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A Randomized Trial of a Low-Fat Diet Intervention on Blood Pressure and Hypertension: Tertiary Analysis of the WHI Dietary Modification Trial

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BACKGROUND
This *post hoc analysis* determined if the Women's Health Initiative (WHI) Diet Modification intervention (DM-I) resulted in a significantly different rate of incident hypertension (HTN), as well as longitudinal changes in blood pressure.

METHODS
Participants were 48,835 postmenopausal women aged 50–79 years who were randomly assigned to either the intervention or comparison group. HTN was defined as self-report of treated HTN collected semiannually or blood pressure ≥140/90 mm Hg at one of the annual follow-up clinic visits.

RESULTS
After a mean follow-up of 8.3 years, and among those who did not have HTN at baseline (n = 31,146), there were 16,174 (51.9%) HTN cases and those assigned to the intervention group had a 4% lower overall risk of developing incident HTN (hazard ratio (HR): 0.96, 95% confidence interval (CI): 0.93–0.99). Although the risk of HTN was lower in the DM-I group in the first few years, the HR became greater than 1 after year 5 (P-trend < 0.01). Similarly, randomization to the DM-I arm resulted in a small but significantly lower average systolic blood pressure (SBP) at 1 year of follow-up (−0.66 mm Hg, 0.44–0.89) that increased over the following 8 years (0.16 mm Hg/year, 0.11–0.21), such that any early benefit was eliminated by year 5 and a minimal deleterious effect emerged by year 7.

CONCLUSION
Randomization to an intensive behavioral dietary modification program aimed at a lower total fat intake is not associated with sustained reductions in blood pressure or risk of HTN in postmenopausal women.

CLINICAL TRIAL REGISTRATION
url http://www.clinicaltrials.gov, unique identifier nct00000611

Keywords: blood pressure; diet; hypertension; trial; women.

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The Women's Health Initiative (WHI) Dietary Modification Trial (DMT) tested the effect of an intensive behavioral dietary intervention on the risk for incident breast and colon cancer and, secondarily, incident cardiovascular disease (CVD).[1] The trial intervention aimed at a reduction in total fat intake, as well as increases in vegetable, fruit, and grain consumption. Compared to those in the comparison group, women randomized to the Diet Modification intervention (DM-I) arm reported significantly lower daily intakes of total calories, cholesterol, total and saturated fat, as well as mono- and polyunsaturated fats, while also reporting significantly higher intakes of total carbohydrate to include dietary fiber.[2] Despite these changes, the DM-I participants did not demonstrate clinically meaningful improvements in blood lipid levels or a difference in the risk for incident coronary heart disease (hazard ratio (HR), 0.97; 95% confidence interval (CI), 0.90–1.06), stroke (1.02; 0.90–1.15), incident carotid disease to include revascularization (1.08, 0.90–1.40) or total CVD (0.98; 0.92–1.05).[2–4]

Since hypertension (HTN) is a strong and consistent risk factor for CVD, especially carotid artery disease and stroke,[5] determining the *post hoc* effect of the DM-I on blood pressure and incident HTN might provide partial explanation of the null findings in the DMT. In this regard, both the Premier trial and Trials of Hypertension Prevention demonstrated that comprehensive lifestyle changes, including those that utilize a behavioral dietary intervention, can control rates of incident HTN,

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while also significantly reducing blood pressure.[6,7] Therefore, we hypothesized that randomization to the DM intervention arm would result in *modest* reductions in systolic blood pressure (SBP) and incident HTN rates over the trial period.

METHODS

Study population

In brief, 48,835 postmenopausal women aged 50–79 years were recruited from 40 sites within the United States from 1993 to 1998.[1,2] During enrollment 40% (n = 19,541) were randomly assigned to a low-fat (20% total kcal) DM-I group, while the remaining 60% (n = 29,294) were allocated to the usual diet comparison group (Figure 1).[8] Exclusion criteria for the DMT included type I diabetes mellitus, a history of cancer (except for nonmelanoma skin cancer), medical conditions predictive of a survival time of less than 3 years or a high risk of lack of retention or intervention nonadherence such as those who had special dietary requirements that were incompatible with the intervention program, consuming less than 600 kcal/d or greater than 5,000 kcal/day, consuming less than 32% of total energy from fat or greater than or equal to 10 meals/week prepared outside of the home.[9]

