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Interdisciplinary Weight Loss and Lifestyle Intervention for Daily Functioning and Psychiatric Symptoms in Obstructive Sleep Apnea:

The INTERAPNEA Randomized Clinical Trial

Almudena Carneiro-Barrera, PhD; Francisco J. Amaro-Gahete, PhD; Germán Sáez-Roca, MD; Carlos Martín-Carrasco, MD; António Labisa Palmeira, PhD; and Jonatan R. Ruiz, PhD

ABSTRACT

Objective: Impaired daily functioning and psychiatric symptoms are highly prevalent in obstructive sleep apnea (OSA); however, the effects of weight loss and lifestyle interventions on these symptoms remain uncertain. This study aimed to evaluate the efficacy of an interdisciplinary weight loss and lifestyle intervention on impaired functioning, psychological distress, anxiety, and depression among men with moderate-to-severe OSA and obesity.

Methods: This study was a randomized clinical trial conducted from April 2019 to October 2020. Men aged 18–65 years with moderate-to-severe OSA and obesity were randomly assigned to usual care (continuous positive airway pressure) or an 8-week weight loss and lifestyle intervention. Primary outcomes were changes from baseline to intervention endpoint and 6 months after intervention in daily functioning (measured by the Functional Outcomes of Sleep Questionnaire [FOSQ]); psychological distress (evaluated through the General Health Questionnaire [GHQ]); and anxiety and depression symptoms (measured by the State-Trait Anxiety Inventory [STAI], State-Trait Depression Inventory [STDI], and Beck Depression Inventory [BDI]).

Results: Eighty-nine participants underwent randomization (mean [± SD] age, 54 ± 8 years; mean apnea-hypopnea index, 41 ± 22 events/h); 49 were assigned to usual care and 40 to the intervention. As compared with usual care, the intervention group had greater improvements in daily functioning (mean between-group difference in FOSQ score, 2.3; 95% confidence interval, 1.5 to 3.2), psychological distress (GHQ score, −10.3; −15.3 to −5.1), state anxiety (STAI-State score, −7.0; −11.0 to −3.0), trait anxiety (STAI-Trait score, −6.1; −9.5 to −2.8), state depression (STDI-State score, −2.4; −4.3 to −0.4), trait depression (STDI-Trait score, −3.8; −5.6 to −2.1), and general depression (BDI score, −2.0; −3.2 to −0.8) at intervention endpoint. Similar changes were observed at 6 months after intervention.

Conclusions: This study provides the first evidence suggesting that an interdisciplinary weight loss and lifestyle intervention improves OSA-related impaired daily functioning and psychiatric symptoms. These findings should be considered when evaluating the potential benefits of this behavioral approach for OSA.

Trial Registration: ClinicalTrials.gov Identifier: NCT03851653

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Author affiliations are listed at the end of this article.

Obstructive sleep apnea (OSA), a major public health problem affecting up to 38% of adults in the overall population, is characterized by recurrent episodes of complete or partial upper-airway obstructions during sleep resulting in long-term exposure to hypoxia, hypercapnia, sleep fragmentation, and increased sympathetic activity.[1,2] With obesity as the leading attributable cause, OSA is closely associated with an increased risk of a wide spectrum of metabolic and cardiovascular diseases, psychiatric/psychological disorders, impaired daily functioning, and, thus, diminished quality of life and all-cause mortality.[3–10] Depression and anxiety, similarly highly prevalent major causes of disease burden and cardiovascular risk factors, are the most common psychiatric conditions found in OSA.[8–10] These comorbid psychiatric symptoms have been found to adversely impact self-management, treatment adherence and functioning, symptoms perception, and health care costs in chronic medical illnesses and, specifically, in OSA.[9–11]

Continuous positive airway pressure (CPAP), the first line treatment for OSA, is a mechanical device highly effective at reducing the number of apnea and hypopnea episodes per hour of sleep (ie, apnea-hypopnea index [AHI]).[12] However, the effects of CPAP on OSA-related subjective symptoms such as psychological distress, anxiety, and depression remain controversial.[13,14] Gathered evidence in the field has shown that CPAP is not more effective at reducing these psychological comorbidities than placebo or sham CPAP, which evidences the complex process underlying the reciprocal interaction between OSA and psychiatric conditions.[13–16] Although effective at reducing OSA severity, CPAP may not address OSA major risk factors such as obesity and other cardiometabolic diseases associated to both OSA and psychological distress.[17] Therefore, a sole reduction in AHI after CPAP therapy, without other autonomic and/or metabolic changes, may not be sufficient to contribute to a clinically significant improvement in psychological well-being, anxiety, and depression.[13]

Alternative or combined non-surgical and non-pharmacologic approaches such as weight loss and lifestyle interventions are highly recommended and appear to substantially improve OSA severity and related cardiometabolic comorbidities.[18–25] There are fairly well-established data indicating that these active interventions

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Clinical Points

- Impaired daily functioning and psychiatric symptoms are highly prevalent in obstructive sleep apnea (OSA); however, the effects of weight loss and lifestyle interventions on these symptoms remain uncertain.
- Given the high prevalence of psychiatric symptoms and their adverse impact on OSA and related chronic medical illnesses, clinicians and health care providers should consider combined weight loss and lifestyle approaches to comprehensively address the imperatives of this increasingly common sleep-disordered breathing.

significantly reduce comorbid psychiatric symptoms in other chronic medical illnesses such as obesity, type 2 diabetes, and cardiovascular diseases.[26–28] However, there is no evidence to date on the efficacy of this approach at addressing the psychiatric symptoms found in OSA.

This study based on data from the INTERAPNEA trial was aimed at testing the effects of an 8-week interdisciplinary weight loss and lifestyle intervention on daily functioning and psychiatric symptoms in overweight/obese adults with CPAP-treated moderate-to-severe OSA. The INTERAPNEA trial sought to determine the efficacy of this behavioral approach, as compared with usual care alone (ie, CPAP), on OSA severity, body weight and composition, and cardiometabolic risk in adults with moderate-to-severe OSA and overweight/obesity.[29] At 6 months after intervention, AHI reductions in the intervention and control groups were −23.8 and −0.8, respectively, with 62% of participants in the intervention group no longer requiring CPAP therapy.[21] Furthermore, clinically significant differences in body weight and composition, as well as cardiometabolic risk outcomes, were also found in the intervention group as compared with the control group.[21] Therefore, we hypothesized that the intervention group would also have greater improvements in daily functioning, psychological distress, and anxiety and depression symptoms than the control group. Additionally, we investigated the associations of changes in daily functioning and psychiatric symptoms with changes in OSA severity (as measured by the AHI), body mass index (BMI), excessive daytime sleepiness (as measured by the Epworth Sleepiness Scale[30]), and subjective sleep quality (as measured by the Pittsburgh Sleep Quality Index[31]) outcomes.

METHODS

Study Design and Population

The present study is an ancillary study of the INTERAPNEA trial. The rationale, design, and methodology of this trial have previously been described in detail.[21,29] In brief, this study was conducted from April 2019 to October 2020, and eligible participants were men aged 18–65 years with CPAP-treated moderate-to-severe OSA (AHI equal or greater than 15 events per hour of sleep) and a BMI equal or greater than 25 kg/m^2. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for randomized clinical trials. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by the Research Ethics Committees of (*a*) University of Granada (Granada, Spain); (*b*) Virgen de las Nieves University Hospital (Granada, Spain); and (*c*) Junta de Andalucía (Spain) (0770-N-19). All participants provided written informed consent. This study was registered at ClinicalTrials.gov (identifier: NCT03851653).

Study Recruitment, Enrollment, and Randomization

Potential participants were recruited from the sleep-disordered breathing unit of the collaborating hospital-based referral center. Owing to practical and feasibility reasons, the trial was conducted in 3 consecutive sets of a maximum of 30 participants. Inclusion feasibility and baseline assessments—including an overnight fasting blood test, in-laboratory full-night polysomnography, a set of questionnaires measuring subjective variables, and measurements of anthropometric and body composition parameters—were performed on each participant. Eligible participants were randomly assigned to either usual care (control group) or weight loss and lifestyle intervention combined with usual care (intervention group) by means of a computer-generated simple (unrestricted) randomization.[32]

Owing to the nature of the intervention, clinicians and participants were aware of trial-group assignments after randomization. Nevertheless, the personnel responsible for data collection and analyses were blinded to allocation assignments at the follow-up.

Study Interventions

The INTERAPNEA interdisciplinary weight loss and lifestyle intervention, meticulously designed and based on existing clinical practice guidelines, lasted 8 weeks and was composed of 5 components/modules: nutritional behavior change, moderate aerobic exercise, smoking cessation, alcohol avoidance, and sleep hygiene. Each component, including 60- to 90-minute group-based weekly sessions, was led by trained professionals in each field. A detailed intervention description has previously been published.[21,29]

The usual-care/control group received, apart from CPAP, a single 30-minute session led by a sleep-disordered breathing specialist addressing general advice on weight loss and lifestyle change. In addition, the study intervention was offered to all participants at the end of the trial.

Study Assessments and Outcomes

The primary outcomes of this study were changes from baseline to intervention endpoint and 6 months after intervention in (1) daily functioning, (2) psychological distress, (3) anxiety, (4) and depression, all outcomes being assessed through well-validated questionnaires.

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Daily functioning was subjectively assessed through the Functional Outcomes of Sleep Questionnaire (FOSQ), a disease-specific quality of life instrument assessing OSA and excessive daytime sleepiness impact on the ability to perform different activities related to daily living.[33,34] This questionnaire is composed of 30 items comprising 5 subscales including general productivity, social outcome, activity level, vigilance, and sexual relationships and intimacy. Each item rates the difficulty of performing a given activity on a scale from 1 (extreme difficulty) to 4 (no difficulty). Mean-weighted item scores for each subscale range from 1 to 4 and the total score, from 5 to 20, with higher scores indicating greater functioning. A total score less than 18 indicates impaired functional status.[35,36]

Psychological distress was measured using the General Health Questionnaire (GHQ).[35,36] This 28-item instrument is a widely used measure of psychological distress as the opposite of psychological well-being. It consists of 4 subscales, each composed of 7 items related to the presence of somatic symptoms, anxiety, social dysfunction, and depression. Each item is scored on a Likert-type scale of severity ranging from 0 to 3, with a total score range from 0 to 84. Higher scores indicate greater psychological distress; a total score greater than 23 suggests the presence of psychological distress and/or a psychiatric disorder.[37,38]

The intensity and frequency of displaying anxiety symptoms were assessed with the State-Trait Anxiety Inventory (STAI).[39,40] This 40-item inventory is composed of 2 subscales comprising 20 items each, measuring state anxiety and trait anxiety on a scale from 0 (not at all or almost never) to 3 (very much so or almost always). The total scores range from 0 to 60 for each subscale, with higher scores indicating greater anxiety. The state anxiety subscale evaluates the intensity of current anxiety symptoms including items such as worry, apprehension, nervousness, tension, and autonomic nervous system activation. The trait anxiety subscale assesses anxiety proneness or frequency of feeling anxious, including general states of calmness, confidence, and security. Total scores equal to or greater than 21 and 24 suggest clinical levels of state anxiety and trait anxiety, respectively, in this specific sample.[41]

State-trait and general depression were assessed using the State-Trait Depression Inventory (STDI) and the Beck Depression Inventory-Fast Screen (BDI-FS), respectively.[42–44] These questionnaires are highly reliable screening tools of depression among medical patients, both solely including cognitive-affective symptoms of depression and excluding other overlapping symptoms commonly found in medical illnesses such as somatic symptoms. STDI evaluates both state and trait depression, distinguishing dysthymia (high negative affect) and euthymia (lack of positive affect) components of depression within each subscale. Items are scored from 1 (not at all or almost never) to 4 (very much so or almost always); total scores of each subscale range from 10 to 40, with higher scores indicating greater symptoms of depression. A total score equal to or greater than 20 and 21 suggests clinical levels of state depression and trait depression, respectively, in this sample.[42] Similarly, the BDI-FS consists of 7 items rated from 0 (never) to 3 (high likelihood) related to sadness, pessimism, past failure, loss of pleasure, self-dislike, self-criticalness, and suicidal thoughts. Total scores range from 0 to 21; a score of 4 or higher suggests depression.[43,44]

Statistical Analysis

The intervention effects on the study outcomes were estimated in the context of linear mixed-effects models, including trial group, assessment time, and their interaction terms as the main effect.[45] Estimations were performed using the restricted maximum-likelihood method and an unstructured covariance matrix in order to adjust for within-participant clustering resulting from the repeated-measures design. This model assumed that missing values were missing-at-random, all values presented in the tables being model-based estimates. Yet, attrition propensity was calculated through a logistic model that predicted attrition based on baseline values of set of participants, allocation group, OSA severity, age, and BMI. Owing to the occurrence of the COVID-19 pandemic at the trial endpoint (intervention endpoint assessment of the third set of participants), only the set of participants significantly predicted attrition. Model assumptions of missing values being missing-at-random were therefore sustained, which is also in accordance with recent recommendations for handling missing data in randomized trials affected by a pandemic specific to our case.[46]

All estimations and analyses were performed primarily with an intention-to-treat approach (including all participants as originally allocated after randomization) and an additional per-protocol approach restricted to participants with a CPAP usage equal or greater than 4 hours per night on 70% of nights and, concerning the intervention group, at least 80% of attendance rate at intervention sessions.

