# Antihypertensive Regimen and Quality of Life in a Disadvantaged Population

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*A sample of family practice patients with essential hypertension (N = 106) who were predominantly elderly, black, and disadvantaged were studied to determine psychosocial and physiological side effects from antihypertensive therapy regimens. Patients were assigned randomly to one of four monotherapy treatment groups: Hydrochlorothiazide-triamterene, metoprolol, captopril, and methyldopa. These medications have been reported to have contrasting effects on quality of life. Measurements of quality of life, physical symptoms, and depression taken at baseline and during therapy revealed few significant changes in these indicators. Changes in mean levels of diastolic and systolic hypertension over time were clinically and statistically significant. Findings raise issues regarding medication effectiveness and cost given the disadvantaged population studied.* J FAM PRACT 1990; 30:143-152.

In the past two decades improved surveillance and treatment of high blood pressure, mainly in primary care settings, has dramatically increased the percentage of patients with diagnosed hypertension who have achieved control of their blood pressure. This improvement in overall blood pressure control has been achieved through the use of pharmacologic and nonpharmacologic regimens (ie, weight control, sodium and alcohol restriction, exercise), most frequently in combination.[1,2] This public health achievement is a result of changes in the clinical management of hypertension, including more individualized treatment regimens and greater patient involvement in the therapy.[3]

For progress in the diagnosis and treatment of hypertension to continue, the following issues must be addressed: patient lifestyles, management of associated diseases (eg, diabetes mellitus, congestive heart failure), compliance enhancement, adverse drug effects, and the special needs of patient populations such as blacks, the elderly, the medically indigent, and pregnant women.[4-6] The wide variety of treatment agents and options can be

very confusing and may impair physician prescribing behavior.[7]

Therapeutic efficacy is only one of several factors that warrant consideration when prescribing antihypertensive medications. Cost, dosage schedules favoring compliance, impact on concomitant medical conditions, and potential adverse drug effects all have an impact on therapeutic decisions.

Antihypertensive medications have been reported to cause a variety of adverse physical symptoms. The most troublesome symptoms include orthostatic hypotension (especially in the elderly); hyperlipidemia; blunting of normal physiologic responses to stress; weight gain; nightmares and insomnia; persistent fatigue, headaches, muscle cramps, and sexual dysfunction.[8-11] Other studies suggest an association between the use of $\beta$-blockers and methyldopa and depression.[12] Flawed research designs, however, diminish the impact of these conclusions. In contrast, recent studies have claimed that the angiotensin-converting enzyme (ACE) inhibitor, captopril, effectively lowers blood pressure among hypertensive patients without sacrificing quality of life.[13-16]

Quality-of-life measurements typically include self-assessment of physical and social dysfunction, emotional distress, symptom experience, and pain.[17] These measurements ascertain the subjective impact of serious illness and treatment efficacy on patients' lives. Quality-of-life indicators are usually based on interview questionnaires with patients rather than on traditional

clinical evaluations. Although interviews have acceptable internal validity, interview-related research has not been extensive in poor or disadvantaged populations.

The quality-of-life literature specific to antihypertensive treatments has not assessed the effects of sociocultural, ethnic, sex, or economic characteristics on treatment outcomes. Most studies have been done on active, middle-aged, employed white men.[13,14]

Given the limited external validity of previous research, this study assessed the impact of previously studied antihypertensive medications on quality-of-life indicators in a disadvantaged population. The research hypotheses were as follows:

1. There will be no significant relationship between blood pressure levels and quality-of-life indicators before treatment.

2. There will be no significant differences in the occurrence or type of side effects between treatment groups (patients receiving $\beta$-blockers, methyldopa, thiazide diuretics, or angiotensin-converting enzyme inhibitors will not significantly differ in reported symptoms of depression and physical discomfort over time).

## METHODS

Study participants were patients currently seen at a university-affiliated family practice residency program clinic. In January 1986, 634 patients with a documented diagnosis of hypertension were identified by a computerized chart audit, using a systematic sample design with an overall goal of 150 for inclusion in the study. Because of changes of address and disconnected telephones, a viable sample of only 100 patients was generated. Excluding previously identified patients, an additional 82 names were selected in the same systematic way. Each patient was then contacted by letter, and 4 weeks later by telephone, requesting participation in the study. Free medical care and antihypertensive medications were offered as incentives to participate.

A diagnosis of hypertension currently requiring pharmacological therapy for control was required for enrollment in the study. Exclusion criteria included severe uncontrolled hypertension with systolic blood pressure greater than 180 mmHg or diastolic pressure greater than 120 mmHg, history of rebound hypertension secondary to medication discontinuance, or evidence of significant end-organ damage such as renal failure, hypertensive retinopathy, cerebrovascular disease, or coronary artery disease.

