

# Effect of Soy Nuts on Blood Pressure and Lipid Levels in Hypertensive, Prehypertensive, and Normotensive Postmenopausal Women

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**Background:** Epidemiologic studies suggest a low incidence of cardiovascular disease in populations that consume dietary soy. For people aged 40 to 70 years, each increment of 20 mm Hg in systolic blood pressure (BP) or 10 mm Hg in diastolic BP doubles the risk of cardiovascular disease for BPs of 115/75 to 185/115 mm Hg.

**Methods:** To determine the effect of soy nuts on systolic and diastolic BP and lipid levels, 60 healthy postmenopausal women were randomized in a crossover design to a Therapeutic Lifestyle Changes (TLC) diet alone and a TLC diet of similar energy, fat, and protein content in which soy nuts (containing 25 g of soy protein and 101 mg of aglycone isoflavones) replaced 25 g of nonsoy protein. Each diet was followed for 8 weeks.

**Results:** Compared with the TLC diet alone, the TLC diet plus soy nuts lowered systolic and diastolic BP 9.9% and 6.8%, respectively, in hypertensive women (sys-

tolic BP  $\geq$  140 mm Hg) and 5.2% and 2.9%, respectively, in normotensive women (systolic BP  $<$  120 mm Hg). Further subdivision of normotensive women revealed that systolic and diastolic BPs were lowered 5.5% and 2.7%, respectively, in prehypertensive women (systolic BP of 120-139 mm Hg) and 4.5% and 3.0%, respectively, in normotensive women. Soy nut supplementation lowered low-density lipoprotein cholesterol and apolipoprotein B levels 11% and 8% ( $P = .04$  for both), respectively, in hypertensive women but had no effect in normotensive women.

**Conclusions:** Substituting soy nuts for nonsoy protein in a TLC diet improves BP and low-density lipoprotein cholesterol levels in hypertensive women and BP in normotensive postmenopausal women. These findings may explain a cardioprotective effect of soy.

*Arch Intern Med.* 2007;167:1060-1067

**T**HE AMERICAN HEART ASSOCIATION estimates that 50 million Americans and 1 billion individuals worldwide have hypertension.<sup>1</sup>

With 35 million office visits, hypertension is the most common primary diagnosis in the United States.<sup>2</sup> The prevalence of hypertension increases with age, and because of their survival advantage, women with hypertension outnumber men with hypertension in the older age groups.<sup>3</sup> The estimated prevalence of hypertension in women older than 45 years is 60% for white women and 79% for African American women.<sup>4</sup>

Coronary heart disease (CHD) is the most common and lethal outcome of hypertension. Women with hypertension have a 4-fold risk of CHD compared with normotensive women.<sup>4,5</sup> The relationship between blood pressure (BP) and cardiovascular disease risk is continuous such that the higher the BP, the greater the chance of myocardial infarction, heart fail-

ure, stroke, and kidney disease.<sup>6</sup> For people aged 40 to 70 years, each increment of 20 mm Hg in systolic BP or 10 mm Hg in diastolic BP doubles the risk of cardiovascular disease for BPs of 115/75 to 185/115 mm Hg.<sup>7</sup> Therefore, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure included a new category of prehypertension, with systolic BP of 120 to 139 mm Hg and diastolic BP of 80 to 89 mm Hg.<sup>6</sup> Stage 1 hypertension is systolic BP of 140 to 159 mm Hg and diastolic BP of 90 to 99 mm Hg. Stages 2 and 3 have been combined into stage 2, with systolic BP of 160 mm Hg or greater and diastolic BP of 100 mm Hg or greater.<sup>6</sup>

Antihypertensive therapy has been associated with 35% to 40% mean reductions in stroke, 20% to 25% reductions in myocardial infarction, and greater than 50% reductions in heart failure in clinical trials.<sup>8</sup> The Seventh Report of the Joint National Committee guidelines state that lifestyle

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management is important in BP control.<sup>6</sup> A 6-month trial of dietary and lifestyle changes has been recommended before initiation of medications in stage 1 hypertension.<sup>9</sup> Lifestyle modifications (and their predicted reductions in systolic BP) include weight reduction (5-20 mm Hg per 10-kg weight loss),<sup>10</sup> the Dietary Approaches to Stop Hypertension eating plan (8-14 mm Hg),<sup>11</sup> dietary sodium reduction (2-8 mm Hg),<sup>6,10-13</sup> exercise (4-9 mm Hg),<sup>14</sup> and moderation of alcohol consumption.<sup>15</sup>