In addition, exploratory analyses using *t* test were also performed to examine differences on changes on the study outcomes by group and clinical status on the corresponding symptoms at baseline. Association of changes in daily functioning and psychiatric symptoms over time with changes in OSA severity, BMI, excessive daytime sleepiness, and subjective sleep quality outcomes were also examined by repeated measures correlation analysis—a statistical technique used to determine the within-individual association for paired measures assessed on 2 or more occasions for multiple individuals.[47] All analyses were performed using R version 4.0.3 (R Project for Statistical Computing). All analyses were performed using R version 4.0.3 (R Project for Statistical Computing).

RESULTS

Study Participants

A total of 89 participants with CPAP-treated moderate-to-severe OSA and overweight/obesity were enrolled from April 2019 through February 2020; data collection concluding

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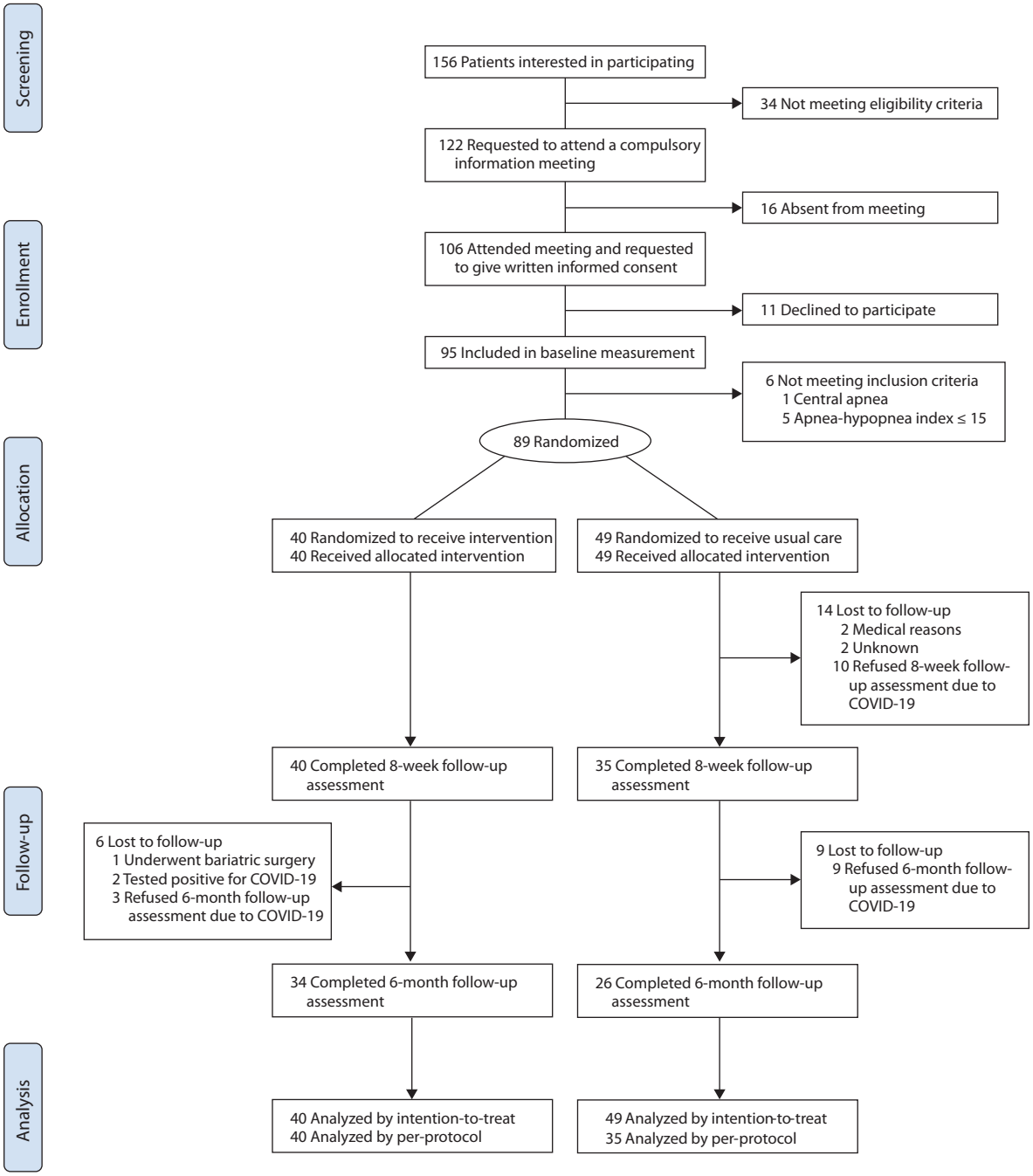
Figure 1. Flowchart of the INTERAPNEA Randomized Clinical Trial



by October 2020 (Figure 1). Participants were randomly assigned to the control group (49 participants) or the intervention group (40 participants). The loss to follow-up was 14 participants from the control group (15.7%), which was mainly due to the emergence of the COVID-19 pandemic (10 participants). A total of 89 participants were included in the intention-to-treat analyses, and 75 in the per-protocol approach according to the prespecified adherence criteria. The two randomized groups were well balanced with respect to baseline characteristics; there were no differences in clinical measures at baseline values between the control group and the intervention group (Table 1). The mean (SD) age was 54.1 (8.0) years, the mean (SD) BMI was 34.4 (5.4) kg/m^2, and the mean (SD) AHI was 41.3 (22.2) events/h. The mean (SD) time since OSA diagnosis and CPAP use was 7.0 (6.1) years. Baseline characteristics were equivalent when adopting a per-protocol approach (Supplementary Table 1).

Daily Functioning

Participants in the intervention group had statistically significant greater improvements from baseline to intervention endpoint and 6 months after intervention in

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Table 1. Baseline Characteristics of the Study Participants

Characteristic[a]	Control (n = 49)[b]	Intervention (n = 40)[b]
Age, mean (SD), y	55.3 (8.5)	52.6 (7.1)
Educational level		
Primary education	13 (26.5)	10 (25.0)
Secondary education	10 (20.4)	6 (15.0)
Vocational education	13 (26.5)	17 (42.5)
Higher education	13 (26.5)	7 (17.5)
Marital status		
Single	7 (14.3)	2 (5.0)
Married	34 (69.4)	34 (85.0)
Divorced	8 (16.3)	4 (10.0)
Occupational status		
Employed	27 (55.1)	21 (52.5)
Self-employed	8 (16.3)	12 (30.0)
Unemployed	4 (8.2)	5 (12.5)
Retired	10 (20.4)	2 (5.0)
Medical conditions[c]		
Hypertension	33 (67.4)	27 (67.5)
Diabetes mellitus type II	12 (24.5)	10 (25.0)
Cardiovascular disease	9 (18.4)	7 (17.5)
Other medical conditions	29 (59.2)	26 (65.0)
Medication[c]		
Antihypertensive	31 (63.3)	24 (60.0)
Statins	15 (30.6)	7 (17.5)
Oral antidiabetic	5 (10.2)	2 (5.0)
Insulin	3 (6.1)	1 (2.5)
β-blockers	7 (14.3)	5 (12.5)
Polymedication[d]	14 (28.6)	6 (15.0)
Body mass index, mean (SD), kg/m^2	33.9 (4.8)	35.0 (6.0)
Body weight status		
Overweight	10 (20.4)	5 (12.5)
Class I obesity	21 (42.9)	19 (47.5)
Class II obesity	16 (32.7)	11 (27.5)
Class III obesity	2 (4.1)	5 (12.5)
Apnea-hypopnea index, mean (SD), events/h	41.1 (21.3)	41.6 (23.5)
Obstructive sleep apnea severity		
Moderate	20 (40.8)	15 (37.5)
Severe	29 (59.2)	25 (62.5)
Epworth Sleepiness Scale score, mean (SD)[e]	9.0 (5.0)	10.3 (5.0)
Pittsburgh Sleep Quality Index score, mean (SD)[f]	8.8 (4.8)	7.2 (3.3)

[a]No significant between-group differences were observed in any of the baseline characteristics.
[b]Values shown as n (%) unless otherwise specified.
[c]Participants could have more than 1 condition or medication.
[d]Defined as the use of 5 or more medications.
[e]The Epworth Sleepiness Scale evaluates excessive daytime sleepiness (range, 0–24; higher scores indicate more daytime sleepiness; score > 10 indicates presence of hypersomnolence).[30]
[f]The Pittsburgh Sleep Quality Index assesses subjective sleep quality (range, 0–21; higher scores indicate worse sleep quality; score > 5 suggests poor sleep quality).[31]

daily functioning than those in the control group, with a mean between-group difference in FOSQ total score of 2.3 (95% confidence interval [CI], 1.5 to 3.2; $P < .001$) and 2.5 (95% CI, 1.5 to 3.4; $P < .001$) (Table 2, Figure 2, and Supplementary Figure 1). Accordingly, participants in the intervention group also had significantly greater improvements in general productivity, social function, activity level, vigilance, and sexual and intimacy functioning (FOSQ subscales; all $P < .05$). Similar results were obtained using the per-protocol approach (Supplementary Table 2). According to changes from intervention endpoint to 6 months after intervention, participants in the intervention group maintained improvements in all daily functioning outcomes (Supplementary Table 3).

Participants in the intervention group who reported impaired daily functioning (FOSQ total score less than 18) at baseline (62.5%) had significantly greater improvements in this outcome than those with no/minimal impaired daily functioning at baseline ($P < .001$) (Supplementary Table 4 and Supplementary Figure 2). At the intervention endpoint and 6 months after intervention, impaired daily functioning was only reported by 17.5% and 7.5 of participants in the intervention group, respectively. No discernible differences in daily functioning changes between those with impaired daily functioning (59%) and without it at baseline were found in the control group ($P > .05$).

Psychological Distress

There was a significantly greater reduction in psychological distress in the intervention group than in the control group, with a mean between-group difference in GHQ total score of −10.3 (95% CI, −15.3 to −5.1; $P < .001$) and −11.8 (95% CI, −17.3 to −6.3; $P < .001$) from baseline to intervention endpoint and 6 months after intervention, respectively (Table 2, Figure 2, and Supplementary Figure 1). Correspondingly, participants in the intervention group also had significantly reduced somatic, social dysfunction, and anxiety and depression symptoms (GHQ subscales; all $P < .05$). Similar results were obtained using the per-protocol approach (Supplementary Table 2). According to changes from intervention endpoint to 6 months after intervention, participants in the intervention group maintained improvements in all psychological distress outcomes (Supplementary Table 3).

Participants in the intervention group who reported psychological distress (GHQ total score greater than 23) at baseline (45%) had significantly greater improvements in this outcome than those with no/minimal impaired daily functioning at baseline ($P < .001$) (Supplementary Table 5 and Supplementary Figure 3). After the intervention, no participants in this group reported psychological distress. No discernible differences in psychological distress changes between those with psychological distress (41%) and without it at baseline were found in the control group ($P > .05$).

Anxiety

Compared with participants in the control group, participants in the intervention group significantly reduced both state anxiety (mean between-group difference in STAI-State, −7.0; 95% CI, −11.0 to −3.0; $P < .001$) and trait anxiety (mean between-group difference in STAI-Trait, −6.1; 95% CI, −9.5 to −2.8; $P < .001$) at intervention endpoint (Table 2 and Figure 2). At 6 months after intervention, mean between-group differences for state anxiety and trait anxiety were −9.3 (95% CI, −13.6 to −4.9; $P < .001$) and −8.8 (95% CI, −12.4 to −5.2; $P < .001$), respectively (Table 2 and Supplementary Figure 1). Similar results were obtained using the per-protocol approach (Supplementary Table 2). According to changes from intervention endpoint to 6 months after intervention, participants in the intervention group maintained improvements in all anxiety outcomes (Supplementary Table 3).

