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Wolters Kluwer

# Management of severe asymptomatic hypertension (hypertensive urgencies) in adults

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## INTRODUCTION AND DEFINITION

Severe hypertension in adults (often defined as systolic blood pressure  $\geq 180$  mmHg and/or diastolic blood pressure  $\geq 120$  mmHg) can be associated with a variety of acute, life-threatening complications, any one of which is considered a hypertensive emergency [1-3]. These include hypertensive encephalopathy, retinal hemorrhages, papilledema, or acute and subacute kidney injury. A review of the manifestations and treatment of hypertensive emergencies is discussed separately. (See "[Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults](#)".)

Much more common, however, is the relatively asymptomatic or completely asymptomatic patient with a blood pressure in the "severe" range (ie,  $\geq 180/\geq 120$  mmHg), often a mild headache, but **no** signs or symptoms of acute end-organ damage [4-6]. This entity of severe asymptomatic hypertension is sometimes called hypertensive urgency and, as with hypertensive emergencies, occurs more frequently among patients who have been nonadherent with either their chronic antihypertensive drug regimen or their low-sodium diet [1,7]. Severe hypertension can also develop in medication-adherent patients following ingestion of large quantities of salt [8] and can be controlled by resuming a low-salt diet [9]. (See "[Initial evaluation of adults with hypertension](#)" and "[Overview of hypertension in](#)

[acute and chronic kidney disease".](#))

This topic reviews the treatment of severe asymptomatic hypertension, or hypertensive urgency. The recommendations below apply only to patients **without** signs of acute or ongoing end-organ damage.

The evaluation of patients with hypertension, the treatment of hypertensive emergencies, and the treatment of the pregnant woman with severe hypertension are discussed separately:

- (See ["Initial evaluation of adults with hypertension"](#).)
- (See ["Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults"](#).)
- (See ["Evaluation and treatment of hypertensive emergencies in adults"](#).)
- (See ["Treatment of hypertension in pregnant and postpartum patients"](#).)
- (See ["Preeclampsia with severe features: Delaying delivery in pregnancies remote from term"](#).)

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## EVALUATION

The most important aspect of the initial assessment of the patient with severely elevated blood pressure is to exclude acute, ongoing, target-organ damage, which would indicate a diagnosis of hypertensive emergency rather than severe asymptomatic hypertension. (See ["Evaluation and treatment of hypertensive emergencies in adults"](#).)

In addition, severely elevated blood pressure should be swiftly confirmed with repeated measurement utilizing proper technique ( [table 1](#)). The technique of measuring blood pressure is presented in detail elsewhere. (See ["Blood pressure measurement in the diagnosis and management of hypertension in adults"](#).)

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## TREATMENT

The optimal management of patients with severe asymptomatic hypertension is unclear. Data from the Studying the Treatment of Acute Hypertension (STAT) registry indicate that the outpatient management of patients with acute severe hypertension is poor and that many patients are lost to follow-up soon after evaluation [10]. In addition, many of these

patients will return to the emergency department for recurrent uncontrolled hypertension within three months.

**Overall approach** — There are several questions related to the management of patients with severe asymptomatic hypertension:

- **How quickly should the blood pressure be reduced?** – The blood pressure should be reduced over a period of hours to days, although slower reductions may be needed in older adult patients at high risk for cerebral or myocardial ischemia resulting from excessively rapid reduction of blood pressure. Determining how rapidly to lower the blood pressure is discussed below. (See '[Rapidity of blood pressure lowering](#)' below.)
- **What is the blood pressure target during this time period?** – The blood pressure should usually be lowered to <160/<100 mmHg. However, the mean arterial pressure should not be lowered by more than 25 to 30 percent over the first two to four hours [10-17]. Thus, the short-term blood pressure target, during the first several hours, may need to be above 160/100 mmHg in patients who present with very high pressures. This approach has not been well studied and is based mostly upon experience. In the long-term, the blood pressure should usually be reduced further (eg, <140/<90 mmHg or <130/<80 mmHg) [2,3]. (See '[Blood pressure reduction goal](#)' below.)
- **How should this goal be achieved?** – The strategy to lower blood pressure in such patients depends upon whether the blood pressure should be lowered more quickly (period of hours) or less quickly (period of days). In addition, moving patients to a quiet room to rest can lead to a fall in systolic pressure of 10 to 20 mmHg or more. (See '[Therapeutic strategies](#)' below.)
  - If the blood pressure needs to be lowered over a period of hours, some clinicians use oral [clonidine](#) or oral [captopril](#), despite the variable efficacy and known adverse effects of these agents [11-14]. Short-acting drugs are most commonly used when the blood pressure must be below an arbitrary threshold before discharge. Otherwise, many clinicians prefer long-acting drugs (eg, [amlodipine](#), [chlorthalidone](#)) and a follow-up primary care office visit in the next one to two days.

