uric acid is controlled to <6 mg/dl with allopurinol. |
| Renal Disease                          |   |  |   |
| Chronic Renal                          | ACEI, ARB if ACEI not tolerated   | DHP CCB (alone)                                    | Avoid potassium-sparing agents<br>due to increased risk of<br>hyperkalemia. Loop diuretics<br>preferred if creatinine is ≥ 2.5  |

|  |   |                                       | (GFR < 30 ml/min).   |
|--|---|---------------------------------------|--|
| GU   |   |                                       |  |
| Impotence  | ACEI (ARB if ACEI not tolerated), DHP CCB   |                                       |  |
| Bilateral (or<br>equivalent)<br>Renal Artery<br>Stenosis | β blocker, DHP CCB  | ACEI and<br>ARB                       |  |
| Pulmonary  |   |                                       |  |
| Reactive Airway<br>Diseases                              |   |                                       | β blockers should be started at low dose and slowly titrated.                            |
| Psychiatric/<br>CNS                                      |   |                                       |  |
| Headaches<br>(Vascular)                                  | β blocker, non-DHP CCB  |                                       | Verapamil (not diltiazem) useful for cluster headaches and, to lesser extent, migraines. |
| Pregnancy  |   |                                       |  |
|  | methyldopa, β blocker (except<br>atenolol and propranolol),<br>calcium channel blocker,<br>labetalol, hydralazine | atenolol,<br>propranolol<br>ACEI, ARB | ACEI and ARB are absolutely contraindicated.   |
| Drug<br>Interactions                                     |   |                                       |  |
| Cyclosporine<br>HTN                                      | β blocker, DHP CCB  |                                       |  |
| Lithium Usage  | β blocker, DHP<br>CCB, Non-DHP CB   | Diuretics,<br>ACEI and<br>ARB         | Thiazides may increase level by 25-40%. Potassium sparing diuretics have minor effects.  |

| *<br>Antihypertensive<br>Drug Classes   | Abbreviations | Antihypertensive Drug<br>Classes (cont.)                                      | Abbreviations  | **May still be used<br>under certain<br>circumstances |
|---|---------------|---|----------------|---|
| Alpha 1 blocker   | α1 blocker    | Direct vasodilator  | NA             |   |
| Angiotensin converting enzyme inhibitor   | ACEI          | Diuretic  | NA             |   |
| Angiotensin II receptor antagonist  | ARB           | Hydralazine   | HYD            |   |
| Beta blocker  | β blocker     | Isosorbide Dinitrate  | ISDN           |   |
| Centrally acting alpha-2 agonist  | NA            | Non-dihydropyridine calcium<br>channel blocker (e.g<br>diltiazem, verapamil). | Non-DHP<br>CCB |   |
| Dihydropyridine<br>calcium channel<br>blocker<br>(e.gamlodipine,<br>felodipine) | DHP CCB       |   |                |   |

# **Table 2. Antihypertensive Medications: Common Doses and Costs**



| Drug Class              | Brand                |                           | Usual Dosage | Regimer          | าร                        | 30 Da    | y Cost*   |
|-------------------------|----------------------|---------------------------|--------------|------------------|---------------------------|----------|-----------|
| (generic name)          | Name                 |                           |              |                  |                           | Generic  | Brand     |
| Thiazide Diuretics      |                      |                           |              |                  |                           |          |           |
| hydrochlorothiazide     | generic              |                           | 12.5mg.daily | 25mg<br>daily    | 50 mg<br>daily            | \$4      | n/a       |
| chlorthalidone          | generic              |                           |              |                  | 25 mg<br>daily            | \$21     | n/a       |
| Potassium Sparing       | /Thiazide Co         | mbination                 | Diuretics    |                  |                           |          |           |
| amiloride /HCTZ**       | generic              |                           |              | 5 mg/50          | 0 mg daily                | \$12     | n/a       |
| triamterene/HCTZ        | generic              |                           |              | 37.5 mg<br>daily | g/25 mg                   | \$11     | n/a       |
| spironolactone/<br>HCTZ | generic              |                           |              | 25 mg/2          | 25 mg daily               | \$28     | \$43      |
| ACE Inhibitors          |                      |                           |              |                  |                           |          | 1         |
| captopril               | Capoten              |                           | 12.5 mg BID  | 25 mg<br>BID     | 50 mg TID                 | \$23-40  | n/a       |
| benazepril              | Lotensin             | 5 mg<br>daily             | 10 mg daily  | 20 mg<br>daily   | 40 mg<br>daily            | \$5 all  | \$62 all  |
| quinapril               | Accupril             |                           | 10 mg daily  | 20 mg<br>daily   | 40 mg<br>daily            | \$9 all  | \$75 all  |
| lisinopril              | Prinivil/<br>Zestril | 5 mg<br>daily             | 10 mg daily  | 20 mg<br>daily   | 40 mg<br>daily            | \$4-5    | \$42-67   |
| enalapril               | Vasotec              | 2.5 mg<br>daily           | 5 mg daily   | 10 mg<br>daily   | 10 mg BID                 | \$7-11   | \$107-272 |
| fosinopril              | Monopril             |                           | 10 mg daily  | 20 mg<br>daily   | 40 mg<br>daily            | \$8 all  | n/a       |
| trandolapril            | Mavik                |                           | 1 mg daily   | 2 mg<br>daily    | 4 mg daily                | \$16 all | \$52 all  |
| moexipril               | Univasc              |                           |              | 7.5 mg<br>daily  | 15 mg<br>daily            | \$18-30  | \$84-88   |
| ramipril                | Altace               |                           | 2.5 mg daily | 5 mg<br>daily    | 10 mg<br>daily            | \$6-7    | \$92-113  |
| perindopril             | Aceon                |                           |              | 4 mg<br>daily    | 8 mg daily                | 20-22    | \$79-96   |
| ACE Inhibitor / Diur    | etic Combina         | ations                    |              |                  |                           |          | 1         |
| benazepril/HCTZ         | Lotensin<br>HCT      | 5 mg/<br>6.25 mg<br>daily | 10 mg/12.5 r | ng daily         | 20 mg/<br>12.5mg<br>daily | \$15     | \$56      |

