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Effect of Escitalopram on Insomnia Symptoms and Subjective Sleep Quality in Healthy Menopausal Women with Hot Flashes: A Randomized Controlled Trial

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Abstract

Objective—Determine effect of escitalopram on insomnia symptoms and subjective sleep quality in healthy menopausal women with hot flashes.

Methods—Randomized, blinded, multi-center, placebo-controlled, parallel group 8-week trial in 205 women (95 African American; 102 white; 8 other) conducted between July 2009 and June 2010. Participants received escitalopram (10–20 mg/day) or placebo. Insomnia symptoms (Insomnia Severity Index [ISI]) and subjective sleep quality (Pittsburgh Sleep Quality Index [PSQI]) at week 4 and 8 were prespecified secondary outcomes. A total of 199 women (97%) provided ISI data and 194 (95%) provided PSQI data at follow-up.

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Results—At baseline, mean hot flash frequency was 9.78/day (SD 5.60), mean ISI was 11.4 (SD 6.3), and mean PSQI was 8.0 (SD 3.7). Treatment with escitalopram reduced ISI at week 8 (mean difference -2.00 , 95% CI: -3.43 to -0.57 , $p < 0.001$ overall treatment effect), with mean reductions of -4.73 (95% CI -5.72 to -3.75) in the escitalopram group and -2.73 (95% CI -3.78 to -1.69) in the placebo group. Reduction in PSQI was greater in the escitalopram versus placebo group at week 8 (mean difference -1.31 , 95% CI -2.14 to -0.49 , $p < 0.001$ overall treatment effect).

Clinical improvement in insomnia symptoms and subjective sleep quality (50% decreases in ISI and PSQI from baseline) was observed more frequently in the escitalopram group versus placebo group (ISI: 50.0% versus 35.4%, $p = 0.04$; PSQI 29.6% versus 19.2%, $p = 0.09$).

Conclusions—Among healthy menopausal women with hot flashes, escitalopram at 10–20 mg/day compared with placebo reduced insomnia symptoms and improved subjective sleep quality at 8 weeks of follow-up.

Keywords

Randomized trial; Escitalopram; Sleep; Hot flashes; Menopause

INTRODUCTION

Self-reported sleep complaints are common in perimenopausal and postmenopausal women(1–3) and have been identified as a key symptom of the menopause transition.(4) Menopause-related sleep disturbance has often been attributed at least in part to nocturnal hot flashes. Prior cross-sectional studies have reported a graded association between hot flashes and insomnia symptoms(5; 6), though the exact role that hot flashes play in sleep complaints of menopausal women remains controversial.(7; 8)

Hormone therapy (estrogen with or without progestin) remains the predominant and only FDA approved treatment for menopausal hot flashes, but use markedly decreased following the release of findings from the Women's Health Initiative Estrogen Plus Progestin Trial that identified the delicate balance of risks versus benefits of combined hormone therapy.(9; 10) Increasingly prescribed to women in midlife(11), selective serotonin and serotonin norepinephrine reuptake inhibitors (SSRIs and SNRIs) have shown modest efficacy in reducing hot flash frequency and severity in prior randomized controlled trials,(12),(13) but use of SSRIs/SNRIs for treatment of hot flashes is limited by concerns about commonly reported side effects, including insomnia and somnolence.(4; 14) However, it is also plausible that SSRIs/SNRIs may improve sleep in parallel with reducing hot flash frequency and severity.

We systematically collected validated, self-reported sleep measures in a randomized double-blind placebo-controlled trial designed primarily to evaluate the effect of the SSRI escitalopram on the frequency and severity of menopausal hot flashes. As previously reported(15), treatment with escitalopram compared with placebo resulted in fewer and less severe hot flashes at 8 weeks. We now report the effect of escitalopram versus placebo on insomnia symptoms and subjective sleep quality (*a priori* specified secondary outcomes) and examine whether any observed effect varied across risk subgroup at baseline.

