An Economic Evaluation of the JNC Hypertension Guidelines Using Data From a Randomized Controlled Trial

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Background: **We wanted to determine the clinical cost of managing hypertension when following the Joint National Committee on Hypertension (JNC) guidelines, including drug therapy, the cost of monitoring for and treating side effects, compliance, and the cost of switching after therapeutic failures.**

Methods: **The base-case analysis considers antihypertensive agents from four therapeutic classes that were recently evaluated in a large randomized trial: enalapril, amlodipine, acebutolol, and chlorthalidone. Clinical evaluation, therapy, and monitoring for hypertension are modeled with an incidence-based Markov model. Clinical inputs include agent efficacy, side effects, and compliance with dosing schedules. JNC-recommended clinical and laboratory monitoring schedules are followed for each agent. Switches between classes occur for therapeutic failures. Drug and medical care costs are valued in 1995 US dollars.**

Results: **Although patients whose hypertension was initially treated with amlodipine achieved control more readily than patients who were given the other agents, the initial costs to achieve and maintain hypertension control were lowest for chlorthalidone ($641), followed by acebutolol ($920), amlodipine ($946), and enalapril ($948). Maintenance costs were lowest for chlorthalidone. For all agents except chlorthalidone, drug costs were the largest component of overall costs, followed by the costs of office visits, laboratory monitoring, and switching between classes for therapeutic failures.**

Conclusions: **By following JNC guidelines, a slightly higher percentage of patients will achieve hypertension control with a newer class calcium channel blocker (amlodipine) but at a substantially higher cost than with a generic diuretic (chlorthalidone). (J Am Board Fam Pract 1999;12:105-14.)**

Hypertension is a common and costly condition that affects 43 million people in the United States[1] and consumes more than $10 billion in direct medical expenditures annually.[2] When initiating pharmacologic therapy for their hypertensive patients, health care providers are able to choose from dozens of antihypertensive agents encompassing several therapeutic classes, each varying in efficacy, side effects, dosing schedules, and cost. Guidelines for managing essential hypertension have been created to simplify the decision-making process, reduce practice pattern variation, and improve patient outcomes.[3] The most widely cited guideline for hypertension was written by the fifth Joint National Committee on Hypertension (JNC-V).[4] The sixth Joint National Committee (JNC-VI) report has also recently been published.[5] The JNC guidelines recommend diuretics or β-blockers as first-line agents for managing essential hypertension, in part because of their proved efficacy in reducing hypertension-related morbidity and mortality in large, randomized trials.

Published hypertension management guidelines (including the JNC reports) have not formally considered economic evidence when making recommendations regarding initial selection of agents and management of this condition. This oversight might be an important. Given that hypertension is widespread and that the most expensive antihypertensive medications can be 100 times more costly than the least expensive agents,

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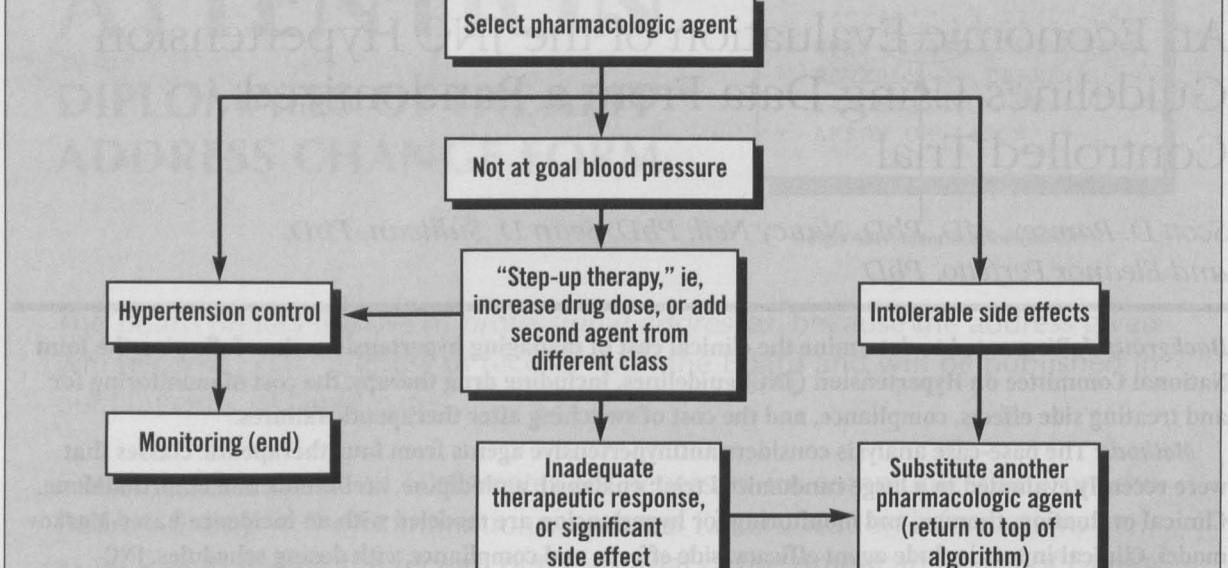

