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Nutritional Treatment of Blood Pressure: Major Nonpharmacologic Trials of Prevention or Treatment of Hypertension

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Major Nonpharmacologic Trials of Prevention or Treatment of Hypertension

Primary Prevention Trials

Primary Prevention of Hypertension (PPH) Trial

The purpose of PPH was to determine whether intense lifestyle modifications would reduce the incidence of hypertension and lower blood pressure in the intervention versus the monitored (control) group.[1] "Hypertension-prone" individuals between the ages of 30 to 44 years were screened. Diastolic blood pressure < 90 mmHg was required for enrollment. Greater than 50% above desirable weight, excess alcohol use, diabetes mellitus, and major cardiovascular diseases precluded participation in the trial. Diastolic blood pressure ≥90 mmHg or initiation of antihypertensive drug therapy was the primary endpoint. Interventions by nutrition counselors and physicians included either:

The greater of a 4.5 kg decrease or 5% weight loss in overweight subjects

Decreased sodium intake to ≤1800 mg (4.5g NaCl)

Reduced alcohol intake (≤26g)

Increased physical activity (30 minutes for 3 days per week)

The group that did not receive the intervention was monitored. Baseline characteristics are shown in Table 48.1. The incidence of hypertension was 8.8% of 102 intervention and 19.2% of monitored subjects (p = 0.027) over 5 years. The odds ratio for hypertension development in the control group was 2.4 (90% CI 1.2-4.8, p <0.027).

TABLE 48.1

Nonpharmacologic Interventions in High Normal Blood Pressure*

Trial	n	Mean Age (Yr)	% Male	% White	Study Duration	Intervention	Initial Blood Pressure	Systolic/ Diastolic Change	Relative Risk of Hypertension*
Primary Prevention of Hypertension[1]	201	38	87	82	5 yr	↓calories & NaCl ↓ethanol ↑physical activity	123/83	-1.3/-1.2	0.46†
Hypertension Prevention Trial[2]	252	38	68	80	3 yr	↓calories	125/83	-2.4/-1.8	0.77
	392	39	62	84	3 yr	↓NaCl	124/83	+0.2/+0.1	0.79
	255	39	62	82	3 yr	↓calories & NaCl	125/83	-1.0/-1.3	0.95
	391	38	63	85	3 yr	↓NaCl & ↑ KCl	124/83	-1.2/-0.7	0.77
Trial of Hypertension Prevention[3] (Phase 1)	564	43	72	79	18 mo	↓calories & ↑physical activity	124/84	-2.9/-2.3	0.49†
	744	43	72	79	18 mo	↓NaCl	125/84	-1.7/-0.9	0.76
	562	43	71	84	18 mo	Manage Stress	125/84	-0.5/-0.8	1.07
	471	43	68	85	6 mo	↑ Calcium	126/84	-0.5/+0.2	0.91
	461	43	68	85	6 mo	↑ Magnesium	125/84	-0.2/-0.1	0.63
	351	43	72	87	6 mo	↑ Potassium	122/81	+0.1/-0.4	0.87
	350	43	70	86	6 mo	↑ Fish Oil	123/81	-0.2/-0.6	1.11
Trial of Hypertension Prevention[4] (Phase 2)	1191	43	66	79	36 mo	↓calories	127/86	-1.3/-0.9	0.81†
	1190	43	67	80	36 mo	↓NaCl	128/86	-1.2/-0.7	0.88
	1193	43	69	79	36 mo	↓calories & NaCl	127/86	-1.1/-0.6	0.84†

* Defined as diastolic blood pressure of ≥90 mmHg or antihypertensive drug therapy during followup.

† $p < 0.05$.

Modified from *Arch Intern Med* 1993;153 January 2 :186-208.[19] Used with permission and Copyright 1993, American Medical Association.

TABLE 48.2

Hypertension Prevention Trial (HPT): Six-Month Change in Interventions

	High BMI				Low BMI		
	Control	Kcalories	Sodium	Sodium/ Calories	Control	Sodium	Sodium/ Potassium
Number of subjects	121	112	109	113	191	173	180
ΔSBP/DBP (mmHg)	-1.8/-2.5	-6.9†/-5.3‡	-3.6/-3.4	-5.8/-4.0	-2.1/-3.0	-3.8/-3.4	-3.4/-3.7
ΔWeight (kg)	+0.18	-5.58†	-0.04	-3.90	+0.27	+0.00*	+0.27
ΔNa+Excretion (mmol/8h)	-4.5	-4.2	-7.8	-8.4	-3.9	-9.4¶	-11.4
ΔK+Excretion (mmol/8h)	0.3	-1.1	0.9	-0.1	-0.1	0.2	1.2

* p = 0.025; † p <0.001; ‡ p <0.01; ¶ p = 0.002.

