Control of Blood Pressure and Risk of Stroke Among Pharmacologically Treated Hypertensive Patients

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Background and Purpose—Despite improved control of blood pressure during the last decades in the United States, a considerable proportion of treated hypertensives have not achieved target blood pressure levels. We estimated the proportion of strokes occurring among treated hypertensive patients that may be attributable to uncontrolled blood pressure.

Methods—A population-based case-control study was conducted among treated hypertensive members of Group Health Cooperative of Puget Sound. Cases were treated hypertensive patients who sustained a first fatal or nonfatal, ischemic (n=460) or hemorrhagic (n=95) stroke during 1989–1996. Controls were a random sample of stroke-free, treated hypertensive Group Health Cooperative enrollees (n=2966), similar in age to the stroke cases. Multiple measurements of blood pressure and other cardiovascular risk factors were collected from medical records. Logistic regression was used to estimate the risk of ischemic stroke and hemorrhagic stroke associated with uncontrolled blood pressure, defined as diastolic blood pressure >90 mm Hg or systolic blood pressure >140 mm Hg. The fraction of strokes attributable to uncontrolled blood pressure among treated hypertensives was calculated.

Results—Blood pressure was uncontrolled in 78% of ischemic stroke cases, 85% of hemorrhagic stroke cases, and 65% of controls. After adjustment for potential confounders, uncontrolled blood pressure among treated hypertensive patients was moderately associated with ischemic stroke (risk ratio=1.5 [95% CI, 1.2 to 1.9]) and strongly related to hemorrhagic stroke (risk ratio=3.0 [95% CI, 1.7 to 5.4]). We estimated that 27% (95% CI, 11% to 39%) of the ischemic strokes and 57% (95% CI, 26% to 75%) of the hemorrhagic strokes among treated hypertensive patients were attributable to uncontrolled blood pressure. Overall, 32% (95% CI, 14% to 45%) of all strokes were attributable to uncontrolled blood pressure.

Conclusions—A considerable proportion of incident strokes among treated hypertensive patients may be prevented by achieving control of blood pressure. **(*Stroke*. 2000;31:420-424.)**

Key Words: hypertension ■ pharmacology ■ risk ■ stroke, hemorrhagic ■ stroke, ischemic

Although the rates of treatment and control of hypertension in the United States have increased over the past 3 decades, these rates appear to have leveled off during the mid 1990s.[1,2] The earlier favorable trends in treatment and control of hypertension coincided with a decline in mortality from stroke and coronary heart disease. However, since 1993, the stroke rate has risen slightly, and the decline in coronary heart disease appears to have leveled off.[3] Data from the third National Health and Nutrition Examination Survey (NHANES-III) suggest that only approximately half of those taking antihypertensive drugs achieve blood pressure (BP) levels at or below the treatment goal of 140/90 mm Hg.[4] Studies in the United Kingdom and the Netherlands have demonstrated that the quality of control of hypertension is strongly related to the occurrence of stroke in the population.[5,6] Using data from a population-based case-control study, we estimated the proportion of incident strokes occurring among treated hypertensive patients that may be attributable to uncontrolled BP in the United States.

Subjects and Methods

Setting

The setting was the Group Health Cooperative of Puget Sound (GHC) in Seattle, a large-staff model health maintenance organization serving >500 000 members in western Washington.

We used data from a population-based case-control study that was originally conducted to study the associations between antihypertensive therapies and myocardial infarction and stroke. Our methods were similar to those used in previous case-control studies.[7]

Subjects

Cases were GHC enrollees, aged 30 to 79 years, who were treated pharmacologically for hypertension and who sustained an incident

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TABLE 1. Characteristics of Cases and Controls

