Primary Prevention of Hypertension by Nutritional-Hygienic Means

Final Report of a Randomized, Controlled Trial

Rose Stamler, MA; Jeremiah Stamler, MD; Flora C. Gosch, MD; Jean Civinelli, Joan Fishman, RD; Patricia McKeever, RD; Arline McDonald, PhD; Alan R. Dyer, PhD

A 5-year trial involving 201 men and women with high-normal blood pressure at baseline demonstrated the ability to reduce the incidence of hypertension in participants randomized to nutritional-hygienic intervention compared with a control group. The incidence of hypertension was 8.8% among 102 intervention group participants vs 19.2% among 99 control group members. The odds ratio for the incidence of hypertension in the control group was 2.4. Mean trial blood pressure also was lower in the intervention compared with the control group (−1.2 and −1.9 mm Hg, respectively, for diastolic blood pressure at work-site and office visits and −1.3 and −2.0 mm Hg, respectively, for systolic blood pressure at the two sites). Net weight loss in the intervention group averaged 2.7 kg during the trial; sodium intake was reduced by 25% and reported alcohol intake decreased by 30%. The majority of intervention participants also reported an increase in physical activity. Effect on blood pressure was related particularly to degree of weight loss. Results indicate that even a moderate reduction in risk factors for hypertension among hypertension-prone individuals contributes to the primary prevention of the disease.

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CONTROL of hypertension in the United States has advanced greatly over the last 20 years.[1] Today, with recognition of the risks that accompany elevated blood pressure (BP), millions of hypertensives are receiving pharmacologic treatment that normalizes pressure. Despite gratification with this change, there is legitimate concern about the balance between benefit and risk with decades-long use of drugs, on a mass scale, particularly for persons with less severe hypertension. This is a concern that the favorable results of short-term trials cannot fully allay.[2-5]

A reasonable way to cope with this dilemma is to attempt, using nonpharmacologic means, to influence BP favorably before hypertension has been established, before untreated hypertension has caused damage, and before worries about unwanted drug effects have to be faced.

There are convincing data, from both epidemiologic studies and trials in hypertensive persons, on the relation of several life-style traits to BP: overweight, high salt intake, high alcohol intake, and physical inactivity.[1,6-9] Intervention on these variables formed the basis of the present randomized, controlled trial on the primary prevention of hypertension in persons at above-average risk of becoming hypertensive. The aim of the trial was to assess whether a program to improve these aspects of life-style resulted in a lower incidence of hypertension and a lower BP in the intervention compared with the control group.

From the Department of Community Health and Preventive Medicine, Northwestern University Medical School, Chicago, Ill.

Reprint requests to 680 N Lake Shore Dr, Suite 1102, Chicago, IL 60611 (Professor R. Stamler).

METHODS

Participants

Two-stage screening identified men and women aged 30 to 44 years who were hypertension-prone, ie, who had a high-normal diastolic BP: a first-screen diastolic BP of 80 to 99 mm Hg, with a second-screen value of 85 to 89 mm Hg or 80 to 84 mm Hg plus overweight (10% to 49% above desirable weight[10]) and/or a rapid resting pulse rate (≥80 beats per minute). Blood pressure was the average of two readings at a visit, with use of the random zero mercury manometer. Those least likely to cooperate with recommended life-style changes were not invited to participate (persons ≥50% above desirable weight, those reporting having five or more alcoholic drinks daily, and persons expressing unwillingness to change). Other reasons for exclusion were major electrocardiographic abnormalities, history or findings of major cardiovascular disease, diabetes, life-limiting conditions, frequent travel limiting clinic attendance,

special diets not compatible with program recommendations, and contraceptive pill use.

Participants were identified at work-site screening in Chicago, Ill, companies that agreed to give individuals time off during the day to participate in the study.

End Points, Sample Size, and Study Duration

The end points of the primary trial were comparison of mean BPs and incidence of definite hypertension in the two study groups. Definition of *hypertension* was initiation of antihypertensive medication therapy by the participant's personal physician or sustained elevation of diastolic BP (a rise in the work-site value to ≥90 mm Hg followed by a mean level ≥90 mm Hg for the remainder of the trial). Sample size originally was calculated on the basis of the first end point (BP difference), and it was determined that with a sample size of 200 the power was .80 to detect a diastolic BP difference of 2.5 mm Hg between groups, with an α of .05 (one sided). Before the start of the trial, inadequate data were available to estimate the incidence of hypertension; it was decided to use the first 2 years of trial experience to determine whether sample size had to be expanded to test the incidence end point. Original calculations indicated a sample of 200 would be adequate to detect a difference in incidence of .15 between the two groups, with power between .70 and .80, depending on the actual incidence of hypertension in the intervention group. In the first 2 years, 12 monitored (control) group members developed hypertension compared with 3 in intervention. It therefore was decided to maintain sample size at 200. Study duration was set to permit all to reach their fifth anniversary.

