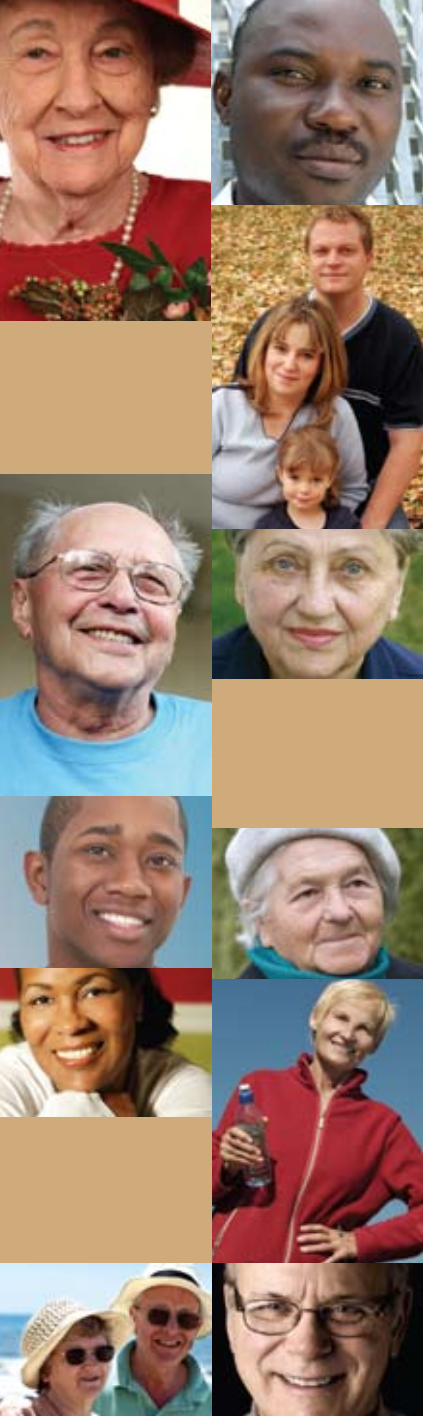
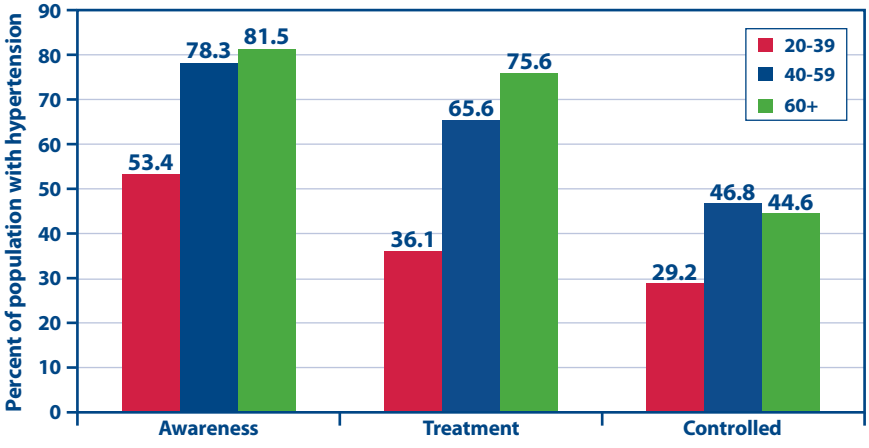


The "Silent Killer" – still at large

Most Americans over age 60 have hypertension. Even among those whose blood pressures are normal at age 55, the lifetime risk of hypertension is 90%.[1] Despite the availability of dozens of effective treatments and decades of data, less than two-thirds of patients in the U.S. with hypertension are receiving treatment, and less than half are adequately controlled.[2] In hypertensive patients, achieving a 12 mmHg reduction in systolic blood pressure (SBP) over 10 years will prevent 1 death for every 11 patients treated, making this one of the most powerful tools a physician can use to prevent devastating illness and disability.[3]

Figure 1. Percentage of U.S. patients with hypertension aware of their disease, on treatment, and adequately controlled (by age).