- If the blood pressure needs to be lowered over a period of days, our approach depends upon the circumstances. In general, the treatment is resumption of antihypertensive therapy (in nonadherent patients), initiation of antihypertensive therapy (if patients are treatment naïve), or the addition of another antihypertensive drug (in patients who are currently treated).

**Rapidity of blood pressure lowering** — The rapidity with which blood pressure should be brought to safe levels is controversial and **not** based upon high-quality medical evidence. In the absence of symptoms, a gradual reduction in pressure is suggested over a period of several hours to several days [1,11].

This suggestion stems from and seeks to balance two major concerns. These include:

- The risk of adverse events (eg, stroke, acute kidney injury, or myocardial infarction) that may occur if the blood pressure is lowered too rapidly or to a level below the ability for autoregulation to maintain adequate tissue perfusion [12,18,19].
- The potential risk of imminent cardiovascular events that may result from severe hypertension if the blood pressure is not quickly and sufficiently reduced. In patients visiting an emergency department for severe hypertension, potential legal ramifications partially motivate lowering the blood pressure in a short period of time.

There is no proven benefit from rapid reduction of blood pressure in patients with severe asymptomatic hypertension [3,11,15,16,18,20], and most such patients who present in the ambulatory setting can be managed as outpatients. The following findings are illustrative:

- In one retrospective study of 59,535 patients who presented in the ambulatory setting with severe asymptomatic hypertension, there appeared to be no substantial benefit from emergency department referral compared with sending the patient home from the office for outpatient management of blood pressure [20]. At six months, rates of major cardiovascular events were similar and low in both groups (0.9 percent), and patients sent home had lower 30-day hospital admission rates (48 versus 59 percent). Although blood pressure control rates were higher at one month in patients referred to the emergency department, there was no difference at six months.
- Another large retrospective study examined 1016 such patients who presented to an

emergency department; 435 patients received acute treatment of the blood pressure, and 581 patients were not given acute treatment [21]. There were no differences in return to the emergency department at 24 hours and at 30 days, and there were no differences in mortality at 30 days and at one year.

On the contrary, rapid and aggressive antihypertensive therapy can induce cerebral or myocardial ischemia or infarction, or acute kidney injury, if the blood pressure falls below the range at which tissue perfusion can be maintained by autoregulation [12,19,22]. This has been most often described with sublingual **nifedipine**, which often leads to an unpredictable and uncontrolled blood pressure reduction as well as severe ischemic complications [19]. However, other agents may also produce rapid, marked, and unpredictable reductions in blood pressure. In one study, for example, 147 patients presenting to a single center with a systolic pressure  $\geq 220$  mmHg or a diastolic pressure  $\geq 120$  mmHg were monitored after administration of antihypertensive medications [23]. At five hours, systolic pressure had fallen to  $< 140$  mmHg in 30 patients and to  $< 120$  mmHg in nine patients; 14 patients (9 percent) had a decline in systolic pressure of more than 100 mmHg. **Clonidine** was associated with the most precipitous fall in blood pressure.

The individual patient's risk for an adverse event and the probable duration of severe hypertension must be considered when deciding how quickly to reduce the blood pressure. As an example, older adult patients may be at particularly high risk for cerebral or myocardial ischemia if the blood pressure is lowered excessively and/or too rapidly. In such patients, who often will have a high pulse pressure (eg, diastolic blood pressure  $< 90$  mmHg with systolic blood pressure  $\geq 180$  mmHg), the initial goal blood pressure may need to be achieved even more slowly (eg, over a week or more).

**Blood pressure reduction goal** — In adults with severe asymptomatic hypertension, the shorter-term goal of management is to reduce the blood pressure to  $\leq 160/\leq 100$  mmHg. However, the mean arterial pressure should not be lowered by more than 25 to 30 percent over the first several hours [11,15].

**Therapeutic strategies** — All patients should be provided a quiet room in which to rest. In one study, for example, 30 minutes of rest in a quiet room produced a fall in blood pressure  $\geq 20/10$  mmHg in 32 percent of adults with severe asymptomatic hypertension [24]. If this is not effective, antihypertensive drugs may be given.

