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Association between Physical Activity and Depressive Symptoms: Midlife Women in SWAN

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Abstract

Introduction—The relationship of physical activity (PA) and positive mood has been the focus of considerable research, primarily cross-sectional. This study was done to evaluate the relationship between PA and high depressive symptoms across time and to examine whether being physically active attenuates the risk of depressive symptoms in midlife women.

Methods—The present study is a longitudinal observation study of the menopausal transition in a multiethnic population. Ten years of data on 2891 women were analyzed. The participants were women from seven geographic areas nationwide, aged 42 to 52 years at baseline, still menstruating and not using exogenous reproductive hormones. Physical activity was measured with the Kaiser Permanente Physical Activity Scale (KPAS). The main outcome measure, depressive symptoms, was assessed with the Center for Epidemiological Studies Depression Scale (CES-D) with primary outcome CES-D score of 16 or higher.

Results—In mixed effect logistic regression models adjusted for covariates, compared to inactivity, physical activity Meeting PA Guidelines (approximating public health guidelines) and physical activity Below PA Guidelines were each associated with lower risk of High Depressive Symptoms (CES-D score of 16 or higher) [odds ratio (OR) =0.52, 95% confidence intervals (CI) 0.40-0.70; OR =0.81, 95% CI 0.67-0.98, respectively] across 10 years. Being married, Japanese and Hispanic ethnicity, current smoking, reporting very upsetting life events, using anti-depressive medications, having hot flashes, and high BMI were all positively associated with High Depressive Symptoms, while high social support was negatively associated.

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Conclusions—Higher PA was associated with lower levels of depressive symptoms persistently over ten years independent of potential confounders. Our findings suggest that reaching moderate intensity PA levels during midlife may be protective against depressive symptoms.

Keywords

Depression; Moderate Intensity Exercise; Menopause; Guidelines

Introduction

It is well-known that depression is a leading cause of disability. In the United States, it is estimated that approximately 16% of the population will meet criteria for Major Depressive Disorder (MDD) in their lifetime, with women being 1.7 times more likely than men to develop the disorder. [24] The predominance of women in those with MDD has generated considerable research focused on the endocrine/biological differences between males and females and the increased risk of MDD during periods of reproductive changes and events in women. In the Study of Women's Health Across the Nation (SWAN), a multi-center, multi-ethnic, community-based cohort study of women, we have shown that that change in menopausal status from pre- to early peri-menopause and late peri-menopause is independently associated with increased risk of a high level of depressive symptoms.[5] Thus, the menopausal transition represents a period of vulnerability to depression that would benefit from better methods of prevention and intervention, particularly non-pharmacological approaches.

We were particularly interested in the possible protective role moderate intensity physical activity (PA) might have on depression in midlife women and the persistence of this association across time. The public health recommended dose of 150 minutes of moderate intensity PA weekly has been associated with multiple health benefits. [19] Cross sectional studies in midlife women consistently demonstrate a positive association between PA and positive mood, vigor, and general well-being [8-9,11,15,28,44-45] and a negative association with negative symptoms, such as depression, anxiety, and perceived stress [11,13,28,35,46] but the study populations, covariates, PA measures and depression outcomes varied. The Melbourne Women's Midlife Health Project looked longitudinally at change in well being (rather than depression or depressive symptoms) and found a marginally significant positive association with change in well-being and PA over a three year follow-up period.[18] In the Belgian National Health Interview Survey of more than 6,800 adults aged 25 to 64 years of age, for women, positive correlations were found for self reported walking and emotional well being, different from men with positive correlations between vigorous activity and mood. [1]