Derived from Tables 4 and 5 in the report of The Hypertension Prevention Trial, *Arch Intern Med* 150: 153; 1990.

Hypertension Prevention Trial (HPT)

Men and women between the ages of 25 to 49 years with a diastolic blood pressure ≤89 mmHg were randomized.[2] Group and individual dietary counseling was performed. This primary prevention trial allocated subjects (see Table 48.1) on the basis of body mass index (BMI) into several interventions. Low BMI (men <25 kg/m^2 and women <23 kg/m^2 were randomized to either a control group (n = 70), sodium restriction (n = 70) ≤70 mmol/d (≤1610 mg/d) or sodium restriction and potassium augmentation (n = 71) ≥100 mmol/d (3900 mg/d). High BMI individuals were randomized to control (n = 126), caloric restriction (n = 125), sodium restriction (n = 126), sodium and caloric restriction (n = 129), and sodium restriction and potassium augmentation (n = 124).

The mean change in blood pressure for the interventions is displayed for both systolic and diastolic blood pressure at six months in Table 48.2. Caloric restriction reduced blood pressure significantly. Caloric and sodium restriction was a less effective strategy in this cohort. Sodium restriction with or without caloric restriction or potassium supplementation had no effect on blood pressure reduction. After three years, weight reduction was still significant (3.5 kg, p <0.001) and was associated with a significant blood pressure reduction of –2.4/–1.8 mmHg. After three years, the incidence of hypertension was significantly reduced in the low BMI group only (p <0.01), but only marginally so in the high BMI group (p = 0.066) as shown in Figure 48.1.

Trials of Hypertension Prevention (TOHP), Phase I

The TOHP (Phase I) was designed to assess the effect of various nonpharmacologic interventions in nonhypertensive subjects to lower blood pressure, and to determine the long-term impact on preventing the development of hypertension (see Table 48.1).[3] The trial was a multicenter, randomized study that examined three lifestyle interventions — weight reduction (n = 308), sodium restriction (n = 327), and stress management (n = 242) — compared to usual care (n = 589), and various nutritional supplements in two stages with an intervening washout period:

1. 25 mmol or 1g QD of calcium carbonate (n = 237), 15 mmol or 360 mg QD of magnesium diglycine (n = 227), and placebo (n = 234)
2. 6 g of fish oil containing 3g of ω-3 fatty acids (n = 175), 60 mmol or 4.5 g of potassium chloride (n = 178), and placebo (n = 175)

Weight reduction used a combination of caloric reduction, exercise increase, and behavioral self-management. Stress management involved teaching slow breathing, progressive