Of the 182 patients initially contacted, 56 individuals declined to participate. Reasons for patient attrition included fear of discontinuation of current medication, bet-

### TABLE 1. SOCIODEMOGRAPHIC CHARACTERISTICS OF STUDY VOLUNTEERS (N=106), IN PERCENT

| Characteristics | Percent |
|---|---|
| Age (years) | |
| 30–49 | 32.3 |
| 50–64 | 35.4 |
| 65 + | 32.3 |
| Sex | |
| Male | 20.0 |
| Female | 80.0 |
| Race | |
| Black | 75.5 |
| White | 20.0 |
| Other | 5.0 |
| Marital status | |
| Married | 39.0 |
| Not married* | 61.0 |
| Occupation | |
| Low prestige | 52.6 |
| Medium prestige | 28.0 |
| High prestige | 19.4 |
| Education | |
| Elementary or less | 27.0 |
| Quit high school | 33.0 |
| High school graduate | 20.0 |
| College or + | 20.0 |
| Income | |
| <$5,000/y | 32.2 |
| $5,000 to $10,000/y | 25.8 |
| $10,000 to $20,000/y | 14.8 |
| >$20,000/y | 17.2 |
| Eligible for Medicaid or Medicare | |
| Not eligible | 56.6 |
| Medicaid | 8.5 |
| Medicare | 26.4 |
| Both | 8.5 |

*Never married, widowed, divorced, or separated

ter controlled hypertension, and moving out of the community. An additional 20 patients were excluded because they were too ill to discontinue medication for the washout period.

The remaining 106 patients received an initial medical evaluation with a complete history and physical examination. All antihypertensive medications were discontinued for a washout period of 1 week. Patients who were normotensive after the washout period were dropped from the study, leaving 82 patients for baseline evaluation. Informed consent was obtained at this visit.

Table 1 represents the sociodemographic characteristics of the sample population. The sample consisted mainly of black, lower income, elderly women with below-average educational and occupational skills.

During the baseline visit, patients underwent initial psychosocial testing and were randomly assigned to one of four medication groups. Medication groups consisted of the following initial drug regimens: hydrochlorothiazide-

triamterene, one capsule daily; metoprolol, 100 mg once daily; captopril, 25 mg three times daily; and methyldopa, 250 mg three times daily. If blood pressure was controlled, patients remained on the same regimen throughout the study.

Patients returned for follow-up visits at 2 weeks, 1 month, 2 months, and 4 months after the baseline visit. At each visit blood pressure was checked and medication was adjusted to maximize blood pressure control. Patients uncontrolled after 1 month were either switched to another medication or given an additional study drug. Compliance checks conducted by the clinical pharmacist at each visit involved pill counts, medication refills, and review for potential adverse drug reactions.

All patients were evaluated and managed by the same physician throughout the study to avoid variability in clinical judgment. Medical problems, other than hypertension, were referred to each patient's regularly assigned physician for management.

Psychological measures of depression and quality of life, obtained by two co-investigators and a graduate assistant, were conducted at the baseline visit, and at the 2-month and 4-month follow-up visits. All interviewers were blinded to the drug therapy of the patients. The physician investigator was not involved in psychosocial data collection.

The following inventories were used to assess psychosocial well-being:

1. Beck Depression Inventory[18]—a 21-item forced-choice, self-report inventory that assesses many aspects of depression including mood, pessimism, fatigability, irritability, loss of appetite and weight, loss of libido, and so on

2. Brief Symptom Inventory[19]—a 53-item five-point Likert-scaled self-report symptom inventory that has been given in a wide variety of settings of which an abbreviated form was used consisting of 24 items with four subscales (somatization, depression, anxiety, and hostility)

3. Composite Index of Well-Being[20]—an 11-item semantic differential index that assesses general affect

Self-reported physical health was evaluated by the Spectrum of Physical Health Index,[21] from which three separate indices were created:[21]

1. Illness severity—a weighted index based on checklist items

2. Physical health—a four-item index based on questions about energy level

3. Symptom number—the number of acute physical symptoms reported

To further assess the reliability of these quality-of-life measures, internal consistency reliabilities were calculated for each test. Cronbach's alpha, a statistic for internal consistency reliability, shows the extent to which each test item relates to the total score on that inventory.[22] Alpha values were as follows: Beck Depression Inventory 0.87; Campbell's Index of General Well-Being 0.88; Brief Symptom Inventory (BSI) somatization 0.78; BSI-depression 0.83; BSI-anxiety 0.76; BSI-hostility 0.66; physical health 0.60; and illness severity 0.62.

