

Effects of Comprehensive Lifestyle Modification on Blood Pressure Control

Main Results of the PREMIER Clinical Trial

Writing Group of the PREMIER Collaborative Research Group

HIGH BLOOD PRESSURE (BP) IS a common, powerful, and independent risk factor for cardiovascular disease (CVD). Almost 50 million US adults, or approximately 25% of the US adult population, have hypertension, defined as BP of 140/90 mm Hg or higher and/or current use of antihypertensive medication.¹ The prevalence of hypertension increases progressively with age, so that more than half of all individuals aged 60 years or older in the United States have hypertension.² The estimated lifetime risk of developing hypertension is 90%.³

Above-optimal BP that is not in the hypertensive range also confers excess CVD risk.⁴ In fact, almost a third of BP-related deaths from coronary heart disease are estimated to occur in nonhypertensive individuals with a systolic BP of 120 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg.⁵ Therefore, reduction of BP to optimal levels, control of hypertension, and prevention of the age-related increase in BP remain major public health priorities.

Current national recommendations for the prevention and treatment of high BP emphasize nonpharmacological therapy, also termed “lifestyle modification.”^{6,7} Lifestyle modifications that effectively lower BP are weight loss, reduced sodium intake, increased physical activity, limited alcohol consumption,

For editorial comment see p 2131.

Context Weight loss, sodium reduction, increased physical activity, and limited alcohol intake are established recommendations that reduce blood pressure (BP). The Dietary Approaches to Stop Hypertension (DASH) diet also lowers BP. To date, no trial has evaluated the effects of simultaneously implementing these lifestyle recommendations.

Objective To determine the effect on BP of 2 multicomponent, behavioral interventions.

Design, Setting, and Participants Randomized trial with enrollment at 4 clinical centers (January 2000–June 2001) among 810 adults (mean [SD] age, 50 [8.9] years; 62% women; 34% African American) with above-optimal BP, including stage 1 hypertension (120–159 mm Hg systolic and 80–95 mm Hg diastolic), and who were not taking antihypertensive medications.

Intervention Participants were randomized to one of 3 intervention groups: (1) “established,” a behavioral intervention that implemented established recommendations (n=268); (2) “established plus DASH,” which also implemented the DASH diet (n=269); and (3) an “advice only” comparison group (n=273).

Main Outcome Measures Blood pressure measurement and hypertension status at 6 months.

Results Both behavioral interventions significantly reduced weight, improved fitness, and lowered sodium intake. The established plus DASH intervention also increased fruit, vegetable, and dairy intake. Across the groups, gradients in BP and hypertensive status were evident. After subtracting change in advice only, the mean net reduction in systolic BP was 3.7 mm Hg ($P<.001$) in the established group and 4.3 mm Hg ($P<.001$) in the established plus DASH group; the systolic BP difference between the established and established plus DASH groups was 0.6 mm Hg ($P=.43$). Compared with the baseline hypertension prevalence of 38%, the prevalence at 6 months was 26% in the advice only group, 17% in the established group ($P=.01$ compared with the advice only group), and 12% in the established plus DASH group ($P<.001$ compared with the advice only group; $P=.12$ compared with the established group). The prevalence of optimal BP (<120 mm Hg systolic and <80 mm Hg diastolic) was 19% in the advice only group, 30% in the established group ($P=.005$ compared with the advice only group), and 35% in the established plus DASH group ($P<.001$ compared with the advice only group; $P=.24$ compared with the established group).

Conclusion Individuals with above-optimal BP, including stage 1 hypertension, can make multiple lifestyle changes that lower BP and reduce their cardiovascular disease risk.

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tion, and the Dietary Approaches to Stop Hypertension (DASH) diet.^{6–8} The DASH diet emphasizes consumption of fruits, vegetables, and low-fat dairy products; includes whole grains, poultry, fish, and nuts; and is reduced in fats,

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red meat, sweets, and sugar-containing beverages. As such, the DASH diet has reduced levels of total fat, saturated fat, and cholesterol and increased levels of potassium, calcium, magnesium, fiber, and protein.⁹

These lifestyle modifications are recommended in nonhypertensive individuals with above-optimal BP. Lifestyle modification is also recommended as initial therapy in stage 1 hypertension (for up to 12 months in those without other risk factors [risk class A] or for up to 6 months in those with other risk factors [risk class B]).⁷ For individuals taking BP medication, lifestyle modification is recommended as adjunctive therapy to lower BP. Although lifestyle therapies are generally recommended as a group, no previous trial has evaluated the effects of implementing these recommendations simultaneously, and no trial has tested the feasibility of implementing the DASH diet in free-living persons.

METHODS

The rationale for the PREMIER clinical trial¹⁰ has been published. Partici-

pating institutions included the National Heart, Lung, and Blood Institute Project Office (Bethesda, Md), the coordinating center (Kaiser Permanente Center for Health Research in Portland, Ore), and 4 clinical centers (Johns Hopkins University, Baltimore, Md; Pennington Biomedical Research Center, Baton Rouge, La; Duke University Medical Center, Durham, NC; and Kaiser Permanente Center for Health Research, Portland, Ore). Institutional review boards at each center and an external protocol review committee approved the protocol. Each participant provided written consent.

Study Participants

The target population consisted of generally healthy adults with above optimal BP including individuals with stage 1 hypertension who met Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) criteria for at least a 6-month trial of nonpharmacological therapy.⁷ Persons were eligible if they were not taking antihypertensive medication and had a systolic BP of 120 to 159 mm Hg

and diastolic BP of 80 to 95 mm Hg, based on the mean BP across 3 screening visits. Nonhypertensive individuals with above optimal BP (120-139 mm Hg systolic and/or 80-89 mm Hg diastolic) were included because of the potential for preventing hypertension and the excess CVD risk associated with BP in this range.⁴ Individuals with stage 1 hypertension (140-159 mm Hg systolic and/or 90-95 mm Hg diastolic) were included because of the potential for nonpharmacological control of hypertension.