METHODS

Overview

The study was a double-blind, placebo-controlled randomized trial conducted at 4 MsFLASH network sites (see Appendix, Supplemental Digital Content 1, which lists funding sources, sites and investigators of the MsFLASH research network, <http://links.lww.com/MENO/A19>) with enrollment stratified by race (African American and

White as self reported). The study design, methods and main trial results have been reported elsewhere.(15) The primary objective of the trial was to determine the efficacy of escitalopram on self reported hot flash frequency and severity (7-day averages for both measures) at 4 and 8 weeks. Self reported sleep measures (insomnia symptoms as assessed by the Insomnia Severity Index [ISI] and subjective sleep quality as assessed by the Pittsburgh Sleep Quality Index [PSQI]) at 4 and 8 weeks were *a priori* specified secondary outcomes. The protocol was approved by the appropriate institutional review board at each site. All women provided written informed consent.

Participants

Between July 2009 and June 2010, the study enrolled 205 women. Eligible women were aged 40–62 years and in general good health; in the menopause transition (amenorrhea 60 days in the past year), postmenopausal (12 months since last menstrual period or bilateral oophorectomy), or had undergone hysterectomy with 1 or more ovaries remaining and had follicle stimulating hormone level >20 mIU/mL and estradiol level 50 pg/mL; and reported 28 hot flashes/night sweats per week (recorded on daily diaries for 3 weeks) rated as bothersome or severe on 4 days per week. Exclusion criteria, described in detail elsewhere(15) included: use of psychotropic medications in the past month; use of prescription, nonprescription or herbal therapies for hot flashes in the past month; use of hormone therapy, hormonal contraceptives, selective estrogen receptor modulators or aromatase inhibitors in the past 2 months; current severe illness; major depressive episode, drug or alcohol abuse in the past year; suicide attempt in the past 3 years; and lifetime diagnosis of bipolar disorder or psychosis. Women with uncontrolled hypertension; history of myocardial infarction, angina, or cerebrovascular events; or history of endometrial or ovarian cancer were also excluded from participation.

Treatment and Study Procedures

After a telephone screen, women potentially eligible and interested in participation were mailed a baseline questionnaire and daily diaries for recording frequency, severity, and bother of hot flashes each morning and evening. Women who continued to meet eligibility criteria were scheduled for 2 clinic visits (screening and randomization) within a 2–3 week interval. At the randomization visit, eligible women were randomized using a dynamic algorithm(15) in a 1:1 ratio to treatment groups of escitalopram 10 mg/day or identical-appearing placebo for 8 weeks. Participants, investigators, and clinical center staff were blinded to treatment assignment. After randomization, a telephone contact was made at one week (to assess protocol adherence and adverse events) and clinic visits were conducted at 4 and 8 weeks. The dose of study medication was increased to 20 mg/day in a blinded manner at 4 weeks for women reporting a <50% decrease in hot flash frequency or no decrease in hot flash severity, unless precluded by unacceptable side effects.

Assessment of Insomnia Symptoms

Participants completed the Insomnia Severity Index (ISI)(16–18) at baseline and 4 and 8 weeks of treatment, a valid and reliable self-administered instrument that measures perception of current (past two weeks) insomnia symptoms. The index consists of 7 items assessing difficulty falling asleep, difficulty staying asleep, problems with early awakening, satisfaction with current sleep pattern, interference of sleep problem with daily functioning, noticeability of impairment attributed to the sleep problem, and degree of distress caused by the sleep problem. Each item is rated on a 0–4 point scale (total score 0–28), with higher scores suggesting more severe insomnia symptoms. The absence of insomnia is indicated by scores 0–7, subthreshold or mild insomnia by scores 8–14, clinical insomnia of moderate severity by scores 15–21, and severe clinical insomnia by scores 22–28. Trials of

pharmacologic and behavioral interventions in patients with insomnia have suggested that the ISI is sensitive in measuring treatment response.(19; 20)

Assessment of Subjective Sleep Quality

Participants also completed the Pittsburgh Sleep Quality Index (PSQI) at baseline and 4 and 8 weeks of treatment. A validated measure of subjective sleep quality and sleep disturbances over a one-month time period, the PSQI assesses subjective sleep quality, latency, duration, and efficiency; sleep disturbances; use of sleeping medication; and daytime dysfunction.(21; 22) Global PSQI scores range from 0–21 with higher scores indicating poorer sleep quality. Cutoffs of 5 (21) and 8 (23) have been reported to indicate poor sleep quality; the higher cutpoint was used in this trial due to previous studies suggesting that self-reported sleep disturbance is common among perimenopausal and postmenopausal women.(1–3) The PSQI has been shown to be sensitive in measuring response to cognitive behavioral therapy in randomized trials conducted in patients with insomnia.(24)

