The Economic Impact of Hypertension

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High blood pressure is the most common chronic medical problem prompting visits to primary health care providers, yet it is estimated that only 34% of the 50 million American adults with hypertension have their blood pressure controlled to a level of <140/90 mm Hg. Thus, about two thirds of Americans with hypertension are at increased risk for cardiovascular events. The medical, economic, and human costs of untreated and inadequately controlled high blood pressure are enormous. Adequate management of hypertension can be hampered by inadequacies in the diagnosis, treatment, and/or control of high blood pressure. Health care providers face many obstacles to achieving blood pressure control among their patients, including a limited ability to adequately lower blood pressure with monotherapy and a typical reluctance to increase therapy (either in dose or number of medications) to achieve blood pressure goals. Patients also face important challenges in adhering to multidrug regimens and accepting the need for therapeutic lifestyle changes. Nonetheless, the achievement of blood pressure goals is possible, and, most importantly, lowering blood pressure significantly reduces cardiovascular morbidity and mortality, as proved in clinical trials. The medical and human costs of treating preventable conditions such as stroke, heart failure, and end-stage renal disease can be reduced by antihypertensive treatment. The recurrent and chronic morbidities associated with hypertension are costly to treat. Pharmacotherapy for hypertension therefore offers a substantial potential for cost savings. Pharmacoeconomic analyses regarding antihypertensive drug therapies, their costs, and the relevant reductions in health care expenditures are a useful framework for optimizing current strategies for hypertension management. (J Clin Hypertens. 2003;5(3 suppl 2):3–13) ©2003 Le Jacq Communications, Inc.

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Cardiovascular disease (CVD) consistently ranked as the No. 1 cause of death in the United States throughout most of the 20th century, and was listed as the primary cause of death in 35.7% of the 2,417,798 deaths reported in 2001.[1] Approximately 20% of the entire US population (or about 62 million Americans) has at least one type of CVD; of these, 50 million (about 81%) have high blood pressure.[2] Unfortunately, whether the hypertension is treated or untreated, only 34% of Americans with hypertension have their blood pressure controlled to <140/90 mm Hg during a home visit.[3] Thus, an estimated 30–35 million Americans have uncontrolled hypertension, and are therefore at unduly increased risk of cardiovascular morbidity and mortality.[4] On a population basis, hypertensive individuals are at greater risk for disability and earlier death than individuals with normal blood pressure.

In 1972, the National Heart, Lung, and Blood Institute of the National Institutes of Health launched The National High Blood Pressure Education Program,[5] to improve the awareness, treatment, and control of hypertension (defined as blood pressure ≥140/90 mm Hg) in the United States. Since then, the National Health and Nutrition Examination Surveys (NHANES) have demonstrated important gains in all three parameters between NHANES II (1976–1980) and NHANES III, phase 1 (1988–1991). These beneficial trends were reversed in NHANES III, phase 2 (1991–1994) (Figure 1).[6] However, preliminary data from a more recent national survey using the same methodology indicate a slight improvement in the percentage of people with controlled hypertension, to 34%.[3] Surveys conducted in other developed countries have found an even lower prevalence of treatment and control of hypertension.[7]

High blood pressure is currently defined as a systolic blood pressure (SBP) ≥140 mm Hg and/or a diastolic blood pressure (DBP) ≥90 mm Hg. Normal blood pressure is defined as both SBP <120 mm Hg and DBP <80 mm Hg.[3] Many authorities have moved toward a lower threshold for hypertension treatment, due to emerging data from epidemiologic studies. About 60% of the deaths from coronary heart disease (CHD) that were attributed to elevated SBP among men screened for the Multiple Risk Factor Intervention Trial (MRFIT) occurred in the groups with high-normal SBP (130–139 mm Hg) and stage 1 systolic hypertension (140–159 mm Hg).[8] In the Framingham Heart Study,[9] only 5% of individuals with optimal blood pressure at study entry (<120/80 mm Hg) eventually developed high blood pressure, compared with 37% of those with high-normal blood pressure at entry. Furthermore, those with high-normal blood pressure had a much higher risk of events, compared with people with normal (120–129/80–84 mm Hg) or optimal blood pressure at entry.[10] These data provide strong evidence that even people with blood pressures lower than those which are generally treated may be at increased risk for adverse sequelae; however, it is not yet known whether active treatment of these people will significantly reduce cardiovascular events. Some argue that these data provide enough evidence for setting blood pressure targets even lower