Other inclusion criteria were 25 years of age or older and body mass index (BMI) of 18.5 to 45.0 (measured as weight in kilograms divided by the height in meters squared). Major exclusion criteria were regular use of drugs that affect BP, JNC-VI risk category C (target organ damage and/or diabetes), use of weight-loss medications, prior cardiovascular event, congestive heart failure, angina, cancer diagnosis or treatment in past 2 years, consumption of more than 21 alcoholic drinks per week, and pregnancy, planned pregnancy, or lactation. Although individuals with diabetes were excluded, persons with other cardiovascular risk factors (ie, cigarette smoking and dyslipidemia) could enroll. Vitamin and mineral supplement use was not an exclusion.

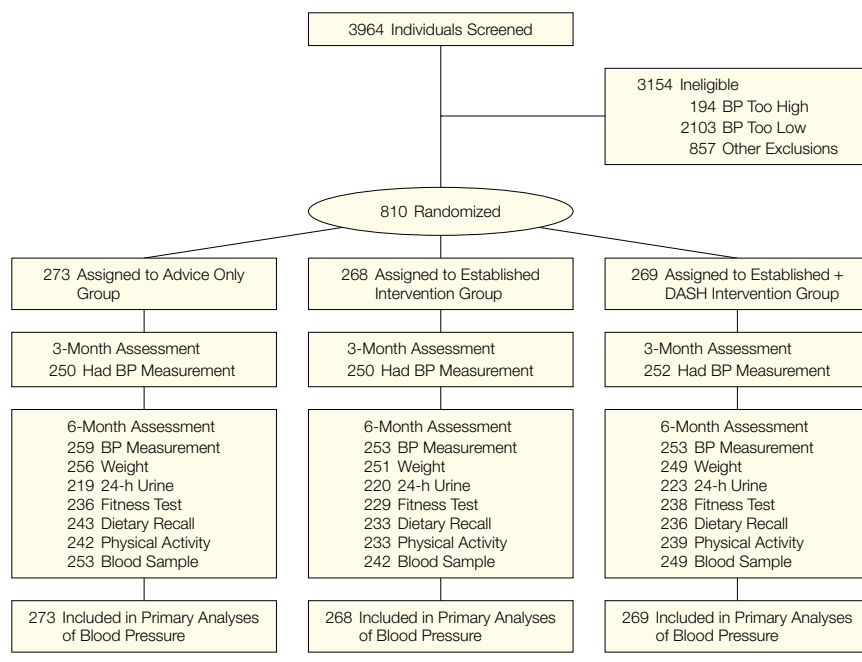
Trial Conduct

Participants were recruited using mass mailings, community-based screening, and mass-media announcements. Enrollment began in January 2000 and ended in June 2001. For logistical purposes, participants were enrolled in 3 or 4 cohorts at each center. Baseline data were collected during 3 screening visits and a randomization visit, each scheduled at least 7 days apart. Follow-up data were collected at 1 visit 3 months after randomization and at 3 visits 6 months after randomization. Participant flow during the trial is shown in FIGURE 1.

Randomization

Randomization assignments were made centrally by a computer program. Clini-

Figure 1. Participant Flow in the PREMIER Clinical Trial



BP indicates blood pressure; DASH, Dietary Approaches to Stop Hypertension.

cal center staff then notified participants of their assigned group. Assignments were stratified by clinic and hypertension status; the randomization block size was 24. Eligible participants were randomly assigned to 1 of 3 groups: (1) an "advice only" comparison group; (2) a behavioral intervention, termed "established" that implemented traditional lifestyle recommendations,¹¹ ie, weight loss among those who were overweight, reduced sodium intake, increased physical activity, and limited alcohol intake among those who drank alcohol; or (3) a behavioral intervention, termed "established plus DASH" that implemented the same traditional recommendations plus the DASH diet.⁷

Advice Only Group

An interventionist, typically a registered dietitian, discussed nonpharmacological factors that affect BP (weight, sodium intake, physical activity, and the DASH diet) and provided printed educational materials. This advice was provided in a single 30-minute individual session immediately following randomization. Counseling on behavior change was not provided. No further contact with the interventionist occurred until after completion of the data collection visits at 6 months.

Behavioral Interventions

Participant goals for both the established and established plus DASH interventions were as follows: (1) weight loss of at least 15 lb (6.8 kg) at 6 months for those with a BMI of at least 25, (2) at least 180 min/wk of moderate-intensity physical activity, (3) daily intake of no more than 100 mEq of dietary sodium, and (4) daily intake of 1 oz or less of alcohol (2 drinks) for men and ½ oz of alcohol (1 drink) for women.

The established and the established plus DASH interventions differed from each other with respect to certain dietary goals and the strategies to achieve weight loss. Only the participants in the established plus DASH intervention received instruction and counseling on

the DASH diet. In this intervention, participant goals designed to accomplish the DASH diet were increased consumption of fruits and vegetables (9-12 servings/d) and low-fat dairy products (2-3 servings/d), and reduced intake of saturated fat ($\leq 7\%$ of energy) and total fat ($\leq 25\%$ of energy). The established intervention did not have goals for fruit, vegetable, or dairy intake; the goal for saturated fat was 10% of energy or less, and the goal for total fat was 30% of energy or less. To achieve weight loss, both interventions emphasized increased physical activity and reduced total energy intake; in addition to these strategies, the established plus DASH intervention also emphasized substitution of fruits and vegetables for high-fat, high-calorie foods.

The format and contact pattern of the established and established plus DASH interventions were identical. During the initial 6 months, there were 18 face-to-face intervention contacts (14 group meetings and 4 individual counseling sessions). Participants in both interventions kept food diaries, recorded physical activity, and monitored calorie and sodium intake. Participants in the established plus DASH group also monitored intake of fruits, vegetables, and dairy products and monitored their intake of fat.

