Effect of Physical Activity on Menopausal Symptoms among Urban Women

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ABSTRACT

NELSON, D. B., M. D. SAMMEL, E. W. FREEMAN, H. LIN, C. R. GRACIA, and K. H. SCHMITZ. Effect of Physical Activity on Menopausal Symptoms among Urban Women. *Med. Sci. Sports Exerc.*, Vol. 40, No. 1, pp. 50–58, 2008. **Purpose:** To determine whether physical activity, measured by expended kilocalories per week (kcal·wk^{-1}), decreases the risk of menopausal symptoms among African American and Caucasian women. **Methods:** Level of physical activity and menopausal symptoms, including hot flashes, depression, anxiety, stress, and vasomotor, physiological, and somatic symptom summaries were measured in 401 women during an 8-yr period. Tertiles of physical activity at each assessment were defined as kilocalories per week: top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}). Regression models were used to estimate the independent effect of physical activity at each time period on menopausal symptoms after adjusting for covariates and hormone levels. Results were also stratified by race, smoking status, and menopausal status. **Results:** Overall, only perceived stress was related to level of physical activity, with women in both the middle and top tertiles of physical activity reporting lower mean levels of stress compared with women in the lowest tertile of activity. In the analysis by menopausal stage, active postmenopausal women continued to report lower mean levels of anxiety, stress, and depressive symptoms compared with inactive postmenopausal women. We did not find an association between level of physical activity and reports of hot flashes, even after adjusting for the variability in the hormonal changes. **Conclusions:** Among a cohort of community-dwelling women, high levels of physical activity were related to lower levels of stress during an 8-yr follow-up period. In addition, levels of anxiety, stress, and depression were lowest among physically active postmenopausal women compared with inactive women in the same menopausal grouping. **Key Words:** KILOCALORIES, DEPRESSION, ANXIETY, STRESS

Menopausal symptoms are experienced by the majority of women as they move through the menopausal transition, and they are a common reason for seeking medical attention during this phase of life (19,15). More recently, women have been seeking alternative therapies for menopausal symptoms, including increasing or maintaining a high level of physical activity. Physical activity has been proposed as an intervention for preventing or attenuating menopause-related vasomotor symptoms as well as other psychological symptoms such as anxiety and depression, but, to date, the evidence regarding the benefit of physical activity is varied (7,24,36).

Current studies examining the usefulness of physical activity in preventing or attenuating vasomotor symptoms have been mixed, and the number of studies assessing the role of physical activity on other symptoms, such as depression, stress, and anxiety, has been minimal (2,29,35,39). Daley et al. (5) and others have examined the role of current physical activity among women of menopausal age; they report higher quality-of-life scores, but they did not find a reduction in vasomotor symptoms among physically activity menopausal-aged women (5,6,7,16,24). In a recent, small, randomized clinical trial, Villaverde-Gutierrez et al. (37) found an improvement in quality-of-life scores, and they report menopausal symptoms among women assigned to the experimental activity group consistently of a 12-month program of cardiorespiratory, stretching, muscle-strengthening, and relaxation twice at week. Other studies have examined activity level before the final menstrual period and have also produced conflicting reports. Sternfeld et al. (34) examined reported physical activity before the

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final menstrual period and did not find activity level related to reported vasomotor symptoms, depressive symptoms, psychological disorders, or somatic symptoms, indicating a potential lack of long-term effects of premenopausal activity and menopausal symptoms. However, one study found an increase in the frequency and severity of hot flashes among the group of women reporting high levels of physical activity before the final menstrual period (38).

Adding to the current confusion regarding the benefits of physical activity on menopausal symptoms, subgroups of menopausal women have been shown to have varying changes in hormone levels and/or symptom reports during the menopausal transition. For example, we have found that African American women have significantly lower levels of estradiol and DHEAS during the menopausal transition and a higher prevalence of hot flashes compared with Caucasian women, although the racial difference in hot flash prevalence was removed after adjustment for hormones and BMI (8,23). Other studies have indicated that smokers have an earlier onset of menopause and/or more severe menopausal symptoms and that women with high levels of anxiety or depressive symptoms report more menopausal symptoms, including hot flashes, but these findings need further study (14,17,18).

We were interested in examining the role of current physical activity level and a variety of menopausal symptoms among a large, diverse group of community-dwelling women for an extended follow-up period. In addition, we were interested in exploring the role of physical activity and menopausal symptoms among the subgroups of smokers, African American women, and women with depressive symptoms. The Penn Study of Ovarian Aging is an ongoing, longitudinal cohort study examining hormonal, clinical, behavioral, and demographic factors associated with ovarian aging, with physical activity surveys administered at four time points during the 8 yr of follow-up. In this report, we describe an analysis to assess whether physical activity level measured at these four points is associated with hot flashes, depression, anxiety, stress, and indicators of menopausal symptom summaries reported at the same time periods. In addition, we assessed the role of physical activity on reported symptoms among particular groups, including smokers, African American women, and by menopausal stage. We hypothesized that higher levels of physical activity, measured by expended kilocalories per week, decrease menopausal symptoms among this group of women approaching menopause.

