ORIGINAL STUDY

The Women’s Study for the Alleviation of Vasomotor Symptoms (WAVS): a randomized, controlled trial of a plant-based diet and whole soybeans for postmenopausal women

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Abstract

Objective: This study aimed to assess the effects of the combination of a low-fat plant-based diet and soybeans on the frequency and severity of menopausal hot flashes.

Methods: Postmenopausal women (n = 38) reporting two or more hot flashes/day were randomly assigned to a low-fat, vegan diet, including 1/2 cup (86 g) of cooked soybeans daily, or to no diet changes for 12 weeks. Frequency and severity of hot flashes were recorded using a mobile application, and vasomotor, psychosocial, physical, and sexual symptoms were assessed using the Menopause-Specific Quality of Life Questionnaire. Significance was assessed using t-tests (continuous outcomes) and chi-squared/McNemar tests (binary outcomes).

Results: Total hot flashes decreased 79 % in the intervention group (P < 0.001) and 49% in the control group (P = 0.002; between-group P = 0.01). Moderate-to-severe hot flashes decreased 84% in the intervention group (P < 0.001) and 42% in the control group (P = 0.009; between-group P = 0.01). From 0 to 12 weeks, 59% (10/17) of intervention-group participants reported becoming free of moderate and severe hot flashes (P = 0.002). There was no change in this variable in the control group (between-group P < 0.001). The Menopause-Specific Quality of Life Questionnaire revealed significantly greater reductions in the intervention group in vasomotor (P < 0.0001), psychosocial (P = 0.04), physical (P < 0.002), and sexual (P = 0.01) domains.

Conclusions: The combination of a low-fat, vegan diet and whole soybeans was associated with reduced frequency and severity of hot flashes and improved quality of life in vasomotor, psychosocial, physical, and sexual domains in postmenopausal women. During the 12-week study period, the majority of intervention-group participants became free of moderate-to-severe hot flashes.

Key Words: Diet – Hot flashes – Isoflavones – Menopause – Nutrition – Plant-based – Soy – Vegan.

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M any peri- and postmenopausal women experience hot flashes—episodes of peripheral vasodilation causing sensations of warmth in the chest, neck, and face, accompanied by sweating and flushing. Hot flashes can also be caused by medications and procedures that alter hormone function. Evidence suggests that dietary factors influence the occurrence of menopause-related hot flashes. In the 1980s, a large study of women living in Japan found hot flashes to occur less frequently than in Western countries.\(^1\) Similar findings were reported in other Asian countries.\(^2,3\) Cultural differences in symptom reporting may have contributed to these differences. It is also noteworthy that traditional diets in these areas emphasized plant-derived staples, such as rice, vegetables, and, in some cases, soy products. As Japan’s diet westernized late in the last century, hot flashes were reported twice as frequently as in the 1980s.\(^4\) In randomized trials, soy products have been shown to reduce the frequency of hot flashes.\(^5\) Soy products contain the isoflavones genistein, daidzein, and glycitein and their respective glycosides. In turn, daidzein can be metabolized by gut bacteria into equol, a nonsteroidal compound that binds to both estrogen receptors \(\alpha\) and \(\beta\), but functions mainly as an estrogen receptor-\(\beta\) agonist.\(^6\) Reportedly, 50% to 60% of Asian adults produce equol, compared with only 20% to 30% of western adults, apparently due to dietary differences that influence gut bacterial populations.\(^6\) Plant-based diets rapidly modify gut bacterial populations.\(^7\) Some studies have found that people following mostly vegetarian diets produce equol more frequently than do omnivores.\(^6,8\)

These studies suggest that a plant-based diet and daily soybean consumption may reduce the frequency of hot flashes and that this combination may be more helpful than either a diet change or soy supplementation alone. Of particular clinical value are studies in women preparing their own foods in real-life conditions. Because such studies cannot be blind, appropriately chosen control groups and redundant measures for vasomotor symptoms are helpful. Therefore, a controlled trial tested the hypothesis that a low-fat, vegan diet, including soybeans, would reduce the frequency and severity of postmenopausal hot flashes.

