Dose-response effects of exercise training on the subjective sleep quality of postmenopausal women: exploratory analyses of a randomised controlled trial

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Dose–response effects of exercise training on the subjective sleep quality of postmenopausal women: exploratory analyses of a randomised controlled trial

Christopher E Kline,1 Xuemei Sui,2 Martica H Hall,1 Shawn D Youngstedt,2,3,4 Steven N Blair,2,5 Conrad P Earnest,6 Timothy S Church7

ABSTRACT

Objective: To investigate whether a dose–response relationship existed between exercise and subjective sleep quality in postmenopausal women. This objective represents a post hoc assessment that was not previously considered.

Design: Parallel-group randomised controlled trial.

Setting: Clinical exercise physiology laboratory in Dallas, Texas.

Participants: 437 sedentary overweight/obese postmenopausal women.

Intervention: Participants were randomised to one of four treatments, each of 6 months of duration: a non–exercise control treatment (n=92) or one of three dosages of moderate-intensity exercise (50% of VO2peak), designed to meet 50% (n=151), 100% (n=99) or 150% (n=95) of the National Institutes of Health Consensus Development Panel physical activity recommendations. Exercise dosages were structured to elicit energy expenditures of 4, 8 or 12 kilocalories per kilogram of body weight per week (KKW), respectively.

Analyses were intent to treat.

Primary outcome measures: Continuous scores and odds of having significant sleep disturbance, as assessed by the Sleep Problems Index from the 6-item Medical Outcomes Study Sleep Scale. Outcome assessors were blinded to participant randomisation assignment.

Results: Change in the Medical Outcomes Study Sleep Problems Index score at 6 months significantly differed by treatment group (control: −2.09 (95% CI −4.58 to 0.40), 4 KKW: −3.93 (−5.87 to −1.99), 8 KKW: −4.06 (−6.45 to −1.67), 12 KKW: −6.22 (−8.68 to −3.77); p=0.04), with a significant dose–response trend observed (p=0.02). Exercise training participants had lower odds of having significant sleep disturbance at postintervention compared with control (4 KKW: OR 0.37 (95% CI 0.19 to 0.73), 8 KKW: 0.36 (0.17 to 0.77), 12 KKW: 0.34 (0.16 to 0.72)). The magnitude of weight loss did not differ between treatment conditions. Improvements in sleep quality were not related to changes in body weight, resting parasympathetic control or cardiorespiratory fitness.

Conclusion: Exercise training induced significant improvement in subjective sleep quality in postmenopausal women, with even a low dose of exercise resulting in greatly reduced odds of having significant sleep disturbance.

ARTICLE SUMMARY

Article focus

- Sleep disturbance is prevalent in postmenopausal women, with 35%–60% reporting significant sleep problems.
- Effective, safe and easily available treatment options for disturbed sleep in postmenopausal women are lacking.
- There has been equivocal evidence as to whether exercise improves sleep in postmenopausal women, though possible dose–response effects have been noted.

Key messages

- Exercise resulted in significant improvement in subjective sleep quality in postmenopausal women, with reduced odds of having sleep disturbance at postintervention with even 50% of the recommended dose of exercise for adults.
- The effects of exercise on sleep quality were independent of changes in body weight, resting parasympathetic control or cardiorespiratory fitness.

Strengths and limitations of this study

- The study constitutes the largest randomised controlled trial on exercise and sleep quality, using a structured dose of exercise and a validated measure of sleep quality.
- Only self-reported sleep was assessed; objective measurement of sleep, with either actigraphy or polysomnography, was not conducted.
- Despite the high prevalence of sleep disturbance in the sample, participants were not selected on the basis of sleep complaints.

postmenopausal women, with even a low dose of exercise resulting in greatly reduced odds of having significant sleep disturbance.

Trial registration number: clinicaltrials.gov identifier: NCT00011193.
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INTRODUCTION
Disturbed sleep is a common complaint among women, with increasing prevalence beginning at the menopausal transition. Postmenopausal women are more likely to report sleep problems than premenopausal or perimenopausal women, with 35%–60% of postmenopausal women reporting significant sleep problems. The first-line treatment options for sleep complaints, hypnotic medication and cognitive behavioural therapy have associated concerns about the safety of long-term use or treatment availability, respectively. Furthermore, results are conflicting on the effect of hormone replacement therapy (HRT) on sleep quality, despite the effectiveness of HRT at reducing other menopausal symptoms.

