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Lifestyle and Demographic Factors in Relation to Vasomotor Symptoms: Baseline Results from the Study of Women's Health Across the Nation

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Results of recent trials highlight the risks of hormone therapy, increasing the importance of identifying preventive lifestyle factors related to menopausal symptoms. The authors examined the relation of such factors to vasomotor symptoms in the multiethnic sample of 3,302 women, aged 42–52 years at baseline (1995–1997), in the Study of Women's Health Across the Nation (SWAN). All lifestyle factors and symptoms were self-reported. Serum hormone and gonadotropin concentrations were measured once in days 2–7 of the menstrual cycle. After adjustment for covariates using multiple logistic regression, significantly more African-American and Hispanic and fewer Chinese and Japanese than Caucasian women reported vasomotor symptoms. Fewer women with postgraduate education reported vasomotor symptoms. Passive exposure to smoke, but not active smoking, higher body mass index, premenstrual symptoms, perceived stress, and age were also significantly associated with vasomotor symptoms, although a dose-response relation with hours of smoke exposure was not observed. No dietary nutrients were significantly associated with vasomotor symptoms. These cross-sectional findings require further longitudinal exploration to identify lifestyle changes for women that may help prevent vasomotor symptoms.

diet; ethnic groups; menopause; reproductive history; signs and symptoms; smoking; tobacco smoke pollution

Abbreviation: SWAN, Study of Women's Health Across the Nation.

Vasomotor symptoms affect most women during the menopausal transition (1–3), although frequencies differ significantly by race/ethnicity (4, 5). Results of recent trials have shown significant risks associated with the use of hormone therapy (6–9). Thus, identifying modifiable lifestyle factors that might prevent menopausal symptoms has increased in importance.

Dietary factors may play a role in estrogen production and metabolism and in symptom occurrence. Asian women consume less fat (10), report less vasomotor symptoms (4, 11–14), excrete more estrogen, and have lower plasma estrone and estradiol concentrations than do Caucasian women (15–18).

Phytoestrogens are composed of mainly isoflavones (found in legumes and beans, especially soybeans) and lignans (found in cereals, fruits, and vegetables, especially flaxseed). Phytoestrogens structurally resemble estradiol, compete with estradiol for binding to estrogen receptors (19–21), and have weak estrogenic and antiestrogenic effects, depending on the concentrations of endogenous estrogens and estrogen receptors (22, 23). Japanese women excrete 100 times more phytoestrogens than do American and Finnish women (24). With only modest ingested amounts,

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isoflavones may reach circulating concentrations that can exceed endogenous estrogen levels (25). Urinary excretion of phytoestrogens and plasma concentrations of sex hormone binding globulin are positively associated with dietary fiber intake, which is inversely related to the percentage of free estradiol in the plasma (26). One trial demonstrated a small, statistically significant reduction in hot flashes in breast cancer survivors treated with vitamin E compared with placebo (27), although the relation of total antioxidant intake to vasomotor symptoms is unknown. The relation of dietary intake of other nutrients to vasomotor symptoms also has not been well studied. Smokers may have lower serum estradiol and estrone concentrations (28) and lower urinary estrogen concentrations than nonsmokers (29), as well as greater symptom reporting, during the menopausal transition (4, 30–34). However, little information exists about the relation of passive smoke exposure to symptoms.

The literature thus suggests a role for lifestyle factors in affecting endogenous hormone concentrations and vasomotor symptoms. However, the independent roles of specific lifestyle factors have not been assessed (35). We, therefore, examined the relation of lifestyle factors to vasomotor symptoms in the multiethnic sample of midlife women in the Study of Women's Health Across the Nation (SWAN) at baseline, when the participants were premenopausal or in the early perimenopause.

MATERIALS AND METHODS

Study participants

SWAN first conducted a cross-sectional screening of 16,065 women for eligibility for a longitudinal cohort from 1995 through 1997 at seven sites (36). Each site screened one minority population (African Americans in Pittsburgh, Pennsylvania; Boston, Massachusetts; Ypsilanti, Michigan; and Chicago, Illinois; Japanese in Los Angeles, California; Chinese in Oakland, California; and Hispanics in New Jersey) and a Caucasian population, using community-based sampling of women aged 40–55 years who resided near each site. Women were included who spoke English, Spanish, Cantonese, or Japanese at the sites where these languages were used. The institutional review boards at all sites approved the protocol.