The incidence of CHD and hormone-dependent cancers (breast and prostate) is lower in Asian than in Western countries, a finding thought, at least in part, to be related to consumption of dietary soy.<sup>16,17</sup> The Therapeutic Lifestyle Changes (TLC) diet is currently recommended by the Adult Treatment Panel of the National Cholesterol Education Program to lower the risk of CHD.<sup>18</sup> The present study examines the effect of soy nuts (dry-roasted soybeans) added to the TLC diet on BP in 60 postmenopausal hypertensive and normotensive women in a randomized crossover trial during an 8-week period. We sought to determine whether dietary soy had an additional benefit to the currently recommended heart-healthy diet.

## METHODS

### PARTICIPANTS

Women with absence of menses for at least 12 months or irregular periods and hot flashes were recruited. Exclusion criteria were current cigarette smoking or smoking in the previous year; clinical coronary artery disease, peripheral artery disease, or cerebrovascular disease; known diabetes mellitus or a fasting glucose level of 126 mg/dL or greater ( $\geq 7.0$  mmol/L); a history of breast cancer; a fasting triglyceride level greater than 400 mg/dL ( $> 4.52$  mmol/L); systolic BP of 165 mm Hg or greater or diastolic BP of 100 mm Hg or greater; untreated hypothyroidism; systemic or endocrine disease known to affect lipid, mineral, or bone metabolism; and consumption of more than 21 alcoholic drinks per week. Use of lipid-lowering drugs, hormone therapy, medications for osteoporosis, and soy products was discontinued for 2 months before entering the study. Participants took a multivitamin but no additional vitamin or mineral supplements or other soy products during the study. The institutional review board of the Beth Israel Deaconess Medical Center approved the protocol, and all participants gave informed consent.

### STUDY DESIGN AND DIETS

This was a randomized controlled crossover trial of the effect of one-half cup of soy nuts daily for 8 weeks on systolic and diastolic BP and lipid levels in 60 postmenopausal women. A registered dietitian instructed the participants to eat a TLC diet, which consisted of 30% of energy from total fat ( $\leq 7\%$  saturated fat, 12% monounsaturated fat, and 11% polyunsaturated fat), 15% from protein, and 55% from carbohydrate; less than 200 mg of cholesterol per day<sup>18</sup>; and 1200 mg of calcium and 2 fatty fish meals per week. Hypertensive women were counseled to limit sodium intake to less than 2 g daily. Those ingesting suboptimal dietary calcium were given calcium carbonate supplementation.

After a 4-week diet run-in, participants adherent to the TLC diet (from review of two 3-day food records) were randomized in a crossover design between 2 diet sequences for 8-week

**Table 1. Nutritional Composition of One-half Cup of Soy Nuts (56 g)**

Ingredient	Content
Calories	240
Total fat, g	8
Saturated fat, g	0
trans fat, g	0
Polyunsaturated fat, g	6
Monounsaturated fat, g	2
Cholesterol, mg	0
Total carbohydrate, g	18
Dietary fiber, g	10
Sugars, g	6
Protein, g	24
Sodium, mg	20
Potassium, mg	780
Calcium, mg	236
Aglycone isoflavones, mg	
Genistein	61
Daidzein	30
Glycitein	10

periods: the TLC diet without soy or the TLC diet with pre-packaged daily allowances of one-half cup of unsalted soy nuts (Genisoy, Fairfield, Calif) containing 25 g of soy protein and 101 mg of aglycone isoflavones (**Table 1**) divided into 3 or 4 portions spaced throughout the day. After a 4-week washout on the TLC diet alone, participants crossed over to the other arm for an additional 8 weeks. Participants were individually advised from which sources to decrease their protein intake to compensate for the 25 g of soy protein in the soy diet arm to keep protein amounts similar on both diet arms. At the end of each 8-week period, fasting blood was collected for measurement of lipid levels, and participants collected a 24-hour urine sample for measurement of isoflavone and creatinine levels.