	Controls		Ischemic Stroke Cases		Hemorrhagic Stroke Cases	
Characteristic	n*	Mean or %	n*	Mean or %	n*	Mean or %
Age, y	2966	65.8	460	70.0	95	66.9
Female, %	2966	33.9	460	56.1	95	57.9
Average BP on treatment						
Systolic, mm Hg	2966	144.1	460	151.6†	95	154.1†
Diastolic, mm Hg	2966	84.2	460	84.3	95	87.6†
Pretreatment BP						
Systolic, mm Hg	2103	162.7	306	168.0†	66	166.9
Diastolic, mm Hg	2103	99.4	306	99.6	66	101.6
Duration of treated hypertension, y	2680	11.0	395	13.0†	87	11.4
Cholesterol, mg/dL	2820	226.6	439	240.2†	85	229.4
Body mass index, kg/m^2	2892	28.5	448	28.5	88	27.8
Current smoking, %	2940	12.4	453	15.2	92	26.1†
Educational level						
Less than high school, %	2214	13.4	267	16.5†	57	15.8
High school or vocational school, %	2214	34.6	267	40.1	57	36.8
College or university, %	2214	52.0	267	43.5	57	47.4
Married, %	2966	74.3	460	60.2†	95	68.4
White, %	2906	89.5	441	89.9	89	79.8†
Diabetes, %	2966	11.3	460	31.3†	95	11.6
Any cardiovascular disease, %	2966	30.3	460	50.2†	95	31.6
History of myocardial infarction, %	2966	8.5	460	10.7	95	6.3
History of transient ischaemic attack, %	2966	6.2	460	19.6†	95	14.7†
Atrial fibrillation, %	2966	5.3	460	14.1†	95	5.3
Angina, %	2966	17.2	460	23.9†	95	16.8
Coronary bypass surgery, %	2966	6.0	460	7.4	95	3.2
Coronary angioplasty, %	2966	2.2	460	2.2	95	1.1
Carotid endarterectomy, %	2966	1.0	460	2.6†	95	2.1
Peripheral vascular surgery, %	2966	2.3	460	3.0	95	2.1

*Number of cases and controls for whom data were available.
†$P<.05$ for comparison of cases and controls.

fatal or nonfatal stroke during July 1989 through December 1996. Potential cases were identified from computerized GHC hospital discharge abstracts, Washington state death files, and the billing records for GHC enrollees who received medical care or services from non-GHC providers. Controls were obtained from a companion study of risk factors for myocardial infarction at GHC.[7] Controls were a random sample of GHC enrollees who were treated pharmacologically for hypertension, frequency matched to the myocardial infarction cases by sex, age, and calendar year. Each subject was assigned an index date. For the cases, the index date was the date of the stroke; for controls, the index date was a random date within the calendar year for which they had been selected as controls. In most strata based on sex, 10-year age categories, and index year, the ratio of controls to cases was >3:1. We excluded subjects (1) who were enrollees for <1 year or who had <4 visits before their index dates; (2) who had had a prior stroke; (3) who had a diagnosis of congestive heart failure; (4) whose stroke was a complication of a procedure or surgery; and (5) who had no recorded BP in their medical records within the year before the index date.

Data Collection and Definitions

Information on BP and other cardiovascular disease risk factors was abstracted from medical records and obtained from a telephone interview of consenting survivors. Abstraction of the information from the medical records was done by trained research assistants who were not blinded to case-control status but were unaware of the study hypothesis. Subjects were considered pharmacologically treated for hypertension when a recording of antihypertensive drug use for the indication of hypertension was present in the medical records and indicated that the subject was treated at the index date. Control of BP was defined according to the mean of the last 3 treated BP readings recorded in the medical records during the year before the index date. If <3 readings were available, we used either the mean of 2 readings (n=563) or a single reading (n=473) to assess the level of BP achieved by treatment.

The level of BP achieved by treatment was categorized according to the classification scheme of hypertension of the sixth report of the Joint National Committee (JNC-VI) on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[4] According to this classification, a diastolic blood pressure (DBP) <90 mm Hg and a systolic blood pressure (SBP) <140 mm Hg are considered controlled. This classification would provide the most informative results for clinicians and policy makers in the United States to assess the implications of managing hypertension according to these national practice guidelines.

TABLE 2. Risk of Stroke Associated With Uncontrolled BP Among Pharmacologically Treated Hypertensives

	Cases		Controls			
	n	%	n	%	RR (95% CI)*	PAR (95% CI)
Ischemic strokes						
DBP <90 and SBP <140 mm Hg	103	22.4	1029	34.7	1.00 (reference)	
DBP 90–100 or SBP 140–160 mm Hg	203	44.1	1412	47.6	1.26 (0.97–1.64)	9 (−1–19)
DBP 100–110 or SBP 160–180 mm Hg	128	27.8	439	14.8	2.16 (1.60–2.94)	15 (9–20)
DBP ≥110 or SBP ≥180 mm Hg	26	5.7	86	2.9	2.27 (1.35–3.83)	3 (1–5)
DBP ≥90 or SBP ≥140 mm Hg	357	77.6	1937	65.3	1.52 (1.19–1.94)	27 (11–39)
Hemorrhagic strokes						
DBP <90 and SBP <140 mm Hg	14	14.7	1029	34.7	1.00 (reference)	
DBP 90–100 or SBP 140–160 mm Hg	46	48.4	1412	47.6	2.41 (1.31–4.44)	28 (10–43)
DBP 100–110 or SBP 160–180 mm Hg	21	22.1	439	14.8	3.36 (1.67–6.78)	16 (7–23)
DBP ≥110 or SBP ≥180 mm Hg	14	14.7	86	2.9	11.52 (5.17–25.66)	13 (9–18)
DBP ≥90 or SBP ≥140 mm Hg	81	85.3	1937	65.3	3.03 (1.69–5.41)	57 (26–75)