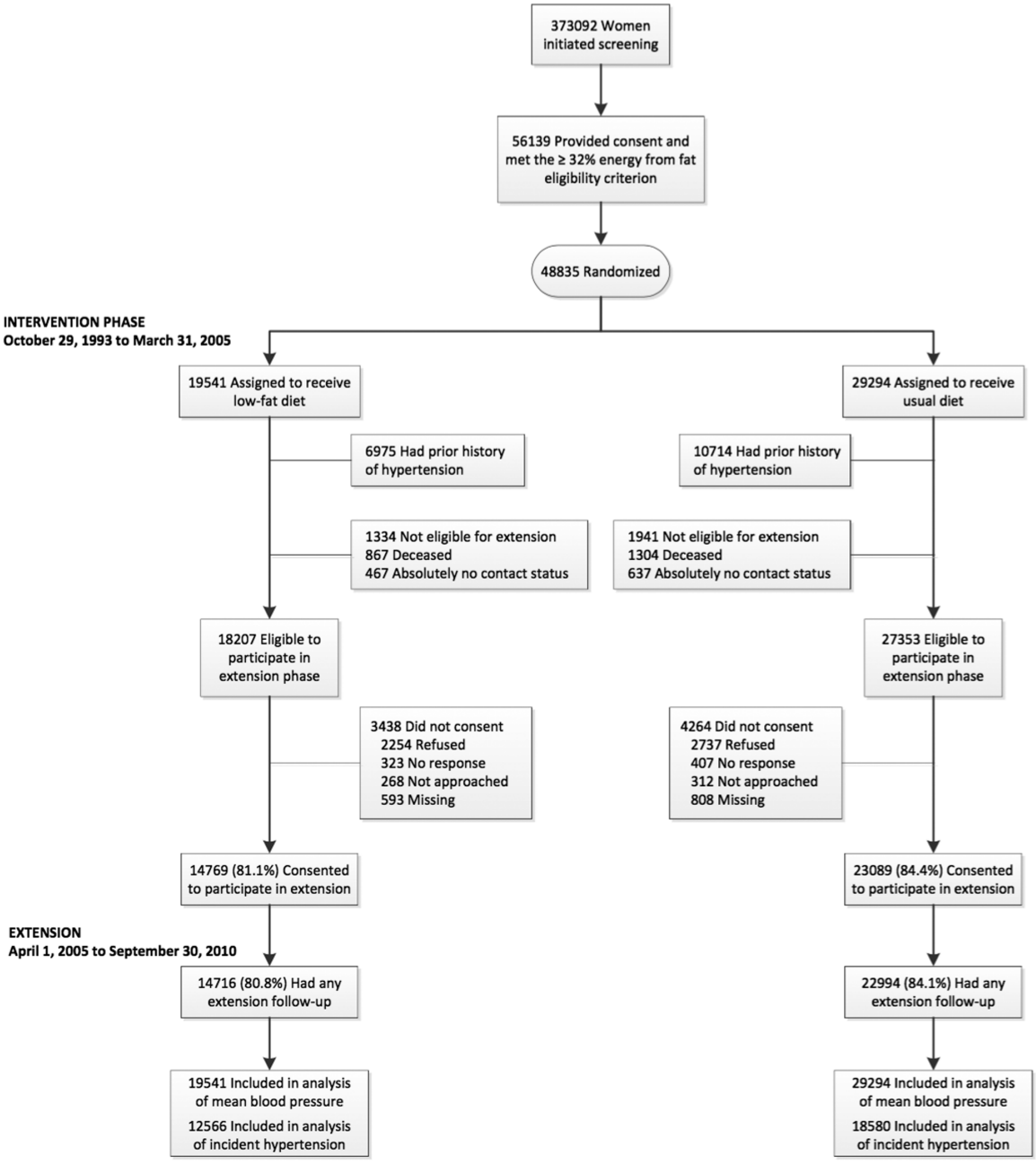

Figure 1. Participant flow in the Dietary Modification Trial.

At baseline, women could also be randomized to the postmenopausal hormone therapy trial ("HT"; conjugated equine estrogen alone or conjugated equine estrogen + medroxyprogesterone acetate). Details about eligibility and treatments for the HT have been published previously.[10]

The WHI was conducted in accordance with the Declaration of Helsinki and all participants provided written informed consent approved by the Institutional Review Boards at all participating institutions.

Intervention

The primary goal of DM-I was to reduce risk of breast cancer by limiting total fat intake to 20% of total energy. Additional goals included increased vegetable and fruit intakes to greater than or equal to 5 servings per day and increased grain intake to greater than or equal to 6 servings per day.[1]

Women in the DM-I group participated in an intensive behavioral modification program consisting of 18 group sessions in the first year and quarterly maintenance sessions until the trial ended in 2005.[9] Women randomly assigned to the comparison group were given a copy of Nutrition and Your Health: Dietary Guidelines for Americans and asked to maintain their usual diet.[11] Dietary intake data for all participants was assessed using the WHI food frequency questionnaire, which was administered at baseline, year 1 and thereafter on a rotating sample of one-third of participants every 3 years. After the intervention period ended in 2005, extended follow-up of 83.1% of surviving participants who provided written consent continued through 30 September 2010 (Figure 1).

Data collection

Personal characteristics, anthropometrics, and self-reported medical history were collected at baseline.[9] History of diabetes mellitus was defined as the self-reported current or past use of antidiabetic pills or injectable insulin. History of treated HTN was defined as self-report of a physician diagnosis of HTN or current use of an anti-HTN medication. Smoking status was coded as former, current, or never. Self-reported physical activity levels were calculated by using a standardized classification system.[12] Anthropometric data included measured height and weight and repeat weight measures at annual clinic visits during the trial intervention.