Eligibility criteria for the cohort study at baseline included the following: age of 42–52 years, intact uterus and at least one ovary, not currently using exogenous hormones affecting ovarian function, a menstrual period in the previous 3 months, and self-identification with each site's designated race/ethnic groups. All women were pre- or early perimenopausal at baseline. Each site recruited approximately 450 eligible participants (total n = 3,302), which formed the study population for the present analyses.

Data collection

The 3-hour baseline clinic visit consisted of an in-person interview, food frequency and self-administered questionnaires, and measurement of blood pressure, weight, height (using calibrated scales and a stadiometer), and waist and hip circumferences. One fasting blood sample was drawn on any of days 2–7 of the menstrual cycle for women enrolled during the first 6 months and on any of days 2–5 thereafter. Serum concentrations of estradiol, testosterone, follicle-stimulating hormone, dihydroepiandrosterone sulfate, and sex hormone binding globulin were determined. Common protocols, manual of operations, training, and staff certification were used at all sites.

The food frequency questionnaires were modifications of the 1995 Block food frequency questionnaire (37, 38), with four versions (English only and three bilingual versions with English and Spanish, Chinese, or Japanese). The English food frequency questionnaire contained a 103-item core food list. The Spanish, Chinese, and Japanese versions included this core list plus 9–16 additional foods appropriate for each ethnic group. The core list was based on responses of African Americans and Caucasians in the Second National Health and Nutrition Examination Survey (37, 39). Commonly consumed sources of dietary phytoestrogen were also included in the core food list (40), including tofu, soymilk, soy sauce, and meat substitutes made from soy. Additional soy products and other foods consumed by Chinese and Japanese women were added to their food frequency questionnaires, based on ethnic-specific focus groups and food records from non-SWAN participants. Additional foods for Hispanics were identified from the Hispanic Health and Nutrition Examination Survey (41) and focus groups.

Respondents reported their usual dietary intake for the previous year. Nine consumption frequency response categories ranged from "never" to "every day" for most foods, but for some foods (e.g., bread and rice), "≥2/day" could be reported. Portion size (four response categories), using three-dimensional models, was asked for each food.

Exclusions

Women were excluded from the present analyses because of a missing food frequency questionnaire (n = 11), vasomotor symptoms (n = 104), hormone concentrations (n = 2), smoke exposure (n = 59), day of blood draw (n = 52), or other covariate information (n = 106), or because of more than 10 foods skipped on the food frequency questionnaire, out-of-range values for number of foods (<4, >17/day), or <500 or >5,000 calories/day (n = 145). The final sample size for the present analyses was thus 2,823.

Outcomes

The number of days in the past 2 weeks that the participant experienced vasomotor symptoms (hot flashes, cold sweats, night sweats) was self-reported (42–44). Factor analyses of vasomotor symptoms showed similar high loadings for cold sweats, night sweats, and hot flashes of 0.73, 0.81, and 0.78, respectively. Because of the infrequency of some symptoms within the smaller ethnic groups, each symptom was treated as binary (any vs. none), and these binary outcomes were summed (possible sums being 0, 1, 2, or 3), with values of 2 and 3 combined because of the small number of women reporting all three symptoms.

Independent variables

From the baseline interview, data were obtained on active and passive smoke exposure, based on the American Thoracic Society questions (45) and validated questions on passive exposure (46). Medians and interquartile ranges and quartiles of nonzero values were computed for current cigarettes smoked per day and total weekly person-hours of passive smoke exposure at home, at work, or in other public/social settings.

Nutrient intakes (antioxidants, fat, total calories, and fiber) were determined by applying a nutrient database to the food frequency questionnaire data. Antioxidant intake was evaluated for individual nutrients and for total antioxidant intake. Antioxidant intakes were calculated for diet alone for nonsupplement users and, separately, for total diet plus supplements used for more than 1 year (excluding users who began supplement use recently, perhaps for symptoms). Total antioxidant values were computed by standardizing each antioxidant item by subtracting the sample mean (which resulted in some negative values) and dividing by the sample standard deviation. Total antioxidant intake was natural log transformed in bivariate and multivariate analyses, adding 3 to the total antioxidant score to avoid negative values. Because most other nutrients were not normally distributed, medians (and interquartile ranges) were computed for descriptive statistics, and log-transformed values were included in multivariate modeling.

Phytoestrogen (genistein, daidzein, and coumestrol) intakes varied sharply by ethnicity; thus, analyses for all participants compared any versus none. In addition, the relation of intake amount to hormone levels and symptoms was examined within each ethnic group, using ethnic-specific quartiles. Because genistein and daidzein are the largest components of isoflavones and because intakes of the three phytoestrogens were so highly correlated, final analyses were performed only for genistein.