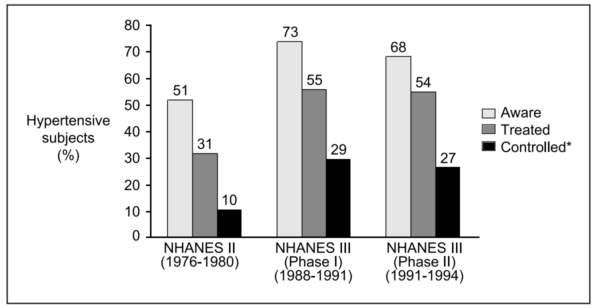

*Figure 1. Awareness, treatment, and control of hypertension in the United States assessed during three time periods. Increases in all parameters that occurred between 1976–1989 and 1988–1991 have leveled off or even decreased in the most recent time period, 1991–1994. *Controlled blood pressure (BP) is defined as systolic BP <140 mm Hg and diastolic BP <90 mm Hg.*[6]

than <140/90 mm Hg for many patients with high blood pressure. This view has so far been substantiated only for diabetic patients.

While the prevalence of hypertension is high (typically about 80%) among patients with existing CVD, the death rate directly attributable to hypertension is small (Table I). These vital statistics data tend to obscure the true impact and benefits of treating hypertension, since high blood pressure is usually not listed as a secondary (or "contributing") cause in the majority of deaths attributed to CVD. Epidemiologic and clinical trial evidence gathered over the past three decades shows a continuous, graded, independent relationship to adverse outcomes for both DBP and SBP,[8] although SBP tends to be a much better predictor among people over age 55 years.[11] Randomized clinical trials have shown that reducing blood pressure with antihypertensive agents

Table I. Prevalence and Deaths (In Millions) Related to Cardiovascular Diseases (CVD) in the United States[1,2]

CVD	Prevalence (% of US Population)	Primary Cause of Death (% of Total Deaths)*
All CVD	61.8 (22.6%)	1.415 (39.4%)
High blood pressure**	50.0 (18.3%)	0.045 (1.8%)
CHD	12.9 (4.6%)	0.515 (21.3%)
Angina pectoris	6.6 (2.3%)	
MI	7.6† (2.7%)	
Diabetes††	10.9 (3.9%)	0.068 (2.8%)
HF	4.9 (1.7%)	0.052 (2.1%)
Stroke	4.7‡ (1.7%)	0.167 (7.0%)
ESRD	0.379 (0.1%)	0.067 (2.8%)

CVD=cardiovascular disease; CHD=coronary heart disease; MI=myocardial infarction; HF=heart failure; ESRD=end-stage renal disease; *based on 2,417,798 deaths from all causes; **defined as blood pressure ≥140/90 mm Hg or taking antihypertensive medication; †estimate of number of current survivors of MI; ††physician-diagnosed diabetes; ‡estimate of number of current survivors of stroke decreases the risk of stroke, CHD, myocardial infarction (MI), heart failure (HF), and progression of renal disease, as well as death from all causes. These rigorous studies were conducted in numerous countries in both men and women, over a wide range of ages, ethnicities, blood pressure levels, and socioeconomic strata.[7] Larger absolute risk reductions have been found in patients at higher absolute risk at baseline, especially patients with type 2 diabetes, the elderly, and those with renal disease.[6] Lower blood pressure targets and larger blood pressure reductions have often been associated with greater benefits, particularly in high-risk populations (e.g., diabetic patients).[8,12,13] A recent meta-analysis[14] of all four trials involving 20,408 patients who were randomized to a higher and lower blood pressure target showed, in aggregate, the lower blood pressure target led to a significant 15% reduction in major cardiovascular events, a 20% reduction in stroke, and a 19% reduction in CHD events. Using data from MRFIT, Stamler and colleagues[8] estimated that each 10 mm Hg reduction in SBP resulted in a 26% overall reduction in all-cause mortality. Because there are millions of Americans with high-normal or elevated blood pressure, a population-wide reduction of only 10 mm Hg in the average SBP should translate to a substantial number of prevented deaths.