Outcome ascertainment. All trial participants were evaluated annually at a clinic visit that included completion of selected survey questionnaires and physical measurements. At these visits, and after a 5-minute rest, blood pressures were measured twice in the right arm by certified staff with the participant in the seated position using a conventional mercury sphygmomanometer and appropriately sized cuffs. SBP was defined as the pressure level at which the first of 5 regular Korotkoff sounds were heard while diastolic blood pressure (DBP) was the pressure level of the last of these sounds. The average of the measurements was used in the analysis. Pulse pressure was computed as the difference between SBP and DBP.

Incident HTN was defined as self-report of treated HTN collected semiannually or blood pressure ≥ 140/90 mm Hg at one of the annual follow-up clinic visits. Of note, our definition was intended to identify women considered to be hypertensive under the JNC7 classification of SBP ≧ 140 or DBP ≧ 90, where drug therapy should be initiated. Those with a history of treated HTN at baseline, as well as self-report or of use of antihypertensive medication, were not eligible to be classified with incident disease.

To investigate the effect of the DM-I on incident HTN during extended follow-up, a secondary analysis of incident HTN, based solely on self-report from randomization through extended follow-up, was performed. Blood pressure was not measured during this period.

Statistical methods. For the longitudinal analysis of SBP, DBP, and pulse pressure, a linear mixed effects regression model was used to estimate the effect of DM-I at the first annual visit and estimate annual change in the effect DM-I through the remainder of follow-up. Statistical significance for the effect of DM-I on the mean trajectories of these blood pressure endpoints was based on a 2-degree-of-freedom test of these 2 parameters (Table 2). *P*-values for the 1-degree-of-freedom tests of these parameters are mentioned in the text to qualify the statistical significance of the trajectory.

The analyses of incident HTN excluded participants with a prior history of HTN and used time-to-event methods. Follow-up time was censored at the time of a woman's last documented follow-up contact or death. HRs were estimated using Cox proportional hazards models stratified by age group and HT randomization group. To address treatment for HTN, a sensitivity analysis was conducted that excluded women who self-reported HTN at baseline or were taking antihypertensive medication, and sensible constants of 0, 10, or 20 mm Hg were added to SBP measurements that occurred on or after any of the remaining participants reported treatment for incident HTN. These results did not markedly differ from the primary analysis.

Statistical significance of 13 prespecified subgroups was based on tests of interaction between randomization group and subgroup. For each endpoint, at most 1 interaction was expected to be significant by chance alone. For the analysis of incident HTN, tests provided evidence against the assumption of proportional hazards, so risk depends on time and was further qualified by linear time-varying HRs with functional form $\exp(a \pm b \times t)$, where a and b are estimated from a Cox regression model and t is time since randomization. All primary analyses were intention-to-treat with 2-sided *P*-values of ≤0·05 being statistically significant.

RESULTS

The baseline characteristics of the participants by DMT arm assignment are presented in Table 1. At baseline, there were no statistically significant differences between women randomized to the intervention and comparison groups for all characteristics except mean SBP, which was quite small (0.4 mm Hg).

Table 1. Baseline characteristics of the women's Health Initiative Dietary Modification Trial participants

Characteristic	Intervention arm (*N* = 19,541)		Comparison arm (*N* = 29,294)		*P*-value[a]
	Mean or *N*	SD or %	Mean or *N*	SD or %	
Age (years)	62.3	6.9	62.3	6.9	0.99
Race/ethnicity					0.74
White	15,871	81.2	23,891	81.6	
Black	2,135	10.9	3,127	10.7	
Hispanic	751	3.8	1,094	3.7	
American Indian	88	0.5	114	0.4	
Asian/Pacific Islander	431	2.2	674	2.3	
Unknown	265	1.4	394	1.3	
Body mass index (kg/m^2)	29.1	5.9	29.1	5.9	0.53
Systolic blood pressure (mm Hg)	127.5	17.2	127.9	17.2	0.02
Diastolic blood pressure (mm Hg)	75.9	9.1	76.0	9.1	0.07
Hypertensive (self-report or high BP)	8,382	46.7	12,734	47.4	0.17
Antihypertensive medication use	6,036	30.9	9,230	31.5	0.15
Cholesterol medication use	2,034	11.8	3,138	12.1	0.29
Treated diabetes	866	4.4	1,337	4.6	0.49
Never smoker	9,918	51.4	15,029	51.9	0.23
Pack years of smoking	9.6	17.9	9.6	18.0	0.69
Percent calories from total fat	37.8	5.1	37.8	5.0	0.91
Physical activity energy (MET-hours/week)	10.0	11.7	10.1	12.0	0.44
Education after high school	15,158	78.0	22,641	77.8	0.65
Annual income <35K	7,275	39.5	11,117	40.3	0.36
History of bilateral oophorectomy	3,884	20.3	5,997	20.9	0.12
History of coronary heart disease	482	2.5	709	2.5	0.75
Family history of myocardial infarction	9,722	52.5	14,341	51.8	0.12
Hormone therapy trial arm					
CEE alone	615	3.1	1,039	3.5	0.41[b]
CEE alone placebo	670	3.4	1,068	3.6	
CEE + MPA	972	5.0	1,457	5.0	0.30[c]
CEE + MPA placebo	925	4.7	1,304	4.5	
Not randomized	16,359	83.7	24,426	83.4	
Calcium-Vitamin D Trial arm					
Active	4,767	24.4	7,827	26.7	0.18[d]
Placebo	4,878	25.0	7,738	26.4	
Not randomized	9,896	50.6	13,729	46.9	