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Table 2. Daily Functioning, Psychological Distress, Anxiety, and Depression Outcomes

Endpoint	Control (n = 49)			Intervention (n = 40)			Mean difference between groups at 8 weeks(95% CI)	Mean difference between groups at 6 months (95% CI)
	Baseline (95% CI)[a]	Change at 8 weeks (95% CI)	Change at 6 months (95% CI)	Baseline (95% CI)[a]	Change at 8 weeks (95% CI)	Change at 6 months (95% CI)		
Functional Outcomes of Sleep Questionnaire[b]								
General productivity score	3.4 (3.3 to 3.6)	0.2 (0.01 to 0.3)	0.04 (−0.1 to 0.2)	3.5 (3.4 to 3.7)	0.4 (0.2 to 0.5)	0.3 (0.2 to 0.5)	0.2 (0.02 to 0.4)[c]	0.3 (0.1 to 0.5)[d]
Social outcome score	3.4 (3.2 to 3.7)	−0.01 (−0.3 to 0.3)	−0.3 (−0.7 to 0.1)	3.5 (3.2 to 3.8)	0.4 (0.1 to 0.7)	0.4 (0.1 to 0.8)	0.4 (0.04 to 0.8)[c]	0.7 (0.3 to 1.1)[e]
Activity level score	3.2 (3.0 to 3.3)	0.1 (−0.04 to 0.3)	0.1 (−0.1 to 0.2)	3.3 (3.1 to 3.5)	0.4 (0.3 to 0.6)	0.5 (0.3 to 0.6)	0.3 (0.1 to 0.5)[d]	0.4 (0.2 to 0.6)[e]
Vigilance score	3.3 (3.1 to 3.5)	−0.1 (−0.3 to 0.2)	0.1 (−0.2 to 0.4)	3.3 (3.1 to 3.5)	0.4 (0.1 to 0.6)	0.5 (0.2 to 0.8)	0.4 (0.1 to 0.7)[d]	0.4 (0.1 to 0.7)[c]
Sexual relationships and intimacy score	3.1 (2.8 to 3.4)	−0.4 (−0.9 to 0.03)	−0.1 (−0.6 to 0.4)	3.3 (3.0 to 3.6)	0.6 (0.2 to 1.0)	0.6 (0.2 to 1.1)	1.0 (0.5 to 1.5)[e]	0.7 (0.2 to 1.3)[c]
Total score	16.5 (15.8 to 17.2)	−0.2 (−0.9 to 0.6)	−0.2 (−1.0 to 0.6)	16.9 (16.2 to 17.7)	2.2 (1.5 to 2.9)	2.3 (1.5 to 3.0)	2.3 (1.5 to 3.2)[e]	2.5 (1.5 to 3.4)[e]
General Health Questionnaire[f]								
Somatic symptoms score	6.1 (5.1 to 7.0)	−1.1 (−2.4 to 0.3)	0.8 (−0.7 to 2.3)	6.6 (5.5 to 7.7)	−5.1 (−6.4 to −3.8)	−3.9 (−5.3 to −2.5)	−4.0 (−5.6 to −2.4)[e]	−4.8 (−6.4 to −3.1)[e]
Anxiety symptoms score	6.6 (5.6 to 7.6)	−1.1 (−2.8 to 0.6)	−0.2 (−2.1 to 1.6)	6.2 (5.1 to 7.3)	−3.6 (−5.3 to −1.9)	−3.7 (−5.5 to −1.9)	−2.5 (−4.5 to −0.5)[c]	−3.5 (−5.6 to −1.4)[d]
Social dysfunction symptoms score	8.8 (8.1 to 9.4)	−1.2 (−2.4 to 0.02)	−0.9 (−2.2 to 0.4)	7.9 (7.2 to 8.6)	−3.1 (−4.3 to −1.8)	−2.7 (−3.9 to −1.4)	−1.9 (−3.3 to −0.4)[c]	−1.8 (−3.3 to −0.3)[c]
Depression symptoms score	2.6 (1.7 to 3.4)	−0.2 (−1.4 to 0.9)	−0.2 (−1.5 to 1.1)	2.7 (1.7 to 3.6)	−2.2 (−3.3 to −1.1)	−2.1 (−3.3 to −0.9)	−1.9 (−3.2 to −0.6)[d]	−1.9 (−3.3 to −0.5)[d]
Total score	24.0 (21.3 to 26.8)	−3.6 (−8.0 to 0.8)	−0.6 (−5.4 to 4.3)	23.4 (20.3 to 26.4)	−13.9 (−18.2 to −9.5)	−12.4 (−17.0 to −7.8)	−10.3 (−15.3 to −5.1)[e]	−11.8 (−17.3 to −6.3)[e]
State-Trait Anxiety Inventory[g]								
Anxiety-state total score	15.7 (13.2 to 18.1)	1.3 (−2.2 to 4.8)	2.2 (−1.7 to 6.0)	16.7 (13.9 to 19.4)	−5.7 (−9.1 to −2.3)	−7.1 (−10.8 to −3.5)	−7.0 (−11.0 to −3.0)[e]	−9.3 (−13.6 to −4.9)[e]
Anxiety-trait total score	19.9 (17.1 to 22.7)	0.05 (−2.9 to 3.0)	0.6 (−2.7 to 3.8)	20.7 (17.5 to 23.8)	−6.1 (−8.9 to −3.3)	−8.2 (−11.2 to −5.2)	−6.1 (−9.5 to −2.8)[e]	−8.8 (−12.4 to −5.2)[e]
State-Trait Depression Inventory[h]								
Euthymia-state score	11.5 (10.5 to 12.4)	−0.5 (−1.7 to 0.8)	0.8 (−0.5 to 2.1)	11.6 (10.6 to 12.7)	−1.9 (−3.0 to −0.7)	−1.6 (−2.9 to −0.4)	−1.4 (−2.8 to −0.02)	−2.4 (−3.9 to −1.0)[d]
Dysthymia-state score	6.0 (5.5 to 6.5)	0.2 (−0.6 to 1.1)	0.7 (−0.2 to 1.6)	6.1 (5.5 to 6.6)	−0.7 (−1.5 to 0.2)	−0.3 (−1.2 to 0.5)	−0.9 (−1.8 to −0.1)	−1.0 (−2.0 to −0.01)
Depression-state total score	17.4 (16.1 to 18.8)	−0.1 (−1.9 to 1.6)	1.5 (−0.4 to 3.5)	17.7 (16.2 to 19.2)	−2.5 (−4.2 to −0.8)	−2.0 (−3.8 to −0.2)	−2.4 (−4.3 to −0.4)[c]	−3.5 (−5.7 to −1.3)[d]
Euthymia-trait score	10.9 (9.9 to 11.9)	−0.4 (−1.5 to 0.8)	0.3 (−1.0 to 1.6)	11.3 (10.2 to 12.4)	−2.6 (−3.7 to −1.4)	−1.6 (−2.8 to −0.4)	−2.2 (−3.5 to −0.8)[d]	−1.9 (−3.4 to −0.5)[c]
Dysthymia-trait score	6.7 (6.1 to 7.4)	0.4 (−0.4 to 1.1)	0.3 (−0.4 to 1.1)	7.0 (6.3 to 7.7)	−1.3 (−1.9 to −0.6)	−1.0 (−1.7 to −0.3)	−1.6 (−2.4 to −0.8)[e]	−1.4 (−2.2 to −0.5)[d]
Depression-trait total score	17.6 (16.1 to 19.1)	0.01 (−1.5 to 1.6)	0.7 (−1.1 to 2.4)	18.3 (16.6 to 20.0)	−3.8 (−5.3 to −2.3)	−2.6 (−4.2 to −1.0)	−3.8 (−5.6 to −2.1)[e]	−3.3 (−5.2 to −1.4)[e]
Beck Depression Inventory-Fast Screen[i] total score	2.8 (2.0 to 3.5)	−0.3 (−1.3 to 0.8)	0.2 (−0.9 to 1.4)	3.2 (2.3 to 4.0)	−2.3 (−3.3 to −1.2)	−1.9 (−3.0 to −0.8)	−2.0 (−3.2 to −0.8)[d]	−2.1 (−3.4 to −0.8)[d]

[a]No significant between-group differences were observed in mean baseline values.
[b]The Functional Outcomes of Sleep Questionnaire assesses the impact of excessive daytime sleepiness on daily functioning (range, 5–20; higher scores indicate greater functioning; score < 18 reflects negative effect of sleepiness on daily functioning).[33–36]
[c]$P < .05$.
[d]$P < .01$.
[e]$P < .001$.
[f]The General Health Questionnaire evaluates psychological distress (range, 0–84; higher scores indicate greater psychological distress; score > 23 indicates presence of psychological distress).[37,38]
[g]The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0–60; higher scores indicate greater anxiety; scores of ≥ 21 and ≥ 24 suggest clinical levels of state and trait anxiety, respectively).[39–41]
[h]The State-Trait Depression Inventory measures state depression and trait depression (range, 10–40; higher scores indicate greater depression; scores of ≥ 20 and ≥ 21 suggest clinical levels of state and trait depression, respectively).[42]
[i]The Beck Depression Inventory-Fast Screen evaluates depression (range, 0–21; higher scores indicate greater depression; score ≥ 4 suggests presence of depression).[43,44]
Abbreviation: CI = confidence interval.

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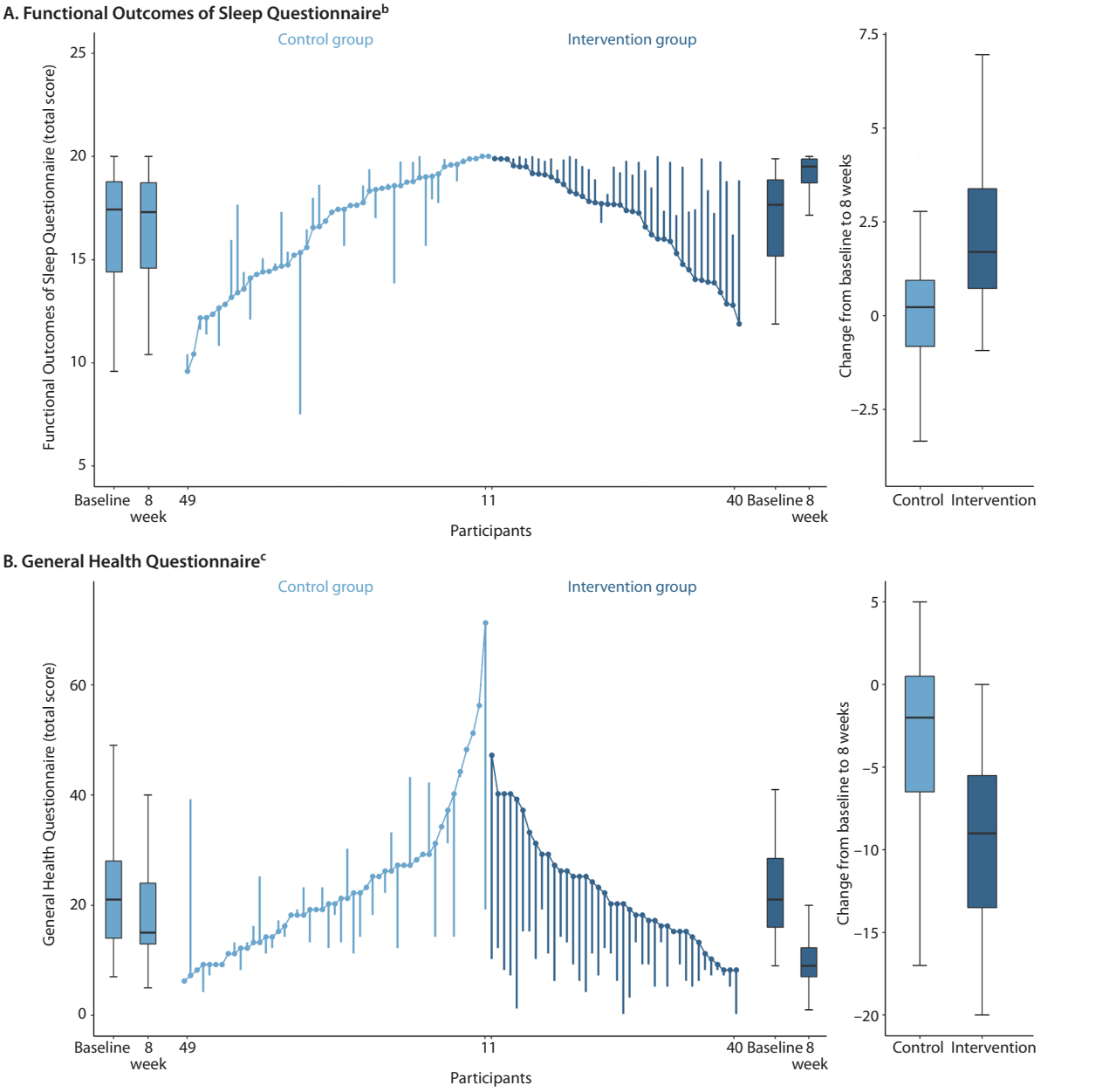
Figure 2. Daily Functioning, Psychological Distress, and Anxiety Outcomes[a]



(continued)

Those participants in the intervention group reporting state anxiety and/or trait anxiety (STAI scores equal or greater than 21 and 24, respectively) at baseline (28% and 38%, respectively) had greater reductions in these outcomes than those with no/minimal state anxiety and/or trait anxiety at baseline (both $P < .001$) (Supplementary Table 6 and Supplementary Figure 4). At the intervention endpoint, only 8% of participants in this group reported state and/or trait anxiety symptoms; which was reduced to 5% at 6 months after intervention. In the control group, a significant difference was only found in state anxiety change between those reporting state anxiety at baseline (29%) and those with no/minimal state anxiety at baseline ($P < .05$).