THE CHALLENGE OF CONTROLLING HIGH BLOOD PRESSURE

Although there is widespread agreement among public health authorities regarding the benefits of controlling high blood pressure, achieving this goal in clinical practice is beset with challenges. Primary care settings should be the site for efforts to improve the detection and treatment of hypertension, since it is in these settings that adults with high blood pressure are most likely to be encountered. In fact, in the United States, hypertension is the leading reason for visits to health care providers.[15]

Most reviews of hypertension treatment[4,7] cite nonadherence to prescribed medication and insufficiently intensive treatment as the two major obstacles to controlling high blood pressure. Trilling and Froom[4] identified five major areas where the quality of hypertension care should be improved: technique used for blood pressure measurement; therapeutic lifestyle changes; inadequate antihypertensive drug treatment; inadequate attainment of blood pressure targets as recommended by current guidelines from the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI)[6]; and low utilization of ambulatory and self-measured blood pressure measurements (particularly when the diagnosis is uncertain). Failure on the part of the health care provider to adhere to clinical guidelines may be due to lack of awareness or disagreement with recommendations. Many health care providers and patients also have low expectations that blood pressure *can* be controlled, particularly in high-risk patients.

In 1996, Hyman and Pavlik[16] surveyed 1200 American primary care physicians and found that more than one third of the responding physicians (n=408) would not start drug therapy for middle-aged (40–60 years of age) or elderly (≥70 years) non-diabetic patients unless the DBP was consistently ≥95 mm Hg. Only 48% of the physicians said they would start treatment for middle-aged adults with an SBP between 140 and 160 mm Hg, and only 24% would do so for patients older than 70 years. In this survey, 41% of respondents reported either limited or no familiarity with the JNC V guidelines, which were in effect at that time. Physicians who were unfamiliar with the current guidelines were consistently less likely to favor initiation of appropriate drug therapy than the group who claimed familiarity with current guidelines. Mehta and colleagues[17] surveyed a random sample of 500 primary care providers (N=500; 54% response rate) and found that the 270 respondents frequently did not adhere to guidelines when initiating antihypertensive treatment in African American patients, older patients, and patients with comorbidities such as HF and renal impairment.

Population subgroups such as elderly or African American patients with hypertension may be less likely to achieve blood pressure control due to health care providers' incorrect perceptions or beliefs. For example, some providers fear that the dangers of lowering SBP in an elderly patient outweigh the benefits; others believe that angiotensin-converting enzyme (ACE) inhibitors are completely ineffective in African American and other black patients. In an analysis of Medicare claims for 23,748 patients over age 65 with newly diagnosed hypertension, between 1991–1995,[18] Knight and colleagues found that the initial drug prescribed for these older hypertensive patients was often inconsistent with JNC V, the current guidelines at that time. Diuretics were prescribed in only 22% of patients with uncomplicated hypertension; a β blocker was given to only 15% of patients with a prior history of MI; and an ACE inhibitor was initially prescribed for only 29% of diabetic patients.

The tendency of some physicians to accept higher-than-recommended blood pressures was also found in an important observational study within the US Department of Veterans' Affairs outpatient clinic system, where economic factors are less of an issue, as the care and prescriptions are provided at very low (and sometimes no) cost.[19] The charts of 800 hypertensive male veterans who received regular medical care over a 2-year period were reviewed. When an elevated blood pressure measurement was recorded, approximately 75% of the time physicians did not change the treatment plan, by either increasing the dose of a current antihypertensive medication or adding another medication. Although the physicians were closely monitoring patients' blood pressures, they repeatedly delayed intensifying the regimen. These data indicated physician inaction as a contributing cause to uncontrolled hypertension, and the findings were so persuasive that soon thereafter the VA Central Office implemented an improved record-keeping and management system throughout the country. A similar problem with provider inaction was identified in an analysis of NHANES III data. Hyman and Pavlik[20] determined that most cases of uncontrolled hypertension (blood pressure ≥140/90 mm Hg) were found in older adults with adequate access to health care and relatively frequent contact with physicians. Further, in this representative sample of the US population the majority of uncontrolled blood pressures consisted of older people with isolated systolic hypertension.

The absolute risk for CVD in patients with hypertension is determined not only by the degree of blood pressure elevation, but also by the presence or absence of target organ damage or other risk factors, such as smoking, dyslipidemia, or diabetes.[6] Conducting a cardiovascular risk assessment is central to determining the intensity of treatment that will be needed to lower that risk. Yet, perhaps largely due to time constraints, primary care providers often give insufficient attention to the link between cardiovascular and renal risk and the initiation of appropriate preventive measures.[21] Some primary care providers are inattentive to achieving the blood pressure targets, as seen in both the VA study and the nationwide NHANES data of Hyman and Pavlik. There is now compelling evidence that lower-than-usual blood pressure targets reduce cardiovascular morbidity and mortality and slow the progression of renal disease for patients with diabetes or renal disease.[22–26]