Covariates

Potential confounding variables were considered on the basis of the literature and analyses of their relation to both independent and dependent variables. The variables examined included age, race/ethnicity, use of alternative therapies, income, education, employment, income, site, physical activity, menopausal status, social support (47), perceived stress (48), acculturation (a score of preferred language for reading, speaking, thinking, and radio/television programs) (49), body mass index (weight (kg)/height $(m)^2$), history of premenstrual symptoms (abdominal cramps, breast tenderness, bloating, or mood changes), menopausal status (pre- or early peri-), comorbidities (history of stroke, high cholesterol, migraine, gallstones, osteoarthritis, thyroid disease, hypercalcemia, anemia, liver disease, epilepsy, phlebitis, anorexia, bulimia, tuberculosis, acquired immunodeficiency syndrome, lupus erythematosus, hypertension, diabetes, heart disease, arthritis, osteoporosis, fibroids, or cancer), use of heart or cholesterol-lowering medications, and use of over-the-counter pain medications. Primary race/ethnicity was self-defined as Black or African American, non-Hispanic Caucasian, Chinese or Chinese American, Japanese or Japanese American, or Hispanic (Central American, Cuban or Cuban American, Dominican, Mexican or Mexican American, Puerto Rican, South American, Spanish or other Hispanic). Menopausal status was classified as "premenopausal" if a woman reported no decreased predictability in menses in the prior 12 months and as "early perimenopausal" if she reported decreased predictability. Nineteen questions on physical activity were adapted from the Kaiser Physical Activity Survey, which was adapted from the Baecke physical activity questionnaire (50, 51), to cover activity in occupation, household and caregiving, sports and exercise, and daily routine.

Data analyses

Univariate frequencies and summary statistics were computed to describe the study population and to summarize the primary independent and dependent variables. Characteristics among ethnic groups were compared using chi-square tests and analysis of variance. Unadjusted associations of smoke exposure and nutrients with number of vasomotor symptoms were estimated using ordinal logistic regression (52). Associations of hormones with symptoms were similarly estimated, adjusting for menstrual cycle day of blood draw. To assess whether any associations of lifestyle factors with symptoms were due in part to hormones, we also modeled each hormone as a function of each lifestyle factor using linear regression, adjusting for menstrual cycle day of blood draw. Multivariate logistic regression models were estimated to identify characteristics associated with symptoms, including nutrients, smoke exposure, and covariates. Estimated odds ratios for the final model were compared with models with and without estradiol or follicle-stimulating hormone to assess whether key independent variables might affect symptoms through these hormonal mechanisms. Race/ethnicity and lifestyle factors of interest were forced into final multivariate models, and backward elimination ($p < 0.05$) was used to obtain a parsimonious final multivariate model. Interactions of nutrients and smoke exposure with confounders were tested.

Nutrients, smoking exposure variables, and body mass index were log transformed to handle skewness. Odds ratios for those variables with a "none" category (e.g., nonsmoking) were computed as the difference between none and the median nonzero value. For those variables with no "none" category (e.g., total calories), odds ratios were computed as the difference between the 75th and 25th percentiles (the interquartile range). Model fit was assessed using chi-square statistics (53, 54) and the Akaike Information Criterion (55). For variables not satisfying the proportional odds assumption, a partial proportional odds model was estimated (54) (i.e., the coefficient for the variable could differ for ≥1 vs. 0 and for ≥2 vs. 0–1 symptoms).

RESULTS

Study population

With the exception of age and follicle-stimulating hormone levels, all covariates varied significantly by race/ethnicity (table 1). Despite similar age distributions, fewer Chinese (37.7 percent) and Japanese (42.6 percent) women were in the early perimenopause than African-American (50.2 percent), Caucasian (46.9 percent), or Hispanic (43.5 percent) women at baseline, consistent with findings from SWAN's screening data regarding ethnic differences in age at menopause (56). In addition, significantly more African-American (46.5 percent) and Hispanic (49.4 percent) women reported vasomotor symptoms, and fewer Japanese (34.3 percent) and Chinese (28.9 percent) women reported vasomotor symptoms than did Caucasian (36.6 percent) women ($p < 0.0001$). Previously SWAN showed that nutrient intakes also varied considerably by race/ethnicity, with dietary antioxidant and fiber intake highest in Chinese women, phytoestrogen intake highest in Japanese women, fat and total calorie intake highest in African-American women, and any alcohol intake highest in Caucasian and lowest in Chinese women (10).