Other Measurements

Frequency and severity of hot flashes/night sweats were recorded on daily diaries in the morning and evening throughout the study. Hot flash frequency was calculated as the total number of hot flashes/night sweats in a 24-hour period. Demographic factors, smoking status, alcohol intake, menopausal status (menopause transition, postmenopause), and health status were assessed by questionnaire at baseline. Validated questionnaires at baseline also evaluated depressive symptoms (9-item scale from the Patient Health Questionnaire [PHQ-9])(25), anxiety (7-item Generalized Anxiety Disorder scale [GAD-7])(26), and pain intensity and interference (3-item PEG scale).(27) Height and body weight were measured at baseline and used to calculate a standard body mass index (BMI).

Statistical analysis

All analyses included all randomized participants with follow-up sleep measurements, which were collected irrespective of adherence to study medication. Of the cohort of 205 randomized participants, 199 women (97%) completed the ISI and 194 (95%) completed the PSQI at follow-up (Figure 1).

Primary analyses consisted of treatment group contrasts from repeated measures linear regression models summarizing ISI and PSQI at both 4 and 8 weeks as a function of treatment assignment and baseline value of the sleep outcome measure. The model was adjusted for race, visit, and clinical center. Robust standard errors were calculated using generalized estimating equations to account for correlation between repeated measures from each participant. We hypothesized that the effect of treatment on sleep outcome measures might be modified by the following characteristics measured at baseline: race, menopausal status, nocturnal hot flash frequency, depressive symptoms (PHQ-9), anxiety (GAD-7), pain intensity and interference (PEG) and body mass index (BMI). Tests of interaction between treatment assignment and each of these variables were performed within the linear regression models estimating mean week 8 ISI (PSQI) as a function of treatment arm, the covariate of interest, and the interaction between treatment assignment and covariate; models were adjusted for race, site and baseline ISI (PSQI). Nominal p-values are presented for the 14 potential interactions examined. Thus, on average, about 1 p-value would be expected to be statistically significant by chance alone at the 0.05 level.

Secondary analyses examined the proportion of women in each treatment group with clinical improvement in sleep measures, defined as a 50% decrease from baseline to 8 weeks in the ISI (PSQI); comparisons between treatment groups were performed using unadjusted Chi-squared tests. To determine the effect of treatment among women with moderate to severe

clinical insomnia, we repeated the primary ISI analysis limiting the cohort to the 67 women with an ISI >14 at baseline. To examine the effect of treatment among women with poor sleep quality, we repeated the primary PSQI analysis limiting the cohort to the 81 women with a PSQI >8 at baseline.

The planned sample size of the trial (90 women per treatment group) was determined by the primary trial endpoints (hot flash frequency and severity).¹⁵ Reported p-values are based on the Wald statistic. Analyses were conducted using SAS Version 9.2 (SAS Institute, Cary, NC) with 2-sided p-value <0.05 considered statistically significant.

Role of the Funding Source

NIH staff critically reviewed the study protocol and drafts of the manuscript prior to journal submission. Forest Research Institute, a subsidiary of Forest Laboratories, Inc. (New York, NY), provided escitalopram and matching placebo, but had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, or in the preparation of the manuscript.

RESULTS

A total of 205 women were randomly assigned to receive escitalopram (N= 104) or placebo (N=101) (Figure 1). The mean age of the participants was 53.9 (SD 4.0) years and mean daily hot flash frequency was 9.78 (SD 5.60). There were no significant differences in baseline characteristics between the treatment groups (Table 1).