Measurements

Staff who were masked to randomization assignment collected measurements. Blood pressure measurements were obtained by trained, certified individuals who used a random zero sphygmomanometer. The BP measurement protocol was similar to protocols used in prior studies.^{12,13} After the participant sat quietly for 5 minutes, the observer measured BP in the right arm with an appropriately sized cuff. At each visit, 2 BP measurements separated by at least 30 seconds were obtained. Systolic BP was the appearance of the first Korotkoff sound, and diastolic BP was the disappearance of Korotkoff sounds. At each assessment point, BP was the mean of all available measurements (baseline [8 BP measurements across 4 visits], 3-month

assessment [2 BP measurements at 1 visit], and 6-month assessment [6 BP measurements across 3 visits]).

Weight was measured using a calibrated scale, and height was measured using a wall-mounted stadiometer. Other data included the Rose Angina questionnaire¹⁴; a medication questionnaire; a symptoms/adverse effects questionnaire; 24-hour urine collections for sodium, potassium, phosphorus, and urea nitrogen; submaximal treadmill tests; waist circumference; 24-hour dietary recalls; fasting blood analysis; and 7-day physical activity recalls. Each of these measurements was obtained at baseline and 6 months after randomization.

Intake of nutrients and food groups was assessed from unannounced 24-hour dietary recalls conducted by telephone interviewers.¹⁵ Two recalls (one obtained on a weekday and the other on a weekend day) were obtained at baseline and 6 months by the Diet Assessment Center of Pennsylvania State University. Nutrient and food group intakes were then calculated using the Nutrition Data System Version NDS-R 1998 (University of Minnesota). Biomarkers of dietary intake were 24-hour urinary excretion of sodium, potassium (reflecting fruit and vegetable intake), phosphorus (reflecting dairy intake), and urea nitrogen (reflecting protein intake). Alcohol intake was obtained from questionnaire.

Cardiorespiratory fitness was assessed using a submaximal treadmill exercise test developed for the PREMIER trial. This 2-stage, 10-minute protocol was designed to achieve an age- and sex-specific effort of moderate intensity.¹⁶ The first stage achieved a light-intensity effort (approximately 40% estimated maximal metabolic equivalents [METs]), followed by a second stage of moderate intensity (approximately 60% estimated maximal METs). The main fitness outcome was heart rate at the end of stage 2 or the last available heart rate from stage 1 for participants who did not complete stage 2. A 7-day physical activity recall was used to assess physical activity.¹⁷ Participants who reported 35 kcal/kg or less

daily of physical activity were classified as sedentary.¹⁸

Specific Aims and Outcomes

The specific aims of the trial were to test the effects of the established intervention compared with the advice only intervention; the effects of the established plus DASH intervention compared with the advice only intervention; and the effects of the established plus DASH intervention compared with the established intervention. The primary outcome was change in systolic BP from baseline to 6 months. Hypertension status and change in diastolic BP at 6 months were secondary outcomes. Blood pressure measurements were censored if the participant reported taking any antihypertensive medication or other medications known to have major BP effects (eg, oral steroids). Hypertension was defined as a mean BP of 140/90 mm Hg or higher or use of antihypertensive medication.

Although the intervention programs lasted 18 months, the protocol-specified, primary outcome assessment occurred at 6 months because national guidelines recommend that individuals with persistent BP of 140/90 mm Hg or higher after a period of lifestyle modification be referred for medication treatment.⁷ During the design of the trial, we anticipated that approximately 30% of participants would have stage 1 hypertension at baseline.¹⁰ Hence, we expected that a large number of individuals would need to be referred for medication treatment at 6 months, requiring censoring of their BP data, and that medication treatment would occur differentially across the 3 randomized groups. Defining the primary outcome at 6 months reduced the risk of bias and ensured that we would have a maximum number of BP measurements for analysis.

Data Analysis

Blood pressure data were analyzed using a linear regression model in which change in BP (mean 6-month value – mean baseline) was regressed on indicators of the 2 behavioral interven-

tions, indicators of clinical center and cohort, and baseline BP. In prespecified subgroup analyses (hypertensive and nonhypertensive), the models also included a main effect for the subgroup indicator and interactions between this indicator and the 2 treatment group indicators. The effects of the interventions did not differ by clinical center ($P = .62$ for center \times treatment interaction for systolic BP and $P = .54$ for diastolic BP).

Primary analyses of BP change are based on intention to treat. For individuals without BP at the 6-month assessment and for those who had been taking antihypertensive medication, 3-month BP measurements were carried forward; if a 3-month BP measurement was unavailable, values were imputed using a “hot deck” procedure that drew values from participants in the advice only group.¹⁹ We also conducted post-hoc “on treatment” analyses limited to those participants in the established and established plus DASH groups who attended at least 15 intervention sessions.

For all other variables, including hypertension status, we used available data and did not impute values for missing data. To analyze continuous indicators of intervention effects, such as change in body weight, we used a similar analytic model. We used the Mantel-Haenszel χ^2 test for 2×2 tables to compare the proportion of individuals meeting intervention targets at 6 months.²⁰ Because the focus of these analyses was the proportion actually meeting target at 6 months in each group and not necessarily the change from baseline status, these analyses did not condition on initial status.

Hypertension status at 6 months was assessed separately for those who were and were not hypertensive at baseline, reflecting persistent and incident hypertension, respectively. We also compared the prevalence of hypertension in all participants. Pairwise differences in the incidence, persistence, and overall prevalence of hypertension between treatment groups were also assessed using the Mantel-Haenszel test.²⁰

Based on a planned sample size of 800 (267 per group), the study had 90% power to detect pairwise between-group differences in systolic BP of 1.6 to 1.8 mm Hg in the whole sample, 3.2 to 3.6 mm Hg among hypertensive participants (assuming that 30% of the individuals in the sample were hypertensive), and 1.7 to 1.9 mm Hg among nonhypertensive participants.