| lisinopril/HCTZ    | Prinzide/<br>Zestoretic | 10 mg/<br>12.5 mg<br>daily | 20 mg/12.5 mg daily | 20 mg/25<br>mg daily        | \$4-5     | \$45 all  |
|--------------------|-------------------------|----------------------------|---------------------|-----------------------------|-----------|-----------|
| fosinopril/HCTZ    | Monopril<br>HCT         |                            | 10 mg/12.5 mg daily | 20 mg/<br>12.5 mg<br>daily  | \$38 all  | \$42      |
| quinapril/HCTZ     | Accuretic               | 10 mg/<br>12.5 mg<br>daily | 20 mg/12.5 mg daily | 20 mg/25<br>mg daily        | \$23 all  | \$79-96   |
| Angiotensin Recept | or Blockers             |                            |                     |                             |           |           |
| telmisartan        | Micardis                |                            | 40 mg daily         | 80 mg<br>daily              | \$116 all | \$145 all |
| olmesartan         | Benicar                 |                            | 20 mg daily         | 40 mg<br>daily              | n/a       | \$115-160 |
| valsartan          | Diovan                  | 80 mg<br>daily             | 160 mg daily        | 320 mg<br>daily             | n/a       | \$127-136 |
| irbesartan         | Avapro                  |                            | 150 mg daily        | 300 mg<br>daily             | \$12-15   | \$92-111  |
| candesartan        | Atacand                 | 8 mg<br>daily              | 16 mg daily         | 32 mg<br>daily              | \$86-107  | \$95-128  |
| eprosartan         | Teveten                 | 50 mg<br>daily             | 400 mg daily        | 600 mg<br>daily             | \$98      | \$125     |
| losartan           | Cozaar                  |                            | 100 mg daily        | 50 mg BID                   | \$6-12    | \$113-156 |
| azilsartan         | Edarbi                  |                            | 40 mg daily         | 80 mg<br>daily              | n/a       | \$132     |
| Angiotensin Recept | or Blocker / I          | Diuretic Co                | mbinations          |                             |           |           |
| valsartan/HCTZ     | Diovan<br>HCT           | 40 mg/<br>12.5 mg<br>daily | 80 mg/12.5 mg daily | 160 mg/<br>12.5 mg<br>daily | \$16 all  | \$120-142 |
| telmisartan/HCTZ   | Micardis<br>HCC         |                            | 80 mg/12.5 mg daily | 80 mg/25<br>mg daily        | n/a       | \$145 all |
| candesartan/HCTZ   | Atacand<br>HCT          |                            | 16 mg/12.5 mg daily | 32 mg/<br>12.5 mg<br>daily  | \$60-63   | \$125 all |
| losartan/HCTZ      | Hyzaar                  |                            | 50 mg/12.5 mg daily | 100 mg/<br>25 mg<br>daily   | \$6-8     | \$92-118  |
| olmesartan/HCTZ    | Benicar<br>HCT          | 20 mg/<br>12.5 mg<br>daily | 40 mg/12.5 mg daily | 40 mg/25<br>mg daily        | n/a       | \$160     |

| eprosartan/HCTZ            | Teveten<br>HCT               |                 | 600 mg/12.5<br>daily | mg                    | 600 mg/<br>25 mg<br>daily | n/a       | \$132     |
|----------------------------|------------------------------|-----------------|----------------------|-----------------------|---------------------------|-----------|-----------|
| azilsartan/CTD             | Edarbyclor                   |                 | 40 mg/ 12.5n         | ng daily              | 40 mg/25<br>mg daily      | n/a       | \$120     |
| Calcium Channel Bl         | lockers                      |                 |                      |                       |                           |           |           |
| Non-DHP                    |                              |                 |                      |                       |                           |           |           |
| verapamil SR               | Calan SR                     |                 |                      |                       |                           |           |           |
| diltiazem                  | Cardizem                     | 30 mg<br>QID    | 60 mg TID            | 60 mg<br>QID          | 90 mg TID                 | \$6       | \$104     |
| diltiazem CD               | Cardizem<br>CD<br>Dilacor    | 120 mg<br>daily | 180 mg daily         | 240 mg<br>daily       | 300 mg<br>daily           | \$20-32   | \$328-554 |
| <b>DHP</b> (dihydropyridir | nes)                         |                 |                      |                       |                           |           |           |
| amlodipine                 | Norvasc                      |                 |                      | 5 mg<br>daily         | 10 mg<br>daily            | \$2-4     | \$96-131  |
| felodipine                 | Plendil                      |                 |                      | 5 mg<br>daily         | 10 mg<br>daily            | \$19-29   | \$41-73   |
| nifedipine CC              | Adalat CC<br>Procardia<br>XL |                 | 30 mg daily          | 60 mg<br>daily        | 90 mg<br>daily            | \$15-28   | \$106-203 |
| nisoldipine                | Sular                        |                 | 20 mg daily          | 30 mg<br>daily        | 40 mg<br>daily            | \$239-260 | \$429     |
| isradipine CR              | Dynacirc<br>CR               |                 |                      | 5 mg<br>daily         | 10 mg<br>daily            | \$64-85   | n/a       |
| Calcium Channel Bl         | locker / ACE I               | nhibitor Co     | mbinations           |                       |                           |           |           |
| amlodipine/<br>benazepril  | Lotrel                       | 2.5mg/10        | mg daily             | 5mg/<br>10mg<br>daily | 5mg/<br>20mg<br>daily     | \$10-21   | \$155-158 |
| trandolapril/<br>verapamil | Tarka                        | 1mg/<br>240mg   | 2mg/180mg            | 2mg/<br>240mg         | 4mg/<br>240m all<br>daily | n/a       | \$125 all |
| Aldosterone Antago         | onists                       |                 |                      |                       |                           |           |           |
| spironolactone             | Aldactone                    |                 |                      | 25 mg<br>daily        | 50 mg<br>daily            | \$12-18   | \$69-116  |
| eplerenone                 | Inspra                       |                 |                      | 50 mg<br>daily        | 50 mg BID                 | \$54-128  | \$176-352 |
| Beta Blockers              |                              |                 |                      |                       |                           |           |           |
| atenolol                   | Tenormin                     |                 | 25 mg daily          | 50 mg<br>daily        | 100 mg<br>daily           | \$4-5     | \$50-77   |