Figure 1. Treatment algorithm recommended by the sixth Joint National Committee (JNC-VI) guideline for management of mild to moderate essential hypertension after the decision to prescribe has been made. Hypertension control-patient has achieved goal blood pressure or is making considerable progress toward that goal.

recommendations that influence practice patterns could have a tremendous economic impact on national expenditures for this condition.

We created a decision analysis model that follows the hypertension management strategy outlined in the JNC guideline for treating uncomplicated adult hypertensive patients. The model compares alternative scenarios in which patients are initially given a β-blocker, diuretic, calcium channel antagonist, or angiotensin converting enzyme (ACE) inhibitor as single-agent therapy. The model was designed to address the question, what antihypertensive agent(s) should be recommended for initial therapy as part of a treatment guideline, given the goals of maximizing control while minimizing the total cost of care for patients with hypertension? We consider the entire cost of managing hypertension, including the cost of the drug itself, hypertension-related office visits, costs of monitoring for and treating adverse effects, and the costs incurred when patients are switched to a new agent after a therapeutic failure or adverse experience. Clinical efficacy data for the model are taken from the Treatment of Mild Hypertension Study (TOMHS)[6] and other literature. We then subject the model to a variety of sensitivity analyses to test the cost and outcome predictions across a rage of clinical management and economic scenarios.

Methods

Decision Analysis Model

The model was designed to simulate clinical decisions and outcomes that would occur when physicians follow the JNC hypertension management guideline in a primary care setting. The clinical decision-making component was based on the treatment algorithm proposed by the JNC-V and JNC-VI for management of mild hypertension in patients who had no preexisting contraindications to therapy with any class of antihypertensive agents. The analysis begins at the point where a decision to initiate drug therapy has been made (Figure 1).

The primary care management pathway begins with selection of a single agent at a low dose as monotherapy. Patients who do not achieve adequate control at low dose are given a higher dose of the same agent or combination therapy with another agent from a different class. If control is still not achieved, the patient is switched to a low-dose, single agent from another therapeutic class, and the course of therapy outlined above is repeated. The process continues until control of hy-

pertension is achieved or all agents have been tried at all doses. Those who experience intolerable side effects with low-dose, high-dose, or combination therapy are randomly assigned a different pharmacologic agent at low dose from among the alternatives. Patients achieving goal blood pressure and tolerating the prescribed therapy remain on that regimen for the duration of the simulations.

In accordance with JNC guidelines, our model assumes a comprehensive initial evaluation visit and follow-up visit 4 weeks after drug therapy begins. In cases in which a medication change is made, patients are reevaluated monthly until control is achieved. The model includes periodic laboratory monitoring for adverse events when using specific agents (Table 1). To account for concerns regarding the effect of β-blockers and diuretics on serum lipid levels, the model includes a one-time posttreatment serum lipid evaluation after starting therapy with these agents. We assume that 2 percent of patients on chlorthalidone and 1 percent of patients on acebutolol will require switching to another agent as a result increased lipid levels caused by therapy. After hypertension control is achieved, patients are reevaluated every 12 weeks for the remainder of the simulation.