Baseline Assessment

After screening, those who initially were eligible attended a fasting visit for standard biochemical tests and a medical visit including a resting electrocardiogram, a submaximal graded treadmill test using the Bruce protocol, and a chest roentgenogram. Those then eligible were invited into the study.

Recruitment and Randomization

After signed consent was obtained, 201 eligible men and women were randomized into one of two study groups using computer assignment, with stratification by average screening BP. Randomization was into either the intervention group, which received individualized guidance to achieve life-style changes, or the monitored (control) group, seen every 6 months.

Intervention Goals, Methods, and Assessments

Goals.—Goals for the intervention group were (1) reduction in overweight of at least 4.5 kg or 5% of weight (whichever was greater) with a fat-modified American Heart Association–type diet, (2) reduction in daily sodium intake to 1800 mg or less (4.5 g of salt), (3) reduction of alcohol intake to no more than two drinks daily (26 g of alcohol), and (4) increase in moderate isotonic physical activity, typically with a target heart rate 70% to 75% of maximum for age, unless contraindicated. Recommendations were for 30 minutes of exercise at least 3 days per week.

Intervention Methods.—Since the various life-style factors are linked closely (eg, exercise, alcohol use, and weight control), intervention was multifactorial. An intensive individualized approach involved both physician and nutrition counselors to help each individual develop a realistic plan to meet intervention goals. Food diaries were used to describe usual eating patterns so recommendations could take account of both tastes and problems. Visit frequency varied from biweekly in the early days of intervention to quarterly, depending on goal status and participant preference. Family members were included whenever possible to discuss meal patterns, identify important sources of calories and sodium, suggest reasonable nutritional alternatives, and provide ideas about opportunities for exercise. Some group counseling also was included, eg, special sessions on weight control. Material was prepared on restaurant ordering, suggestions for holiday eating, and recipes. Periodic newsletters exchanged experiences, answered common questions, and reinforced goals. As part of appropriate medical practice, all smokers—in both the intervention and monitored groups—were advised to quit smoking.

Dietary Intake Assessment.—Intervention participants were asked to collect 7-day food diaries at baseline and annually and 4-day records at least semiannually. Monitored participants were to keep annual 7-day diaries. All were instructed in keeping an accurate record, with use of food models and plates of various sizes to judge portion sizes. Completed records were reviewed with them. Records were coded for computer analysis, based on methods of the Nutritional Coding Center, University of Minnesota, Minneapolis; for analyses, Nutrition Coding Center tape 6 was used.

Measurement of Urinary Sodium, Potassium, and Creatinine Levels.—The dietary coding did not provide for salt added in cooking or at the table, so the main assessment of sodium intake was obtained from urinary values. At baseline and annually, all participants were asked to collect seven consecutive, timed, overnight urine samples for determination of sodium, potassium, and creatinine content. Intervention group participants also were asked to collect four such samples semiannually.

Overnight specimens were requested since complete collections during 24 hours were judged to be more difficult and multiple, timed, overnight specimens standardized to 8 hours have been shown to yield reasonably accurate estimates of habitual sodium intake.[11] Results were converted to 24-hour estimates with multipliers from a substudy that compared overnight 8-hour with total 24-hour values. Multipliers obtained in the substudy and then applied to the main study were 3.8 for sodium, 5.0 for potassium, and 3.1 for creatinine.[12]

Urine aliquots were analyzed at Northwestern Memorial Hospital Clinical Research Laboratory, Chicago, with 1 in 14 samples as a blind replicate. Sodium and potassium were analyzed by ion-selective electrode by an electrolyte analyzer. Creatinine was analyzed by the Jaffé alkaline picrate method by spectrophotometer.

Other Measurements

BP.—Blood pressure was measured every 6 months. These measurements were at the work site so the two groups would have similar familiarity with the surroundings. In addition, BP was measured at annual office visits. Since the office setting was more familiar to intervention group participants because of frequent counseling visits, there could be a bias toward lower readings there for them compared with the monitored group. Therefore, unless otherwise indicated, work-site levels were used for group comparisons. Measurements were made by staff members trained and certified in procedures used by the Hypertension Detection and Follow-up Program, based on recommendations of the American Heart Association.[13] Observers of BP were tested for vision, hearing acuity, and accuracy and were retested each 6 months.