All analyses were performed using SAS version 8 (SAS Institute Inc, Cary, NC). Nominal P values are presented. For a given outcome, we only considered the pairwise contrasts vs the advice only intervention to be significantly different if at least one of them achieved a P value of $< .025$; in that case, the other contrast with advice only and the contrast between the established and established plus DASH interventions were evaluated at the .05 level.²¹

RESULTS

A total of 810 participants were enrolled in the trial (Figure 1). Baseline characteristics were similar in the randomized groups (TABLE 1). The mean (SD) age was 50.0 (8.9) years, 62% were women, and 34% were African Americans. Of the 279 African Americans, 74% were women. The participants were generally overweight and sedentary. Mean (SD) systolic and diastolic BP were 134.9 (9.6) and 84.8 (4.2) mm Hg. Among the 38% of participants with hypertension, mean (SD) systolic and diastolic BP were 143.9 (7.6) and 87.5 (4.3) mm Hg; corresponding BP measurements in the nonhypertensive participants were 129.5 (5.8) and 83.2 (3.1) mm Hg. Six months after randomization, 94% of participants had their BP measured at 1 or more visits; 87% attended all 3 visits.

Intervention Attendance and Effects

Of the 18 intervention sessions offered during the initial 6 months, 70% of participants in the established group attended at least 15 sessions; just 8% attended 5 sessions or less. In the established plus DASH group, corresponding data were 78% and 7%. Mean

(SD) attendance was 14.5 (4.5) and 15.4 (4.4) sessions, respectively.

Differences in weight, physical fitness, and diet among the randomized groups were achieved. TABLE 2 displays intervention outcomes, and TABLE 3 lists the number of individuals who reached the intervention goals. Weight loss occurred in each group, including the advice only group. While changes in physical activity did not differ among the groups, fitness significantly improved in both behavioral interventions. Alcohol intake was low and did not change in any group.

Mean reductions in urinary sodium excretion occurred in both behavioral interventions, but only the reduction in the established group differed significantly from that of advice only group. However, in both behavioral intervention groups, the percentage of individuals who achieved the trial goal of less than 100 mEq/d differed significantly from the advice only group (Table 3). Also, based on 24-hour dietary recall data, both behavioral interventions significantly reduced sodium intake in comparison with the advice only group (data not shown).

In the established plus DASH group, fruit and vegetable intake increased significantly compared with the other 2 groups; parallel changes in urinary potassium excretion occurred. One third of participants in the established plus DASH group, but only 6% of participants in the other 2 groups, consumed the goal of 9 or more servings of fruits and vegetables per day at 6 months. Compared with the advice only and established groups, consumption of dairy products increased significantly in the established plus DASH group as did dietary calcium intake and net urinary phosphorus excretion. The percentage of established plus DASH participants who consumed 2 or more dairy servings was 59%. Saturated and total fat consumption significantly decreased in both intervention groups.

Blood Pressure Effects

Blood pressure declined progressively over time in each group (FIGURE 2).

Table 1. Baseline Characteristics by Randomized Group*

Characteristic	Advice Only (n = 273)	Established (n = 268)	Established + DASH (n = 269)
Age, mean (SD), y	49.5 (8.8)	50.2 (8.6)	50.2 (9.3)
Female	172 (63.0)	174 (64.9)	154 (57.2)
Race or ethnicity			
African American	100 (36.6)	100 (37.3)	79 (29.4)
Non-Hispanic white	167 (61.2)	163 (60.8)	181 (67.3)
All others	6 (2.2)	5 (1.9)	9 (3.3)
BMI, mean (SD)†	32.9 (5.6)	33.0 (5.5)	33.3 (6.3)
Weight classification			
Nonoverweight (BMI, <25)	15 (5.5)	13 (4.9)	16 (6.0)
Overweight (BMI, 25-29.9)	76 (27.8)	80 (29.9)	82 (30.5)
Obese (BMI, ≥30)	182 (66.7)	175 (65.3)	171 (63.6)
Alcohol, mean (SD), drinks/d	0.21 (0.41)	0.24 (0.47)	0.29 (0.52)
Sedentary (kcal/kg/d ≤35)	223 (81.7)	217 (81.0)	224 (83.6)
Annual household income			
<\$30 000	31 (11.4)	26 (9.7)	27 (10.0)
\$30 000-\$60 000	91 (33.3)	83 (31.0)	82 (30.5)
>\$60 000	142 (52.0)	151 (56.3)	148 (55.0)
Unknown (no answer)	9 (3.3)	8 (3.0)	12 (4.5)
Education			
High school or less	21 (7.7)	20 (7.5)	33 (12.3)
Some college	175 (64.1)	157 (58.6)	144 (53.5)
Some graduate school	77 (28.2)	91 (34.0)	92 (34.2)
Current cigarette smokers	14 (5.1)	18 (6.7)	7 (2.6)
Dyslipidemia‡	59 (21.6)	68 (25.4)	64 (23.8)
Blood pressure, mean (SD), mm Hg			
Systolic	134.2 (10.1)	135.5 (9.2)	134.9 (9.4)
Diastolic	84.8 (4.3)	85.0 (4.1)	84.6 (4.0)
Hypertensive	104 (38.1)	100 (37.3)	100 (37.2)

Abbreviations: BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension.

*Data are presented as No. (%) unless otherwise indicated.

†Body mass index is calculated as weight in kilograms divided by the square of the height in meters.

‡Total cholesterol ≥240 mg/dL (6.21 mmol/L) and/or use of lipid-lowering medication.

From baseline to 6 months, mean (SD) reductions in systolic BP were 6.6 (9.2) mm Hg in the advice only group, 10.5 (10.1) mm Hg in the established group, and 11.1 (9.9) mm Hg in the established plus DASH diet group. Corresponding diastolic BP reductions were 3.8 (6.3), 5.5 (6.7), and 6.4 (6.8) mm Hg, respectively. In hypertensive participants, mean (SD) reductions in systolic BP were 7.8 (10.3), 12.5 (11.5), and 14.2 (10.1) mm Hg, and mean (SD) reductions in diastolic BP were 3.8 (7.1), 5.8 (7.0), and 7.4 (7.1) mm Hg, respectively. In nonhypertensive participants, mean (SD) reductions in systolic BP were 5.8 (8.4), 9.4 (9.1), and 9.2 (9.3) mm Hg, and mean (SD) reductions in diastolic BP were 3.8 (5.8), 5.3 (6.5), and 5.8 (6.6) mm Hg, respectively.