Insomnia Symptoms

At baseline, the mean ISI was 11.4 (SD 6.3). A total of 77 women (37.6%) were classified with mild (subthreshold) insomnia (ISI 8–14), 55 (26.8%) with moderate clinical insomnia (ISI 15–21), and 12 (5.9%) with severe clinical insomnia (ISI 22–28). Treatment with escitalopram reduced the ISI compared with placebo, adjusted for race, site, and baseline ISI ($p<0.001$ overall treatment effect) (Table 2, Figure 2a). The overall effect of escitalopram on insomnia symptoms was consistent with its effect on insomnia symptoms at the individual timepoints of week 8 and 4. The average ISI at week 8 in the escitalopram group decreased to 6.75 (95% CI 5.54–7.95), a 41% decrease or an average of 4.73 points compared to baseline, while the average ISI at week 8 decreased in the placebo group to 8.41 (95% CI 7.16–9.66), a 24% decrease or an average of 2.73 points compared with baseline. Findings were similar at week 4 (a 43% decrease in ISI relative to baseline in the escitalopram group versus a 21% decrease relative to baseline in the placebo group). Clinical improvement at week 8 (50% decrease from baseline in ISI) was greater in the escitalopram group compared with the placebo group (50.0% in escitalopram group and 35.4%, in placebo group, $p=0.04$).

The effectiveness of escitalopram in reducing ISI was similar across strata of baseline participant characteristics (Figure 3a). There was no evidence of an interaction between treatment assignment and race, menopausal status, nocturnal hot flash frequency, depressive symptoms, anxiety symptoms, pain intensity and interference, or BMI (p for interaction terms = 0.17).

The effect of escitalopram treatment on insomnia symptoms among the 67 women with moderate to severe clinical insomnia (ISI >14) at baseline was similar to its effect in the overall study population. Among these women, the average ISI in the escitalopram group decreased from 18.56 to 11.77 at week 8, a 37% decrease or an average reduction of 6.86 points compared to baseline, while the average ISI decreased in the placebo group from

18.48 to 13.65 at 8 weeks, a 26% decrease or an average of 4.84 points compared with baseline ($p=0.02$ overall treatment effect).

Subjective Sleep Quality

At baseline, the mean PSQI was 8.0 (SD 3.7). A total of 81 women (39.5%) were classified with poor subjective sleep quality (PSQI >8). Treatment with escitalopram reduced the PSQI compared with placebo, adjusted for race, site, and baseline PSQI ($p<0.001$ overall treatment effect) (Table 2, Figure 2b). The overall effect of escitalopram on subjective sleep quality was consistent with its effect on sleep quality at the individual timepoints of week 8 and 4. The average PSQI at week 8 in the escitalopram group decreased to 5.56 (95% CI, 4.92–6.21), a 32% decrease or an average of 2.64 points compared with baseline, while the average PSQI at week 8 decreased in the placebo group to 6.40 (95% CI, 5.64–7.16), a 17% decrease or an average of 1.33 points compared with baseline. Findings were similar at 4 weeks (a 32% decrease in PSQI relative to baseline in the escitalopram group versus a 16% decrease relative to baseline in the placebo group). Clinical improvement at week 8 (50% decrease from baseline in PSQI) occurred more often in the escitalopram group compared with the placebo group (29.6% in escitalopram group and 19.2% in placebo group), but the difference did not reach statistical significance ($p=0.09$).

The effectiveness of escitalopram in reducing the PSQI was similar across strata of baseline participant characteristics (Figure 3b). There was no evidence of an interaction between treatment assignment and race, menopausal status, nocturnal hot flash frequency, depressive symptoms, symptoms of anxiety, pain intensity and interference, or BMI (p for interaction terms 0.11).

The effect of escitalopram treatment on subjective sleep quality among the 81 women with poor sleep quality (PSQI >8) at baseline was similar to its effect in the overall study population. Among these women, the average PSQI in the escitalopram group decreased from 11.60 to 7.68 at 8 weeks, a 34% decrease or an average of 3.89 points compared with baseline, while the average PSQI decreased in the placebo group from 11.94 to 9.21 at 8 weeks, a 24% decrease or an average of 2.88 points compared with baseline ($p=0.06$ overall treatment effect).