Group assignment was unknown to the BP technicians. To further minimize observer bias, the random zero mercury manometer was used. Participants were asked to avoid smoking or eating for 30 minutes before measurement, to empty the bladder, and to remain seat-

ed in a quiet room for 5 minutes. Blood pressure was measured on the right arm with an appropriate-sized cuff. Systolic BP was the appearance of the first sound (K1) and diastolic BP was the disappearance of sound (K5). Two pressures with the random zero mercury manometer were averaged as the measures of record.

Blood Chemistry.—At baseline and annually, all participants received a standard battery of tests done by computerized sequential multiple analyzer. Blood samples were drawn after a 15-hour overnight fast and analyzed at the Northwestern Memorial Hospital laboratory; 1 in 10 specimens was a blind replicate.

Weight and Height.—Participants were weighed on a beam-balance scale, without shoes and heavy clothing. Height was measured with the scale's rule. Weight was measured at semiannual work-site and annual office visits. Relative weight was calculated using 1959 life insurance actuarial tables.[10]

Statistical Methods

Since there is considerable variability in BP as well as in intake of sodium and alcohol, and often also in weight in persons attempting to lose weight, and since length of time in the study also varied, trial average values for each person were used for these variables in the main analyses. In addition, comparisons were made based on findings at fixed intervals. In this way, total trial experience of the entire sample was used.

In calculating trial average diastolic BP for persons prescribed antihypertensive treatment by their personal physicians, the value recorded at the last work-site visit prior to initiation of treatment (or 90 mm Hg, whichever was higher) was used for subsequent visits. Most of these relatively young individuals were taking medication because of elevated diastolic, not systolic, BP. Therefore, it would have been inappropriate to assign systolic values of 140 or 150 mm Hg for posttreatment visits; the actual systolic pressure of the last pretreatment visit was retained for future visits and included in the trial average. Trial average for work-site BP and weight was the average of all semiannual measurements for these variables; trial average for office visit BP, urinary sodium intake, and reported alcohol intake included all annual measurements.

Differences between baseline and trial average for key variables were compared for intervention and monitored groups by Student's t tests for continuous variables. One-sided tests were used based on prior study hypotheses of direction of change. Differences in proportions were compared using the χ^2 test corrected for continuity. Relative risk for incidence of hypertension was calculated using the odds ratio, with 90% confidence intervals.

For examination within the intervention group of the relation of life-style changes to BP end points, use was made of simple correlation and multiple linear regression.

RESULTS

Baseline Comparability

The randomized groups were comparable on most variables (Table 1). Participants were 21% to 23% overweight and excreted about 4000 mg of sodium daily, and about 20% reported high alcohol intake (four or more drinks at least 1 day per week). They were similar in age-sex-race distribution, with a mean age of 37 years; 86% were men and 82% were white. Reported cigarette smoking was higher in the monitored group (38%) than in the intervention group (25%).

Study Participation

Median length of time in the study was 5.2 years for the intervention group and 5.4 years for the monitored group. Dropout was small for both groups, with 87% participating for 4 years or more. A high proportion of intervention participants supplied multiple-day food records and multiple, timed overnight urine specimens at least twice a year. The median number of multiple-day food records (4 or 7 days on each occasion) was 8.1; the median for urine collections (4 or 7 nights on each occasion) was 9.0. Monitored participants supplied similar records and specimens annually, and comparison between groups on these variables is based on annual findings.

Trial End Points

Incidence of Hypertension.—During the 5 years of the trial, the incidence of hypertension was more than twice as high in the monitored as in the intervention group (Table 2). The proportion moving from hypertension-prone to definite hypertension was 19.2% of monitored participants vs 8.8% of intervention group members ($\chi^2=3.68$ with continuity correction; $P=.027$). The odds ratio for the incidence of hypertension in the control group was 2.4 (90% confidence interval, 1.2 to 4.8).

Hypertension occurred later in the trial for intervention than monitored participants. Three of 9 incident cases in the intervention group occurred in the first 2 years, with the remaining 6 in the third year and beyond. This proportion was reversed in the monitored group, with 12 of 19 cases in the first 2 years and the remaining one third thereafter. The odds ratio for incidence of hypertension in the monitored group was greater than 1.00 in both periods but