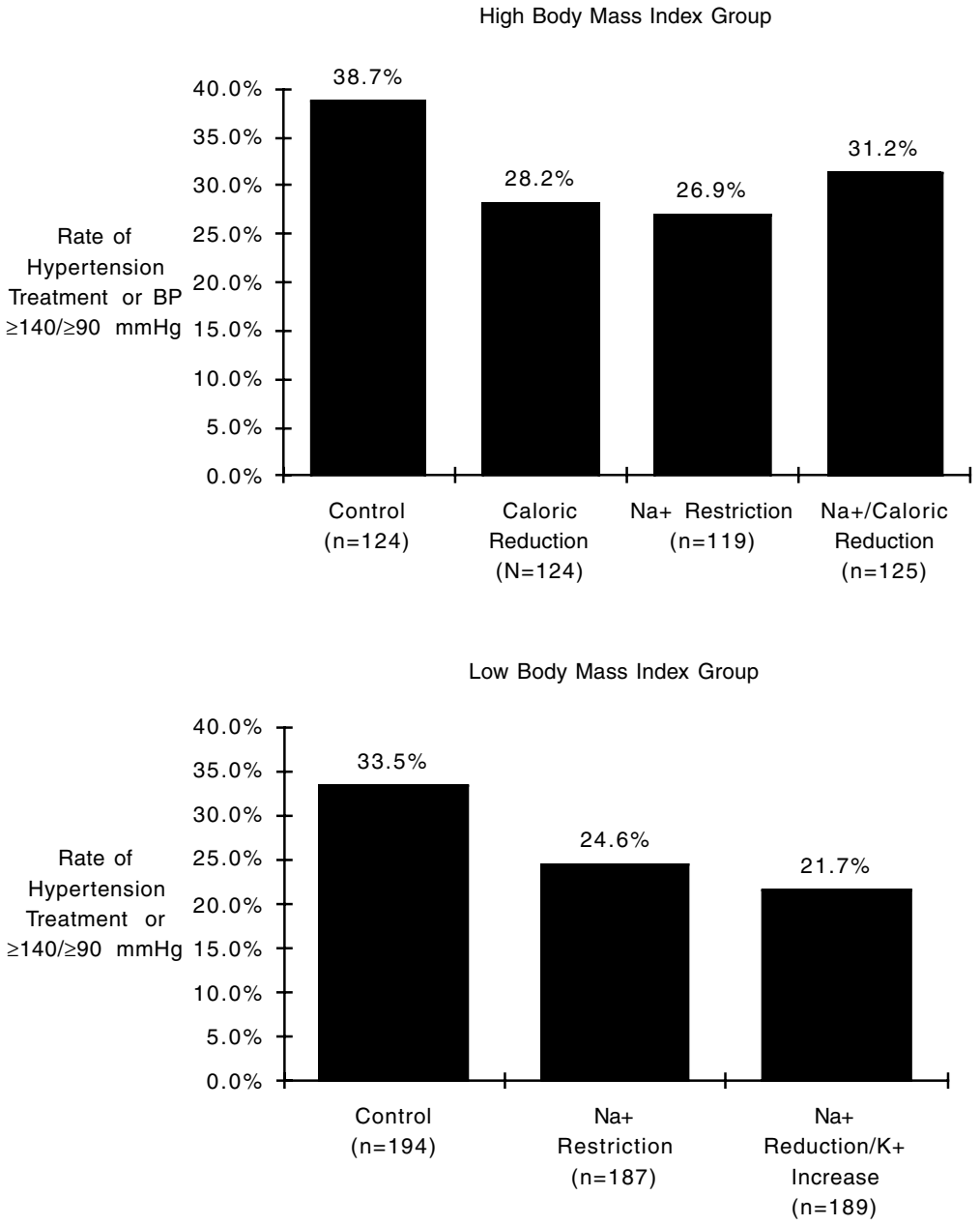

FIGURE 48.1
The Hypertension Prevention Trial: three-year rate of elevated blood pressure or treatment for hypertension, according to BMI and intervention.

muscular relaxation, mental imagery, stretching, and managing stress perceptions, reactions, and situations. The lifestyle modifications lasted 18 months and used blinded measurement of blood pressure as an endpoint. The nutritional supplements were placebo controlled, doubled blinded, and lasted 6 months.

The primary outcomes are displayed in Table 48.3 and Figure 48.2. Only weight reduction significantly lowered blood pressure and reduced the development of hypertension

TABLE 48.3

Intervention Outcome, Treatment Effect, and Blood Pressure Effect (Active – Control) in Trial of Hypertension Prevention, Phase I

Intervention	Outcome Treatment Effect	Blood Pressure Effect
18 Months Maximum Followup		
Sodium excretion (mmol/24h)	-43.86†	-1.69†/-0.85*
Weight change (kg)	-3.90†	-2.90†/-2.28†
Stress score frequency/intensity	+2.35†/-0.01	-0.47/-0.82
6 Months Maximum Followup		
Magnesium excretion (mmol/24h)/serum (mmol/L)	1.31†/+0.04†	-0.20/-0.05
Calcium excretion (mmol/24h)	0.91†	-0.46/+0.20
Potassium excretion (mmol/24h)	42.29†	+0.06/-0.42
% Eicosapentaenoic/Docosahexaenoic fatty acid	2.90†/2.04†	-0.22/-0.62

* $p < 0.05$; † $p < 0.01$.

Derived from Tables 2 and 3 in Trial of Hypertension Prevention, Phase 1, *JAMA* 267: 1213; 1992.