For high-risk patients—in particular, those with diabetes or renal disease—lowering blood pressure to <140/90 mm Hg may not provide optimal protection from adverse cardiovascular and renal events. Hypertension in the diabetic patient significantly increases the risk of end-stage renal disease, CHD, stroke, peripheral vascular disease, and diabetic retinopathy. Based on data from the United Kingdom Prospective Diabetes Study 38,[25] tight blood pressure control (defined in 1982 as <150/85 mm Hg) had a much greater impact on reducing cardiovascular events and the progression of renal disease than did tight glucose control (glycosylated hemoglobin [HbA_{1c}] <7%). A blood pressure target goal of <130/80 mm Hg is currently recommended by the American Diabetes Association (ADA),[27] the National Kidney Foundation (NKF),[28] the British Hypertension Society,[29] and the Canadian Consensus Conference on Hypertension,[30] for all patients with diabetes. Achieving these lower blood pressure goals in the approximately 11 million Americans who have both diabetes and hypertension presents an enormous challenge, both due to the greater number of medications required and the increased costs associated with the more intensive treatment.

Many patients face major barriers to blood pressure control. These obstacles may include suboptimal adherence to medical treatment; lack of a consistent health care provider; inadequate knowledge or incorrect perceptions or beliefs about hypertension; lack of social support, transportation, or control over dietary choices; and complexity of the treatment regimen (inconvenient dosing, undesirable drug-related effects, and/or difficulty integrating therapeutic lifestyle changes).[31]

THE COSTS OF TREATING HYPERTENSION

The estimated direct and indirect costs of treating CHD, stroke, hypertension, and HF in the United States in 2003 are shown in Table II. The American Heart Association (AHA) estimates that the total cost of treating hypertension in the United States in 2003 will be $50.3 billion—$37.2 billion in direct medical costs, and $13.1 billion in indirect costs owing to lost productivity related to morbidity and mortality.[2] The AHA also estimates that the costs of treating "total CVD" will be $351.8 billion—$209.3 billion in direct costs, and $142.5 billion in indirect costs inclusive of lost future earnings for those who will die in 2002. According to an analysis by the AHA,[2] 45% of the direct costs of treating hypertension are related to medications (drugs or other medical durables), compared with 16% for total CVD. Conversely, 63% of expenditures associated with CVD are related to hospital or nursing home expenditures, compared with 25% for hypertension. The costs of hypertension in the United States may be greater in the southeastern states—often referred to as the "Stroke Belt"—where the prevalence of high blood pressure and death rates from stroke are higher than in other regions.[2]

These AHA estimates of the cost of hypertension in the United States do not include costs related to

Table II. Estimated Direct and Indirect Costs (In US$ Billions) of CHD, Stroke, Hypertension, and HF in the United States in 2003[2]					
Direct Costs	CHD	Stroke	Hypertension	HF	Total CVD*
Inpatient	43.4	24.7	8.7	16.0	130.1
Professional services	9.2	2.5	9.2	1.7	31.8
Drugs/medical durables	7.2	0.9	17.8	2.3	36.6
Home health care	1.4	2.9	1.5	2.2	10.8
Total direct costs	61.2	31.0	37.2	22.2	209.3
Indirect Costs of Lost Productivity					
Related to morbidity	8.8	5.9	7.0	N/A	32.4
Related to mortality	59.9	14.3	6.1	2.1	110.1
Total indirect costs	68.7	20.2	13.1	2.1	142.5
Total costs	129.9	51.2	50.3	24.3	351.8

CHD=coronary heart disease; HF=heart failure; CVD=cardiovascular disease; N/A=not available; *totals do not add up due to rounding and overlap

the treatment of hypertension in patients with renal impairment; however, uncontrolled hypertension is the cause of about 25% of the cases of end-stage renal disease in the United States. Comprehensive estimates for the cost of renal diseases are somewhat difficult to obtain since data for renal diseases are in the purview of other voluntary health organizations, including the NKF and the American Society of Nephrology (ASN). Thus, estimates are less precise regarding the cost of antihypertensive therapy to postpone renal failure; the proportion of hypertensive people who eventually receive renal replacement therapy (dialysis or kidney transplants); and the medical care-related costs for these patients. The NKF estimated that in the United States in 2002 approximately $14–$25 billion would be spent for these purposes. When the estimates of the cost of hypertension from both the NKF and the ASN are pooled, and allowances made for potential overlap, the total comes to approximately $66 billion. Even this estimate is conservative; using these projections, the average expenditure for a hypertensive person in the United States would be about $1320 per year.

