



Self-reported menopausal symptoms in a racially diverse population and soy food consumption

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ABSTRACT

Objectives: Evaluate the association of self-reported vasomotor symptom (VMS) frequency with race/ethnicity among a diverse midlife US population and explore menopause symptom differences by dietary soy isoflavone (genistein + daidzein) consumption.

Study design: Cross-sectional population-based study of peri- and postmenopausal women, ages 45–58. **Outcomes:** Recent VMS frequency, VMS ever; recent symptom bother (hot flashes, night sweats, headache and joint-ache).

Results: Of 18,500 potentially eligible women, 9325 returned questionnaires (50.4% response); 3691 were excluded (premenopausal, missing data, taking hormones). Of 5634 remaining women, 82.1% reported hot flashes ever, 73.1% reported night sweats ever; 48.8% and 38.6% reported recent hot flashes or night sweats, respectively. Compared with White women, Chinese, Japanese, Vietnamese, other Asian (each $p < 0.001$) and Filipino ($p < 0.01$) women less commonly reported ever having hot flashes; Asian women less commonly reported recent VMS bother ($p < 0.001$). Black women more commonly reported hot flashes ever ($p < 0.05$) and recent VMS bother ($p < 0.05$). Compared with non-Hispanic White women, Hispanic women were less likely to report hot flashes ($p < 0.05$) or night sweats ($p < 0.001$) ever. Women were classified by isoflavone consumption: (1) none ($n = 1819$), (2) 0.01–4.30 mg/day ($n = 1931$), (3) 4.31–24.99 mg/day ($n = 1347$) and (4) ≥ 25 mg/day ($n = 537$). There were no group differences in recent VMS number/day: (1) 7.0 (95% CI 6.5, 7.5); (2) 6.4 (95% CI 6.0, 7.1); (3) 7.0 (95% CI 6.3, 8.2); and (4) 6.8 (95% CI 6.1, 7.7).

Conclusions: Menopausal symptoms, independent of isoflavone intake, varied considerably by race/ethnicity and were least common among Asian races.

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1. Introduction

The prevalence of vasomotor symptoms (VMS), or hot flashes and night sweats, is lower in Asian than in North American and European countries; 10–25% of Chinese women and 10–20% of Indonesian women report VMS compared with 60–90% of North American and European women [1–3]. These findings are hypothesized, at least in part, to be related to soy-rich diets [4], but a full understanding of how race/ethnicity affect menopausal symptoms remains elusive. The Study of Women's Health Across the Nation (SWAN) evaluated VMS by race/ethnicity and found that, in the United States, Black and Hispanic women were more likely, and Japanese and Chinese women less likely than White women to

report VMS; diet did not appear to modify this association [3]. Little additional information about VMS among midlife US women from diverse ethnic backgrounds exists, particularly related to soy diet intake. Other studies have compared cross cultural differences in the menopausal experience, but mainly describe differences in the menopausal experience observed between countries [5].

Soy intake varies dramatically country to country and by racial/ethnic groups within a country. The average daily soy intake is four to nine times greater in Asian countries than in North American and European countries (e.g. soy intake of 17–36 g in Japan, Korea, Taiwan, and Indonesia compared with approximately 4 g in the United States) [6]. It is suggested that variation in hot flash relief from soy may be due to variability in a woman's ability to metabolize isoflavones, possibly related to race [7–9]. Soy foods are a rich source of three isoflavones: daidzein, genistein, and glycitein. A daidzein metabolite, equol, is a principal isoflavonoid produced by gut bacteria [10], and it is hypothesized that equol may be primarily responsible for VMS symptom relief [9,11,12]. Approximately 50% of Japanese women and 20–30% of US women have gut bacteria able

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to produce equol [9,13–15]. Thus, a large study is needed to appreciate differences in relief of VMS associated with soy diet when evaluated in US populations due to a low prevalence of women capable of producing equol and an even lower prevalence of soy consumed by US women.

Questions remain about the impact of race/ethnicity on VMS [5] and the effects of soy diet on this association. In this large, cross-sectional analysis we describe the associations between self-reported hot flashes and night sweats with race/ethnicity among healthy midlife US women of diverse racial and ethnic backgrounds, living in the greater Seattle area, and not using hormone therapy. This cross-sectional survey was the first part of the Lifetime Exposures And Vasomotor (e) Symptoms, LEAVeS, study designed to evaluate the association of VMS with isoflavone-metabolizing phenotypes, specifically equol. Using baseline survey data, we report differences in frequencies and bother of reported menopausal symptoms by race/ethnicity, independent of soy intake, and stratified by soy intake. Findings from the smaller subset of women analyzed by equol phenotype will be reported separately.

2. Methods

2.1. Location

This study was performed at Group Health (GH), a large, mixed-model, nonprofit health care system, located in the Pacific Northwest that coordinates care and coverage for approximately 675,000 enrollees.

