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Long-Term Weight Loss and Changes in Blood Pressure: Results of the Trials of Hypertension Prevention, Phase II

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Background: **Weight loss appears to be an effective method for primary prevention of hypertension. However, the long-term effects of weight loss on blood pressure have not been extensively studied.**

Objective: **To present detailed results from the weight loss arm of Trials of Hypertension Prevention (TOHP) II.**

Design: **Multicenter, randomized clinical trial testing the efficacy of lifestyle interventions for reducing blood pressure over 3 to 4 years. Participants in TOHP II were randomly assigned to one of four groups. This report focuses only on participants assigned to the weight loss ($n = 595$) and usual care control ($n = 596$) groups.**

Patients: **Men and women 30 to 54 years of age who had nonmedicated diastolic blood pressure of 83 to 89 mm Hg and systolic blood pressure less than 140 mm Hg and were 110% to 165% of their ideal body weight at baseline.**

Intervention: **The weight loss intervention included a 3-year program of group meetings and individual counseling focused on dietary change, physical activity, and social support.**

Measurements: **Weight and blood pressure data were collected every 6 months by staff who were blinded to treatment assignment.**

Results: **Mean weight change from baseline in the intervention group was −4.4 kg at 6 months, −2.0 kg at 18 months, and −0.2 kg at 36 months. Mean weight change in the control group at the same time points was 0.1, 0.7, and 1.8 kg. Blood pressure was significantly lower in the intervention group than in the control group at 6, 18, and 36 months. The risk ratio for hypertension in the intervention group was 0.58 (95% CI, 0.36 to 0.94) at 6 months, 0.78 (CI, 0.62 to 1.00) at 18 months, and 0.81 (CI, 0.70 to 0.95) at 36 months. In subgroup analyses, intervention participants who lost at least 4.5 kg at 6 months and maintained this weight reduction for the next 30 months had the greatest reduction in blood pressure and a relative risk for hypertension of 0.35 (CI, 0.20 to 0.59).**

Conclusions: **Clinically significant long-term reductions in blood pressure and reduced risk for hypertension can be achieved with even modest weight loss.**

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See editorial comment on pp 72-74.

Approximately one fourth of the U.S. adult population—nearly 50 million people—has hypertension (1, 2). Taking a broader perspective, more than half of the adult population has higher than optimal blood pressure (1), defined as systolic blood pressure greater than 120 mm Hg and diastolic blood pressure greater than 80 mm Hg (2). These persons are at significantly increased risk for cardiovascular disease and stroke (3). Although pharmacologic treatment for hypertension significantly reduces morbidity and mortality from cardiovascular diseases (4, 5), long-term pharmacologic therapy can have undesirable side effects and requires the expense of continuing medical supervision. Furthermore, pharmacologic therapy is not usually initiated when blood pressure is higher than optimal yet below diagnostic thresholds for hypertension. Thus, lifestyle interventions for primary prevention and initial treatment of high blood pressure remain a vital strategy for controlling this highly prevalent condition (2).

Weight loss has been shown to reduce blood pressure in overweight hypertensive patients (6–9) and in overweight persons with high-normal blood pressure (10–12). Two reviews of randomized trials of weight reduction to reduce blood pressure examined the results of nine studies (13, 14). Most of these trials were small, only one had more than 500 participants (11), and most had short-term follow-up (1 year or less). Only three studies had follow-up of 3 to 5 years (8, 10, 11). Compared with controls, weight loss averaged nearly 7 kg in the short-term trials and approximately 3 kg in the three longer-term trials. In almost all trials, systolic blood pressure and diastolic blood pressure were reduced in

the intervention groups. Since these reviews were published, the Trials of Hypertension Prevention (TOHP) Phase I reported mean weight reduction of 3.9 kg at 18 months in 564 overweight participants with high-normal blood pressure, resulting in significant decreases in systolic blood pressure and diastolic blood pressure compared with a usual care control group (12, 15).

To investigate whether nonpharmacologic interventions can prevent hypertension over the long term, TOHP II was initiated. This was a randomized, controlled trial examining the effects of weight loss and dietary sodium reduction, alone and in combination, in reducing blood pressure in overweight adults with high-normal diastolic blood pressure (16). This target population is at high risk for hypertension as they age. The primary outcome paper from this trial (17) provided only a brief overview of the effects of weight loss on blood pressure.

Here, we provide more detailed analysis of weight loss and blood pressure in TOHP II. Of special interest are the long-term effects of weight loss on blood pressure, the magnitude of the dose–response relationship at 36 months, the effect of patterns of weight loss on blood pressure, and the predictors of weight loss and blood pressure response.