Because of the association of hypertension with subsequent adverse cardiovascular events, the cost of diagnosing and treating the cardiovascular complications of high blood pressure is also important, as these complications are potentially preventable if hypertension is controlled. The estimated numbers of inpatient cardiovascular procedures performed in hospitals in the United States in 1999 are shown in Table III. According to a report published by the Health Care Cost and Utilization Project (HCUP),[32] which is based on an extensive, nationwide, hospital-reporting database, CVD (including CHD, HF, MI, and stroke) is the most frequent reason for hospitalization. Further, hypertension is the leading comorbidity associated with these hospitalizations, occurring in about 20% of all patients who are hospitalized for any reason. In a separate publication from HCUP regarding procedures tracked by the Diagnosis Related Group (DRG) system,[33] cardiovascular procedures represented more than one fourth of all inhospital procedures. Diagnostic cardiac catheterization was the most frequently performed procedure and was carried out in more than 20% of inpatients aged 45–79 years during 1997. Despite the fact that HCUP data exclude patients with a "short-stay admission" (<24 hours),[33] more than 3.8 million cardiac catheterizations were reported for 1997. In 2000, the average cost of cardiac catheterization was $16,838 per procedure[2]; Medicare paid for a large percentage of these procedures.

Five of the top 10 procedures paid for by Medicare are related to CVD, including diagnostic cardiac catheterization, coronary artery bypass grafting, diagnostic echocardiography, and percutaneous transluminal coronary angioplasty.[33] Older individuals account for a large percentage of patients receiving cardiac procedures; however, about one third to one half of estimated cardiovascular procedures in the United States in 2000 were performed for patients younger than 65 years of age (Table III).[2]

The direct annual health care costs of treating a patient with hypertension can be categorized as: costs related to drug acquisition; office visits relat-

Table III. Estimated* Numbers (In Thousands) of Inpatient Cardiovascular Procedures Performed in Hospitals in the United States in 2000[2]

Procedure	Number of Procedures Performed in 2000**	Number of Procedures Performed in Patients Younger Than 65 Years
Total angioplasty	1025	499 (49%)
PTCA	561	266 (47%)
Stenting	456	223 (49%)
Cardiac revascularization (bypass)	519	233 (45%)
Diagnostic cardiac catheterizations†	1318	672 (51%)

PTCA=percutaneous transluminal coronary angioplasty. *Breakdowns are not available for some procedures, so entries for some categories do not add up to totals. These data include codes where the estimated number of procedures is fewer than 5000. Categories of such small numbers are considered unreliable by the Centers for Disease Control and Prevention (CDC)/National Center for Health Statistics (NCHS), and in some cases may have been omitted. **Estimated inpatient cardiovascular procedures performed; †this number is much lower than that reported by the Health Care Cost and Utilization Project (HCUP), which is >3.8 million and includes procedures performed in the outpatient setting.[33]

ed to blood pressure management; required laboratory tests; and in-office or inhospital costs associated with adverse effects of treatment. Sometimes, lower costs in one category (e.g., drugs) are offset by higher costs in another (e.g., office visits). In 1994, Hilleman and colleagues[34] found that, compared with ACE inhibitors and calcium channel blockers, drug acquisition costs for diuretics or β blockers were lower, but the costs of office visits, laboratory tests, and follow-up for adverse effects were higher, leading to no significant differences in total cost of care across the four drug classes. According to a study by Paramore and colleagues,[35] poor control of hypertension for any reason was associated with higher drug costs and more physician visits. Uncontrolled blood pressure may be due at least partly to patient-related factors—for example, nonadherence to prescribed medications, adverse effects, costs of medications, or inconvenience.

Office visits related to adverse effects of medications may be an important, albeit hidden cost of treating hypertension. In hypertension, a largely asymptomatic condition, the long-term effect that adverse effects of a medication may have on a patient's motivation to continue treatment should not be ignored. More than 75% of adverse drug effects are dose related,[36] and are often provoked when health care providers initiate therapy at a high dose or up-titrate a single drug when blood pressure is not controlled. Some health care providers are reluctant to use low-dose combination therapy that may enhance both efficacy and tolerability.

Adherence to pharmacologic therapy for hypertension is known to be low; it is estimated to range from 50%–70% over a 1-year period.[37] Discontinuation of drug therapy may be related to patient- or physician-related factors, or insufficient efficacy. However, a large portion of patient nonadherence may be attributed to real or perceived adverse effects of medications, their cost, or a lack of understanding of the goals of therapy—problems that could be successfully addressed in the clinical setting. Caro[38] found that patients are most likely to discontinue taking antihypertensive medicines in the first year of therapy; however, patients who have been adherent during initiation of treatment tend to remain in treatment longer. Thus, the goal should be to achieve the blood pressure target as quickly as possible following initiation of treatment, with a regimen that satisfies the concerns of the patient. This may require more clinic visits immediately following the diagnosis of hypertension, but also offers the potential to reduce the long-term costs of both visits and medications.