PAR indicates population attributable risk.

*Adjusted for age, sex, index year, pretreatment SBP, total cholesterol, diabetes, current smoking, and clinical cardiovascular disease (diagnoses of angina, claudication, atrial fibrillation, history of myocardial infarction, transient ischaemic attack, coronary angioplasty, coronary bypass surgery, carotid endarterectomy, or peripheral vascular surgery).

Statistical Analysis

Complete data were uniformly available from the medical records for case-control status and medical conditions such as pharmacological treatment of hypertension, angina, and diabetes.

In preliminary analyses of demographic and behavioral risk factor data such as smoking, physical activity, race, marital status, and education, the agreement between medical record and self-reported measures was good to excellent. Self-reported data, available for 52.4% of the subjects, were used for these variables; if not available, then data from the medical record were used. After information from these 2 sources was combined, data were missing on smoking (1.0%), physical activity (8.0%), race (2.4%), education (28.1%), cholesterol (5.0%), duration of treatment for hypertension (10.2%), and pretreatment BP (29.7%). We used an approximate Bayesian bootstrap method to impute these missing values. This multiple imputation method is a modification of the hot-deck method and takes account of the imputation variability.[8] In sensitivity analyses, the results using multiply-imputed data were similar to those seen in the analysis of subjects with complete data.

All statistical tests were 2-tailed. We used stratification and logistic regression to control for potential confounding factors of the association between BP control and stroke. We used odds ratios to estimate the risk of stroke associated with the various JNC-VI stages of hypertension,[4] compared with the risk in subjects with controlled BP (DBP <90 mm Hg and SBP <140 mm Hg). The population attributable fractions and their 95% CIs were calculated according to Whittemore.[9] We also examined the relation between tertile of DBP (bottom tertile, DBP <82 mm Hg; middle tertile, DBP 82 to 90 mm Hg; top tertile, DBP >90 mm Hg) and SBP (bottom tertile, SBP <146 mm Hg; middle tertile, SBP 146 to 159 mm Hg; top tertile, SBP ≥159 mm Hg) and risk of stroke. All analyses were performed separately for ischemic and hemorrhagic strokes.

Results

During 1989–1996, 791 treated hypertensive patients were hospitalized for or died out of hospital from an incident stroke. We also identified 3654 controls who were eligible. We excluded 38 cases and 149 controls who were enrolled for <1 year or had <4 visits before their index date, 110 cases and 199 controls with chronic heart failure, 17 cases and 64 controls who had no treated BP recorded in their medical records, 60 cases and 289 controls whose most recent BP reading was taken >1 year before the index date, and 23 cases for whom no determination of the type of stroke (ischemic or hemorrhagic) could be made on the basis of the available information. This analysis included 460 ischemic stroke cases, 95 hemorrhagic stroke cases, and 2966 controls.

Compared with controls, ischemic stroke cases had higher mean levels of treated SBP, pretreatment SBP, and total cholesterol (Table 1). A number of risk factors, including diabetes and history of cardiovascular disease, were more prevalent among ischemic stroke cases than among controls. Compared with controls, hemorrhagic stroke cases had higher mean levels of treated SBP and DBP, were more often current smokers, and more often had a history of transient ischemic attack, but not of cardiovascular disease (Table 1).

The mean BP during the year before the index date was more often uncontrolled among ischemic (77.6%) and hemorrhagic (85.3%) stroke cases than among controls (65.3%) (Table 2). Uncontrolled BP was moderately associated with ischemic stroke (risk ratio [RR]=1.52 [95% CI, 1.19 to 1.94]) and strongly related to hemorrhagic stroke (RR=3.03 [95% CI, 1.69 to 5.41]). The relative risks progressively increased with the level of uncontrolled BP defined according to the JNC-VI classification of hypertension, more so for hemorrhagic stroke than for ischemic stroke (Table 2).