METHODS

Participants

Participants in TOHP II were overweight adults with nonmedicated diastolic blood pressure of 83 to 89 mm Hg and systolic blood pressure less than 140 mm Hg. Other eligibility criteria included age 30 to 54 years and a body mass index of 26.1 to 37.4 kg/m^2 for men and 24.4 to 37.4 kg/m^2 for women, approximately 110% to 165% of ideal weight (18). Principal exclusion criteria were current treatment with medications that might affect blood pressure, clinical or laboratory evidence of cardiovascular disease, diabetes mellitus, renal insufficiency (serum creatinine concentration $\geq$ 150 μmol/L [$\geq$1.7 mg/dL] for men and $\geq$ 132 μmol/L [$\geq$1.5 mg/dL] for women), and current or planned pregnancy. Detailed descriptions of recruitment and participant characteristics have been published elsewhere (19, 20). The study was reviewed and approved by the institutional review boards at all nine TOHP centers and the coordinating center, and all participants signed informed consent forms.

Design

Eligible participants were randomly assigned with equal probability to one of four groups: weight loss only, sodium reduction only, combined weight loss and sodium reduction, or usual care (controls).

Measurements

Age, sex, ethnicity, and years of education were obtained by questionnaire. Baseline blood pressure measurements were taken at three screening visits, each separated by 7 to 45 days. At each visit, three readings of systolic blood pressure and diastolic blood pressure were obtained and averaged. Certified staff obtained measurements in seated participants by using a Hawksley random-zero sphygmomanometer (21). Body weight was measured to the nearest 0.2 kg (0.5 lb) by using a calibrated balance-beam scale; participants wore indoor clothing (without shoes).

Blood pressure and weight were measured every 6 months after randomization to the end of follow-up at 36, 42, or 48 months, depending on randomization date. Clinic staff who were blinded to study group assignment made these assessments. Blood pressure measurements were obtained during a single visit at all follow-up points except for 18 and 36 months, when measurements were taken at a series of three visits approximately 1 week apart. Multiple measurements were taken at 18 and 36 months to provide a more precise assessment of average blood pressures at these primary outcome points. Dietary intake was assessed by 24-hour recall, and physical activity was assessed by questionnaire.

Intervention

Participants assigned to the weight loss intervention group sought to lose at least 4.5 kg (10 lb) during the first 6 months of the intervention and to maintain their weight loss for the remainder of the trial. A brief description of the intervention methods is presented here; a more detailed description has been published elsewhere (22).

The intervention started with an individual counseling session, followed by 14 weekly group meetings led by dietitians or health educators. After this 14-week intensive phase, participants attended six biweekly group meetings and then monthly group meetings. Beginning in the 18th month, participants were offered a variety of

options to keep them involved in the intervention, including individual counseling sessions and special group sessions focused on selected weight loss topics.

The intervention focused on self-directed behavior change (behavioral self-management), nutrition education, information on physical activity, and social support for making and maintaining behavior changes. Specific behavior change techniques included self-monitoring (food diaries and graphs of minutes of physical activity per day), setting explicit short-term goals and developing specific action plans to achieve those objectives, and developing alternative strategies for situations that trigger problem eating.

The dietary intervention focused on reducing caloric intake by decreasing consumption of excess fat, sugar, and alcohol. Keeping daily food diaries was emphasized for monitoring intake and assessing progress. With experience, the participants determined the caloric intake that produced moderate weight loss for them. It was suggested that men not consume less than 1500 kcal/d and women not less than 1200 kcal/d. Weight loss of more than 0.9 kg (2 lb) per week was discouraged.

The physical activity goal was to gradually increase activity to 30 to 45 minutes per day, four to five days per week. Exercise intensity was moderate, approximately 40% to 55% of heart rate reserve, and consisted primarily of brisk walking.

Table 1. **Baseline Characteristics of Participants in the Weight Loss and Usual Care Groups in Phase II of the Trials of Hypertension Prevention***

Characteristic	Weight Loss Group (n = 595)	Usual Care Group (n = 596)	Overall (n = 1191)
Demographic and social			
Age, *y*	43.4 ± 6.1	43.2 ± 6.1	43.3 ± 6.1
Men, %	63.0	68.3	65.7
White, %	78.0	79.5	78.8
Black, %	17.8	17.3	17.5
College graduate, %	50.8	50.8	50.8
Health status			
Weight, *kg*			
Men	98.9 ± 12.3	98.5 ± 11.7	98.7 ± 12.0
Women	84.1 ± 11.9	82.9 ± 10.9	83.6 ± 11.5
Body mass index, kg/m^2			
Men	31.0 ± 2.9	31.0 ± 2.9	31.0 ± 2.9
Women	31.0 ± 3.6	30.8 ± 3.5	30.9 ± 3.6
Systolic blood pressure, *mm Hg*	127.6 ± 6.1	127.3 ± 6.4	127.4 ± 6.2
Diastolic blood pressure, *mm Hg*	86.0 ± 1.9	85.8 ± 1.9	85.9 ± 1.9
Vigorous exercise, *times/wk*	2.0 ± 4.0	1.8 ± 1.9	1.9 ± 3.1
Energy intake, *kJ/24 h*†	9480 ± 3605	9353 ± 3803	9416 ± 3703
Energy from fat, %†	36.0 ± 9.6‡	33.9 ± 10.3	34.9 ± 10.0
Energy from saturated fat, %†	12.2 ± 3.9§	11.2 ± 4.1	11.7 ± 4.0

* Data with the plus/minus sign are the mean ± SD.
† Data were available for 230 participants in the weight loss group and 234 participants in the usual care group.
‡ $P < 0.05$.
§ $P < 0.01$.