TABLE 4 displays pairwise differences in BP. In all participants, nonhypertensive participants, and hypertensive participants, the established and established plus DASH interventions significantly reduced systolic and diastolic BP in comparison with the advice only group. Although BP change in the established plus DASH group was consistently greater than corresponding BP change in the established group, none of the pairwise differences was statistically significant.

The pattern of results was similar in the "on treatment" analyses, which included those individuals in the established and established plus DASH groups (70% and 78% of participants, respectively) who attended more than 15 intervention sessions. For contrasts with the advice only group, BP

Table 2. Intervention Outcomes at Baseline and at 6 Months by Randomized Group

Intervention Outcome	Mean (SD)			P Value*		
	Advice Only	Established	Established + DASH	Established vs Advice Only	Established + DASH vs Advice Only	Established + DASH vs Established
Weight, kg†	n = 242	n = 238	n = 233			
Baseline	95.8 (17.0)	96.2 (17.8)	98.8 (19.3)			
6 Months	94.7 (17.2)	91.3 (18.2)	93.0 (19.0)			
Change	-1.1 (3.2)	-4.9 (5.5)	-5.8 (5.8)	<.001	<.001	.07
Physical activity (estimated energy expenditure, kcal/kg/d)	n = 239	n = 229	n = 233			
Baseline	33.7 (2.6)	33.8 (2.6)	33.8 (3.5)			
6 Months	34.0 (2.4)	34.2 (2.2)	34.4 (3.2)			
Change	0.3 (2.9)	.4 (2.9)	0.6 (2.4)	.66	.10	.23
Fitness (heart rate at stage 2 of exercise test, beats/min)	n = 235	n = 226	n = 232			
Baseline	130.3 (14.7)	130.6 (14.2)	130.1 (14.6)			
6 Months	125.0 (15.6)	122.6 (15.7)	121.1 (15.8)			
Change	-5.3 (9.7)	-8.0 (11.1)	-9.0 (10.7)	.005	<.001	.28
Alcohol intake, drinks/d	n = 228	n = 226	n = 229			
Baseline	0.2 (0.4)	0.2 (0.5)	0.3 (0.5)			
6 Months	0.2 (0.4)	0.2 (0.4)	0.3 (0.5)			
Change	0.0 (0.3)	0.0 (0.3)	0.0 (0.4)	.53	.87	.42
Urine collections	n = 215	n = 212	n = 211			
Sodium, mEq/24 h						
Baseline	173.3 (66.7)	167.8 (70.0)	178.2 (78.9)			
6 Months	152.8 (66.3)	136.2 (64.6)	145.6 (71.6)			
Change	-20.6 (71.6)	-31.6 (74.7)	-32.6 (78.1)	.01	.12	.36
Potassium, mEq/24 h						
Baseline	66.4 (28.7)	66.6 (23.8)	67.9 (26.1)			
6 Months	65.1 (27.5)	67.5 (24.9)	87.3 (36.0)			
Change	-1.3 (28.7)	0.9 (22.3)	19.3 (32.1)	.35	<.001	<.001
Urea nitrogen, mg/24 h						
Baseline	11 325.6 (4237.8)	11 415.1 (3819.1)	11 933.6 (3987.5)			
6 Months	10 651.2 (3805.3)	11 042.5 (3632.8)	12 085.3 (3991.9)			
Change	-674.4 (4246.6)	-372.6 (3457.0)	151.7 (3507.2)	.28	<.001	.01
Phosphorus, mg/24 h						
Baseline	919.4 (433.0)	903.8 (333.5)	976.4 (368.4)			
6 Months	827.3 (341.3)	833.3 (331.0)	978.8 (372.7)			
Change	-92.1 (441.0)	-70.4 (333.2)	2.4 (350.4)	.75	<.001	<.001
Dietary recalls	n = 232	n = 227	n = 230			
Fruits and vegetables, servings/d						
Baseline	4.4 (2.3)	4.6 (2.4)	4.8 (2.5)			
6 Months	4.9 (2.7)	5.1 (2.5)	7.8 (3.2)			
Change	0.5 (2.8)	0.5 (2.6)	3.0 (3.6)	.79	<.001	<.001
Dairy, servings/d						
Baseline	1.6 (1.2)	1.7 (1.3)	1.8 (1.3)			
6 Months	1.7 (1.4)	1.5 (1.1)	2.3 (1.2)			
Change	0.1 (1.6)	-0.2 (1.5)	0.5 (1.6)	.02	<.001	<.001
Dietary calcium, mg/24 h‡						
Baseline	732.3 (350.2)	728.8 (336.5)	763.0 (365.7)			
6 Months	699.2 (402.4)	683.9 (350.7)	940.2 (403.5)			
Change	-33.1 (418.1)	-44.9 (327.6)	177.2 (439.7)	.55	<.001	<.001
Total fat, % kcal						
Baseline	32.9 (7.1)	33.4 (8.0)	33.3 (7.8)			
6 Months	31.9 (7.6)	29.4 (8.4)	23.8 (8.6)			
Change	-1.0 (7.9)	-3.9 (9.8)	-9.5 (9.5)	<.001	<.001	<.001
Saturated fat, % kcal						
Baseline	11.0 (3.3)	10.8 (3.2)	11.0 (3.1)			
6 Months	10.6 (3.5)	9.4 (3.5)	7.7 (3.2)			
Change	-0.4 (3.9)	-1.5 (4.0)	-3.3 (3.9)	<.001	<.001	<.001

Abbreviation: DASH, Dietary Approaches to Stop Hypertension.