Depression

Participants in the intervention group had significantly greater reductions in depression from baseline to intervention endpoint and 6 months after intervention than the control group as shown by the STDI and BDI-FS total scores (Table 2, Figure 3, and Supplementary Figure 5). The mean between-group difference was −2.4 (95% CI, −4.3 to −0.4; $P < .05$) in state depression and −3.8 (95% CI, −5.6 to −2.1; $P < .001$) in trait depression at intervention endpoint. At 6 months after intervention, the mean between-group difference was −3.5 (95% CI, −5.7 to −1.3; $P < .01$) in state depression and −3.3 (95% CI, −5.2 to −1.4; $P < .001$) in trait depression. Consistently, the mean between-group

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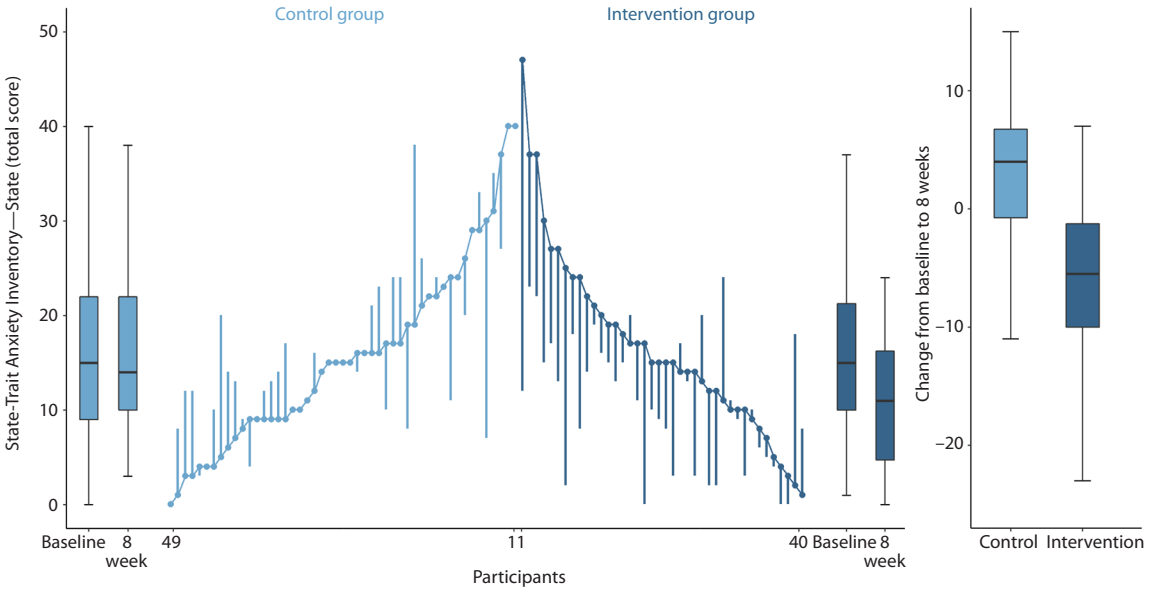
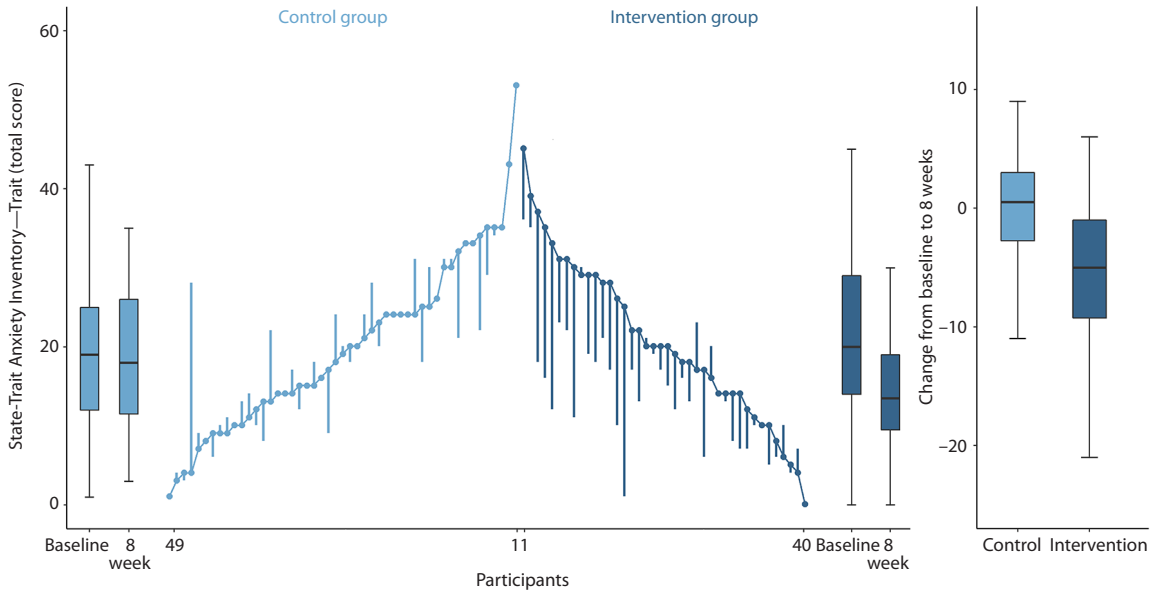
Figure 2 (continued).

C. State-Trait Anxiety Inventory—State[d]



D. State-Trait Anxiety Inventory—Trait[d]



[a]The ends of the boxes in the boxplots are located at the first and third quartiles, with the black line in the middle illustrating the median. Whiskers extend to the upper and lower adjacent values, the location of the furthest point within a distance of 1.5 interquartile ranges from the first and third quartiles. The parallel line plot contains 1 vertical line for each patient, which extends from their baseline value to their 8-week value. Baseline values are placed in ascending order for the control group and descending order for the intervention group.

[b]The Functional Outcomes of Sleep Questionnaire assesses the impact of excessive daytime sleepiness on daily functioning (range, 5–20; higher scores indicate greater functioning; score < 18 reflects negative effect of sleepiness on daily functioning).[33–36] Ascending lines indicate an improvement in the outcome.

[c]The General Health Questionnaire evaluates psychological distress (range, 0–84; higher scores indicate greater psychological distress; score > 23 indicates presence of psychological distress).[37,38] Descending lines indicate an improvement in the outcome.

[d]The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0–60; higher scores indicate greater anxiety; score ≥ 21 and ≥ 24 suggests clinical levels of state and trait anxiety, respectively).[39–41] Descending lines indicate an improvement in the outcome.

difference in depression as measured by the BDI-FS was −2.0 (95% CI, −3.2 to −0.8; $P < .01$) and −2.1 (−3.4 to −0.8; $P < .01$) at intervention endpoint and 6 months after intervention, respectively. Similar results were obtained using the per-protocol approach (Supplementary Table 2). According to changes from intervention endpoint to 6 months after intervention, participants in the intervention group maintained improvements in all depression outcomes (Supplementary Table 3).

Participants in the intervention group reporting state, trait, and/or general depression (STDI-State score equal or greater than 20; STDI-Trait score equal or greater than

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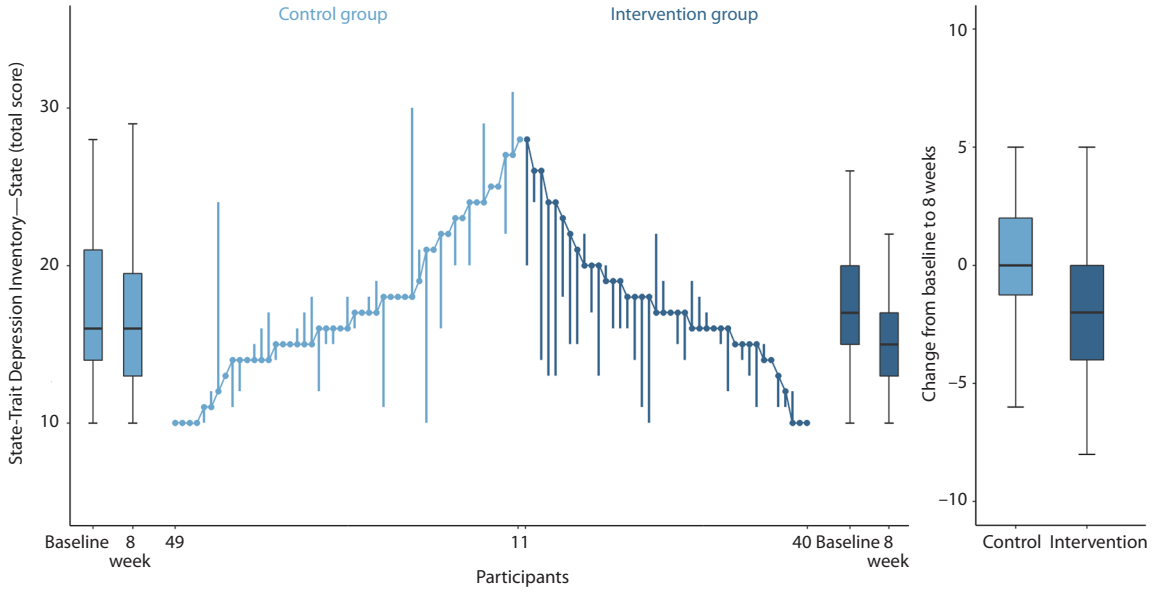
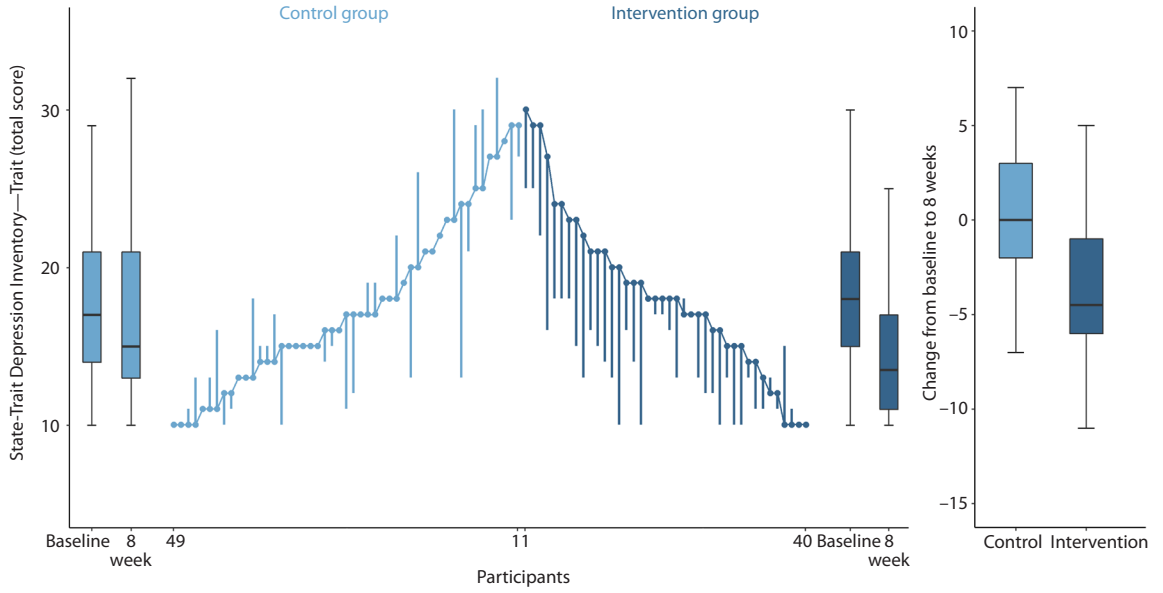
Figure 3. Depression Outcomes[a]

A. State-Trait Depression Inventory—State[b]



B. State-Trait Depression Inventory—Trait[b]



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21; BDI-FS score equal or greater than 4) at baseline (28%, 30%, and 40%, respectively) had greater reductions in these outcomes than those with no/minimal state, trait, and/or general depression at baseline (all $P < .001$) (Supplementary Tables 7 and 8 and Supplementary Figures 6 and 7). After the intervention, 12.5% and 7.5% of participants in this group reported state and/or trait depression, respectively; only 3% reported general depression. At 6 months after intervention, 15% and 17.5% reported state and/or trait depression, respectively, with general depression being reported by 5% of participants. In the control group, no significant differences in state, trait, and/or general depression changes from baseline to intervention endpoint by depression status at baseline were found (all $P > .05$).

Association of Changes in Daily Functioning and Psychiatric Symptoms Over Time With Changes in OSA Severity, BMI, Excessive Daytime Sleepiness, and Subjective Sleep Quality Outcomes

Changes in daily functioning and psychiatric symptoms over time as measured by the FOSQ, GHQ, STAI, STDI, and BDI-FS total scores were significantly associated with

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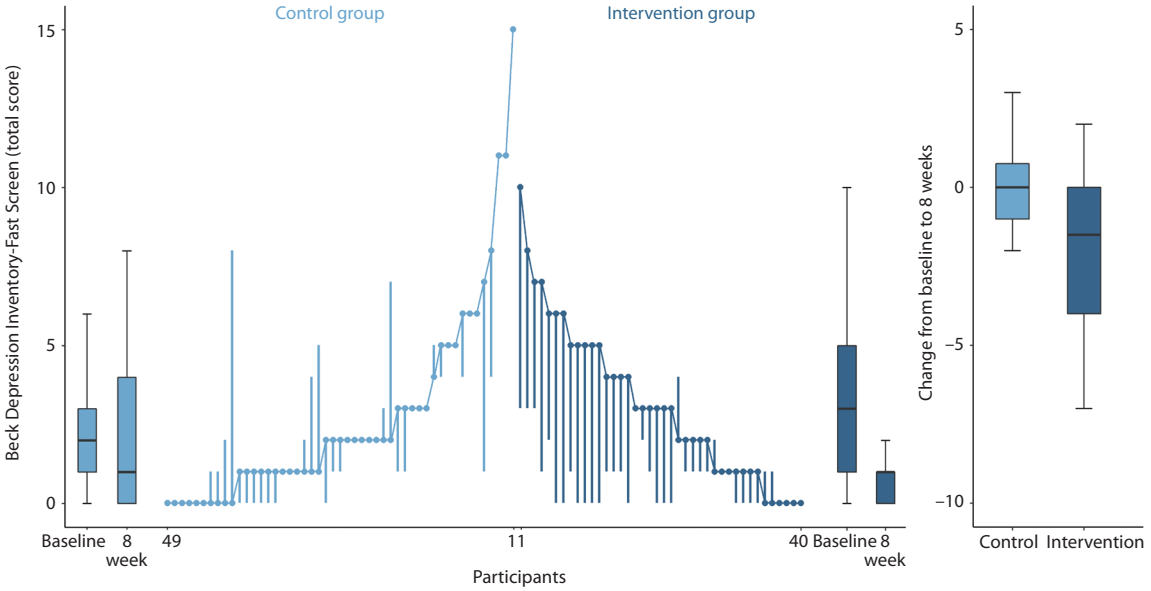
Figure 3 (continued).