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Begin with lifestyle changes…

Some patients may be able to control their blood pressure with improved diet, reductions in salt or alcohol, weight reduction, and exercise. These measures, as shown below, are key components of management for nearly all patients.

Table 1. Lifestyle modifications for blood pressure control.

Modification	Recommendation	Approximate reduction in systolic blood pressure
Weight reduction	Achieve or maintain normal body weight (BMI=18.5-25)	5-20 mmHg/10 kg of weight loss
Adopt "DASH" eating plan	Consume a low-fat diet rich in fruits, vegetables	8-14 mmHg
Dietary sodium reduction	Less than 100 mmol/day (2.3 g/day)	2-8 mmHg
Physical activity	Aerobic physical activity 30 min/day on most days	4-9 mmHg
Moderation of alcohol consumption	Men < 2 oz/day Women < 1 oz/day	2-4 mmHg

Adapted from JNC 7 Guidelines[4]

When a drug is needed…

Many antihypertensive medications are available, but direct comparisons between classes were scarce prior to the ALLHAT study.[5] This trial was an NIH-supported head-to-head randomized comparison of common treatment choices in >42,000 patients with hypertension: a thiazide-like diuretic (chlorthalidone), a calcium channel blocker (CCB: amlodipine [Norvasc]), an ACE inhibitor (ACEI: lisinopril), and an alpha-blocker (doxazosin [Cardura]).

Highlights from the ALLHAT trial[5]

- **Thiazides achieved better systolic blood pressure control** (Fig 2)**, and as good or better health outcomes compared to the other drugs studied, and were just as well tolerated.**

- ☑ Thiazides were superior to CCBs and ACEIs in preventing congestive heart failure (Fig 3).
- ☑ Thiazides were superior to ACEIs in preventing cardiovascular events (Fig 4).
- ☑ Thiazides were superior to alpha-blockers in preventing cardiovascular events, including both CHF and coronary artery disease.

Figure 2. BP reduction by treatment group: compared to chlorthalidone, SBP was significantly higher in the amlodipine (1mmHg) and lisinipril (2mmHg) groups.