Adherence

During the 8 week treatment period, 87% (179/205) of the women were adherent to their study dose as defined by taking at least 70% of dispensed pills. At 8 weeks, the average absolute difference between escitalopram and placebo groups among adherent women was 2.36 points in ISI ($p<0.001$ overall treatment effect) and 1.16 points in PSQI ($p<0.001$ overall treatment effect).

Sleep Adverse events

Newly-emergent adverse events (AEs) were reported by 53% of women in the escitalopram group and 63% of women in the placebo group ($p=0.20$). There were no differences between the escitalopram and placebo groups in newly emergent complaints of fatigue/tiredness (24.1% versus 20.3%, $p=0.15$), difficulty sleeping/insomnia (17.7% versus 23.8%, $p=0.61$), or drowsiness 17.3% versus 15.9%, $p=0.84$).

DISCUSSION

In healthy women with menopausal hot flashes, treatment with escitalopram at doses of 10 or 20 mg/d relative to placebo reduced insomnia symptoms and improved subjective sleep quality. These results do not support the concern(4) that insomnia is an anticipated side

effect of escitalopram treatment in this population and should provide reassurance to clinicians and women considering use of escitalopram therapy for relief of hot flash symptoms.

It is notable that insomnia and poor subjective sleep quality were common in this cohort, despite excluding women with a diagnosis of major depression or anxiety disorder from participation and enrolling women who, on average, reported minimal depressive or anxiety symptoms. Over one-third of women at baseline had an ISI >14 suggestive of a clinical diagnosis of moderate to severe insomnia and nearly 40% had poor subjective sleep quality (defined using a conservative cutpoint of 8 on the PSQI). These findings are consistent with those reported in a similar randomized trial study population(5) and are in agreement with population-based studies in women not selected on the basis of hot flashes that have reported a strong association between the presence of hot flashes or greater hot flash frequency and self-reported sleep complaints.(1; 6; 28)

Contrary to conventional wisdom that sleep difficulties may emerge with initiation of SSRI treatment, we found that treatment with escitalopram compared with placebo reduced ISI by 2.0 points and PSQI by 1.3 points at week 8 demonstrating a modest benefit of escitalopram in decreasing insomnia symptoms and improving subjective sleep quality. One-half of the women in the escitalopram group versus 35% in the placebo group reported that insomnia symptoms decreased by at least 50% from baseline; clinical improvement in self-reported sleep quality was similar to the reduction in insomnia symptoms, though the comparison did not reach statistical significance. The effects of escitalopram versus placebo on insomnia symptoms and subjective sleep quality were consistent across risk subgroups. Few previous placebo-controlled randomized trials of SSRIs for treatment of menopausal hot flashes have systematically collected sleep outcome data with one trial of citalopram reporting benefit, (29) a dose-ranging trial of paroxetine reporting mixed results,(30) and another dose-ranging trial of paroxetine reporting no effect.(31)

Systematic reviews of the evidence from efficacy studies evaluating SSRIs(32) including escitalopram(33) for the treatment of major depression and anxiety disorders have noted that insomnia is a commonly reported adverse event. The applicability of findings from trials of patients selected on the basis of major depression or anxiety disorder to this population of healthy women with hot flashes without clinical psychiatric diagnoses is uncertain. We found no differences in the frequency of newly emergent adverse events of insomnia, fatigue, or drowsiness between escitalopram and placebo groups. In contrast, previous trials of paroxetine(31), citalopram(34), venlafaxine (a SNRI)(35) and desvenlafaxine (a SNRI) (36) in women with hot flashes reported that these adverse events were more common among women assigned to active treatment versus placebo, albeit not always at the level of significance. Differences in effects of specific SSRIs on self-reported sleep in women with hot flashes may be due to several reasons including differences in pharmacologic properties of specific drugs, study populations, choice of sleep outcome measures, and reporting of adverse events.

This trial has limitations as well as strengths. The study population was comprised of healthy women selected on the basis of hot flash frequency. Thus, results may not be generalizable to other groups such as unselected midlife women or women selected on the basis of psychiatric conditions. The effects of escitalopram treatment on self-reported sleep measures beyond 8 weeks are unknown. We evaluated several potential modifiers of treatment response, but analyses were limited by suboptimal power and multiple comparisons were performed. In-home overnight polysomnography was not performed; results of a trial with objectively measured sleep outcomes might differ from findings of this study of self-reported sleep measures. Strengths of this trial include the use of valid and

reliable instruments to measure insomnia symptoms and subjective sleep quality, representation of African American women, high adherence to treatment, and nearly complete collection of sleep outcome measures.