Randomized trials of exercise show that women in exercise groups report improvements in mood symptoms, relative to controls, with structured, supervised programs for several hours per week over several months, including aerobic and strength training. [14,27,39,42] For example, Dennerstein and colleagues compared the public health guidelines recommendation of 150 minutes of moderate intensity PA weekly with a lower dose of PA and found that after 12 weeks of supervised exercise in individuals with MDD, only the dose

meeting public health guidelines was associated with reduced depressive symptoms at a rate similar to other anti-depressant interventions.[11] A community based, controlled trial of strength training using elastic bands with women with mean age of 68 years old demonstrated improvements in strength but not in mental health functioning. [10] In an intervention study of sedentary midlife African American women, adherence to a community based walking program at moderate intensity was associated with lower depressive symptoms at six months. [47] Trivedi and colleagues, in the TReatment with Exercise Augmentation for Depression (TREAD) study, tested the efficacy of 2 different doses of aerobic exercise in patients with MDD who had not remitted with antidepressant medication and found a trend toward a higher remission rate in the higher-dose exercise group. [38] Further, they concluded that higher-dose exercise may better for women without a family history of mental illness. Researchers in the UK used accelerometers to correlate objectively measured level of physical activity with daily positive emotional style but not psychophysiological stress responses in 40 healthy females (aged 28.7 ± 6.1 yrs). [30] Of interest, using cut-points for the accelerometer data, the positive correlation with daily mood was found for light and moderate intensity but not vigorous intensity PA.

SWAN provides the opportunity to examine in midlife women the independent association between naturally occurring changes in PA and changes in depression across time, adjusting for covariates that might confound this association The current analyses tested the hypothesis that a level of PA that approximates the public health recommendation of 150 minutes per week of moderate intensity PA (referred to here as “Meeting PA Guidelines”) is associated longitudinally with lower levels of depressive symptoms over ten years independent of potential confounders. In addition, we tested the hypothesis that women who reported some exercise but not at a level that approximates the public health recommended dose (“Below PA Guidelines”) would also report fewer depressive symptoms over ten years than women with no reported exercise or sports activity (“Inactive”). Results of this evaluation can increase our understanding of the extent to which physical activity may be useful in managing depression in midlife women and how persistent the relationship may be over midlife, a time of vulnerability.

Methods

Participants

Participants for the current analysis were from the Study of Women's Health Across the Nation (SWAN). Between 1995 and 1997, SWAN recruited over 3,000 women from five ethnic/racial groups who self identified as Caucasian, African American, Japanese, Chinese or Hispanic. Recruiting from seven sites allowed for recruitment of Caucasian women and one specified minority group (African Americans in Pittsburgh, Boston, the Detroit area, and Chicago; Japanese in Los Angeles; Chinese in the Oakland region; and Hispanics in Newark) at each site. Women aged 42-52 years of age with an intact uterus and at least one ovary were invited to participate in SWAN as long as they had menstruated in the previous three months, were not currently pregnant or breast feeding, and had not used reproductive hormone preparations affecting ovarian or pituitary function in the past three months. Several population sampling techniques were used and IRB approval and informed consent

were obtained by all sites, as previously described. [36]. At study entry and annually thereafter women at all sites completed a standard assessment that included self-administered and interviewer-administered questionnaires assessing sociodemographic, behavioral, psychological, physical, health and lifestyle characteristics. Interviews and questionnaires were available in English, Spanish, Cantonese, and Japanese. All women provided written informed consent. Of 3,302 midlife women enrolled in SWAN, this analysis includes data from 2,891 participants who provided data on PA level, depressive symptoms, and relevant covariates in one or more annual assessments.

Study Variables

Data for the current study were obtained from self-administered and interviewer-administered questionnaires at baseline and at annual follow up (F/U) visits for 10 years. Data on PA were collected at baseline and F/U years 3, 6, and 9. Sociodemographic data including age, ethnicity, marital status and education were collected at baseline. Time varying covariates included depressive symptoms, menopausal status, body mass index (BMI), social support, very stressful life events, antidepressant medication use and hormone replacement therapy (HT), smoking status, frequent hot flashes or night sweats were assessed at baseline and at each of the following visits.