MATERIAL AND METHODS

Data collection. From 1996 to 1997, a population-based sample of 436 women living in the city of Philadelphia was identified through random digit dialing. More than 70% of households identified were screened for eligibility. To ensure a racially diverse population, eligible women were stratified by race (African American or Caucasian), were between the ages of 35 and 47 yr, reported menstrual cycles in the normal range (22–35 d) for the previous 3 months, and reported at least one intact ovary. Exclusion criteria at baseline included any serious illness that might compromise ovarian or hormonal function, such as diabetes, liver disease, breast or endometrial cancer; current use of exogenous sex hormones or psychotropic drugs; self-reported chronic alcohol or drug abuse within the past year; or current pregnancy, lactation, or intention to become pregnant. The institutional review board of the University of Pennsylvania approved the study, and all women provided written informed consent.

At enrollment, eligible women were asked to participate in a long-term women's health study with no specific emphasis on the examination of menopause. In-person project-related data were collected at approximately 9-month intervals for the first 5 yr of the study and annually during the subsequent 3 yr for the entire 8-yr period. For this manuscript, 380 subjects participating in 10 follow-up assessments during the 8-yr period and contributing physical activity information at each of the four assessment periods were included. A prior assessment of women lost to follow-up found no significant differences between women lost and women participating in the project (26).

At each assessment period, an extensive in-person structured interview questionnaire was administered by trained research interviewers who collected information on demographic background information, menstrual cycle characteristics, menopausal symptoms, physical activity, menstrual and reproductive history, general health status, medication use (including hormone replacement), and substance use. In addition, subjects completed a set of standard self-report questionnaires, including the Center for Epidemiological Studies' Depression Scale (CES-D) (21), the Zung Anxiety Scale (40), and the Perceived Stress Scale (3). Level of physical activity was collected at four points during the 8-yr follow-up (assessment period 2, 6, 8, and 10), using the Paffenbarger Physical Activity Questionnaire (27,28). Body mass index ($kg \cdot m^{-2}$) was calculated from the average of two measurements of weight and height at each assessment. Research interviewers were rotated among the study participants to reduce the influence of interviewer bias.

During each assessment period, two visits were scheduled between days 1 and 6 of two consecutive menstrual cycles, to obtain blood samples for hormone assays. The narrow visit window was selected to assess reproductive hormone levels in the early follicular phase, when levels are the most reliable (25,31) and changes associated with ovarian aging are most pronounced (4). Thus, each woman provided two blood samples per assessment period and a maximum of eight blood samples per subject in this report. The hormone levels from these two visits were used to calculate a mean hormone level for each assessment period.

Blood samples were centrifuged and plasma frozen in aliquots at −80°C. Assays were conducted in the general

clinical research center at the Hospital of the University of Pennsylvania in batches that included four visits per subject, to reduce the within-subject variability attributable to assay conditions. Estradiol (E2), follicle-stimulating hormone (FSH), and testosterone were measured by radioimmunoassay, using Coat-A-Count (Diagnostic Products, Los Angeles, CA) commercial kits. Assays were performed in duplicate. The inter- and intraassay coefficients of variation were below 5%.

Study measures. Physical activity at each of the four assessment periods was collected, using the Paffenbarger Physical Activity Questionnaire (27). This survey has been found to be both valid and reliable and to have excellent predictive validity when compared with other similar surveys (28). To examine the role of current physical activity and current reported menopausal symptoms during the 8-yr follow-up period, the individual kilocalories of leisure-time physical activity per week were calculated (28) and categorized into data-derived tertiles for analysis, defined as the top third ($\geq$ 1450 kcal·wk^{-1}), the middle third ($<$ 1450 to 644 kcal·wk^{-1}), and the bottom third ($<$ 644 kcal·wk^{-1}) of reported current activity. As described by Ainsworth et al. (1), the rate of energy expenditure for each reported leisure-time physical activity was classified by each woman and reported as kilocalories per week for each assessment period. The median value in each tertile of 2260, 957, and 392 kcal·wk^{-1} can be roughly translated into five sessions per week of walking 4.0 mph for 1.5 h, 38 min, and 16 min, respectively (1).

We used the Penn Menopausal Symptoms List (MSL) to collect information on the frequency and severity of 12 menopausal symptoms: hot flashes; vaginal dryness or discomfort; concentration or memory problems; irritability; mood swings; feeling sad, down, or blue; feeling anxious, on edge, or nervous; trouble sleeping; aches, joint pain, or stiffness; headaches; losing or leaking urine; and decreased libido or interest in sex (11). This list was adopted and validated from the Kupperman Menopausal Index. The symptoms were rated by the subjects for their presence and severity in the past month. Three menopausal symptom summaries were developed statistically, and a weighted combination of the specific symptom severity measures was used to assess 1) psychological symptoms, which included the reports of irritability, anxiety, feeling sad, mood swings, poor concentration/memory, trouble sleeping, or headaches; 2) vasomotor symptoms, which included the reports of hot flashes or aches; and 3) somatic symptoms, which included the reports of urine leaks, vaginal dryness, or decreased interest in sex. In the factor analysis, aches and hot flashes were significantly related and, thus, grouped together; recent reports have significantly linked reported aches with menopausal stage, similar to prior findings regarding reported hot flashes and menopausal stage (9). We previously have documented that these three dimensions of menopause-related symptoms had high internal consistency and acceptable psychometric properties and are sensitive markers of menopausal symptoms in a population-based cohort (11). In this cohort, the severity of reported symptoms was relatively mild; thus, we were unable to examine the role of physical activity on severity of symptoms.