Baseline Variable	Intervention Group (n=102) Mean	Intervention Group (n=102) SD	Monitored Group (n=99) Mean	Monitored Group (n=99) SD
Age, y	37.4	4.1	37.7	4.0
Men, %	86.3	...	86.9	...
White, %	81.4	...	82.8	...
Weight, kg	83.3	11.0	85.3	11.0
Relative weight	120.5	13.1	123.4	11.2
Urinary sodium level, mg/d	3982.3	1413.1	4252.9	1445.3
Urinary potassium level, mg/d	2683.9	969.7	2661.5	905.2
Alcohol intake				
Drinkers, %	83.3	...	87.9	...
Mean g/d consumed by drinkers	33.1	28.0	34.7	31.9
% Who consume ≥52 g/d*	20.9	...	19.5	...
Cigarette smokers, %	24.5	...	38.4	...
No. of cigarettes per d by smokers	16.8	17.5	15.8	13.9
Serum creatinine level, μmol/L	100.0	15.0	100.8	15.0
Serum cholesterol level, mmol/L	5.1	0.8	5.3	1.0
Serum fasting glucose level, mmol/L	5.1	0.5	5.2	0.7
Serum uric acid level, μmol/L	370.0	80.0	370.0	80.0
Serum triglyceride level, mmol/L	1.4	0.8	1.4	0.8
Pulse rate, beats per minute	74.0	8.5	74.0	8.5
Blood pressure, mm Hg				
Diastolic	82.2	3.0	82.2	2.9
Systolic	122.1	6.8	122.4	7.0

*On one or more days per week.

Table 2.—Incidence of Hypertension

Group	No. In Group	No. (%) of Hypertensives*
Intervention	102	9 (8.8)
Monitored	99	19 (19.2)
	$\chi^2=3.68$; $P=.027$	

*Hypertensives are participants who were prescribed antihypertensive medication by their personal physician and/or who sustained an elevated work-site diastolic blood pressure (see text).

Table 3.—Mean Blood Pressure at Work-Site and Annual Office Visits

	No. of Participants	Mean (±SD) Blood Pressure, mm Hg: Baseline	Trial Average*	Change	Net Change†	Student's t Test	P‡
Diastolic							
Work-site visit							
Intervention group	102	82.5 (2.9)	81.2 (5.2)	−1.3 (4.7)	−1.2 (0.7)	1.67	.049
Monitored group	99	82.6 (2.9)	82.5 (5.5)	−0.1 (4.9)	...	...	...
Annual office visit							
Intervention group	99	82.4 (2.6)	81.8 (5.9)	−0.7 (5.6)	−1.9 (0.8)	2.31	.011
Monitored group	95	82.6 (3.0)	83.8 (6.3)	+1.2 (5.6)	...	...	...
Systolic							
Work-site visit							
Intervention group	102	122.5 (6.8)	119.8 (7.6)	−2.6 (6.4)	−1.3 (0.9)	1.55	.061
Monitored group	99	122.7 (7.0)	121.5 (8.9)	−1.3 (6.1)	...	...	...
Annual office visit							
Intervention group	99	122.2 (6.7)	118.5 (7.5)	−3.7 (6.4)	−2.0 (0.9)	2.10	.019
Monitored group	95	122.9 (7.0)	121.2 (9.0)	−1.7 (6.4)	...	...	...

*Median number of years from baseline to the last visit at the work site was 5.0 for the intervention group and 5.1 for the monitored group and at the annual office visits was 5.2 for the intervention group and 5.4 for the monitored group. Median number of periodic measurements per participant at the semiannual work-site visits was 9.2 for the intervention group and 9.3 for the monitored group and at the annual office visits was 4.3 for the intervention group and 4.5 for the monitored group.
†Values in parentheses are SEs.
‡One-sided test.

was larger in the first 2 years than in the second 2 years (4.1 and 1.3, respectively).

As described in the "Methods" section, an individual was designated as hypertensive if given antihypertensive medication by his/her personal physician or if work-site diastolic BP rose to greater than or equal to 90 mm Hg and the mean work-site level thereafter was 90 mm Hg or higher. The second criterion was included since intervention group participants might be more reluctant than monitored participants to use medication for elevated BP. In fact, of 19 monitored participants with incident hypertension, 16 had antihypertensive medication prescribed by their personal physicians, while in the intervention group 5 of the 9 defined as hypertensive were taking antihypertensive drugs, but the remaining 4 declined drug treatment.

Since smoking was less frequent at baseline in the intervention group, and since cigarette smoking might contribute to hypertension, incidence was compared separately for smokers and nonsmokers. The incidence of hypertension was higher among monitored than intervention participants for both smokers and nonsmokers, but the difference apparently was larger among smokers. Among smokers, the incidence was 28.9% for monitored vs 8.0% for intervention (odds ratio, 3.9; 90% confidence interval, 1.1 to 13.5); among nonsmokers, the comparable proportions were 11.5% (monitored) vs 7.8% (intervention) (odds ratio, 1.5; 90% confidence interval, 0.6 to 3.6). With the given sample size, the difference between smokers and nonsmokers was not significant. The odds ratio for the overall association of randomized group with incidence, adjusted for smoking distribution, was 2.1 (90% confidence interval, 1.0 to 4.2).