Independent Variable

Physical activity was measured using a version of the Kaiser Physical Activity Survey (KPAS), originally adapted from the Baecke questionnaire. [2], that consists of 38 items. [37] The KPAS is self-administered, asks about PA in the past year, and assesses PA in four domains (sports/exercise, active living, occupational, household/caregiving). Most of the items have categorical responses that are combined to provide domain-specific indices as well as a total score. For this analysis, the results in the sports/exercise domain were used (an open-ended question about participation in most frequent sport or exercise, and 3 questions with categorical responses for frequency, duration and relative intensity). Women reported a broad range of sports and exercise, including team sports, individual sports, and recreational activities including walking. Women who reported playing sports or exercising more than once a week, for at least 2 hours per week, with a moderate or greater increase in heart rate and breathing, and for more than 9 months per year were classified into the “Meeting PA Guidelines” group. We considered this level of PA to approximate the public health guidelines recommendation of 150 minutes of moderate intensity PA weekly for health benefits.[19] Women who reported sports or exercise but not at the frequency, relative intensity or duration approximating the public health guideline were classified as the “Below PA Guidelines” group. Women who never reported any participation in sports or exercise were classified as the “Inactive” group (referent). The 3 groups were mutually exclusive. Those who were Inactive reported not participating in any sports or exercise. The Below PA Guidelines group could report sports or exercise activity ranging from a very small or irregular amount of PA to just below guidelines. Likewise, the Meeting PA Guidelines group could range from just meeting guidelines to very active.

Dependent Variables

Depressive Symptoms

Depressive symptoms were measured with the 20-item Center for Epidemiological Studies Depression Scale (CES-D), which assesses the frequency of being bothered by depressive symptoms in the past week on a scale from 0 (rarely) to 3 (most or all of the time). [33] Responses to the 20 items are summed for a total score ranging from 0-60. CES-D scores of 16 or higher indicate 'High Depressive Symptoms' with possible clinical implications. [3] The CES-D has been shown to be valid and reliable in diverse ethnic populations. [22,48]

Covariates

Covariates were chosen for inclusion in statistical analyses due to their established relationship with physical activity and/or relevance to the possible relationship between physical activity and depressive symptoms based on the literature. [4,6,16,23] Standard self-report questions frequently used in epidemiological studies were used to assess most of the covariates. Age was self-reported in years. Cigarette smoking (yes/no) and hot flashes (present < 6 days or ≥ 6 days in previous 14 days) were self-reported. Interviewer-administered questions included race/ethnicity self identification as African American, Chinese, Hispanic, Japanese or Caucasian (referent category). Respondents were classified to high education (some college education or higher) or not. Marital status was defined as either married and/or living as married or not married. Menopausal status was considered in 2 groups: premenopausal/early perimenopausal versus late peri-menopausal/post menopausal (no menstrual bleeding for at least 3 months/12 months). Anti-depressant medication and HT use was based on use in the past month. Body mass index was calculated from measured height and weight using a standardized protocol. Psychosocial variables included social support, 4 items from the Medical Outcomes Study Social Support Survey, summed and used continuously with possible scores ranging from 0 for least social support to 16 for most social support [34] and stressful life events based on a checklist of 18 life events rated according to how stressful they were. Number of very stressful events since the last study visit was categorized as 0, 1 or 2 or more.

Statistical Analyses

Four assessment TIME PAIRs were created and used in the analyses, linked to the four available PA measurements, as PA was not measured annually. We paired PA measured at baseline, F/U visit 3, F/U visit 6 and F/U visit 9 with CES-D in the following visit (F/U visit 1, F/U visit 4, F/U visit7 and F/U visit 10) for the TIME PAIR 0, TIME PAIR 1, TIME PAIR 2 and TIME PAIR 3 analyses, respectively. Each TIME PAIR analysis included baseline variables and time-varying covariates collected at each of the four PA visits. This allowed us to examine if the association between PA and depressive symptoms changed over time independent of the effect of the covariates.

