PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Dose-Response Effects of Exercise Training on the Subjective Sleep Quality of Postmenopausal Women: Exploratory Analyses of a Randomised Controlled Trial
AUTHORS	Kline, Christopher ; Sui, Xuemi; Hall, Martica; Youngstedt, Shawn; Blair, Steven; Earnest, Conrad; Church, Timothy

VERSION 1 - REVIEW

REVIEWER	Jennifer Hellier Statistician King's Clinical Trials Unit Institute of Psychiatry, Kings College London UK
REVIEW RETURNED	27-Apr-2012

GENERAL COMMENTS	1) The statistical models are adjusted for age, BMI, sleep medication use and HRT use. How were the covariates in the model decided upon? 2) Last Observation Carried Forward is used for the ITT analysis to deal with missing data. Were any other methods considered for the missing data? Please could the authors describe the missing data pattern (for example missing at random). 3) Please could the authors describe how the assumptions of the statistical modelling checked / met?

VERSION 1 – AUTHOR RESPONSE

REVIEWER #1 COMMENTS:
1. The statistical models are adjusted for age, BMI, sleep medication use and HRT use. How were the covariates in the model decided upon?

Authors' response: We adjusted for baseline age (years), BMI (kg/m2), sleep medication use (yes/no), baseline sleep quality (continuous score or yes/no sleep disturbance) and HRT use (yes/no). The covariates, as well as the primary analytic plan, were selected a priori (with the exception of sleep medication) based upon the overall study methods (Morss et al., 2004): "All analyses will take into account prespecified covariates, including age, BMI, HRT status, and baseline values of outcome measures. Analyses of continuous outcome measures will be based on ANCOVA models of 6-month change scores since baseline, and treatment effects will be summarized as least-squares adjusted means (p. 343)."

It may be suggested that randomization reduces or eliminates the need for covariate adjustment. In our view, randomization helps to ensure pre-treatment equivalence on unknown confounders. However, for variables known or strongly suspected to confound the experiment, additional statistical control is warranted. We believe that statistically controlling for these confounds allows for greater certainty in attributing observed changes in the dependent variable to the intervention.

When running the analyses without covariate adjustment, the results do not change from those already reported, and this is noted in the manuscript ('Statistical Analysis' subsection of Methods, last sentence of second paragraph).

2. Last Observation Carried Forward is used for the ITT analysis to deal with missing data. Were any other methods considered for the missing data? Please could the authors describe the missing data pattern (for example missing at random)?

Authors' response: We also dealt with missing data by imputing missing values with mean values. However, the patterns of the association were not significantly different from the LOCF analysis. We now note this in the Methods section (last paragraph of 'Statistical Analysis' section).

Baseline characteristics of the participants with missing post-intervention data were not significantly different from those with post-intervention data on any demographic, covariate, or sleep variables. We believe this indicates that the missing data pattern is likely missing at random, and that the participants with missing post-intervention data were similar to the participants with valid post-intervention data.

3. Please could the authors describe how the assumptions of the statistical modelling were checked/met?

Authors' response: From the residual plots and normal plots, we found that the homogenous, linearity and normal distribution assumptions held for the models that we selected. From the students residual plot we also found that there were no obvious outliers. When we performed the multicollinearity diagnostics, we found that there was no problem of collinearity.

Regarding the Homogeneity of Variances assumption: the variances of each dependent MOS SPI change variable were equal for each level of the group assignments and covariates (baseline age, BMI, sleep medication use, and HRT use). This assumption was tested by Levene's test of equality of error variances.

Regarding the Homogeneity of Regression Slopes assumption: the slope of the line predicting each MOS SPI change variable from the above covariates was equal for each level of the group assignment. This assumption was tested by adding the interaction term in the ANCOVA models. We found there was no significant interaction.

We now note in the revised manuscript that the assumptions underlying the ANCOVA were checked and met ('Statistical Analysis' subsection of Methods, second sentence of second paragraph).