Trial Average BP.—For intervention participants, trial average BP was lower than baseline at both work-site and annual office visits for diastolic and systolic BPs (Table 3). In all four comparisons, BP changes were favorable to the intervention group, but mean differences between changes in intervention and monitored group members were small. They nonetheless were statistically significant for diastolic BP in both locations and for systolic BP at the annual office visit, while of borderline significance at the work site ($P=.061$). These net differences based on trial average were almost identical to those observed at 5 years.

Changes in Life-style Variables for the Intervention and Monitored Groups

Parallel with the more favorable outcome in BP status, there were larger changes in life-style in the intervention compared with the monitored group.

Weight Change.—Mean weight loss in overweight intervention group participants was 2.0 kg (trial average weight compared with baseline weight) (Table 4). Since monitored group participants gained an average of 0.8 kg during the trial, net weight change for intervention was −2.7 kg ($P<.001$). More than 25% of overweight intervention participants met the goal of loss of 4.5 kg or more (trial average). The largest group weight change was in the first year, −4.1 kg. In following years, some weight was regained by intervention participants so that the mean difference from baseline was −2.4, −1.6, −0.9, and −0.7 kg for succeeding anniversaries. However, because monitored participants gained weight after the first year, net difference in weight change between the groups was −3.9 kg at 1 year and −2.6, −2.4, −2.3, and −2.8 kg at succeeding years.

Urinary Sodium and Potassium.—Sodium intake, as assessed by repeated measurement of urinary sodium output, was reduced by approximately 25% in intervention participants vs 6% in the monitored group (Table 4) ($P<.001$). Approximately 13% of intervention participants achieved and maintained the sodium intake goal of less than 1800 mg/d (vs 1% at that level in the monitored group). At baseline, 18% of the intervention group had a daily intake above 5400 mg (13.5 g of salt). The proportion at this high level was reduced to 2% in the intervention group but remained at 17% in the monitored group. Modification in sodium intake among intervention participants was maintained throughout the trial and was greatest in the third and fourth years (−31% and −26%). As noted in the "Methods" section, monitored participants supplied urine samples annually, so only annual samples (and not interim collections) from the intervention group are included for comparability. Intervention participants (n = 10) supplying only interim samples are excluded from Table 4. When the analysis was repeated including these 10 individuals, results were unchanged.

Potassium excretion indicated little change in intake, from 2684 mg/d at baseline to a trial average of 2702 mg for intervention and from 2662 to 2697 mg/d for monitored participants. The sodium/potassium molar ratio changed from 2.5 to 1.9 in the intervention group but was almost unchanged in the monitored group—2.7 at baseline and a trial average of 2.6.

Alcohol Intake.—Among self-reported drinkers, mean daily intake at baseline was 30.2 g of alcohol for intervention members and 32.5 g for monitored participants, slightly more than two alcoholic drinks daily (Table 4).

Table 4.—Change in Weight, Sodium Output, and Alcohol Intake

	Baseline	Trial Average	Change	Net Change*	Student's t Test	P	Median No. of Periodic Measurements per Participant
Weight, kg (SD)†							
Intervention group (n = 95)	85.0 (11.5)	83.0 (11.1)	−2.0 (4.5)	−2.7 (0.6)	4.62	<.001	9.2 (semiannual)
Monitored group (n = 98)	85.7 (10.8)	86.5 (11.3)	+0.8 (3.7)	...	...	...	9.3 (semiannual)
Urinary sodium output, mg/d (SD)							
Intervention group (n = 92)	3980.4 (1446.8)	3038.9 (1137.9)	−941.5 (1215.9)	−700.3 (164.0)	4.27	<.001	4.5 (annual)
Monitored group (n = 95)	4296.2 (1545.1)	4055.0 (1252.8)	−241.2 (1014.8)	...	...	...	4.7 (annual)
Alcohol intake, reported g/d (SD)							
Intervention group (n = 86)	30.2 (29.3)	20.3 (19.6)	−9.9 (18.8)	−2.2 (3.1)	0.70	.242, not significant	4.1 (annual)
Monitored group (n = 90)	32.5 (32.4)	24.8 (20.6)	−7.7 (23.1)	...	...	...	3.4 (annual)

*Net change is the change in the intervention group minus the change in the monitored group. Values in parentheses are SEs.
†Participants with relative weight greater than 1.00.

Both groups reported a reduction during the trial, by an average 9.9 g for intervention (−33%) and by 7.7 g for monitored (−24%) participants, a nonsignificant difference between the groups in amount of change. The largest reduction among intervention participants was in the first year (−35%); reductions in subsequent years (compared with baseline) were 29% at the second year and 31% at the third, fourth, and fifth annual visits.