Participant characteristics at TIME PAIR 0 were summarized using mean (SD) for continuous variables and N (%) for categorical variables for the overall cohort and by PA group. Group differences were tested using ANOVA for continuous variables and chi-squared tests for categorical variables. In order to summarize changes of depressive

symptoms and physical activity, the proportions of participants with High Depressive Symptoms and of those Meeting PA Guidelines were computed in each TIME PAIR. Similarly, the proportions of participants with High Depressive Symptoms and of those Below PA Guidelines were computed in each TIME PAIR. Persistence of High Depressive Symptoms was defined as having High Depressive Symptoms over at least two consecutive TIME PAIRs (0 and 1, 1 and 2, or 2 and 3). Similarly persistence of Meeting PA Guidelines was defined as Meeting PA Guidelines over at least two consecutive TIME PAIRs (0 and 1, 1 and 2, or 2 and 3).

The associations between PA and depressive symptoms in the four TIME PAIRs were assessed using mixed effects logistic regression.[20] PA and covariates collected at a given visit were included as time-varying predictors of depressive symptoms in the subsequent visit year. All analyses included baseline time-invarying covariates. A random intercept for each participant represented her depressive tendency over time, e.g. the greater the exhibition of High Depressive Symptoms, the higher the random intercept. Therefore, the mixed model provides the association between PA and depressive symptoms controlling for participants' depressive tendency. In order to determine if the associations between PA and depressive symptoms were similar over TIME PAIRs, two models were run, one which allowed for associations to vary by TIME PAIRs and another with a fixed association across TIME PAIRs. This step was taken to determine the feasibility of performing the analyses assuming a fixed association. The final analyses were conducted first as bivariate models without including any covariates, then as multivariable models controlling for covariates. All statistical tests were two-tailed, with statistical significance set at $P < .05$. All analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC).

Results

Among 2891 total eligible participants, the number of participants providing data included in TIME PAIR 0, TIME PAIR 1, TIME PAIR 2, and TIME PAIR 3 was 2682, 1951, 1554, and 1447, respectively. Because one of the variables in TIME PAIR 0 was missing (either baseline Physical Activity measurement, a time-varying covariates, or CES-D at follow-up visit 1) in 209 participants, their data were included in TIME PAIR 1, TIME PAIR 2 and/or TIME PAIR 3 when all variables were completed. Table 1 shows the characteristics of the cohort overall and by physical activity level at TIME PAIR 0 for 2682 participants (2891-209=2682). At baseline the participants were 46 years of age on average with 49% self identifying as Caucasian. They were well educated with 77% reporting education beyond high school. Their mean BMI was 28.0 (SD=7.1). One-fifth of the participants (20.0%, N=535) had High Depressive Symptoms (CESD> or =16). Only 17% reported Meeting PA Guidelines. There were statistically significant physical activity group differences for multiple covariates such that among women Meeting PA Guidelines, lower average BMI and higher average social support were each associated with a lower proportion of participants who reported High Depressive Symptoms. (Table 1)

Over the decade of data collection in SWAN, different trends in High Depressive Symptoms and Meeting PA Guidelines were noted. The proportion of participants with High Depressive Symptoms decreased while the proportion of those Meeting PA Guidelines

increased over time. (Table 2) The individuals in the group with High Depressive Symptoms or Meeting PA Guidelines were not consistent over time. About half of the participants who had High Depressive Symptoms in a previous TIME PAIR also had High Depressive Symptoms in the subsequent TIME PAIR. Similarly, about half to two thirds of the participants Meeting PA Guidelines in a previous TIME PAIR engaged in this level of PA in the subsequent TIME PAIR. (Table 3)

