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EYE ON THE ELDERLY

Hypertension care: Striking the proper balance

How aggressive should treatment be? Which drug combinations should raise red flags? Which drugs should you avoid entirely? Here's how to safely customize your care.

Practice recommendations

- Treat systolic hypertension in the elderly to reduce their risk of cardiovascular events and mortality (B).
- Don't shy away from treating the very old. Hypertension treatment is beneficial even in patients who are 80 years of age or older (B).
- Don't prescribe an angiotensin-converting enzyme inhibitor and an angiotensin receptor blocker for elderly patients without heart failure; the combination increases the risk of adverse effects without reducing cardiovascular events (B).

Strength of recommendation (SOR)

- A Good-quality patient-oriented evidence
- B Inconsistent or limited-quality patient-oriented evidence
- C Consensus, usual practice, opinion, disease-oriented evidence, case series

Esther V. is an 81-year-old Caucasian woman who has been in your practice for a number of years. Her history is significant for a hip fracture 5 years ago and a subsequent diagnosis of osteoporosis. But she's still able to live on her own, and takes only 1 medication—alendronate 70 mg once a week. Today Mrs. V.'s blood pressure is 150/80 mm Hg, and a chart review indicates that it has been in that

range for the past 2 years. In view of her history and her age, would you proceed with treatment, and if so, how would you address her elevated systolic pressure?

Treating high blood pressure in elderly patients like Esther V. is a complicated proposition: While it's important to mitigate hypertension's negative effects, physicians need to be mindful that for this patient population, antihypertensive therapy itself involves elevated risks and unique concerns. These include:

- **drug-drug interactions**, exacerbated by the multiple medications that many older patients take;
- **the side effect profile** of antihypertensive agents, including orthostatic hypotension and the possibility of exacerbating an already heightened risk of falls; and
- **uncertainty about when to initiate therapy**, which drugs to choose if a second antihypertensive agent is needed, and when (or whether) a patient is too old to benefit from treatment.

Noncompliance is another potential complication in the elderly, who may have difficulty following a drug regimen or avoid prescription medications because they're worried about the adverse effects—or the cost—of the drugs.

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Thus, it's not surprising that hypertension so often remains under- or untreated in older patients, a problem highlighted by a 2003 review in which only 27% of elderly patients were found to have reached their blood pressure goal.¹

Despite the difficulty of adequately addressing hypertension in this patient population, the benefits do outweigh the risks. The following practical guide will help you overcome common barriers to treatment, avoid dangerous drug combinations, and customize your patient's care to maximum benefit.

■ **Treat hypertension, regardless of age**

The Seventh Report of the Joint National Committee on Prevention, Evaluation, and Treatment of Hypertension (JNC 7) recommends a goal of <140/90 mm Hg for most individuals, and <130/80 mm Hg for those with diabetes mellitus or chronic kidney disease.² But as patients age, presentations like that of Mrs. V.—elevated systolic pressure and normal diastolic pressure—are increasingly common. Isolated systolic hypertension is thought to be a consequence of the aging process, which results in a reduction in elasticity and compliance of the large arteries, degradation of arterial elastin, and atherosclerosis-associated accumulation of arterial calcium and collagen.³

Certainly, we know that hypertension of any kind is a major risk factor for a number of conditions with significant morbidity and mortality, including coronary artery disease,⁴ stroke,⁵ and heart failure.⁶ In the elderly, treatment of systolic hypertension, even in the absence of diastolic hypertension, has been proven to reduce cardiovascular and renal disease and death.⁷⁻⁹

Extending lives: What the evidence shows

Treating the very old. Hypertension in the Very Elderly (HYVET), the most recent trial, randomized more than 3800 hy-



pertensive patients over the age of 80 in Europe, China, Australia, and Tunisia to receive either a diuretic or placebo. After 2 years, the treatment group had significant reductions in fatal and nonfatal stroke (number needed to treat [NNT]=19), all-cause mortality (NNT=8), cardiovascular death (NNT=15), and heart failure (NNT=67).¹⁰

A subset of this trial (HYVET-COG) reviewed the effects of antihypertensive therapy on the development of dementia in the very old. The researchers did not find a statistically significant reduction in the incidence of dementia in the treatment group. But when the HYVET-COG data were combined in a meta-analysis with data from 3 other antihypertensive trials in the elderly, treatment for hypertension was associated with a 13% relative risk reduction for dementia.¹¹ Despite a major limitation of the HYVET trial—participants were typically healthier than the general population within their age

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group—the findings highlight the benefits of treating hypertension even in the very old.