**METHODS**

The study was approved by the Advarra Institutional Review Board on September 2, 2020 (Pro00045315). Women with postmenopausal hot flashes were recruited through social media and screened by telephone (Fig. 1). Inclusion criteria were postmenopausal women aged 40 to 65 years, moderate-to-severe hot flashes at least twice daily, last period within the preceding 10 years, no menses in the preceding 12 months, and willingness to follow a low-fat vegan diet, including soybeans. Exclusion criteria were use of hormonal medications in the preceding 2 months, an explanation for hot flashes other than natural menopause, smoking, substance abuse, history of an eating disorder, use of weight-loss medications in the preceding 6 months, a current attempt to lose weight, a body mass index less than 18.5 kg/m\(^2\), soy allergy, and current consumption of a low-fat vegan diet with daily soy intake. Volunteers who met the eligibility criteria, provided consent, and completed a practice dietary record were assigned to an intervention group or control group using a computer-generated random-number table. Because assignment was done simultaneously, allocation concealment was unnecessary.

**Outcome measures**

The following measures were assessed at baseline and week 12, except as noted:

**Dietary intake**

A 3-day dietary record, including 2 weekdays and 1 weekend day, was analyzed using Nutrition Data System for Research software version 2020, by staffers of the Nutrition Coordinating Center, University of Minnesota.

**Body weight**

Participants used identical digital scales (Renpho Model ES-CS20 M, Anaheim, CA) accurate to 0.05 kg.

**Height**

Participants were asked to report their height to the nearest 0.5 cm, using a tape measure at home (baseline only).

**Health status and medications**

Participants were asked to report their general health status and all medication use.

**Physical Activity**

The International Physical Activity Questionnaire short form quantifies recent physical activity, multiplying MET values for specific activity levels by the minutes activities were carried out and by the number of days each activity was undertaken.\(^6\)

**Menopausal symptoms**

Using the My Luna mobile application (Blue Trail Software Holding, San Francisco, CA), participants were asked to record hot flashes as they occurred, including times of onset and cessation, and their intensity, for 7 days. Hot flashes that awakened participants during sleep were to be registered on the application the following morning.

The Menopause-Specific Quality of Life Questionnaire (MENQOL) assessed the effect of menopausal symptoms on quality of life in four domains: vasomotor, psychosocial, physical, and sexual.\(^10,11\) The vasomotor domain asks participants to rate the degree to which they are bothered by (1) hot flushes or flashes, (2) night sweats, or (3) sweating, using a scale ranging from 0 (not bothered at all) to 6 (extremely bothered).

**Dietary intervention**

The intervention group was asked to follow a low-fat, vegan diet, based on fruits, vegetables, whole grains, and legumes and to minimize added oils and fatty foods (eg, nuts,
nut butters, and avocados). They were provided with non-genetically modified soybeans (Laura Soybeans, Corwith, IA) and were asked to consume \( \frac{1}{2} \) cup (86 g) of cooked whole soybeans daily. No other foods were provided. To facilitate soybean preparation, participants (in both groups) who did not already have pressure cookers were provided with them (Instant Pot, Instant Brands, Kanata, Ontario, Canada). Intervention group participants were asked to attend weekly, 1-hour group sessions via an Internet conference platform (Zoom). All sessions were conducted by a registered dietitian, physician, or members of the research staff and included information on meal planning, shopping, food preparation, and handling everyday dietary challenges. Each participant was asked weekly about adherence to the dietary intervention (omission of animal-derived foods, minimizing oils, and consuming soybeans), although formal dietary adherence assessment was limited to analysis of 3-day dietary records.