Bivariate analyses

In unadjusted analyses, the amount of cigarettes smoked, passive smoke exposure, and higher total calorie and fat intakes were significantly associated with vasomotor symptoms (table 2). Neither individual dietary nor total antioxidant intake (with or without supplements and either as a continuous variable or as quartiles) or dietary fiber or alcohol intake was associated with vasomotor symptoms. Genistein consumption also was not associated with vasomotor symptoms in any ethnic group, although an over fourfold but nonsignificant odds ratio was observed in Japanese women. Serum estradiol levels were significantly negatively associated, and follicle-stimulating hormone was significantly positively associated with vasomotor symptoms in unadjusted analyses.

In analyses adjusted only for menstrual cycle day of the blood draw, active and passive smoke exposure and dietary intakes were not significantly associated with estradiol concentrations, although estradiol tended to be lower in women smoking a higher number of cigarettes/day (data not shown). Follicle-stimulating hormone was higher in women smoking a higher number of cigarettes/day. An increased alcohol concentration was associated with somewhat higher estradiol levels but not with follicle-stimulating hormone. Body mass index was significantly negatively associated with estradiol and follicle-stimulating hormone, as previously reported from SWAN (15).

Multivariate analyses

In multivariate analyses adjusting simultaneously for ethnicity, all lifestyle factors, and confounding factors (table 3), the odds of reporting vasomotor symptoms remained significantly higher in early perimenopausal than premenopausal women and significantly higher in African-American and Hispanic women and lower in Chinese than in Caucasian women. No significant interaction of menopausal status with race/ethnicity was observed.

With both passive and active smoke exposure in the model, only passive but not active smoke exposure remained significantly associated with vasomotor symptoms, although a dose response was not observed for person-hours of exposure (table 3). No dietary factors (fat, fiber, total calories, genistein, antioxidants, or alcohol consumption) were significantly related to reporting of vasomotor symptoms. Because of significant ethnic differences in genistein intake, with medians near zero in African Americans, Caucasians, and Hispanics and median concentrations of greater than 3,000 μg for Japanese and Chinese women, we examined ethnic-specific genistein intake amounts in relation to vasomotor symptoms in multivariate models. Although genistein × ethnicity interactions were statistically nonsignificant, ethnic-specific slopes of lognormal (genistein + 1) and vasomotor symptoms differed in magnitude and direction by ethnicity, as did odds ratios for ethnic-specific medians of nonzero genistein values versus no consumption (data not shown). In both cases, only in Japanese and Chinese women was a suggestion of a positive, although nonsignificant, association observed; in the other three ethnic groups, no association was observed.

Being in early perimenopause, increased body mass index, history of premenstrual symptoms, use of over-the-counter pain medications, history of comorbidities, use of physical alternative therapies, perceived stress, and age were all significantly positively and independently associated with vasomotor symptoms. No interaction of smoke exposure, nutrients, and confounders was statistically significant or improved model fit.

Estradiol level was significantly negatively associated, while follicle-stimulating hormone was significantly positively associated, with vasomotor symptoms. Results excluding hormones as predictors were compared with those including hormones as predictors, to assess their potential mechanistic involvement in the relation of lifestyle factors to vasomotor symptoms. Odds ratios for nonhormonal factors were similar in all models, reflecting the general lack of associations of lifestyle behaviors with estradiol and follicle-stimulating hormone, so that only models without estradiol and follicle-stimulating hormone have been presented.

DISCUSSION

SWAN includes one of the largest and most racially and ethnically diverse populations of pre- and perimenopausal women ever studied. In addition, SWAN's community-based sampling enhances the generalizability of results. Several new findings emerged.

Demographic, hormonal, and health factors

Symptom reporting varied significantly by race/ethnicity. Significantly more African Americans and Hispanics and significantly fewer Chinese women reported vasomotor symptoms than did Caucasian women. Similar ethnic differences in vasomotor symptoms have been reported by others

TABLE 1. Characteristics of baseline study population by race/ethnicity, Study of Women's Health Across the Nation, 1995–1997