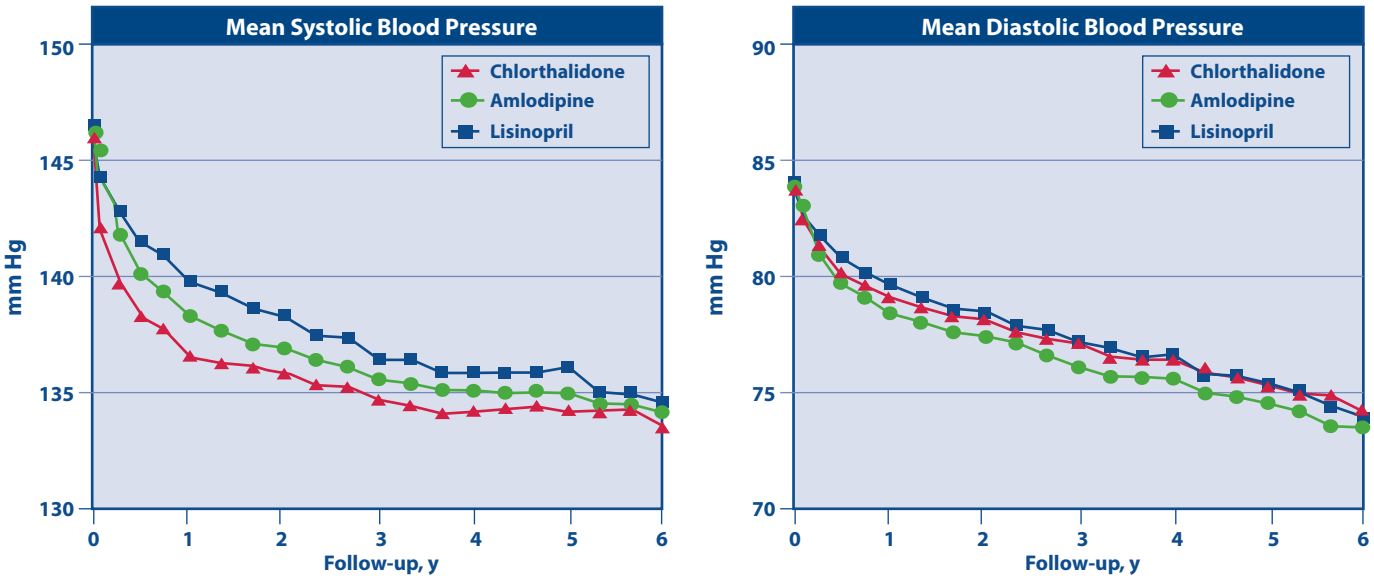


Figure 3. Rates of congestive heart failure.

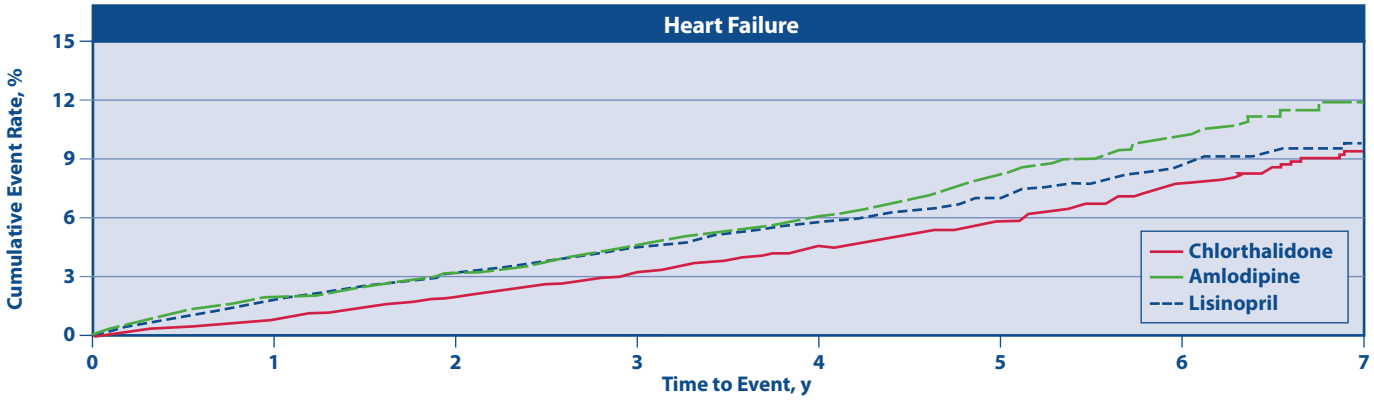
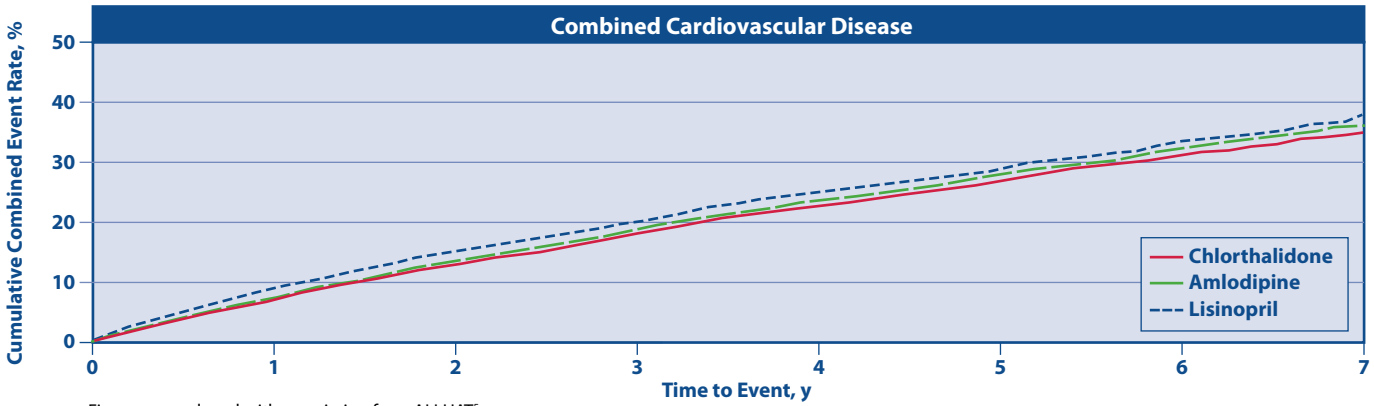