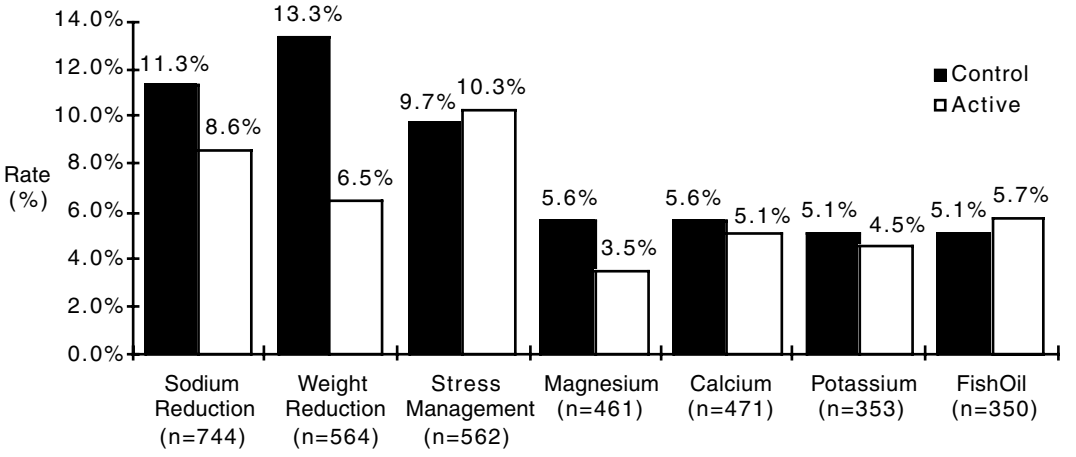

FIGURE 48.2

Trial of Hypertension Prevention, Phase 1. Incidence of hypertension in each lifestyle change and nutritional supplement group. Only weight reduction significantly reduced incidence of hypertension, relative risk = 0.49 (95% CI, 0.29 to 0.83). Derived from corrected table in *JAMA* 1992; 267(17): 2330.

at maximal followup at 18 months. Sodium restriction significantly lowered systolic and diastolic blood pressure, –1.7/–0.9 mmHg, but did not significantly reduce the incidence of hypertension.

The weight loss goal was 4.5 kg for the participants with 115 to 165% of desirable body weight that were enrolled. 45% of men and 26% of women in the intervention group compared with 12% of men and 18% of women in the control group met the weight loss goal at 18 months. The net change in weight at 18 months was 4.7 kg for men and 1.8 kg for women ($p < 0.01$). Rather than being related to gender, the treatment effect was related to the higher baseline weight in males. In fact, the amount of blood pressure change, by gender related more to the quintile of weight change as shown in Table 48.4.

TABLE 48.4

Trial of Hypertension Prevention, Phase 1: Effect of Weight Change on Blood Pressure Reduction at 18 Months by Gender

	Quintile of Weight Change, kg				
	<-9.5	**-9.5 to <-4.5**	**-4.5 to <-2.0**	**-2.0 to <1.0**	**≥1.0**
Δ Systolic Blood Pressure (mmHg)					
Men	-9.0	-6.6	-4.8	-3.3	-1.6
Women	-5.7	-7.5	-5.0	-0.8	-1.2
Δ Diastolic Blood Pressure (mmHg)					
Men	-9.4	-6.8	-5.5	-4.2	-2.6
Women	-9.1	-7.1	-4.3	-4.9	-4.1

Derived from Figures 3, 4, and 5 in Trial of Hypertension Prevention, Phase 1, *JAMA* 267: 1213; 1992.

TABLE 48.5

Baseline Characteristics and Outcomes of Trials of Hypertension Prevention (Phase II)

	Weight Loss	**Sodium Restriction**	**Combined**	**Usual Care**
Number	595	594	597	596
Age, y	43.4	44.2	43.6	43.2
Male, %	63.0	64.8	68.8	68.3
White, %	78.0	81.1	78.4	79.5
Weight, kg	93.4	94.0	93.6	93.6
Baseline sodium excretion, mmol/d	180.9	186.1	179.3	188.0
Baseline blood pressure, mmHg	127.6/86.0	127.7/86.1	127.4/86.0	127.3/85.8
Six Month Followup				
Weight change, kg	-4.4 p <0.001*	-1.1 p <0.001*	-4.1 p <0.006*	0.1
Sodium excretion change, mmol/d	-18.2 p = 0.48*	-78.0 p <0.001*	-64.3 p = 0.006*	-27.6
Change in blood pressure, mmHg	-6.0/-5.5 p <0.001/<0.001†	-5.1/-4.4 p <0.001/<0.001†	-6.2/-5.6 p <0.001/<0.001†	-2.2/-2.8
Incidence of hypertension, %	4.2 p = 0.02*	4.5 p = 0.04*	2.7 p <0.001*	7.3
36 Month Followup				
Weight change, kg	-0.2 p <0.001*	+1.7 p = 0.92*	-0.3 p <0.001*	+1.8
Sodium excretion change, mmol/d	-9.0 p = 0.79*	-50.9 p <0.001*	-34.1 p <0.001*	-10.5
Change in blood pressure, mmHg	-0.8/-3.2 p = 0.01/0.04†	-0.7/-3.0 p = 0.02/0.10†	-0.5/-3.0 p = 0.05/0.19†	+0.6/-2.4
Incidence of hypertension, %	31.9	34.4	32.8	39.2

* significance vs. usual care group

† significance of systolic and diastolic blood pressure vs. usual group

Derived from Tables 1 through 4 from The Trials of Hypertension Prevention (Phase II) Prevention Collaborative Research Group, *Arch Intern Med* 157: 657; 1997.