Characteristic	African American (*n* = 750)	Caucasian (*n* = 1,418)	Chinese (*n* = 218)	Hispanic (*n* = 239)	Japanese (*n* = 198)	Total (*n* = 2,823)
Age (years)* (median (IQR†))	46.2 (4.3)	46.1 (4.2)	46.5 (4.0)	46.0 (3.8)	46.2 (4.2)	46.1 (4.2)
Education (% (no.))						
<High school	4.4 (32)	1.5 (20)	11.6 (25)	47.0 (103)	0.5 (1)	6.6 (181)
High school graduate	21.0 (152)	14.0 (193)	16.2 (35)	26.0 (57)	14.7 (29)	17.0 (466)
Some college	40.0 (290)	30.7 (424)	19.9 (43)	16.9 (37)	34.5 (68)	30.5 (862)
College graduate	16.7 (121)	22.1 (306)	29.6 (64)	8.2 (18)	28.9 (57)	20.7 (566)
Graduate school	17.9 (130)	31.8 (439)	22.7 (49)	1.8 (4)	21.3 (42)	24.2 (664)
Employed (% (no.))	79.3 (593)	85.4 (1,210)	89.5 (195)	56.1 (133)	78.3 (155)	81.1 (2,286)
Annual household income ($) (% (no.))						
<20,000	19.2 (138)	6.7 (94)	5.1 (11)	55.8 (129)	2.1 (4)	13.6 (376)
20,000–34,999	20.1 (145)	13.7 (192)	15.0 (32)	23.8 (55)	9.5 (18)	16.0 (442)
35,000–49,999	21.1 (152)	17.6 (247)	16.4 (35)	10.2 (24)	12.1 (23)	17.5 (481)
50,000–74,999	21.7 (156)	27.0 (378)	25.2 (54)	5.6 (13)	29.0 (55)	23.8 (656)
75,000–99,999	10.7 (77)	16.2 (227)	15.9 (34)	2.6 (6)	20.5 (39)	13.9 (383)
≥100,000	7.2 (52)	18.8 (263)	22.4 (48)	1.7 (4)	26.8 (51)	15.2 (418)
Body mass index (kg/m^2) (median (IQR))	32.1 (8.1)	27.8 (6.9)	23.5 (4.2)	29.5 (6.1)	23.2 (3.8)	28.5 (7.4)
Current smokers						
% (no.)	22.4 (168)	15.4 (219)	1.8 (4)	17.6 (42)	14.6 (29)	16.4 (462)
Cigarettes/day (median (IQR))‡	10 (10)	20 (10)	9 (10.5)	10 (15.0)	10 (15.0)	15 (13.0)
Passive smoke exposure						
Any (% (no.))	64.0 (480)	60.5 (858)	22.0 (48)	37.7 (90)	38.4 (76)	55.0 (1,552)
Hours/week (median (IQR))‡	7.0 (28.0)	4.0 (19.0)	2.0 (4.5)	8.5 (27.0)	2.0 (6.0)	5.0 (22.0)
Perceived stress score (median (IQR))§	8.0 (5.0)	8.0 (4.0)	8.0 (4.0)	11.0 (4.0)	9.0 (4.0)	8.0 (5.0)
Total physical score (median (IQR))§	7.3 (2.3)	8.1 (2.4)	7.3 (2.5)	6.6 (1.9)	7.8 (2.3)	7.6 (2.5)
Estradiol (pg/ml) (median (IQR))	55.4 (56.8)	56.4 (55.2)	48.1 (51.9)	61.9 (70.3)	49.6 (51.1)	55.3 (56.0)
Follicle-stimulating hormone (mIU/ml) (median (IQR))*	16.4 (17.5)	15.3 (14.6)	16.2 (16.9)	15.6 (17.8)	14.2 (12.1)	15.7 (15.6)
Premenopausal (% (no.))	49.8 (364)	53.1 (732)	62.3 (134)	56.5 (122)	57.4 (112)	53.5 (1,464)
Total kcal (median (IQR))	1,797 (1,035)	1,710 (784)	1,664 (826)	1,546 (655)	1,762 (779)	1,717 (830)
Total fat (g) (median (IQR))	68.6 (48.6)	61.9 (36.7)	53.1 (25.1)	55.1 (30.7)	57.0 (30.1)	61.5 (37.8)
Dietary fiber (g) (median (IQR))	10.8 (6.9)	11.4 (6.6)	13.7 (7.6)	11.5 (6.3)	10.9 (6.3)	11.4 (6.7)
Genistein						
Any (% (no.))	55.5 (416)	65.4 (928)	99.5 (217)	31.0 (74)	99.5 (197)	64.9 (1,832)
μg (median (IQR))‡	3.9 (21.7)	7.1 (502)	3,662 (7,783)	216.8 (916)	5,440 (10,107)	48.7 (1,704)
Alcohol						
Any (% (no.))	57.5 (431)	61.1 (866)	22.0 (48)	50.2 (120)	38.9 (77)	50.7 (1,430)
% of calories (median (IQR))‡	35.3 (85.8)	50.1 (107)	19.8 (36.9)	23.9 (23.9)	53.1 (107)	37.2 (94.8)
Dietary vitamin C (mg) (median (IQR))¶	90.5 (90.2)	93.8 (77.0)	119.9 (72.4)	88.6 (89.8)	80.3 (59.0)	93.4 (81.6)
Dietary vitamin E (mg) (median (IQR))¶	8.7 (5.7)	8.0 (4.6)	8.8 (3.9)	6.9 (3.2)	7.3 (3.6)	8.0 (4.5)
Dietary provitamin A (μg) (median (IQR))¶	2,031 (1,742)	1,908 (1,677)	3,733 (3,178)	1,891 (1,473)	1,909 (1,784)	2,030 (1,874)
Dietary retinol (μg) (median (IQR))¶	441 (518)	426 (308)	266 (310)	363 (381)	242 (251)	400 (364)
Total antioxidants (median (IQR))#	−1.1 (2.6)	−1.0 (2.9)	−0.7 (2.5)	−1.7 (2.2)	−0.9 (3.2)	−1.1 (2.8)
Over-the-counter pain medication (% (no.))	24.9 (187)	29.9 (423)	6.4 (14)	38.1 (91)	12.6 (25)	26.2 (740)
History of premenstrual symptoms (% (no.))	96.3 (721)	95.4 (1,353)	85.9 (182)	97.1 (232)	90.4 (178)	94.7 (2,666)
Any comorbidities (% (no.))	82.2 (608)	72.9 (1,019)	57.0 (122)	81.4 (188)	63.8 (125)	74.2 (2,062)