C. Beck Depression Inventory-Fast Screen[c]



[a]The ends of the boxes in the boxplots are located at the first and third quartiles, with the black line in the middle illustrating the median. Whiskers extend to the upper and lower adjacent values, the location of the furthest point within a distance of 1.5 interquartile ranges from the first and third quartiles. The parallel line plot contains 1 vertical line for each patient, which extends from their baseline value to their 8-week value. Baseline values are placed in ascending order for the control group and descending order for the intervention group.
[b]The State-Trait Depression Inventory measures state depression and trait depression (range, 10–40; higher scores indicate greater depression; score ≥ 20 and ≥ 21 suggests clinical levels of state and trait depression, respectively).[42] Descending lines indicate an improvement in the outcome.
[c]The Beck Depression Inventory-Fast Screen evaluates psychological distress (range, 0–21; higher scores indicate greater depression; score ≥ 4 suggests presence of depression).[43,44] Descending lines indicate an improvement in the outcome.

changes in OSA severity (as measured by the AHI), BMI, excessive daytime sleepiness (as measured by the Epworth Sleepiness Scale total score), and subjective sleep quality (as measured by the and the Pittsburgh Sleep Quality Index total score); improvement in daily functioning and psychiatric symptoms was related with reduced OSA severity, BMI, excessive daytime sleepiness, and increased subjective sleep quality (all $P \leq .001$; Supplementary Table 9 and Supplementary Figures 8–11).

DISCUSSION

The current study demonstrates the efficacy of an interdisciplinary weight loss and lifestyle intervention, designed to reduce OSA severity, at improving daily functioning and comorbid psychiatric symptoms in CPAP-treated moderate-to-severe OSA. At intervention endpoint, the intervention group had a significant improvement in daily functioning of 13% and an outstanding reduction in psychological distress of 59%. Similarly, participants in the intervention group significantly reduced both state anxiety by 34% and trait anxiety symptoms by 29% at intervention endpoint. Regarding depression symptoms, these participants had significant reductions of 14%, 21%, and 72% in state depression, trait depression, and general depression, respectively. Remarkably, all improvements were maintained at 6 months after intervention. Importantly, these improvements in daily functioning and psychiatric symptoms over time were closely related to improvements in OSA severity, BMI, excessive daytime sleepiness, and subjective sleep quality. These results extend previous findings on the efficacy of weight loss and lifestyle interventions at reducing comorbid psychiatric symptoms in obesity and other related medical conditions such as type 2 diabetes and provide the strongest evidence to date of the effects of this approach on OSA.[26–28]

Furthermore, according to the standard thresholds of the measures used, those participants in the intervention group reporting clinically significant levels of impaired daily functioning, psychological distress, anxiety, and/or depression at baseline had significantly greater improvements in these symptoms than those with no/minimal symptoms at the start of the trial. Remarkably, 72% and 100% of those with clinical levels of impaired daily functioning and psychological distress at baseline, respectively, reported resolution of these symptoms after the intervention. Similarly, 82% achieved resolution of state anxiety and 80%, resolution of trait anxiety at the intervention endpoint. Of those reporting state, trait, and/or general depression at baseline, 73%, 75%, and 100%, respectively, also reported resolution of these symptoms after the intervention. These results, apart from strengthening the evidence supporting

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that weight loss and lifestyle interventions protect patients from psychiatric disorders rather than precipitating them,[26,48] question the consideration of these symptoms as risk factors that could undermine the effects of or adherence to these interventions.[49–51]

Improvements in functional and psychiatric symptoms after a weight loss and lifestyle intervention, as compared with CPAP alone, may be explained by the underlying biological, metabolic, and neurologic dysregulations contributing to both OSA and psychiatric conditions.[7–9,13] According to current models, the functional and psychiatric disturbances found in OSA are not only the result of sleep fragmentation, hypoxia, and neurotransmitter alterations but also secondary to the chronic illness burden and its comorbidities including obesity and cardiometabolic diseases.[7–9,13] As compared to CPAP alone, the INTERAPNEA intervention had significant effects on OSA severity, weight, cardiometabolic risk factors, and, thus, health-related quality of life,[21] factors that are well-related to impaired functional status, psychological distress, and anxiety and depression symptoms.[52,53] Thus, addressing all these factors, as opposed to OSA severity alone, exacerbates the improvement and even resolution of these symptoms.

Strengths and Limitations

A major strength of this study is that it provides the first evidence to date on the effects of a weight loss and lifestyle approach on daily functioning and psychiatric symptoms in OSA. Given the intervention design and results obtained, this study may be a clear rationale for an effective approach readily adaptable to real-world practice settings. Another noteworthy strength is the use of well-validated questionnaires, measuring depression through instruments adapted to medical patients by excluding overlapping/somatic symptoms that are commonly found in both OSA and depression and complicate the determination of one condition in the presence of the other.

A main study limitation is the study duration, which may be an obstacle in the determination of longer-term intervention effects. Nevertheless, the behavioral approach used has been well-established as a key factor for sustainable weight loss and benefits maintenance.[54] The sole inclusion of men with obesity and moderate-to-severe OSA also limits the generalizability of results to women and men without obesity and/or with mild OSA. Certain demographic factors of participants such as employment status and marital status, as well as the reduced number of participants with class III obesity, may have favored weight loss and lifestyle change and, consequently, psychiatric symptoms amelioration; the generalization of our findings is therefore limited to this population.

CONCLUSION

This study provides the first evidence suggesting that an interdisciplinary weight loss and lifestyle intervention is effective at improving and even resolving impaired functioning, psychological distress, and anxiety and depression symptoms comorbid to moderate-to-severe OSA. Given the high prevalence of these psychiatric symptoms and their adverse impact on OSA and related chronic medical illnesses, clinicians and health care providers should consider combined weight loss and lifestyle approaches to comprehensively address the imperatives of this increasingly common sleep-disordered breathing.

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Author Affiliations: Department of Psychology, Universidad Loyola Andalucía, Seville, Spain (Carneiro-Barrera); Department of Physical Education and Sports, Faculty of Sport Sciences, Sport and Health University Research Institute (iMUDS), University of Granada, Granada, Spain (Amaro-Gahete, Ruiz); EFFECTS-262 Research group, Department of Medical Physiology, School of Medicine, University of Granada, Granada, Spain (Amaro-Gahete); Unidad de Trastornos Respiratorios del Sueño, Servicio de Neumología, Hospital Universitario Virgen de las Nieves, Granada, Spain (Sáez-Roca, Martín-Carrasco); Centro de Investigação em Desporto, Educação Física, Exercício e Saúde, Faculdade de Educação Física e Desporto, Universidade Lusófona de Humanidades e Tecnologias, Lisbon, Portugal (Palmeira).

Corresponding Author: Almudena Carneiro-Barrera, PhD, Department of Psychology, Universidad Loyola Andalucía, 41704 Seville, Spain (acarneiro@uloyola.es).

Author Contributions: Funding acquisition, conceptualization, data analysis and interpretation, and writing (original draft): (Carneiro-Barrera); conceptualization and writing (review and editing): (Amaro-Gahete, Sáez-Roca, and Martín-Carrasco); conceptualization, data interpretation, and writing (review and editing): (Palmeira); funding acquisition, conceptualization, and writing (review and editing): (Ruiz). All authors read and approved the final version of the manuscript.

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Additional Information: Requests for data can be made to Dr Carneiro-Barrera (acarneiro@ugr.es). Data, code book, and analytic code will be made available upon request subject to team review and approval of the proposed analysis.

Supplementary Material: Available at Psychiatrist.com.

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Supplementary Material

Article Title: Interdisciplinary Weight Loss and Lifestyle Intervention for Daily Functioning and Psychiatric Symptoms in Obstructive Sleep Apnea: The INTERAPNEA Randomized Clinical Trial

Authors: Almudena Carneiro-Barrera, PhD; Francisco J. Amaro-Gahete, PhD; Germán Sáez-Roca, MD; Carlos Martín-Carrasco, MD; António Labisa Palmeira, PhD; and Jonatan R. Ruiz, PhD

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Supplementary Table 1. Baseline Characteristics of the Study Participants (Per-Protocol Approach)

Characteristics[b]	No. (%)[a]	
	Control (n = 49)	Intervention (n = 40)
Age, mean (SD), y	55.4 (8.9)	52.6 (7.2)
Educational level		
Primary Education	8 (22.9)	10 (25.0)
Secondary Education	6 (17.1)	6 (15.0)
Vocational Education	11 (31.4)	17 (42.5)
Higher Education	10 (28.6)	7 (17.5)
Marital status		
Single	4 (11.4)	2 (5.0)
Married	25 (71.4)	34 (85.0)
Divorced	6 (17.1)	4 (10.0)
Occupational status		
Employed	19 (54.3)	21 (52.5)
Self-employed	6 (17.1)	12 (30.0)
Unemployed	3 (8.6)	5 (12.5)
Retired	7 (20.0)	2 (5.0)
Medical Conditions[c]		
Hypertension	22 (62.9)	27 (67.5)
Diabetes Mellitus II	12 (34.3)	10 (25.0)
Cardiovascular disease	8 (22.9)	7 (17.5)
Other medical conditions	18 (51.4)	26 (65.0)
Medication[c]		
Antihypertensive	21 (60.0)	24 (60.0)
Statins	9 (25.7)	7 (17.5)
Oral antidiabetic	4 (11.4)	2 (5.0)
Insulin	3 (8.6)	1 (2.5)
Beta-blockers	5 (14.3)	5 (12.5)
Polymedication[d]	9 (25.7)	6 (15.0)
Body mass index, mean (SD), kg/m^2	33.7 (4.5)	35.0 (6.0)
Body weight status		
Overweight	7 (20.0)	5 (12.5)
Class I obesity	17 (48.6)	19 (47.5)
Class II obesity	10 (28.6)	11 (27.5)
Class III obesity	1 (2.9)	5 (12.5)
Apnea-hypopnea index, mean (SD), events/hr	39.2 (20.7)	41.6 (23.5)
Obstructive sleep apnea severity		
Moderate	15 (42.9)	15 (37.5)
Severe	20 (57.1)	25 (62.5)
Time since obstructive sleep apnea diagnosis, mean (SD), y	8.6 (6.0)	6.5 (6.5)

[a] No. (%) reported unless otherwise specified.

[b] No significant between-group differences were observed in any of the baseline characteristics.

[c] Participants could have more than one condition or medication.

[d] Defined as the use of five or more medications.