Control group participants were asked to maintain their customary diets, maintain weekly contact with the research team to report body weight and symptoms, and attend four 1-hour group sessions during the study, and were provided with pressure cookers. At the study’s conclusion, control group participants were offered detailed instruction in the dietary intervention. For both groups, alcoholic beverages were limited to one per day. Appropriately planned plant-based diets are generally adequate in all nutrients, except for vitamin B\(_{12}\). All participants in both groups were provided with a daily 100 \( \mu \)g vitamin B\(_{12}\) supplement. Participants wishing to follow a vegan diet after study completion were counseled to use a vitamin B\(_{12}\) supplement. All participants were asked to avoid other new dietary supplements and to keep their physical activity and medications constant, except as recommended by their personal physicians. Because the study occurred during the

**FIG. 1.** Participant flow through the trial. MENQOL, The Menopause Specific Quality of Life Questionnaire.
Covid-19 pandemic, it was conducted via telephone, email, and videoconferencing. All questionnaires and data sheets were coded with identification numbers and were maintained on a passcode-protected, secure server. Data collected via Qualtrics Survey Software were stored on a secure Qualtrics account using Transport Layer Security encryption and maintaining FEDramp and ISO 27001 certifications.

**Statistical procedures**

To the investigators’ knowledge, no prior study has examined the effects of a vegan diet along with whole cooked soybeans on hot flashes; studies using soy extracts or isoflavones did not provide an adequate basis for a power analysis. The current study was therefore conducted to generate initial data on effect sizes and variability. The investigators aimed to enroll up to 40 participants evenly divided between study groups.

Descriptive statistics for demographic and clinical variables were calculated for each group. To assess significance of baseline differences between the study groups, t-tests were calculated for continuous measures and exact versions of appropriate chi-squared-type tests used for categorical measures.

For all measures, descriptive statistics (means, standard deviations, standard errors) were calculated. As distributions of all outcomes did not substantially depart from approximate normality, parametric tests were used to assess treatment effects. Specifically, hypotheses were examined by performing t tests for two independent samples on the difference score denoting change from baseline to week 12. For binary outcomes, the chi-square test or Fisher exact test was used to assess between-group differences, whereas the exact McNemar test was used for assessing significance of within-group changes.

**RESULTS**

Of 786 individuals replying to the request for volunteers, 631 were excluded before a personal interview, and 155 were interviewed by telephone (Fig. 1). After exclusions, 38 participants were randomly assigned to the two study groups. Intervention-group participants were slightly younger than controls, with slightly more recent cessation of menses (Table 1). One intervention-group participant and one control-group participant failed to complete the MENQOL at week 12, leaving 36 participants for the MENQOL analysis. These 2 individuals and 1 additional participant in each group failed to provide final body weights and mobile application data, leaving 34 participants for the analysis of body weight and hot flash frequency and intensity. Clinical changes are reported in Table 2. Significant nutrient intake changes were reported in the intervention group. Physical activity did not change significantly in either group. Mean body weight decreased by 3.5 kg in the intervention group and increased by 0.8 kg in the control group ($P = 0.0021$). The frequency of total hot flashes, as reported with the My Luna application, decreased 79% in the intervention group ($P < 0.001$) and 49% in the control group ($P = 0.002$; between-group $P = 0.01$). Moderate-to-severe hot flashes decreased 84% (from 4.9 to 0.8/day) in the intervention group ($P < 0.001$) and 42% (from 3.8 to 2.2/day) in the control group ($P = 0.009$; between-group $P = 0.013$). Nighttime moderate-to-severe hot flashes also decreased significantly more in the intervention group ($P = 0.0286$). From 0 to 12 weeks, 59% (10/17) of intervention-group participants reported becoming free of moderate or severe hot flashes ($P = 0.002$). In the control arm, there was no change in this variable (6% at each time point, between-group $P = 0.0003$). The MENQOL questionnaire revealed significant reductions in the intervention group in hot flashes, night sweats, sweating, and the composite vasomotor, psychosocial, physical, and sexual domains, all of which were