### BP MEASUREMENTS

Women were seated quietly for at least 5 minutes in a chair at 60° to 85° with feet on the floor and the right arm supported at heart level.<sup>6</sup> A cuff bladder encircling at least 80% of the arm was used to ensure accuracy. Measurements of BP were performed using cycling Dinamaps (GE Medical Systems Information Technologies, Inc, Milwaukee, Wis) at the end of each diet period. Two readings were obtained at the beginning of each visit at least 30 seconds apart, as in the Treatment of Mild Hypertension Study.<sup>19</sup> If there was more than a 5-mm Hg difference in systolic BP between the 2 readings, a third reading was obtained. The hypertensive group of women was defined by a systolic BP of 140 mm Hg or greater or diastolic BP of 90 mm Hg or greater. The primary analysis defined normotensive women as all those with a systolic BP less than 140 mm Hg and diastolic BP less than 90 mm Hg. Normotensive women were then further divided into 2 groups: one with prehypertension (systolic BP of 120-139 mm Hg and diastolic BP of 80-89 mm Hg) and the second with systolic BP less than 120 mm Hg.

### LIPID AND APOLIPOPROTEIN B MEASUREMENTS

Plasma was separated from red blood cells at 3000 rpm for 30 minutes at 4°C and stored at -80°C. All lipid analyses were performed in a single run at the end of the study. Total cholesterol, high-density lipoprotein cholesterol, and triglyceride lev-

**Table 2. Baseline Characteristics by Blood Pressure Status\***

Characteristic	Normotensive Women (n = 48)	Hypertensive Women (n = 12)	P Value
Age, y	53.5 ± 5.3	58.3 ± 6.5	.01
BMI	25.4 ± 4.9	28.0 ± 4.3	.008
Years since menopause	4.5 ± 4.3	7.4 ± 6.1	.01
Exercise, min/wk	156 ± 118	127 ± 120	.25
Total C, mg/dL	228 ± 39	248 ± 62	.01
LDL-C, mg/dL	143 ± 32	164 ± 57	.01
HDL-C, mg/dL	58 ± 15	56 ± 10	.70
Triglyceride, mg/dL	128 ± 97	128 ± 74	.96
Apolipoprotein B, mg/dL	111 ± 19	126 ± 37	.01
Glucose, mg/dL	98 ± 10	97 ± 11	.77

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); C, cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113; glucose to millimoles per liter, multiply by 0.0555.

\*Values are given as mean ± SD.

els were measured simultaneously in the laboratory of Nader Rifai, MD, PhD, which is certified by the National Heart, Lung, and Blood Institute/Centers for Disease Control and Prevention Lipid Standardization program.<sup>20</sup> Direct low-density lipoprotein cholesterol (LDL-C) level was measured by means of a homogeneous direct method (Genzyme Corp, Cambridge, Mass).<sup>21</sup> The coefficient of variation for lipid levels was less than 3.1%. Apolipoprotein B (apoB) was measured using an immunoturbidimetric technique on the Hitachi 911 analyzer and reagents and calibrators from Wako Chemicals USA (Richmond, Va). The coefficient of variation for apoB ranged from 3.9% to 5.1% for 42.6, 88.3, and 132.8 mg/dL.

#### URINE ISOFLAVONE MEASUREMENTS, DIETARY ANALYSIS, AND EXERCISE

Isoflavones and metabolites in 24-hour urine samples were analyzed using high-performance liquid chromatography with electrochemical detection.<sup>22,23</sup> Intra-assay precision, as a percentage of relative standard deviation, ranged from 1.7% to 10.2%. An equol producer is defined as having an equol level greater than 1000 nmol/L in the urine.<sup>24,25</sup>

Nutrient intake was assessed from 3 sets of 3-day food records (with 1 day being a weekend day) for each diet arm using a software program (Nutritionist V, version 3.0; N-Squared Computing, Salem Park, Ore).

Study participants were counseled to adhere to their current exercise regimen (if active exercisers) or to walk 30 minutes daily (if sedentary) and not change their exercise throughout the study to prevent a confounding effect of weight change or exercise on study results. Study participants recorded the number of minutes of exercise performed daily throughout the study.