Three additional psychological factors that may be potentially related to symptom report—anxiety, depression and perceived stress—were collected and assessed. At each assessment period, the Zung Anxiety Scale was used to measure anxiety in the past week. The questionnaire included 20 items that are internally consistent and sensitive to the frequency of affective and somatic anxiety symptoms (40). Subjects rated each item from 1 (none or a little of the time) to 4 (most or all of the time), and the ratings were summed for a total continuous anxiety score. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). Subjects rated 20 items that relate to depressed mood, from 0 (rarely or none of the time) to 4 (most of the time); positive item scores were reversed, the ratings were summed, and the standard cut point of $\geq$ 16 was used to indicate depressed mood (30). Recently, among a sample of older African Americans, the CES-D was found to have high internal consistency (alpha = 0.86) (21). Stress was measured using the Cohen's Perceived Stress Scale, which measures the degree to which situations in the past month are appraised as stressful (3). Prior research has reported adequate reliability scores and high correlation of the Perceived Stress Scale with life event scores (3).

Menopausal status at each assessment period was constructed, using data from the menstrual dates concurrent with each study interview, plus the dates of the two previous menstrual periods recorded at each of the two interview visits, the self-reported number of menstrual periods between assessment periods, and cycle length and number of days of bleeding. At each assessment period, each subject was assigned to one of the following five menopause categories on the basis of the available information: *premenopausal*, defined as having regular menstrual cycles in the 22- to 35-d range; *late premenopause*, defined as within-subject change in cycle length > 7 d, in either direction, for one cycle compared with the subject's baseline at enrollment in the cohort; *early transition*, defined as within-subject change in cycle length > 7 d, in either direction, for at least two cycles compared with the subject's baseline at enrollment in the cohort; *late transition*, defined as 3–11 months of amenorrhea; or *postmenopausal*, defined as > 12 months of amenorrhea, with no hysterectomy (13).

Statistical analysis. To examine the relationship between concurrent measures of physical activity and continuous outcomes of menopausal symptoms such as depression, anxiety, stress, and vasomotor, psychological, and somatic symptom summaries for the 8-yr period, linear mixed-effects regression models were developed. Generalized linear mixed models were employed to estimate the

effect of physical activity on the dichotomous report of hot flashes (yes/no). The reporting of flashes also include reported night sweats. All models were fit using SAS Proc Genmod, and variance estimates for the Wald statistics of the true regression coefficients were adjusted for the repeated observations from each participant, using the generalized estimates equations approach (20). The lowest physical activity tertile was used as the reference group. All available data for each subject at each assessment period were included in the repeated-measures models, and time (time since entry into the study) was included in the model to account for the increased frequency of menopausal symptoms attributable to the aging of the cohort during the follow-up period. The final selection of covariates included in the models was guided by whether the variable remained statistically significant at $P < 0.05$ and whether inclusion modified other significant associations in the model by 15% or more (22). Menopausal status (assessed at each assessment period), race, smoking (assessed at each assessment period), and age at enrollment met these criteria and were included as covariates in the final multivariable models. Women were censored from the analysis for the assessment period that they reported exogenous hormone use.

Separate multivariable analyses were also conducted for smokers, African American women, women with a history of depression (defined as a CES-D score over 16), and by menopausal stage to examine the role of physical activity on menopausal symptoms among these select groups of women.

Additional models were developed that adjusted for estradiol, testosterone, and FSH levels measured at each assessment period. Because BMI was considered to be along the causal pathway between physical activity and symptoms (i.e., physical activity influences BMI, and BMI has a role in symptoms), it would be inappropriate to include BMI as a potential confounding variable. We did, however, develop models that included BMI, to explore possible mediation of the effects of interest. However, these results were very similar and are not presented. All analyses were performed using the SAS statistical package, version 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

Sample characteristics. The average age of the group at baseline was 42 yr old (±3.5), 49% were African American, 58% reported more than a high school education, 38% smoked cigarettes, and 44% reported a baseline CES-D score of 16 or higher. By design, all of the women were premenopausal at baseline. At assessment 10, 8 yr after enrollment into the cohort, 20% of the women were menopausal, with an additional 18% classified in the late transitional phase. More than 50% of women reported hot flashes (53%), 31% reported smoking cigarettes, 28% reported a CES-D score of 16 or higher at assessment 10, and the average kilocalorie-per-week expenditure at the end of the follow-up period (1355 ± 2033 kcal·wk^{-1}) was substantially lower compared with baseline levels (1424 ± 1759 kcal·wk^{-1}).

As shown in Table 1, the level of physical activity varied significantly by race, with African American women more likely to expend fewer kilocalories per week compared with Caucasian women. In addition, there was an inverse association between obesity and physical activity. Smoking was marginally related to physical activity, with 30% of women in the top-third physical activity group reporting smoking cigarettes compared with 40% of smokers in the bottom-third physical activity group ($P = 0.09$). In these unadjusted analyses, physical activity did not vary by education, marital status, parity, depressive symptoms, age, stress, or anxiety level at baseline. In addition, none of the hormone

TABLE 1. Demographic characteristics of participants in the Penn Study of Ovarian Aging by baseline physical activity.