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Supplementary Table 2. Daily Functioning, Psychological Distress, Anxiety and Depression Outcomes (Per-Protocol Approach)

Endpoints	Control (n=49)			Intervention (n=40)			Mean difference between groups at 8 weeks (95% CI)	Mean difference between groups at 6 months (95% CI)
	At baseline (95% CI)[a]	Change at 8 weeks (95% CI)	Change at 6 months (95% CI)	At baseline (95% CI)[a]	Change at 8 weeks (95% CI)	Change at 6 months (95% CI)		
Functional Outcomes of Sleep Questionnaire[b]								
General productivity score	3.4 (3.3 to 3.6)	0.2 (-0.001 to 0.3)	0.04 (-0.1 to 0.2)	3.5 (3.4 to 3.7)	0.4 (0.2 to 0.5)	0.3 (0.2 to 0.5)	0.2 (0.03 to 0.4)[g]	0.3 (0.1 to 0.5)[h]
Social outcome score	3.5 (3.3 to 3.8)	-0.1 (-0.4 to 0.3)	-0.4 (-0.7 to 0.02)	3.5 (3.2 to 3.8)	0.4 (0.1 to 0.8)	0.4 (0.1 to 0.8)	0.5 (0.1 to 0.9)[g]	0.8 (0.4 to 1.2)[i]
Activity level score	3.2 (3.0 to 3.4)	0.1 (-0.1 to 0.3)	0.05 (-0.1 to 0.2)	3.3 (3.1 to 3.5)	0.4 (0.3 to 0.6)	0.5 (0.3 to 0.6)	0.3 (0.1 to 0.5)[h]	0.4 (0.2 to 0.6)[i]
Vigilance score	3.2 (3.0 to 3.5)	-0.03 (-0.3 to 0.3)	0.1 (-0.2 to 0.4)	3.3 (3.1 to 3.5)	0.4 (0.1 to 0.6)	0.5 (0.2 to 0.8)	0.4 (0.1 to 0.7)[g]	0.4 (0.03 to 0.7)[g]
Sexual relationships and intimacy score	3.0 (2.6 to 3.3)	-0.3 (-0.8 to 0.2)	0.02 (-0.5 to 0.6)	3.3 (3.0 to 3.6)	0.6 (0.2 to 1.1)	0.6 (0.2 to 1.1)	0.9 (0.4 to 1.4)[h]	0.6 (0.02 to 1.2)[g]
Total score	16.4 (15.6 to 17.2)	-0.1 (-0.9 to 0.6)	-0.1 (-1.0 to 0.7)	16.9 (16.2 to 17.7)	2.2 (1.5 to 2.9)	2.3 (1.5 to 3.0)	2.3 (1.5 to 3.2)[i]	2.4 (1.5 to 3.4)[i]
General Health Questionnaire[c]								
Somatic symptoms score	5.8 (4.7 to 6.9)	-0.9 (-2.3 to 0.5)	0.9 (-0.6 to 2.5)	6.6 (5.6 to 7.6)	-5.1 (-6.4 to -3.8)	-3.9 (-5.3 to -2.5)	-4.1 (-5.7 to -2.6)[i]	-4.9 (-6.6 to -3.1)[i]
Anxiety symptoms score	5.9 (4.7 to 7.0)	-0.5 (-2.2 to 1.3)	0.5 (-1.4 to 2.4)	6.2 (5.2 to 7.3)	-3.6 (-5.2 to -1.9)	-3.7 (-5.4 to -2.0)	-3.1 (-5.1 to -1.1)[h]	-4.2 (-6.3 to -2.1)[i]
Social dysfunction symptoms score	8.5 (7.8 to 9.3)	-1.0 (-2.2 to 0.3)	-0.7 (-2.1 to 0.7)	7.9 (7.2 to 8.6)	-3.1 (-4.2 to -1.9)	-2.7 (-3.9 to -1.4)	-2.1 (-3.5 to -0.7)[h]	-2.0 (-3.5 to -0.5)[g]
Depression symptoms score	2.1 (1.2 to 3.0)	-0.03 (-1.1 to 1.2)	-0.1 (-1.2 to 1.4)	2.7 (1.8 to 3.5)	-2.2 (-3.3 to -1.1)	-2.1 (-3.3 to -1.0)	-2.2 (-3.5 to -0.9)[h]	-2.2 (-3.6 to -0.8)[h]
Total score	22.3 (19.2 to 25.3)	-2.3 (-6.8 to 2.1)	0.8 (-4.2 to 5.7)	23.4 (20.5 to 26.2)	-13.9 (-18.1 to -9.7)	-12.5 (-16.9 to -8.1)	-11.5 (-16.6 to -6.5)[i]	-13.2 (-18.6 to -7.8)[i]
State-Trait Anxiety Inventory[d]								
Anxiety-state total score	14.5 (11.6 to 17.3)	1.9 (-1.7 to 5.5)	2.8 (-1.2 to 6.8)	16.7 (14.0 to 19.3)	-5.7 (-9.1 to -2.4)	-7.2 (-10.7 to -3.6)	-7.6 (-11.7 to -3.6)[i]	-10.0 (-14.4 to -5.6)[i]
Anxiety-trait total score	18.5 (15.3 to 21.6)	0.5 (-2.5 to 3.5)	1.1 (-2.2 to 4.4)	20.7 (17.7 to 23.6)	-6.1 (-8.9 to -3.3)	-8.2 (-11.2 to -5.3)	-6.6 (-9.9 to -3.2)[i]	-9.3 (-13.0 to -5.7)[i]
State-Trait Depression Inventory[e]								
Euthymia-state score	11.3 (10.2 to 12.4)	-0.3 (-1.6 to 0.9)	1.0 (-0.4 to 2.4)	11.6 (10.6 to 12.7)	-1.9 (-3.0 to -0.7)	-1.6 (-2.9 to -0.4)	-1.5 (-2.9 to -0.1)[g]	-2.6 (-4.1 to -1.1)[i]
Dysthymia-state score	5.7 (5.1 to 6.3)	0.4 (-0.4 to 1.3)	0.9 (-0.1 to 1.8)	6.1 (5.5 to 6.6)	-0.7 (-1.4 to 0.1)	-0.4 (-1.2 to 0.5)	-1.1 (-2.0 to -0.1)[g]	-1.2 (-2.2 to -0.2)[g]
Depression-state total score	17.0 (15.4 to 18.5)	0.1 (-1.7 to 1.9)	1.9 (-0.1 to 3.8)	17.7 (16.2 to 19.1)	-2.5 (-4.2 to -0.8)	-2.0 (-3.7 to -0.2)	-2.6 (-4.6 to -0.6)[g]	-3.8 (-6.0 to -1.6)[i]
Euthymia-trait score	10.9 (9.7 to 12.0)	-0.3 (-1.5 to 0.9)	0.4 (-0.9 to 1.8)	11.3 (10.2 to 12.4)	-2.6 (-3.7 to -1.4)	-1.6 (-2.8 to -0.4)	-2.2 (-3.6 to -0.9)[h]	-2.0 (-3.5 to -0.6)[h]
Dysthymia-trait score	6.5 (5.7 to 7.3)	0.5 (-0.3 to 1.2)	0.5 (-0.3 to 1.3)	7.0 (6.2 to 7.7)	-1.3 (-1.9 to -0.6)	-1.0 (-1.7 to -0.3)	-1.7 (-2.5 to -0.9)[i]	-1.5 (-2.4 to -0.6)[h]
Depression-trait total score	17.4 (15.6 to 19.2)	0.1 (-1.4 to 1.7)	1.0 (-0.8 to 2.7)	18.3 (16.6 to 20.0)	-3.8 (-5.3 to -2.3)	-2.6 (-4.2 to -1.1)	-3.9 (-5.7 to -2.2)[i]	-3.6 (-5.5 to -1.7)[i]
Beck Depression Inventory-Fast Screen[f]								
Total score	2.3 (1.5 to 3.1)	-0.000 (-1.1 to 1.1)	0.6 (-0.6 to 1.7)	3.2 (2.4 to 3.9)	-2.3 (-3.2 to -1.3)	-1.9 (-2.9 to -0.9)	-2.3 (-3.4 to -1.1)[i]	-2.5 (-3.7 to -1.2)[i]

Abbreviations: CI, confidence interval.

[a] No significant between-group differences were observed in mean baseline values.

[b] The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4]

[c] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6]

[d] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9]

[e] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10]

[f] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

[g] $P < 0.05$

[h] $P < 0.01$

[i] $P < 0.001$

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Supplementary Table 3. Daily Functioning, Psychological Distress, Anxiety and Depression Outcomes (Changes from 8 weeks to 6 months)

Endpoints	Control (n=49)			Intervention (n=40)		
	8 weeks Mean (95% CI)	6 months Mean (95% CI)	Mean change (95% CI)	8 weeks Mean (95% CI)	6 months Mean (95% CI)	Mean change (95% CI)
Functional Outcomes of Sleep Questionnaire[b]						
General productivity score	3.6 (3.4 to 3.7)	3.5 (3.3 to 3.6)	-0.1 (-0.3 to 0.1)	3.9 (3.7 to 4.0)	3.8 (3.7 to 4.0)	-0.03 (-0.2 to 0.1)
Social outcome score	3.4 (3.1 to 3.7)	3.1 (2.8 to 3.4)	-0.3 (-0.7 to 0.1)	3.9 (3.7 to 4.2)	3.9 (3.6 to 4.2)	0.01 (-0.3 to 0.4)
Activity level score	3.3 (3.1 to 3.5)	3.2 (3.1 to 3.4)	-0.1 (-0.2 to 0.1)	3.7 (3.6 to 3.9)	3.8 (3.6 to 3.9)	0.04 (-0.1 to 0.2)
Vigilance score	3.2 (3.0 to 3.4)	3.4 (3.1 to 3.6)	0.1 (-0.2 to 0.4)	3.7 (3.5 to 3.9)	3.8 (3.6 to 4.0)	0.1 (-0.2 to 0.4)
Sexual relationships and intimacy score	2.7 (2.4 to 3.1)	3.0 (2.7 to 3.4)	0.3 (-0.2 to 0.8)	3.9 (3.6 to 4.2)	3.9 (3.6 to 4.3)	0.02 (-0.4 to 0.5)
Total score	16.3 (15.6 to 17.1)	16.3 (15.5 to 17.1)	-0.02 (-0.9 to 0.8)	19.1 (18.3 to 19.8)	19.2 (18.4 to 20.0)	0.1 (-0.6 to 0.9)
General Health Questionnaire[c]						
Somatic symptoms score	5.0 (3.9 to 6.1)	6.9 (5.7 to 8.1)	1.9 (0.4 to 3.5)[g]	1.5 (0.5 to 2.6)	2.7 (1.6 to 3.8)	1.2 (-0.2 to 2.6)
Anxiety symptoms score	5.5 (4.4 to 6.7)	6.4 (5.1 to 7.7)	0.9 (-1.1 to 2.8)	2.7 (1.5 to 3.8)	2.5 (1.3 to 3.7)	-0.1 (-1.9 to 1.6)
Social dysfunction symptoms score	7.6 (6.8 to 8.4)	7.9 (7.0 to 8.8)	0.3 (-1.1 to 1.7)	4.9 (4.1 to 5.6)	5.2 (4.4 to 6.0)	0.4 (-0.9 to 1.7)
Depression symptoms score	2.4 (1.4 to 3.3)	2.4 (1.3 to 3.4)	0.02 (-1.3 to 1.3)	0.5 (-0.5 to 1.4)	0.5 (-0.4 to 1.5)	0.1 (-1.1 to 1.2)
Total score	20.4 (17.2 to 23.7)	23.5 (19.8 to 27.1)	3.0 (-2.1 to 8.1)	9.5 (6.4 to 12.6)	11.0 (7.7 to 14.2)	1.5 (-3.1 to 6.0)
State-Trait Anxiety Inventory[d]						
Anxiety-state total score	16.9 (14.1 to 19.8)	17.8 (14.7 to 20.9)	0.9 (-3.1 to 4.9)	11.0 (8.2 to 13.7)	9.5 (6.6 to 12.4)	-1.4 (-5.0 to 2.2)
Anxiety-trait total score	19.9 (16.9 to 23.0)	20.5 (17.2 to 23.8)	0.5 (-2.8 to 3.9)	14.6 (11.4 to 17.7)	12.4 (9.2 to 15.7)	-2.1 (-5.1 to 0.9)
State-Trait Depression Inventory[e]						
Euthymia-state score	11.0 (9.9 to 12.1)	12.3 (11.1 to 13.4)	1.3 (-0.1 to 2.6)	9.8 (8.7 to 10.8)	10.0 (8.9 to 11.1)	0.2 (-1.0 to 1.4)
Dysthymia-state score	6.2 (5.6 to 6.8)	6.6 (6.0 to 7.3)	0.4 (-0.5 to 1.4)	5.4 (4.8 to 6.0)	5.7 (5.1 to 6.3)	0.3 (-0.5 to 1.1)
Depression-state total score	17.3 (15.8 to 18.8)	19.0 (17.3 to 20.6)	1.7 (-0.3 to 3.7)	15.2 (13.7 to 16.7)	15.7 (14.1 to 17.3)	0.5 (-1.3 to 2.3)
Euthymia-trait score	10.5 (9.4 to 11.6)	11.2 (10.0 to 12.4)	0.7 (-0.7 to 2.0)	8.8 (7.6 to 9.9)	9.7 (8.5 to 10.9)	0.9 (-0.3 to 2.1)
Dysthymia-trait score	7.1 (6.4 to 7.8)	7.1 (6.3 to 7.8)	-0.02 (-0.8 to 0.8)	5.7 (5.0 to 6.4)	6.0 (5.2 to 6.7)	0.2 (-0.5 to 1.0)
Depression-trait total score	17.6 (16.0 to 19.3)	18.3 (16.5 to 20.0)	0.7 (-1.1 to 2.4)	14.5 (12.8 to 16.2)	15.7 (13.9 to 17.4)	1.2 (-0.4 to 2.8)
Beck Depression Inventory-Fast Screen[f]						
Total score	2.5 (1.7 to 3.4)	3.0 (2.1 to 4.0)	0.5 (-0.7 to 1.7)	0.9 (0.1 to 1.7)	1.3 (0.4 to 2.1)	0.4 (-0.7 to 1.4)

Abbreviations: CI, confidence interval.

[a] No significant between-group differences were observed in mean baseline values.