The perspective of the model is that of a health care payer responsible for all direct medical expenditures, including drug costs. The time horizon for the model is 5 years from the start of therapy. Clinical outcomes and costs at years 1, 3, and 5 are presented. Clinical outcomes are presented as the proportion of patients on each therapy with controlled hypertension at the end of the period of observation. Economic outcomes include the cost to achieve control after starting treatment and the cost of maintenance therapy once successful control has been achieved. The costs of treating rare, serious adverse events and long-term major disease endpoints (eg, stroke, myocardial infarction) are not included in the analysis. All costs reported here are in 1995 US dollars. Costs beyond the first year are discounted at a rate of 3 percent per annum.

Hypertension-related expenditures include both drug and nondrug-related care. Drug costs include the cost of each agent plus a dispensing fee; drug costs used in this analysis are based on the 1995 average wholesale price list published in *Drug Topics Red Book*.[7] Nondrug costs include the cost of the baseline assessment, routine monitoring and follow-up (office visits and laboratory testing), and for treatment failures, the cost of switching therapeutic classes. All nondrug costs (eg, office visits, laboratory tests) are based on modal reimbursement schedules obtained from a large managed care organization in Washington State.

Table 1. Laboratory and Monitoring.

Therapeutic Class	Laboratory and Monitoring
All: baseline assessment	Urinalysis, complete blood cell count, blood glucose, potassium, calcium, creatinine, uric acid, cholesterol, triglycerides, electrocardiography
ACE inhibitors	Scheduled creatinine and potassium follow-up
β-Blockers	One-time follow-up serum cholesterol and triglycerides
Calcium channel blockers	None
Diuretics	Scheduled creatinine and potassium follow-up One-time follow-up serum cholesterol and triglycerides

ACE - angiotensin-converting enzyme.

Treatment effectiveness—the probability of achieving hypertension control with a specific pharmacologic agent in clinical practice—is usually less than the efficacy rates observed in clinical trials. We modeled effectiveness as a function of treatment efficacy and expected compliance after accounting for patients who immediately switch agents because they experience intolerable side effects. The efficacy rates for each antihypertensive agent are based on results from TOMHS,[6] a prospective, randomized placebo controlled trial of hypertension treatments in a community practice setting. Patient compliance with therapy is a function of the dosing schedule.[8] Patients who achieve control are assumed to have controlled hypertension for the duration of the simulation. Patients whose hypertension is not controlled with any of the available therapeutic options (because of side effects, inadequate therapeutic response, or both) are classified as having uncontrolled hypertension at the end of the simulation period.

Our base-case analysis considers the antihypertensive agents from four commonly prescribed therapeutic classes that were evaluated in TOMHS.[6] The treatment options were as follows: (1) monotherapy; enalapril (ACE inhibitor),

Table 2. First-Year Expected Costs Based on Therapeutic Outcomes of TOMHS.

Agent Selected for Initial Therapy	Daily Dose (mg)	Daily Medication Cost* ($)	Percent Effectiveness† Initial Agent	First-Year Expected Costs for Control Achieved ($) Initial Agent	First-Year Expected Costs for Control Achieved ($) Any Agent‡	Expected Annual Maintenance Costs ($)
Acebutolol						
Low dose	400	1.12	77.8	920	938	616
High dose	800	2.24				1020
Amlodipine						
Low dose	5	1.22	82.5	946	940	642
High dose	10	2.11				963
Enalapril						
Low dose	5	0.95	68.1	948	949	631
High dose	10	1.00				649
Chlorthalidone						
Low dose	15	0.08	67.5	641	645	328
High dose	30	0.09				331
Acebutolol (800 mg) + chlorthalidone (15 mg)§		2.32				1038
Amlodipine (10 mg) + chlorthalidone (15 mg)§		2.19				992
Enalapril (10 mg) + chlorthalidone (15 mg)§		1.08				678
Chlorthalidone (30 mg) + enalapril (2.5 mg)§		0.84				591