Trials of Hypertension Prevention (TOHP II), Phase II

The randomized TOHP II was conducted as a two-by-two factorial design study to assess the effect of weight reduction, sodium restriction, or both compared to usual care in lowering blood pressure and preventing the development of hypertension after three to four years of followup.[4] Diastolic blood pressure was required to be 83 to 89 mmHg at the third screening visit, and weight 110 to 165% of desirable body weight. Intervention goals for the weight reduction group was weight loss ≥4.5 kg, and for the sodium reduction group a decrease in sodium intake ≤80 mmol/d. Blinded observers measured blood pressure. 2382 subjects were recruited.

Baseline and treatment outcomes are displayed in Table 48.5. By 6 months, neither the weight loss nor sodium restriction goals were met by the groups; however, the net blood pressure reduction compared to the usual care group was significant ($p < 0.001$ for each intervention): weight loss, –3.7/–2.7 mmHg; sodium restriction, –2.9/–1.6 mmHg; and the combination, –4.0/–2.8 mmHg. At 36 months, many of the treatment effects were lost. The 38% incidence of hypertension was similar in all treatment groups, compared to 44% in the usual care group, and did not appear additive at 36 months. The relative risk of hypertension (compared with the usual care group) was 0.87 for the weight loss group ($p = 0.06$), 0.86 for the sodium reduction group ($p = 0.04$), and 0.85 for the combined intervention group ($p = 0.02$).[4]

Secondary Prevention Trials

Dietary Intervention Study of Hypertension (DISH)

Participants in DISH were former medicated participants of the Hypertension Detection and Follow-up Program.[5] The cohort (n = 496) was grouped into obese (≥120% of ideal body weight) or nonobese. The obese group was randomized into one of four groups: 1) continue drug therapy or 2) discontinue drug therapy and a) receive no dietary intervention, the control group, b) decrease sodium intake, or c) lose weight. The nonobese group was randomized to 1) continue drug therapy or 2) discontinue drug therapy and a) receive no dietary intervention, the control group, or b) decrease sodium intake.

Demographics and outcomes are shown in Table 48.6. Among overweight persons, 46.3% lost an average of 5% of weight, or greater than 4.5 kg after 56 weeks. The average weight

TABLE 48.6

Dietary Intervention Study in Hypertension: Demographics and Outcome

	Obese Drug Therapy Control	Obese No Drug Control	Obese Sodium Restriction	Obese Weight Reduction	Lean Drug Therapy Control	Lean No Drug Control	Lean Sodium Restriction
Number	48	89	101	87	33	70	68
Age (Yr)	59	57	57	56	58	57	56
% Black	75	70	64	62	58	73	56
% Women	69	64	59	68	52	50	47
BP (mmHg)	131/80	128/80	128/81	128/81	126/80	124/80	127/81
ΔWeight (kg)	-0.46	-0.46	0	-4.0	+0.46	0	+0.46
Δ Urine Na+ (mEq/d)	-13	-10	-59	0	+2	-5	-44
% on *no* BP Drugs	0	35	45	60	0	45	53

Derived from Tables 1, 2, and 3 in article by Langford, H.G., et al. *JAMA* 253: 657; 1985.

TABLE 48.7

Hypertension Control Program: Demographics and Outcome

	No BP Drugs Nutritional Therapy	No BP Drugs No Nutritional Therapy	BP Drugs No Nutritional Therapy
Number	97	44	48
Age (Yr)	57	55	55
% Female	35	39	38
% Black	11	21	15
BP (mmHg)	122/78	118/77	119/79
Δ Weight (kg)*	-1.8‡	+2.0	+2.0
Δ Urinary Na+ (mEq/d)	-60‡	+20	-5
Δ Ethanol (g/d)†	-12.5	-7.1	-10.2
% Without BP Drugs	39%‡	5%	0%

* Among obese subjects only; † Among drinkers only; ‡ $p < 0.001$

Derived from tables and manuscript of Stamler, R. et al. *JAMA* 257: 1484; 1987.

loss in this group was 4.0 kg ($p < 0.05$ versus the no-medication control group). Among obese and nonobese persons who were sodium restricted, the mean decrease in urine sodium output was –59 mEq/24 hr and –44 mEq/24 hr (each $p < 0.05$ versus the no-medication control group) after 56 weeks. The percent not taking antihypertensive medication among obese individuals was 35.3% in the control group, 44.9% in the sodium restricted group, and 59.5% in weight loss group ($p = 0.0015$ versus control). In the lean group, the percent not taking antihypertensive medication was 45% in the control group and 53.4% in the sodium-restricted group (not significantly different).