*Corresponding to pairwise differences in change.

†Among overweight or obese participants (body mass index ≥ 25).

‡Not including supplemental calcium.

reductions in the on treatment analyses were approximately 20% to 40% greater than corresponding reductions in the intention to treat analyses.

FIGURE 3 displays the percentage of nonhypertensive participants who became hypertensive, the percentage of hypertensive participants who remained hypertensive, and the percentage of all participants who were hypertensive at 6 months. In each instance, there was a gradient in hypertensive status across the 3 groups. The lowest

prevalence of hypertension (12%) occurred in the established plus DASH group; this prevalence corresponds to a 53% risk reduction (ie, 1 – relative risk) compared with the advice only group. By 6 months, antihypertensive medication had been started in 19 participants in the advice only group, 2 participants in the established group, and 5 participants in the established plus DASH group. The established and established plus DASH groups significantly increased the percentage of

individuals who achieved an optimal BP (<120 mm Hg systolic and <80 mm Hg diastolic; FIGURE 4).

Other Effects

A serious musculoskeletal injury occurred in 20 participants in the advice only group, 17 in the established group, and 16 in the established plus DASH group. One stroke, 1 transient ischemic attack, and 1 myocardial infarction occurred in the advice only group. No cardiovascular event occurred in the

Table 3. Participants Meeting Intervention Goals at Baseline and at 6 Months by Randomized Group

Intervention Goal	No./Total (%)			P Value*		
	Advice Only	Established	Established + DASH	Established vs Advice Only	Established + DASH vs Advice Only	Established + DASH vs Established
Weight loss >15 lb (6.8 kg)† 6 Months	15/242 (6.2)	68/238 (28.6)	80/233 (34.3)	<.001	<.001	.18
Urinary sodium ≤100 mmol/d						
Baseline	25/215 (11.6)	38/212 (17.9)	32/211 (15.2)			
6 Months	42/215 (19.5)	80/212 (37.7)	59/211 (28.0)			
Change	17 (7.9)	42 (19.8)	27 (12.8)	<.001	.04	.03
Alcoholic drinks, ≤2 drinks/d (men), ≤1 drink/d (women)						
Baseline	225/228 (98.7)	218/226 (96.5)	221/229 (96.5)			
6 Months	223/228 (97.8)	221/226 (97.8)	224/229 (97.8)			
Change	2 (–0.9)	3 (1.3)	3 (1.3)	.99	.99	.98
Fruits and vegetables, ≥9 servings/d						
Baseline	7/232 (3.0)	11/227 (4.9)	16/230 (7.0)			
6 Months	15/232 (6.5)	14/227 (6.2)	78/230 (33.9)			
Change	8 (3.5)	3 (1.3)	62 (26.9)	.90	<.001	<.001
Dairy products, ≥2 servings/d						
Baseline	72/232 (31.0)	72/227 (31.7)	83/230 (36.1)			
6 Months	78/232 (33.6)	64/227 (28.2)	136/230 (59.1)			
Change	6 (2.6)	8 (–3.5)	53 (23.0)	.21	<.001	<.001
Fat ≤30% kcal/d‡						
Baseline	83/232 (35.8)	74/227 (32.6)	75/230 (32.6)			
6 Months	87/232 (37.5)	123/227 (54.2)	180/230 (78.3)			
Change	4 (1.7)	49 (21.6)	105 (45.7)	<.001	<.001	<.001
Fat ≤25% kcal/d§						
Baseline	33/232 (14.2)	33/227 (14.5)	38/230 (16.5)			
6 Months	41/232 (17.7)	66/227 (29.1)	135/230 (58.7)			
Change	8 (3.5)	33 (14.6)	97 (42.2)	.004	<.001	<.001
Saturated fat ≤10% kcal/d‡						
Baseline	92/232 (39.7)	95/227 (41.9)	94/230 (40.9)			
6 Months	103/232 (44.4)	139/227 (61.2)	182/230 (79.1)			
Change	11 (4.7)	44 (19.3)	88 (38.2)	<.001	<.001	<.001
Saturated fat ≤7% kcal/d§						
Baseline	27/232 (11.6)	29/227 (12.8)	22/230 (9.6)			
6 Months	36/232 (15.5)	60/227 (26.4)	107/230 (46.5)			
Change	9 (3.9)	31 (13.6)	85 (36.9)	.004	<.001	<.001

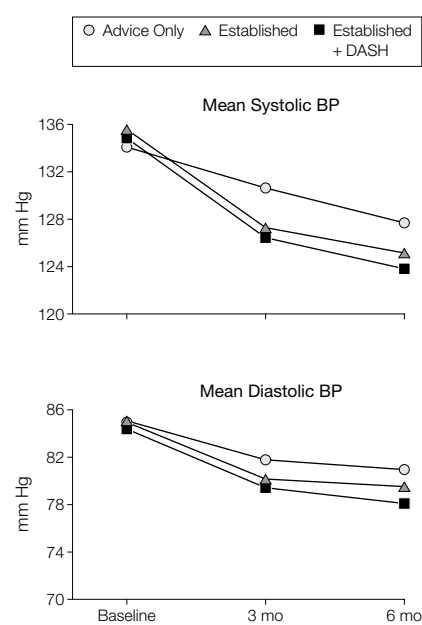
Abbreviation: DASH, Dietary Approaches to Stop Hypertension.

*Corresponding to pairwise differences at 6 months from logistic regression analysis.

†Among overweight or obese participants (body mass index ≥25).

‡Dietary fat goals for the established group.

§Dietary fat goals for the established + DASH group.

Figure 2. Mean Systolic and Diastolic Blood Pressure (BP) Over Time by Randomized Group

DASH indicates Dietary Approaches to Stop Hypertension.

established group, and 1 myocardial infarction occurred in the established plus DASH group.