The relationship between PA and High Depressive Symptoms did not differ over time either in the bivariate analysis (Chi-square = 1.7, df=6, p= 0.94) or multivariate analysis (Chi-square = 27.5, df=33, p = 0.74). Therefore, we present only results of the analysis where we assumed a constant association over time. In unadjusted analyses, Physical Activity, either Meeting PA Guidelines or Below, was negatively associated with High Depressive Symptoms in the following year. Odds of having High Depressive Symptom for participants Meeting PA Guidelines and Below PA Guidelines were about two thirds (OR=0.34) and one third (OR=0.65) lower, respectively, compared to Inactive participants. Controlling for covariates, odds ratios for Physical Activity, Meeting Guidelines or Below PA Guidelines, were reduced but still significantly negatively associated with High Depressive Symptoms. The odds of having High Depressive Symptoms for participants Meeting PA Guidelines and Below PA Guidelines were about half (0.52, 95% confidence intervals 0.40-0.70) and one-fifth (0.81, 95% confidence intervals 0.67-0.98), respectively, compared to Inactive participants. (Table 4) Despite the finding that the individuals in the group with High Depressive Symptoms or Meeting PA Guidelines were not consistent over time, the relationship between the two variables persisted over the TIME PAIRs.

Married individuals were less likely to report High Depressive Symptoms and Japanese and Hispanic individuals were more likely than Caucasians to report High Depressive Symptoms. Time-varying covariates include the following: current smoker, very upsetting life events, anti-depressive medications use, hot flashes, and BMI. These covariates were all positively associated with High Depressive Symptoms. Higher social support was associated with reduced odds ratios. Menopausal status was not associated with High Depressive Symptoms in this analysis.

Discussion

In this study we assessed whether physical activity levels, in particular at the dose, frequency and relative intensity approximating public health guidelines, were associated longitudinally with lower levels of depressive symptoms over ten years independent of potential confounders. To our knowledge, this is the first study exploring the longitudinal relationship between physical activity and depressive symptoms in midlife women over a decade. Consistent with previous studies, we found that physical actively is inversely related to depressive symptoms, possibly conferring a protective effect. This inverse relationship is particularly meaningful during midlife as menopause and its accompanying hot flashes, which can last for a number of years, have been associated with increased risk of potentially clinically significant levels of depressive symptoms.[5] Our study demonstrates the positive effects of voluntary exercise and PA on mental health, with greater impact at the dose recommended by Centers for Disease Control and Prevention.[7] Given the high prevalence

of depression in the United States, for women in particular, exercise is still not considered a first line treatment option, even though exercise can be low cost and low risk, can be sustained indefinitely, and has additional benefits for multiple aspects of physical health and physical function. A twelve week exercise program for MDD non remitted with SSRI treatment has shown positive outcomes at 2 different doses of PA. [38] This is particularly important to menopausal women who are accumulating greater health risks and disability. Further, our results are strengthened by our analysis demonstrating a persistent relationship between PA and mood over time despite the finding that the individuals in the group with High Depressive Symptoms or Meeting PA Guidelines were not consistent over time.

Of interest, the menopausal variable in the mixed model is non-significant. It may be that PA is a stronger correlate of depressive symptoms than menopausal status. However, this finding may be related to the variable construct we used. It is likely that combining pre- and early peri-menopausal as the reference group accounts for the differences in results from the previous analysis. The previous analysis compared pre-menopausal to early peri-, late peri- and post-menopausal. [5] Early peri- had significantly higher odds of high CESD than pre-menopausal. Additionally, hot flashes are strongly associated with menopausal status, particularly prevalent during late peri- and post-menopause, and are apparently a better predictor of high depressive symptoms than the status variable itself in these analyses. Other covariates were significantly associated with High Depressive Symptoms. Married individuals and women with greater than a high school education were less likely to report High Depressive Symptoms and Japanese and Hispanic individuals were more likely than Caucasians to report High Depressive Symptoms. Over time smokers, women experiencing very upsetting life events, taking anti-depressive medications, having hot flashes, reporting low social support and higher BMI, were at greater risk for High Depressive Symptoms. The associations observed are consistent with what has been observed in other studies of depression in midlife women. [4,17] Importantly, these data suggest that even when common predictors of depression are accounted for, PA, particularly PA that meets guidelines, is associated with reduced risk for high depressive symptoms.