Statistical Analysis

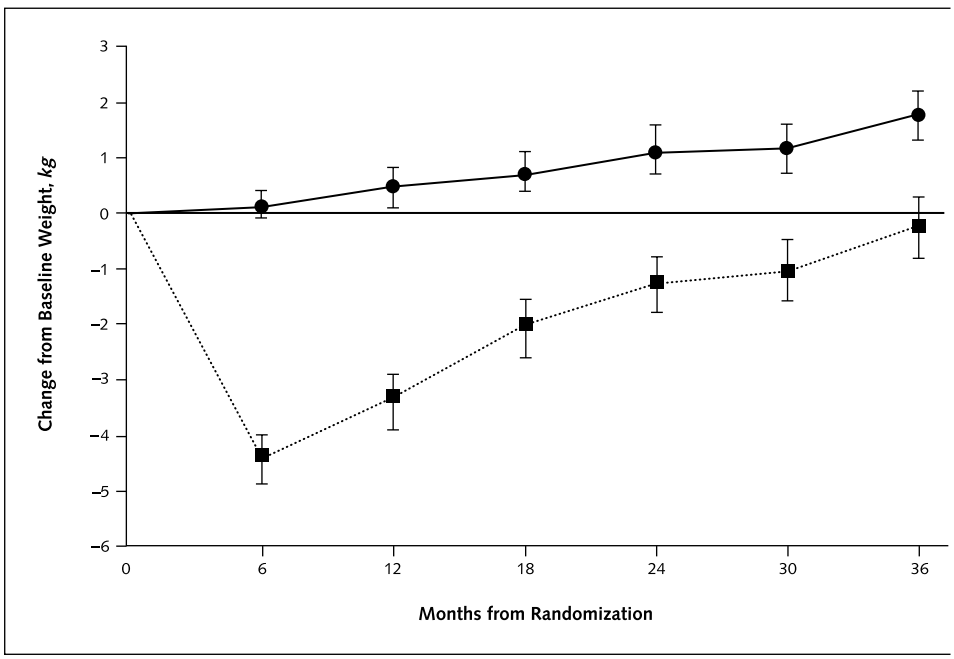
Baseline characteristics of the weight loss and usual care groups were compared overall and by sex by using *t*-tests for means and chi-square tests for proportions. Although weight and blood pressure data were collected every 6 months, special efforts were made to achieve high follow-up rates at 18 and 36 months; at each of these two time points, nine blood pressure readings were collected over three visits and were averaged.

For participants prescribed antihypertensive medication, follow-up blood pressure for all subsequent visits was taken to be the last study blood pressure before therapy was started. Participants receiving medications that affect blood pressure for reasons other than hypertension or who became pregnant were treated as missing at that visit.

We used two-sample *t*-tests to compare changes in weight and blood pressure from baseline in the weight loss intervention and usual care groups overall, by sex, by ethnicity, and by sex and ethnicity. The effects of the intervention in terms of changes in weight and blood pressure were examined overall and in subgroups defined by sex, ethnicity, and sex and ethnicity. Subgroup differences were tested by using terms for the interaction of treatment group with sex and with ethnicity in multiple linear regression models. Regression analyses were also used to analyze the dose–response relationship between change in weight and change in blood pressure, overall and within sex and ethnicity subgroups. Differences in dose response were tested by using interaction terms in linear regression models. All regressions were adjusted for age and baseline weight. We also adjusted for baseline blood pressure in the blood pressure regression models.

Change in blood pressure was also examined in relation to quintile of weight loss. Quintiles were computed by using the distribution of weight change in the weight loss intervention group. Additional multiple regression analyses were performed in which weight loss

Figure 1. **Mean change in weight over 36 months.**



Dotted lines represent the weight loss group; solid lines represent the usual care group. Error bars represent 95% CIs.

participants were categorized according to patterns of weight loss at 6 and 36 months. The PROC MIXED function of SAS software (SAS Institute, Inc., Cary, North Carolina) was used to perform repeated-measures analyses that tested differences over time by pattern of weight loss. Cox proportional hazards models were used for survival analyses, with onset of hypertension as the outcome.

RESULTS

Baseline Findings

The baseline characteristics of participants assigned to the weight loss ($n = 595$) and usual care ($n = 596$) groups have been described in detail elsewhere (20). To summarize, 66% were men, 79% were white, 18% were black, and 51% were college graduates; the mean age was 43 years at baseline (**Table 1**).