**When the pressure should be lowered over a period of hours** — Patients judged to be

at high risk for imminent cardiovascular events due to severe hypertension, including those with known aortic or intracranial aneurysms, should have their blood pressure lowered over a period of hours.

A wide variety of therapeutic modalities have been used to lower blood pressure over this short period of time, including oral or sublingual [nifedipine](#), nitrates, [captopril](#), or oral [clonidine](#) or [hydralazine](#) [13,17,25]. However, **sublingual nifedipine is contraindicated** in this setting and should **not** be used. As noted above, cerebral or myocardial ischemia or infarction can be induced by aggressive antihypertensive therapy if the blood pressure falls below the range at which tissue perfusion can be maintained by autoregulation [12,19,22]. This has been most often described with sublingual nifedipine, which may produce an unpredictable and uncontrolled blood pressure reduction as well as severe ischemic complications [19]. This was a major reason why the use of nifedipine capsules for hypertension is not approved by the United States Food and Drug Administration (US FDA), and why most hospitals' intensive care units and emergency departments restrict the use of this medication [26].

There are regional and national variations in the initial choice of oral drug therapy for patients with severe asymptomatic hypertension. In some places, local policy dictates that blood pressures must be treated and lowered below an arbitrary threshold before the patient can be discharged; in such cases, the two most common agents are [14]:

- Oral [clonidine](#) (but not intended as long-term therapy)
- Oral [captopril](#) (if the patient is not volume overloaded)

However, other oral agents are sometimes used to quickly lower the blood pressure [14,23]. In addition, some experts select longer-acting agents (ie, those commonly used to treat chronic hypertension) rather than short-acting drugs.

Following administration of an antihypertensive agent, the patient is observed for a few hours to ascertain a reduction in blood pressure of 20 to 30 mmHg. Thereafter, a longer-acting agent is prescribed, and the patient is sent home to follow-up within a few days. The drop in blood pressure may take relatively longer with [captopril](#) and may be too large among patients with hemodynamically significant renal artery stenosis.

A potentially safer alternative approach is to forgo these shorter-acting agents and initiate a long-acting agent (eg, [amlodipine](#), [chlorthalidone](#)) with follow-up in clinic after one or

two days. This strategy may be superior to the strategy that includes the use of shorter-acting agents [20,21] and may eventually lead to reevaluation of policies mandating the use of shorter-acting antihypertensive agents. (See '[When the pressure should be lowered over a period of days](#)' below.)

**When the pressure should be lowered over a period of days** — Patients with severe asymptomatic hypertension who do not require rapid lowering of their blood pressure (see above) should have their blood pressure lowered over a period of days. In previously nonadherent patients, resumption of their routine medications is usually sufficient.

**Previously treated hypertension** — Among patients recently treated with antihypertensive medications, the following (depending upon the circumstances) may be appropriate interventions [16,18]:

- Reinstitution of prior medications (while attempting to avoid those associated with rebound hypertension, eg, central alpha-2-agonists, high-dose beta blockers) in nonadherent patients.
- Increase the dose of existing antihypertensive medications, or add another agent. In many instances, patients receive subtherapeutic doses of antihypertensive agents.
- Addition of a diuretic appropriate to the patient's level of kidney function, and reinforcement of dietary sodium restriction, in patients who have worsening hypertension due to high sodium intake.

**Untreated hypertension** — In the previously untreated patient, several options are available. The approach should take into consideration the individual patient's risk with persistence of severe hypertension, the likely duration of severe hypertension, and risk of cerebrovascular or myocardial ischemia with rapid reduction in blood pressure [15,16,18].

There are no data supporting the use of a particular agent in patients whose blood pressure should be reduced over a period of several days. A calcium channel blocker (but **not** sublingual [nifedipine](#)), beta blocker, an angiotensin-converting enzyme (ACE) inhibitor, or angiotensin receptor blocker (ARB) can be started. Examples in these categories are oral nifedipine (the long-acting preparation), oral [metoprolol XL](#), or [ramipril](#).

The choice of drug should take into consideration the type of antihypertensive agent that is most appropriate in the long term and underlying conditions that may be favorably or



adversely affected by the antihypertensive agent ( [table 2](#)). (See "[Choice of drug therapy in primary \(essential\) hypertension](#)".)