* All characteristics, except age and follicle-stimulating hormone concentrations, differed significantly by race/ethnicity.
† IQR, interquartile range.
‡ Nonzero values only.
§ Higher score indicates greater stress or physical activity.
¶ Nonsupplement users only (*n* = 1,374).
# Sum of standardized nutrients, omitting women initiating supplements within the past year (*n* = 2,421).

TABLE 2. Unadjusted odds ratios and 95% confidence intervals for vasomotor symptoms by lifestyle factors and hormones, proportional odds logistic regression, Study of Women's Health Across the Nation (*n* = 2,823) at baseline, 1996–1997

Log-transformed factor	Unadjusted odds ratio	95% confidence interval
Active smoking*	1.6	1.3, 1.9
Passive smoke exposure*	1.3	1.2, 1.4
Total calories†	1.2	1.1, 1.4
Fat†	1.3	1.2, 1.4
Fiber†	1.0	0.9, 1.1
Alcohol consumption*	0.9	0.8, 1.0
Genistein*		
African Americans	0.9	0.8, 1.0
Caucasians	1.0	0.9, 1.0
Chinese	1.0	0.2, 4.0
Hispanics	1.2	0.7, 2.1
Japanese	4.2	0.7, 27.3
Vitamin C†,‡	1.0	0.8, 1.1
Viatmin E†,‡	1.2	1.0, 1.3
Provitamin A†,‡	1.0	0.9, 1.2
Retinol†,‡	1.1	1.0, 1.3
Total antioxidants§	1.0	0.9, 1.1
Body mass index†	1.5	1.3, 1.6
Physical activity†,¶	0.9	0.8, 1.0
Estradiol†,#	0.9	0.8, 1.0
Follicle-stimulating hormone†,#	1.3	1.2, 1.5

* Median for nonzero values versus none.
† 75th percentile versus 25th percentile.
‡ Nonsupplement users only (*n* = 1,374).
§ Omitting women who initiated supplement use within the past year (*n* = 2,421 remaining).
¶ Not natural log transformed.
# Adjusting for day of menstrual cycle.

TABLE 3. Adjusted† odds ratios and 95% confidence intervals for vasomotor symptoms from backward elimination logistic regression models, Study of Women's Health Across the Nation (*n* = 2,823) at baseline, 1996–1997