TOMHS - Treatment of Mild Hypertension Study.[6]
*Average wholesale price, 1995 *Drug Topics Red Book*.[7]
†Effectiveness - number of patients who achieve control on initial therapy at end of first year. Effectiveness modeled as function of drug efficacy, expected compliance, and dropouts from intolerable side effects.
‡Includes cost of managing those switched to alternative agents after therapeutic failure with initial agent.
§Not used as initial therapy.

amlodipine (calcium channel blocker), acebutolol (β-blocker), or chlorthalidone (diuretic); or (2) combination therapy of each agent plus chlorthalidone or chlorthalidone plus enalapril. We ran the model four times, each time using one of the four agents as initial monotherapy. Efficacy and safety data for each agent were based on the results published in the TOMHS report.[6]

Sensitivity Analysis

Sensitivity analysis tested the effect of modifying the input parameters on the economic endpoints. We adjusted the input parameters in the model to determine how they affected the cost of hypertension care with each agent at years 1, 3, and 5. The drugs used in the TOMHS study are neither the most common nor least costly agents in each antihypertensive class. To determine the sensitivity of the economic endpoints to the price of the antihypertensive agent, we substituted the cost of highest, lowest, and median-priced agents in the same therapeutic class for the price of each agent used in TOMHS. Unit prices for the highest, lowest, and median-priced agents in the each therapeutic class were taken from the 1995 *Drug Topics Red Book*. Next, efficacy rates for each agent were also adjusted upward and downward 50 percent from the base-case levels. Base-case rates for compliance were also adjusted from 100 percent (perfect compliance) to one half of the base-case level. Finally, the rate of intolerable side effects was adjusted from 0 percent to 100 percent higher than the base-case levels. One-way sensitivity analyses were performed on all inputs and two-way sensitivity analyses were performed on drug cost and efficacy parameters.

Results

Data from TOMHS reveal that the initial agent controlling the highest proportion of the cohort as single agent therapy was amlodipine (82.5 percent), followed by acebutolol (77.8 percent),

Table 3. Expected Costs at 1, 3, and 5 Years From Start of Therapy for Patients Who Achieve Control on Initial Therapeutic Agent, by Category.

Initial Therapeutic Agent	Medication Cost ($)	Percent of Total Cost	Office Visits* ($)	Percent of Total Cost	Laboratory Monitoring ($)	Percent of Total Cost	Total Cost ($)
Chlorthalidone							
Year 1	29	5	322	50	289	45	641
Year 3	84	7	711	57	453	36	1248
Year 5	136	7	1077	59	608	33	1821
Acebutolol							
Year 1	408	44	322	35	189	21	920
Year 3	1180	57	711	34	189	9	2080
Year 5	1907	60	1077	34	189	6	3173
Amlodipine							
Year 1	445	47	322	34	179	19	946
Year 3	1285	59	711	33	179	8	2175
Year 5	2078	62	1077	32	179	5	3334
Enalapril							
Year 1	346	37	322	34	279	29	948
Year 3	1000	46	711	33	443	21	2154
Year 5	1617	49	1077	33	598	18	3292

Note: Costs are cumulative and, after year 1, discounted at 3% per annum.
*Includes initial comprehensive examination at baseline (year 1 only).

enalapril (68.1 percent), and chlorthalidone (67.5 percent). Most of the TOMHS patients whose hypertension was not controlled on initial therapy were able to achieve control with one of the other agents using single-agent therapy. For example, 97 percent of patients who were initially given acebutolol achieved hypertension control on acebutolol or another drug as single-agent therapy; only 3 percent required combination therapy.