Some experts initiate therapy with two drugs or a combination agent in such patients. The rationale is that most patients with a blood pressure  $\geq 20/10$  mmHg above goal will require two or more chronic antihypertensive agents to achieve the goal blood pressure [[3,15,27,28](#)]. If, in a previously untreated patient with severe asymptomatic hypertension, the goal is to lower the blood pressure over a period of days (rather than hours) and to use a combination of drugs that will be continued as long-term antihypertensive therapy, we would begin a long-acting dihydropyridine calcium channel blocker plus a long-acting ACE inhibitor/ARB. This choice is based upon the results of the ACCOMPLISH trial, which is discussed elsewhere (See "[Choice of drug therapy in primary \(essential\) hypertension](#)".)

It is unlikely that a combination of two long-acting drugs in modest doses will cause a rapid and dangerous reduction in blood pressure. However, initiation of two agents simultaneously must be done with close blood pressure follow-up since the full effects of both agents may not occur for a few days and adverse consequences may ensue if the blood pressure is lowered too quickly. This is particularly true among patients with cerebrovascular disease in whom more cautious blood pressure reduction is generally warranted.

**Monitoring and follow-up** — The patient with severe asymptomatic hypertension is usually managed in the emergency department since exclusion of acute end-organ damage requires laboratory testing and the patient may require administration of medications and several hours of observation. However, the patient can often be safely managed in the clinician's office if the evaluation and management can be carried out in that setting. (See "[Initial evaluation of adults with hypertension](#)".)

The management of a patient who does not have established follow-up is difficult. Rarely, such patients may require admission. In addition, patients at high risk for acute cardiovascular events (eg, longstanding diabetes, known coronary artery disease or prior stroke) should probably be admitted. (See "[Cardiovascular risks of hypertension](#)", [section on 'Additive effects of hypertension and other risk factors'](#).)

Ideally, the patient should be observed for a few hours to ascertain that the blood pressure is stable or improving, that they indeed remain asymptomatic, and that they have received referral to an appropriate source of long-term medical care. If this occurs,



the patient can be sent home with close follow-up over the subsequent days directed toward evaluation for symptoms related to hypertension or hypotension and adjustment of medications to achieve the initial blood pressure goal of  $\leq 160/100$  mmHg. In reliable patients who can monitor their blood pressure at home, close phone follow-up may substitute for direct clinician visits. If the patient does not have a clinician, follow-up may need to be in the emergency department, urgent care, or other acute care setting.

Over the subsequent weeks and months, the dose and selection of medications should be adjusted as needed to achieve the desired blood pressure goals. These issues are discussed elsewhere:

- (See "[Choice of drug therapy in primary \(essential\) hypertension](#)".)
- (See "[Goal blood pressure in adults with hypertension](#)".)

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## SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "[Society guideline links: Hypertension in adults](#)".)

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## INFORMATION FOR PATIENTS

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Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "[Patient education: High blood pressure emergencies \(The Basics\)](#)")

- Beyond the Basics topics (see "[Patient education: High blood pressure in adults \(Beyond the Basics\)](#)" and "[Patient education: High blood pressure treatment in adults \(Beyond the Basics\)](#)" and "[Patient education: High blood pressure, diet, and weight \(Beyond the Basics\)](#)")

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## SUMMARY AND RECOMMENDATIONS

- **Definition** – Severe hypertension in adults (often defined as systolic blood pressure  $\geq 180$  mmHg and/or diastolic blood pressure  $\geq 120$  mmHg) can be associated with a variety of acute, life-threatening complications, any one of which is considered a hypertensive emergency. Much more common, however, is the relatively or completely asymptomatic patient with a blood pressure in the "severe" range (ie,  $\geq 180/\geq 120$  mmHg), often a mild headache, but **no** signs or symptoms of acute end-organ damage. This entity of severe asymptomatic hypertension is sometimes called hypertensive urgency. (See '[Introduction and definition](#)' above.)
- **Management** – The optimal management of patients with severe asymptomatic hypertension is unclear. However, in such patients, our overall approach is as follows (see '[Overall approach](#)' above):
  - **Rapidity of therapy** – We suggest lowering the blood pressure over a period of hours to days rather than longer periods of time (**Grade 2C**). The rapidity with which blood pressure should be brought to safe levels is controversial and **not** based upon high-quality medical evidence. This suggestion stems from and seeks to balance two major concerns. These include:
    - The risk of adverse events (eg, stroke or myocardial infarction) that may occur if the blood pressure is lowered too rapidly or to a level below the ability for autoregulation to maintain adequate tissue perfusion.
    - The potential risk of imminent cardiovascular events that may result from severe hypertension if the blood pressure is not quickly and sufficiently reduced. In patients visiting an emergency department for severe hypertension, potential legal ramifications partially motivate lowering the blood pressure over several hours.
  - **Initial goal blood pressure** – Over this period, we suggest lowering the blood