	Physical Activity: Bottom Third, $N = 129$ (kcal·wk^{-1})	Physical Activity: Middle Third, $N = 131$ (kcal·wk^{-1})	Physical Activity: Top Third, $N = 120$ (kcal·wk^{-1})
Race*			
Caucasian	37.5%	58.8%	56.6%
African American	62.5%	41.2%	43.4%
Education			
High school or lower	44.2%	42.7%	41.9%
Greater than high school	55.8%	57.3%	58.1%
Marital status			
Married	59.2%	66.4%	54.3%
Not married	40.8%	33.6%	45.7%
BMI*			
Obese (≥ 30)	52.1%	32.0%	25.0%
Overweight (25–29)	21.0%	33.6%	37.1%
Normal (< 25)	26.9%	34.4%	37.9%
Smoking			
Yes	40.0%	42.8%	30.2%
No	60.0%	57.2%	69.8%
Parity (mean)	2.9	3.4	3.3
CES-D at baseline			
≥ 16	46.7%	39.7%	44.9%
< 16	53.3%	60.3%	55.1%
Age (yr)	41.9	42.6	42.1
Stress score at baseline	22.1	19.9	20.6
Anxiety score at baseline	35.0	34.1	35.2
Mean/median levels at baseline			
Estradial	43.3/35.1	47.8/41.5	42.9/36.5
FSH	8.6/7.1	8.5/7.0	9.7/6.9
Testerone	11.9/10.7	13.4/12.7	15.3/10.8
Menopausal status at 8 yr			
Postmenopausal	20.5%	18.5%	20.9%
Late transition	16.2%	17.4%	20.9%
Early transition	30.8%	27.2%	17.3%
Late premenopausal	2.6%	2.2%	6.2%
Premenopausal	29.9%	34.8%	34.6%

* $P < 0.001$.

Baseline tertiles of physical activity by kilocalories per week: top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}).

Age, smoking, BMI, depression, stress, and anxiety reported in this table were from the baseline assessment.

Menopausal status was measured at assessment 10 with menopausal status groupings defined as premenopausal (regular menstrual cycles in the 22- to 35-d range), late premenopausal (change in cycle length > 7 d, in either direction, for one cycle), early transition (change in cycle length > 7 d, in either direction, for at least two cycles), late transition (3–11 months of amenorrhea), or postmenopausal (>12 months of amenorrhea with no hysterectomy).

Anxiety was measured by Zung Anxiety Scale, stress was measured by Cohen's Perceived Stress Scale, and depression was measured by the Center for Epidemiologic Studies Depression Scale (CES-D).

TABLE 2. Effect of physical activity on menopausal symptoms.

	Vasomotor Symptom Summaries	Somatic Symptom Summaries	Psychological Symptom Summaries	Hot Flashes	Depression	Anxiety	Stress
Kilocalories*							
Top third	−0.13, −0.28, 0.02	−0.06, −0.021, 0.08	−0.26, −0.62, 0.09	0.82, 0.60, 1.11	−0.26, −1.51, 0.99	−0.24, −1.14, 0.66	−1.10, −2.05, −0.15
Middle third	−0.09, −0.21, 0.03	−0.10, −0.22, 0.02	−0.08, −0.36, 0.20	0.79, 0.61, 1.04	0.25, −0.79, 1.29	−0.40, −1.14, 0.34	−1.15, −1.96, −0.33
Bottom third	—	—	—	—	—	—	—

* Adjusted for menopausal status, race, smoking, and age. Odds ratios/95% confidence intervals reported for hot flashes and coefficient estimates reflecting differences in the average group/95% confidence intervals were reported for all other, continuous outcomes.
Vasomotor symptoms overall were defined by at least one report of hot flashes or aches.
Somatic symptoms overall were defined by at least one report of urine leaks, vaginal dryness, or decreased interest in sex.
Psychological symptoms overall were defined by at least one report of irritability, anxiety, feeling sad, mood swing, poor concentration, trouble sleeping, or headaches.
Depression was measured by the Center for Epidemiologic Studies–Depression Scale (CES-D).
Anxiety was measured by the Zung Anxiety Scale.
Stress was measured by the Cohen's Perceived Stress Scale.
Kilocalories are reported in tertiles as the top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}).

levels were significantly different between the three physical activity groups.

Physical activity and menopausal symptom summaries. Women in the top and middle tertiles of physical activity had lower vasomotor symptom summary scores during the study period compared with women in the bottom tertile, but these differences were not clinically large or statistically significant (Table 2). Physical activity was not associated with somatic and psychological symptom summaries during the study period. Among the subgroups of smokers, African American women, or women with depressive symptoms, physical activity was not significantly related to vasomotor, somatic, or psychological symptom summaries for the 8-yr follow-up period (Tables 3 and 4), although the trend of lower mean summary scores remained. Adjustment for estradiol, testosterone, and FSH did not significantly influence any of these findings. Physical activity was not related to vasomotor or somatic symptom summaries among any of the menopausal groups, although we found that active women in the late-transitional group had higher psychological symptoms summary scores (difference between group scores = 2.28, 95% CI: 1.46, 3.09) (Table 5).

Physical activity and hot flashes. As shown in Table 2, we did not find a relationship between reports of hot flashes during the study period and level of physical activity (OR = 0.82, 95% CI: 0.60, 1.11, P value = 0.20; and OR = 0.79, 95% CI: 0.61, 1.04, P value = 1.09 for the top and middle tertiles of physical activity, respectively), and physical activity was not related to hot flashes among the subgroup of smokers, African American women, or by menopausal group (Tables 3–5), or among women with depressive symptoms (data not shown). Including the hormones in the multivariate models, which adjusts for the variability in hormone levels by activity group, did not change these null findings.

Physical activity and depressive symptoms. Among the overall cohort, physical activity was not associated with mean levels of depressive symptoms for the 8-yr follow-up period (difference = −0.26, 95% CI: −1.51, 0.99 for the top tertile; and difference = 0.25, 95% CI: −0.79, 1.29 for the middle tertile). However, a significant relationship was found for the subset of postmenopausal women in the highest tertile of physical activity (difference = −4.05, 95% CI: −7.28, −0.82) (Table 5). Active, postmenopausal women had, on average, a four-point-lower depression score compared with postmenopausal women in the lowest tertile of physical activity. Among postmenopausal women in the middle tertile, physical activity was not significantly related to

TABLE 3. Effect of physical activity on menopausal symptoms among smokers.