The Hypertension Control Program (HCP)

Participants in the HCP were former drug-treated participants of the Hypertension Detection and Follow-up Program. Subjects (n = 189) were randomized to three groups:

1. Discontinue antihypertensive therapy and reduce overweight, excess salt, and alcohol
2. Stop medication without nutritional intervention (the control group)
3. Continue drug treatment with no nutritional program

The primary endpoint was the percentage of subjects remaining hypertensive in the intervention versus the control group.

As shown in Table 48.7, in the nutritional intervention group, weight decreased ($p < 0.001$) and sodium output increased ($p < 0.001$) significantly after four years. 39% of the nutritional therapy group were maintained on no drug therapy compared to only 5% of the control group ($p < 0.001$).

Trial of Antihypertensive Intervention and Management (TAIM)

This multicenter, placebo-controlled trial randomized 787 overweight (110 to 160% ideal body weight) hypertensive (baseline diastolic pressure 90 to 100 mmHg) men and women to one of three drugs (placebo, chlorthalidone 25 mg QD, or atenolol 50 mg QD) and three dietary interventions (usual diet, weight loss, or sodium decrease/potassium increase).[6] The weight loss goal was 10% of baseline weight or 4.54 kg, whichever was greater. Sodium reduction was 52 to 100 mmoles/d and potassium increase 62 to 115 mmoles/d, and depended on weight. Both weight reduction and electrolyte changes required group nutri-

TABLE 48.8

Trial of Antihypertensive Intervention and Management: Change in Blood Pressure from Baseline by Treatment Group at Six Months

	Usual Diet	Weight Loss	Low Na+/High K+
Placebo	-10.34/-7.96 (n = 90)	-11.49/-8.78 (n = 90)	-8.66/-7.91 (n = 79)
Chlorthalidone	-17.41/-10.78 (n = 87)	-21.72/-15.06 (n = 87)	-19.51/-12.18 (n = 89)
Atenolol	-15.06/-12.43 (n = 87)	-18.11/-14.81 (n = 88)	-18.29/-12.76 (n = 90)

Derived from Tables 2 and 3 from Langford, H.G. et al. *Hypertension* 17: 210; 1991.

tional counseling weekly for 10 weeks, and individually thereafter every 6 to 12 weeks. There was no change in the drugs or their dosages during the first six months of the trial unless critical diastolic blood pressures were reached (treatment crossovers). Change in diastolic blood pressure treatment failure (as assessed by the need to increase drug treatment), quality of life, and calculated cardiovascular risk were assessed.

Table 48.8 shows the change in systolic and diastolic blood pressure from baseline to six months by treatment group. In the weight loss group, the average decrease in weight was 4.5 kg after six months. Weight loss was more effective than usual diet ($p = 0.001$) or the low sodium/high potassium diet ($p = 0.019$) in lowering diastolic blood pressure. Weight loss in combination with either a diuretic (–4.3 mmHg, $p = 0.002$), added significantly to blood pressure reduction compared to usual diet with a diuretic. The combination of weight loss with a β-blocker (–2.4 mmHg, $p = 0.07$) did not add to the effect of the drug alone.

45% of the weight loss cohort lost ≥4.5 kg. For patients who were not treatment crossovers, placebo and usual diet (n = 71) was associated with a 7 mmHg decrease in blood pressure and a 0.63 kg change in weight, and was less effective than placebo with >4.5 kg weight loss and diastolic blood pressure decrease of 11.6 mmHg ($p < .01$). There was a graded relationship with the amount of weight reduction and blood pressure decrease: <2.25 kg, –6.9 mmHg; –2.25 to 4.5 kg, –8.9 mmHg; and >4.5 kg, –11.6 mmHg. The change in diastolic blood pressure inversely correlated with the baseline plasma renin indexed to the 24-hour urinary sodium in the weight loss diet group.[7] In fact, the change in diastolic blood pressure with >4.5 kg weight change is comparable to low-dose drug therapy as seen in Table 48.9. After 24 months, there was gradual return of weight toward the baseline.[8] Among the weight-loss diet patients, the least mean change in weight occurred among atenolol-treated subjects. In fact, among atenolol-treated subjects assigned to usual diet or electrolyte modification, there was a mean weight gain. The 5-year incidence of treatment failure was lower in the weight loss group (49.8 per 100 subjects) than in the usual diet group (56.7 per 100 subjects).[9]

TABLE 48.9

Trial of Antihypertensive Intervention and Management: Change in Diastolic Blood Pressure with >4.5 kg Weight Change — Comparable to Low-Dose Drug Therapy

	Usual Diet	≥4.5 kg Weight Loss
Placebo	-7.0 (n = 71)	-11.6 (n = 33)*
Chlorthalidone	-11.1 (n = 80)	-15.3 (n = 53)†
Atenolol	-12.4 (n = 79)	-18.4 (n = 26)‡

* $p < 0.01$, † $p = .002$, and ‡ $p = 0.0005$ compared to usual diet.