COMMENT

The PREMIER trial documented that individuals with above-optimal BP, including stage 1 hypertension, can make multiple lifestyle changes that lower BP and control hypertension. Both of the PREMIER behavioral interventions accomplished substantial weight loss, reduced sodium intake, and increased physical fitness. Individuals assigned to the established plus DASH intervention also made dietary changes consistent with the DASH diet, ie, increased their intake of fruits, vegetables, and dairy products. In aggregate, these lifestyle changes should substantially lower the risk of CVD as well as the risk of other chronic diseases, including diabetes, osteoporosis, and perhaps cancer.

Trial participants were demographically heterogeneous. More than 50% were women, and more than 30% were African American. The distributions of

educational attainment and household income were broad, but slightly skewed toward persons with higher education and income. The BP inclusion criteria of PREMIER would include approximately 50% of US adults. These aspects of the study suggest that trial results should be applicable to a large portion of the US population.

Markers of adherence, including several objective measurements, confirmed that participants in the behavioral interventions made lifestyle changes. Each behavioral intervention led to substantial weight loss as well as increased fitness. The reduced heart rate on the treadmill test, an objective measure of improved fitness, suggests that participants increased their physical activity, even though self-reported physical activity as measured by 7-day physical activity recalls did not change significantly. Both behavioral interventions significantly reduced sodium intake, although not to the same extent as behavioral interventions that focused exclusively on this factor.^{12,13,22}

Table 4. Mean Between-Group Differences in Blood Pressure (BP) Change in All Participants, Nonhypertensive Participants, and Hypertensive Participants

	Change in Established Minus Change in Advice Only*		Change in Established + DASH Minus Change in Advice Only		Change in Established + DASH Minus Change in Established	
	Mean (95% CI)	P Value	Mean (95% CI)	P Value	Mean (95% CI)	P Value
Intention-to-Treat Analyses						
Systolic BP						
All	-3.7 (-5.3 to -2.1)	<.001	-4.3 (-5.9 to -2.8)	<.001	-0.6 (-2.2 to 0.9)	.43
Nonhypertensive	-3.1 (-5.1 to -1.1)	.003	-3.1 (-5.1 to -1.1)	.002	0.0 (-2.0 to 2.0)	.97
Hypertensive	-4.6 (-7.2 to -2.1)	<.001	-6.3 (-8.9 to -3.8)	<.001	-1.7 (-4.3 to 0.9)	.20
Diastolic BP						
All	-1.7 (-2.8 to -0.6)	.002	-2.6 (-3.7 to -1.5)	<.001	-0.9 (-2.0 to 0.2)	.11
Nonhypertensive	-1.6 (-2.9 to -0.2)	.027	-2.0 (-3.4 to -0.6)	.005	-0.4 (-1.8 to 0.9)	.53
Hypertensive	-2.0 (-3.8 to -0.3)	.025	-3.6 (-5.4 to -1.9)	<.001	-1.6 (-3.4 to 0.2)	.08
On Treatment Analyses†						
Systolic BP						
All	-4.9 (-6.6 to -3.3)	<.001	-5.7 (-7.2 to -4.1)	<.001	-0.7 (-2.5 to 1.0)	.41
Nonhypertensive	-4.3 (-6.4 to -2.2)	<.001	-4.7 (-6.7 to -2.7)	<.001	-0.4 (-2.6 to 1.8)	.69
Hypertensive	-5.9 (-8.5 to -3.2)	<.001	-7.1 (-9.7 to -4.5)	<.001	-1.3 (-4.1 to 1.6)	.38
Diastolic BP						
All	-2.5 (-3.7 to -1.3)	<.001	-3.2 (-4.3 to -2.0)	<.001	-0.7 (-1.9 to 0.6)	.29
Nonhypertensive	-2.2 (-3.7 to -0.7)	.003	-2.5 (-3.9 to -1.1)	.001	-0.3 (-1.8 to 1.3)	.72
Hypertensive	-3.0 (-4.9 to -1.1)	.002	-4.2 (-6.1 to -2.4)	<.001	-1.3 (-3.3 to 0.7)	.22

Abbreviation: DASH, Dietary Approaches to Stop Hypertension.

*Change is 6-month BP minus baseline BP.

†Analyses include all advice only participants (n = 273) and those persons in the established group (n = 188, 71% of randomized participants) and established + DASH group (n = 210, 78% of randomized participants) who completed 15 or more of the 18 possible intervention sessions.

The established plus DASH intervention also increased consumption of fruits, vegetables, and dairy products; analyses of urinary potassium and phosphorus were consistent with data from the 24-hour dietary recalls.

Across the 3 groups, gradients in BP and hypertensive status were evident. The smallest BP reduction occurred in the advice only group, while the greatest BP reduction occurred in the established plus DASH group. Hypertension control was most successful in the established plus DASH group, in which 77% of individuals with stage 1 hypertension at baseline had a systolic BP of less than 140 mm Hg and a diastolic BP of less than 90 mm Hg at 6 months. In the established group, the corresponding figure was 66%. These rates compare favorably with survey data² and trial data,²³ in which drug therapy controls BP in approximately half of hypertensive individuals. Hence, these behavioral interventions should be viable treatment options, at least among those hypertensive individuals who are motivated to make lifestyle changes.

The established and established plus DASH interventions also reduced BP in nonhypertensive individuals with above-optimal BP. Specifically, an optimal BP level (<120 mm Hg systolic and <80 mm Hg diastolic) was achieved in 40% and 48% of participants assigned to these 2 interventions, respectively. Overall, this pattern of findings suggests that even in the context of other effective lifestyle modifications, adoption of the DASH diet further improves BP control.