Exercise. — Assessment depended, first, on self-reporting by intervention group members, and 75% reported an increase in moderate physical activity. Stationary bicycling, brisk walking, and jogging were the main activities. Decrease in resting pulse rate was only slightly higher in intervention than monitored participants (−2.6 vs −2.2 beats per minute, respectively). However, improvement from baseline in response to graded exercise tests performed at 2 to 3 years was significantly greater in the intervention than in the monitored group, as reported earlier.[14]

Nutritional Changes. — Intervention participants reported a 30% trial average decrease in daily energy intake (from 11 437 to 8068 J [from 2723 to 1921 calories]) vs a 12% decrease for the monitored group (from 11 621 to 10 256 J [from 2767 to 2442 calories]). In recommendations to the intervention group, dietary modification to achieve both weight loss and improved composition emphasized reduction in total fat, saturated fat, and dietary cholesterol. For intervention participants, reported total fat was reduced from 42.0% of calories at baseline to 35.3% of total calories, saturated fat from 15.8% to 12.5%, and dietary cholesterol from 188 mg per 4200 J (1000 calories) to 169 mg per 4200 J (1000 calories). In contrast, changes in the monitored group were small for total fat (from 41.6% to 40.2% of calories) and saturated fat (from 15.6% to 14.8%), while dietary cholesterol remained essentially unchanged (178 and 177 mg per 4200 J [1000 calories]). With reported calorie reduction, absolute values of other nutrients (protein, polyunsaturated fat, carbohydrates, and potassium) fell in both groups but changed little as a percentage of calories. Reported calcium intake was reduced in the intervention group from 800 to 650 mg/d but increased per 4200 J (1000 calories) (from 293 to 342). Change was minimal in the monitored group.

Smoking cessation was reported by 3 of 25 intervention smokers and 10 of 38 monitored smokers; the lower quit rate in the intervention group perhaps related to the multiplicity of life-style changes recommended to that group, with a major focus on nutritional change.

Relationship Between Nutritional Changes and Changes in BP and Other Variables in the Intervention Group

Changes in BP.—All results described previously herein compared the two randomized groups, intervention and monitored. To examine further the relation between the nutritional program and BP, epidemiologic analyses were made of outcome within the intervention group based on amount of change made in two major intervention areas: weight and sodium intake.

In one analysis, for each of these variables the group was divided into those above and those below median change. Median weight change in the whole intervention group was a loss of 1.4 kg. The average decrease in the half losing more weight was 5.3 kg; the average change in the other half was a gain of 1.4 kg (Table 5). Diastolic BP was reduced 2.3 mm Hg in the successful losers vs 0.5 mm Hg in the other half of the intervention group ($P = .035$). Those who lost weight had a reduction of 4.4 mm Hg in systolic BP vs 1.1 mm Hg in those with little or no weight loss or with weight gain ($P = .007$).

A similar analysis was performed regarding change in sodium intake. Median group change was a reduction of 1012 mg/d. In the half making more change (−1842 mg of sodium per day), trial average diastolic BP was reduced by 1.5 mm Hg and systolic BP was reduced by 3.0 mm Hg. In the half with less sodium change (−88 mg), BP reduction was less than that in the successful sodium changers (1.2 mm Hg for diastolic and 1.9 for systolic BP); the difference between the two halves was not significant. In simple correlation analyses, weight reduction in the intervention group was related significantly to average change during the trial in both systolic and diastolic BP ($r = .31$ for both, $P < .001$). Sodium restriction also was related to systolic BP changes; the coefficient was smaller than for weight ($r = .14$, $P = .089$). Correlation of sodium intake change with diastolic BP was small ($r = .03$) and nonsignificant. Changes in these two intervention variables were related significantly to each other ($r = .28$, $P = .040$). The spontaneous changes in weight in the monitored group also were related significantly to changes in BP.

Weight increased by 1% in the 9 persons with incident hypertension in the intervention group but decreased by 3% in the 93 intervention participants who remained nonhypertensive. Sodium reduction was 717 mg/d in incident hypertensives and 984 mg/d in nonhypertensives; reported daily alcohol intake was reduced by 5 g in incident hypertensives and 9 g in the remainder.

In multiple regression analyses there was a significant relationship between weight change and change in BP, while for sodium and alcohol change the relationship was not independently significant. The regression coefficient for weight change indicated that a difference of 4.5 kg was associated with a difference of 2.1 mm Hg in systolic BP

Table 5.—Weight Change and Work-Site Trial Average Blood Pressure for the Intervention Group*

	Those Who Lost More Than the Median Group Loss† (n=47)	Those Who Lost Less Than the Median Group Loss (n=48)
Mean weight change, kg‡	−5.3	+1.5
Diastolic blood pressure, mm Hg (SD)		
Baseline	83.0 (2.6)	82.1 (3.3)
Trial average	80.6 (5.4)	81.6 (5.1)
Change	−2.3 (5.0)	−0.5 (4.5)
	$t=1.84$, $P=.035$	
Systolic blood pressure, mm Hg (SD)		
Baseline	123.5 (6.2)	121.2 (6.2)
Trial average	119.1 (8.1)	120.1 (6.4)
Change	−4.4 (6.7)	−1.1 (6.0)
	$t=2.53$, $P=.007$	

*Participants with baseline relative weight greater than 100.0 were included.
†Median change for the intervention group in trial average weight was −1.4 kg.
‡Difference between baseline and trial average.

and 1.5 mm Hg in diastolic BP.