The economic model revealed that the average, per-patient cost to achieve control on any agent—including initial evaluation, therapy, monitoring and treatment of side effects, and switching costs for therapeutic failures—was lowest when the initial therapy was chlorthalidone ($645) and highest when the initial therapy was enalapril ($949) (Table 2). After hypertension was controlled, annual maintenance costs were lowest for those who were treated with low-dose chlorthalidone ($328) alone and highest for those controlled with high-dose acebutolol alone ($1020). Annual maintenance costs were much higher for patients taking combination therapies, ranging from $591 for 30 mg of chlorthalidone plus 2.5 mg of enalapril to $1038 for those taking 800 mg of acebutolol plus 15 mg of chlorthalidone.

The relative economic outcomes for each agent did not change for years 1, 3, and 5, although the magnitude of the difference in expected costs increased steadily with time (Table 3). For 5 years of treatment, costs per patient were lowest when the initial therapy was chlorthalidone ($1821) and highest when initial therapy was amlodipine ($3334). For all agents except chlorthalidone, drug costs dominated the cost of hypertension care for the entire period of observation (Table 3).

Sensitivity Analyses

The cost of achieving hypertension control and the subsequent costs of maintenance therapy were most sensitive to changes in the prices of each agent (Figure 2). Lowering the price of enalapril by 50 percent, for example, reduced by about 12 percent the cost to achieve control (on any agent) when using enalapril as initial therapy. Similarly, annual maintenance therapy costs (for hypertension controlled on enalapril) decrease by nearly 25 percent with a 50 percent reduction in the price of this medication.

The cost of achieving control was modestly sensitive to changes in efficacy, compliance, and side effects that result in drug switching for therapeutic failures. The cost to achieve control on any agent decreased as the efficacy rate was reduced for the more expensive agents, because patients started on the more expensive agents were then more likely to be switched to a less expensive β-blocker or diuretic. Changes in efficacy, compliance, and side effects did not affect maintenance costs. Overall, antihypertensive treatment costs