Derived from Figures 2 and 3 from Wassertheil-Smoller, S. et al. *Arch Intern Med* 152: 131; 1992.

In the low sodium/high potassium group, the average decrease in urinary sodium was 27.4 mmol/d and the average increase in urinary potassium 10.9 mmol/d. The effect on blood pressure of the low sodium/high potassium diet did not differ from that of the usual diet ($p = 0.347$) on blood pressure. The low sodium/high potassium diet did not further lower diastolic blood pressure, but the baseline urinary sodium excretion was already relatively low (133 mmol/d). However, in the placebo group, when urinary sodium excretion ≤70 mEq/d was achieved, systolic and diastolic blood pressure reduction was greater than in the usual diet group (–23.7/–13.9 mmHg versus –9.6/–7.0 mmHg, each $p < 0.005$).[10]

After 3 years, compared to the usual diet, the net difference of urinary sodium excretion reduction was 30 mmol/d and urinary potassium excretion augmentation was 11 mmol/d.[11] There was a 41% decrease ($p = 0.01$) in the risk of treatment failure for women and 34% decrease ($p = 0.03$) among less obese patients. After 3.5 years among patients assigned to low sodium/high potassium diet, treatment failures occurred in 68% of placebo-, 47% of diuretic-, and 35% of β-blocker-assigned subjects.

Quality of life was improved with weight reduction.[12] Weight reduction significantly reduced symptoms of physical problems, especially sexual problems, and improved satisfaction with physical health. Weight loss improved the erectile dysfunction reported with chlorthalidone and usual diet (12.1 versus 26.2%).[13] Weight reduction reduced symptoms of sexual problems in both men and women significantly. The low sodium/high potassium diet with placebo was associated with greater fatigue (34.3%) than was either usual diet (18.1%, $p = 0.04$) or weight reduction (14.6%, $p = 0.009$). The electrolyte intervention group in combination with chlorthalidone (32.0%, $p = 0.04$) was associated with more sleep disturbances than chlorthalidone versus usual diet (16%). A nonsignificant ($p = 0.07$) similar trend was observed with atenolol.

Overall calculated cardiovascular risk worsened with chlorthalidone therapy in the usual diet group at six months due to the changes in cholesterol and glucose.[14] Those persons treated with atenolol or weight reduction showed the lowest relative risk.

Trial of Nonpharmacologic Interventions in the Elderly

This was a randomized, multicenter, controlled trial of 975 men and women aged 60 to 80 years with blood pressure of <145/<85 mmHg on a single hypertensive drug.[15] Patients were randomized to treatment based on their body habitus. 585 obese patients either received usual care, sodium restriction (a dietary intake of less than 80 mmoles per day as measured by 24-hour urine sodium collection), a weight loss program to achieve a loss of 4.5 kilograms or greater, or a combination of sodium restriction and weight loss. 390 nonobese patients were randomized to either usual care or sodium restriction.

The mean change in blood pressure prior to attempted medication withdrawal for each group was: sodium reduction, –3.4/–1.9 mmHg; weight reduction, –4.0/–1.1 mmHg; combination intervention, –5.3/–3.4 mmHg; and usual care, –0.8/–0.8 mmHg. Sodium reduction, weight reduction, and the combination intervention lower blood pressure significantly more than usual care. After three months of nonpharmacological therapy, antihypertensive medication withdrawal was attempted. After 30 months, 44% of patients in the combined sodium and weight reduction group were free of a primary endpoint (sustained blood pressure of 150/90 mmHg or higher, pharmacologic treatment of hypertension, or occurrence a clinical cardiovascular event). Compared to 16% in the usual care group, 34% of the sodium restriction group and 37% of the weight reduction group did not have a primary endpoint at 30 months. The sodium-restricted group reduced average sodium intake about 40 mmoles per day. In the weight loss group, average body weight decreased by 3.5 kilograms. Sodium restriction was equally effective in the obese and lean

subjects; however, the combined intervention was not more effective than either single intervention. Predictors of successful long-term withdrawal of pharmacologic treatment include lower baseline systolic blood pressure, shorter duration of hypertension or drug treatment, and absence of a history of cardiovascular disease.[16]

Dietary Approaches to Stop Hypertension (DASH)