Figure 4. Rates of combined cardiovascular disease events.



Figures reproduced with permission from ALLHAT[5]

Back to basics…

The Joint National Commission on Hypertension (JNC), funded by the NIH, is the nation's premier authority on blood pressure treatment. Its most recent guidelines emphasize the central role of thiazides in the management of hypertension. **When used in moderate doses, thiazides are very effective, very well tolerated, and inexpensive.** JNC has identified specific co-exisiting conditions as "compelling indications" for the addition or use of other drug classes, such as ACEIs and beta-blockers (BBs). These include diabetes, coronary artery disease and congestive heart failure (Table 2).

Thiazide diuretics: Good drugs with a bad rap
Some physicians are reluctant to prescribe thiazides because of concern over side effects such as hypokalemia. However, much of the bad reputation of thiazides arose in earlier times, when excessively high doses were used. At moderate doses (e.g., 12.5 mg of hydrochlorothiazide [HCTZ]), they provide effective blood pressure control, with a rate of side effects no higher than other antihypertensives, and only 2% higher than placebo.

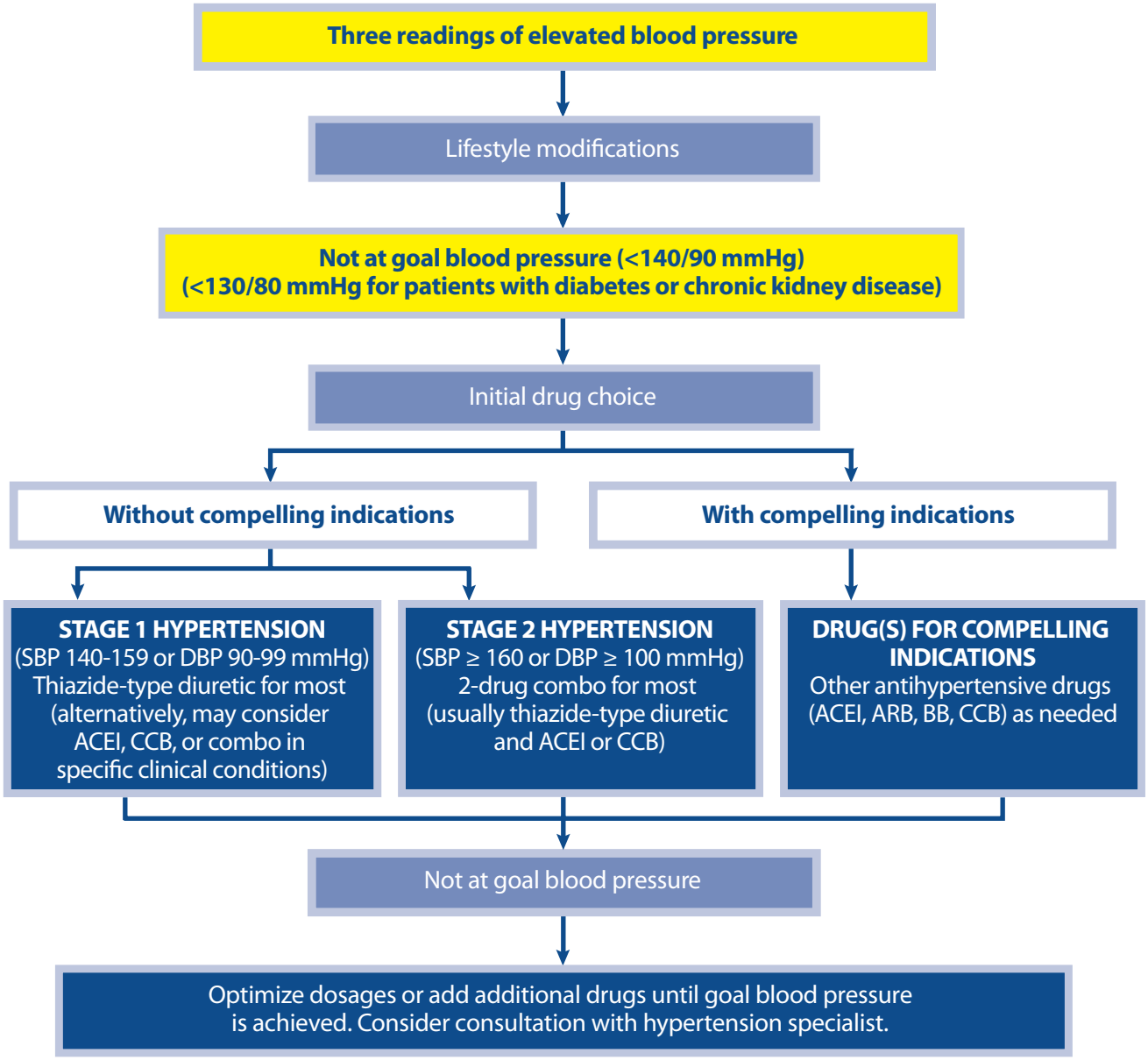
Table 2. Compelling indications for use of other medications for hypertension.

Compelling Indication	Drug Class	Target Subgroups
CHF	ACEI (ARB if intolerant) Beta blocker Aldosterone blocker	All EF <40% EF <40% and symptoms
MI/Ischemic heart disease	Beta blocker ACEI	All All
High risk of CAD, CAD, angina, or silent ischemia	Beta blocker (CCB if intolerant)	All
Diabetes	ACEI (ARB if intolerant)	All
Chronic kidney disease	ACEI (ARB if intolerant)	All
Cerebrovascular disease	No clear agent preference	