Over the course of the study there was a 20% attrition rate from the first follow-up visit at 2 weeks to the visit at 2 months, and a 14% attrition rate between the 2-month visit and the 4-month visit, giving an overall attrition rate of 30%. A total of 74 patients completed the whole study. Attrition was distributed evenly across treatment groups. Follow-up telephone calls to dropouts revealed that lack of transportation to the clinic and lack of adherence to study protocol (ie, missed appointments, seeing the wrong physician, not feeling sick enough to come) largely accounted for this significant attrition rate. Drug side effects, a significant attrition factor in the study by Croog et al,[13] were ruled out.

## ANALYSIS

Preliminary data analyses determined that scores on the inventories used in this study could be analyzed by parametric multivariate analyses of variance (MANOVA). MANOVA is similar to analysis of variance (ANOVA) but generalizes to multiple intercorrelated dependent variables, such as quality-of-life indicators (Table 2).[23] MANOVA determines the equality of means and the equality of dispersion matrices (variance/covariance matrices) between groups. Compared with ANOVA, the multivariate tests of MANOVA are more sensitive to group differences, although MANOVA produces less power than a univariate test under certain conditions. In this study, MANOVA suggests overall trends among indicators from baseline to follow-up. Differences between groups found at baseline are simultaneously adjusted by the use of the Bonferroni method for significance levels. Chi-square tests were used for categorical indicators.

## RESULTS

Data collected at baseline (n=82) indicated no significant zero-order correlations between diastolic blood pressure and any of the quality-of-life indicators (Table 2). Systolic blood pressure positively correlated with illness severity. Individuals with more self-reported chronic or disabling

TABLE 2. CORRELATION MATRIX: AGE, BLOOD PRESSURE, AND QUALITY-OF-LIFE VARIABLES AT BASELINE

| | Age (yr) | Diastolic Blood Pressure | Systolic Blood Pressure | Physical Well-Being | Illness Severity | Number of Symptoms | General Well-Being |
|---|---|---|---|---|---|---|---|
| Diastolic blood pressure | −.01 | | | | | | |
| Systolic blood pressure | .39* | .59* | | | | | |
| Physical well-being | .09 | .10 | .18 | | | | |
| Illness severity | .26* | .04 | .21† | −.24† | | | |
| Number of symptoms | −.05 | −.11 | −.08 | −.51* | .40* | | |
| General well-being | .26* | .09 | .23† | .55* | −.02 | −.33* | |
| Beck Depression Scale | −.23† | −.10 | −.17 | −.57 | .05 | .40* | −.67* |

*$P < .01$
†$P < .05$

conditions also had higher systolic blood pressure readings. In contrast, higher systolic blood pressure readings positively correlated with general well-being scores. Age is possibly a confounding factor. There were no consistent relationships between elevated blood pressure and depression or self-reported indicators of well-being.

Multivariate results were based on complete sets of data from 74 patients in the four treatment groups: hydrochlorothiazide-triamterene (n = 34), metoprolol (n = 17), captopril (n = 13), and methyldopa (n = 10). These differences in group size occurred at the 1-month visit and reflect adjustments in initially assigned medications to achieve better blood pressure control. There were no statistically significant differences between persons in different treatment groups on quality-of-life measures at baseline.

Figures 1 through 4 illustrate the univariate results of a between-groups repeated-measures multivariate analysis of variance for both blood pressure and quality-of-life measures. Lowering of blood pressure over time was shown for both diastolic blood pressure (F = 50.55, P < .001) and systolic blood pressure (F = 48.32, P < .001). This main effect is attributable to metoprolol, captopril, and methyldopa. The hydrochlorothiazide-triamterene group did not demonstrate any significant lowering of blood pressure.

There were no clinically or statistically significant between-group changes for quality-of-life indicators of depression, general well-being, psychosocial distress, illness severity, and physical health. In contrast to a previous finding,[13] captopril patients, who, although a randomly assigned group, had more severe levels of blood pressure at baseline, failed to demonstrate significant improvements in quality-of-life scores associated with lowering of blood pressure.

Table 3 represents summary statistics concerning the number of physical symptoms reported. In all treatment groups, except for the hydrochlorothiazide-triamterene group, the number of self-reported symptoms decreased over time. These improvements included decreased headaches, stiffness, swelling, or aching of joints or muscles, and fatigue. These improvements may directly relate either to blood pressure control or to the halo effect of study participation, since these symptoms are not typically associated with blood pressure elevation. Sample size precludes more specific analysis of these effects.