A non-pharmacological treatment that has been traditionally thought to improve sleep is exercise. In epidemiological research, exercise has frequently been associated with better sleep. However, experimental research has provided less compelling evidence, particularly when regarding postmenopausal women. Of the four randomised trials that have investigated the effect of exercise on sleep quality in this population, only one reported a significant improvement in subjective sleep quality following an exercise intervention. However, despite the generally negative findings from these studies involving postmenopausal women, possible dose–response effects of exercise on sleep quality were noted. In one of these studies, women who performed at least 225 min of morning exercise per week had less trouble falling asleep compared with those who exercised <180 min per week in the morning. Likewise, another study reported a positive association between walking frequency and improvements in sleep.

To our knowledge, no research has directly investigated the effects of different doses of exercise on sleep quality. The Dose–Response to Exercise in postmenopausal Women (DREW) trial was conducted to investigate the health effects of 50%, 100% and 150% of the National Institutes of Health (NIH) Consensus Development Panel physical activity recommendations in a group of sedentary postmenopausal women. Results on the primary outcomes of the study, cardiorespiratory fitness and blood pressure, have already been reported. Subjective sleep quality was also assessed in this trial as an exploratory outcome, and the data provided herein give the first systematic examination of whether a dose–response relationship exists between exercise and subjective sleep quality. It was hypothesised that, in comparison to a non-exercise control group, subjective sleep quality would improve with increasing dosage of exercise.

METHODS
A complete description of the recruitment and screening procedures has been published elsewhere. Briefly, the study was a randomised, controlled, multi-arm, parallel-group trial in which the primary purpose was to examine whether there were dose–response effects on cardiorespiratory fitness and blood pressure with incrementally increasing doses of energy expenditure. The study was approved annually by the Cooper Institute Institutional Review Board, and written informed consent was obtained by all participants prior to study involvement.

Participants
Participants were recruited from the Dallas, Texas, metropolitan area from April 2001 to June 2005. Of 4545 women screened for eligibility, those who were aged 45–75 years, postmenopausal, sedentary (<20 min of exercise on ≤2 days/week and <8000 steps/day, averaged over 1 week), overweight or obese (body mass index (BMI) of 25–43 kg/m²) and had normal to mildly elevated resting blood pressure (systolic blood pressure of 120–159 mm Hg and diastolic blood pressure ≤99 mm Hg) were eligible to participate (figure 1). Exclusion criteria included significant cardiovascular disease, recent hospitalisation for mental illness or significant symptoms of depression (score ≥10 on the Center for Epidemiologic Studies Depression Scale) or any other health condition that would contraindicate participation in an exercise programme. Overall, 464 women were randomised to treatment, with baseline sleep data available for 437 participants.

Randomisation and retention
Prior to randomisation, participants completed a 2-week run-in period, in which participants received lifestyle modification instruction over the course of six laboratory visits. The primary purpose of this run-in period was to maximise retention and adherence to the subsequent intervention. Participants were compensated for completing baseline and postintervention assessments, with additional compensation based on intervention adherence.

Allocation of participants to treatment conditions was accomplished using a computer-generated randomisation sequence, determined from randomly permuted blocks of equal length with fixed numbers of treatment allotments to balance treatment enrolments over time. Allocation concealment was achieved by placing treatment assignment letters into sequentially numbered opaque envelopes sealed by the study statistician. At the time of randomisation, envelopes were opened by a staff member not affiliated with the randomisation process.

Participants were randomised to one of four treatment conditions: a non-exercise control group, or one of three exercise groups expending 4, 8 or 12 kilocalories per kilogram of body weight per week (KKW). Energy expenditure levels for the exercise groups were designed to correspond with 50%, 100% and 150% of the NIH Consensus Development Panel physical activity recommendations, respectively.
Interventions

Women assigned to the exercise groups participated in three to four training sessions/week for 6 months, alternating between semirecumbent cycle ergometer and treadmill exercise. Training sessions were conducted in a supervised laboratory setting, and exercise dosage was closely monitored for each session. Training intensity was moderate, set at the heart rate associated with 50% of each woman’s VO$_{2peak}$ and continuously monitored by heart rate telemetry. To determine the number of calories that needed to be expended each week, participants were weighed weekly and their weight was multiplied by the exercise dosage.