Repeated assessment of the association over time revealed that the magnitude of the association was not affected by chronological age, but was constant from a mean age of 46 years old, in TIME PAIR 0, to a mean age of 55 years old, in TIME PAIR 3. Finally, both PA level and level of depressive symptoms changed considerably over time (e.g., about half of subjects Meeting PA Guidelines at TIME PAIR 0 did not meet it at TIME PAIR 1), suggesting the importance of interventions that not only increase but sustain regular PA. Similarly, it is noteworthy that depressive symptom reports also change over time, but persist in about half of the subjects. The importance of the varying symptoms and behaviors may be taken into account by clinicians caring for midlife women who will need to reinforce not only adopting but sustaining healthy behaviors.

Both psychological and physiologic mechanisms, including reduced inflammation [32], increased levels of neurotransmitters (specifically, dopamine and serotonin), and enhanced brain aminergic synaptic transmission [43], increased endorphin secretion [21], distraction from stressful stimuli[25], and improved self-efficacy and self-esteem[29] may be responsible for these observed protective effects. In the TReatment with Exercise

Augmentation for Depression (TREAD) study, pro inflammatory cytokines were measured before and after the 12 week exercise intervention, with higher baseline levels of TNF- α associated with greater decrease in depression symptoms. [32] In addition, a significant positive correlation between change in IL 1β levels and change in depression symptoms scores was observed. Endocannabinoids, like the endogenous opioids, are known to have anxiolytic and analgesic properties and to be present in elevated concentrations in the body following exercise and may be another plausible mechanism for the physiologic basis for the benefits of PA on mental health.[12] The positive role of physical activity in brain health has been linked to increased expression of Brain-Derived Neurotrophic Factor (BDNF), a protein hypothesized to limit or repair the damage caused by stress.[26] Exercise is known to increase levels of a number of neurotrophic factors in both experimental animals and humans [41] and induce activity in the pre-frontal cortex on neuroimaging that parallel those seen with anti-depressant medications. [31] Our results suggest that the ‘dose’ of moderate intensity PA that has been recommended for other health benefits , including increased longevity, decreased risk of cardiorespiratory and metabolic diseases and some cancers (most notably colon and breast), maintenance of energy balance, and improved musculoskeletal health and function[40], also appears to be protective for depressive symptoms.

Given the myriad positive effects of this level of PA, it is likely that for each individual there is a unique and important benefit to one's physical and emotional health bestowed by Meeting PA Guidelines. Sadly, less than half of the population regularly participates in physical activity at the guideline level linked to health benefits, and adherence to physical activity guidelines is even lower among women ages 40 to 60.[7] This finding persists in our current study with only 17% of participants reporting PA at the Meeting Guidelines level. Maintenance of the recommended level over a decade in midlife is even more challenging. Behavior change models that focus on sustained changes in physical activity need to be the focus of public health research and clinical care. Sustaining even modest levels of physical activity may prevent depressive symptoms so public health messages should support all physical activity behavior. There may be gender differences relative to PA and mood that should be considered in tailoring these messages.

Strengths of this study include: a large multiracial sample of women from a well-characterized cohort study; 10 years of follow up data; adjustment for important covariates; an extensive validated PA questionnaire allowing for a calculation of dose of PA approximating public health guidelines; repeated assessments of the association over a decade which revealed the robust association; and the opportunity to study persistence of the relationship between PA and depressive symptoms.

Limitations of this study include recall survey methodology of the dependent and independent variables; there was no objective measure of physical activity and no measure of clinical depression. We were not able to determine the exact volume of exercise, allowing only an approximate comparison between the recommended public health dosing of exercise and our approximation of the recommended amount. We were constrained by the SWAN study protocol which measured PA on average every three years rather than annually. This led to our paired groupings of PA in one year and CESD in the subsequent year, at TIME

PAIRs 0-3. Covariate time frames reflected recall from the past four weeks, i.e. social support, up to the past one year, i.e. upsetting life events, while the time frame of the CESD was the past one week and the KPAS was the past one year. As in all longitudinal studies, participant drop outs played a role and may have biased our sample and hence our findings. The proportion of participants with High Depressive Symptoms decreased while the proportion of those Meeting PA Guidelines increased over time, which might reflect a tendency for women with lower depressive symptom levels to continue in the study while those with higher symptom levels dropped out. Likewise, women who were more active may have been more committed to attending follow up visits than inactive women. Finally, we had very small frequencies of participant data in some of the cells, i.e. Hispanics Meeting guidelines, which limited inferences in regards to racial differences.