Abbreviations: *N*, sample size; MET, metabolic equivalent of task; CEE, conjugated equine estrogens; MPA, medroxyprogesterone acetate.
[a]Based on chi-square test of association for categorical variables and *t*-test for continuous variables. [b]*P*-value corresponds to test of association between DM trial group and CEE alone trial group. [c]*P*-value corresponds to test of association between DM trial group and CEE + MPA trial group. [d]*P*-value corresponds to test of association between DM trial group and CaD trial group.

Figure 2 shows the main effect for randomization to the DM-I group on SBP, DBP, and pulse pressure during the WHI intervention period; the linear mixed effects model fit the data well. Contrasted to the comparison group, randomization to the DM-I arm resulted in a small but significantly lower average SBP at 1 year of follow-up (−0.66 mm Hg, 0.44–0.89). After the first year, there was a significant trend for increasing SBP over the following 8 years (0.16 mm Hg/year, 0.11–0.21), such that any early benefit was eliminated by year 5 and a minimal deleterious effect emerged by year 7. Similarly, those in the DM-I arm had, on average, a 0.64 mm Hg lower DBP (0.51–0.76) than those in the comparison group at year 1, but the DBP difference between groups diminished significantly

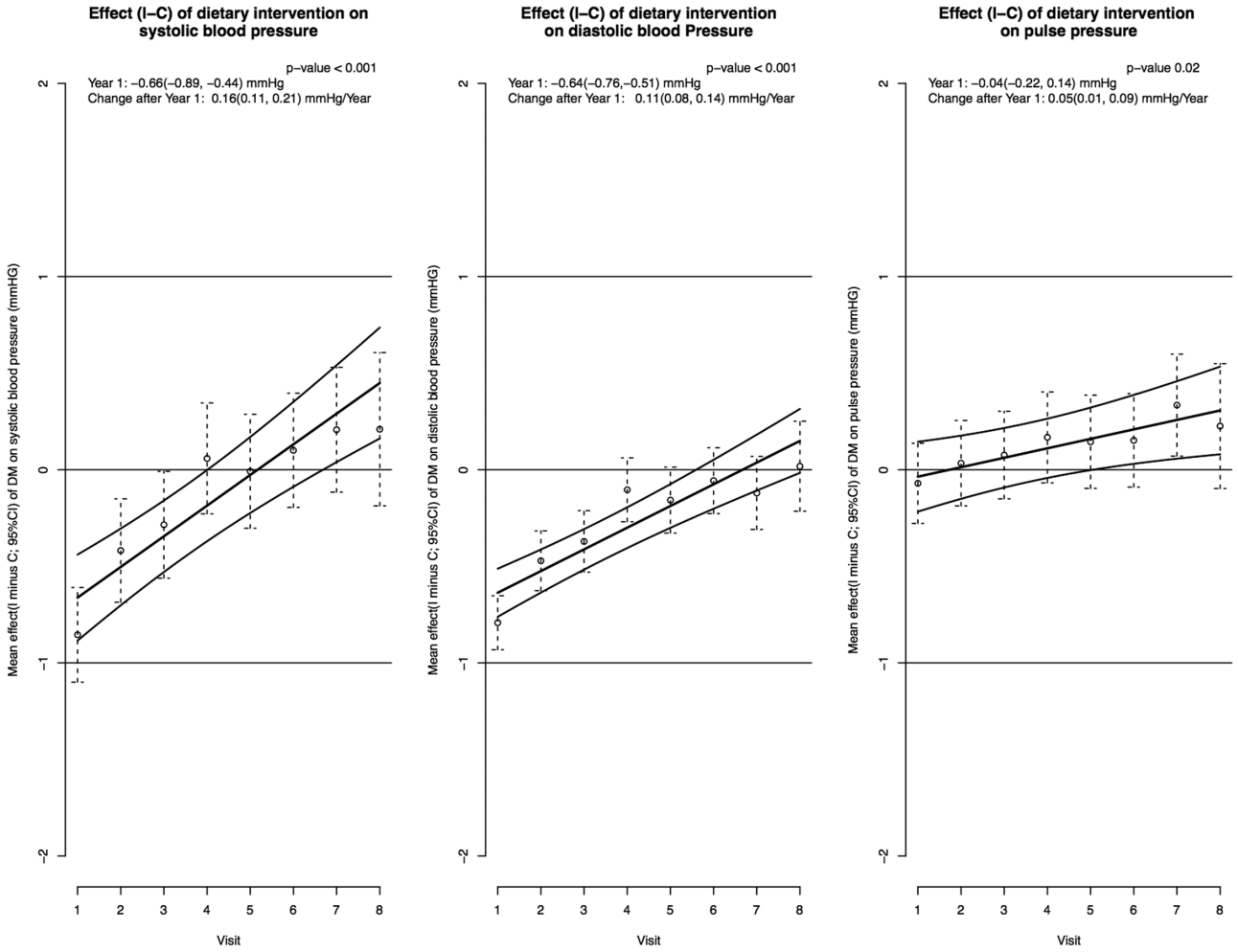

Figure 2. Mean longitudinal effect of randomization to the DM-I arm compared to DM-C on systolic blood pressure, diastolic blood pressure, and pulse pressure. Estimate (95% CI) is from a linear mixed effects (LME) regression model shown by a solid (dotted) lines. The LME model included the corresponding baseline BP measurement as a covariate, a cubic polynomial to model time since randomization, an indicator variable for randomization group, an interaction term for randomization group × time (linear), along with a random intercept and random slope for time (linear). To confirm the LME model was reasonable, estimates for mean BP (95% CI; bowties) were also computed from a classical repeated measures model, where annual visits were coded categorically, and therefore do not assume a cubic relationship with time, nor a linear intervention effect.

by an average rate of 0.11 mm Hg/year (0.08–0.14) after that point.

The results of randomization in the DMT on (i) mean values at visit 1 and (ii) mean change in slope for the blood pressure measures by selected subgroups are shown in Table 2. Participants in the DM-I arm who were also randomized to the conjugated equine estrogen alone intervention arm had significantly lower SBP at year 1 (−2.74 mm Hg, $P < 0.01$), which increased at a higher rate after this time (0.60 mm Hg/year, $P < 0.01$). Moreover, DM-I participants who did not report a history of HTN at baseline had a significantly lower SBP at year 1 (−0.95 mm Hg, $P = 0.01$), but the change after that point was not significantly different from those who did not report having HTN (0.18 vs. 0.14 mm Hg/year respectively, $P = 0.50$). In contrast, there were no significant differences in the year 1 DBP or slope of annual change in DBP by the different subgroups.

The Kaplan–Meier estimates for incident HTN by DMT arm are depicted in Figure 3. Contrasted to those in the comparison group, those assigned to the intervention group had a 4% lower overall risk of developing incident HTN (HR: 0.96, 95% CI: 0.93–0.99). Although the risk of HTN was lower in the DM-I group in the first few years, the HR became greater than 1 after year 5 (P-trend ≤ 0.01).