Changes in Biochemical Variables.—Successful weight change in the intervention group also was related to favorable trial average changes in levels of serum cholesterol, glucose, and triglycerides. The net difference was calculated by comparing differences between trial average and baseline levels in the more vs the less successful weight losers. In these comparisons, the net difference in serum cholesterol levels was 0.17 mmol/L, in serum fasting glucose levels was 0.28 mmol/L, and in fasting triglyceride levels was 0.26 mmol/L, all favorable to the half of the group losing more weight.

COMMENT

While recent randomized trials report positive results using nutritional therapy as replacement for drug treatment in persons with confirmed hypertension,[9,15] the trial reported herein is the first long-term trial on efficacy of multifactor nutritional-hygienic intervention for primary prevention of hypertension. To our knowledge, the only other trial in adults with a similar aim is the 3-year Hypertension Prevention Trial.[16] The central finding of the present investigation was the significant difference during the 5 years of study in the incidence of hypertension between the life-style intervention group (8.8%) and the monitored (control) group (19.2%). The relative risk of incidence of hypertension in the control group was 2.4.

There also were small differences in favor of the intervention group compared with the monitored group in trial average BPs measured at the work site, in both diastolic BP (−1.2 mm Hg, $P=.049$) and systolic BP (−1.3 mm Hg, $P=.061$). While from a clinical viewpoint such differences in BP in a single patient are considered small, group differences of that dimension have importance since a higher group average reflects a shift of the group to higher BP levels, with a concomitant higher proportion frankly hypertensive. This was seen herein in the more than two-to-one difference in the incidence of hypertension in the monitored vs intervention group.

Since a randomized trial using lifestyle modifications could not be completely blinded, several steps were taken to reduce bias in the assessment of end points. In regard to the incidence of hypertension, the decision to initiate treatment with antihypertensive medication for participants was not made by the study physician but rather by the personal physician. While the study could not ensure that the private physician followed standard criteria for initiating drug therapy, a review of study records indicated that for monitored participants taking medication, diastolic BP measured at the work site 6 months prior to prescription was, in fact, elevated (average diastolic BP, 91.7 mm Hg).

Since intervention participants could be less motivated to turn to pharmacologic treatment of elevated BP, to reduce possible bias a second criterion for incidence of hypertension was used, namely, a rise in work-site diastolic BP (≥90 mm Hg), with a sustained average at that level thereafter. Further, staff who measured BP were blinded as to group assignment of participants and they used the random zero mercury manometer, which also helps reduce measurement bias.

Together with the central comparisons between the two randomized groups, relation within the intervention group of change in life-style to change in BP was examined. In these essentially epidemiologic analyses, the greater the weight change, the greater the change in BP. The half of the intervention group that lost more than the median group weight loss had a reduction in work-site systolic BP of 4.4 mm Hg, significantly greater than the 1.1-mm Hg reduction in the half with less weight loss or even weight gain. A similar difference was observed for diastolic BP (−2.3 vs −0.5 mm Hg). Similar though smaller differences were seen when comparison of BP change was made within the intervention group based on reduction in sodium intake.

An additional benefit observed within the intervention group was the effect of weight loss on levels of serum cholesterol, serum glucose, and serum triglycerides.

Overall, study results indicate that a modest program based on nutritional steps to reduce overweight, high salt intake, and high alcohol intake, accompanied by an increase in moderate exercise, can contribute to prevention of hypertension. A finding possibly of considerable practical importance was the much higher incidence of hypertension in smokers than nonsmokers in the monitored group. A few previous data sets from population studies have indicated such a relationship,[6] but prospective data on smoking and risk of high BP are sparse.

While a sizable proportion of intervention participants (from one fourth to one third) met study goals for reduction of overweight and excess salt and alcohol intake, overall changes in the intervention group were modest. Based on the greater BP response of those who made greater changes, it is reasonable to assume that if more substantial improvements in life-styles were made, the effect on BP would be more sizable than that observed in the present study.