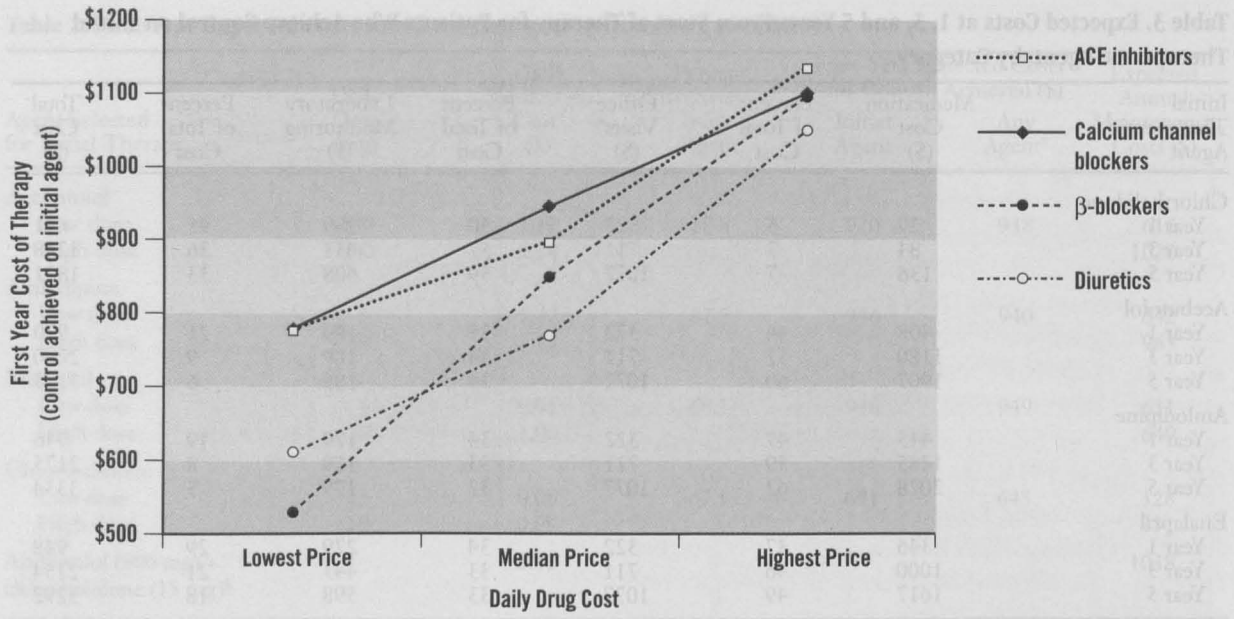

Figure 2. Relationship between drug cost and first-year cost of therapy (when control is achieved on initial agent). Price ranges for available agents in each drug class taken from 1995 *Drug Topics Red Book.*[7] Daily drug costs (lowest, median, highest) used were angiotensin-converting enzyme (ACE) inhibitors ($0.50, 0.81, 1.46), β-blockers ($0.05, 0.93, 1.60), calcium channel blockers ($0.78, 1.23, 1.64), and diuretics ($0.01, 0.43, 1.20). Only therapies with once- or twice-daily dosing schedules were considered.

were more sensitive to changes in the cost of routine office visits or laboratory monitoring than changes in efficacy, compliance, and side effects. Office visit and monitoring costs affected the cost to achieve control, switching costs, and maintenance costs for patients with controlled hypertension. In contrast, compliance and side effects affected only the cost to achieve control.

Changing the laboratory monitoring schedule had a modest impact on costs for agents for which routine laboratory monitoring is recommended. Recent evidence suggests that very low dose diuretics are effective for controlling blood pressure.[9,10] Moreover, since there are considerably fewer metabolic effects at very low doses, routine patient monitoring might not be necessary. When we model initial therapy with very low dose chlorthalidone (7.5 mg/d versus 15 mg/d) and include one-time only monitoring of creatinine and potassium, first-year treatment costs fall from $645 to $542, and annual maintenance costs fall by about 30 percent. Chlorthalidone is not currently available in 7.5-mg tablet form, however, and these estimates do not account for potential reductions in patient compliance that could result from the need to split 15-mg tablets.

In a two-way sensitivity analysis of daily drug cost and drug efficacy, we found that the efficacy required to maintain a constant cost of care (annual cost of care when hypertension is controlled on any therapy) rose substantially for modest increases in drug price (data not shown). For example, if the price of enalapril is increased by 6 percent (about 5 cents per day), the efficacy of enalapril would have to rise by approximately 15 percent to maintain the same cost to achieve control on this agent.

Discussion

The JNC hypertension guidelines call for the use of β-blockers and diuretics as first-line therapies and recommend switching treatment to an agent from another therapeutic class when control is not achieved on initial therapy at the maximum tolerated dose. We created a decision analysis model of the JNC guidelines to compare therapeutic outcomes and costs to achieve and maintain hypertension control when initial therapy is selected from each of the four most commonly used classes of antihypertensive agents: β-blockers, diuretics, ACE inhibitors, and calcium channel blockers. Our analysis shows that even though the highest percentage of patients achieve control after initial therapy with the calcium channel blocker, the cost

to achieve and maintain control on this medication can be three times as high as when a diuretic or β-blocker is selected as initial therapy. Sensitivity analyses reveal that the cost of the initially selected antihypertensive agent drives the cost of hypertension care far more than other factors, including drug efficacy, side effects, switching for therapeutic failures, or the cost of monitoring the patient.

Pharmaceutical manufacturers often claim that the reduced likelihood of switching as a result of better efficacy or side effect profiles justifies the higher per-unit expenditures for many of the newer agents. Our message for primary care clinicians is that their preferred initial choice for treating essential hypertension has important economic consequences, even accounting for patients who ultimately must be switched to other agents.

The method of analysis was somewhat conservative (ie, less favorable to β-blockers and diuretics) in several ways. We assumed that diuretic therapy included regular monitoring of serum potassium and creatinine; however, many patients on low-dose diuretics (eg, those on a stable regimen) might not need regular monitoring of creatinine and potassium. Similarly, we assumed that patients on β-blockers and diuretics would receive a one-time posttreatment evaluation of serum lipids, although the clinical impact of these drugs on lipids is controversial.[11-14] Finally, we assumed that patients with stable, controlled hypertension would receive follow-up visits every 12 weeks (according to JNC guidelines), although in practice such patients might require fewer visits. Each of these assumptions raises slightly the cost of β-blockers and diuretic therapy relative to treatment with ACE inhibitors and calcium channel blockers.