Treating systolic hypertension. A Cochrane review conducted more than 10 years ago to assess the effectiveness of treating systolic hypertension in otherwise healthy older patients found that treatment reduced cardiovascular morbidity and mortality by 53 events per 1000 patient-years.¹² Several prospective, double-blind, randomized, placebo-controlled studies found that treatment of systolic hypertension in healthy elderly patients reduced the incidence of total mortality (NNT=59), fatal and nonfatal cardiovascular events (NNT=26), and fatal and nonfatal stroke (NNT=79).¹³

■ Getting past common barriers to treatment

Despite these findings, many elderly patients with hypertension do not receive adequate treatment, often because of clinicians' concerns about uncertain parameters and treatment risks. We've identified some common barriers and suggested ways to get beyond them.

BARRIER Unclear parameters, concerns about aggressive Tx

There is little doubt of the value of treating stage 2 systolic hypertension (≥ 160 mm Hg) in the elderly. Not so for stage 1 systolic hypertension (140-159 mm Hg): A 2004 systematic review of studies evaluating the treatment of elevated systolic pressure in this patient population concluded that evidence for treating stage 1 systolic hypertension was not as strong.¹⁴

Observational studies suggesting a link between aggressive blood pressure-lowering and increased mortality in elderly patients have also been a cause for concern among some physicians.^{15,16} The INDANA meta-analysis, conducted in 1999, reviewed data from patients 80 years of age and older enrolled in anti-

hypertensive trials and found a nonsignificant increase in death rates among patients who received treatment.¹⁷

How to respond? Carefully weigh the potential benefits of antihypertensive therapy in view of the overall health, functional status, and risks of side effects for a particular patient. The findings of the INDANA meta-analysis, while not statistically significant, serve as a reminder of the need to individualize treatment.

In the absence of a definitive treatment approach, it is also important to discuss the options with the patient. The authors of the systematic review that evaluated the benefits of treatment for stage 1 systolic hypertension recommended that antihypertensive therapy be based, in part, on patient preference and tolerance of therapy.¹⁴

BARRIER Risks associated with multiple medications

The concurrent use of multiple medications, which is very common in the elderly, can interfere with treatment of hypertension in 2 ways: Some drugs have the potential to cause (or exacerbate) elevated blood pressure. Others may counter the effects of antihypertensive therapy.

Among the drugs that contribute to hypertension are the sympathomimetic agents found in many over-the-counter (OTC) cough and cold preparations in which the mechanism of action is direct vasoconstriction.¹⁸ Tricyclic antidepressants, which are commonly used to treat pain syndromes in the elderly, have also been shown to raise both systolic and diastolic pressure.¹⁹

On the other hand, nonsteroidal anti-inflammatory drugs (NSAIDs), often used by elderly patients to treat osteoarthritis, may counter the effects of many antihypertensive agents. Both OTC and prescription NSAIDs inhibit cyclo-oxygenase-2 (COX-2) in the kidneys, resulting in a reduction in sodium excretion and an increase in plasma volume.²⁰

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Caution patients to avoid NSAIDs, OTC cough and cold preparations, and excessive caffeine, all of which may elevate their blood pressure.

TABLE

Which drugs, for which patients?²

DRUG CLASS*	INDICATIONS	CONSIDERATIONS
ACE inhibitors	Heart failure, post-MI, diabetes, high risk for CAD, chronic kidney disease, recurrent stroke prevention	Avoid concurrent use of ARBs in patients without heart failure. Avoid concurrent use of NSAIDs. If a second drug is needed, add a thiazide diuretic or CCB.
ARBs	Heart failure, diabetes, chronic kidney disease	Avoid concurrent use of ACE inhibitors in patients who don't have heart failure.
Beta-blockers	Heart failure, post-MI, high risk for CAD, diabetes	Not recommended as first-line therapy for uncomplicated hypertension.
CCBs	High risk for CAD, diabetes	Avoid prescribing verapamil for elderly patients.
Thiazide diuretics	Heart failure, high risk for CAD, diabetes, recurrent stroke prevention	Avoid concurrent use of NSAIDs. Will not work with reduced GFR or hypokalemia. Use with caution in patients prone to orthostatic hypotension.