To our knowledge, the current study is the first longitudinal study of physical activity, at and below PA guidelines, and depressive symptoms to be conducted in a large and diverse sample of midlife women traversing the menopause. The results are independent of multiple relevant and confounding covariates, including BMI, sociodemographics, HT and anti depressive medication use. Notably, the association between physical activity and high depressive symptoms was found for both PA groups, Meeting or Below Guidelines, relative to the Inactive group and persisted over time. Our findings suggest that motivating midlife women to maintain at least some level of moderate intensity PA may be protective against depressive symptoms, with some activity better than inactivity. Depression leads to extensive social, emotional and economic impairments and raising awareness of approaches to prevent or reduce its symptoms at this vulnerable time for women would be extremely valuable, even life changing. Our findings provide another example to share with midlife women and their healthcare and wellness providers as they make suggestions for robust sustained lifestyle behavior changes that diminish one's risk of depressive symptoms and their sequelea during midlife, a particularly vulnerable time for women.

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Table 1

Sociodemographics By Physical Activity Level at Baseline (TIMEPAIR 0)

*Meeting PA Guidelines=sports or exercise > once a week, 2 hours or more per week, mod or large increase in heart rate & breathing, > 9 months per year	Inactive (N=1174)		*Below PA Guidelines (N=1051)		*Meeting PA Guidelines (N=457)		All Participants in TIME PAIR 0 (N=2682)		P-Value
	N	%	N	%	N	%	N	%	
CESD Score ≥ 16[†]	288	28.7%	197	19.8%	50	14.7%	535	19.9%	<0.0001
Education > High School	802	68.3%	866	82.4%	409	89.5%	2077	77.4%	<0.0001
Married	749	63.8%	731	69.6%	341	74.6%	1821	67.9%	<0.0001
Antidepressant Medication	115	9.8%	108	10.3%	35	7.7%	258	9.6%	0.2748
Current Smoker	233	19.8%	136	12.9%	33	7.2%	402	15.0%	<0.0001
Hot Flashes ≥6 days past 14 days	112	9.6%	67	6.4%	29	6.4%	208	7.8%	<0.0001
Late Peri or Post Menopausal	0	0.0%	0	0.0%	0	0.0%	0	0.0%	N.A.[#]
Hormone Replacement Therapy	0	0.0%	0	0.0%	0	0.0%	0	0.0%	N.A.[§]
Race									<0.0001
African American	365	31.1%	252	24.0%	68	14.9%	685	25.5%	
Caucasian	476	40.5%	538	51.2%	310	67.8%	1324	49.4%	
Chinese	103	8.8%	95	9.0%	26	5.7%	224	8.4%	
Hispanic	152	12.9%	37	3.5%	4	0.9%	193	7.2%	
Japanese	78	6.6%	129	12.3%	49	10.7%	256	9.5%	
Upsetting Life Events									0.3117
None	612	52.1%	519	49.4%	233	51.0%	1364	50.9%	
One	219	18.7%	234	22.3%	97	21.2%	550	20.5%	
Two or more	343	29.2%	298	28.4%	127	27.8%	768	28.6%	

	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age	45.9	2.7	45.9	2.7	46.0	2.7	45.9	2.7	0.6266
Body Mass Index	29.8	7.9	27.4	6.5	25.1	5.2	28.0	7.1	<0.0001
Social Support	12.0	3.5	12.7	3.0	13.1	2.8	12.4	3.2	<0.0001

[†]CESD=Center for Epidemiologic Studies Depression Scale

[#] Women had to be pre- or early peri-menopausal at study entry (TIME PAIR 0) so none of the women were late peri- or postmenopausal at this visit.