The effect of randomization to the DM-I group on incident HTN differed significantly by baseline statin medication use (Table 3). Those in the intervention group and who reported statin medication use at baseline had a 16% higher risk for developing HTN whereas those who did not report statin use had a 5% lower risk ($P < 0.01$). The results were essentially unchanged when those with a history of CVD were excluded from this analysis. There were no other significant differences in the risk for incident HTN by the other tested subgroups.

As the risk of incident HTN may be falsely elevated when the definition includes a single measure of blood pressure, we performed a secondary analysis using self-report of HTN. During the intervention period, there was a similar pattern

Table 2. Subgroup analysis for the effect of dietary modification on systolic, diastolic, and pulse pressures

			SBP			DBP			PP		
Subgroup (baseline)	**Intervention (*N*)**	**Comparison (*N*)**	**Mean[a]**	**Slope[b]**	***P***	**Mean[a]**	**Slope[b]**	***P***	**Mean[a]**	**Slope[b]**	***P***
Age (years)					0.29			0.13			0.24
50–54	2,673	3,982	−0.54	0.12		−0.59	0.13		0.04	0.00	
55–59	4,255	6,319	−0.69	0.12		−0.54	0.07		−0.18	0.05	
60–69	8,778	13,044	−0.61	0.16		−0.53	0.1		−0.10	0.06	
70–79	3,119	4,660	−0.94	0.26		−1.13	0.19		0.20	0.07	
Race/ethnicity					0.29			0.34			0.84
White	15,357	22,947	−0.78	0.18		−0.70	0.12		−0.1	0.06	
Black	2,023	2,910	−0.25	0.05		−0.40	0.05		0.17	0.00	
Hispanic	688	1,011	0.08	0.07		−0.28	0.07		0.32	0.01	
American Indian	79	108	−2.07	−0.17		−2.31	0.06		0.24	−0.22	
Asian	423	657	0.26	0.15		−0.41	0.12		0.63	0.05	
Body mass index					0.10			0 .01			0.8
<25	4,906	7,369	−0.69	0.12		−0.72	0.09		0.00	0.03	
25 to < 30	6,708	10,059	−1.00	0.19		−0.76	0.11		−0.25	0.08	
≥ 30	7,133	10,454	−0.40	0.17		−0.50	0.14		0.11	0.03	
CEE alone Trial					0.01			0.2			0.02
Active	591	989	−2.74	0.6		−1.32	0.25		−1.40	0.34	
Placebo	641	1,010	−0.45	0.09		−0.45	0.13		0.08	−0.06	
Not randomized	6,871	10,154	−0.55	0.15		−0.53	0.09		−0.03	0.07	
CEE+MPA Trial					0.85			0.46			0.96
Active	943	1,404	−0.71	0.23		−0.61	0.16		−0.06	0.07	
Placebo	903	1,242	−1.04	0.32		−1.11	0.24		0.07	0.07	
Not randomized	8,875	13,204	−0.55	0.12		−0.64	0.11		0.06	0.02	
CaD Trial					0.14			0.33			0.31
Active	4,876	7,736	0.06	0.17		0.33	0.08		−0.25	0.10	
Placebo	4,764	7,827	−1.05	0.06		−0.31	0.04		−0.73	0.02	
Not randomized	9,185	12,442	−0.72	0.17		−0.71	0.14		−0.02	0.03	
% Energy from fat (tertiles)					0.07			0.06			0.45
< 34.8%	6,235	9,256	−0.41	0.06		−0.51	0.08		0.09	−0.01	
34.8 to <39.4%	6,342	9,520	−0.94	0.21		−0.81	0.11		−0.16	0.10	
≥ 39.4%	6,139	9,116	−0.60	0.20		−0.59	0.16		−0.01	0.05	
Smoking status					0.20			0.60			0.38
Never	9,620	14,474	−0.83	0.15		−0.73	0.12		−0.12	0.03	
Past	7,789	11,417	−0.54	0.18		−0.54	0.11		−0.01	0.07	
Current	1,200	1,839	−0.12	0.12		−0.57	0.11		0.43	0.00	
Treated diabetes					0.97			0.58			0.78
No	18,006	26,772	−0.66	0.16		−0.62	0.11		−0.05	0.05	
Yes	817	1,231	−0.72	0.19		−0.94	0.13		0.21	0.05	
Hypertension[c]					0.03			0.17			0.12
No	9,214	13,574	−0.95	0.18		−0.71	0.11		−0.24	0.07	
Yes	8,047	12,098	−0.38	0.14		−0.53	0.12		0.15	0.03	
History of statin use					0.66			0.61			0.65