*Peripheral alpha-blockers, centrally acting alpha-agonists, and vasodilators should not be routinely used to treat hypertension in elderly patients. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CCB, calcium channel blocker; GFR, glomerular filtration rate; MI, myocardial infarction; NSAIDs, nonsteroidal anti-inflammatory drugs.

How to respond? Take a thorough medication history, including OTC and prescription drugs and supplements, before initiating treatment. Caution patients to avoid NSAIDs, OTC cough and cold preparations, and excessive caffeine, all of which may elevate their blood pressure. Remind patients that any new medication prescribed by another physician may affect their blood pressure, and advise them to maintain a current list of all medications to be reviewed at each visit.

BARRIER Concerns about side effects

The elderly are more susceptible to orthostatic hypotension than younger patients because of age-related decreases in the baroreflex.²¹ Estimates suggest that anywhere from 5% to 50% of individuals older than 65 years are affected.²¹ Orthostatic hypotension, a side effect of many antihypertensive agents, is associated with higher rates of dizziness, syncope, and falls—a particular concern in elderly patients with a history of osteoporosis, pathological fracture, or gait dysfunction

(See “Screening for hearing loss, risk of falls” on page 471).

How to respond? Before initiating antihypertensive therapy, take your patient's blood pressure in both a sitting and standing position. Educate the patient and his or her family about the presentation of orthostatic hypotension, and advise the patient to stop taking the new medication and contact you if he or she develops the associated signs and symptoms. Schedule frequent follow-up appointments to closely monitor the effects of antihypertensive therapy, as well.

Stress the importance of lifestyle interventions

JNC 7 recommends several nonpharmacological treatments for all hypertensive patients, regardless of age. These include:

- healthy diet (such as Dietary Approaches to Stop Hypertension [DASH])
- sodium restriction (daily intake of <100 mmol/d)
- limited alcohol intake
- weight reduction (a decrease of

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For every 10 kg of weight lost, a decrease of 5 to 20 mm Hg has been reported.

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- regular physical activity (reported decrease of 4-9 mm Hg).²

No long-term trials have assessed the effects of lifestyle modification on morbidity and mortality. A subset of patients in the original DASH trial with stage 1 systolic hypertension did benefit from the diet, but the subgroup was small and the median age was 54.7 years.²² No large-scale studies have addressed the effectiveness of the diet in older patients with systolic hypertension.

■ Customizing therapy: What to consider

Evidence supports the use of various classes of antihypertensive medications in the treatment of high blood pressure, including thiazide diuretics, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs).^{10,23-27} JNC 7 recommends starting with 1 medication for patients with stage 1 hypertension (140-159/90-99 mm Hg) and 2 medications for patients with stage 2 hypertension ($\geq 160/100$ mm Hg).² As previously noted, however, clear-cut evidence in support of treating elderly patients with stage 1 hypertension is lacking.

When you do initiate treatment for an elderly patient, begin with a low dose and titrate slowly, carefully monitoring for side effects. If 2 antihypertensive agents are needed, start 1 agent at a time in patients who are at risk for significant side effects. The type of antihypertensive agent you prescribe should be based on your patient's health status, comorbidities, and treatment for other conditions, as well as on the known effects of the particular class of drugs (TABLE).

Thiazide diuretics. JNC 7 recommends thiazide diuretics as first-line treatment based on cost and effectiveness. Because thiazide diuretics decrease the urinary ex-

cretion of calcium, JNC 7 recommends their use in patients with osteoporosis.²

But potential side effects, such as dehydration, orthostatic hypotension, and hypokalemia, are more common in elderly patients, and may limit the use of these drugs in clinical practice. NSAIDs may reduce the antihypertensive effects of thiazide diuretics through a decrease in sodium excretion and an increase in plasma volume, and should be used with caution—if at all—in this patient population.²⁰