Intervention Attendance

The number of intervention sessions a participant could attend in the first 6 months after randomization depended on the delay before their first group session. Eighty-one percent of the participants attended at least half of the sessions they were expected to attend during the first 6 months, and 64% attended at least 80% of their assigned sessions. The median number of sessions attended in the first 6 months was 12. Between 6 and 18 months, the median number of sessions attended was 11, about half the expected attendance rate. Between 18 and 36 months, the median number of sessions attended was 7.5.

Follow-up

Rates of data collection at 36 months were high. Respective follow-up rates in the weight loss intervention and usual care groups were 92% and 93% for weight measurement and 89% and 86% for blood pressure measurement.

Weight Loss

Mean weight change from baseline in the intervention group was −4.4 kg at 6 months, −2.0 kg at 18 months, and −0.2 kg at 36 months. The respective mean weight change in the control group was 0.1, 0.7, and 1.8 kg (**Figure 1**). Group differences in mean weight change (net weight change) were statistically significant at each follow-up point ($P < 0.001$).

Linear multiple regression analyses tested the inter-

action of weight loss with sex and ethnicity, each adjusting for the other demographic variable. Model fit was best at 6 months, with R^2 values of 0.25 at 6 months, 0.09 at 18 months, and 0.05 at 36 months. In the intervention group, men had greater net weight loss than women by 1.6 kg at 6 months ($P = 0.006$), 1.2 kg at 18 months ($P = 0.07$), and 1.7 kg at 36 months ($P = 0.02$). A significant ethnicity-by-treatment interaction was also observed at 6 and 18 months; white persons lost a net 1.8 kg more than black persons at both time points ($P = 0.01$ and 0.03, respectively). At 36 months, weight loss did not differ significantly between white persons and black persons ($P > 0.2$). Age was associated with greater weight loss only at the 36-month assessment.

Baseline weight correlated with weight change at 6 months only. For every 10 kg of higher baseline weight, the net weight loss was greater by 0.8 kg ($P < 0.001$ for baseline-by-treatment interaction; data not shown). At 6 months, the larger effect of the weight loss intervention seen in men compared with women was no longer significant after controlling for higher baseline weight in men. When the two-way interaction terms of treatment with sex, ethnicity, and baseline weight were all included in the model, the interaction term of treatment-by-sex was no longer significant at 6 months (data not shown).

Table 2. **Mean Change in Body Weight from Baseline**

Group	6 Months		18 Months		36 Months	
	Participants	Mean Weight Change (95% CI)	Participants	Mean Weight Change (95% CI)	Participants	Mean Weight Change (95% CI)
	n	*kg*	*n*	*kg*	*n*	*kg*
All participants						
Intervention	565	−4.4 (−4.8 to −3.9)	545	−2.0 (−2.5 to −1.5)	547	−0.2 (−0.7 to 0.3)
Control	561	0.1 (−0.1 to 0.4)	551	0.7 (0.4 to 1.6)	554	1.8 (1.3 to 2.2)
Difference		−4.5 (−5.0 to −4.0)		−2.7 (−3.3 to −2.1)		−2.0 (−2.6 to −1.3)
All men						
Intervention	358	−5.1 (−5.7 to −4.5)	348	−2.5 (−3.1 to −1.8)	344	−0.7 (−1.3 to −0.1)
Control	387	0.1 (−0.2 to 0.4)	381	0.8 (0.4 to 1.3)	384	1.9 (1.4 to 2.4)
Difference		−5.2 (−5.9 to −4.6)		−3.3 (−4.1 to −2.5)		−2.6 (−3.4 to −1.8)
All women						
Intervention	207	−3.1 (−3.7 to −2.5)	197	−1.2 (−2.0 to −0.5)	203	0.7 (−0.2 to 1.5)
Control	174	0.2 (−0.3 to 0.7)	170	0.4 (−0.2 to 1.1)	170	1.5 (0.6 to 2.4)
Difference		−3.3 (−4.0 to −2.5)		−1.7 (−2.6 to −0.7)		−0.8 (−2.0 to 0.4)
White persons						
Intervention	442	−4.9 (−5.4 to −4.4)	422	−2.5 (−3.1 to −1.9)	426	−0.4 (−1.0 to 0.2)
Control	446	0.1 (−0.2 to 0.4)	442	0.6 (0.2 to 1.0)	444	1.6 (1.1 to 2.1)
Difference		−5.0 (−5.6 to −4.4)		−3.1 (−3.8 to −2.4)		−2.0 (−2.8 to −1.3)
Black persons						
Intervention	101	−2.3 (−3.1 to −1.5)	99	−0.2 (−1.1 to 0.7)	96	0.7 (−0.4 to 1.9)
Control	96	0.4 (−0.2 to 1.0)	91	0.7 (−0.1 to 1.5)	91	2.2 (1.2 to 3.2)
Difference		−2.7 (−3.6 to −1.7)		−0.9 (−2.1 to 0.3)		−1.5 (−2.9 to 0.0)
White men						
Intervention	308	−5.5 (−6.1 to −4.9)	295	−2.9 (−3.6 to −2.1)	295	−0.9 (−1.6 to −0.3)
Control	325	0.0 (−0.3 to 0.4)	324	0.7 (0.2 to 1.2)	327	1.7 (1.2 to 2.3)
Difference		−5.5 (−6.3 to −4.8)		−3.6 (−4.4 to −2.7)		−2.7 (−3.5 to −1.8)
White women						
Intervention	134	−3.6 (−4.4 to −2.8)	127	−1.7 (−2.6 to −0.7)	131	0.8 (−0.3 to 1.9)
Control	121	0.2 (−0.4 to 0.7)	118	0.4 (−0.3 to 1.2)	117	1.4 (0.3 to 2.5)
Difference		−3.7 (−4.7 to −2.8)		−2.1 (−3.3 to −0.9)		−0.6 (−2.2 to 1.0)
Black men						
Intervention	37	−2.6 (−4.2 to −1.0)	39	0.0 (−1.5 to 1.6)	34	1.2 (−0.4 to 2.8)
Control	47	0.5 (−0.4 to 1.4)	42	1.1 (0.1 to 2.1)	42	2.8 (1.5 to 4.1)
Difference		−3.1 (−4.9 to −1.4)		−1.1 (−2.9 to 0.7)		−1.6 (−3.6 to 0.4)
Black women						
Intervention	64	−2.1 (−3.0 to −1.3)	60	−0.4 (−1.6 to 0.9)	62	0.5 (−1.1 to 2.0)
Control	49	0.3 (−0.6 to 1.2)	49	0.4 (−0.8 to 1.6)	49	1.7 (0.2 to 3.1)
Difference		−2.4 (−3.6 to −1.2)		−0.7 (−2.5 to 1.0)		−1.2 (−3.3 to 1.0)