Independent variable	Adjusted odds ratio	95% confidence interval
Ethnicity		
Caucasian	Referent	
African American		
≥1 vs. 0	1.4	1.1, 1.7**
≥2 vs. 0–1	1.5	1.2, 1.9
Chinese		
≥1 vs. 0	0.7	0.4, 1.0
≥2 vs. 0–1	0.4	0.2, 0.7
Hispanic		
≥1 vs. 0	1.6	0.9, 2.6
≥2 vs. 0–1	2.6	1.5, 4.4***
Japanese		
≥1 vs. 0	0.9	0.6, 1.5
≥2 vs. 0–1	0.6	0.3, 1.0
Age‡ (per year)	1.3	1.2, 1.5****
Early peri- vs. premenopause		
≥1 vs. 0	1.7	1.4, 2.0****
≥2 vs. 0–1	2.1	1.7, 2.6****
Education		
<High school	1.2	0.8, 1.7
High school	Referent	
Some college	1.1	0.8, 1.3
College	0.8	0.6, 1.1
Postcollege	0.7	0.6, 1.0
Log body mass index‡	1.2	1.0, 1.3*
Log (no. of cigarettes + 1)§	1.0	0.8, 1.4
Log (passive smoke hours + 1)§	1.2	1.0, 1.3**
Log (alcohol + 1)§	1.0	0.9, 1.2
Log fat‡	1.0	0.8, 1.2
Log fiber‡	1.0	0.9, 1.2
Any genistein	1.2	1.0, 1.4
Log total calories‡	1.2	0.9, 1.6
Physical activity‡	1.0	0.9, 1.2
Premenstrual symptoms	1.8	1.2, 1.7**
Over-the-counter pain medications	1.3	1.1, 1.6**
Any comorbidities	1.5	1.2, 1.8****
Perceived stress‡	1.4	1.2, 1.6****

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.
† Also adjusted for cycle day of blood draw among only those women not missing the day of blood draw.
‡ 75th percentile versus 25th percentile.
§ Median for nonzero values versus none.

(3, 4, 12, 14). It is possible that language and/or acculturation contributed to our observed differences, since 83.5 percent of Hispanics, 36 percent of Chinese, and 25 percent of Japanese women completed non-English versions of the questionnaire assessing symptoms. However, no difference in the number of symptoms reported was observed in those that completed the questionnaire in English compared with those who did not complete it in English in any of these three ethnic groups. Fewer Hispanic women were acculturated, yet more reported vasomotor symptoms, while more Japanese and Chinese women were acculturated, but fewer reported vasomotor symptoms. In addition, the food frequency questionnaires contained both English and the appropriate non-English language for each of these three groups. Thus, it is unlikely that acculturation or language accounted for much of the observed differences.

Body mass index was significantly associated with vasomotor symptoms. Increased body fat provides more insulation, which would increase core body temperature and thus might increase hot flashes (57, 58), and might counterbalance the preventive potential of increased circulating estrogens due to aromatization in adipose tissue. However,

increased plasma estrogen levels have not been observed in premenopausal obese women (59). History of premenstrual symptoms was also significantly associated with vasomotor symptoms, consistent with prior work (60, 61).

Smoke exposure

Passive but not active smoke exposure was significantly associated with vasomotor symptoms after adjustment for covariates and each other, although no dose response was observed for hours of passive smoke exposure. The relation of smoke exposure to vasomotor symptoms is unlikely to be related to antiestrogenic effects as previously reported (62–64), given the lack of change in point estimates when estradiol was included in the multivariate models. Although the exact physiologic mechanism of hot flashes is unknown, estrogen withdrawal (not just low estrogen levels) is involved (65–68). Additionally, small changes in core body temperature precede hot flashes (69, 70). Although many studies have reported an association of current cigarette smoking with vasomotor symptoms (3, 4, 33, 34, 71, 72), none has also simultaneously examined the relation of passive smoke exposure. In our analyses, current smoking did not remain in final models when passive smoke exposure was included. This may explain the discrepancy between our present results and those of others (that did not include passive smoke exposure) regarding current smoking. Further examination is needed in longitudinal studies of the relation of passive smoke exposure to symptoms.

Phytoestrogens

Genistein intake was not related to the reporting of vasomotor symptoms after adjustment for covariates among SWAN's participants. Isoflavones, the most common class of phytoestrogens, have hormonal effects in animals (73). Phytoestrogens have chemical structures similar to those of estradiol and selective estrogen receptor modulators (74), bind to estrogen receptors (75), and have weak estrogenic or antiestrogenic effects, depending on their concentration and the concentrations of endogenous estrogens and other dietary factors (76, 77). The antiestrogenic effects are partially explained by competition with endogenous estrogens for estrogen receptors (78). Supplementation with isoflavones decreases estradiol, progesterone (79), luteinizing hormone, follicle-stimulating hormone, and dihydroepiandrosterone sulfate (79–82), which could lead to lower levels of free estradiol (83), but most studies have had small sample sizes and various types and doses of phytoestrogens and lengths of follow-up (80, 84–87).