#### STATISTICAL ANALYSIS

Results are expressed as mean ± SD. Continuous variables were compared using 2-tailed paired (within BP group) and unpaired (normotensive to hypertensive) *t* tests. Triglyceride values were log transformed to attain a normal distribution. To examine whether there was a carryover effect from the order of diets for the 2-period crossover design, a repeated-measures analysis of variance with order and treatment as independent variables and outcome as the dependent variable

was performed. Pearson correlation coefficients were used to assess relationships between continuous variables. *P* < .05 was considered significant.

## RESULTS

**Table 2** provides the baseline characteristics by BP status. Hypertensive women (n = 12) were significantly older and heavier and had higher total cholesterol, LDL-C, and apoB levels than normotensive women (n = 48).

#### ISOFLAVONE LEVELS AND DIETARY CONTENT

Soy nut compliance was assessed using urinary isoflavone levels, which were significantly higher in the soy diet arm compared with the control diet arm for daidzein, genistein, equol, and glycitein (**Table 3**). Thirty-five women (58%) were equol producers. Levels of enterolactone, a lignan phytoestrogen found in fruits and vegetables,<sup>26</sup> were similar in the control and soy diet arms for normotensive and hypertensive women, a finding suggesting that fruit and vegetable intake was similar in the soy and control diet arms.

Analysis of dietary content revealed that polyunsaturated fat and protein levels were significantly higher and carbohydrate levels lower in the soy diet arm compared with the control diet for normotensive women, whereas there was no difference in hypertensive women (**Table 4**). Total and saturated fat contents were significantly lower on the soy diet compared with the control diet for normotensive and hypertensive women. Calcium intake was approximately 1200 mg in both diet arms. Compliance was achieved with less than 200 mg of cholesterol per day in each diet arm and close to the goal (7%) for saturated fat. These results suggest that study participants were compliant with the TLC diet.

#### EFFECT OF SOY NUTS ON BP

Soy nut supplementation significantly reduced systolic and diastolic BP in all 12 hypertensive women and in 40 of the 48 normotensive women (**Figure**). Order of diets did not affect response. Hypertensive women (mean baseline systolic BP of 152 mm Hg and diastolic BP of 88 mm Hg) had a mean 9.9% decrease in systolic BP (*P* = .003) and a 6.8% decrease in diastolic BP (*P* = .001) on the soy diet compared with the control diet (**Table 5**). Normotensive women (mean systolic BP of 116 mm Hg) had a 5.2% decrease in systolic BP (*P* < .001) and a 2.9% decrease in diastolic BP (*P* = .02) on the soy diet compared with the control diet. There was no change in BMI (calculated as weight in kilograms divided by the square of height in meters) or exercise on the soy diet vs the control diet for the normotensive and hypertensive women; therefore, neither weight change nor exercise level accounts for the lower BP in the soy diet arm. When normotensive women were subdivided into prehypertensive and normotensive women, both groups had significant reductions in systolic BP, and there was a trend toward a reduction in diastolic BP in the soy diet arm compared with the control diet arm (**Table 6**).

**Table 3. Isoflavone Concentrations in the Control vs Soy Diet Arms in Normotensive and Hypertensive Women\***

Isoflavone	Normotensive Women (n = 48)			Hypertensive Women (n = 12)		
	Control Diet	Soy Diet	P Value	Control Diet	Soy Diet	P Value
Diadzein	0.28 ± 0.66	21.25 ± 14.72	<.001	0.15 ± 0.17	14.92 ± 7.76	<.001
Genistein	0.43 ± 0.99	6.22 ± 8.39	<.001	0.21 ± 0.47	4.96 ± 3.715	.001
Equol	0.05 ± 0.19	3.97 ± 6.78	<.001	0	5.87 ± 7.11	.02
Glycitein	0.19 ± 0.68	1.61 ± 1.06	<.001	0.02 ± 0.04	1.04 ± 0.68	<.001
Enterolactone	2.70 ± 5.34	2.45 ± 3.81	.74	1.37 ± 2.06	1.41 ± 1.31	.95

\*Values are given as mean ± SD micrograms per milligram of creatinine.