## DISCUSSION

A predominantly disadvantaged, black, female population was investigated to determine whether antihypertensive medications had any effect on quality-of-life indicators. Data based on three standardized measures of quality of life and collected through personal interviews in a clinical setting had internal consistency. Moreover, relationships between quality-of-life indicators conformed to previous research. High-scale reliability and cross-validated correlations, similar to those found in a study of middle-class white respondents,[24] support construct validity.

Surprisingly, quality-of-life indicators were not significantly affected by type of antihypertensive agent administered. A number of possible explanations could account for these findings. Methodologically, it may be that quality-of-life measures were inappropriate for this population,[25,26] or perhaps these patients gave socially desirable answers, underestimating psychosocial distress.[27,28]

Clearly, antihypertensive therapy does not have a discernible relationship to quality of life or to changes in quality of life within this predominantly disadvantaged, undereducated black population. These findings contradict recent studies, which show that captopril increases quality of life while other medications decrease quality of life.[13–16] Further research with variations in the sociodemographic characteristics of study populations is necessary to clarify these discrepancies.
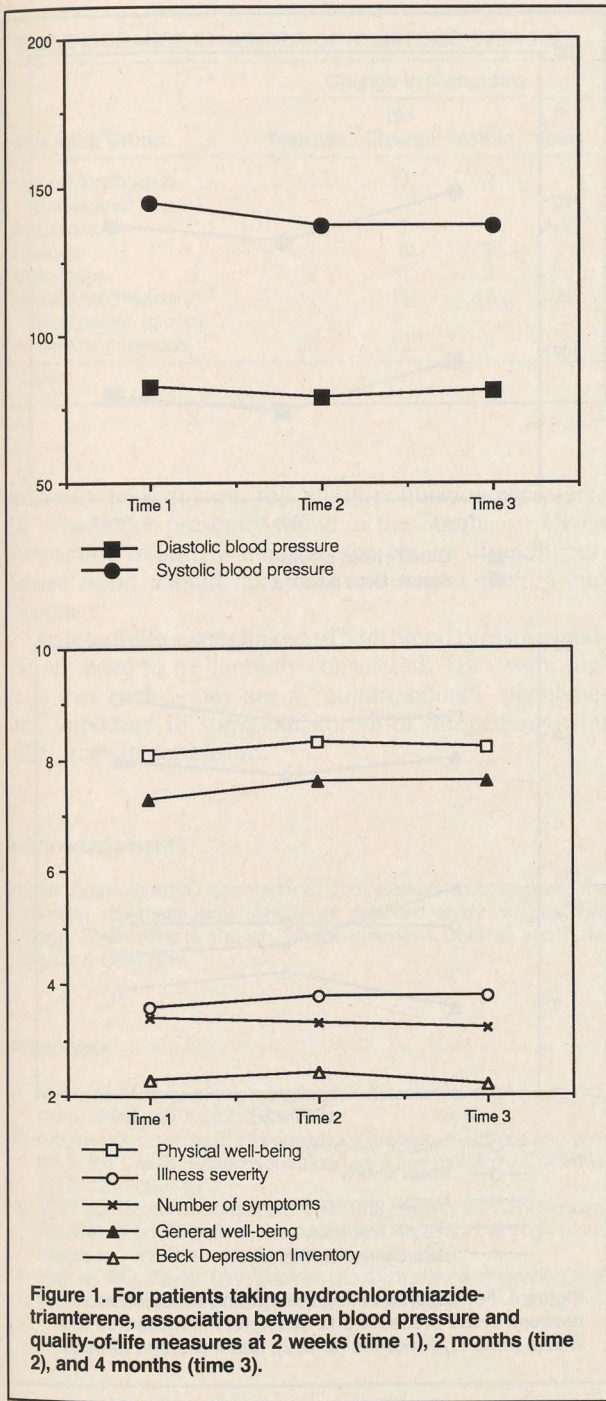
Figure 1. For patients taking hydrochlorothiazide-triamterene, association between blood pressure and quality-of-life measures at 2 weeks (time 1), 2 months (time 2), and 4 months (time 3).
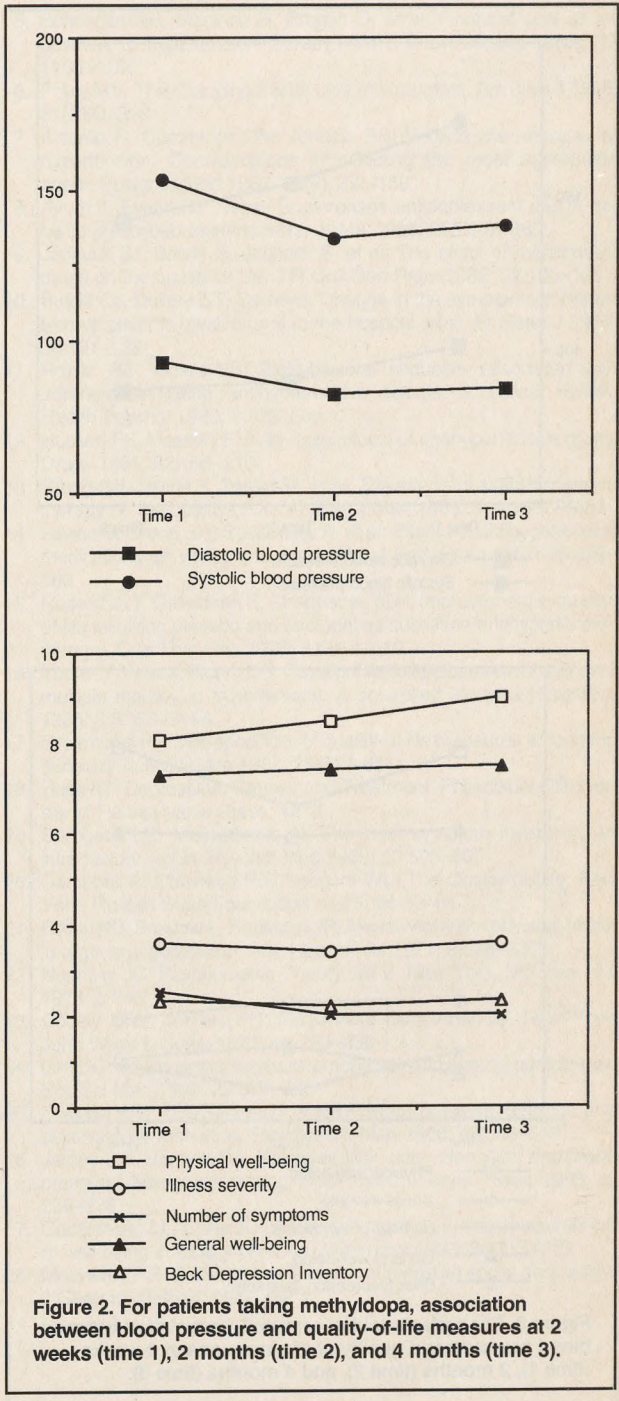
Figure 2. For patients taking methyldopa, association between blood pressure and quality-of-life measures at 2 weeks (time 1), 2 months (time 2), and 4 months (time 3).