In 1995, Bobal and colleagues[39] distributed a survey regarding utilization patterns and costs of hypertension medications to a random sample of pharmacy directors of large managed-care plans throughout the United States. Twenty-nine pharmacy directors responded, representing more than 8 million covered lives. The overall annual drug budgets ranged from $5.7–$225 million, and the typical allocation for hypertension products was about 15% of the overall budget (range, 8%–26%). The pharmacy directors estimated that the number of changes in drug regimens (including increasing the dose of a current medication, switching to another drug, or adding another drug) that the average hypertensive patient would require to achieve blood pressure control was 3.3

(range, 1–15). Respondents reported that the factors considered most likely to have the greatest impact on the need to change therapy were adverse effects (93%), nonadherence (69%), and lack of efficacy (72%). Pharmacy directors also noted that frequently changing medications potentially leads to additional, often uncounted costs associated with product wastage, drug dispensing fees, patient copayments, and pharmacy administrative costs; this may further contribute to patient nonadherence with the prescribed therapy.

PHARMACOECONOMIC ANALYSIS OF TREATMENT OF HYPERTENSION

Perhaps because hypertension is so common and its treatment often requires the use of more than a single medication, antihypertensive drug therapy is a common target of cost-cutting efforts. This approach may be faulty if it fails to take into account health care expenditures that may be offset by savings that occur due to blood pressure reduction (e.g., fewer MIs, strokes, or HF hospitalizations). Statewide initiatives to reduce health care costs by restricting outpatients' access to chronic medications have resulted in higher health care expenditures in a number of instances.[40] For example, New Hampshire noted a 35% decline in the use of medications after implementation of a three-prescriptions/month/patient limit, compared with a similar Medicaid cohort in New Jersey that had no limitation. However, among the frail elderly population in New Hampshire, this initiative was associated with several unintended adverse effects, including a significant two-fold increased risk of admission to nursing homes.[41] Although cost containment is a legitimate concern that must be addressed by health care providers, consumers, third-party payors, and public policy efforts, limitation of access to useful medications by administrative action appears to be "penny-wise, but pound foolish."

The use of economic analyses has become increasingly common in health care management. These studies are often conducted by health economists who try to assess the costs and benefits of providing medical care, using data from a wide range of sources to develop a decision model.[42] These types of analyses provide information that must be interpreted according to the values and perspective of the user. A good example is a treatment that prevents death among elderly people, which might be considered "good" from the patient's and health care provider's perspective, but costly (and therefore "bad") to Medicare, since more Social Security benefits would need to be paid during those years of extended life.

Economic analyses may be relatively simple or extremely complex. For example, a relatively straightforward cost-minimization analysis is usually performed to assess differing costs related to similar medical regimens within a population; sometimes these analyses have surprising results. Small and colleagues[43] performed a retrospective analysis of the total costs of treatment for 6176 hypertensive patients older than 65 years of age with different ACE inhibitors, categorized as "older agents" (captopril, enalapril, and lisinopril) and "newer agents" (benazepril, ramipril, quinapril, and fosinopril). Total costs included the cost of the ACE inhibitors and concurrent antihypertensive medications, laboratory costs, medical office visit costs to monitor outcomes, and treating adverse drug reactions or complications arising from therapy. The total median cost per month was higher for older agents than for newer agents ($59.82 vs. $53.02, respectively; $p<0.0009$), and the mean percentage of patients persisting with therapy (as determined by refill rates) was greater with newer vs. older agents (66% vs. 58%, respectively; $p<0.0001$). The investigators recommended using the newer rather than older ACE inhibitors for elderly patients.

Probably the most common type of cost analysis is the cost-effectiveness calculation, which compares costs associated with hard clinical outcomes (i.e., morbidity and mortality) with the costs of treatment. These analyses consider both the direct costs of care and the cost savings associated with prevented outcomes, and are typically expressed in the units of "dollars of cost per year of life saved." Cost-utility analyses take these concepts one-step further, by "discounting" each year of extended life after an event by a "utility" score typically gathered from a large group of individuals before they have such an event. For example, in a cost-utility analysis for stroke prevention, each year of life after a nonfatal stroke would be "downgraded" by an increment that depends on the severity of the stroke. A year with hemiplegia might be worth, for example, only 33% of a year of good health, and loss of the use of an arm only 50%. Cost-utility analyses typically have units of "dollars per year of quality-adjusted life-year gained." Cost-utility analyses would probably be greatly improved if there were well-validated, widely accepted utility scales. These analyses have not become quite as popular as the "cost-effectiveness" variety.