The association between both types of stroke and uncontrolled BP did not significantly differ between men and women, between older and younger subjects (above and below the median age), or between subjects with or without a history of cardiovascular disease, with or without diabetes, or with high or low pretreatment DBP or SBP (above and below the median pretreatment BP). The results remained virtually unchanged after adjustment for pretreatment DBP, duration of treated hypertension, body mass index, educational level, marital status,

TABLE 3. Risk of Stroke Associated With Tertiles of DBP and SBP Among Pharmacologically Treated Hypertensives

	Cases		Controls		
	n	%	n	%	RR (95% CI)*
Ischemic strokes					
DBP <82 mm Hg	176	38.3	1121	37.8	1.00 (reference)
DBP 82–90 mm Hg	175	38.0	1192	40.2	1.26 (0.99–1.68)
DBP >90 mm Hg	109	23.7	653	22.0	1.87 (1.40–2.50)
SBP <146 mm Hg	189	41.1	1742	58.7	1.00 (reference)
SBP 146–159 mm Hg	123	26.7	720	24.3	1.30 (1.01–1.68)
SBP ≥159 mm Hg	148	32.2	504	17.0	1.92 (1.48–2.48)
Hemorrhagic strokes					
DBP <82 mm Hg	32	33.7	1121	37.8	1.00 (reference)
DBP 82–90 mm Hg	31	32.6	1192	40.2	1.05 (0.63–1.75)
DBP >90 mm Hg	32	33.7	653	22.0	2.28 (1.33–3.89)
SBP <146 mm Hg	31	32.6	1742	58.7	1.00 (reference)
SBP 146–159 mm Hg	33	34.7	720	24.3	2.59 (1.56–4.31)
SBP ≥159 mm Hg	31	32.6	504	17.0	3.29 (1.93–5.61)

*Adjusted for age, sex, index year, pretreatment SBP, total cholesterol, diabetes, current smoking, and clinical cardiovascular disease (diagnoses of angina, claudication, atrial fibrillation, history of myocardial infarction, transient ischaemic attack, coronary angioplasty, coronary bypass surgery, carotid endarterectomy, or peripheral vascular surgery).

race, physical activity, and current use of aspirin. Exclusion of subjects who had <3 BP readings in their medical records before the index date did not substantially change the results.

Estimation of the population attributable fractions suggests that 27% (95% CI, 11% to 39%) of ischemic and 57% (95% CI, 26% to 75%) of hemorrhagic strokes may have been attributable to uncontrolled BP. One third of the ischemic strokes and one half of the hemorrhagic strokes that were attributable to uncontrolled BP occurred among those with mildly elevated BP levels (JNC-VI stage I). Overall, 32% (95% CI, 14% to 45%) of all strokes may have been attributable to uncontrolled BP.

The association between ischemic stroke risk and tertile of BP was similar for DBP and SBP, whereas the risk of hemorrhagic stroke was more strongly associated with SBP than with DBP (Table 3).

Discussion

In this study we demonstrated that a large proportion of pharmacologically treated hypertensive patients in this population-based study had elevated BP. During the year before the index date, approximately 65% of the control subjects, 78% of the ischemic stroke cases, and 85% of the hemorrhagic stroke cases had a BP >90 mm Hg diastolic or 140 mm Hg systolic. Approximately 27% of incident ischemic strokes and 57% of incident hemorrhagic strokes among pharmacologically treated hypertensive patients were attributable to uncontrolled BP. Patients with mild elevations of BP accounted for approximately one third of the excess incident ischemic strokes and approximately one half of the excess incident hemorrhagic strokes.

The strengths of this observational study include the use of population-based case and control subjects, the comparable ascertainment of potential confounding factors, and the use of multiple measurements of BP to assess control of BP. Although we adjusted for potential confounding factors, residual confounding cannot be excluded because of the possibility of incomplete or inaccurate measurement of covariates and unknown or unmeasured confounding factors for which adjustment was not possible. Furthermore, the medical records abstractors were not blinded to case-control status and may have classified potential confounding factors differently for cases and controls. In approximately 30% of subjects there were no data on pretreatment BP values. Although the confounding effects of pretreatment BP levels were virtually the same in the analysis of subjects with complete data as in the analysis of subjects with missing pretreatment BP values, we cannot completely rule out the possibility that subjects with uncontrolled BP had higher pretreatment BP levels and therefore a higher risk of stroke.