pressure to  $<160/<100$  mmHg or to a level that is no more than 25 to 30 percent lower than the baseline blood pressure (**Grade 2C**). Thus, the short-term blood pressure target may need to be above 160/100 mmHg in patients who present with very high pressures, because cerebral or myocardial ischemia or infarction, or acute kidney injury, can be induced by rapid and aggressive antihypertensive therapy if the blood pressure falls below the range at which tissue perfusion can be maintained by autoregulation. This approach has not been well studied and is based mostly upon experience. In the long-term, the blood pressure should usually be reduced further (eg,  $<140/<90$  or  $<130/<80$  mmHg). (See '[Blood pressure reduction goal](#)' above.)

- **Therapeutic options** – There are a variety of options for lowering the blood pressure in patients with severe asymptomatic hypertension. All patients should be provided a quiet room in which to rest. This may produce a fall in blood pressure  $\geq 20/10$  mmHg in approximately one-third of adults. If this is not effective, antihypertensive drugs may be given. The antihypertensive strategy depends upon whether the goal is to lower the blood pressure more quickly (period of hours) or less quickly (period of days) (see '[Therapeutic strategies](#)' above):
  - To lower the blood pressure over a period of hours, some use oral [clonidine](#) (but should not be maintained as long-term therapy) or oral [captopril](#) (if the patient is not volume overloaded). However, **sublingual nifedipine is contraindicated** in this setting and should **not** be used. (See '[When the pressure should be lowered over a period of hours](#)' above.)
  - To lower the blood pressure over a period of days, our approach depends upon the circumstances. In general, the treatment is resumption of antihypertensive therapy (in nonadherent patients), initiation of antihypertensive therapy (if patients are treatment naïve), or the addition of another antihypertensive drug (in patients who are currently treated). (See '[When the pressure should be lowered over a period of days](#)' above.)
- **Triage** – The patient with severe asymptomatic hypertension is usually managed in the emergency department since exclusion of acute end-organ damage requires laboratory testing, and the patient may (depending on local policies and procedures)

receive medications and several hours of observation. However, the patient can often be safely managed in the clinician's office if the evaluation and management can be carried out in that setting. The management of a patient who does not have established follow-up is difficult. Rarely, such patients may require admission. In addition, patients at high risk for acute cardiovascular events (eg, longstanding diabetes, known coronary artery disease or prior stroke) should probably be admitted. Ideally, if treated acutely, patients should be observed for a few hours to ascertain that the blood pressure is stable or improving, that they indeed remain asymptomatic, and that they have received referral to an appropriate source of long-term medical care. (See '[Monitoring and follow-up](#)' above.)

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## GRAPHICS

### Checklist for accurate measurement of blood pressure

Key steps for proper BP measurements	Specific instructions
Step 1: Properly prepare the patient	<ol style="list-style-type: none"> <li>1. Have the patient relax, sitting in a chair (feet on floor, back supported) for &gt;5 minutes.</li> <li>2. The patient should avoid caffeine, exercise, and smoking for at least 30 minutes before measurement.</li> <li>3. Ensure patient has emptied their bladder.</li> <li>4. Neither the patient nor the observer should talk during the rest period or during the measurement.</li> <li>5. Remove all clothing covering the location of cuff placement.</li> <li>6. Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria.</li> </ol>
Step 2: Use proper technique for BP measurements	<ol style="list-style-type: none"> <li>1. Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically.*</li> <li>2. Support the patient's arm (eg, resting on a desk).</li> <li>3. Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum).</li> <li>4. Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used.</li> <li>5. Either the stethoscope diaphragm or bell may be used for auscultatory readings.</li> </ol>
Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/hypertension	<ol style="list-style-type: none"> <li>1. At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings.</li> <li>2. Separate repeated measurements by 1 to 2 minutes.</li> <li>3. For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP. Inflate the cuff 20 to 30 mmHg above this level for an auscultatory determination of the BP level.</li> <li>4. For auscultatory readings, deflate the cuff pressure 2 mmHg per second, and listen for Korotkoff sounds.</li> </ol>
Step 4: Properly document accurate BP readings	<ol style="list-style-type: none"> <li>1. Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and</li> </ol>



	<p>disappearance of all Korotkoff sounds, respectively, using the nearest even number.</p> <p>2. Note the time of most recent BP medication taken before measurements.</p>
Step 5: Average the readings	<p>1. Use an average of <math>\geq 2</math> readings obtained on <math>\geq 2</math> occasions to estimate the individual's level of BP.</p>
Step 6: Provide BP readings to patient	<p>1. Provide patients the SBP/DBP readings both verbally and in writing.</p>

BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.