Table 2. Continued

Subgroup (baseline)	Intervention (*N*)	Comparison (*N*)	SBP			DBP			PP		
			Mean[a]	Slope[b]	*P*	Mean[a]	Slope[b]	*P*	Mean[a]	Slope[b]	*P*
No	17,671	26,294	−0.64	0.15		−0.63	0.11		−0.02	0.05	
Yes	1,153	1,711	−1.04	0.24		−0.68	0.17		−0.38	0.08	
History of CHD					0.99			0.55			0.78
No	18,146	26,985	−0.66	0.16		−0.62	0.11		−0.05	0.05	
Yes	443	666	−0.72	0.16		−0.82	0.05		0.21	0.08	
History of stroke					0.35			0.21			0.47
No	18,639	27,697	−0.65	0.16		−0.64	0.11		−0.02	0.05	
Yes	186	308	−1.90	0.53		−0.69	0.35		−1.16	0.18	

Abbreviations: CaD, Calcium and Vitamin D Trial; CHD, coronary heart disease.

[a]Difference (DM-I minus DM-C) in mean blood pressure (mm Hg) at year 1. [b]Difference (DM-I minus DM-C) in slope of change in mean blood pressure (in mm Hg/year) after year 1. Aforementioned estimates were from a linear mixed effects model that included a random intercept, random slope, and the corresponding baseline BP measure as a covariate. [c]Self-report or SBP > 140 mm Hg or DBP > 90 mm Hg

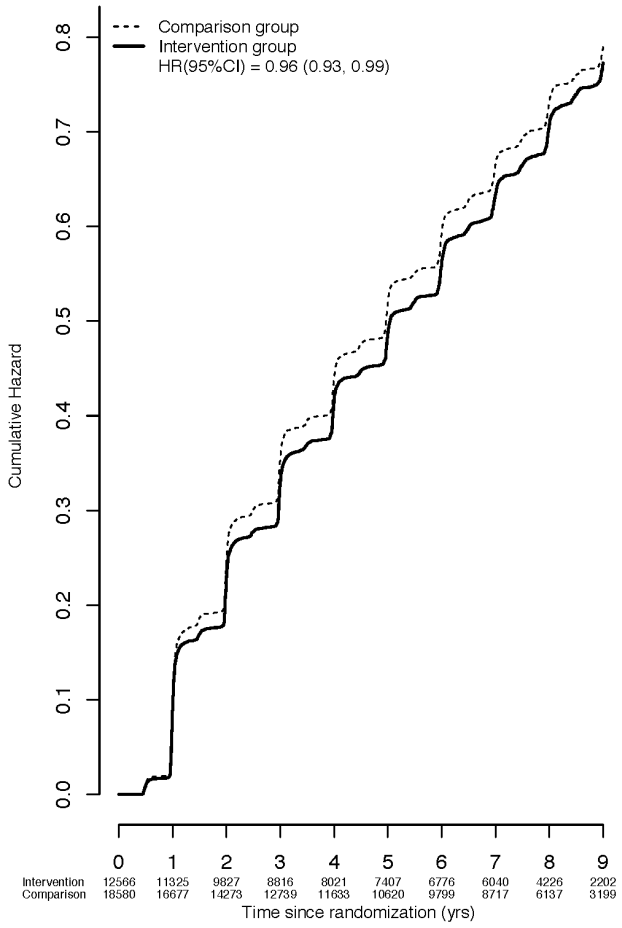

Figure 3. Kaplan–Meier estimates for incident hypertension during the intervention period by DMT arm. Solid black line, intervention group; dashed black line, control group.

of risk for self-reported incident HTN, which later leveled off and possibly diminished during the post-intervention period (*P*-value for difference in trends between periods = 0.02, see Supplementary Appendix). Consequently, there were no differences in incident HTN during extended follow-up.