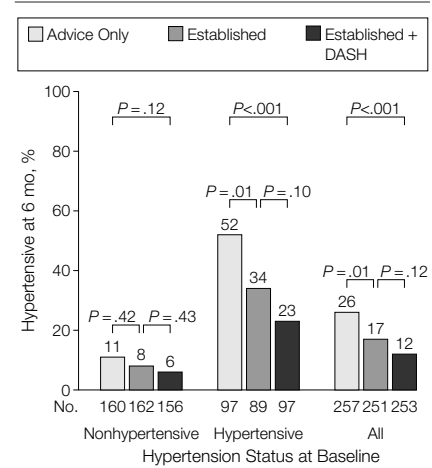
Still, the BP effects attributed to the DASH diet, specifically the BP differences between the established plus DASH and the established interventions, were less than previously found in the DASH feeding studies,^{8,24} and none of the contrasts in hypertension status was statistically significant. One potential reason is that participants received an inadequate "dose" of the DASH diet. For instance, even though mean fruit and vegetable intake increased from 4.8 to 7.8 servings per day in the established plus DASH interven-

tion, the latter is below what was provided in the DASH feeding studies, namely, 9.6 servings per day.

Another plausible reason is subadditivity of intervention effects. Specifically, the net BP effect of the DASH diet in the PREMIER trial likely underestimates the BP effects of the DASH diet if it were implemented alone.^{8,25} It has been well documented that the combined effect of an intervention that implements 2 or more BP-reducing components is less than the sum of BP reductions from interventions that implement each component alone. Subadditivity can occur from reduced adherence¹³ because of the effort and complexity of making more than 1 lifestyle change. For example, participants in the established plus DASH intervention were advised to increase their intake of dairy products while reducing total caloric intake. Still, even in the setting of high adherence, such as feeding studies, subadditivity occurs.²⁴

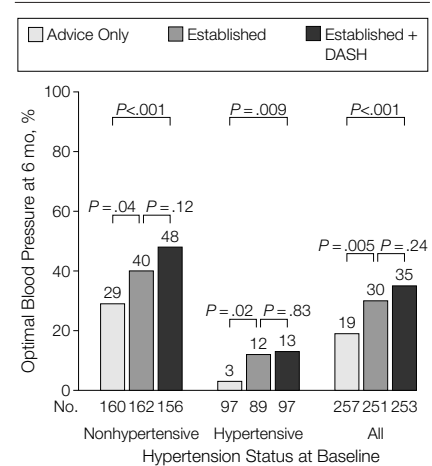
The advice only comparison group in the PREMIER trial likely accomplished some lifestyle modifications. Such behavior changes might have resulted from recruitment of motivated participants; secular trends (eg, growing awareness of the obesity epidemic); the 30-minute intervention session postrandomization; and the multiple, regular data collection visits and contacts (4 visits and 2 dietary recalls at baseline; 1 visit at 3 months and 3 visits at 6 months, along with telephone calls and reminders). Although before-after changes must be interpreted cautiously, the weight loss of 1.1 kg at 6 months in this group exceeded what has occurred in other trials, which have often reported weight gain in the control group.¹³ Also, the 20-mEq reduction in sodium excretion may reflect efforts to lower salt intake. Such modest changes in behavior might have reduced BP in this group, thereby attenuating the pairwise differences in BP between the advice only group and the 2 behavioral interventions. In fact, the within-group BP reductions observed in the advice only group (systolic BP reduction of 6.6 mm Hg and diastolic BP

Figure 3. Percentage of Participants With Hypertension at 6 Months by Randomized Group Among Nonhypertensive, Hypertensive, and All Participants at Baseline



DASH indicates Dietary Approaches to Stop Hypertension.

Figure 4. Percentage of Participants With Optimal Blood Pressure at 6 Months by Randomized Group Among Nonhypertensive Participants at Baseline, Hypertensive Participants at Baseline, and All Participants



DASH indicates Dietary Approaches to Stop Hypertension.

reduction of 3.8 mm Hg) greatly exceed what was observed in the control groups of other studies.^{8,12,13,22}

In the PREMIER trial, the primary outcome variables were collected at 6 months postrandomization. The inclusion of hypertensive individuals in the PREMIER trial precluded use of BP

measured at a later follow-up visit as the primary outcome because national guidelines recommend initiation of drug therapy for individuals with Class B hypertension who remain hypertensive after a 6-month period of nondrug therapy.⁷ Still, evidence from clinical trials suggests that as long as adherence is sustained, BP effects persist.^{26,27} Also, in longitudinal observational studies, healthy dietary patterns indicative of long-term habits are associated with reduced CVD^{28,29} and mortality.³⁰

In addition to hypertension, high-normal BP is also associated with excess CVD risk.⁴ Of the general population, about 34% have BP in the nonhypertensive yet above optimal BP range and another 14% have stage 1 hypertension.² Furthermore, the majority of BP-related events occur in the range of BP studied in the PREMIER trial.⁵ In this setting, it is reasonable to speculate that widespread implementation of the PREMIER behavioral interventions, particularly the established plus DASH intervention, should decrease CVD risk through reduced BP in nonhypertensive individuals and increased BP control in hypertensive individuals.

Yet most health care insurers do not cover behavioral interventions for the prevention and treatment of hypertension.³¹ Given the substantial health benefits of these programs in improving BP control, preventing diabetes,^{32,33} and controlling dyslipidemia,³⁴ it is time to consider how such programs might be implemented, particularly for those patients at elevated CVD risk. The costs of such programs should be balanced against the benefits of preventing hypertension, diabetes, heart disease, and other conditions, thereby preventing the need for medical treatments that may be costly.

In summary, our trial results demonstrate the feasibility of comprehensive behavioral interventions and their beneficial effects on BP and hypertension control. Benefits extend to both nonhypertensive individuals at risk for

tensive individuals who are not receiving medication therapy. Although we did not study individuals receiving drug therapy, available data indicate that nonpharmacological interventions also reduce BP in these individuals.^{35,36} Ultimately, population-wide adoption of healthy lifestyles as promoted in the PREMIER interventions should substantially reduce the societal burden of CVD and other chronic diseases.

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If I had a device, it would be the True, the True only, leaving the Beautiful and the Good to settle matters afterwards as best they could.

—Charles Augustin Sainte-Beuve (1804-1869)