Exercise dose was gradually increased to minimise injury risk. All exercise training groups expended 4 KKW during the first intervention week, with the 4 KKW group continuing at that dose for 6 months. The 8 and 12 KKW groups increased their energy expenditure by 1 KKW until they reached their appointed exercise doses.

Blinding

Although participants could not be blinded to their treatment, staff were separated into intervention and assessment teams to ensure blinding of all assessment staff to participant randomisation assignment. Participants were consistently reminded to refrain from discussing their randomisation assignments with outcome assessment staff.

Sleep measure

Subjective sleep quality was assessed with six items from the Medical Outcomes Study (MOS) Sleep Scale. At
Exercise and sleep quality in postmenopausal women

Baseline and postintervention, participants were asked to respond based on their sleep during the previous 4 weeks. One question, which addressed the length of time to fall asleep, was framed with five response options ranging from 0 to 15 min to >60 min. For the remaining five questions (ie, restless sleep, daytime drowsiness, difficulty falling asleep, awakening from sleep and experiencing difficulty returning to sleep, staying awake during the day), participants were asked to respond on a 5-point scale, ranging from ‘none of the time’ to ‘all of the time’. Item responses were assigned scores using conventional scoring rules, with higher scores indicating a greater severity of sleep disturbance. A modified Sleep Problems Index (SPI), using all six sleep items, provided a measure of overall sleep quality.17 SPI scores >25 were considered to indicate significant sleep disturbance, as prior work using a 9-item SPI reported that a cutpoint of >25 identified individuals who considered themselves to have a sleep problem with a sensitivity of 86.2% and specificity of 66.3%.17

Scores on the MOS Sleep Scale have been shown to correlate with other MOS health items,16 differentiate between those with and without chronic health conditions17 and improve with treatment of chronic health conditions.18 Normative values for the general population have also been developed.17

Other measures

Baseline demographic and health characteristics were assessed by completion of a comprehensive medical history questionnaire. Height and weight were measured with a calibrated stadiometer and electronic scale, respectively. Diet was assessed before and following the intervention using a semiquantitative food-frequency questionnaire, whereas unsupervised physical activity was monitored throughout the study with a pedometer (Accusplit Eagle, Livermore, California).

Cardiorespiratory fitness (VO2peak) was assessed from maximal exercise testing using a cycle ergometer (Excalibur Sport, Lode Medical Technology, Groningen, the Netherlands), as previously described.14 Testing was performed twice at baseline and twice at postintervention, with values from each timepoint averaged. Heart rate variability (HRV) was measured from the final 5 min of a 25-min resting assessment, as previously described.19 The square root of the mean of the sum of the squares of differences between adjacent R–R intervals (rMSSD), a marker of parasympathetic activity,20 was retained for analysis.

Statistical power

Sample size was originally based on having adequate power to detect changes in the primary outcomes of the overall study, VO2peak and blood pressure.14 Additional participants were allocated to the 4 KKW condition to increase statistical power for detecting smaller anticipated fitness gains in this group. Because sleep was not a primary outcome in the design of the original study, there was no opportunity before data collection to investigate sample size or power for this outcome variable. Nevertheless, given the current enrollment, the study had 84% power (assuming two-tailed α=0.05) to detect an effect size of 0.20 for MOS SPI score reduction.

Statistical analysis

Baseline sleep quality was compared against normative data17 using a one-sample t-test. Continuous MOS SPI values were examined across quartiles of BMI, parasympathetic tone (rMSSD) and cardiorespiratory fitness (VO2peak) with analysis of covariance (ANCOVA), controlling for age, BMI, sleep medication use and HRT use. The likelihood of having significant sleep disturbance at baseline (ie, MOS SPI >25) was evaluated with logistic regression across the same quartiles using the same covariates.