CONCLUSIONS

Treatment with escitalopram 10 to 20 mg/day in healthy menopausal women with hot flashes reduced insomnia symptoms and improved subjective sleep quality. These results should provide reassurance to clinicians and women considering escitalopram treatment for hot flash symptoms who have concerns about insomnia as a potential adverse effect. Future trials should evaluate the efficacy of SSRIs/SNRIs in improving insomnia symptoms in menopausal women selected on the basis of hot flashes and sleep disturbance and directly compare the efficacy of these agents with hormone therapy in the treatment of these commonly co-occurring menopausal complaints.

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APPENDIX

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The network sites that participated in this study were Boston, MA (Massachusetts General Hospital; Principal Investigators: Lee Cohen, MD and Hadine Joffe, MD, MSc); Indianapolis, IN (Indiana University; Principal Investigator: Janet S Carpenter, PhD, RN, FAAN); Oakland, CA (Kaiser Permanente Division of Research; Principal Investigators: Barbara Sternfeld, PhD and Bette Caan, PhD; and Philadelphia, PA (University of Pennsylvania; Principal Investigator: Ellen W. Freeman, PhD). The Data Coordinating Center of the network is based at the Fred Hutchinson Cancer Research Center; Principal Investigators: Andrea LaCroix, PhD and Garnet Anderson, PhD. The chairperson is Kristine E. Ensrud, MD, University of Minnesota.

Other investigators of the MsFLASH Network that contributed to this study include Katherine A. Guthrie, PhD, Joseph Larson, MS: Fred Hutchinson Cancer Research Institute, Seattle WA; Katherine Newton, PhD: Group Health Research Institute, Seattle WA; Susan D. Reed, MD, Nancy F. Woods, PhD, RN, Carol A. Landis, DNSc, RN: University of Washington, Seattle, WA, and Sheryl Sherman, PhD: National Institute on Aging/US National Institutes of Health, Bethesda, MD.

Figure 1.
Participant Flow Diagram for Data Collection of Sleep Outcome Measures

2A

2B

Figure 2.

Figure 2a. Mean Insomnia Severity Index from Baseline to Week 8 by Treatment Assignment

Note: Vertical bars represent standard error

Figure 2b. Mean Pittsburgh Sleep Quality Index from Baseline to Week 8 by Treatment Assignment

Note: Vertical bars represent standard error

Figure 3.

Figure 3a. Mean Change in ISI from Baseline to Week 8 by Treatment Assignment Overall and within Risk Subgroups

The dotted vertical line indicates the overall absolute mean difference between treatment groups ^aAdjusted absolute mean differences and interaction p-values are computed from a linear model estimating mean week 8 ISI as a function of treatment arm, the subgroup of interest, and the interaction between treatment assignment and subgroup. In addition, all models are adjusted for race, site and baseline ISI, with exception of the model examining the effect of treatment within race subgroups, where the model is adjusted for site and baseline ISI.

^bMean week 8 ISI – baseline ISI difference

Figure 3b. Mean Change in PSQI from Baseline to Week 8 by Treatment Assignment Overall and within Risk Subgroups

The dotted vertical line indicates the overall absolute mean difference between treatment groups ^aAdjusted absolute mean differences and interaction p-values are computed from a linear model estimating mean week 8 PSQI as a function of treatment arm, the subgroup of interest, and the interaction between treatment assignment and subgroup. In addition, all models are adjusted for race, site and baseline PSQI, with exception of race subgroup, where the model is adjusted for site and baseline PSQI.