When to treat and how…

- In general, blood pressure should be maintained at 140/90 or less, or less than 130/80 in patients with diabetes or chronic kidney disease.
- Start with a thiazide diuretic unless there is a *compelling indication* for use of a different drug.
- Most regimens requiring two or more drugs should include a thiazide diuretic, unless there is a contraindication.

A practical approach to hypertension control.[4]



Adapted from JNC 7 treatment algorithm[4]

Once you've chosen the drug class, does it matter which individual drug you use?

There is very little data suggesting that any one agent within a drug class (e.g., ACEIs) is superior to another in that class. Only a few trials have directly compared drugs within a class head-to-head and most studies have just assessed blood pressure control and safety. These studies suggest that in general, **all agents within a given drug class are equally effective and equally safe**. There can, however, be substantial differences in cost between agents.

Combination therapy for hypertension

Even at high doses, most drug classes will lower blood pressure by 9-10 mmHg. Therefore, for many patients, **achieving adequate hypertension control can require more than one medication**. In fact, only about **one-quarter** of patients will have good BP control on only one drug. Combination therapy with moderate doses of agents from multiple classes can provide additive effects on blood pressure without increasing the risk of adverse events from high doses of individual drugs. Most combinations are safe, except for beta blocker/CCB combinations (risk of bradycardia) and ACEI/ARB combinations (risk of hyperkalemia, hypotension, syncope, and renal dysfunction).