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*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: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. J Am Coll Cardiol 2017. Table used with the permission of Elsevier Inc. All rights reserved.*

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## Considerations for individualizing antihypertensive therapy

Indication or contraindication	Antihypertensive drugs
<b>Compelling indications (major improvement in outcome independent of blood pressure)</b>	
Heart failure with reduced ejection fraction	ACE inhibitor or ARB, beta blocker, diuretic, aldosterone antagonist*
Postmyocardial infarction	ACE inhibitor or ARB, beta blocker, aldosterone antagonist
Proteinuric chronic kidney disease	ACE inhibitor or ARB
Angina pectoris	Beta blocker, calcium channel blocker
Atrial fibrillation rate control	Beta blocker, nondihydropyridine calcium channel blocker
Atrial flutter rate control	Beta blocker, nondihydropyridine calcium channel blocker
<b>Likely to have a favorable effect on symptoms in comorbid conditions</b>	
Benign prostatic hyperplasia	Alpha blocker
Essential tremor	Beta blocker (noncardioselective)
Hyperthyroidism	Beta blocker
Migraine	Beta blocker, calcium channel blocker
Osteoporosis	Thiazide diuretic
Raynaud phenomenon	Dihydropyridine calcium channel blocker
<b>Contraindications</b>	
Angioedema	Do not use an ACE inhibitor
Bronchospastic disease	Do not use a non-selective beta blocker
Liver disease	Do not use methyldopa
Pregnancy (or at risk for)	Do not use an ACE inhibitor, ARB, or renin inhibitor (eg, aliskiren)

Second- or third-degree heart block	Do not use a beta blocker, nondihydropyridine calcium channel blocker unless a functioning ventricular pacemaker
<b>Drug classes that may have adverse effects on comorbid conditions</b>	
Depression	Generally avoid beta blocker, central alpha-2 agonist
Gout	Generally avoid loop or thiazide diuretic
Hyperkalemia	Generally avoid aldosterone antagonist, ACE inhibitor, ARB, renin inhibitor
Hyponatremia	Generally avoid thiazide diuretic
Renovascular disease	Generally avoid ACE inhibitor, ARB, or renin inhibitor

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker.

\* A benefit from an aldosterone antagonist has been demonstrated in patients with NYHA class III-IV heart failure or decreased left ventricular ejection fraction after a myocardial infarction.

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## Contributor Disclosures

**Joseph Varon, MD, FACP, FCCP, FCCM, FRSM** No relevant financial relationship(s) with ineligible companies to disclose. **William J Elliott, MD, PhD** Consultant/Advisory Boards: Johnson & Johnson [Resistant hypertension]. Other Financial Interest: Elsevier [Hypertension]. All of the relevant financial relationships listed have been mitigated. **George L Bakris, MD** Grant/Research/Clinical Trial Support: Bayer [Diabetic nephropathy]; KBP Biosciences [Resistant hypertension]; Novo Nordisk [Diabetic kidney disease]. Consultant/Advisory Boards: Alnylam [Resistant hypertension]; AstraZeneca [Diabetic nephropathy]; Bayer [Nephropathy]; Ionis [Resistant hypertension]; KBP BioSciences [Resistant hypertension]; Vifor [Hyperkalemia]. All of the relevant financial relationships listed have been mitigated. **William B White, MD** Consultant/Advisory Boards: AB Science [Alzheimer's disease, mastocytosis]; Alynam [Heart failure]; AstraZeneca [Lupus, lung disease]; Bristol-Myers Squibb [Psoriasis]; Cadence [Oral contraception]; Cerevel Therapeutics [Cancer, schizophrenia]; Chinook [IgA nephropathy]; JAZZ [Narcolepsy]; Marius [Hypogonadism]; Medtronic [Renal denervation]; Takeda [Gout, narcolepsy, cancer]; Traverre [IgA nephropathy]; UCB [Psoriasis, arthritis]. All of the relevant financial relationships listed have been mitigated. **John P Forman, MD, MSc** No relevant financial relationship(s) with ineligible companies to disclose.

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