	Vasomotor Symptom Summaries	Somatic Symptom Summaries	Psychological Symptom Summaries	Hot Flashes	Depression	Anxiety	Stress
Kilocalories*							
Top third	0.04, −0.21, 0.29	0.03, −0.22, 0.29	0.01, −0.62, 0.64	1.15, 0.70, 1.90	0.23, −2.07, 2.52	0.02, −1.64, 1.69	−1.29, −2.99, 0.41
Middle third	0.17, −0.05, 0.39	0.03, −0.19, 0.24	−0.08, −0.62, 0.47	1.16, 0.73, 1.82	−0.32, −2.15, 1.52	−0.13, −1.65, 1.38	−1.33, −2.80, 0.15
Bottom third	—	—	—	—	—	—	—

* Adjusted for menopausal status, race, smoking, and age. Odds ratios/95% confidence intervals reported for hot flashes and coefficient estimates reflecting differences in the average group/95% confidence intervals were reported for all other, continuous outcomes.
Vasomotor symptoms overall were defined by at least one report of hot flashes or aches.
Somatic symptoms overall were defined by at least one report of urine leaks, vaginal dryness, or decreased interest in sex.
Psychological symptoms overall were defined by at least one report of irritability, anxiety, feeling sad, mood swing, poor concentration, trouble sleeping, or headaches.
Depression was measured by the Center for Epidemiologic Studies–Depression Scale (CES-D).
Anxiety was measured by the Zung Anxiety Scale.
Stress was measured by the Cohen's Perceived Stress Scale.
Kilocalories are reported in tertiles as the top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}).

TABLE 4. Effect of physical activity on menopausal symptoms among African American women.

	Vasomotor Symptom Summaries	Somatic Symptom Summaries	Psychological Symptom Summaries	Hot Flashes	Depression	Anxiety	Stress
Kilocalories*							
Top third	−0.04, −0.28, 0.19	0.08, −0.12, 0.28	−0.38, −0.91, 0.16	0.96, 0.59, 1.53	0.04, −1.87, 1.94	0.49, −0.86, 1.84	−1.24, −2.47, −0.02
Middle third	−0.11, −0.29, 0.07	−0.06, −0.24, 0.12	−0.41, −0.80, −0.01	0.79, 0.53, 1.16	0.05, −1.53, 1.63	−0.72, −1.85, 0.42	−1.72, −2.94, −0.05
Bottom third	—	—	—	—	—	—	—

* Adjusted for menopausal status, race, smoking, and age. Odds ratios/95% confidence intervals reported for hot flashes and coefficient estimates reflecting differences in the average group/95% confidence intervals were reported for all other, continuous outcomes.
Vasomotor symptoms overall were defined by at least one report of hot flashes or aches.
Somatic symptoms overall were defined by at least one report of urine leaks, vaginal dryness, or decreased interest in sex.
Psychological symptoms overall were defined by at least one report of irritability, anxiety, feeling sad, mood swing, poor concentration, trouble sleeping, or headaches.
Depression was measured by the Center for Epidemiologic Studies–Depression Scale (CES-D).
Anxiety was measured by the Zung Anxiety Scale.
Stress was measured by the Cohen's Perceived Stress Scale.
Kilocalories are reported in tertiles as the top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}).

depressive symptoms over time. In contrast, among women in the late-transition group, higher depressive symptoms were found among women in the middle physical activity grouping, but not among the highest physical activity group (difference = 3.17, 95% 1.39, 4.94).

Physical activity at any level was not related to depressive symptoms among smokers, African American women, or women with a history of depressive symptoms during the study period (Tables 3 and 4). Adjustment for estradiol, testosterone, or FSH did not change any of these findings.

Physical activity and anxiety. Level of anxiety was not significantly related to physical activity in the overall cohort (Table 2). The only difference in anxiety during the study period was among active, late-transition, or postmenopausal women. Among active, postmenopausal women, anxiety was lower compared with the lowest activity group, but among active, late-transition women, the anxiety was higher among the active group (difference = 3.12, 95% CI: 1.45, 4.79) (Table 5). Level of physical activity was not related to anxiety among smokers, African American women, or women with depressive symptoms (Tables 3 and 4). Adjustment for each of the three hormones did not impact any of these relationships.

Physical activity and stress. As shown in Table 2, during the 8-yr study period, a reduction in stress was related to higher physical activity among women in both the top and middle tertiles of physical activity (difference = −1.10, 95% CI: −2.05, −0.15; and difference = −1.15, 95% CI: −1.96, −0.33, respectively). The relationship between stress and physical activity was most pronounced among postmenopausal women and African American women (Tables 4 and 5), with postmenopausal women in the top and middle physical activity groups reporting the largest mean differences in stress compared with postmenopausal women in the reference physical activity group (difference = −3.01, 95% CI: −7.88, 0.08; and difference = −4.61, 95% CI: −7.71, −1.49, respectively). These relationships remained after adjustment for estradiol, testosterone, and FSH levels. In addition, physical activity was related to stress among the subset of women with depressive symptoms (difference = −1.9, 95% CI: −3.22, −0.64; and difference = −2.2, 95% CI: −3.48, −0.87 among women reporting depressive symptoms in the top and middle tertiles, respectively).