Two primary outcomes were evaluated for the current study: (1) change in continuous MOS SPI score across treatment groups and (2) odds of having significant sleep disturbance at postintervention across treatment groups. Change in continuous MOS SPI scores across groups was tested by ANCOVA, with adjustment for age, BMI, sleep medication use, HRT use and baseline MOS SPI values. All assumptions underlying the ANCOVA models were checked and verified to be met. Individual treatment groups were compared with the control group with Tukey–Kramer adjustment for multiple comparisons. An α level of 0.05 was used because it was our a priori intention to compare only the separate treatment groups with the control group. Dose–response trends were analysed using least-squares regression of MOS SPI change across groups. Logistic regression examined the odds of having significant sleep disturbance at postintervention, following adjustment for age, BMI, sleep medication and HRT use, and baseline sleep disturbance (SPI >25, SPI ≤25). Unadjusted analyses provided similar results to those with covariate control, so only those results with full covariate adjustment were reported.

Finally, to examine whether improved sleep quality was significantly influenced by body weight, parasympathetic tone or cardiorespiratory fitness, changes in weight, rMSSD and VO2peak were added to the ANCOVA and logistic regression analyses. Additionally, among completed participants, changes in MOS SPI score were evaluated across quartiles of change in body weight, rMSSD and VO2peak following adjustment for age, treatment, BMI, sleep medication use, HRT use and baseline MOS SPI score.

Analyses were limited to participants with baseline MOS Sleep data. Primary analyses were conducted using the intent-to-treat principle; if postintervention data were missing, baseline values were carried forward for analysis. When analyses were restricted to only those participants with baseline and postintervention MOS Sleep data (n=359), results were not substantively changed; similarly, when missing postintervention data
were imputed with mean values, results were unchanged. Therefore, only intent-to-treat analyses were presented. All analyses were performed using SAS V.9.2 (SAS Institute). All tests were two-tailed, with statistical significance set at p≤0.05.

RESULTS

Participant characteristics

A summary of participant characteristics is provided in table 1. Mean age and BMI of the 437 participants were 57.3±6.6 years and 31.8±3.9 kg/m², respectively.

Baseline MOS SPI values and prevalence of sleep disturbance are provided in Table 1. Of the 437 participants, 46% of the sample (n=200) were considered to have significant sleep disturbance at baseline, as defined as MOS SPI >25. Baseline sleep quality of the participants was significantly worse than normative values (normative value: 25.79; t_{436}=2.42, p=0.02), a magnitude of 0.12 SD.

Baseline continuous MOS SPI values and odds of sleep disturbance across quartiles of BMI, rMSSD and VO₂peak are shown in Table 2. Sleep quality significantly differed among quartiles of rMSSD (F_{3,343}=2.55, p=0.05), with the lowest quartile of rMSSD having significantly worse baseline sleep quality than the other quartiles of rMSSD. Similarly, each quartile of rMSSD was associated with lower odds of having significant sleep disturbance at baseline compared with the lowest quartile of rMSSD. No differences in MOS SPI values or odds of having significant sleep disturbance were observed across quartiles of BMI or VO₂peak.

Exercise training adherence, diet and unsupervised activity

Treatment adherence was calculated as the percentage of exercise energy expenditure achieved compared with the amount of exercise energy expenditure that was prescribed. Adherence was similar between exercise groups (4 KKW: 95.1±16.1%, eight KKW: 88.5±26.1%, 12 KKW: 92.5±20.9%), as previously reported.

Changes in diet and unsupervised activity have been previously reported. Preintervention to post-intervention changes in energy intake did not differ between treatment conditions. Pedometer-assessed unsupervised activity ranged from 4766 to 5067 steps/