| Renin Inhibitors           |                        |               |              |                      |                 |          |           |
|----------------------------|------------------------|---------------|--------------|----------------------|-----------------|----------|-----------|
| Prazosin                   | Minipress              |               | 1mg BID      | 2mg<br>BID           | 5mg BID         | \$17-33  | \$68-160  |
| terazosin                  | Hytrin                 |               | 1mg daily    | 2mg<br>daily         | 5mg daily       | \$4-5    | \$42-43   |
| Doxazosin                  | Cardura                |               | 1mg daily    | 2mg<br>daily         | 4mg daily       | \$17-24  | \$66-70   |
| Alpha Blockers             |                        |               |              |                      |                 |          |           |
| Methyldopa                 | generic                |               | 25 0mg TID   | 500 mg<br>TID        | 1000 mg<br>TID  | \$20-42  | n/a       |
| clonidine                  | Catapres               |               |              | 0.1 TID              | 0.3 TID         | \$8 all  | \$180-275 |
| Centrally-acting alp       | ha-2 agonists          | 3             |              |                      |                 |          |           |
| minoxidil                  | generic                |               |              | 5mg<br>BID           | 20mg BID        | \$11-28  | n/a       |
| Hydralazine                | generic                |               | 25 mg TID    | 50 mg<br>TID         | 100 mg<br>TID   | \$10-25  | n/a       |
| <b>Direct Vasodilators</b> |                        |               |              |                      |                 |          |           |
| carvedilol                 | Coreg CR               | 10mg<br>daily | 20 mg daily  | 40 mg<br>daily       | 80 mg<br>daily  | n/a      | \$158 all |
| nebivolol                  | Coreg                  |               | 3.125 BID    | 12.5-25<br>mg BID    | 25 BID          | \$6-7    | \$90-160  |
|                            | Bystolic               |               | 2.5 mg daily | 10-20<br>mg<br>daily | 40 mg<br>daily  |          | \$78-159  |
| metoprolol succinate       | Toprol XL              |               |              | 100 mg<br>daily      | 200 mg<br>daily | \$27-45  | \$58-93   |
| metoprolol tartrate        | Lopressor              |               |              | 50 mg<br>BID         | 100 mg<br>BID   | \$11-15  | \$134-268 |
| nadolol                    | Corgard                |               | 40 mg daily  | 80 mg<br>daily       | 160 mg<br>daily | \$96-153 | \$127-350 |
| labetalol                  | Trandate/<br>Normodyne |               | 100 mg BID   | 200 mg<br>BID        | 300 mg<br>BID   | \$24-41  | \$40-69   |
|                            | Inderal XL             |               | 60 mg daily  | 80 mg<br>daily       | 120 mg<br>daily | \$27-54  | \$178-356 |
| propranolol                | Inderal LA             |               |              | 40 mg<br>BID         | 80 mg BID       | \$4-5    | \$150-300 |

| Torsemide   | Demadex | 5 mg<br>daily | 10 mg<br>daily | \$11-13 | \$54-60 |  |
|---|---------|---------------|----------------|---------|---------|--|
| (Furosemide –generic or Lasix – has no blood pressure indication, only volume control.) |         |               |                |         |         |  |

<sup>\*</sup> Pricing information for brand drugs, Average Wholesale Price minus 10% from Red Book Online 11/1/13. For generic drugs, Maximum Allowable Cost plus \$3 from BCBS of Michigan MAC List, 11/1/13. \*\* HCTZ = hydrochlorothiazide, CTD = chlothalidone

## Table 3. Errors in Measurement of Blood Pressure

#### **Faulty Technique Patient Related** No effect on BP readings Back not Pseudo- Menstrual phase supported hypertension · Chronic caffeine ingestion Arm not Atrial Phenylephrine nasal spray supported fibrillation · Cuff self-inflation Elbow too · Pain or Examinee and examiner discordance in high anxiety sex or race Elbow too Acute Bell vs diaphragm of stethoscope low smoking Room temperature Missed Acute caffeine Thin shirtsleeve under cuff (growing auscultatory evidence, not universally endorsed) (<30 min.) Feet not on ground Acute ethanol (<2 **Faulty BP Equipment** hours) Talking Gauge during BP inaccurate reading Cuff not correct size

### **Table 4. Classification of Office BP Readings**

| Category               | Systolic | Diastolic |
|------------------------|----------|-----------|
| Normal                 | <120     | and <80   |
| Prehypertension        | 120-139  | or 80-89  |
| Hypertension • Stage 1 | 140-159  | or 90-99  |
| • Stage 2              | ≥160     | or ≥100   |

### Table 5. Reversible Causes of Sustained Elevated Blood Pressure Readings

| Medications:  NSAIDs *  oral contraceptive agents  glucocorticoid or mineralocorticoid steroids | Medications (continued): | <ul> <li>Lifestyle factors</li> <li>alcohol &gt; 2<br/>drinks/day</li> <li>sedentary<br/>lifestyle</li> </ul> | • High sodium (esp. elderly or African-American) |
|---|--------------------------|---|--|
| * interferes with antihypertensive medications  |                          | <ul><li>Illicit drugs</li><li>cocaine</li><li>amphetamines</li><li>anabolic<br/>steroids</li></ul>            | Associated Conditions  • Sleep apnea             |

## **Rationale for Recommendations**

Recommendations are organized under headings for:

- · Diagnosis of hypertension
- · Initial evaluation of newly diagnosed patient
- Treatment of hypertension
- Monitoring blood pressure control

### **Diagnosis of Hypertension**

**Performing BP measurement.** BP readings need to be performed accurately to provide useful information. BP in the office should be checked after 5 minutes of sitting quietly in a chair, with feet on the floor, and arm supported at the heart level, and the results recorded on the medical record. Standardizing the use of the same arm by all staff can facilitate comparisons for sequential measurement. The choice of which arm does not matter if at the initial measurement there are no differences between blood pressures taken on both sides. Caffeine, exercise, and smoking should be avoided for at least 30 minutes prior to measurement. (See Appendix for detail about devices and proper technique.) Patients should be informed of the readings, interpretation and necessary follow-up if indicated.

**Frequency of BP screening.** Frequency depends on patient risk status regarding hypertension.

- If **normotensive** (<120/80), at least every 2 years (current expert opinion). However one should consider BP measurement for every adult visit.
- If risk factors, at least annually.

Although a single, carefully taken BP reading may predict future cardiovascular risk, risk is better identified by taking the mean BP level from recordings over several visits.

**HTN classification and follow-up assessment.** The average initial BP readings should be staged according to JNC 7 expert opinion guidelines (Table 4).

For prehypertension (120-139 / 80-89 mm Hg), measure BP annually.

If the BP average is ≥140/90, consider assessing for and correcting the reversible causes of hypertension (Table 5). Aortic regurgitation may be a cause of isolated systolic hypertension.

**BP monitoring**. BP can be monitored at home in two ways.

- Home blood pressure monitoring (HBPM) Patient or caregiver records blood pressures at home with a blood pressure cuff. This requires knowledge and training in proper technique.
   Upper arm BP cuffs are preferred, since wrist and finger monitors are not reliable. Proper technique and calibration of home BP cuffs should be verified in a clinic setting if HBPM is to be utilized for clinical decision making.
- Ambulatory blood pressure monitoring (ABPM) Automated cuff sent home from the clinic, worn for a pre-specified period of time (usually 24 hours). It is expensive, but is reliable and has been shown to be an independent predictor of cardiovascular morbidity and mortality when added to office based BP measures.

HBPM and ABPM identify patients whose BP at clinic visits differs from BP outside the office. They may also be useful in resistant hypertension.