**Table 4. Dietary Intake in the Control vs Soy Diet Arms in Normotensive and Hypertensive Women\***

Dietary Intake	Normotensive Women (n = 48)			Hypertensive Women (n = 12)		
	Control Diet	Soy Diet	P Value	Control Diet	Soy Diet	P Value
Kilocalories	1399 ± 317	1554 ± 349	.002	1465 ± 358	1869 ± 626	.01
Total fat, g	23.8 ± 7.0	19.1 ± 7.2	<.001	29.8 ± 6.3	23.0 ± 8.1	.003
Saturated fat, g	7.5 ± 3.3	6.3 ± 2.9	.001	8.5 ± 2.4	6.6 ± 3.0	.01
Monounsaturated fat, g	7.4 ± 4.4	6.9 ± 2.3	.37	10.5 ± 2.8	8.6 ± 3.1	.09
Polyunsaturated fat, g	4.8 ± 2.7	7.4 ± 2.3	<.001	7.1 ± 2.5	8.3 ± 2.9	.18
Protein, g	16.8 ± 3.8	20.7 ± 4.0	<.001	18.4 ± 3.8	20.0 ± 3.5	.30
Carbohydrate, g	57.2 ± 3.8	53.3 ± 4.0	<.001	48.1 ± 5.5	48.1 ± 10.9	.99
Cholesterol, mg	142 ± 62	125 ± 81	.08	192 ± 41	182 ± 70	.60

\*Values are given as mean ± SD.

#### EFFECT OF SOY NUTS ON LIPID, apoB, AND GLUCOSE LEVELS

Levels of LDL-C and apoB were significantly higher in hypertensive vs normotensive women at baseline (Table 2). Levels of LDL-C and apoB were lowered 11% and 8%, respectively ( $P = .04$  for both), on the soy diet compared with the control diet in hypertensive women, but there was no effect in normotensive participants (Table 7). In the 8 hypertensive women with LDL-C levels greater than 140 mg/dL ( $>3.63$  mmol/L), the percentage reduction in systolic BP was positively correlated with the level of equol in the soy diet arm ( $r = 0.80$ ;  $P = .02$ ). Otherwise, there were no significant correlations with BP reduction. There were no changes in glucose levels.