Table 1 Baseline participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>All (N=437)</th>
<th>Control (n=92)</th>
<th>4 KKW (n=151)</th>
<th>8 KKW (n=99)</th>
<th>12 KKW (n=95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.32 (6.46)</td>
<td>57.14 (5.91)</td>
<td>57.78 (6.53)</td>
<td>57.58 (6.63)</td>
<td>56.47 (6.72)</td>
</tr>
<tr>
<td>Education, years</td>
<td>14.03 (2.11)</td>
<td>14.01 (2.12)</td>
<td>13.80 (2.02)</td>
<td>13.47 (2.06)</td>
<td>14.00 (2.28)</td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>398 (91)</td>
<td>86 (93)</td>
<td>141 (94)</td>
<td>87 (88)</td>
<td>84 (88)</td>
</tr>
<tr>
<td>Ethnicity/race, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>278 (64)</td>
<td>58 (63)</td>
<td>92 (61)</td>
<td>60 (61)</td>
<td>68 (72)</td>
</tr>
<tr>
<td>Hispanic/other</td>
<td>31 (7)</td>
<td>11 (12)</td>
<td>10 (7)</td>
<td>7 (7)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Employed, n (%)</td>
<td>304 (70)</td>
<td>62 (67)</td>
<td>105 (70)</td>
<td>67 (68)</td>
<td>70 (74)</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake, kcal/day</td>
<td>2277.2 (952.6)</td>
<td>2277.4 (947.9)</td>
<td>2213.1 (941.6)</td>
<td>2290.7 (930.7)</td>
<td>2364.7 (1003.5)</td>
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<td>Anthropometrics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84.46 (11.82)</td>
<td>85.77 (12.43)</td>
<td>83.56 (11.42)</td>
<td>84.74 (12.43)</td>
<td>84.33 (11.24)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>31.77 (3.85)</td>
<td>32.29 (3.94)</td>
<td>31.54 (3.80)</td>
<td>31.98 (4.08)</td>
<td>31.44 (3.58)</td>
</tr>
<tr>
<td>Cardiorespiratory fitness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative VO₂peak, ml/kg/min</td>
<td>15.37 (2.92)</td>
<td>15.56 (3.00)</td>
<td>15.44 (3.00)</td>
<td>14.70 (2.49)</td>
<td>15.77 (3.05)</td>
</tr>
<tr>
<td>Absolute VO₂peak, l/min</td>
<td>1.29 (0.26)</td>
<td>1.33 (0.28)</td>
<td>1.28 (0.24)</td>
<td>1.24 (0.24)</td>
<td>1.32 (0.26)</td>
</tr>
<tr>
<td>Heart Rate Variability*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rMSSD, ms</td>
<td>22.83 (11.56)</td>
<td>23.35 (11.01)</td>
<td>23.58 (12.24)</td>
<td>23.25 (11.29)</td>
<td>20.68 (11.19)</td>
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<tr>
<td>Subjective sleep quality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOS Sleep Problems Index</td>
<td>27.92 (18.40)</td>
<td>28.37 (19.71)</td>
<td>27.03 (17.92)</td>
<td>27.35 (18.10)</td>
<td>29.47 (18.32)</td>
</tr>
<tr>
<td>Sleep disturbance, n (%)</td>
<td>200 (46)</td>
<td>38 (41)</td>
<td>65 (43)</td>
<td>49 (49)</td>
<td>48 (51)</td>
</tr>
</tbody>
</table>

Data presented as mean (SD) unless otherwise indicated.

*Samples for rMSSD data were 351, 79, 123, 73 and 76 participants for all, control, 4 KKW, 8 KKW and 12 KKW groups, respectively. KKW, kilocalories of energy expenditure per kilogram of body weight per week; MOS, Medical Outcomes Study; rMSSD, square root of the mean of the sum of the squares of differences between adjacent R–R intervals; VO₂peak, peak rate of oxygen consumption.
day at baseline and did not differ between groups. Compared with baseline, daily steps increased for each group at month 1 (each $p < 0.05$), with greater steps in the control group than the three exercise groups (each $p < 0.05$). However, no differences in daily steps between the control and exercise groups were observed by months 5 and 6. Among the exercise groups, daily steps did not change from months 1 through 6. Therefore, the results reported here are unlikely to be due to changes in diet or spontaneous activity outside the exercise training laboratory.

Changes in sleep quality with exercise training

Changes in sleep quality with exercise training are depicted in figure 2. A significant effect of the intervention was noted in the full model ($F_{8,428}=17.35$, $p<0.001$), with treatment group being an independent predictor of change in continuous MOS SPI score ($F_{3,428}=2.79$, $p=0.04$) following control for age, BMI, HRT use, sleep medication use and baseline MOS SPI values. Moreover, a significant linear dose–response effect was found for MOS SPI scores across treatment groups ($p=0.02$). When compared against control, a significantly greater improvement in MOS SPI score was found for the 12 KKW group ($p=0.02$).