Table 3. **Change in Body Weight by Number of Counseling Sessions Attended***

Baseline to 6 Months			6 to 18 Months			18 to 36 Months		
Counseling Sessions Attended	Participants	Mean Weight Change ± SE	Counseling Sessions Attended	Participants	Mean Weight Change ± SE	Counseling Sessions Attended	Participants	Mean Weight Change ± SE
n		*kg*	*n*		*kg*	*n*		*kg*
0–2	44	−2.2 ± 0.7	0–2	68	2.3 ± 0.5	0–2	128	2.2 ± 0.4
3–9	133	−1.5 ± 0.4	3–10	199	2.9 ± 0.3	3–10	176	1.8 ± 0.4
10–13	166	−4.2 ± 0.4	11–20	208	2.8 ± 0.4	11–20	127	1.4 ± 0.6
14	226	−6.6 ± 0.3	>20	60	1.6 ± 0.3	>20	93	1.6 ± 0.4
P for trend		<0.001		0.031		>0.2		

* Adjusted for age, ethnicity, sex, and weight at baseline.

At 18 and 36 months, baseline weight-by-treatment interaction was not significant and did not affect the differential weight loss experienced by men compared with women.

Weight loss at 6 months was strongly related to attendance at the intervention sessions, but the relationship between attendance and weight loss diminished later in the trial. **Table 3** shows weight change by number of intervention sessions attended.

Blood Pressure

At all follow-up points, the weight loss and usual care groups differed significantly in diastolic blood pressure and systolic blood pressure. The differences between the group means (usual care vs. intervention) in diastolic blood pressure were −2.7 mm Hg (95% CI, −3.5 to −2.0 mm Hg; $P < 0.001$) at 6 months, −1.3 mm Hg (CI, −2.0 to −0.6 mm Hg; $P < 0.001$) at 18 months, and −0.9 mm Hg (CI, −1.7 to −0.0 mm Hg; $P < 0.05$) at 36 months. For systolic blood pressure, the group differences at the same time points were −3.7 mm Hg (CI, −4.7 to −2.8 mm Hg; $P < 0.001$), −1.8 mm Hg (CI, −2.7 to −0.9 mm Hg; $P < 0.001$), and −1.3 mm Hg (CI, −2.4 to −0.3 mm Hg; $P < 0.01$).

As expected, participants who lost the most weight had the largest reductions in blood pressure. **Figure 2** shows the change in blood pressure in all participants, categorized by quintile of weight change at 36 months. The quintile of participants with the greatest weight loss had a mean reduction from baseline of 7.0 mm Hg in diastolic blood pressure and 5.0 mm Hg in systolic blood pressure. In contrast, the quintile of participants with the least weight loss had a mean reduction in diastolic blood pressure of 0.7 mm Hg and a mean increase in systolic blood pressure of 2.5 mm Hg. The mean weight change in each quintile was −8.8 kg (<−4.4 kg), −2.6 kg (−4.4 to −1.1 kg), −0.1 kg (−1.1 to 1.2), 2.6 kg (1.2 to 4.2 kg), and 7.3 kg (>4.2 kg).