While stroke risk is clearly reduced by BP treatment in clinical trials,[10–12] the population attributable fractions that we estimated may not directly apply to other settings in which population characteristics and levels of BP control differ. The general US population includes more blacks, Hispanics, and uninsured people who are more likely to have poor BP control,[1,2,13,14] and this difference may limit the generalizability of our findings. The rate of control of hypertension in the United States according to the NHANES-III survey (1988–1991)[2] was, however, higher (45%) than the rate of control of hypertension among the controls in our study population (34.7%). This difference may have been due to the smaller number of BP measurements in our study (3 during 1 year) compared with the NHANES-III survey (6 during 2 visits), which would tend to overestimate the prevalence of hypertension.[14a]

This study not only confirms the strong association between achieved BP and risk of stroke among treated hypertensive patients[5,15–17] but also provides separate estimates for ischemic and hemorrhagic stroke and the proportion of these strokes that may have been attributable to inadequate control of BP. SBP was more strongly associated with the risk of hemorrhagic stroke than DBP, whereas DBP and SBP were similarly associated with the risk of ischemic stroke. Several studies have found a stronger association between hypertension and hemorrhagic stroke than with ischemic stroke.[18–20] However, several studies in Chinese populations have demonstrated a similar risk of ischemic and hemorrhagic stroke in relation to hypertension.[21]

Previously it was demonstrated in this same population that 15% of the incident myocardial infarctions among treated hypertensive patients were attributable to uncontrolled BP.[22] Possible causes of uncontrolled BP include treatment-resistant hypertension,[23] recent start of antihypertensive drug therapy, lack of access to medical care,[14] suboptimal treatment by physicians, and patient noncompliance. Lack of compliance with antihypertensive drugs[24–28] and lack of appropriate treatment[29–31] have been identified as the most important barriers to hypertension control. Interventions directed at improvement of compliance[32] and optimization of antihypertensive drug treatment[33] may lead to improved BP control.

The findings of our study suggest that achieving control of BP among pharmacologically treated hypertensive patients might prevent 57% of hemorrhagic and 27% of ischemic strokes.