DISCUSSION

Among a cohort of urban, community-dwelling women, we found that higher physical activity levels, translating into walking 4.0 mph for 1.5 h, five times a week, was only associated with lower levels of stress. These findings remained consistent in the models when adjusting for important covariates as well as hormone levels, indicating

TABLE 5. Effect of physical activity on menopausal symptoms: postmenopausal women (N = 90).

	Vasomotor Symptom Summaries	Somatic Symptom Summaries	Psychological Symptom Summaries	Hot Flashes	Depression	Anxiety	Stress
Kilocalories*							
Top third	−0.22, −0.85, 0.42	−0.06, −0.57, 0.44	−0.93, −2.03, 0.17	0.89, 0.14, 5.62	−4.05, −7.28, −0.82	−5.69, −8.41, −2.98	−3.90, −7.88, 0.08
Middle third	−0.09, −0.46, 0.28	−0.07, −0.46, 0.32	−0.33, −1.27, 0.62	0.79, 0.22, 2.89	−2.04, −5.38, 1.31	−2.36, −5.06, 0.34	−4.61, −7.71, −1.49
Bottom third	—	—	—	—	—	—	—

* Adjusted for menopausal status, race, smoking, and age. Odds ratios/95% confidence intervals reported for hot flashes and coefficient estimates reflecting differences in the average group/95% confidence intervals were reported for all other, continuous outcomes.
Vasomotor symptoms overall were defined by at least one report of hot flashes or aches.
Somatic symptoms overall were defined by at least one report of urine leaks, vaginal dryness, or decreased interest in sex.
Psychological symptoms overall were defined by at least one report of irritability, anxiety, feeling sad, mood swing, poor concentration, trouble sleeping, or headaches.
Depression was measured by the Center for Epidemiologic Studies–Depression Scale (CES-D).
Anxiety was measured by the Zung Anxiety Scale.
Stress was measured by the Cohen's Perceived Stress Scale.
Kilocalories are reported in tertiles as the top third (≥ 1450 kcal·wk^{-1}), middle third (< 1450 to 644 kcal·wk^{-1}), and bottom third (< 644 kcal·wk^{-1}).

the independent role of current physical activity level on current reported perceptions of stress. Similar to the majority of other studies, we did not find a relationship between physical activity and a decrease or increase in the frequency of vasomotor symptoms, including hot flashes.

Among the subset of active, postmenopausal women, we also found that physical activity was related to significantly lower levels of depressive symptoms as well as lower levels of perceived stress and anxiety. Others have reported a role of physical activity on lower anxiety and depression among women completing the menopausal transition (2,8). Using a single assessment of physical activity, a low level of physical activity was related to higher levels of perceived stress in the SWAN study (33). In addition, Mirzaiinjmabadi et al. (24) have reported that exercise was effective in relieving depression and anxiety among women participating in the Queensland Midlife Womens Health Study. Similar to this report, these authors also did not find a relationship between physical activity and vasomotor symptoms, including hot flashes (24). Paradoxically, we did find that physically active women in the late-transitional phase of menopause had higher levels of anxiety, depression, and overall psychological symptoms summaries. We feel that these findings illustrate the difficulty in categorizing and adjusting for fluctuations in sex hormone levels during this very transitional phase of the menopause. In fact, in preliminary analysis we found that depressive symptoms increase during the late-transitional phase among the group of women with an extreme, quadratic profile of fluctuations in sex hormones (i.e., increasing, then decreasing, levels of estradiol). Perhaps the role of physical activity may exacerbate psychological symptoms of menopausal among women in the late-transition phase, given the extreme variability in hormone levels. These findings may provide insight into the prior work of Whitcomb et al. (38) reporting an increase in hot flashes among physical active women.

Thurston et al. (35) recently have reported a role of physical activity and decreased vasomotor symptoms only among women with a history of depressive symptoms. We examined the role of physical activity level and menopausal symptoms, including hot flashes, anxiety, and stress, among the subset of women with current depressive symptoms. We did find that among women with current depressive symptoms, those with high levels of physical activity reported lower levels of anxiety. However, we did not find a relationship between physical activity and hot flashes in this subgroup. Given the low prevalence of women with current depressive symptoms, this study may not have adequate power to detect such associations.

Previous analyses of this cohort of women have found hormone levels to be related to menopausal symptoms; in particular, a quadratic estradiol profile (increasing, then decreasing, level of estradiol over time) has been linked to higher levels of vasomotor symptoms, including hot flashes; fluctuations in testosterone level have been related to decreased libido; and high levels of FSH, LH, and variability over time in FSH, LH, and estradiol levels have been related to new-onset depressive symptoms among women approaching the transition to menopause (10,12). In addition, a recent evaluation of this cohort of women has concluded that self-reported physical activity of > 1455 kcal·wk^{-1} was associated with 54% and 47% lower estradiol and testosterone levels, respectively, among women in the late-transition and postmenopausal groups. However, physical activity did not affect hormone levels in any of the other menopausal groups (32). Thus, although hormone levels have been previously linked to symptom reports in this cohort, the present study, which focused on the independent role of physical activity on a variety of menopausal symptoms, adjusting for variability in hormone levels, found that the level of physical activity was related only to reduced perceived stress. These data also indicate that higher levels of physical activity influence lower somatic/psychological symptoms most directly among women in the postmenopausal group.