The choice of combination therapy for hypertension should be guided by the JNC-7 guidelines:[4]

- Thiazides should be a part of most multi-drug regimens
- The choice of other medications should be driven by compelling indications

Many anti-hypertensive combinations can be prescribed as a single pill in a once-daily generic form, allowing for simple and affordable regimens. Combinations of hydrochlorothiazide (HCTZ) and generic ACEIs are especially appealing.

Effect of standard dose antihypertensive on SBP.

Drug class	SBP reduction (mmHg)
Thiazide	8.8
Beta-blocker	9.2
ACEI	8.5
ARB	10.3
CCB	8.8
Renin Inhibitor	8.7

From initial treatment to control

Most patients with hypertension do not achieve adequate blood pressure control. The two main reasons are poor compliance and lack of treatment intensification by the physician.

Patient compliance

Up to 50% of patients stop their antihypertensive medications after only a short time – and many patients never even fill the first prescription. Improving patients' adherence with their prescribed regimens is an effective way to improve blood pressure control.

What works to promote compliance?

- ☑ MAKE THE REGIMEN AS **SIMPLE** AS POSSIBLE
- ☑ BE SURE YOU PRESCRIBE THE MOST **AFFORDABLE** MEDICATIONS
- ☑ **ASK THE PATIENT** IF HE OR SHE IS HAVING DIFFICULTY TAKING THE PRESCRIBED MEDICATIONS

At each visit, **re-educate** the patient about the importance of controlling blood pressure.

Overcoming inertia

Even with good compliance, adequate control of blood pressure often requires using multiple agents. In many cases "clinical inertia" can impede the addition of additional antihypertensive medications.[6] Physicians must be willing to add medications when blood pressure is not adequately controlled.