Hydrochlorothiazide, a commonly used thiazide diuretic, should not be used in doses >50 mg/d because higher doses increase the risk of side effects without increasing efficacy.²⁸ In the Systolic Hypertension in the Elderly Program (SHEP) study, the positive effects of another thiazide diuretic—chlorthalidone—were lost in elderly patients with serum potassium <3.5 mmol/L, so serum electrolytes should be routinely assessed during therapy.^{2,7} Thiazide diuretics lose their effectiveness in patients with a glomerular filtration rate of <30 mL/min/1.73 m² and should not be used in this group.²⁹

Beta-blockers. Beta-blockers are indicated in patients with a previous history of myocardial infarction, as they have been shown to decrease the rate of new coronary events.³⁰ Other comorbidities that may be mitigated by beta-blocker administration include angina pectoris, atrial fibrillation with a rapid ventricular rate, compensated heart failure, preoperative hypertension, and essential tremor.²

Side effects of beta-blockers include sedation, depression, sexual dysfunction, bradycardia, conduction abnormalities, and exacerbation of severe reactive airway disease.² Central nervous system effects of beta-blockers tend to be lowest in hydrophilic agents, such as atenolol, and highest in lipophilic agents, such as propranolol, which readily cross the blood-brain barrier.³¹

A 2007 Cochrane review looked at the effectiveness of beta-blockers as

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JNC 7 recommends the use of thiazide diuretics in patients with hypertension and osteoporosis, but potential side effects may limit their use.

first-line agents in uncomplicated hypertension and concluded that the evidence does not support their use. The reviewers noted, however, that the majority of the trials used atenolol and cautioned that the results might not apply to other beta-blockers—or to subgroups, such as the elderly.³²

ACE inhibitors and ARBs. Both ACE inhibitors and ARBs inhibit the renin-angiotensin-aldosterone pathway, and both classes are indicated in patients with diabetes, chronic kidney disease, or heart failure.² Cough is a side effect of ACE inhibitors that affects 5% to 35% of patients,³³ but angioedema—estimated to occur in 0.1% to 0.7% of patients taking ACE inhibitors—is the most serious side effect.³⁴

An elevation in serum potassium and serum creatinine may occur after starting an ACE inhibitor in patients with heart failure, dehydration, or significant renal insufficiency, so assess serum creatinine and potassium 1 week after initiating therapy. An increase in serum creatinine >30% may require discontinuation or dose reduction.^{2,35}

Elderly patients who take NSAIDs while on ACE inhibitors are at particular risk for acute renal failure; reviews of iatrogenic acute renal failure in the elderly have shown that most cases are related to the concurrent use of these medications.^{36,37} This is yet another reason to avoid giving NSAIDs to elderly patients with hypertension, particularly if they're taking diuretics or ACE inhibitors.

Beware of ACE inhibitor-ARB combinations. The American College of Cardiology and the American Heart Association recommend substituting an ARB if side effects from an ACE inhibitor occur in patients with heart failure, but extreme caution is required if the patient experienced ACE inhibitor-associated angioedema.³⁸ TRANSCEND, a randomized controlled trial of almost 6000 patients, specifically studied the use of ARBs in patients unable to tolerate ACE inhibitors

and concluded that they can be safely given to patients who had side effects from ACE inhibitors.³⁹

Since ACE inhibitors and ARBs affect the renin-angiotensin-aldosterone pathway at different points, there has been interest in the effectiveness of combining these agents. The CHARM-Added trial found that the combination of these agents reduced both cardiovascular events and mortality in patients with heart failure.⁴⁰

Combining ACE inhibitors and ARBs in patients *without* heart failure was evaluated in the ONTARGET trial. While the combination treatment group had a greater reduction in blood pressure, there was no significant cardiovascular benefit over patients who were on ACE inhibitors alone. But there was an increase in hypotension, syncope, and renal dysfunction among those in the combination treatment group, all of which are significant concerns in the elderly. The authors concluded that the ACE inhibitor-ARB combination should not be used in patients who do not have heart failure.⁴¹

Calcium channel blockers. CCBs block the entrance of calcium into vascular cells, producing dilation in the coronary arteries and peripheral vasculature, and are effective in the treatment of hypertension in elderly patients.⁴² Nondihydropyridine CCBs (diltiazem and verapamil) are useful in patients with atrial fibrillation and supraventricular tachycardia because of their negative chronotropic effects.² And African American patients respond better to CCBs—with a greater reduction in blood pressure and cardiovascular complications—than to ACE inhibitors.^{2,25}

Dihydropyridine CCBs (amlodipine and long-acting felodipine and nifedipine) are safe in patients with heart failure or chronic stable angina,⁴³ but short-acting nifedipine has been found to increase the risk of mortality.⁴⁴

Dihydropyridine CCBs have been reported to cause peripheral edema in

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Avoid using alpha-blockers, centrally acting alpha-agonists, or vasodilators to treat hypertension in elderly patients.