In conclusion, these findings have a number of implications for the practicing physician. Many study patients were living on fixed incomes. Fifty-eight percent were living on less than $10,000 a year. Yet only 43% were eligible for Medicaid or Medicare. Sixty percent had less than a high school education. Limited Medicaid coverage

**Figure 3. For patients taking captopril, association between blood pressure and quality-of-life measures at 2 weeks (time 1), 2 months (time 2), and 4 months (time 3).**



**Figure 4. For patients taking metoprolol, association between blood pressure and quality-of-life measures at 2 weeks (time 1), 2 months (time 2), and 4 months (time 3).**
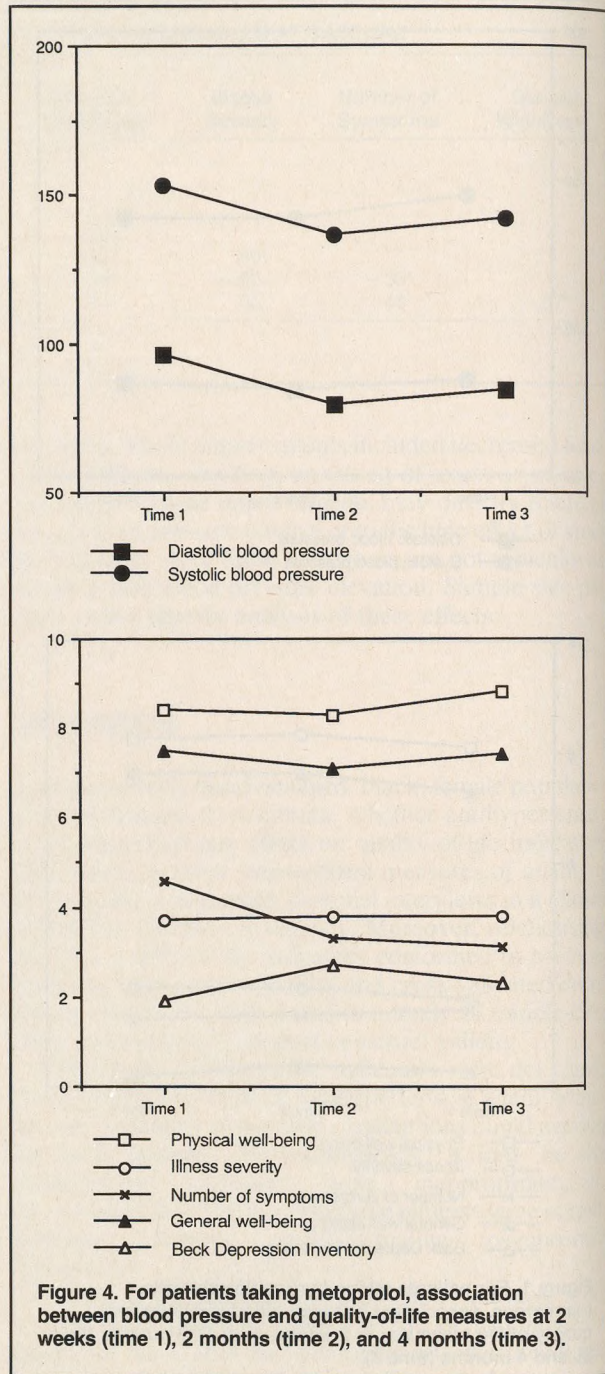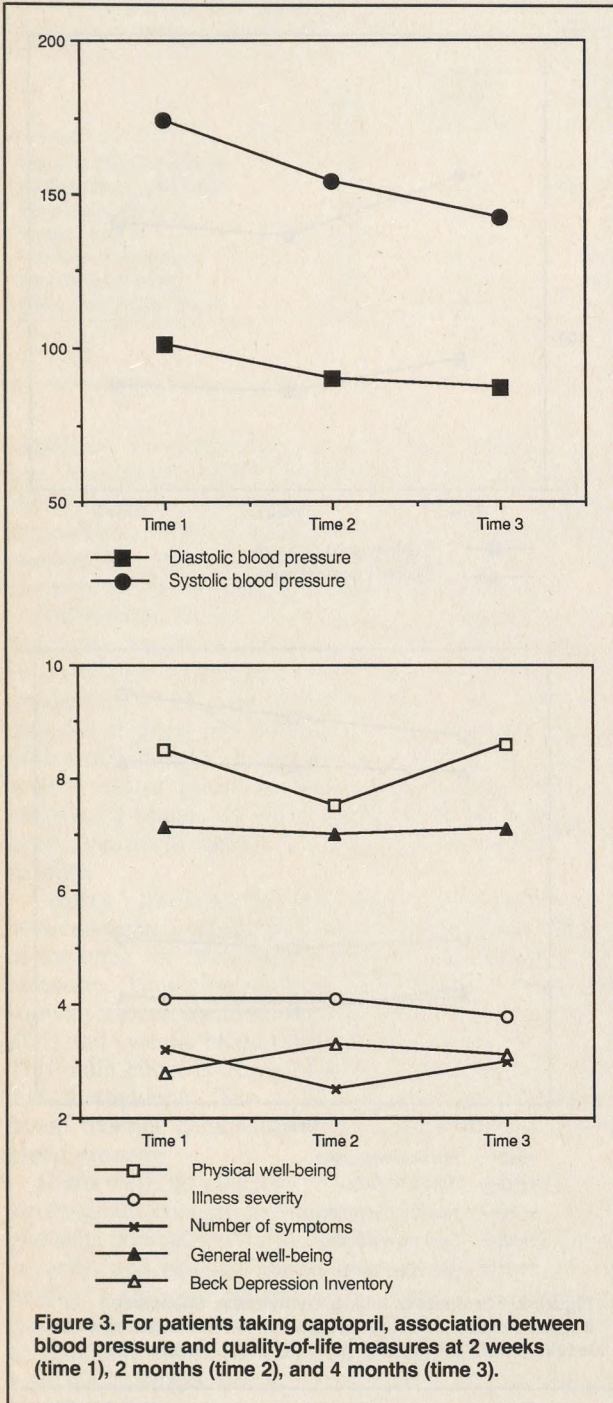
of prescription medications and no provision for outpatient drug coverage by Medicare creates a dilemma for persons on a fixed income. When care was available at no

charge, as in this study, most patients managed to find transportation to the clinic and chose to comply with treatment regimens. In education, income, and lack of

## TABLE 3. CHANGE IN NUMBER OF SYMPTOMS OVER TIME

| | Change in Symptoms | | | |
| Treatment Group | Improve | No Change | Worse | P Value |
|---|---|---|---|---|
| Hydrochlorothiazide/ triamterene* | 11 | 11 | 12 | |
| Metoprolol | 9 | 7 | 1 | NS |
| Captopril | 7 | 4 | 2 | |
| Methyldopa | 7 | 1 | 2 | |
| Hydrochlorothiazide/ triamterene* (group) | 11 | 11 | 12 | <.05 |
| All treatment (groups) | 23 | 12 | 5 | |

*Diuretic*

access to medical care, this study population represents the urban poor presently found in the Southeast. Given comparable treatment efficacy, the choice of antihypertensive agent should take cost and access factors into account.[5,6]

Quality-of-life issues linked to high blood pressure medications need to be carefully considered. This study suggests that such issues are a "culture-bound" phenomenon, important to some but not all of the persons who suffer from hypertension.