[§] Women had to not be on Hormone Replacement Therapy at study entry (TIME PAIR 0).

Table 2

Proportions of Subjects with High Depressive Symptom Based on Physical Activity Level at 4 TIME PAIRs

		TIME PAIR 0 (N=2682)	TIME PAIR 1 (N=2285)	TIME PAIR 2 (N=1822)	TIME PAIR 3 (N=1627)
High Depressive Symptoms		20.0%	18.3%	14.9%	15.2%
Physical Activity Level	Meeting PA Guidelines	17.0%	16.4%	19.1%	21.1%
	Below PA Guidelines	39.2%	38.4%	41.5%	39.7%
	Inactive	43.8%	45.2%	39.5%	38.2%

Table 3

Proportions* of Subjects who had High Depressive Symptom (or Meeting Physical Activity Guidelines) in Two Consecutive TIME PAIRs.

	TIME PAIRs 0 and 1		TIME PAIRs 1 and 2		TIME PAIRs 2 and 3	
	N	%*	N	%*	N	%*
High Depressive Symptoms	338	50.9%	220	45.5%	163	53.4%
Meeting PA Guidelines	326	50.6%	238	54.2%	221	65.2%

*Denominator is subjects who High Depressive Symptom (or Meeting Physical Activity Guidelines) in two consecutive TIME PAIRs.

Table 4

Mixed Effect Logistic Regression for Physical Activity and High Depressive Symptoms[#] in the Following Year

		ESTIMATES	S.E.	p-value	ODDS RATIO	ODDS RATIO 95% CONFIDENCE INTERVAL	
	Physical Activity			<0.0001			
	Inactive (Reference)						
	Meeting PA Guidelines	−0.646	0.144	0.000	0.52	0.40	0.70
	Below PA Guidelines	−0.205	0.096	0.033	0.81	0.67	0.98
Time-varying Covariates	Very upsetting life events			<0.0001			
	No (Reference)						
	One	0.576	0.110	0.000	1.78	1.43	2.21
	Two or more	0.849	0.102	0.000	2.34	1.91	2.85
	Smoker	0.375	0.135	0.006	1.45	1.12	1.90
	BMI[§]	0.016	0.007	0.035	1.02	1.00	1.03
	On Antidepressive Medication	0.967	0.121	0.000	2.63	2.07	3.33
	Late Peri-menopausal or Post-menopausal[†]	0.042	0.135	0.759	1.04	0.80	1.36
	Hot flashes	0.463	0.115	0.000	1.59	1.27	1.99
	High social support[§]	−0.154	0.014	0.000	0.86	0.83	0.88
	Hormone Replacement Therapy	−0.273	0.237	0.249	0.76	0.48	1.21
Baseline covariates	Ethnicity			0.001			
	Caucasian (Reference)						
	African American	−0.012	0.130	0.925			
	Chinese	0.104	0.200	0.604			
	Japanese	0.492	0.180	0.006			
	Hispanic	0.744	0.226	0.001			
	Age[§]	−0.027	0.020	0.177			
	Married	−0.342	0.113	0.003			
	Higher Education (>High school)	−0.377	0.127	0.003			
Intercept	TIME PAIR 1	−2.060	0.182	0.000			

	ESTIMATES	S.E.	p-value	ODDS RATIO	ODDS RATIO 95% CONFIDENCE INTERVAL
TIME PAIR 2	−2.189	0.192	0.000		
TIME PAIR 3	−2.491	0.213	0.000		
TIME PAIR 4	−2.467	0.228	0.000		
Variance of random intercept	2.418	0.27	0.000		

[#] High Depressive Symptoms defined as CESD score > or = 16

[§] Continuous variables are centered at their mean

[†] Reference group is Pre-menopausal or Early Peri-menopausal