The association between sleep disturbance (ie, MOS SPI >25) at postintervention and treatment is summarised in table 3. Compared with control and following covariate adjustment, each exercise training group had lower odds of having significant sleep disturbance following the intervention, with the odds of having significant sleep disturbance decreasing while exercise dose increased (linear trend $p=0.01$).

Influences of change in weight, fitness and parasympathetic tone on sleep

Postintervention changes in body weight, parasympathetic tone and cardiorespiratory fitness for the overall DREW sample have been previously reported.14–19 In the present study’s sample, the magnitude of weight loss did not differ between treatment groups (control: $-1.08 (3.70)$ kg, 4 KKW: $-1.23 (3.43)$ kg, 8 KKW: $-1.60 (3.23)$ kg, 12 KKW: $-1.25 (2.83)$ kg; $F_{3,433}=0.43$, $p=0.73$). Cardiorespiratory fitness improved with exercise training in a dose-dependent manner (control: $-0.20 (1.88)$ ml/kg/min).

<table>
<thead>
<tr>
<th>Variable</th>
<th>MOS SPI score (95% CI)</th>
<th>OR of MOS SPI &gt;25 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1: $&lt;34.7$</td>
<td>27.95 (24.54 to 31.36)</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Q2: 31.7 to $&lt;34.7$</td>
<td>24.37 (20.92 to 27.82)</td>
<td>0.60 (0.35 to 1.03)</td>
</tr>
<tr>
<td>Q3: 28.6 to $&lt;31.7$</td>
<td>30.48 (27.03 to 33.94)</td>
<td>1.14 (0.67 to 1.96)</td>
</tr>
<tr>
<td>Q4: $&lt;28.6$</td>
<td>28.85 (25.46 to 32.24)</td>
<td>0.98 (0.58 to 1.68)</td>
</tr>
<tr>
<td>Linear p</td>
<td>0.26</td>
<td>0.53</td>
</tr>
<tr>
<td>rMSSD (ms)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1: $&lt;15.0$</td>
<td>31.77 (27.95 to 35.59)</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Q2: 15.0 to $&lt;20.9$</td>
<td>24.77 (21.04 to 28.51)*</td>
<td>0.53 (0.29 to 0.97)</td>
</tr>
<tr>
<td>Q3: 20.9 to $&lt;29.0$</td>
<td>25.22 (21.36 to 29.09)*</td>
<td>0.43 (0.23 to 0.81)</td>
</tr>
<tr>
<td>Q4: $&lt;29.0$</td>
<td>26.50 (22.64 to 30.35)*</td>
<td>0.46 (0.25 to 0.86)</td>
</tr>
<tr>
<td>Linear p</td>
<td>0.08</td>
<td>0.01</td>
</tr>
<tr>
<td>VO₂peak (ml/kg/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1: $&lt;13.4$</td>
<td>29.55 (25.86 to 33.25)</td>
<td>1.00 (Referent)</td>
</tr>
<tr>
<td>Q2: 13.4 to $&lt;15.2$</td>
<td>28.80 (25.35 to 32.25)</td>
<td>1.22 (0.70 to 2.13)</td>
</tr>
<tr>
<td>Q3: 15.2 to $&lt;17.0$</td>
<td>28.60 (25.05 to 32.15)</td>
<td>1.04 (0.58 to 1.87)</td>
</tr>
<tr>
<td>Q4: $&lt;17.0$</td>
<td>24.91 (21.41 to 28.42)</td>
<td>0.63 (0.34 to 1.14)</td>
</tr>
<tr>
<td>Linear p</td>
<td>0.10</td>
<td>0.09</td>
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</tbody>
</table>

Continuous baseline MOS SPI scores (left panels) and ORs of having significant sleep disturbance at baseline (MOS SPI >25) (right panels) across quartiles of baseline BMI, rMSSD and VO₂peak. All analyses adjusted for age, BMI, sleep medication use and HRT use, except when the covariate quartile was the independent variable.

*Significant difference ($p<0.05$) in MOS SPI score compared with quartile 1 (referent group).