## Acknowledgments

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# Commentary

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The preceding study by Glik and co-workers[1] addresses an important clinical issue, the effects of antihypertensive drugs on the quality of life. Following a series of studies of mild to moderate hypertension that have variably supported the positive effects of treatment,[2,3] hypertension has become the second most common reason to visit the family physician.[4] It is significant that in 1984 an estimated 10 million people in the United States were receiving antihypertensive medications at a cost of $2.5 billion.[5]

The quality of life has been defined as an individual's perceived ability to function normally in society.[6,7] This broadly defined concept includes functional capacity (in terms of physical, behavioral, cognitive, social, and economic dimensions) as well as symptoms. While there are no "gold standards" for measuring the quality of life, numerous instruments purporting to measure these dimensions and others have been developed. Criteria appropriate for the development of these instruments and the instruments themselves have been reviewed elsewhere.[8,9] The applications of quality-of-life data in the treatment of hypertension have been reviewed in the pages of this and other journals.[6,10]

Although mild hypertension is unlikely to produce symptoms, the wide range of symptom side effects associated with pharmacologic treatment may cause patients to discontinue therapy. For example, during the 5 years of the British Medical Research Council Trial of Mild Hypertension, 16% of patients receiving drug treatment withdrew because of such side effects as impotence, gout, lethargy, nausea, dizziness, and headache.[11] A group of 3844 patients who had not received antihypertensive medications at the beginning of the Hypertension Detection and Follow-up Program was followed for 5 years. A total of 9.3% had probable or definite side effects severe enough to require discontinuation of therapy, and an additional 23.4% discontinued treatment because of possible side effects.[12]

Surely the development of side effects reduces compliance with a medication regimen. When patients feel worse with therapy than without, it is difficult to convince them of the long-term benefits of treatment. Theoretically, compliance should increase if side effects are minimal and the patient's quality of life is enhanced.

Most often in the clinical setting, a measurable evidence of change in patient status is anticipated in terms of patient report, physical findings, and laboratory or imaging studies. In quality-of-life studies, the appraisal of benefit is made by the patient rather than by the physician. The construction of such measures must therefore reflect those areas of dysfunction with which patients are concerned, and must to some degree be disease-specific.[9] In addition, these measures should enable patients to describe the relative undesirability of various symptoms and states. Thus, Taylor[7] calls for modifications in the design of quality-of-life measures to include more explicitly the perspective and preference of patients.

In their study, Glik and co-workers[1] asked whether there was an association between blood pressure levels and quality-of-life indicators before treatment, and whether there was a difference in the quality-of-life experience of patients receiving the different drugs. One hundred eighty-two patients were "systematically sampled" from a group of 634 hypertensive individuals receiving pharmacotherapy in a university-affiliated family practice program. People with severe hypertension or evidence of end-organ damage were excluded. Of the 182, 56 refused to participate and 20 were judged too ill to risk discontinuation of medication for the washout period. Twenty-four patients were normotensive after the washout, leaving 82 patients available for randomization to one of four drug treatment groups. The authors followed both the blood pressure and quality-of-life data for these people over a 4-month period, using all or portions of previously validated instruments that demonstrated good internal consistency. The authors concluded that there were no apparent differences in most quality-of-life measures as experienced by the participants. In addition, there was no association between initial blood pressure and quality-of-life indices. Should these "negative" results have been anticipated?

First, improvement in the quality of life from baseline (after the patient had been on no drugs) would be surprising in a disease state that is usually asymptomatic (mild to moderate hypertension). In this trial, in which individuals with severe hypertension and those with evidence of end-organ damage were excluded, one would expect both a higher level of quality of life at baseline and a lower

potential benefit of therapy on the patient's quality of life. The previous two studies demonstrating enhanced quality of life with the use of captopril acquired baseline quality-of-life measures when patients were still on or had just discontinued the previous antihypertensive regimen.[13,14]

Second, perhaps the instruments used in the study by Glik et al could not detect meaningful changes in the quality of life. The usefulness of an evaluative quality-of-life questionnaire depends on its responsiveness[9] or clinical sensitivity,[7] that is, its ability to detect clinically significant changes even if the changes are small. Responsiveness is defined as the ratio between the score seen in changed patients to the variability of the score in stable patients. This determination sometimes requires studies of two groups of patients, one group stable on therapy and another treated by a known efficacious drug. In a single clinical trial, responsiveness can be estimated by comparing the results in the placebo group with the effects seen in the treatment group. Unfortunately, in a clinical trial such as this one, in which no differences were detected between groups, two outcomes are possible. Either there was no real difference in quality of life between the treatment groups, or the questionnaire was insufficiently responsive to detect differences.