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References

1. Burt VL, Cutler JA, Higgins M, Horan MJ, Labaharthe D, Whelton P, Brown C, Roccella EJ. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the Health Examination Surveys, 1960 to 1991. *Hypertension*. 1995;26:60–69.
2. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, Horan MJ, Labarthe D. Prevalence of hypertension in the US adult population: results from the Third National Health and Nutrition Examination Survey, 1988–1991. *Hypertension*. 1995;25:305–313.
3. National Heart, Lung, and Blood Institute. *Fact Book Fiscal Year 1996*. Bethesda, Md: US Dept of Health and Human Services, National Institutes of Health; 1997.
4. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med*. 1997;157:2413–2446.
5. Du X, Cruickshank K, McNamee R, Saraee M, Sourbutts J, Summers A, et al. Case-control study of stroke and the quality of hypertension control in north west England. *BMJ*. 1997;314:272–276.
6. Klungel OH, Stricker BHC, Paes AHP, Seidell JC, Bakker A, Voko Z, Breteler MB, de Boer A. Excess stroke among hypertensive men and women attributable to undertreatment of hypertension. *Stroke*. 1999;30:1312–1318.
7. Psaty BM, Heckbert SR, Koepsell TD, Siscovick DS, Raghunathan TE, Weiss NS, Rosendaal FR, Lemaitre RN, Smith NL, Wahl PW. The risk of myocardial infarction associated with antihypertensive drug therapies. *JAMA*. 1995;274:620–625.
8. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. *Stat Med*. 1991;10:585–598.
9. Whittemore AS. Statistical methods for estimating attributable risk from retrospective data. *Stat Med*. 1982;1:229–243.
10. Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). *Lancet*. 1991;338:1281–1285.
11. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension: final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA*. 1991;265:3255–3264.
12. Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, Bulpitt CJ, de Leeuw PW, Dollery CT, Fletcher AE, Forette F, Leonetti G, Nachev C, O'Brien ET, Rosenfeld J, Rodicio JL, Tuomilehto J, Zanchetti A, for the Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet*. 1997;350:757–764.
13. Stockwell DH, Madhavan S, Cohen H, Gibson G, Alderman MH. The determinants of hypertension awareness, treatment, and control in an insured population. *Am J Public Health*. 1994;84:1768–1774.
14. Ahluwalia JS, McNagny SE, Rask KJ. Correlates of controlled hypertension in indigent, inner-city hypertensive patients. *J Gen Intern Med*. 1997;12:7–14.
14a. Klungel OH, de Boer A, Paes AHP, Nagelkerke NJD, Bakker A. Undertreatment of hyperension in a population-based study in the Netherlands. *J Hypertens*. 1998;16:1371–1378.
15. Manolio TA, Kronmal RA, Burke GL, O'Leary DH, Price TR. Short-term predictors of incident stroke in older adults: the Cardiovascular Health Study. *Stroke*. 1996;27:1479–1486.
16. Bulpitt CJ, Palmer AJ, Fletcher AE, Beevers DG, Coles EC, Ledingham JG, O'Riordan PW, Petrie JC, Rajagopalan BE, Webster J. Optimal blood pressure control in treated hypertensive patients: report from the Department of Health Hypertension Care Computing Project (DHCCP). *Circulation*. 1994;90:225–233.
17. Trafford JA, Horn CR, O'Neal H, McGonigle R, Halford-Maw L, Evans R. Five year follow-up of effects of treatment of mild and moderate hypertension. *BMJ (Clin Res Ed)*. 1981;282:1111–1113.
18. How Lin C, Shimizu Y, Kato H, Robertson TL, Furonaka H, Kodama K, Fukunaga Y. Cerebrovascular disease in a fixed population of Hiroshima and Nagasaki, with special reference to relationship between type and risk factors. *Stroke*. 1984;15:653–660.
19. Stemmermann GN, Hayashi T, Resch JA, Chung CS, Reed DM, Rhoads GG. Risk factors related to ischemic and hemorrhagic cerebrovascular disease at autopsy: the Honolulu Heart Study. *Stroke*. 1984;15:23–28.
20. Al-Roomi K, Heller RF, Holland T, Floate D, Wlodarczyk J. The importance of hypertension in the aetiology of infarctive and haemor-rhagic stroke: the Lower Hunter Stroke Study. *Med J Aust*. 1992;157:452–455.
21. He J, Klag MJ, Wu Z, Whelton PK. Stroke in the People's Republic of China, II: meta-analysis of hypertension and risk of stroke. *Stroke*. 1995;26:2228–2232.
22. Kaplan RC, Psaty BM, Heckbert SR, Smith NL, Lemaitre RN. Blood pressure level and incidence of myocardial infarction among patients treated for hypertension. *Am J Public Health*. 1999;89:1414–1417.
23. Alderman MH, Budner N, Cohen H, Lamport B, Ooi WL. Prevalence of drug resistant hypertension. *Hypertension*. 1988;11(suppl II):II-71–II-75.
24. Peterson GM, McLean S. Determinants of patient compliance and clinical response in general-practice treatment of hypertension. *Med J Aust*. 1982;2:230–233.
25. Stockwell DH, Madhavan S, Cohen H, Gibson G, Alderman MH. The determinants of hypertension awareness, treatment, and control in an insured population. *Am J Public Health*. 1994;84:1768–1774.
26. Haynes RB, Gibson ES, Hackett BC, Sackett DL, Taylor DW, Roberts RS, Johnson AL. Improvement of medication compliance in uncontrolled hypertension. *Lancet*. 1976;1:1265–1268.
27. Morisky DE, DeMuth NM, Field-Fass M, Green LW, Levine DM. Evaluation of family health education to build social support for long-term control of high blood pressure. *Health Educ Q*. 1985;12:35–50.
28. Eisen SA, Woodward RS, Miller D, Spitznagel E, Windham CA. The effect of medication compliance on the control of hypertension. *J Gen Intern Med*. 1987;2:298–305.
29. Berlowitz DR, Ash AS, Hickey EC, Friedman RH, Glickman M, Kader B, Moskowitz MA. Inadequate management of blood pressure in a hypertensive population. *N Engl J Med*. 1998;339:1957–1963.
30. Klein LE. Compliance and blood pressure control. *Hypertension*. 1988;11(suppl II):II-61–II-64.
31. Wilber JA, Barrow JG. Hypertension: a community problem. *Am J Med*. 1972;52:653–663.
32. Miller NH, Hill M, Kottke T, Ockene IS. The multilevel compliance challenge: recommendations for a call to action: a statement for healthcare professionals. *Circulation*. 1997;95:1085–1090.
33. Dickerson JE, Hingorani AD, Ashby MJ, Palmer CR, Brown MJ. Optimisation of antihypertensive treatment by crossover rotation of four major classes. *Lancet*. 1999;353:2008–2013.