^bMean week 8 PSQI – baseline PSQI difference

Table 1**Baseline Characteristics by Treatment Assignment**

Baseline Characteristic^a	Escitalopram (n=104)	Placebo (n=101)
Age at screening, mean (SD)	53.45 (4.20)	54.36 (3.86)
Age group, n (%)		
42 – 49	16 (15.4)	8 (7.9)
50 – 54	48 (46.2)	47 (46.5)
55 – 59	30 (28.8)	36 (35.6)
60 – 62	10 (9.6)	10 (9.9)
Race, n (%)		
White	53 (51.0)	49 (48.5)
African American	47 (45.2)	48 (47.5)
Other	4 (3.8)	4 (4.0)
Clinic Site, n (%)		
Boston	24 (23.1)	19 (18.8)
Indianapolis	17 (16.3)	18 (17.8)
Oakland	31 (29.8)	26 (25.7)
Philadelphia	32 (30.8)	38 (37.6)
Education, n (%)		
High school diploma or GED	15 (14.4)	23 (22.8)
School/training after high school	46 (44.25)	41 (40.6)
College graduate	43 (41.3)	37 (36.6)
Marital Status, n (%)		
Never married	18 (17.3)	13 (12.9)
Divorced	18 (17.3)	26 (25.7)
Widowed	4 (3.8)	6 (5.9)
Married or living with partner	64 (61.5)	56 (55.4)
Smoking, n (%)		
Never	53 (51.0)	46 (45.5)
Past	30 (28.8)	29 (28.7)
Current	21 (20.2)	26 (25.7)
Alcohol use, drinks/week, n (%)		
0	41 (39.4)	41 (40.6)
1–6	51 (49.0)	41 (40.6)
7	12 (11.5)	17 (16.8)
BMI, kg/m ² , mean (SD)	28.58 (6.59)	29.70 (6.42)
Menopause status, n (%)		
Post-menopause	84 (80.8)	83 (82.2)
Late Transition	17 (16.3)	15 (14.9)
Early Transition	3 (2.9)	3 (3.0)
Self-reported health, n (%)		
Excellent	18 (17.3)	13 (12.9)

Baseline Characteristic ^a	Escitalopram (n=104)	Placebo (n=101)
Very Good	41 (39.4)	40 (39.6)
Good	36 (34.6)	37 (36.6)
Fair	7 (6.7)	11 (10.9)
Poor	1 (1.0)	0 (0.0)
PEG score (range 0–10), mean (SD)	1.62 (2.21)	1.58 (2.40)
PHQ-9 Depression score (range 0–13), mean (SD)	3.24 (3.06)	2.94 (3.24)
GAD-7 Anxiety score (range 0–19), mean (SD)	2.50 (3.34)	2.19 (3.33)
Hot flashes/24 hr, mean (SD)	9.88 (3.34)	9.66 (4.88)
Nocturnal Hot Flashes, mean (SD)	3.83 (2.82)	4.08 (2.32)

^a $p > 0.05$ for all comparison by treatment groups as tested by t test or chi-square

Table 2

Mean ISI and PSQI by Treatment Assignment

Outcome	Escitalopram			Placebo			P value ^d
	N	Mean (95% CI)	N	Mean (95% CI)	Difference Mean (95% CI)		
ISI							
Baseline	103	11.57 (10.32, 12.83)	100	11.15 (9.93, 12.37)	0.42 (−1.32, 2.16)	<0.001	
Week 4 – Baseline	101	−4.98 (−5.97, −3.99)	98	−2.34 (−3.26, −1.42)	−2.64 (−3.99, −1.30)		
Week 8 – Baseline	101	−4.73 (−5.72, −3.75)	97	−2.73 (−3.78, −1.69)	−2.00 (−3.43, −0.57)		
PSQI							
Baseline	101	8.23 (7.52, 8.93)	97	7.78 (6.99, 8.57)	0.44 (−0.60, 1.49)	<0.001	
Week 4 – Baseline	97	−2.63 (−3.17, −2.08)	95	−1.21 (−1.80, −0.62)	−1.42 (−2.22, −0.62)		
Week 8 – Baseline	98	−2.64 (−3.19, −2.10)	94	−1.33 (−1.96, −0.70)	−1.31 (−2.14, −0.49)		

^a p-values from comparison of escitalopram vs. placebo in repeated measures linear models of each outcome as a function of intervention arm and adjusted for race, visit (week 4 or 8), site, and baseline value of outcome.