- White coat hypertension (WCH) refers to patients with elevated BP at office visits, but normal BP outside the office. This condition is common (>20% of patients with elevated BP) and may result in overtreatment if unrecognized. Both HBPM and ABPM can help identify WCH. Documentation of WCH results in decreased drug cost, with no change in LV mass, cardiovascular outcomes, or well being. WCH may carry a higher long term risk of hypertension, but at least one study has not shown an increase in risk.
- Masked hypertension refers to patients with target BP at clinic, but elevated home BP. This
  condition may be nearly as common as WCH. These patients may have LVH or other target
  organ damage despite normal office BP. Both HBPM and ABPM can help identify masked
  hypertension, resulting in more aggressive medication regimens and improved cardiovascular
  outcomes.

Currently, reimbursement for ABPM by Medicare is covered only for suspected WHC, defined by 3 or more office visit BPs >140/90 mm Hg, at least two documented BPs outside the office <140/90 mm Hg, and no evidence of target organ damage.

### **Initial Evaluation of Newly Diagnosed Patients**

History. Once the diagnosis of hypertension is made, the clinician should determine by history and

physical examination whether the patient has evidence suggesting secondary hypertension, as well as other cardiovascular risk factors. The history should focus on the following:

- Cardiovascular review of systems, including known duration of hypertension
- Symptoms or previous personal/family history that helps to identify secondary hypertension
- Presence or absence of other cardiovascular risk factors
- Psychosocial and environmental factors that may influence BP control
- Medications being taken

**Physical examination.** Based on expert opinion the JNC 7 recommendations for the physical examination of hypertensive patients are:

- Two or more BP measurements separated by 2 minutes with the patient either supine or seated
- Verification in the contralateral arm
- Body mass index (BMI), calculated by weight (kg)/ [height (m)]<sup>2</sup> (possibly waist circumference)
- Funduscopic examination for arteriolar narrowing, nicking, hemorrhages, exudates, etc.
- Neck examination for carotid bruits, distended veins, or enlarged thyroid
- Heart/lung examination
- Abdominal examination for enlarged kidneys, masses, distended bladder, renal bruits, aortic aneurysm
- · Extremity examination for pedal pulses and edema
- Neurological assessment, particularly for signs of cerebrovascular disease

#### Laboratory tests and diagnostic procedures.

**Essential hypertension**. Consider the following tests before therapy is initiated. Screening for diabetes is particularly important.

| Potassium     | • Urinalysis |
|---------------|--------------|
| Blood glucose | Lipid panel  |
| Creatinine    | • EKG        |
| Calcium       | Hematocrit   |

**Secondary and/or complicated hypertension**. Consider other testing and/or referral when secondary hypertension or complicated hypertension (does not respond to usual measures, pre-existing controlled hypertension becomes uncontrolled, sudden onset of hypertension, and/or malignant hypertension) is suspected. History and the above laboratory screening may be helpful in detection.

Secondary hypertension and complicated hypertension etiologies include:

Chronic or acute kidney disease

- Renovascular hypertension
- · Sleep apnea
- · Medications or illicit drugs
- · Chronic kidney disease
- · Renovascular disease
- · Primary aldosteronism
- · Coarctation of the aorta
- · Chronic steroid therapy and Cushing's syndrome
- · Pheochromocytoma
- · Thyroid or parathyroid disease

Medications and other reversible causes are described further in Table 5.

**Risk Stratification.** The risk of cardiovascular disease in patients with hypertension is determined not only by the level of BP but also by the presence or absence of target organ damage:

#### Current diagnoses:

- LVH
- · CHF
- Angina
- Stroke or TIA
- Chronic kidney disease (includes microalbuminu-ria and proteinuria)
- · Peripheral arterial disease
- Retinopathy

#### History of:

- MI
- CABG
- CVA
- TIA

#### Other risk factors:

- Smoking
- Obesity (BMI≥30 kg/m²)
- Physical inactivity
- Dyslipidemia
- Diabetes
- Estimated GFR < 60 mL/min)</li>
- Age (>55 for men, >65 for women)
- Family history of premature cardiovascular disease (men <55 or women <65) disease</li>

### **Treatment of Hypertension**

**Treatment BP goal.** The goal depends on the presence of other risk factors.

**Goal if no risk factors**. Clinical trial data reviewed by the Seventh Report of the Joint National Committee (JNC 7) support reducing SBP to < 140 mmHg and DBP to < 90 mmHg. This has been confirmed by the panel members of the Eighth Joint National Committee for those aged below 60 years. For those aged 60 years and over, the latter recommends reducing SBP to <150 mmHg and DBP to <90 mmHg. A sustained decrease in SBP of 10 mm Hg or DBP of 5-6 mm Hg for patients with hypertension decreases the risk of

stroke by 35-40% and decreases the chance of coronary heart disease by 20-25%.

**Goal if diabetes or end organ damage**. The goals for blood pressure treatment in diabetes have been evaluated in several randomized trials.

For diastolic blood pressure, a target of 90 and possibly 80 mmHg provides marked benefits. Caution is suggested when diastolic BP falls below 70 mmHg. Mortality increased when patients with diabetes had diastolic BP below 70.

Systolic blood pressure has not been evaluated as rigorously. For patients with elevated blood pressure and other end organ damage (e.g. retinopathy, CHF, CAD, PVOD, cerebrovascular disease), aggressive treatment of HTN provides significant improvements in clinical outcomes. Few studies have targeted or achieved systolic pressures below 140 mmHg. However, the available data suggest that a systolic target of < 140 mmHg is reasonable.

**Treatment selection.** While lifestyle modification is always recommended, the addition of medications depends on disease severity and other risk factors.

Patients with prehypertension but without risk factors or target organ damage (TOD) should have lifestyle modification recommended.

Patients with Stage 1 hypertension and no other risk factors can be recommended for a trial of lifestyle modification for up to 12 months. With recent evidence suggesting that early treatment to goal blood pressure levels may attenuate the expression of hypertension and improve clinical outcomes, more experts are recommending both medication and lifestyle modification initially, with plans to reduce or eliminate drug therapy as lifestyle goals are achieved.

Patients with Stage 2 hypertension or with either diabetes, or any TOD should have drug therapy in addition to lifestyle modification. Initial combination therapy with a thiazide plus an additional agent is useful (or other combinations). Additionally, patients that are felt to have resistance to prior therapy or possibly less compliant may achieve better control with initial combination therapy.

**Lifestyle modifications.** Clinical trials have shown that lifestyle modifications can lower BP. Lifestyle modifications are best initiated and sustained through an educational partnership between the patient and a multidisciplinary health care team. While team members may vary by clinical setting, behavior-change strategies should include nutrition, exercise, and smoking cessation services.

**Weight reduction and maintenance.** Many individuals who are both overweight and hypertensive can lower their BP with weight reduction. The effect is usually evident in the early stages of weight loss and frequently occurs with only a ten pound reduction in weight.