[b] The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4]

[c] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6]

[d] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9]

[e] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10]

[f] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

[g] $P < 0.05$

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Supplementary Table 4. Functional Outcomes of Sleep Questionnaire[a] by group and clinical status

	At baseline		At 8 weeks		At 6 months	
Group	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**
Control/usual care						
All	49 (100)	16.48 (2.82)	49 (100)	16.38 (3.16)	49 (100)	16.41 (2.97)
With impaired daily functioning	29 (59.2)	14.65 (2.22)	32 (65.3)	14.78 (2.76)	31 (63.3)	14.72 (2.41)
No impaired in daily functioning	20 (40.8)	19.13 (0.59)	17 (34.7)	19.40 (0.60)	18 (36.7)	19.33 (0.62)
Intervention						
All	40 (100)	16.91 (2.29)	40 (100)	19.09 (1.07)	40 (100)	19.23 (0.93)
With impaired daily functioning	25 (62.5)	15.61 (1.88)	7 (17.5)	17.07 (0.44)	3 (7.5)	16.74 (0.49)
No impaired in daily functioning	15 (37.5)	19.10 (0.61)	33 (82.5)	19.52 (0.52)	37 (92.5)	19.43 (0.60)

[a] The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4]

Supplementary Table 5. General Health Questionnaire[a] by group and clinical status

	At baseline		At 8 weeks		At 6 months	
Group	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**
Control/usual care						
All	49 (100)	24.04 (13.54)	49 (100)	22.37 (12.65)	49 (100)	23.63 (11.98)
With psychological distress	20 (40.8)	36.20 (12.79)	19 (38.8)	35.37 (10.22)	21 (42.9)	34.33 (10.68)
No psychological distress	29 (59.2)	15.66 (4.97)	30 (61.2)	14.13 (4.38)	28 (57.1)	15.61 (3.86)
Intervention						
All	40 (100)	23.38 (10.11)	40 (100)	9.5 (4.29)	40 (100)	10.25 (4.02)
With psychological distress	18 (45.0)	32.44 (7.25)	0 (0.0)	-	0 (0.0)	-
No psychological distress	22 (55.0)	15.96 (4.35)	40 (100)	9.5 (4.29)	40 (100)	10.25 (4.02)

[a] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6]

Supplementary Table 6. State-Trait Anxiety Inventory[a] by group and clinical status

		At baseline		At 8 weeks		At 6 months	
		No. (%)	**Mean (SD)**	**No. (%)**	**Mean (SD)**	**No. (%)**	**Mean (SD)**
State Anxiety	Control/usual care						
	All	49 (100)	15.65 (9.97)	49 (100)	17.02 (9.54)	49 (100)	17.7 (10.22)
	With state anxiety	14 (28.6)	28.43 (6.58)	16 (32.7)	28.31 (6.66)	19 (38.8)	28.3 (6.50)
	No state anxiety	35 (71.4)	10.54 (5.45)	33 (67.3)	11.55 (4.60)	30 (61.2)	11.0 (5.26)
	Intervention						
	All	40 (100)	16.68 (9.89)	40 (100)	10.95 (6.92)	40 (100)	9.60 (6.21)
	With state anxiety	11 (27.5)	29.18 (8.00)	3 (7.5)	23.00 (1.00)	2 (5.0)	22.00 (0.00)
	No state anxiety	29 (72.5)	11.93 (5.34)	37 (92.5)	9.97 (6.23)	38 (95.0)	8.95 (5.65)
Trait Anxiety	Control/usual care						
	All	49 (100)	19.90 (11.03)	49 (100)	20.25 (10.69)	49 (100)	20.35 (11.64)
	With trait anxiety	19 (38.8)	31.00 (7.59)	20 (40.8)	30.45 (7.24)	19 (38.8)	32.11(7.80)
	No trait anxiety	30 (61.2)	12.87 (5.82)	29 (59.2)	13.20 (5.88)	30 (61.2)	12.90 (6.21)
	Intervention						
	All	40 (100)	20.65 (10.36)	40 (100)	14.55 (8.15)	40 (100)	12.60 (8.19)
	With trait anxiety	15 (37.5)	31.67 (5.35)	3 (7.5)	33.67 (3.21)	2 (5.0)	36.00 (0.00)
	No trait anxiety	25 (62.5)	14.04 (6.03)	37 (92.5)	13.00 (6.20)	38 (95.0)	11.37 (6.29)

[a] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9]

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Supplementary Table 7. State-Trait Depression Inventory[a] by group and clinical status

	Group	At baseline		At 8 weeks		At 6 months	
		No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
State Depression	Control/usual care						
	All	49 (100)	17.43 (4.88)	49 (100)	17.49 (5.57)	49 (100)	18.41 (5.81)
	With state depression	14 (28.6)	24.00 (2.22)	15 (30.6)	24.33 (3.64)	17 (34.7)	25.18 (3.66)
	No state depression	35 (71.4)	14.80 (2.61)	34 (69.4)	14.47 (2.98)	32 (65.3)	14.81 (2.61)
	Intervention						
	All	40 (100)	17.68 (4.27)	40 (100)	15.18 (3.48)	40 (100)	15.68 (4.29)
	With state depression	11 (27.5)	23.09 (2.77)	5 (12.5)	21.60 (1.67)	6 (15.0)	24.00 (2.28)
	No state depression	29 (72.5)	15.62 (2.60)	35 (87.5)	14.26 (2.57)	34 (85.0)	14.21 (2.47)
Trait Depression	Control/usual care						
	All	49 (100)	17.59 (5.45)	49 (100)	17.69 (6.08)	49 (100)	18.02 (6.21)
	With trait depression	14 (28.6)	24.86 (2.77)	15 (30.6)	25.47 (3.81)	14 (28.6)	26.36 (3.91)
	No trait depression	35 (71.4)	14.69 (2.94)	34 (69.4)	14.27 (2.83)	35 (71.4)	14.69 (2.93)
	Intervention						
	All	40 (100)	18.28 (5.22)	40 (100)	14.48 (3.88)	40 (100)	15.55 (4.87)
	With trait depression	12 (30.0)	24.50 (3.37)	3 (7.5)	24.00 (1.73)	7 (17.5)	24.14 (3.29)
	No trait depression	28 (70.0)	15.61 (3.19)	37 (92.5)	13.70 (2.82)	33 (82.5)	13.73 (2.70)

[a] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10]

Supplementary Table 8. Beck Depression Inventory-Fast Screen[a] by group and clinical status

Group	At baseline		At 8 weeks		At 6 months	
	No. (%)	Mean (SD)	No. (%)	Mean (SD)	No. (%)	Mean (SD)
Control/usual care						
All	49 (100)	2.78 (3.22)	49 (100)	22.37 (12.65)	49 (100)	3.08 (3.67)
With symptoms of depression	12 (24.5)	7.42 (3.29)	15 (30.6)	6.67 (3.27)	17 (34.7)	6.88 (3.85)
No symptoms of depression	37 (75.5)	1.27 (1.02)	34 (69.4)	1.06 (1.04)	32 (65.3)	1.06 (1.01)
Intervention						
All	40 (100)	3.15 (2.50)	40 (100)	9.5 (4.29)	40 (100)	1.18 (1.74)
With symptoms of depression	16 (40.0)	5.69 (1.66)	1 (2.5)	4 (0.0)	2 (5.0)	7.00 (2.83)
No symptoms of depression	24 (60.0)	1.46 (1.14)	39 (97.5)	0.82 (0.97)	38 (95.0)	0.87 (1.02)

[a] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

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Supplementary Table 9. Repeated measures correlation analyses examining association of changes in daily functioning, psychological distress, anxiety and depression over time (at 8 weeks and 6 months after intervention) with changes in obstructive sleep apnea severity, body mass index, excessive daytime sleepiness and subjective sleep quality outcomes

	Apnea-hypopnea index, events/hr			Body mass index, kg/m2			Epworth Sleepiness Scale, total score[a]			Pittsburgh Sleep Quality Index, total score[b]		
Outcomes	**r**	**95% CI**	**P value**	**r**	**95% CI**	**P value**	**r**	**95% CI**	**P value**	**r**	**95% CI**	**P value**
Functional Outcomes of Sleep Questionnaire, total score[c]	-0.66	-0.78 to -0.51	< 0.001	-0.55	-0.70 to -0.37	<0.001	-0.72	-0.82 to -0.59	< 0.001	-0.69	-0.79 to -0.55	<0.001
General Health Questionnaire, total score[d]	0.67	0.51 to 0.78	<0.001	0.64	0.49 to 0.76	<0.001	0.67	0.52 to 0.78	<0.001	0.75	0.62 to 0.83	<0.001
State-Trait Anxiety Inventory[e]												
Anxiety-state total score	0.53	0.35 to 0.68	<0.001	0.54	0.35 to 0.68	<0.001	0.49	0.29 to 0.65	<0.001	0.53	0.34 to 0.68	<0.001
Anxiety-trait total score	0.62	0.45 to 0.74	<0.001	0.62	0.46 to 0.75	<0.001	0.61	0.45 to 0.74	<0.001	0.65	0.50 to 0.77	<0.001
State-Trait Depression Inventory[f]												
Depression-state total score	0.38	0.17 to 0.56	<0.001	0.40	0.19 to 0.58	<0.001	0.39	0.18 to 0.57	<0.001	0.39	0.18 to 0.57	<0.001
Depression-trait total score	0.57	0.39 to 0.71	<0.001	0.55	0.36 to 0.69	<0.001	0.48	0.28 to 0.64	<0.001	0.50	0.31 to 0.66	<0.001
Beck Depression Inventory-Fast Screen[g]	0.63	0.47 to 0.75	<0.001	0.59	0.42 to 0.72	<0.001	0.53	0.34 to 0.67	<0.001	0.61	0.45 to 0.74	<0.001

Abbreviations: CI, confidence interval.

[a] The Epworth Sleepiness Scale evaluates excessive daytime sleepiness (range, 0-24; higher scores indicate more daytime sleepiness; score >10 indicates presence of hypersomnolence).[13]

[b] The Pittsburgh Sleep Quality Index assess subjective sleep quality (range, 0-21; higher scores indicate worse sleep quality; score >5 suggests poor sleep quality).[14]

[c] The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4]

[d] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6]

[e] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9]

[f] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10]

[g] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

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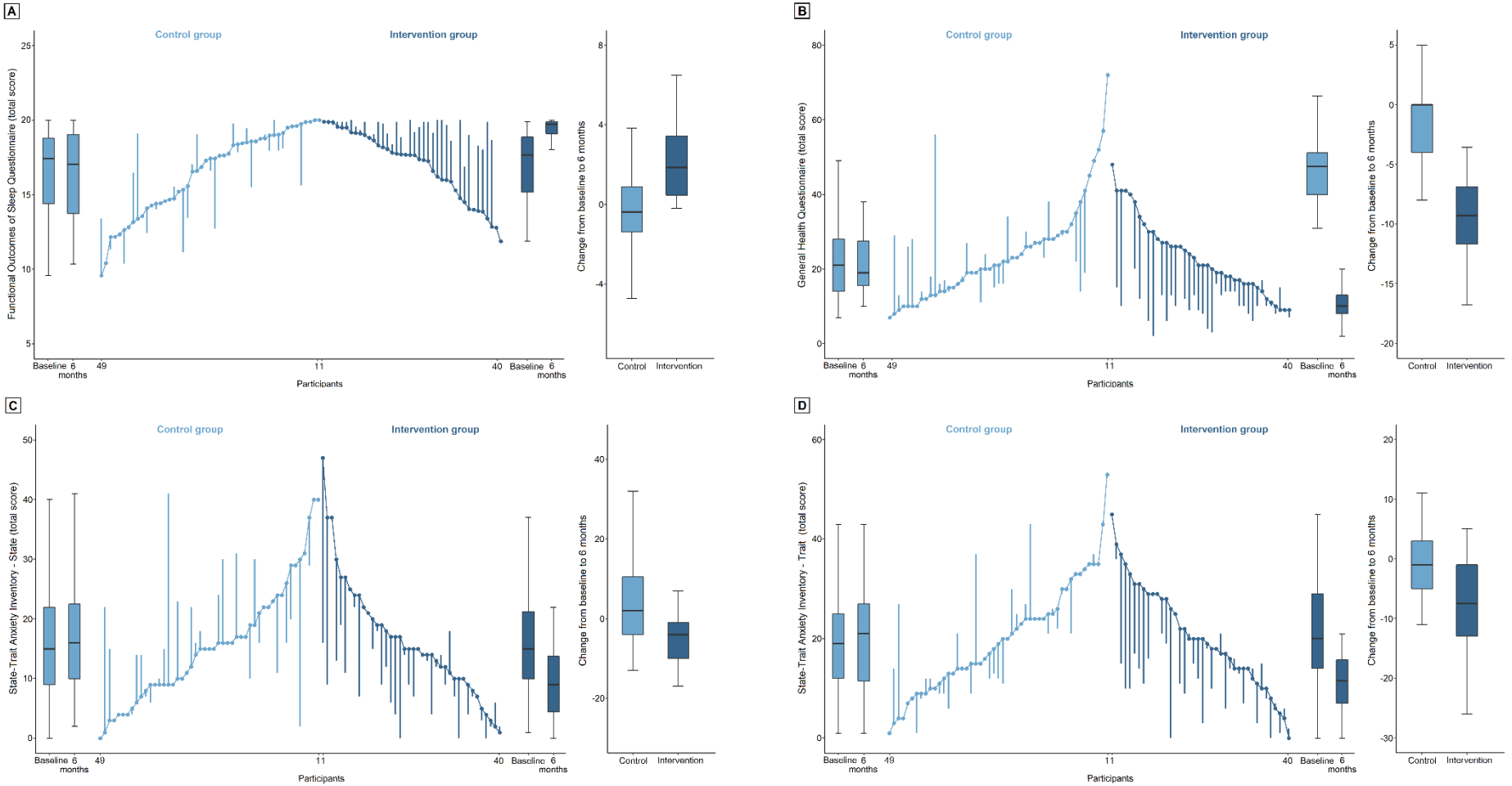
Supplementary Figure 1. Daily Functioning, Psychological Distress, and Anxiety Outcomes (Changes from baseline to 6 months)[a]