In regression analyses adjusting for age, sex, ethnicity, baseline weight, and baseline blood pressure, the overall effect on blood pressure at 36 months was a reduction of 0.35 mm Hg in diastolic blood pressure and 0.45 mm Hg in systolic blood pressure per kg of weight lost. No differences in response of diastolic blood pressure or systolic blood pressure to weight loss were seen according to ethnicity. At 36 months, women had a 0.15–mm Hg smaller reduction in diastolic blood pressure per kg lost than men (0.26 mm Hg vs. 0.41 mm Hg; $P = 0.047$), after adjustment for age, ethnicity, baseline weight, and baseline diastolic blood pressure. The change in systolic blood pressure did not differ between men and women.

To examine the relationship between patterns of weight loss and blood pressure, weight loss intervention participants were divided into three groups: those who lost 4.5 kg or more at 6 months and also maintained at least a 4.5-kg weight loss at 36 months (successful maintenance), those who lost at least 4.5 kg at 6 months but whose weight loss at 36 months was less than 2.5 kg (relapse), and those whose weight loss at 6 and 36 months was 2.5 kg or less (no loss). According to these categories, there were 73 participants in the successful maintenance subgroup, 129 in the relapse subgroup, and 198 in the no-loss subgroup. The remaining participants ($n = 195$) were not classified because their pattern of weight change did not fit one of these categories or because they had missing data at one of the assessments. Mean weight change from baseline at 6, 18, and

36 months was −10.2 kg (CI, −11.2 to −9.2 kg), −9.2 kg (CI, −10.7 to −7.6 kg), and −9.1 kg (CI, −10.0 to −8.1 kg) in the successful maintenance subgroup; −8.5 kg (CI, −9.3 to −7.8 kg), −2.9 kg (CI, −3.7 to −2.1 kg), and 1.7 kg (CI, 1.2 to 2.3 kg) in the relapse subgroup; and 0.0 kg (CI, −0.2 to 0.3 kg), 1.7 kg (CI, 1.2 to 2.3 kg), and 3.6 kg (CI, 2.9 to 4.2 kg) in the no-loss subgroup.

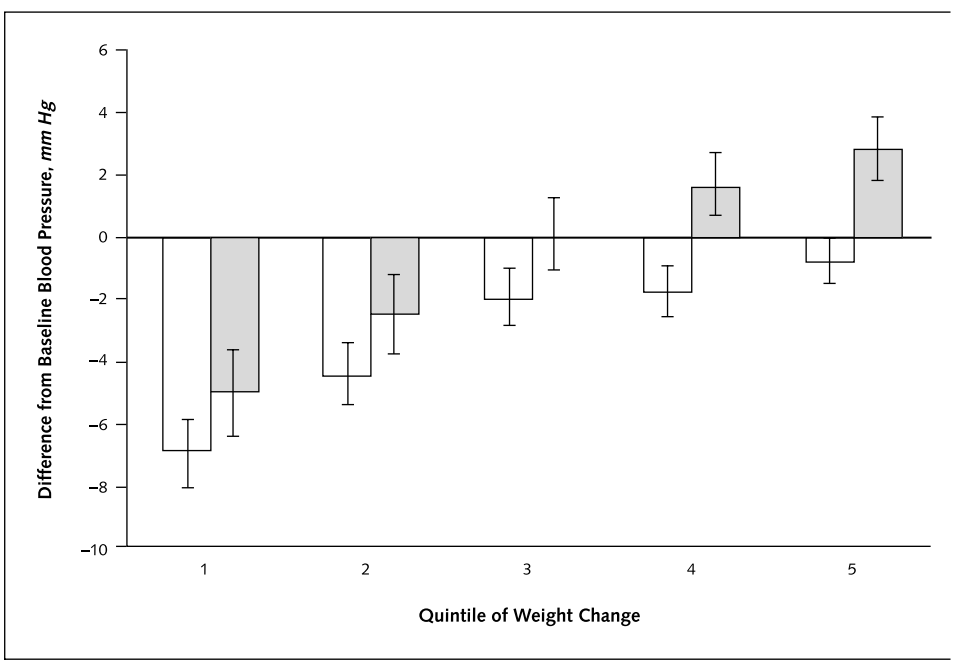
The mean diastolic blood pressure and systolic blood pressure for participants in each of the three weight change subgroups and the usual care control group are shown in **Figure 3**. Although all subgroups experienced a decrease in blood pressure at 6 months, the two groups with weight loss at 6 months had the largest decreases in blood pressure. Participants who subsequently regained much or all of their lost weight (relapse) showed a steady increase in blood pressure to near-baseline levels at 36 months, whereas those who maintained weight loss also maintained substantial reduction in blood pressure. In a repeated-measures analysis adjusting for age, sex, ethnicity, and baseline weight and blood pressure, the three weight change subgroups differed significantly in blood pressure response by time ($P = 0.04$ for systolic blood pressure, $P = 0.007$ for diastolic blood pressure).