**Modification of dietary sodium**. The current recommendation is to lower sodium intake to less than 2.4 grams per day. Encourage patients to lower their sodium intake by not adding salt to their food or in cooking; limiting processed, convenience, or fast foods; and reading food labels for sodium content. Water softeners contribute sodium to the water and may be significant.

**Moderation of alcohol intake**. Patients should not exceed a daily alcohol intake of 1 ounce of ethanol. This amount is contained in 2 ounces of 100 proof whiskey, 8 ounces of wine, or 24 ounces of beer.

**Adequate physical activity**. Regular aerobic physical activity may be beneficial for both prevention and treatment of hypertension. It may enable weight loss, improve functional health status, and diminish mortality and risk for cardiovascular disease. Thirty to forty-five minutes of brisk walking three or four times weekly is adequate and effective. Resistive isotonic activities as sole exercise are not recommended to lower BP in hypertensive patients.

**Tobacco avoidance**. All smokers should be offered assistance in smoking cessation and strongly advised to quit.

**Potassium**. High dietary potassium may protect against hypertension development. Hypokalemia may exacerbate hypertension and induce ventricular arrhythmia. Potassium sparing diuretics and ACE inhibitors retain potassium and magnesium whereas simple potassium chloride replacement does not replace magnesium.

Other dietary factors. Calcium supplementation may result in a very small reduction in BP (systolic -1.27 mm Hg; diastolic -0.24 mm Hg). No definitive data suggest magnesium supplementation lowers blood pressure. Dietary fats have no effect on blood pressure. Acute caffeine ingestion may elevate BP; however, tachyphylaxis to chronic ingestion attenuates this effect. A diet low in sodium and saturated fats, and high in vegetables, fruits, and low fat dairy products has been shown to lower blood pressures (the "DASH" diet).

**Drug therapy.** Hypertension is a chronic disease. Thus, the choice of which medication(s) to prescribe has long term implications.

**Drug selection.** Data from a very large multicenter RCT supported by smaller studies demonstrate that moderate-to-high dose thiazide diuretics (chlorthalidone 25 mg/day) are as good as any other class of agents in reducing cardiovascular adverse outcomes, and superior in secondary outcomes such as stroke and CHF. Most patients will require two or more drugs to achieve control, and a few will not tolerate thiazides. The choice of additional or alternative medication should be individualized to achieve the target BP and the following goals:

- · Once daily administration
- · Reduction in CV complications demonstrated in clinical trials
- Choice of agent(s) that also treat concurrent conditions
- Least potential disruptive side-effects based on concurrent conditions or lifestyles
- Least expensive (both in pharmaceutical and laboratory monitoring costs)
- Fixed combination therapy can be more cost-effective and may improve compliance. Some patients may benefit from beginning with fixed combination therapy (e.g., Stage 2 hypertension or patients resistant to monotherapy in the past).

All agents within a class have similar physiological action, except calcium channel blockers and beta blockers, which have sub-classes with different physiological effects. If monotherapy is not effective in reaching the BP goal, the addition or substitution of a different class with different physiological action is indicated. Combining medications from the same class is not effective. Table 2 shows costs of drug treatment for various antihypertensive agents.

Diuretics, beta blockers, ACE inhibitors, and long-acting dihydropyridine CCBs have been shown in

randomized controlled trials to reduce cardiovascular morbidity and mortality. The ALLHAT study was a large multicenter direct comparison RCT designed to determine if the older or newer agents are more effective in prevention of cardiovascular morbidity and mortality. It compared treatment starting with a thiazide diuretic, an ACE inhibitor, a long-acting dihydropyridine CCB, and an alpha-blocker. Beta blockers and centrally-acting agents were used as the second step drugs; almost three-fourths of patients required two or more drugs. Beta blockers were the most commonly used second agent. The alpha blocker arm was discontinued early because of an excess of adverse outcomes. The other agents performed equally in primary outcome (coronary endpoints), but the thiazide (chlorthalidone), in moderate to high doses, was superior in secondary outcomes (stroke and CHF). This finding was consistent across age and race, and in all subgroups including patients with diabetes, coronary disease, and hyperlipidemia.

Existence of other risk factors, co-morbidities, and concern for untoward drug effects may influence initial drug selection. ACE inhibitors, ARB's, and CCB's may be initial options. Beta blockers are not preferred as initial therapy in the elderly unless compelling other conditions exist, e.g., coronary artery disease (see Table 1). Recent meta-analyses suggest that beta blockers may be less effective in stroke reduction when compared to other classes of antihypertensive therapy. Beta blocker usage for HTN may be deferred unless CAD or CHF exists.

For African Americans without DM or CKD, a thiazide diuretic and/or CCB may be considered as first and second line antihypertensive medications. However, an ACEI or ARB may be more appropriate for African Americans with DM and/or CKD with estimated GFR of <60 ml/min and also for those where a clinical suspicion of milder CKD exists, e.g., positive for microalbuminuria. This recommendation differs from JNC 8, which recommends a thiazide diuretic or CCB as initial antihypertensive therapy for African Americans, including for those with diabetes.

No clear guidelines exist regarding whether specific drug combinations impart superior clinical outcomes (e.g., ACEI/CCB vs. ACEI/diuretic. Large, well-designed trials (ACCOMPLISH with benazepril/amlodipine vs. benazepril/HCTZ, ACCELERATE with aliskiren and amlodipine vs. either alone) raise the possibility that a combination of a blocker of the renin-angiotensin system and calcium channel blocker may be superior to other combinations and single agents. Currently, the combinations of ACEI/ARB, ACEI/direct renin inhibitor (DRI), or ARB/DRI are not recommended in HTN management.

**Diuretics**. Thiazide diuretics have traditionally been the initial treatment for most patients with hypertension. Although the trials that showed a decrease in cardiovascular morbidity and mortality used moderate to high dose diuretics, higher dosages of thiazide diuretics have shown only minimal improvement in BP control. Consequently, the maximum suggested dosage of thiazide diuretics has been lowered in order to avoid metabolic side-effects. The range of hydrochlorthiazide is 12.5mg to 50 mg each morning. In patients more vulnerable to side effects, such as the elderly, even this range should be approached with caution. The most studied thiazide is chlorthalidone, though hydrochlorothiazide is the predominant prescription thiazide in the USA.

Side effects. Thiazide diuretics increase the frequency of sexual dysfunction in men and women and initially may cause interruptions in daily routine for micturition. Thiazides cause a short-term increase in LDL cholesterol; however, long-term trials have shown minimal change and outcome studies show no clinical impact. Thiazides slightly increase risk for diabetes (ALLHAT). While small changes in LDL and glycemic control are not contraindications, the clinical impact of these metabolic aberrations has yet to be

elucidated. Thiazides can increase uric acid and precipitate attacks of gout. Hypokalemia is uncommon at usual (12.5-25 mg) doses but occurs relatively often at doses of 50 mg or more.