Third, variations in quality of life may have been seen in some studies but not others because different instruments were used. The Brief Symptom Inventory (BSI) was the only measure used in common by the current authors and Croog and co-workers.[13] This earlier study found that captopril significantly enhanced the quality of life on some measures compared with methyldopa or propranolol. However, no differences were found in the Brief Symptom Inventories of individuals taking each of these drugs. The scores from subscales of the BSI used in the study by Glik and co-workers were not reported in their paper.

Fourth, an inadequate sample size may have accounted for the negative findings of this study. A predetermined judgment of a clinically significant change in one of the quality-of-life measures used would have enabled a sample size calculation to ensure adequate power in a study with negative results. The issue of power is particularly important when the study hypothesis is that there are no differences. The likelihood of a type II, or beta, error should have been calculated.

Like other clinical trials, quality-of-life studies are susceptible to three major forms of bias. The current study can be examined in terms of the risks of selection bias, misclassification bias, and confounding bias.

Selection bias affects the generalizability of study findings. This study is the first to use a sample of predominantly poor, female, black, and middle-aged patients from a family practice clinic. Thus, while useful information may have been provided on patients not previously studied in quality-of-life studies of antihypertensive medica-

tions, generalizability of results to other settings is problematic. In addition, by providing free medical care and drugs, one of the economic barriers to compliance was removed. In a typical family practice setting, expensive medications may have a negative economic impact on the quality of life.

The patient's or investigator's knowledge of the disease process and the treatment received can substantially affect the responses to questionnaires and the assessments of outcomes. Blinding of the subject and the evaluator to treatment is a technique used to prevent the misclassification of outcomes. In the current study, quality-of-life evaluators were blinded regarding treatment group assignment, but patients and the physician investigator apparently were aware of the drugs used. It is also not clear whether patients knew their blood pressure level at the time they were completing the quality-of-life questionnaire, a factor that could surely affect responses.

The importance of blinding the patient and the investigator was highlighted by a recent trial comparing a centrally acting drug with an angiotensin-converting enzyme (ACE) inhibitor. This study showed a substantial discrepancy in the results between physician-administered and self-administered quality-of-life data that demonstrated a bias resulting from the physician's positive expectations of the new drug.[15]

Confounding occurs when one or more other variables are "mixed up" in the association between exposures and outcomes. This form of bias can occur in a clinical trial when the distribution of clinically significant characteristics differs between the treatment groups. The 82 eligible subjects in the current study were randomly assigned to one of the four drug treatment groups at the beginning of the study, and 4-month follow-up data were available on 74 subjects. Even this modest amount of attrition can contribute to confounding, although the authors assure the reader that the subjects were evenly distributed across treatment groups and that drug side effects were not responsible for attrition.

A much more significant source of confounding threatens the validity of this study, however. Subjects whose blood pressure was not adequately controlled at the first follow-up visit were transferred to another treatment group, apparently almost all to the hydrochlorothiazide-triamterene group ([n = 34], compared with metroprolol [n = 17], captopril [n = 13] and methyldopa [n = 10]). Perhaps for this reason the hydrochlorothiazide-triamterene group did not demonstrate any significant lowering of blood pressure, as this group received the subjects whose blood pressure was the hardest to control. It also means that the subjects in time 1 are not necessarily the same subjects at time 2 and time 3 in Figures 1 through 4. It is not known how different these groups of individuals were by the end of the first month of the study period and

how these differences may have affected subsequent comparisons.

This study points to the challenges of quality-of-life research in the context of a clinical trial with competing objectives. The authors were ethically compelled to change the therapy of subjects whose blood pressure was not adequately controlled. By reassigning individual subjects and analyzing them within their new groups, however, the benefits of random allocation were negated, and the validity of the results is threatened.

With an increasing array of antihypertensive medications available for use by the primary care physician, both clinical response and effects on quality of life (including the economic impact of the therapy) will continue to be important components of medical decision making. Studies of this type are difficult and are subject to numerous methodological pitfalls. Nevertheless, studies of this subject by Glik and co-workers and others should be promoted. In the same context, researchers should also be encouraged to evaluate the effect on quality of life of preventive regimens in other clinical settings such as the drug treatment of hypercholesterolemia and the use of postmenopausal estrogen therapy.

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