Rare, catastrophic side effects were not included in the model because of the low expected economic impact of these events. For example, if the cost of treating angioedema with laryngeal edema in patients with ACE inhibitors (1 case per 100,000 patients) were $50,000 per case,[15] the cost of treatment with these agents would be raised by $0.50 per person per year.[13]

Our selected patient population was young to middle-aged adults with mild, uncomplicated hypertension. The efficacy of some of the agents might vary according to the age of the population. For example, hydrochlorothiazide was shown in at least one study to be more effective at lowering blood pressure and better tolerated in older adults than were other agents.[16]

This model does not address the impact of antihypertensive therapy on health-related quality of life. The TOMHS investigators report that all patients receiving antihypertensive therapy, compared with placebo, experienced an improvement in health-related quality of life, but that only the gains in patients receiving chlorthalidone or acebutolol achieved statistical significance.[17] Thus, the attractiveness of diuretics and β-blockers established by this economic model appears to be enhanced by available quality-of-life data.

This analysis was limited to a population with essential hypertension and no presumed contraindications to any one class of antihypertensive agents. We make the reasonable assumption that hypertension control is the goal of therapy, as none of these agents has been shown to be superior to the others at reducing the hypertension-related endpoints of stroke, myocardial infarction, and death in this population. A recent meta-analysis[18] suggests that low-dose diuretic therapy might be more effective in preventing coronary disease than either high-dose diuretic therapy or β-blocker therapy. Certain agents might be favored in selected populations—such as β-blockers for hypertensive patients who have suffered a myocardial infarction, or ACE inhibitors for hypertensive patients with congestive heart failure. In these cases the relevant endpoint (death) is affected by the choice of therapy in addition to the intermediate goal of hypertension control. These populations are beyond the scope of the model. The model also does not consider patients who chronically fail to comply with clinical management and drug therapy.

Do these results apply to other agents from the four therapeutic classes? Unfortunately we lack high-quality, comparative efficacy data from randomized studies of other antihypertensive agents in representative patient populations. The model suggests, however, that modest differences in efficacy among agents in any therapeutic class will be less important than the unit cost of the agents for determining the ultimate economic outcomes. To further illustrate this concept, we modeled the most commonly prescribed agents in each of the four antihypertensive classes (atenolol, lisinopril, verapamil XL, hydrochlorothiazide) in a large managed care plan in Washington State using

Table 4. Outcomes of Other Commonly Prescribed Antihypertensive Agents.

Agent Selected for Initial Therapy*	Daily Dose (mg)	Daily Medication Cost ($)	Percent Effectiveness Initial Agent†	First-Year Expected Costs for Control Achieved ($)		Expected Annual Maintenance Costs ($)
				Initial Agent	Any Agent	
Lisinopril						
Low dose	10	0.78‡	73	886	891	570
High dose	20	0.84‡				591
Atenolol						
Low dose	50	0.09§	81	544	617	236
High dose	100	0.13§				250
Verapamil XL						
Low dose	240	0.96§	86	851	917	549
High dose	360‖	0.97§				904
Hydrochlorothiazide						
Low dose	25	0.01‡	77	615	687	293
High dose	50	0.02‡				296

*Representative agents in each therapeutic class selected based on prescribing patterns in a large managed care organization in Washington State; most frequently prescribed agent in each antihypertensive class selected.

†Effectiveness denotes number of patients who achieve control on initial therapy at end of observation period. Effectiveness is modeled as function of drug efficacy, expected compliance, and dropouts from intolerable side effects. Efficacy rates for agents listed taken from a large randomized trial similar to TOMHS.[19]

‡Average wholesale price.

§Health Care Financing Administration - maximum allowable cost.