**Loop diuretics.** These diuretics are preferred for individuals with renal impairment (serum creatinine  $\geq 2.5$  mg/dl) and individuals allergic to thiazide diuretics. Loop diuretics are useful for reducing preload, which contributes to hypertension in renal-impaired individuals. Hypokalemia is less common due to the renal impairment, but should still be monitored. Loop diuretics are not as likely as thiazide diuretics to cause gout.

Angiotensin converting enzyme (ACE) inhibitors. As a class, ACE-inhibitors have similar actions and side effects, with the only major difference being duration of action. ACE inhibitors reduce BP with generally few side effects and slow the decline of renal function in most diseases. The renoprotective effect may be augmented when combined with angiotensin receptor blocker. Ramipril was shown in a randomized controlled trial to decrease cardiovascular events in hypertensive and normotensive individuals with systolic heart failure over placebo. However, newer trials have not shown renin-angiotensin blockade to be superior to other medications in decreasing morbidity and mortality. Onset of diabetes was not prevented by ramipril in a study directly addressing this issue.

Side effects. Angioedema is a rare side effect (0.1-0.7%), which may be life-threatening and may occur at any point in the treatment. The incidence may be higher in African Americans. Although renal artery stenosis per se is not a contraindication for ACE therapy, renal impairment may occur in patients with bilateral renal artery stenosis or unilateral renal artery stenosis with a single kidney. All in this class induce cough equally, which may be disabling enough with some patients to result in the need to discontinue the drug; cough occurs more often in women. **This class is contraindicated in pregnancy.** 

Angiotensin II receptor antagonists (ARB) displace angiotensin II (All) from its type 1 receptors. Losartan and irbesartan have been shown in randomized, double-blind trials in diabetics with microalbuminuria or azotemia to decrease the development of frank proteinuria or progression to renal failure requiring dialysis or transplantation. In patients who have systolic heart failure and are intolerant to an ACEI because of cough, ARBs are recommended.

Side effects. Angioedema has been rarely reported with Losartan, but has occurred in patients with prior angioedema on ACE inhibitors. Losartan has a uricosuric effect (i.e. increases excretion of uric acid, lowering concentration in blood) that is unique compared to others in this class. Losartan may be less efficacious compared to others in this group at lowering BP and should be used twice a day. **This class is contraindicated in pregnancy.** 

**Calcium channel blocking (CCB) agents**. There are three classes of calcium channel blocking agents based on different calcium channel receptors, all with different physiological effects and side effects: verapamil, diltiazem, and dihydropyridines. All long acting DHP CCB's have been shown to reduce blood pressure and cardiovascular events.

Of the dihydropyridine CCB's, the longer-acting agents (e.g. amlodipine, felodipine, nislodipine) make single daily dosing possible. These drugs provide the most reliable and significant blood pressure reduction in most patient subtypes. They are particularly effective in stroke reduction and have been shown to reduce overall CVD risk. The short-acting agents are not indicated for hypertension.

Some effects with specific diseases include:

- Acute coronary syndrome. Short-acting dihydropyridines should be avoided in the first 24-48 hours of an acute coronary syndrome.
- Chronic kidney disease. Dihydropyridines should be avoided as a single agent for patients with microalbuminuria, as they will worsen protein loss and renal function, but may be used in combination with ARB or ACE inhibitors.
- Chronic CAD. Verapamil has shown to be as effective as a beta-blocker in patients with CAD or remote history of MI. The long-acting dihydropyridine agents may be used in patients with angina; however, some feel that they only should be used when combined with a beta blocker.
   All CCB's can be used in hypertensive patients with chronic CAD to reduce anginal episodes
- · Aortic regurgitation. Nifedipine may be useful in hypertensive patients with aortic regurgitation.

Side effects. Edema may occur and is more pronounced with the dihydropyridine agents.

Bradycardia is a side effect of verapamil and diltiezem, but renders them useful agents in the treatment of atrial fibrillation/SVT). Verapamil has more pronounced bradycardia effects and often results in constipation. Verapamil and diltiazem may increase risk for statin myopathy (cytochrome 3A4 inhibition).

**Aldosterone inhibitors.** Spironolactone and eplerenone are used in certain conditions associated with hypertension, such as resistant hypertension, hyperaldosteronism, and potassium wasting. However, when used in patients with chronic kidney disease, or concurrently with potassium sparing agents (ACEI, ARB, triamterene), they carry significant risk for **life-threatening hyperkalemia**. Combination therapy is generally restricted to patients with systolic heart failure, and requires close follow-up. Gynecomastia and breast pain are common side effects with spironolactone, causing discontinuation in about 10%.

**Beta blockers** have been shown to reduce cardiovascular morbidity and mortality in controlled clinical trials for both diastolic and isolated systolic hypertension. However, one study showed that diuretics are superior to beta-blockers for stroke reduction, and another showed that losartan is superior to beta blocker for CVD reduction. The results of three meta analyses suggest that other anti-hypertensive agents are superior to most beta-blockers for initial therapy. In addition, atenolol has poorer outcomes when compared to other beta-blockers (an excess stroke risk of 17%).

Beta blockers are indicated for patients with coronary disease or CHF unless specific contraindications or documented intolerance exists. Certain beta blockers (e.g., carvedilol) also have alpha blocking properties and are useful for maintenance therapy of heart failure. Discussion regarding other properties of beta blockers, such as B1 selectivity and lipid solubility, are beyond the scope of this guideline.

While a target heart rate of <60/minute has been suggested in using beta blockers for patients with systolic heart failure, no target has been established for patients with uncomplicated hypertension.

Side effects. Occasionally fatigue and uncommonly impotence are side effects at the recommended low doses. Beta-1 blockers produce the same dramatic reduction in angiotensin II levels as ACE inhibitors, and the two agents together have an additive effect. Though beta blockers may raise triglycerides and lower HDL cholesterol, these effects have not been found to be clinically significant in outcome studies.

**Renin inhibitors** are a novel way of blocking the renin-angiotensin-aldosterone system (RAAS). The first drug in this class is aliskiren. The drug has been shown to lower blood pressure alone or in combination

with other antihypertensives, but its effects on clinical outcomes is unknown. Aliskiren should be used as a fourth line agent in patients who have failed standard therapy.

Side Effects. As with other RAAS agents, aliskiren can cause an increase in serum creatinine and potassium especially is used in combination with an ACE inhibitor or ARB. **This class is contraindicated in pregnancy.** 

Peripheral alpha blockers. Alpha blockers should not be used as initial therapy but may be added to a thiazide or other outcome-improving agent for additional BP control or when prostatism treatment is desired.

Side effects: Alpha blockers may cause first dose syncope, so are generally started at bedtime and slowly titrated up in dose. They may cause fluid retention and edema. The ALLHAT study showed a 25% increase in cardiac events in the doxazosin vs. chlorthalidone group.