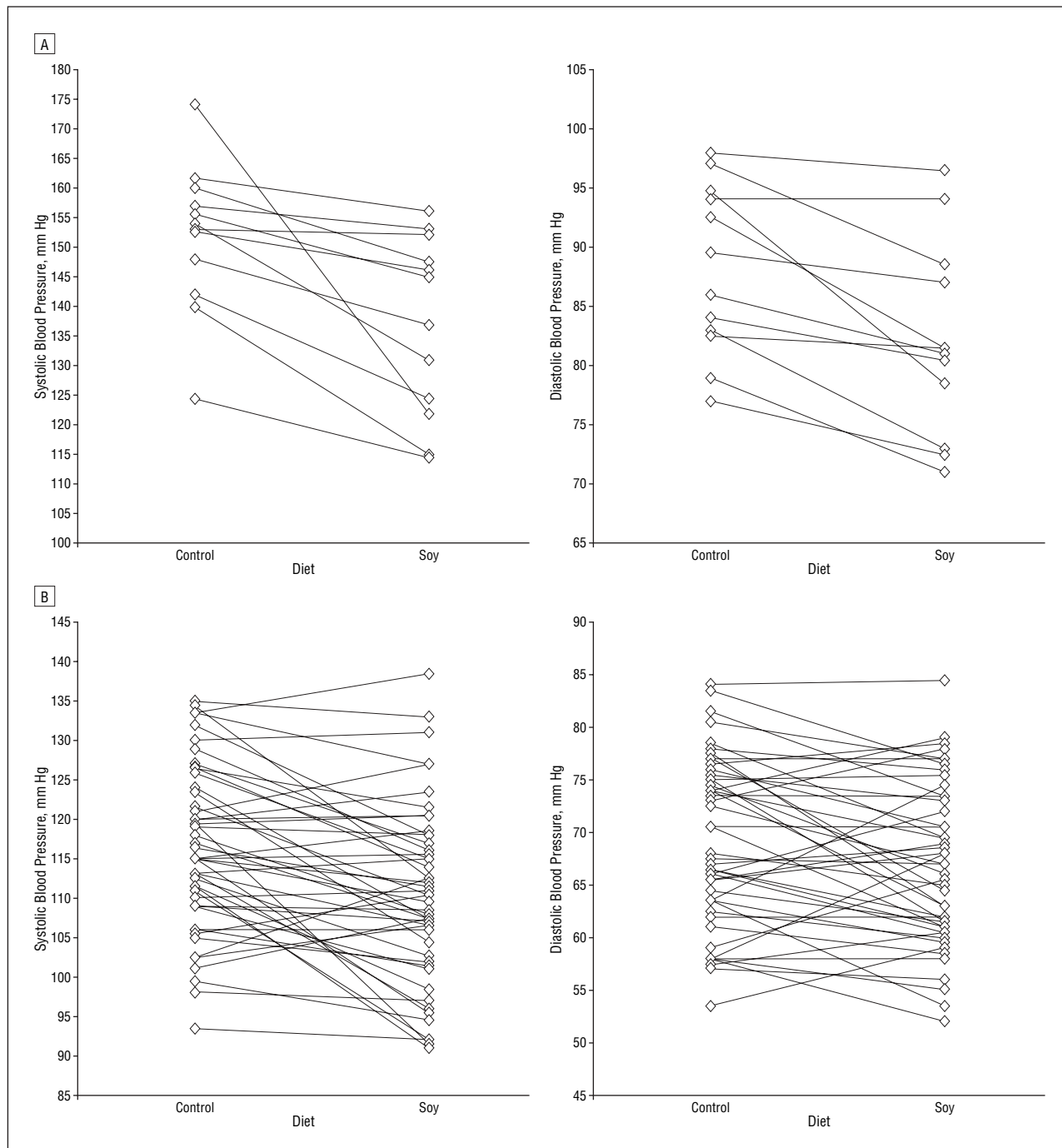
#### COMMENT

In this 8-week crossover trial, soy nuts containing 25 g of soy protein and 101 mg of aglycone isoflavones lowered BP in hypertensive and normotensive postmenopausal women compared with the TLC diet without soy. To our knowledge, this is the first study to directly compare the effects of a whole soy food in normotensive and hypertensive individuals. Hypertensive women had a 10% lower systolic BP and a 7% lower diastolic BP; these reductions in hypertensive women were twice as great as the 5% and 3% reductions, respectively, observed in normotensive women. These results are comparable with those seen with antihypertensive drugs.<sup>6,19</sup>

A 12-mm Hg decrease in systolic BP for 10 years has been estimated to prevent 1 death for every 11 patients with stage 1 hypertension treated<sup>8</sup>; therefore, the average reduction of 15 mm Hg in systolic BP in hypertensive women in the present study could have significant implications for reducing cardiovascular risk and death on a population basis. Because risk of cardiovascular disease doubles with each 20/10-mm Hg increase in BP beginning at 115/75 mm Hg,<sup>7</sup> the BP reductions in normotensive women in the present study are also important. Moreover, subdivision of normotensive women into prehypertensive and normotensive (baseline BP  $<120$  mm Hg) groups showed that both have significant reductions in systolic BP.

Modest decreases in diastolic BP can also reduce cardiovascular risk. One study<sup>27</sup> estimated that a 2-mm Hg reduction in diastolic BP (the mean reduction observed in normotensive and prehypertensive women in the present study) resulted in a 6% reduction in CHD and a 15% reduction in stroke. In a prospective, observational analysis of 420 000 individuals, a 5-mm Hg lower diastolic BP (mean reduction of 6 mm Hg observed in hypertensive women in the present study) was associated with at least 34% less stroke and 21% less CHD at mean follow-up of 10 years.<sup>28</sup> Therefore, the diastolic BP reductions in the present study would be predicted to translate into significant decreases in CHD and stroke for normotensive, prehypertensive, and hypertensive women.

One previous study has reported on the effect of a whole soy food on BP in hypertensive individuals. In a



**Figure.** Individual systolic and diastolic blood pressures after the control (Therapeutic Lifestyle Changes [TLC]) diet and the soy plus TLC diet for 8 weeks each in a crossover design for hypertensive (A) and normotensive (B) women.