Several randomized, controlled, masked trials of soy supplementation have reported statistically significant reductions in hot flashes (88–95), although some studies have not (96–99). A Japanese observational study showed lower soy intake in women with hot flushes than in those without (100). However, our present cross-sectional results show no protective effect on vasomotor symptoms with increased amounts of genistein. One possible explanation for this discrepancy is that of cross-sectional bias; that is, more symptomatic women may have increased their phytoestrogen intake to reduce hot flashes, a possibility which will be better examined in SWAN's longitudinal analyses. In addition, factors that we were unable to measure, such as antibiotic use and bowel disease, may have affected the bioavailability of ingested isoflavones (101, 102).

Fat

The potential role of dietary fat in menopausal symptoms has been inferred from the low fat intake of Asian populations and their reduced symptom reporting. We previously observed Japanese and Chinese women to have lower fat intake than Caucasians and African Americans (10). We found a positive association of fat intake with vasomotor symptoms in unadjusted, but not in multivariate, analyses. Dietary fat has been positively related to plasma estrogen concentrations in premenopausal (103) and postmenopausal (104, 105) women. Lower fat and estrogen levels, and thus possibly less variability in estrogen, in Asians may partially explain their lower reporting of symptoms.

Dietary fiber

Dietary fiber intake was not related to the reporting of vasomotor symptoms in either unadjusted or multivariate analyses. A high-fiber diet diminishes estrogen absorption from the intestinal lumen and its contribution to the total body pool of estrogens (106). Moreover, binding of unconjugated estrogens to fiber in the gut impedes their reabsorption (107, 108). Dietary fiber intake and plasma estradiol concentrations were negatively correlated in a study of premenopausal Asian immigrant and Caucasian women (109). Significant reductions in serum estrogen concentrations were observed in premenopausal women given supplements with wheat bran, but not in those given supplements with oat or corn bran, all of which doubled dietary fiber consumption without reducing fat intake (106).

Total calories

The effect of total calories on estrogen activity or symptoms has not been well studied. Separating the effects of total calories from those of fat intake is difficult. The present results showed that total calorie intake was significantly associated with vasomotor symptoms in unadjusted analyses but nonsignificantly associated after adjustment for covariates.

Antioxidants

In our study, neither dietary not total antioxidant intake was associated with vasomotor symptoms. Debate continues concerning the pro- and antioxidant effect of estrogens (110–112). Decreased antioxidant enzyme activity and total antioxidant status have been observed in healthy women transitioning from premenopause to peri- and postmenopause (113). Estrogens are powerful antioxidants in the prevention of lipid peroxidation (114, 115). However, estrogens are heterogeneous, and the environment may also affect antioxi-

dant properties (116). SWAN's longitudinal analyses may reveal more about antioxidant intake and symptoms.

Limitations

The present study has limitations that may affect its comparison with prior studies and the precision of some findings. First, these analyses were based on cross-sectional data, and women may have changed lifestyle behaviors due to symptoms; thus, whether, for example, dietary intake actually preceded the onset of symptoms is uncertain. Future analyses of SWAN's longitudinal data will help to clarify and minimize this limitation. Second, comparisons were made of a number of lifestyle factors; thus, some statistically significant results may have occurred by chance. In addition, our sample was limited to pre- and early perimenopausal women; thus, new or different findings must be interpreted cautiously. Future longitudinal examinations will help clarify whether the associations are likely to be causal. Finally, inadequacies of dietary assessment may have weakened our ability to uncover relations. Measurement error is inherent in all dietary methods; this was compounded in SWAN by the obtaining of comparable dietary intake measures in four languages for five ethnic groups.

Strengths

Despite these limitations, the present study had a number of notable strengths. As mentioned, this is one of the largest and most racially and ethnically diverse samples of midlife women ever studied for risk factors for symptoms. This, in combination with the community-based sampling used in SWAN, provides greater representativeness, thus enhancing the generalizability of the results. In addition, careful control in multivariate models of a number of demographic, reproductive, and medical variables reduces the likelihood that the results are due to uncontrolled confounding. Indeed, the new finding of a relation of passive smoke exposure to vasomotor symptoms and no relation with current smoking when passive smoke exposure is in the model may reflect lack, in prior studies, of adequate control of covariates, such as passive smoke exposure. Finally, the comprehensiveness of the dietary factors examined is a strength of the study.

Conclusions

The present large, multiethnic, community-based study provides new evidence that passive smoke exposure, hormones, and body mass index are associated with vasomotor symptoms in midlife women and that the reporting of these symptoms varies by race/ethnicity. However, no significant associations were found with dietary factors in this cross-sectional analysis. The associations found here must be further explored in longitudinal analyses, so as to help guide women and clinicians in finding lifestyle changes to prevent symptoms, thus reducing or providing alternatives to use of medications.

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