**Centrally-acting alpha-2 agonists** are less often used due to their side-effects. They have no evidence of outcome benefit. Methyldopa remains a first line agent in pregnancy.

*Side effects.* May induce bradycardia; dry mouth and sedation are common. Rebound hypertension may occur with sudden discontinuation of clonidine.

**Direct vasodilators.** These drugs are fourth line agents for essential hypertension and should be used in patients who have failed standard therapy. Direct vasodilators induce reflex tachycardia and thus should be combined with a beta blocker or non-dihydropyridine calcium channel blocker. Due to increased fluid retention, they should also be combined with a diuretic. These agents have not been shown to reduce left ventricular hypertrophy. They are third or forth line agents, sometimes useful in refractory hypertension.

Hydralazine may produce a lupus erythematosus-like syndrome; the syndrome is extremely rare when the daily dose is less than 200 mg. Side effects include headache, palpitations, anorexia, and nausea. At least twice daily dosing requirements limit the usefulness of this drug. Hydralazine has shown benefit in CHF when combined with a nitrate.

Minoxidil is effective in treating the severest forms of hypertension, although it is used less frequently today because ACE inhibitors and calcium channel blockers may be as effective. Side effects include hypertrichosis and fluid accumulation in serous cavities, including the pericardium.

### **Monitoring Blood Pressure Control**

No studies demonstrate the most appropriate monitoring of BP and follow-up. The following is a consensus opinion of the guideline team.

**Blood pressure measurement.** All patients who have been diagnosed with hypertension should be taught the technique of home BP monitoring, assuming that there are no cognitive deficiencies that would preclude the technique. A handout about the purchase and proper technique may be used. Patients should purchase an electronic, digital home BP cuff. The proper cuff size should be indicated to the patient by the healthcare provider. Automatic (self-inflating) and non-automatic electronic monitors are equally effective, with the non-automatic being cheaper but more labor intensive.

Patients should be instructed to take their BP daily, upon awakening and before dinner (other times as

necessary), until the BP is controlled to the targeted range discussed above. After BP control is achieved, BP may be obtained monthly. The BP readings should be recorded on a BP monitoring sheet and sent or brought to the physician. The wrist and finger units, although easy to use, are not reliable for monitoring blood pressure.

**Prehypertension.** Follow at least annually.

**Stage 1 hypertension.** Once antihypertensive therapy is initiated, most patients should return for follow-up and adjustment of medications at monthly intervals or less until the BP goal is reached. The effect of an antihypertensive agent on BP is typically stabilized in < 2 weeks. At each visit, BP control, adverse medication effects, patient adherence, and new target organ damage should be assessed. If after 1-3 months the BP does not reach the targeted goal:

- 1. Ensure that the patient is believed to be taking the medication as prescribed.
- 2. Ensure that the dose of the medication is adequate.
- 3. Reconsider reversible causes.
- 4. Add a second drug from another class if necessary to reach goal.

After BP is at goal and stable, follow-up visits can usually be at 3- to 6-month intervals. A randomized controlled trial showed that for stable patients that patient outcomes were equivalent for follow-up intervals of 3 and 6 months. No evidence currently exists regarding the equivalence of 6-month and 12-month intervals. Serum potassium and creatinine should be monitored at least annually. Monitoring for microalbuminuria may also be useful.

**Stage 2 hypertension.** Follow-up is generally similar to that for medical therapy for Stage 1 hypertension, except more frequent visits may be necessary, e.g., more frequently than monthly intervals initially to adequately control BP.

**Additional considerations.** Most patients will require two or more medications to reach goal. Fixed dosage combination antihypertensive medications may simplify therapy and improve adherence, but generic individual agents are usually less costly.

If blood pressure is uncontrolled after persistent attempts to do so, or multiple (>3) drugs are needed, consider referral to a hypertension specialist.

Intolerance to multiple medications may be an indication of over-treated hypertension due to a significant white coat effect. Ambulatory or home BP monitoring may then be helpful.

**Controlled BP.** Once BP is controlled, office visits every 3-6 months are appropriate. At any time, for any stage of hypertension, consultation with a clinician skilled in the management of hypertension should be considered if BP cannot be controlled adequately, patient compliance is poor, or there is difficulty identifying exacerbating conditions or medications.

**Resistant hypertension.** Resistant hypertension is the failure to reach goal BP in patients who are adhering to full doses of an appropriate 3-drug regimen that includes a diuretic. After excluding potential identifiable causes of hypertension (Table 5), clinicians should explore reasons why the patient is not at the goal BP. Particular attention should be paid to diuretic type and dose in relationship to renal function because thiazide-type diuretics lose effect once the GFR falls <30 ml/min. Consultation with a

hypertension specialist should be considered if goal BP cannot be achieved.

### **Special Considerations**

**Hypertension and Pregnancy**. The use of anti-hypertensives in pregnancy must consider fetal well-being. Treating uncomplicated Stage 1 hypertension is often not necessary in otherwise low-risk women with normal renal function and no other target organ disease. These women should be closely followed during pregnancy. Pre-eclampsia or other pregnancy-induced hypertension should be treated by a physician experienced in managing these diseases.

Women considering pregnancy, who are hypertensive and require treatment, should be on antihypertensive medication ideally three to six months prior to conception. Medications for treating significant hypertension during pregnancy, in order of preference, are:

- 1. Methyldopa the drug with the longest experience Problems with this medication include frequent side effects and the need to dose multiple times a day.
- 2. Beta-blocker with or without diuretic (avoiding atenolol, which may be associated with intrauterine growth retardation) are relatively popular and the first choice of some.
- 3. Labetalol
- 4. Calcium channel blockers

Diuretics are also acceptable to use.

Contraindicated in pregnancy are ACE inhibitors, ARBs, and renin inhibitors.

**Ongoing diabetes screening.** While screening for diabetes is recommended when a mean BP > 135/80 is first identified, for patients with hypertension an optimal interval for subsequent screening for diabetes is not known. The American Diabetes Association (based on expert opinion) recommends screening at 3-year intervals.

**Elderly patients.** The benefit of treating hypertension in older adults has been well established. The HYVET study confirmed substantial reduction in cardiovascular risk and mortality from treating hypertension in patients age 80 and older, to a target of 150/80 mmHg.

No clear benefit has been shown for systolic BP targets lower than < 150 (e.g., < 140). Lowering diastolic BP to < 65 is a theoretical risk. No clear evidence exists to determine the relative risk of achieving a systolic BP < 150 if that treatment also lowers diastolic BP to < 65.

Orthostasis is a common problem in the elderly and monitoring standing and supine BP is important during treatment to identify this.