BMI, body mass index; MOS, Medical Outcomes Study; Q, quartile; rMSSD, square root of the mean of the sum of the squares of differences between adjacent R–R intervals; SPI, Sleep Problems Index; VO₂peak, peak rate of oxygen consumption.
DISCUSSION

The key finding from exploratory analyses of the DREW randomised controlled trial was that exercise training significantly improved subjective sleep quality in overweight/obese postmenopausal women. Specifically, we observed a dose-response trend for the continuous MOS SPI values and, perhaps most notably, significantly reduced odds of having significant sleep disturbance at postintervention with even 50% of the recommended dose of exercise for adults. Interestingly, the improvements in sleep quality were not related to changes in body weight, parasympathetic tone or cardiorespiratory fitness.

Previous research with postmenopausal women had yielded conflicting findings regarding whether exercise improved sleep.9–12 While suggested by prior studies in this population,9 11 the present study is the first to document a dose-response relationship between exercise and improved subjective sleep quality. Although sleep was an exploratory outcome of the DREW study, it is the largest clinical trial to date that has examined the relationship between aerobic exercise dose and sleep quality. Our current findings mirror the overall body of research indicating that exercise improves sleep, most prominently in those with existing sleep disturbances.8

Clinical implications

When considering the improvements in continuous MOS SPI scores following exercise training, the clinical significance is uncertain. The observation that only those who exercised at a 12-KKW dose experienced a significant improvement in sleep quality compared with control may be viewed as discouraging, as this dose equated to approximately 190 min/week of moderate-intensity aerobic exercise14 and many individuals may not be willing to perform that much exercise to improve sleep. However, the significant dose-response effect suggests that any dose of exercise should benefit sleep, albeit with larger effects noted with higher levels of energy expenditure.

In contrast, the greatly reduced odds of having significant sleep disturbance following exercise training suggests that exercise may hold the most promise as a treatment option for postmenopausal women with significant sleep disturbance. In particular, even an exercise dose consisting of 50% of the NIH Consensus Panel physical activity recommendations significantly reduced the odds of having a postintervention MOS SPI >25. This is noteworthy since sleep complaints are prevalent in postmenopausal women,1 and current treatment options, such as HRT and hypnotic medication, have often been found to be only mildly efficacious at improving sleep quality compared with placebo in postmenopausal women.6 23

The mechanisms by which exercise may improve subjective sleep quality in postmenopausal women are unknown. Although the present study was not specifically designed to address mechanisms of effect, secondary analyses focused on changes in three variables

### Table 3

<table>
<thead>
<tr>
<th>Prevalence and odds of significant sleep disturbance (ie, Medical Outcomes Study SPI &gt;25) at postintervention</th>
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</thead>
<tbody>
<tr>
<td><strong>Prevalence (n (%))</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>4 KKW</td>
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<tr>
<td>8 KKW</td>
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<tr>
<td>12 KKW</td>
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<tr>
<td>Linear trend P</td>
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<tr>
<td>Weight change</td>
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<tr>
<td>VO2peak change</td>
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<td>rMSSD change</td>
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</table>

Model 1 adjusted for age, BMI, sleep medication use, hormone replacement therapy use and baseline sleep quality (SPI ≤25, SPI >25); model 2 adjusted for change in body weight in addition to variables included in model 1; model 3 adjusted for change in VO2peak in addition to variables included in model 1; model 4 adjusted for change in rMSSD in addition to variables included in model 1.

KKW, kilocalories of energy expenditure per kilogram of body weight per week; rMSSD, square root of the mean of the sum of the squares of adjacent R–R intervals; SPI, Sleep Problems Index; VO2peak, peak rate of oxygen consumption.