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**TABLE 1.** Baseline demographics of participants in a randomized trial of a dietary intervention for vasomotor symptoms

|                                      | Intervention group (n = 19) | Control group (n = 19) | $P$  |
|--------------------------------------|----------------------------|------------------------|------|
| Mean age, y (SD)                     | 53.3 (4.4)                 | 55.5 (4.1)             | 0.12 |
| Age range                            | 42-60                      | 49-64                  |      |
| Race and ethnicity                   |                            |                        |      |
| Black, non-Hispanic                  | 2 (11%)                    | 4 (21%)                | 0.66 |
| Native American, non-Hispanic        | 1 (5%)                     | 0 (0%)                 | 1.0  |
| White, non-Hispanic                  | 15 (79%)                   | 14 (74%)               |      |
| White, Hispanic                      | 1 (5%)                     | 1 (5%)                 |      |
| Marital status                       |                            |                        | 0.45 |
| Not married                          | 3 (16%)                    | 6 (32%)                |      |
| Married                              | 16 (84%)                   | 13 (68%)               |      |
| Education                            |                            |                        |      |
| High school, partial or graduate     | 1 (5%)                     | 0 (0%)                 | 1.0  |
| College, partial or graduate         | 9 (47%)                    | 12 (63%)               |      |
| Graduate degree                      | 9 (47%)                    | 7 (37%)                |      |
| Body mass index in kg/m² (SD)        | 26.8 (7.6)                 | 27.4 (5.2)             | 0.77 |
| Years since menopause, mean (SD)     | 3.7 (2.9)                  | 5.6 (2.6)              | 0.044|

$^a$P values refer to t tests for continuous variables and exact test (Fisher for marital status and Mantel-Haenszel for ordered education) for categorical variables.

$^b$P value calculated for race distribution (Black vs Native American vs White): $P = 0.66$ by Fisher exact test. For ethnicity (Hispanic vs non-Hispanic), $P = 1.0$ by Fisher exact test.
### TABLE 2. Nutrient intake, physical activity, body weight, and menopausal symptoms at baseline and 12 weeks<sup>a</sup>

|                      | Intervention group | Control group | Effect size<sup>b</sup> | P<sup>c</sup> |
|----------------------|--------------------|---------------|--------------------------|--------------|
| **Dietary intake**   |                    |               |                          |              |
| Energy (kcal/d)      | 1,505 (1,247-1,764) | 1,558 (1,323-1,839) | 62.1 (349.3 to 225.1) | 0.66         |
| Total fat (g/d)      | 59.1 (43.6-74.5)   | 58.8 (46.1-71.5)   | 22.9 (43.5 to -2.4)   | 0.0297       |
| Saturated fat (g/d)  | 17.8 (10.0-25.5)   | 14.5 (10.0-18.9)   | 12.6 (21.7 to -3.6)   | 0.0081       |
| Carbohydrates (g/d) | 193.2 (152.2-234.2)| 220.7 (175.7-265.7)| 443.3 (1.1 to 84.6)  | 0.0318       |
| Protein (g/d)        | 59.5 (49.5-69.5)   | 57.2 (46.1-68.4)   | 5.0 (8.4 to 18.5)     | 0.45         |
| Fiber (g/d)          | 30.1 (22.8-37.5)   | 32.9 (25.5-40.3)   | 16.0 (8.8 to <23.2)   | <0.001       |
| **Physical activity**|                    |               |                          |              |
| BMI (kg/m²)          | 72.9 (63.4-82.3)   | 74.3 (67.0-81.6)   | 4.3 (6.9 to -1.8)     | 0.0021       |
| Hot flashes total    | 6.2 (4.6-7.7)      | 4.9 (3.0-6.8)      | 2.5 (4.5 to 0.6)      | 0.0104       |
| Hot flashes mod-severe| 4.9 (3.4-6.4)   | 3.8 (2.3-5.4)      | 1.7 (2.8 to -0.5)     | 0.0134       |
| Individuals with any mod-severe hot flashes | 17 (100%) | 16 (94%) | 0 (0%) | 0.0003 |
| Nighttime hot flashes | 4.6 (3.3-6.0) | 3.2 (2.0-4.5) | -2.0 (3.5 to -0.5) | 0.0103 |
| Nighttime hot flashes | 3.6 (2.4-4.8) | 1.7 (0.9-2.4) | -0.8 (1.4 to -0.2) | 0.06 |
| Nighttime hot flashes | 1.6 (1.1-2.1) | 1.0 (0.7-1.6) | -0.2 (0.8-0.1) | 0.0128 |
| **SEXUAL**           |                    |               |                          |              |
| Vasoconstrictor      | 5.9 (5.2-6.7)      | 5.9 (5.5-6.4)      | -2.5 (3.5 to -1.6)    | <0.0001      |
| Psychosocial         | 3.6 (2.5-4.7)      | 3.5 (2.6-4.3)      | -0.1 (1.1 to 0.0)     | 0.0432       |
| Physical             | 3.8 (3.1-4.5)      | 3.6 (3.0-4.3)      | -1.4 (2.2 to -0.6)    | 0.0015       |
| Sexual               | 4.6 (3.3-5.9)      | 3.7 (2.5-4.9)      | -1.9 (3.3 to -0.5)    | 0.0103       |