2.2. Inclusion/exclusion

Women had to have been enrolled in GH for at least one year, received care at a GH-owned facility, and have resided within 50 miles of the research clinic. Women were eligible if they did not use hormones, did not have intestinal or malabsorption syndromes, were without colectomy, without cancer, and did not use antibiotics in the prior 3 months. Women were age 45–58 (the age group most likely to have VMS and to be peri- or early postmenopausal) [16]. Women with regular menses were considered premenopausal and were excluded from the analysis. In addition, those who were unable to read English, or were mentally or legally incapacitated such that informed consent could not be obtained, or those who intended to move within the next month rendering follow-up impossible were also excluded.

2.3. Procedure

The GH electronic databases were used to identify potential study participants using data on age, gender, enrollment start and termination dates, and coverage type. Electronic medical records were used to identify body mass index (BMI; kg/m²), illnesses or medications that could interfere with isoflavone metabolism and medications that could affect VMS. Pharmacy fill dates were used to exclude women who had used systemic estrogen and/or progestin, selective estrogen receptor modulators, or oral contraceptives (prior 6 months) or antibiotics (prior 3 months). Previous studies indicate that enrollees receiving care in GH-owned facilities fill nearly all their prescriptions at GH-owned pharmacies [17]. A total of 18,500 potentially eligible women were identified. The sample was representative of the underlying population of GH.

Recruitment occurred through a series of direct mailings (March 2010–February 2011), a magazine advertisement and announcements on informational screens with rotating messages in all GH pharmacies. An introductory letter, the survey and consent form were mailed to potentially eligible women. A \$2 incentive was

included in the first mailing. Mailings were repeated twice and a reminder postcard was sent between the two mailings.

The mailed survey assessed menopausal status, basic demographics, VMS frequency and bother, soy food intake and confirmed absence of medications or health conditions that precluded participation. The survey also asked detailed information about race/ethnicity, providing 15 different choices and a write-in option. Final analyses included the 10 most common racial groups, “mixed”, “other” and Hispanic (yes/no). Women who reported 2 racial categories and one category was White, were classified in the non-White category. Women who reported 2 or more non-White categories were classified as “mixed” and those who wrote in an uncommon racial grouping were classified as “other”. Self-reported VMS frequency and bother in the past 2 weeks (characterized as none, a little, moderate, a lot) were assessed. Bother from headache and joint ache/pain in the past 3 months were also assessed (yes and no).

Women with a uterus were classified as menopausal transition (skipped at least one menses in the past 12 months) or postmenopausal (absence of menses for greater than 12 months). Women were classified as surgically postmenopausal if they had had bilateral oophorectomy. Women with hysterectomy with retained ovaries were classified as menopausal transition if they were 45–52 years and if they had skipped at least one menses in the 12 months prior to hysterectomy and were classified as postmenopausal if they were over 52 or if they were 45–52 and had absence of menses for over 12 months prior to hysterectomy (without hormone usage).

We estimated daily isoflavone (genistein + daidzein) intake, using a validated soy food questionnaire [18]. Women were classified by isoflavone consumption as: Group 1, 0 mg/day; Group 2, 0.01–4.30 mg/day; Group 3, 4.31–24.99 mg/day; and Group 4, ≥25 mg/day. Values were set by design to divide women into tertiles, with the highest tertile then separated into two (Groups 3 and 4). Women with consumption of ≥25 mg of isoflavone/day had intakes approaching those reported elsewhere among women taking isoflavone extracts who achieved VMS relief [6,19].

2.4. Analyses

We performed descriptive statistics and generalized linear model (GLM) for statistical inference. Specifically, we evaluated whether hot flashes or night sweats ever, VMS bother, headache or joint pain bother varied by detailed classifications of race/ethnicity, using logistic regression, and adjusting for age and BMI. We also evaluated the association of self-reported VMS frequency and bother in the past 2 weeks with isoflavone consumption, controlling for age, race/ethnicity, BMI, and education using the Negative Binomial regression model. This method (interpreted similarly to Poisson) analyzes count data, providing a better fit than Poisson when the conditional mean and variance of the outcome variable are unequal. A statistically significant result implies that the expected VMS count in the low or moderate or high isoflavone intake exposure group as compared to the reference exposure group (none), was either higher or lower. The distribution of the sample mean was calculated using bootstrap resampling; 95% confidence intervals (CIs) were adjusted for bias and skew using the bias corrected and accelerated (BCa) method [20]. If a main effect was noted, we planned to stratify by race/ethnicity.

3. Results

Of the 18,500 potentially eligible women, 9325 women returned questionnaires (50.4% response rate); and 9007 women had usable data with VMS frequency and soy food information. A total of 5634

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