4 KKW: 0.59 (1.83), 8 KKW: 1.13 (1.54), 12 KKW: 1.42 (1.79) ml/kg/min; F3,433=13.32, p<0.001. Among those with usable HRV and sleep data (n=351), rMSSD improved in a dose-dependent fashion with exercise training (control: 0.20 (8.45), 4 KKW: 2.72 (9.20), 8 KKW: 3.72 (11.47), 12 KKW: 5.29 (9.51) ms; F3,347=3.82, p=0.01). When added to the model analysing differences in continuous MOS SPI change among treatment groups, none of these covariates were significant (p≥0.14), and inclusion of these variables did not alter the previously noted treatment group differences or linear dose–response effects. When individually added to logistic regression analyses, none of these covariates significantly affected the odds of having significant sleep disturbance. In particular, even an intervention with even 50% of the recommended dose of exercise for adults. Interestingly, the improvements in sleep quality were not related to changes in body weight, parasympathetic tone or cardiorespiratory fitness.
which have been shown to be related to sleep: body weight, parasympathetic activity and cardiorespiratory fitness. There is a clear association between obesity and disturbed sleep, and weight loss has been found to reduce sleep complaints. Likewise, poor sleepers have been found to have impaired sleep HRV, and exercise training has been well documented to improve autonomic function. Finally, physical fitness has been previously associated with sleep quality, and greater improvements in fitness have been associated with better sleep outcomes in some experimental studies.

Nonetheless, in the present study, changes in body weight, parasympathetic tone or cardiorespiratory fitness were not significantly related to changes in sleep, whether assessed by covariate control, change in sleep quality across quartiles of change in these variables or correlations between change in these variables and change in sleep quality. Although significant improvements were noted for rMSSD and VO2peak following exercise training in this sample, the variability associated with the sleep measure used in the current study may have masked any possible associations. The present study suggests that exercise training can result in improved sleep quality independent of weight loss, increased fitness or improved autonomic balance.

**Strengths and weaknesses**

Strengths of the study include a randomised controlled design, closely supervised intervention, use of a validated measure of sleep quality and the largest experimental sample size to investigate the effects of exercise on sleep. The study population was another strength, as the prevalence of disturbed sleep was high. Finally, assessment of variables that are related to sleep quality and may contribute to improved sleep following exercise training was another strength of the study.

A limitation of the study is that sleep quality was not a primary outcome of the original DREW trial. Therefore, results should be interpreted cautiously. Another study limitation is that sleep was not objectively assessed (ie, via wrist actigraphy or polysomnography). Because of the subjective nature of the outcome and impossibility of blinding participants to their treatment, improvements in self-reported sleep quality may have been subject to expectancy effects, as exercise is commonly believed to improve sleep quality. However, the finding of a significant linear trend between exercise dose and improvement in sleep quality would not necessarily be expected. Moreover, that sleep was not a primary outcome of interest and part of a wide range of study assessments further reduces the chance of expectancy or demand biases. Additionally, there is growing recognition of the merit of assessing subjective sleep quality. For instance, in contrast with subjective sleep quality, objective sleep has not been found to be altered across the menopausal transition. Furthermore, impaired subjective sleep quality is what prompts search for treatment, and recent evidence suggests that traditional objective sleep measures might be inadequate for detecting subtle indicators of disturbed sleep. It is also noteworthy that subjective sleep quality has been associated with quality of life and physical and mental health in postmenopausal women.

A lack of assessment of obstructive sleep apnoea (OSA) was another limitation. Although OSA is considered to be a male-dominated sleep disorder, postmenopausal OSA prevalence is similar between men and women. Moreover, excess weight is the primary cause of OSA for most adults, which would place this overweight/obese sample at even higher risk for OSA. Evidence suggests that exercise, in the absence of more established treatments or significant weight loss, is moderately efficacious at reducing OSA severity and improving sleep. However, dose–response effects of exercise on OSA severity are unknown.

Finally, because aerobic activity was the only mode of exercise studied in the DREW trial, the possible effects of resistance exercise on sleep quality could not be examined in this sample. Resistance training has been shown to improve sleep quality, though there has been minimal work comparing different doses of resistance exercise on sleep quality.

**Conclusions**

In summary, in a sample of overweight/obese postmenopausal women, exercise training significantly reduced the odds of having significant sleep disturbance. These improvements in sleep were independent of the effects of exercise training on body weight, parasympathetic tone or cardiorespiratory fitness. Additional research with more comprehensive measurement of sleep is warranted, but exercise training appears to significantly improve sleep quality in postmenopausal women.

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**Contributors** TSC and SNB designed and organised the study. TSC, CPE and SNB collected the data. CEK and XS performed the statistical analyses. CEK wrote the first draft of the manuscript. XS, MHH, SDY, CPE, SNB and TSC provided critical input at all stages and critically reviewed and contributed to the final draft. CEK and TSC are guarantors.

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**REFERENCES**