<sup>a</sup>Data are for all participants who provided data at both baseline and 12 weeks.

<sup>b</sup>Values in this column represent differences between the mean change scores of the intervention group and those of the control group; 95% CIs in parentheses.

<sup>c</sup>P values refer to t tests for between-group (intervention compared with control) comparisons of changes from baseline to final values, except that proportion of women with any moderate-to-severe hot flashes (at baseline and persisting at week 12) were compared with Fisher exact test.

<sup>d</sup>Nonparametric 95% CI from 10,000 bootstrap samples, as 7/17 Intervention participants had week 12 cholesterol intake of 0.

<sup>e</sup>Numbers signify hot flashes per 24 hours as reported using the My Luna mobile application; N = 17 intervention, 17 control.

<sup>f</sup>Exact 95% CI, among women reporting moderate/severe hot flashes at Week 0.

<sup>g</sup>For the within-group changes, the P values are marked as:

For P < 0.05.

For P < 0.001.
greater than the changes in the control group (effect sizes: vasomotor −2.5 [95% CI −3.5 to −1.6], P < 0.0001; psychosocial −1.2 [95% CI −2.4 to −0.04], P = 0.04; physical −1.4 [95% CI −2.2 to −0.6], P = 0.002; and sexual −1.9 [−3.3 to −0.5], P = 0.01).