‖180-mg tablet taken twice daily.

contracted unit drug prices available to that plan and efficacy rates from a large randomized trial similar to TOMHS.[19] Atenolol was the least expensive therapeutic option, followed closely by hydrochlorothiazide (Table 4). The unit price of atenolol is about one-half that of acebutolol, the second least costly agent in the comparison of the TOMHS therapies.

Although the absolute differences in first-year, per-patient treatment costs between therapeutic classes is relatively small (about $300 per year from Table 4), the widespread occurence of hypertension makes these small differences important. As an example, consider a managed care organization treating 5000 patients with newly diagnosed mild hypertension in a given year. The decision model predicts that by recommending chlorthalidone as initial treatment for these patients, this organization could save up to $1.5 million compared with a policy in which amlodipine was the recommended initial therapy.

Clinicians face a vast array of pharmacologic choices for their hypertensive patients. Multiple competing claims can make the process of selecting an initial agent confusing. Many manufacturers attempt to persuade providers that the use of their antihypertensive medication is justified by higher efficacy rates in controlled trials, more favorable side effect profiles, or lower need for adverse event monitoring compared with alternatives. Hypertension guidelines, such as those written by the JNC, attempt to persuade clinicians on the basis of evidence from clinical trials and recommendations by a panel of experts in the field.

Reducing the cost of managing chronic illnesses such as hypertension is now a priority for many health care providers and managed care plans. To date, however, most groups that create clinical practice guidelines, such as the JNC, do not consider evidence from economic analyses when developing their evaluation and treatment recommendations. It has been suggested elsewhere that minimizing the cost of managing hypertension in a patient population is a reasonable goal for guideline development.[20] The economic analysis presented here provides a mechanism for systematically considering the complete cost of first-year treatment, including the cost of evaluation and monitoring, the unit costs of the drugs, and the cost of switching for therapeutic failures.

Retrospective economic analyses of hypertension care that include costs as outcomes using alternative therapies in individual clinic settings have yielded results similar to those presented

here.[21,22] Edelson and colleagues[23] found that from a societal standpoint, β-blockers and diuretics were the most cost-effective therapy for mild hypertension. Such analyses, however, are often seen as having limited usefulness in settings with different costs of care (including medication costs, which are often different from the prices quoted in the *Drug Topics Red Book*) and different practice styles. As noted above, our model is designed to integrate efficacy, compliance, and safety data from clinical trials with the unique treatment costs and management strategies of a given institution. The model was designed to be a useful source of economic data for decision makers who are adapting hypertension guidelines such as JNC-V and JNC-VI for use in their own organizations.

We also recommend that national groups such as the JNC formally consider economic evidence from clinical studies and decision analysis models, along with drug efficacy and safety data, when updating their recommendations for the evaluation and treatment of hypertension. The JNC-VI recommendations were released while the study was being conducted but did not consider economic outcomes as part of the process. Furthermore, we emphasize that focusing on medication costs alone is insufficient, because the entire cost of hypertension therapy—including evaluation, monitoring, and switching costs in addition to drug costs—is affected by the medication choice. The inclusion of economic end points can only enhance the attractiveness of any guideline to managed care organizations. Additionally, guidelines specifying "lowest cost" management strategies that produce acceptable results can be used to avoid undertreatment of patients with hypertension. Finally, decision analyses might be helpful for the evaluation of the relative clinical and economic outcomes of hypertension treatment in special populations, such as those with coronary disease or diabetes.

Conclusions

This analysis suggests that diuretics and β-blockers, which have been recommended as initial monotherapy for patients with hypertension on the basis of clinical evidence, are also the most attractive options from an economic standpoint. Medication costs are the largest proportion of the overall cost of managing hypertension, and the total cost of antihypertensive care with time is most sensitive to changes in the cost of medications and laboratory monitoring. Differences in efficacy and compliance between therapeutic classes are small enough to have relatively little impact on the overall cost of managing hypertension. We suggest that new guidelines for managing hypertension should consider both clinical and economic endpoints when making recommendations for pathways of care.

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