Several limitations of this study should be noted. First, the measurement of physical activity was conducted approximately every 2 yr during the 8-yr follow-up period. In addition, both physical activity and hot flashes were collected via self-report, which may result in an imprecise measurement in this study. However, the error embedded in self-reported data are generally considered nondifferential, indicating that even if the exact level of physical activity or hot flashes is unknown, the ranking within groups is accurate. Further, such error would bias the results toward the null. For example, any recall bias in physical activity or hot flashes should be nondifferential by group and, thus, result in nonsignificant findings. Part of the reasoning behind our choice to use a between-person repeated-measures regression analytic approach was to minimize the impact of this imprecision in self-reported data by capitalizing on the repeated measurements. Second, we used a limited number of physical activity questions to assess and calculate expended kilocalories per week of leisure activity. Although others have reported high reliability using these measures, there may be individual variation in the kilocalorie expenditure per activity that we could not assess. This misclassification would also be nondifferential and, mostly likely, bias the estimates toward the null. Third, these reported associations are aggregate, cross-sectional assessments of physical activity and menopausal symptoms. Although physical activity and menopausal symptoms were assessed at four separate points during the follow-up period, the assessment periods were almost 2 yr apart. Given the fluctuation in physical activity level between assessment periods, we were concerned about the accuracy of using physical activity at one assessment period to predict symptoms in the next assessment period. In fact, one reason for our null findings may be our inability to evaluate a time lag for the prospective associations of interest. We and others have identified that physical activity has a direct, more immediate effect on psychological symptoms such as anxiety, stress, and depression. However, the current model cannot assess the impact of

physical activity on future vasomotor symptoms and hot flashes, given the large gaps in time between assessments. There is potential for some of the significant findings to be type I error, but, given our large, representative sample size, our *a priori* hypotheses, and the justification for the subgroup comparisons, we have substantially reduced the possibility for a type I error. Fourth, we were unable to examine the role of current physical activity and the severity of hot flashes because of the low number of women included in the cohort reporting severe hot flashes during the follow-up period. Finally, we did not collect information regarding other personality characteristics, including neuroticism or coping styles, and a limited number of women reported the use of other types of complementary and alternative therapies; thus, we could not examine or adjust for the influence of these factors on menopausal symptoms.

The strengths of this study include the recruitment of a large sample of urban, community-dwelling African America and Caucasian women approaching the menopausal transition, with an excellent follow-up rate during the 8-yr period; multiple assessments of a variety of menopausal symptoms and validated physical activity levels during an 8-yr period; conducting multivariate modeling, which allows for change over time in symptom reports and physical activity; censoring women from the analysis if they reported exogenous hormone use; incorporating valid, reproducible instruments to assess vasomotor symptoms, anxiety, depression, and psychosocial stress; and the generalizability of these study results to both Caucasian and African American women, given the initial subject-selection criteria.

In conclusion, we found that high levels of physical activity were related to lower levels of perceived stress, and levels of anxiety, stress, and depression were significantly lower among physically active, postmenopausal women compared with postmenopausal women in the lowest tertile of physical activity. These results suggest that maintaining or increasing physical activity during the menopausal transitional period and postmenopause may assist in reducing a variety of psychological symptoms, including anxiety, stress, and depression. We did not find an association between physical activity and vasomotor symptoms, including hot flashes. In addition, we could not confirm the findings of Whitcomb et al. (38), which indicate that high levels of physical activity before the final menstrual cycle resulted in an increased frequency and severity of hot flashes, because we measured current physical activity among menopausal-age women. It is possible that the conflicting findings regarding the effect of physical activity on vasomotor symptoms reported in the literature could be accounted for by variability in the changes in endogenous reproductive hormones given regular exercise above some undefined threshold. Additional studies of the effects of a wide rage of physical activity levels on vasomotor menopausal symptoms, before and after the final menstrual period, and including measurements of reproductive hormones, are needed to explore this hypothesis.