When we examined changes in SBP by quartile of achieved levels of total and saturated fat, and using the entire comparison group as the reference as previously described,[2] a significant trend ($P < 0.001$) was observed toward greater reduction of SBP at year 1 among those in the intervention group who reached the lowest levels of either total or saturated fat; −1.18 and −1.15 mm Hg, respectively. These results should be interpreted with caution however, as these results utilize post-randomization behavior to characterize participants.[13]

DISCUSSION

In this trial of nearly 49,000 postmenopausal women, randomization to a dietary behavior modification intervention resulted in a small but statistically significant reduction in SBP and DBP, as well as a slightly lower risk for incident HTN, 1 year after enrollment. However, the differences were not maintained after the first few years such that the early benefit was eliminated by the 5th year of follow-up. Overall, these results demonstrate that randomization to an intervention focused on lowering total fat only did not confer long-term reduction in average blood pressure or risk of HTN in this population of postmenopausal women.

As higher blood pressure is the strongest risk factor for essentially all types of atherosclerotic CVD,[14] the lack of long-term effect of the DM-I on blood pressure levels may partially explain the lack of reduction in incident coronary heart disease, carotid disease, stroke, or total CVD reported previously for the WHI-DMT.[2,4] Additional longitudinal analyses could be performed to discern if other risk factors were significantly affected by the DMT and, thereby, provide further insight of the null effect of this trial on incident CVD in postmenopausal women.

The Dietary Approaches to Stop Hypertension (DASH) was a feeding trial that tested the efficacy of diets (i) rich in both fruits and vegetables or (ii) fruits, vegetables, and low-fat dairy products, in combination with reduced saturated and total fat on blood pressure. Compared to the control diet

Table 3. Effect of the dietary intervention on risk of incident hypertension by selected subgroups[a]

Subgroup (baseline)	Intervention *N* (%)	Comparison *N* (%)	HR[b] (95% CI)	*P*-value[c]
Age (years)				0.74
50–54	873 (6.1)	1,322 (6.2)	0.98 (0.90–1.07)	
55–59	1,456 (7.4)	2,197 (7.8)	0.95 (0.89–1.01)	
60–69	3,019 (9.9)	4,603 (10.3)	0.96 (0.92–1.01)	
70–79	1,088 (13.7)	1,616 (14.4)	0.95 (0.88–1.03)	
Race/ethnicity				0.56
White	5,295 (8.6)	8,096 (8.9)	0.95 (0.92–0.99)	
Black	634 (13.3)	878 (13.2)	1.02 (0.92–1.13)	
Hispanic	251 (8.3)	386 (9.3)	0.88 (0.75–1.04)	
African Indian	29 (8.2)	28 (8.0)	0.86 (0.47–1.57)	
Asian	146 (9.8)	228 (9.9)	1.02 (0.83–1.26)	
Body mass index				0.48
<25	1,593 (6.3)	2,465 (6.6)	0.94 (0.89–1.00)	
25 to < 30	2,368 (8.8)	3,657 (9.2)	0.95 (0.90–1.00)	
≥30	2,447 (12.4)	3,578 (12.8)	0.97 (0.92–1.02)	
CEE alone trial				0.67
Active	246 (13.5)	385 (14.1)	0.96 (0.82–1.13)	
Placebo	232 (10.7)	373 (11.5)	0.92 (0.78–1.08)	
No randomized	2,276 (9.8)	3,332 (10.0)	0.98 (0.93–1.03)	
CEE + MPA Trial				0.42
Active	383 (10.2)	552 (10.1)	0.99 (0.87–1.13)	
Placebo	328 (9.2)	478 (10.14)	0.92 (0.80–1.06)	
Not randomized	2,971 (7.8)	4,617 (8.3)	0.95 (0.90–0.99)	
CaD Trial				0.40
Active	1,157 (7.9)	1,820 (7.8)	1.01 (0.94–1.09)	
Placebo	1,138 (7.6)	1,816 (7.8)	0.97 (0.90–1.04)	
Not randomized	4,141 (9.7)	6,102 (10.4)	0.96 (0.93–0.99)	
% Energy from fat (tertiles)				0.43
<34.8%	2,158 (8.6)	3,158 (8.7)	0.99 (0.94–1.05)	
34.8 to < 39.4%	2,108 (8.7)	3,316 (9.2)	0.93 (0.88–0.98)	
≥39.4%	2,130 (9.5)	3,228 (9.9)	0.96 (0.91–1.02)	
Smoking status				0.87
Never	3,279 (8.9)	5,028 (9.4)	0.96 (0.92–1.00)	
Past	2,609 (8.8)	3,906 (9.1)	0.96 (0.91–1.01)	
Current	474 (9.4)	703(9.3)	0.99 (0.88–1.11)	
Diabetes mellitus (treated)				0.40
No	6,255 (8.8)	9,458 (9.1)	0.96 (0.93–0.99)	
Yes	181 (16.5)	278 (17.9)	0.88 (0.73–1.07)	
History of statin use				0.01
No	6,140 (8.8)	9,325 (9.2)	0.95 (0.92–0.98)	
Yes	296 (13.1)	413 (11.1)	1.16 (1.00–1.36)	
History of CHD				0.17
No	6,306 (8.9)	9,531 (9.2)	0.96 (0.93–0.99)	
Yes	50 (12.3)	90 (16.1)	0.75 (0.52–1.07)	