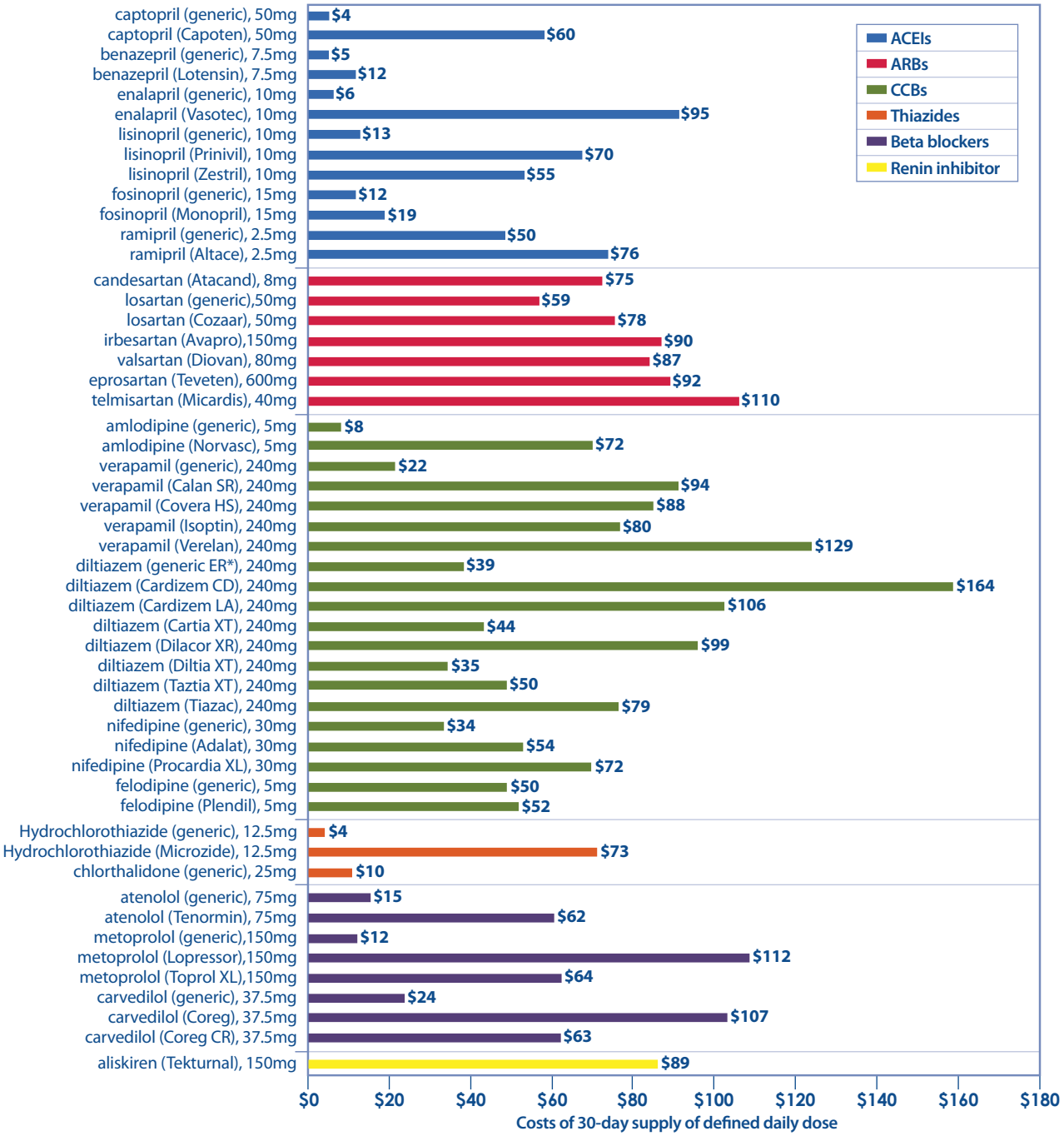
Stopping the "Silent Killer"

Effective hypertension control is one of the best ways a physician can make a real difference in patients' health by preventing myocardial infarction, stroke, renal damage, and premature death.

Several key steps can improve current management:

- ☑ Low-dose thiazides should play a central role as initial therapy for many patients, and as part of combination treatment for others
- ☑ Choose other medications based on compelling indications
- ☑ Combination therapy will often be needed
- ☑ When choosing agents, consider cost and compliance

Monthly cost of antihypertensive agents prescribed at defined daily doses (DDD).



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References: **1.** Vasan, R.S., et al., Residual lifetime risk for developing hypertension in middle-aged women and men:The Framingham Heart Study. *JAMA*, 2002. 287(8): p. 1003-10. **2.** Wong ND, et al. Inadequate control of hypertension in US adults with cardiovascular disease comorbidities in 2003-2004. Arch *Intern Med* 2007;167(22):2431-6. **3.** Ogden, L.G., et al., Long-term absolute benefit of lowering blood pressure in hypertensive patients according to JNC VI risk stratification. *Hypertension* 2000; 35(2):539-43. **4.** Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - Complete Report. JNC 7 Complete Report: The Science Behind the New Guidelines. National Institutes of Health, National Heart, Lung, and Blood Institute. NIH Publication No. 04-5290. 2004. Obtained June 2010 from: http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.htm. **5.** The ALLHAT Collaborative Research Group. Sponsored by the National Heart, Lung, and Blood Institute (NHLBI). Major outcomes in high risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs. diuretic. *JAMA* 2002:2981-2997. Obtained June 2010 from: http://allhat.uth.tmc.edu/Slides/Results.ppt. **6.** Phillips, L.S., et al., Clinical inertia. *Ann Intern Med*, 2001. 135: p. 825-834.

Additional references documenting these recommendations are provided in the evidence document accompanying this material.

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