REFERENCES

1. Ainsworth BE, Haskell HW, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc.* 2000;32(9 suppl):S498–504.
2. Asbury EA, Chandrruangphen P, Collins P. The importance of continued exercise participation in quality of life and psychological well-being in previously inactive postmenopausal women: a pilot study. *Menopause.* 2006;13(4):561–7.
3. Cohen SKT, Mermelstein RA. Global measure of perceived stress. *J Health Soc Behav.* 1983;24:385–96.
4. Cramer DW, Barbieri RL, Xu H, Reichardt JK. Determinants of basal follicle-stimulating hormone levels in premenopausal women. *J Clin Endocrinol Metab.* 1994;79:1105–59.
5. Daley A, Macarthur C, Stokes-Lampard H, McManus R, Wilson S, Mutrie N. Exercise participation, body mass index, and health-related quality of life in women of menopausal age. *Br J Gen Pract.* 2007;57(535):130–5.
6. Elavsky S, McAuley E. Physical activity and mental health outcomes during menopause: a randomized controlled trial. *Ann Behav Med.* 2007;33(2):132–42.
7. Elavsky S, McAuley E. Physical activity, symptoms, esteem, and life satisfaction during menopause. *Maturitas.* 2005;52(3–4): 374–85.
8. Freeman EW, Sammel MD, Grisso JA, Battistini M, Garcia-Espagna B, Hollander L. Hot flashes in the late reproductive years: risk factors for African American and Caucasian Women. *J Womens Health Gend Based Med.* 2001;10(1):67–76.
9. Freeman EW, Sammel MD, Lin H, et al. Symptoms associated with menopausal transition and reproductive hormones in midlife women. *Obstet Gynecol.* 2007;110:230–40.
10. Freeman EW, Sammel MD, Liu L, Gracia CR, Nelson DB, Hollander L. Hormones and menopausal status as predictors of depression in women in the transition to menopause. *Arch Gen Psychiatry* 2004;61(1):62–70.
11. Freeman EW, Sammel MD, Liu L, Martin P. Psychometric properties of a menopausal symptom list. *Menopause.* 2003;10(3): 258–65.
12. Gracia CR, Sammel MD, Freeman EW, Liu L, Hollander L, Nelson DB. Predictors of decreased libido in women during the late reproductive years. *Menopause.* 2004;11(2):144–50.
13. Gracia CR, Sammel MD, Freeman EW, et al. Defining menopausal status: a new definition to identify the earliest changes. *Menopause.* 2005;12(2):128–35.
14. Greenberg G, Thompson SG, Meade TW. Relation between cigarette smoking and use of hormonal replacemtn therapy for menopausal symptoms. *J Epidemiol Community Health.* 1987; 41(1):26–9.
15. Guthrie JR, Dennerstein L, Taffe JR, Donnelly V. Health care-seeking for menopausal problems. *Climacteric.* 2003;6:112–7.
16. Guthrie JR, Smith AM, Dennerstein L, Morse C. Physical activity and the menopause experience: a cross-sectional study. *Maturitas.* 1994;20(2–3):71–80.
17. Hassa H, Tanir HM, Tekin B, Sense T, Oge T, Mutlu FS. Possible factors affecting the age at menopause among women in the central Anatolian religion of Turkey. *Clin Exp Obstet Gynecol.* 2006;33(1):59–60.
18. Juang KD, Wang SJ, Lu SR, Lee SJ, Fuh JL. Hot flashes are associated with psychological symptoms of anxiety and depression in peri- and post- but not premenopausal women. *Maturitas.* 2005;52(2):119–26.

19. Kronenberg F. Hot flashes. In: Lobo RA, editor. *Treatment of the Postmenopausal Woman*. 2nd ed. New York (NY): Raven Press; 1999. p. 157–77.
20. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986;73:13–22.
21. Long FK, Reed PS, Mutran EJ, DeVellis RF. Measuremnt adequacy of the CES-D among a sample of older. *Afr Am Psychiatry Res*. 2002;109(1):1–9.
22. Maldonano G, Greenland S. Simulation study of confounder-selection strategies. *Am J Epidemiol*. 1993;138:923–36.
23. Manson JM, Sammel MD, Freeman EW, Grisso JA. Racial differences in sex hormone levels in women approaching the transition to menopause. *Fertil Steril*. 2001;75(2):297–304.
24. Mirzaiinjmabadi K, Anderson D, Marnes M. The relationship between exercise, body mass index and menopausal symptoms in midlife Australian women. *Int J Nurs Pract*. 2006;12(1): 28–34.
25. Muti P, Trevisan M, Micheli A, et al. Reliability of serum hormones in premenopausal and postmenopausal women over a one-year period. *Cancer Epidemiol Biomarkers Prev*. 1996;5: 917–22.
26. Nelson DB, Sammel MD, Freeman EW, Liu L, Langan E, Gracia CR. Predicting participation in prospective cohort studies. *Menopause*. 2003;11(5):1–6.
27. Paffenbarger RA, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol*. 1978;108:161–75.
28. Pereira MA, FitzerGerald SJ, Gregg EW, et al. A collection of physical activity questionnaires for health-related research. *Med Sci Sports Exerc*. 1997;29:S1–205.
29. Pines A, Fisman EZ. The healing properties of exercise. *Menopause*. 2006;13(4):544–5.
30. Radloff LS. The CES-D scale: a new self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–401.
31. Santoro N, Adel T, Skurnick JH. Decreased inhibin tone and increased activin a secretion characterize reproductive aging in women. *Fertil Steril*. 1999;71:658–62.
32. Schmidt KA, Lin H, Sammel MD, et al. Association of physical activity with reproductive hormones: the Penn Ovarian Aging Study. *Cancer Epidemiol Biomarkers Prev*. 2007;16(10):2042–7.
33. Sternfeld B, Cauley J, Harlow S, Liu G, Lee M. Assessment of physical activity with a single global question in a large, multi-ethnic sample of midlife women. *Am J Epidemiol*. 2000;152:678–87.
34. Sternfeld B, Quesenberry CP Jr, Husson G. Habitual physical activity and menopausal symptoms: a case-control study. *J Womens Health*. 1999;8(1):115–23.
35. Thurston RC, Joffe H, Soares CN, Harlow BL. Physical activity and risk of vasomotor symptoms in women with and without a history of depression: results from the harvard study of mood and cycles. *Menopause*. 2006;13(4):553–60.
36. Treatment of menopause related vasomotor symptoms: position statement of the North American Menopause Society. *Menopause*. 2004;11:11–33.
37. Villaverde-Gutierrez C, Araujo E, Cruz F, Roa JM, Barbosa W, Ruiz-Villaverde G. Quality of life of rural menopausal women in response to a customized exercise programme. *J Adv Nurs*. 2006;54(1):11–19.
38. Whitcomb BW, Whiteman MK, Langenberg P, Flaws JA, Romani WA. Physical activity and risk of hot flashes among women in midlife. *J Womens Health*. 2007;16(1):124–33.
39. Woods NF. Exercise and hot flashes: toward a research agenda. *Menopause*. 2006;13(4):541–3.
40. Zung WWK. A rating instrument for anxiety disorders. *Psychosomatics*. 1971;12:371–9.