Table 3. Continued

Subgroup (baseline)	Intervention *N* (%)	Comparison *N* (%)	HR[b] (95% CI)	*P*-value[c]
History of stroke				0.40
No	6,401 (8.9)	9,671 (9.2)	0.96 (0.93–0.99)	
Yes	35 (11.5)	67 (13.1)	1.17 (0.74–1.83)	

[a]Excluded participants with prior history of hypertension at baseline (based on self-report of hypertension or use of antihypertensive medication). [b]Hazard ratio (95% CI) from a proportional hazards model stratified by age group, HT trial randomization group, and subgroup. [c]Corresponds to a significance test of interaction or trend.

that was low in fruits, vegetables, and dairy products, and a higher fat content, all of the DASH intervention diets resulted in significantly lower SBP and DBP levels at the end of the 8-week feeding period.[15] Notably, in the second DASH trial, participants assigned to the low-fat diet arm and who were also assigned to reduced sodium intake during the intervention period, had the greatest reductions in blood pressure at 30 days of follow-up.[16] Our results not only confirm the short-term benefits of the DASH diet but also demonstrate that long-term benefits may be harder to sustain.

The results of our analyses appear to be somewhat similar to those of the PREDIMED trial. This study randomized healthy adults to a control group or a Mediterranean diet to include selected nuts. All groups participated in quarterly group sessions conducted by dieticians. At year 1, SBP and DBP were lower in all groups. However, after 4 years of follow-up, DBP, but not SBP, was significantly lower in the intervention groups.[17,18] Since nuts are relatively high in fiber and unsaturated fatty acids,[19] this dietary constituent may have beneficial cardiovascular health benefits. Given this, the short-term effect of the DM-I on blood pressure appears to be consistent with some combination of interventions that not only reduced dietary fat intake, but also increased intake of fruits and vegetables.[20]

It is important to note that, unlike the DASH trial, the WHI-DMT intervention did not focus on CVD or, more specifically, blood pressure reduction. Nor was weight reduction a goal. Despite this, the DM-I participants lost an average weight of 2.2 kg in the first year, and maintained statistically significant lower weight than DM-C participants during follow-up, albeit diminishing somewhat over the trial period.[8] As such, the loss in weight may have contributed to the reduction in blood pressure at year 1 compared to DM-C. However, it appears the initial weight loss, and significantly lower weight throughout the study, was not sufficient to overcome other factors that resulted in the increasing SBP. This is concordant with the results of the Trials of Hypertension Prevention where, among those in the intervention group that lost significant weight, SBP rose after the first 6 months of the follow-up period.[21]

Beyond the aforementioned discussion, it is unclear why the DM-I did not result in sustained reductions in blood pressure and risk for incident HTN. One possibility is that the intensity of the intervention changed from 18 group sessions in the first year to quarterly maintenance sessions thereafter. However, prior studies of the WHI DM cohort have demonstrated good adherence to the intervention and that dietary change can be achieved and maintained over the first 5 years of a clinical trial.[22] Another is that there may be compensatory physiologic mechanisms that "resist" changes from long-term interventions. Indeed, Willett described the situation where dietary trials causing reductions in total calories from fat result in transient, but not sustained, reductions in total body fatness.[23] Perhaps this "resistance" phenomenon is translatable to blood pressure.

Strengths of our study include a very large sample size in a well-characterized cohort that was followed for an extended period of time that collected repeated measures of BP along with self-report of medications for HTN. A limitation is that the women enrolled in the WHI were all postmenopausal and relatively healthy. As such, inferences to populations dissimilar to the WHI should be made with caution. Also, the analyses of incident HTN during the WHI extension period was based on self-report.

The results of our study confirm prior findings that randomization to an intensive behavioral dietary modification program can reduce blood pressure in the short term among postmenopausal women, but such reductions may be difficult to sustain. When combined with other results from the WHI, the current findings imply that the absence of more targeted dietary intervention may have contributed to the reasons why the DMT did not significantly reduce incident CVD.

SUPPLEMENTARY MATERIAL

Supplementary materials are available at *American Journal of Hypertension* (http://ajh.oxfordjournals.org).

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DISCLOSURE

The authors declared no conflict of interest.

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