Antihypertensive choice in the elderly is similar to other age groups. Beta blockade should be avoided unless there is a compelling indication such as CAD or CHF. Lower initial antihypertensive drug doses and slower titration is generally recommended.

### **Related National Guidelines**

This guideline is consistent with JNC 7, updated with results of major trials subsequently (see

references). It is consistent with the report from the panel members appointed to JNC 8, except for African Americans without evidence diabetes or CKD, this guideline recommends the same initial drugs as for other patients without evidence of diabetes or CKD.

### **Strategy for Literature Search**

Preliminary evidence was identified using literature considered relevant in JNC 7 (see annotated references). That report utilized literature searches of the preceding reports and added a systematic search of literature from January 1997 through April 2003.

In 2007 a search of literature from 2003–2007 was performed that was also utilized to develop the 2009 version of this guideline. That search was conducted on Medline prospectively using the major keywords of: hypertension, human adults, English language, clinical trials, guidelines, and published from 1/1/03 through 5/1/07. Terms used for specific topic searches within the major key words included: alpha 1 blocker, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonist, beta blockers (selective and non-selective), calcium channel blockers (dihydropyridine and non-dihydropyridine forms), centrally acting alpha-2 agonist, diuretics (thiazide and non-thiazide, loop, potassium-sparing), vasodilator (direct), avoidance (alcohol, stress, tobacco), blood pressure monitoring (ambulatory, home), dietary (caffeine, calcium, garlic, magnesium, onion, potassium, sodium), exercise, disease-based management (stroke, coronary artery disease, cardiac, heart failure, arterial fibrillation, peripheral vascular disease, diabetes, chronic kidney disease, metabolic syndrome), and resistant hypertension.. Detailed search terms and strategy available upon request.

In 2013 the full literature search was deferred while waiting for the search results of JNC 2013 ("JNC 8"). However, expert member of the team identified three topics for which important new evidence had been published and systematic searches were performed on those topics. The search was conducted on Medline prospectively using the major keywords of: hypertension, human adults, English language, guidelines, clinical trials, cohort studies, and published from 1/1/03 through 6/1/13. Terms used for specific topic searches within the major key words included: combination of 'ACE (angiotensin converting enzyme) inhibitors and ARB (angiotensin receptor blockers), combination of ARB and DRI (direct renin inhibitors), and patients age  $\geq 65$  years (older/elderly) and target blood pressure and treatment.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent information available to expert members of the panel, including abstracts from recent meetings and results of clinical trials. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

### **Measures of Clinical Performance**

National programs that have clinical performance measures for care for hypertension include the following.

Centers for Medicare & Medicaid Services:

- Physician Quality Reporting Measures for Group Practice Reporting Option (GPRO)
- Clinical Quality Measures for financial incentives for Meaningful Use of certified Electronic Health Record technology (MU)
- Quality measures for Accountable Care Organizations (ACO)

These program's clinical performance measures for hypertension are summarized below. When programs have measures, the measures are generally similar, although specific details vary (e.g., population inclusions and exclusions).

**Blood pressure measurement.** The percentage of patient visits for patients aged 18 years or older with a diagnosis of hypertension who have been seen for at least 2 office visits, with blood pressure recorded. (MU, ACO, GRPO)

**Controlling high blood pressure.** The percentage of patients aged 18–85 years with a diagnosis of hypertension and whose blood pressure was adequately controlled (< 140/90) (MU, ACO, GRPO)

**Hypertension: Improvement in blood pressure.** The percentage of patients aged 18-85 years with a diagnosis of hypertension whose blood pressure improved during the measurement period (MU, ACO, GPRO)

Preventive care and screening: Screening for high blood pressure and follow-up documented.

Percentage of patients aged 18 years and older seen during the reporting period who were screened for high blood pressure AND a recommended follow-up plan is documented based on the current blood pressure reading (MU, ACO)

Additional measures regarding care for hypertension exist for patients with specific medical conditions, e.g., diabetes, coronary artery disease.

### **Disclosures**

University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

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### **Review and Endorsement**

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Medicine, and Cardiology. The final version was endorsed by the Clinical Practice Committee of the University of Michigan Faculty Group Practice and the Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers.

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

### APPENDIX. Standardized Blood Pressure Measurement

#### **Types of Measuring Devices**

- **Aneroid manometer** could be used. However, the deflated cuff should read exactly zero, and it should be calibrated at least yearly, unless used frequently and then yearly.
- Electronic manometers should be calibrated twice a year if used weekly, or once a year if used less often.
- The cuff should be the appropriate size for the measured arm, and each cuff should have

markers to note the proper selection.

#### **Proper Technique**

- 1. **Prior activity.** Ideally, the patient should **not** have:
  - within 30 minutes smoked, ingested caffeine, or exercised
  - within 2 hours eaten or ingested alcohol
- 2. **Preparation.** The patient should sit with their back supported and feet on the floor (not seated on the exam table) for 5 minutes before the 1st blood pressure is taken.
- 3. **First visit: bilateral measures.** The blood pressure should be measured at least once in each arm (at the patient's first visit) to assure that there is no difference in blood flow (i.e., should be < 10 mm Hg difference), and if there is a significant difference, the higher pressure should be used thereafter.
- 4. **Cuff. Improper cuff size is the most common source of measurement error.** The arm should be bare, and the cuff should be fitted securely so that the bladder midline is over the brachial artery and the lower edge of the cuff is 1 inch above the antecubital fossa.
- 5. **Gauge.** The gauge should be at eye level.
- 6. **Arm.** The patient's arm should be supported, and the stethoscope or measurement point should be at heart level.
- 7. **Inflation.** Inflate the cuff at least 30 mm Hg above the systolic reading and deflate at a maximum of 2-3 mm per second or a maximum of 2 mm per pulse beat between the Korotkoff sounds.
- 8. **Measurement.** Record the systolic reading at the first sound heard Korotkoff phase I and the diastolic reading as the last sound heard Korotkoff phase V. If there is a muffling of the sound, this should also be recorded Korotkoff phase IV (e.g. 150/50/0).
- 9. Repeated measurement. Take the patient's pulse while waiting to repeat a second measurement after 1-2 minutes. If the measurement is performed immediately after walking into the room and the reading is normal, it should be recorded and repeated in 1-2 minutes. If the blood pressure is elevated immediately after walking into the room, it should not be recorded and the blood pressure should be repeated after 5 minutes of rest. At least two readings should be taken, and if the readings vary by more than 5 mm Hg diastolic, the readings should be repeated until there is less variability.
- 10. **Other recorded information.** The arm used, position of the patient, and the size of the cuff (when non-standard cuff size used) should be recorded.
- 11. **Inform.** Inform the patient of the readings.

| Approval : | Signatures |
|------------|------------|
|------------|------------|

Step Description Approver Date

| Quality Review | April Proudlock: Project Senior<br>Manager      | 08/2021 |
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