3-month double-blind randomized study<sup>29</sup> of 40 men and women with mild to moderate hypertension, 500 mL of soy milk twice a day for 3 months lowered systolic BP by 18.4 mm Hg and diastolic BP by 15.9 mm Hg compared with 1.4– to 3.7-mm Hg reductions with cow’s milk ( $P<.001$ ). Several studies have examined the effect of whole soy food on BP in normotensive individuals. Freeze-dried tofu significantly lowered diastolic BP 2 mm Hg compared with meat placebo in 6 participants (2 women).<sup>30</sup> In a 4-week crossover trial,<sup>31</sup> a 52-g soy protein diet lowered BP in male patients but not in female patients, com-

pared with low-fat dairy protein. Three trials<sup>32-34</sup> found no significant effect of whole soy foods compared with nonsoy protein on BP. The active component of soy is not known. In the present study, protein, polyunsaturated fat, and isoflavone content were all higher and carbohydrate content was lower on the soy diet compared with the control diet in normotensive women. In contrast, protein, polyunsaturated fat, and carbohydrate content were similar on the soy and control diets in hypertensive women, but isoflavone content was higher on the soy diet compared with

**Table 5. Blood Pressure, BMI, and Exercise at the End of Each Diet Period in Normotensive and Hypertensive Women\***

Variable	Normotensive Women (n = 48)				Hypertensive Women (n = 12)			
	Control Diet	Soy Diet	Change, %	P Value	Control Diet	Soy Diet	Change, %	P Value
Systolic BP, mm Hg	116 ± 10	110 ± 11	5.2↓	<.001	152 ± 12	137 ± 15	9.9↓	.003
Diastolic BP, mm Hg	69 ± 8	67 ± 7	2.9↓	.02	88 ± 7	82 ± 8	6.8↓	.001
BMI	25.7 ± 5.1	25.7 ± 5.1	None	.26	28.0 ± 4.3	27.7 ± 4.3	1.0↓	.14
Exercise, min/wk	156 ± 118	143 ± 120	NA	.09	127 ± 120	152 ± 128	NA	.08
Exercise, d/wk	4.0 ± 2.3	3.7 ± 2.4	NA	.14	3.2 ± 2.6	3.1 ± 2.5	NA	.38

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); BP, blood pressure; NA, not applicable; ↓, decrease in percentage.

\*Values are given as mean ± SD.

**Table 6. Change in BP at the End of Each Diet Period in Normotensive Women Subdivided Into Prehypertensive and Normotensive Groups\***

Variable	Normotensive Women (n = 31)				Prehypertensive Women (n = 17)			
	Control Diet	Soy Diet	Change, %	P Value	Control Diet	Soy Diet	Change, %	P Value
Systolic BP, mm Hg	110 ± 7	105 ± 8	4.5↓	.003	127 ± 5	120 ± 9	5.5↓	.003
Diastolic BP, mm Hg	67 ± 7	65 ± 7	3.0↓	.06	73 ± 8	71 ± 8	2.7↓	.18
BMI	24.9 ± 4.7	25.0 ± 4.6	None	.21	27.2 ± 5.6	27.2 ± 5.7	None	.95
Exercise, min/wk	170 ± 153	156 ± 144	8.2↓	.19	163 ± 115	144 ± 114	11.7↓	.07
Exercise, d/wk	3.8 ± 2.3	3.5 ± 2.3	7.9↓	.31	4.5 ± 2.4	4.1 ± 2.5	8.9↓	.20

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); BP, blood pressure; ↓, decrease in percentage.

\*Values are given as mean ± SD.

**Table 7. Lipid and Glucose Results at the End of Each Diet Period in Normotensive and Hypertensive Women\***

Variable	Normotensive Women				Hypertensive Women			
	Control Diet	Soy Diet	Change, %	P Value	Control Diet	Soy Diet	Change, %	P Value
Total-C, mg/dL	228 ± 39	224 ± 36	1.7↓	.28	248 ± 62	230 ± 45	7.5↓	.08
LDL-C, mg/dL	143 ± 32	142 ± 31	0.7↓	.55	164 ± 57	146 ± 46	11.0↓	.04
HDL-C, mg/dL	58 ± 15	59 ± 14	1.7↑	.21	56 ± 10	56 ± 11	None	.73
Triglycerides, mg/dL	128 ± 97	119 ± 83	7.0↓	.31	128 ± 74	114 ± 50	10.9↓	.29
Apolipoprotein B, mg/dL	111 ± 19	108 ± 24	2.7↓	.25	126 ± 37	116 ± 32	8.0↓	.04
Glucose, mg/dL	98 ± 10	97 ± 9	1.0↓	.30	97 ± 11	95 ± 12	2.1↓	.27

Abbreviations: C, cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ↓, decrease in percentage.

SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113; glucose to millimoles per liter, multiply by 0.0555.

\*Values are given as mean ± SD.

the control diet. Hypertensive and normotensive women had significant reductions in BP. Taken together, these findings suggest that the isoflavone content may account for the differences in BP in the present study. Phytoestrogen supplements in the form of isolated isoflavone tablets have no effect on BP,<sup>35-41</sup> a finding suggesting that isolated isoflavones have no benefit.

A second major finding in the present study was the reduction of LDL-C and apoB with soy in hypertensive women (mean LDL-C level of 164 mg/dL [4.25 mmol/L]) in the absence of a change in weight or exercise. In these women, equol was correlated with the percentage reduction in

BP. Equol is an isoflavone that is formed during the intestinal metabolism of daidzein; it is not found in soy foods.<sup>42</sup> Not all humans can form equol. The formation of equol has been shown to affect the clinical efficacy of soy food in preventing bone loss.<sup>43,44</sup> In a retrospective analysis<sup>44</sup> of a 2-year study of the effect of 18 g of soy protein with 85 mg of isoflavones on bone mineral density, equol was formed in 45% of women; those forming equol had a 2.4% increase in lumbar spine bone mineral density compared with a 4.2% loss in lumbar spine in those receiving soy protein without isoflavones. In contrast, non-equol producers had no significant change in bone mineral density. Two

factors could potentially account for the increased efficacy of equol: (1) equol has a higher affinity for the estrogen receptor than daidzein, its precursor phytoestrogen, and (2) equol has the highest antioxidant capacity of all the isoflavones.<sup>43</sup>

In contrast to hypertensive women, normotensive women in the present study had a decrease in BP without a change in LDL-C content. These women had an average baseline LDL-C level of 143 mg/dL (3.70 mmol/L), 21 mg/dL (0.54 mmol/L) lower than hypertensive women. These results are similar to those of 2 previous studies<sup>45,46</sup> in which soy protein was more effective in lowering LDL-C levels in hyperlipidemic vs normolipidemic individuals.

Levels of triglyceride were 7% and 11% lower in normotensive and hypertensive women, respectively, in the soy diet arm compared with the control arm. Although these reductions were not statistically significant, their magnitude is similar to reductions in triglyceride levels observed in other soy studies<sup>47,48</sup> and may have clinical relevance, especially since triglyceride levels are stronger predictors of cardiovascular risk in women than in men.<sup>49-51</sup>

In conclusion, soy nuts significantly lowered systolic and diastolic BP in normotensive and hypertensive postmenopausal women and lowered levels of LDL-C and apoB in hypertensive, hyperlipidemic women. This study was performed in the free-living state; therefore, dietary soy may be a practical, safe, and inexpensive modality to reduce BP. If the findings are repeated in a larger group they may have important implications for reducing cardiovascular risk in postmenopausal women on a population basis.

**Accepted for Publication:** January 26, 2007.

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**Author Contributions:** Dr Welty had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Welty and Lee. *Acquisition of data:* Welty, Lee, and Zhou. *Analysis and interpretation of data:* Welty, Lee, Lew, and Zhou. *Drafting of the manuscript:* Welty and Lew. *Critical revision of the manuscript for important intellectual content:* Welty, Lee, Lew, and Zhou. *Statistical analysis:* Welty. *Obtained funding:* Welty. *Administrative, technical, and material support:* Welty, Lee, and Lew. *Study supervision:* Welty and Zhou.

**Financial Disclosure:** None reported.

**Funding/Support:** This study was funded by the Harvard Medical School's Center of Excellence in Women's Health (National Institutes of Health); contract 00T002244 from the Office on Women's Health, Department of Health and Human Services; and in part by grant RR 01032 to the Beth Israel Deaconess Medical Center General Clinical Research Center from the National Institutes of Health.

**Acknowledgment:** We are grateful to the study participants for their time and to Genisoy for donating the soy nuts.

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