**DISCUSSION**

The frequency of hot flashes, particularly moderate-to-severe hot flashes, decreased to a significantly greater degree in the intervention group, compared with the control group. At 12 weeks, the majority of intervention-group participants reported no moderate-to-severe hot flashes at all. This finding, based on real-time reporting on a mobile application, was confirmed in the MENQOL questionnaire responses. Body weight also decreased significantly in the intervention group. In Western countries, vasomotor symptoms occur in up to 80% of menopausal women. In the 1980s, Lock surveyed 1,225 women, aged 45 to 55 years, living in Nagano, Kyoto, and Kobe, Japan. Hot flashes during the previous 2 weeks were reported by 13.5% of perimenopausal women and 15.2% of postmenopausal women. Cultural differences in symptom reporting and in dietary practices that may underlie these differences in vasomotor symptoms have been investigated. Between 1975 and 2009, per capita meat consumption (other than fish and shellfish) in Japan increased from 23 to 45.9 kg, although this figure remained far below the US figures (120.2 kg in 2009). Dairy consumption increased greatly, as did overall fat and protein intake. Dietary changes in Japan were paralleled by changes in menopausal symptoms. In a 2005 study, hot flashes were reported twice as frequently as in the 1980s. Hot flashes in the preceding 2 weeks were reported by 42.1% of late-perimenopausal women. Despite Westernization, soy intake remains much higher in Japan, compared with the United States, suggesting that overall dietary changes, rather than changes in soy intake, may be responsible for the increasing vasomotor symptom frequency. Research in China, Mexico’s Yucatan Peninsula, and other countries has shown marked variations in symptom reporting, reflecting differences in culture, diet, and other factors. Soy isoflavonones have greater affinity for estrogen receptor-β than estrogen receptor-α and have both estrogen-agonist and estrogen-antagonist properties. In controlled trials, soy isoflavonones have proven helpful in the treatment of hot flashes. The soybeans (1/2 cup, 86 g) used in the present study would be expected to deliver approximately 55 to 60 g of isoflavonones, similar to the amounts commonly used in clinical trials (approximately 30-80 mg/day) and slightly greater than amounts consumed in Japan or China (approximately 30-40 mg/day). Daidzein can be metabolized by gut bacteria to produce equol, which has been shown in some studies to reduce hot flash incidence or severity. The conversion of daidzein to equol has been identified in 20% to 30% of Western omnivorous adults and >50% of Asians. These differences are likely attributable, not to genetics or to habitual soy consumption, but to the overall diet. When omnivores increase consumption of plant-derived foods, the gut microbiome changes rapidly. These shifts may favor equol production. An Australian study of 29 individuals following mostly vegetarian diets found that 59% were able to produce equol, compared with 25% of 12 nonvegetarians. In a US study of 15 vegans and 16 omnivores, these figures were 40% and 0%, respectively. Some have suggested that vasodilation is a counter-regulatory neurovascular response to impaired glycemic control caused by reduced estrogen availability. If sustained, it is noteworthy that plant-based diets improve glycemic control in adults with and without type 2 diabetes. Hot flashes also diminished in the control group, albeit to a lesser degree than in the intervention group. This may reflect (1) the natural decline in symptoms after menopause, (2) cooler temperatures approaching the study conclusion in December, or (3) control group participants’ awareness of the vegan dietary intervention (buttressed by weekly staff contact and the provision of pressure cookers) and their eagerness to implement it, despite being asked not to. This study has several advantages. The inclusion of nonconfined individuals provided findings that readily translate to nonclinical settings. The use of whole soybeans complements findings based on extracts. Use of a mobile application for recording vasomotor events may be more thorough than paper-and-pencil recording and is more convenient than galvanic skin response monitoring. The design also has limitations. The sample size was relatively small, and the 12-week intervention did not assess longer-term effects. In intervention trials in noninstitutionalized individuals using whole diets, blinding is impracticable. Such studies are nonetheless crucial. While placebo effects cannot be ruled out in the present study, some confidence comes from the fact that improvements were consistent between questionnaire responses and real-time vasomotor symptom recording using the mobile application (including participants’ recollections of nighttime symptoms awakening them from unconsciousness) and were paralleled by weight changes. Reporting of food intake and menopausal symptoms can be inaccurate. Although contact with volunteers was frequent, the Covid-19 pandemic necessitated that contact be via Zoom, telephone, and email. To address this challenge, participants used identical digital scales and reporting procedures and maintained weekly contact with the research team. The study leaves for future investigations to identify the relative roles of a plant-based diet and soy supplementation, and the role of diet-induced microbiome changes in isoflavone metabolism.

**CONCLUSIONS**

The combination of a low-fat plant-based diet and whole soybeans was associated with reduced frequency and severity of hot flashes, the elimination of moderate-to-severe hot flashes for the majority of participants, and quality-of-life improvements in vasomotor, psychosocial, physical, and sexual domains.

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