Onset of Hypertension

A secondary outcome of TOHP II was onset of hypertension, defined as systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or prescription of an antihypertensive drug by a personal physician. According to this definition, weight loss participants were significantly less likely than usual care controls to develop hypertension. The risk ratios for hypertension in weight loss participants at 6, 18, and 36 months and the end of the study were 0.58 (CI, 0.36 to 0.94), 0.78 (CI, 0.62 to 1.00), 0.81 (CI, 0.70 to 0.95), and 0.79 (CI, 0.65 to 0.96), respectively.

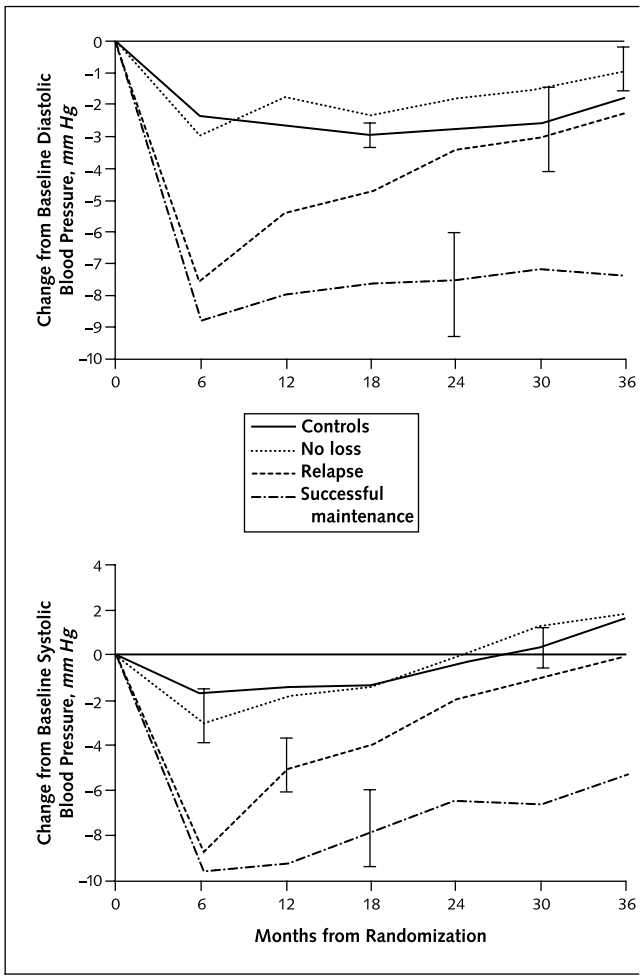
Survival analysis for onset of hypertension, adjusting for sex, age, ethnicity, and baseline weight, showed a significant difference among subgroups of the weight loss intervention group. The relative risk for hypertension (compared with the control group) was 0.35 (CI, 0.20 to 0.59) in the successful maintenance subgroup, 0.75 (CI, 0.53 to 1.04) in the relapse subgroup,

Figure 2. **Mean change in blood pressure.**



White bars represent diastolic blood pressure; gray bars represent systolic blood pressure. Error bars represent 95% CIs. Data are adjusted for age, ethnicity, and sex according to quintile of weight change at 36 months (weight loss and usual care groups combined).

Figure 3. **Mean change in diastolic (*top*) and systolic (*bottom*) blood pressure.**



Data are adjusted for age, ethnicity, and sex, according to patterns of weight change. Usual care controls were not assigned to intervention. Participants with successful maintenance of weight loss were defined as those who lost 4.5 kg or more at 6 months and maintained at least 4.5 kg of weight loss at 36 months. Participants with relapse were those who lost at least 4.5 kg at 6 months but whose weight loss at 36 months was less than 2.5 kg. Participants with no weight loss had weight loss of 2.5 kg or less at 6 and 36 months. Error bars represent 95% CIs.

and 1.10 (CI, 0.85 to 1.42) in the no-loss subgroup. When these subgroups were compared with each other, the relative risk for hypertension in the successful maintenance group compared with the no-loss group was 0.31 (CI, 0.18 to 0.55), the relative risk in the relapse group compared with the no-loss group was 0.68 (CI, 0.47 to 1.00), and the relative risk in the successful maintenance group compared with the relapse group was 0.46 (CI, 0.25 to 0.84).