A cost-effectiveness approach can also be applied to the use of a diagnostic test. In an article recommending screening for microalbuminuria for all hypertensive or diabetic patients,[44] Parving did not perform a formal cost analysis. The cost-effectiveness analysis was performed by Golan and colleagues,[45] comparing three different strategies of testing for microalbuminuria. Despite some unusual baseline cost assumptions (e.g., the ACE inhibitor lisinopril was used at the VA at depot pricing, by law the lowest price available in the United States), these authors concluded that all diabetic patients over age 55 should be treated with an ACE inhibitor, beginning at the time of diagnosis, and no testing for microalbuminuria need be undertaken thereafter. The current recommendation from the ADA is to screen only diabetic patients at high risk for diabetic nephropathy, and then treat those individuals with an angiotensin II receptor blocker.[27]

Perhaps the most interesting pharmacoeconomic analyses are those regarding antihypertensive drug therapy. Johannesson and Jonsson[46] reviewed nine published studies and concluded that the cost effectiveness of treating hypertension with medications is more beneficial (i.e., lower cost per year of life saved) for patients with higher pretreatment blood pressure levels or as age increased, for both men and women. This suggestion has since been borne out in several other studies: the cost-effectiveness ratio is lower (i.e., more beneficial) for individuals at higher levels of absolute risk at baseline. While the costs and efficacy of treatment are usually similar among all subgroups, more events would be postponed or avoided in those groups with higher baseline risk. This phenomenon is perhaps best illustrated in Figure 2, which summarizes the number of strokes prevented in several large, placebo-controlled clinical trials of antihypertensive drugs. The oldest patients in the Swedish Trial of Old Patients With Hypertension (STOP-Hypertension)[47] had both the highest absolute risk (based on the number of strokes observed in the placebo group per 1000 patient-years of follow-up) and the greatest number of strokes prevented (approximately 14 per 1000 patient-years of follow-up). On the other hand, the first Medical Research Council (MRC) trial[48] studied young people at relatively low risk, and, despite about the same intensity and cost of treatment, prevented only about one stroke per 1000 patient-years of follow-up.

Several simpler calculations have been proposed that link clinical end points and cost. The easiest of these to understand is the "number needed to treat" (or "NNT"). This is simply the reciprocal of the absolute risk difference for a given treatment, and provides an estimate of how many individuals need to be treated for a certain time period to prevent one event of interest. In the first MRC trial[48] discussed in the preceding paragraph, the 1-year NNT for stroke was about 856, whereas for STOP-Hypertension, the 1-year NNT was only about 66. If the costs of treatment are similar, a treatment with a lower NNT is generally easier to recommend (as more cost effective) than a similar treatment with a higher NNT. Some jurisdictions (e.g., New Zealand; Ontario, Canada) require that the results of such calculations be below a certain threshold before adding a treatment to the formulary. It is also possible to compare, for a large group of patients, the cost of each millimeter of mercury that blood pressure is lowered. Chen and Lapuerta[49] have recommended this method for understanding the economic implications of comparative studies involving several different antihypertensive agents.[49] Even they caution, however, that there are limitations to this method, including the embedded assumptions that compared agents have similar tolerability and that blood pressure lowering is a valid surrogate for cardiovascular risk reduction.