7% to 8% of patients taking long-acting nifedipine and up to 16% of elderly patient taking amlodipine.⁴⁵ Verapamil has the highest incidence of constipation, and should be avoided in elderly patients.²

■ Steer clear of these drugs

Significant side effects, including hypotension, sedation, depression, and dry mouth, limit the use of other antihypertensives, such as peripheral alpha blockers, centrally acting agents, and vasodilators, in elderly patients.² In the ALLHAT trial, the alpha-blocker arm was stopped prematurely because of an increased rate of cardiovascular events and heart failure compared with the thiazide diuretic arm.²⁵ That finding led to the recommendation that alpha-blockers not be used as first-line agents for treating hypertension.

Centrally acting alpha-agonists (clonidine, methyldopa, and reserpine) have a high incidence of sedation, dry mouth, and depression, and elderly patients are more likely to experience orthostatic hypotension and rebound hypertension if these agents are discontinued abruptly or doses are missed.² Vasodilators, including minoxidil and hydralazine, cause sodium and fluid retention and reflex tachycardia.² Because of their unfavorable side effects and lack of outcomes data, alpha-blockers, centrally acting alpha-agonists, and vasodilators should not be used routinely for the treatment of hypertension in elderly patients.

■ Considerations in selecting a second agent

Patients who fail to achieve adequate blood pressure control despite lifestyle modifications and a single agent, and those who are initially diagnosed with stage 2 hypertension, will require 2 or more medications. An elderly patient who has not responded to a single agent should be asked about any other medications (or substances) that might be

interfering with the antihypertensive agent, especially NSAIDs, tricyclic antidepressants, sympathomimetics, and caffeine. Find out, too, whether the patient is following the prescribed regimen.

When you prescribe 2 antihypertensives, choose agents with complementary mechanisms of action—a diuretic and an ACE inhibitor, for example, or an ACE inhibitor and a CCB. In addition to avoiding an ACE/ARB combination in patients who do not have heart failure, avoid concurrent use of beta-blockers and ACE inhibitors⁴⁶ and a dihydropyridine CCB/thiazide diuretic combination⁴⁷ in all elderly patients.¹⁴

How does the evidence apply to your patient?

As we saw earlier, Esther V. has isolated systolic hypertension, which increases her risk of myocardial infarction, stroke, and heart failure. Even though she is 81 years old, studies such as HYVET support the treatment of her hypertension. Certainly, you'll encourage her to limit her salt intake, follow a healthy diet, and exercise daily, as tolerated.

But because Mrs. V. has stage 1 hypertension, her preference and her ability to tolerate therapy will play a key role in the decision to initiate treatment. If her blood pressure does not respond to lifestyle modifications and she is agreeable to medical therapy, you would recommend 1 antihypertensive agent.

Which drug class is best? Given her history of osteoporosis, a low-dose thiazide diuretic might be a reasonable choice. But because she has a history of hip fracture from a fall, it would be prudent to avoid agents associated with volume depletion—and to opt for either an ACE inhibitor or a CCB as first-line therapy instead. It is extremely important to obtain a list of any OTC medications Mrs. V. is currently taking and to advise her to avoid the use of NSAIDs.

You would also want to obtain the results of Mrs. V.'s most recent bone mineral density test, and talk to her about the

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When it's necessary to add a second antihypertensive, choose agents that have complementary mechanisms of action.

importance of taking calcium with vitamin D. If there are concerns about her gait, you would consider a formal gait evaluation, as well. Finally, you would review potential side effects, including orthostatic hypotension, and tell Mrs. V. to call if they occur, and schedule an appointment to monitor her serum potassium and renal function in a few weeks. ■

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It is prudent to avoid agents associated with volume depletion in a patient with a history of a hip fracture from a fall.

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**1.25
 CME/CE
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Incretin-related therapies:

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