In this group of relatively young adults (30 to 44 years at entry), 1 in 5 persons in the control group moved from a status of hypertension-prone to hypertensive during the 5 years of the trial compared with 1 in 11 persons in the life-style intervention program. Since an estimated 10 million men and women in the Unted States in this age range have high-normal BP,[17] ie, diastolic 80 to 89 mm Hg, the level represented by participants in this study, potential saving in hypertension incidence (and concomitant added risk of coronary disease and stroke) could be as large as 1 million cases over 5 years. Savings in numbers of cases among older persons would enlarge this potential even further.

Participants in the trial apparently were healthy, active people recruited by work-site population screening, not patients in an ambulatory-care or hospital setting. It seems reasonable to infer that the findings in this group are gener-

alizable to wider sections of the population. This is particularly true since these interventional findings on the relation of BP to weight and intake of sodium and alcohol are in keeping with epidemiologic findings in large population studies.[8] Results also are congruent with the interim report of the Hypertension Prevention Trial, whose findings on lower BP with nutrition intervention are similar to those of our group.[16]

Implementation of a strategy of primary prevention of hypertension by safe nutritional-hygienic means would seem to be appropriate as a necessary complement to the ongoing effort of early detection and effective treatment (nonpharmacologic and pharmacologic) for those with high BP already established.[1]

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References

1. Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The 1988 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med.* 1988;48:1023-1038.

2. Blaufox MD, Guest Editor, and the Hypertension Detection and Follow-up Program Cooperative Group Editorial Board. Results and implications of the Hypertension Detection and Follow-up Program. *Prog Cardiovasc Dis.* 1986;29(suppl 1):1-124.

3. Hebert PR, Fiebach NH, Eberlein KA, Taylor JO, Hennekens CH. The community-based randomized trials of pharmacologic treatment of mild-to-moderate hypertension. *Am J Epidemiol.* 1988;127:581-590.

4. Cutler JA, Horan MJ, Roccella EJ, Zusman RM, guest eds. The National Heart, Lung, and Blood Institute workshop on antihypertensive drug treatment: the benefits, costs, and choices. *Hypertension.* 1989;13(suppl I):I-1–I-172.

5. Stamler R. Influence of treatment of 'mild' hypertension on coronary heart disease. *Acta Med Scand.* 1985;(suppl 701):89-99.

6. Stamler J, Berkson DM, Dyer A, et al. Relationship of multiple variables to blood pressure: findings from four Chicago epidemiologic studies. In: Paul O, ed. *Epidemiology and Control of Hypertension.* Miami, Fla: Symposia Specialists; 1975: 307-356.

7. Stamler J. Hypertension: aspects of risk. In: Hunt JC, Cooper T, Frohlich ED, et al, eds. *Hypertension Update: Cardiovascular Risk Factors and Consequences of Hypertension.* Bloomfield, NJ: Health Learning Systems Inc; 1979:22-37.

8. INTERSALT Cooperative Research Group. INTERSALT: an international study of electrolyte excretion and blood pressure: results for 24-hour urinary sodium and potassium excretion. *Br Med J.* 1988;297:319-328.

9. Stamler R, Stamler J, Grimm R, et al. Nutritional therapy for high blood pressure: final report of a four-year randomized controlled trial—The Hypertension Control Program. *JAMA.* 1987; 257:1484-1491.

10. New weight standards for men and women. *Stat Bull Metropol Life Ins Co.* 1959;40:1-4.

11. Liu K, Dyer AR, Cooper RS, Stamler R, Stamler J. Can overnight urine replace 24-hour urine collection to assess salt intake? *Hypertension.* 1979;1:529-536.

12. Dyer A, Stamler R, Grimm R, et al. Do hypertensive patients have a different diurnal pattern of electrolyte excretion? *Hypertension.* 1987;10:417-424.

13. *Recommendations for Human Blood Pressure Determination by Sphygmomanometers: Report of a Subcommittee of the Postgraduate Education Committee of the American Heart Association.* Dallas, Tex: American Heart Association; 1980. Publication 70-019B.

14. Liao Y, Emidy LA, Gosch FC, Stamler R, Stamler J. Cardiovascular responses to exercise of participants in a trial on the primary prevention of hypertension. *J Hypertens.* 1987;5:317-321.

15. Langford HG, Blaufox MD, Oberman A, et al. Dietary therapy slows the return of hypertension after stopping prolonged medication. *JAMA.* 1985;253:657-664.

16. Hypertension Prevention Trial Research Group. Hypertension Prevention Trial: 3 year results. *Circulation.* 1988;78(suppl II):II-568.

17. *Blood Pressure Levels in Persons 18 to 74 Years of Age, 1976 Through 1980, and Trends in Blood Pressure From 1960 to 1980 in the United States: Data From the National Health Survey.* Hyattsville, Md: National Center for Health Statistics; July 1986. Series 11, No. 234.