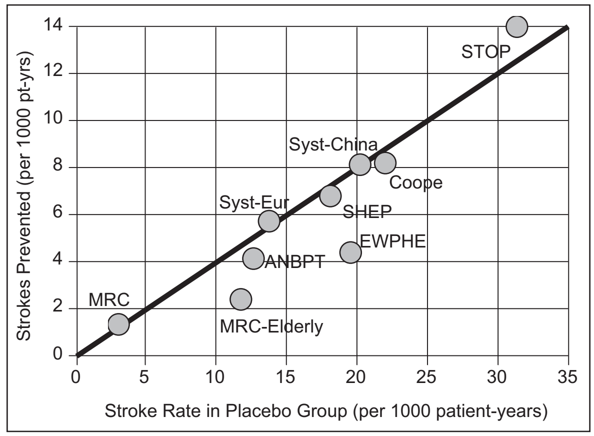

Figure 2. Relationship of absolute risk of stroke (expressed as stroke rate per 1000 patient-years in the control [usually placebo] arm, x-axis) and number of strokes prevented per 1000 patient-years of active drug treatment (y-axis) in several clinical trials of antihypertensive drug therapy MRC=Medical Research Council Trial in Mild Hypertension (principal results)[48]; MRC-Elderly=Medical Research Council Trial in Older Adults[53]; ANBPT=Australian National Blood Pressure Trial[54]; Syst-Eur=Systolic Hypertension Trial in Europe[55]; SHEP=Systolic Hypertension in the Elderly Program[56]; EWPHE=European Working Party on Hypertension in the Elderly[57]; Coope=Study of Coope and Warrender[58]; STOP=Swedish Trial in Old Patients With Hypertension[47]; Syst-China=Systolic Hypertension Trial in China[59]

Many professionals involved in health care financing have expressed concerns regarding the potentially increased costs of implementing the recommendations to lower blood pressure target goals, since doing so will increase drug-use costs. In the UK Prospective Diabetes Study Group (UKPDS 40),[50] a formal cost-effectiveness analysis was conducted, based on the actual resources used and benefits observed during the trial. In this study, tighter blood pressure control in type 2 diabetes actually *saved* £1049 per life-year without diabetic complications, and *saved* £720 per year of extended life, compared with the "usual care standard." Most of these savings occurred because of the substantially reduced rates of costly complications seen with tighter blood pressure control in this very high-risk population. A similar conclusion was recently reached by integrating clinical trial and epidemiologic data from the United States population into a computerized model. We[31] performed a cost-effectiveness analysis comparing the direct costs and potential benefits of two blood pressure goals (<140/90 mm Hg vs. <130/85 mm Hg), based on JNC VI guidelines, for a cohort of 60-year-old diabetic patients who were initially free of CVD or renal failure. The model was designed to calculate, per year, the number of individuals who would be expected to incur a morbid event (stroke, MI, HF, or end-stage renal disease) or to die, and the costs associated with each morbid event and follow-up for prior events. Calculations were carried out until all simulated patients died, after which estimates of the average lifespan and total costs of medical care for each cohort were generated. According to this analysis, reducing blood pressure from <140/90 mm Hg to <130/85 mm Hg in a group of high-risk individuals would result in an increased life expectancy from 16.5 to 17.4 years, while the total lifetime medical costs (including those associated with additional treatment) would decline by $1450. Thus, the analysis suggests both overall cost *savings*, and life extension, with the lower blood pressure goal.[31] The same model, used in a cohort of 50-year-old diabetic patients, would yield an increased life expectancy from 23.0 to 24.0 years, but would increase lifetime medical costs by $801, mostly because the younger patients lived longer while remaining free of morbid events. The results of these two economic analyses suggest that lowering blood pressure in type 2 diabetes joins perhaps four other medical interventions that have proven effective in saving both lives *and* money: aspirin and a low-cost β blocker after an acute MI, childhood immunizations, and prenatal vitamins.

RECOMMENDATIONS

Controlling blood pressure with medications is unquestionably one of the more cost-effective methods of reducing premature cardiovascular morbidity and mortality. Physicians, patients, and health care fiscal policy makers all have important roles to play in enhancing the cost effectiveness of blood pressure management. Early detection and quicker control of blood pressure may prevent or delay the onset of costly CVD or renal disease. Intensive efforts should be undertaken to help patients initiate and maintain therapeutic lifestyle changes. It is paramount to achieve blood pressure goals without compromising quality of life. To achieve these goals concomitantly, more than a single drug is likely to be required in a majority of patients with high blood pressure.[23,25,51,52] Several pills that combine low doses of different antihypertensive agents have the advantages of having fewer adverse effects, lower acquisition costs, and a lower copayment in managed-care pharmacy plans.

The role of patient education should not be minimized. One useful patient education booklet is, "High Blood Pressure—What You Should Know About It and What You Can Do to Help Your Doctor Treat It" (available online at www.hypertensionfoundation.org). Other recommendations to consider include continuing medical education programs for health care providers, developing effective treatment algorithms for specific populations, and encouraging use of home blood pressure monitoring by patients.

Pharmacy and chart audits may provide useful data regarding prescribing practices, efficacy of treatment, and adherence to a given medication regimen. Algorithm-driven, nursing- or pharmacy-based case management has been shown to have a beneficial effect on both blood pressure-lowering efficacy and patient adherence to antihypertensive treatment. As in all quality-improvement efforts, it is important to evaluate the impact of all steps taken to reduce costs and improve outcomes following implementation of these recommendations.

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NOTICE
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