DISCUSSION

The weight loss intervention in TOHP II produced significant weight loss over 36 months compared with usual care, resulting in significant reductions in diastolic blood pressure and systolic blood pressure and in a lower incidence of hypertension. A direct dose–response relationship was observed between weight loss and blood pressure reduction. When data from the intervention and control groups were combined, change in blood pressure was related to quintile of weight change. Participants in the quintile of greatest weight loss (loss of $>$4.4 kg) had reductions in diastolic and systolic blood pressure of 5.0 mm Hg and 7.0 mm Hg, whereas those in the quintile of least weight change (gain of $\geq$4.2 kg) had decreases of 0.7 mm Hg and 2.4 mm Hg. Analyses of subgroups of the intervention group categorized by patterns of weight loss showed that participants who lost at least 4.5 kg and sustained this loss continued to maintain a substantial reduction in blood pressure through 36 months compared with the control group, the no-loss intervention subgroup, and the relapse intervention subgroup. Likewise, the relative risk for hypertension was significantly lower in the successful maintenance subgroup (0.35 [CI, 0.20 to 0.59]; $P < 0.001$). Although this correlational analysis may have been confounded by unidentified factors associated with both weight loss and blood pressure, it seems most likely that sustained weight loss is a key factor in long-term reduction in risk for cardiovascular disease.

Previous trials of weight loss and blood pressure, most of which have had shorter follow-up than TOHP II, have consistently found that weight loss reduces blood pressure (23). Consistent with the results of other studies (15, 24), we found that men had greater weight loss than women. Although baseline weight was a significant predictor of weight loss at 6 months and reduced the significance of the greater weight loss in men compared with women at 6 months, greater weight loss in men persisted consistently thereafter, independent of baseline weight. Higher lean body mass and metabolic rate in men may facilitate their greater weight loss. In the first 18 months, white participants lost more weight than black participants, an effect also seen in other trials (25), but this difference was not evident at 36 months. These results suggest that ethnicity and initial weight may exert their effects only in the short term.

The finding that intervention attendance during the first 6 months was related to greater weight loss has been observed in other reports (15, 26, 27) and is consistent with studies showing that longer duration of intervention produces greater weight loss (28). Developing more effective methods for dealing with early treatment failure may substantially improve overall results.

Although weight loss reduces blood pressure in participants with high-normal blood pressure, the problem of only modest long-term success rates remains. In our study, about 13% of the intervention participants were able to lose 4.5 kg or more and maintain this weight loss over 3 years. When quintiles of weight loss at 3 years of follow-up are examined (**Figure 2**), the top 40% of the weight loss distribution had significantly reduced blood pressure. Although these findings are much better than those in the usual care group, better methods for maintaining weight loss need to be developed.

Our study had limitations. Given the high rate of collection of follow-up data at 36 months (92% for weight), we chose to exclude missing data from the analyses. It seems likely that participants who did not return for data collection visits experienced less weight loss than those who did. In addition, the association between intervention attendance and weight loss may not be a simple dose–response relationship; rather, weight loss and meeting attendance may be related to undetermined personal characteristics, or attendance may have increased in response to weight loss. However, a randomized clinical trial manipulating the number of intervention sessions has shown a direct relationship between number of intervention sessions and initial and long-term weight loss (29).

The fact that weight loss prevented hypertension in TOHP II raises the important issue of whether this intervention can prevent the deleterious pattern of increasing blood pressure with age. Observational studies have documented an age-associated increase in systolic blood pressure that occurs throughout adulthood and stabilization of diastolic blood pressure beginning around 50 years of age (1). In TOHP II, persons who successfully maintained weight loss of 4.5 kg or more experienced a reduction in diastolic blood pressure that was sustained throughout the remainder of follow-up. In contrast, systolic blood pressure decreased over the initial 6 months but subsequently increased halfway to baseline levels even though weight loss was sustained. In fact, from 6 months to 36 months, the slope of systolic blood pressure with time was similar in the successful maintenance and the no-loss subgroups. This pattern suggests that weight loss alone, even if maintained, may not be sufficient to prevent an age-related increase in systolic blood pressure and that other determinants of blood pressure, such as sodium intake, may be important (30).

Participants who lost weight initially, achieved a blood pressure reduction at 6 months, and then subsequently regained their lost weight did not have higher blood pressure at 3 years than those who did not lose weight or those in the control group. Wing and colleagues (31) reported a similar finding. Survival analysis showed that even participants who lost weight for a relatively short time and then relapsed experienced a reduced risk for hypertension over the course of the study compared with those who did not lose weight. This finding suggests that some degree of weight loss, even if not sustained beyond 6 months, confers benefit. Thus, weight loss should continue to be promoted for preventing high blood pressure. The challenge is to develop weight loss programs that achieve higher long-term success rates.

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The so-called survival instinct is often described as an animal urge to preserve oneself. But once the threat of bodily annihilation is relieved, the soul still requires preservation, and a wounded soul becomes the source of its own affliction; it cannot nurse itself directly. So survival can seem a curse, for one of the dominant needs of the needy soul is to be needed. As I came to know survivors, I found that, when it comes to soul preservation, the urge to look after others is often greater than the urge to look after oneself.

Philip Gourevitch
We Wish To Inform You That Tomorrow We Will Be Killed with Our Families: Stories from Rwanda
New York: Farrar, Straus and Giroux; 1998:228

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