The DASH trial was a multicenter, randomized feeding study that sought to assess the impact of nutrients naturally occurring in food in contrast to nutritional supplements.[17] Subjects were required to have a systolic blood pressure less than 160 mmHg and a diastolic blood pressure 80 to 95 mmHg. Persons consuming greater than 14 alcoholic beverages per week were excluded from the study. After screening, all subjects completed a three-week control diet. The control diet included magnesium, potassium, and calcium at the 25th percentile of consumption, and fiber at the average level of consumption. After the control period, 459 study participants received either a control diet, a fruit and vegetable diet, or combination diet for eight weeks. The fruit and vegetable diet provided magnesium and potassium at the 75th percentile of consumption and was also high in fiber. The combination diet was high in protein and fiber, provided increased calcium, magnesium, and potassium to the 75th percentile of consumption, and reduced intake of total fat, total cholesterol, and saturated fat. The sodium content (~3000 mg per day) was similar for all three diets, and caloric intake was adjusted so that weight gain did not occur in the study.

The average age of the subjects was 44 years; 60% were African Americans and 49% were women. About 14% had a diastolic blood pressure ≥90 mmHg, and 23.5% had a systolic blood pressure ≥140 mmHg. Change in the diastolic blood pressure was the primary outcome. The change in blood pressure in the combination group (corrected for the change in the control group) was –5.5/–3.0 mmHg ($p < 0.001$ for each). The change in blood pressure among hypertensive subjects was larger than in nonhypertensive subjects (–11.4/–5.5 mmHg versus –3.5/–2.1 mmHg), and among minority subjects was larger than nonminority subjects (–6.8/–3.5 mmHg versus –3.0/–2.0 mmHg). The change in blood pressure in the fruit and vegetable group minus the change in the control group was –2.8/–1.1 mmHg ($p < 0.001$ for each). Hypertensive subjects had a greater blood pressure reduction (–7.2/–2.8 mmHg) on the fruit and vegetable diet.

The combination diet demonstrated superiority over the fruits and vegetables in reducing blood pressure significantly an average of –2.5/–1.9 mmHg more. The combination diet lowered systolic blood pressure significantly more in African Americans (6.8 mm Hg) than in whites (3.0 mm Hg), and in hypertensive subjects (11.4 mm Hg) than in nonhypertensive subjects (3.4 mm Hg) ($p < 0.05$ for both).[18]

Since the DASH trial showed a blood pressure-lowering effect for a diet rich in vegetables, fruits, grains, low-fat dairy products, fish, poultry, and nuts, a logical question was whether there was an additional benefit of a low sodium diet. To answer this question, 412 subjects were randomly assigned to either the DASH diet or a control diet.[21] Each person for their assigned diet was rotated in random order at 30-day intervals to a low (50 mmol/d), intermediate (100 mmol/d) or high (150 mmol/d) sodium intake diet. The study population included 57% females, 57% blacks, and 41% hypertensives. Since this was a feeding trial, it was not surprising that urinary excretion of sodium was reduced according to treatment assignment in both the DASH and control diet groups. The change in blood pressure in the control diet group from high to intermediate sodium intake was –2.1/–1.1 mmHg, and from intermediate to low sodium intake –4.6/–2.4 mmHg. The corresponding values for the DASH diet were –1.3/–0.6 mmHg and –1.7/–1.0 mmHg. All of these values are statistically significant except for the change in diastolic blood pressure

from high to intermediate sodium intake in the DASH group. The benefit of the DASH diet over the control diet was confirmed by the change in blood pressure in the high (–5.9/–2.9 mmHg), intermediate (–5.0/–2.5 mmHg), and low sodium intake (-2.2/-1.0 mmHg) groups. The greatest benefit was seen in hypertensive subjects, African Americans, and women. There was a less than additive effect of decreased sodium intake and DASH diet, but a greater effect than either intervention individually.

Summary

The primary prevention trials prove that sodium restriction and weight reduction are effective in reducing the rate of development of hypertension. However, the behavioral changes are difficult to sustain over a 36-month period, and the treatment effects are modest. Individual strategies of potassium, calcium, magnesium, or fish oil supplementation are not effective in nonhypertensive subjects in lowering blood pressure or preventing the development of hypertension.

The secondary prevention trials document a clear benefit for sodium restriction and weight reduction in controlling blood pressure. However, the combination of weight reduction and sodium restriction was not additive. Weight loss was additive to diuretic therapy and improved quality of life, including sexual dysfunction. Although individual dietary components of potassium, calcium, magnesium, and fish oil supplementation have not been successful strategies for primary prevention, the DASH feeding study, which reduced intake of total fat, total cholesterol, and saturated fat, and increased protein, fiber, fruit, and vegetable intake, demonstrates the potential that can be achieved with nonpharmacological interventions rich in these individual components.

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