[a] The ends of the boxes in the boxplots are located at the first and third quartiles, with the black line in the middle illustrating the median. Whiskers extend to the upper and lower adjacent values, the location of the furthest point within a distance of 1.5 interquartile ranges from the first and third quartiles. The parallel line plot contains 1 vertical line for each patient which extends from their baseline value to their 6-month value. Ascending lines indicate an improvement in the outcome (A). Descending lines indicate an improvement in the outcome (B, C, D). Baseline values are placed in ascending order for the control group and descending order for the intervention group. A, The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4] B, The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6] C,D, The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9]

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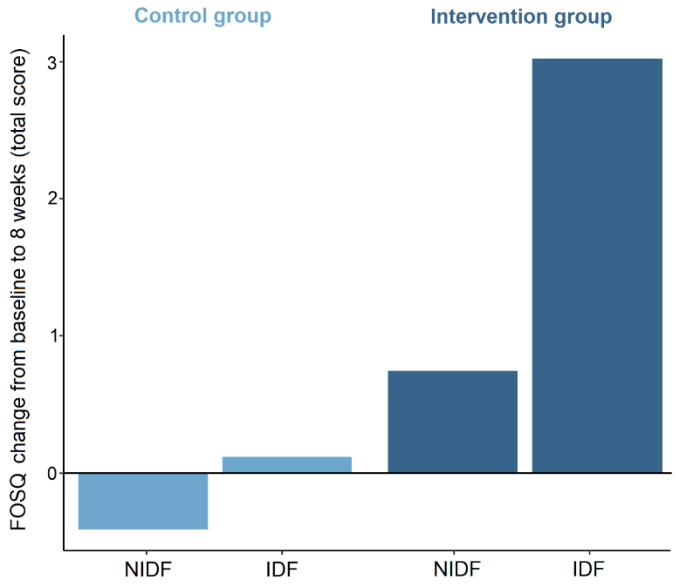
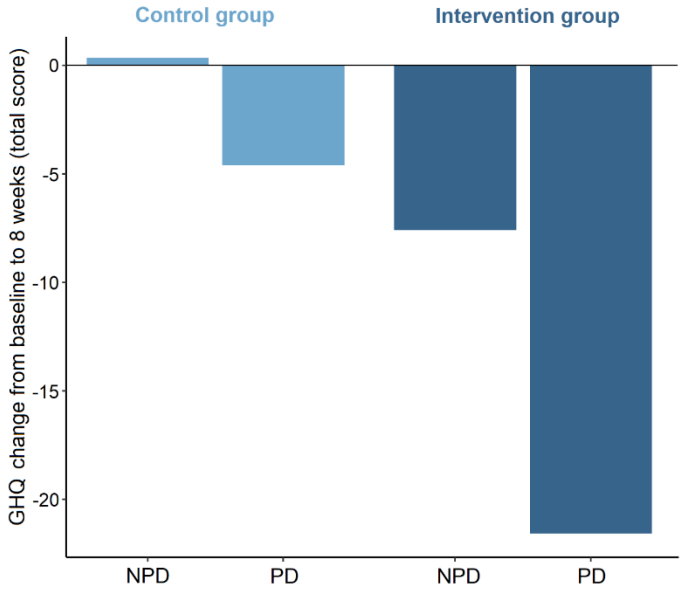
Supplementary Figure 2. Changes in the Functional Outcomes of Sleep Questionnaire (FOSQ) by group and daily functioning status at baseline



Abbreviations: IDF, participants who reported impaired daily functioning at baseline; NIDF, participants with no/minimal impaired daily functioning reported at baseline.

Supplementary Figure 3. Changes in the General Health Questionnaire (GHQ) by group and psychological distress status at baseline



Abbreviations: PD, participants who reported psychological distress at baseline; NPD, participants with no/minimal psychological distress reported at baseline.

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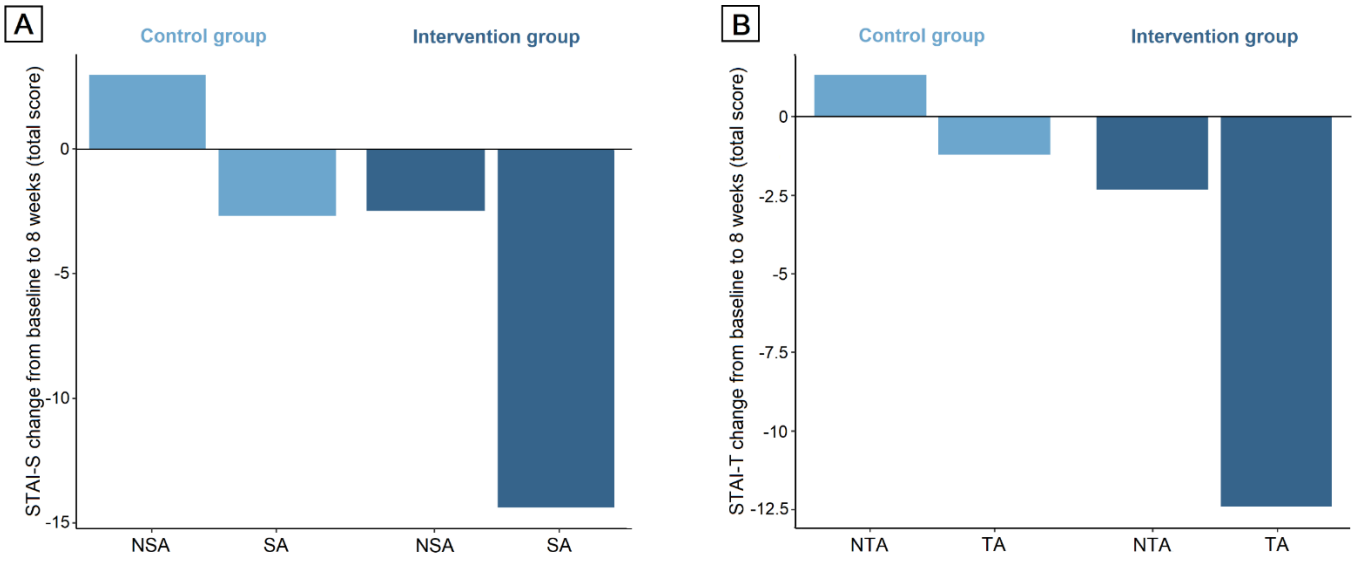
Supplementary Figure 4. Changes in the State-Trait Anxiety Inventory (STAI) by group and anxiety status at baseline



Abbreviations: A, State Anxiety (STAI-S); SA, participants who reported state anxiety at baseline; NSA, participants with no/minimal state anxiety reported at baseline. B, Trait Anxiety (STAI-T);
Abbreviations: TA, participants who reported trait anxiety at baseline; NTA, participants with no/minimal trait anxiety reported at baseline.

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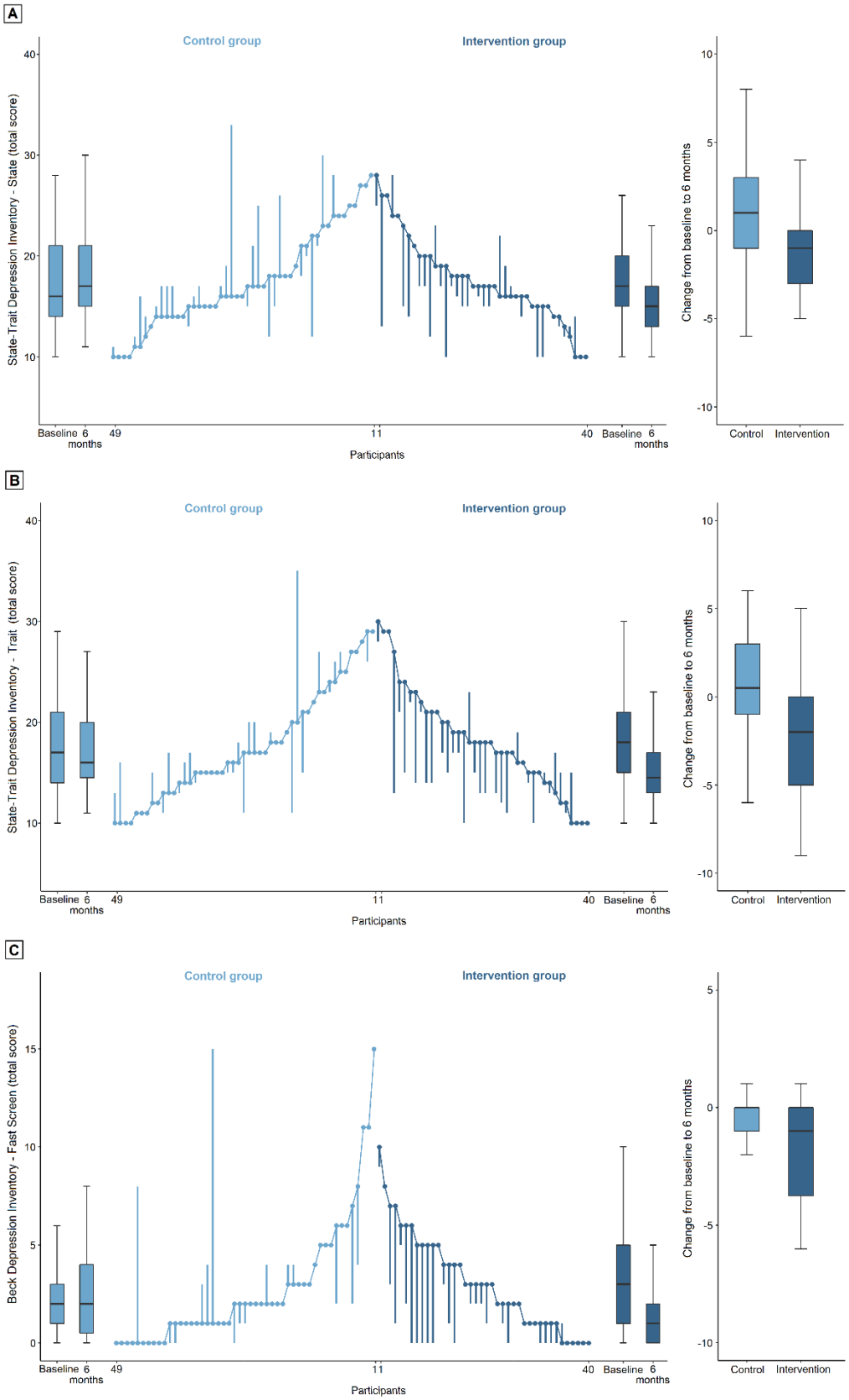
Supplementary Figure 5. Depression Outcomes (Changes from baseline to 6 months)[a]



[a] The ends of the boxes in the boxplots are located at the first and third quartiles, with the black line in the middle illustrating the median. Whiskers extend to the upper and lower adjacent values, the location of the furthest point within a distance of 1.5 interquartile ranges from the first and third quartiles. The parallel line plot contains 1 vertical line for each patient which extends from their baseline value to their 6-month value. Descending lines indicate an improvement in the outcome. Baseline values are placed in ascending order for the control group and descending order for the intervention group. A, B, The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10] C, The Beck Depression Inventory-Fast Screen evaluates psychological distress (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

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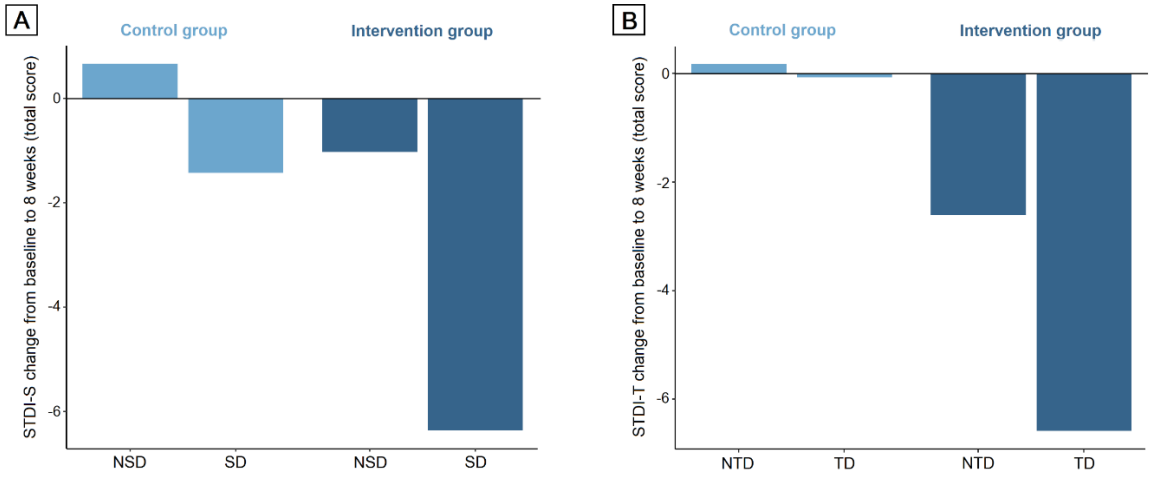
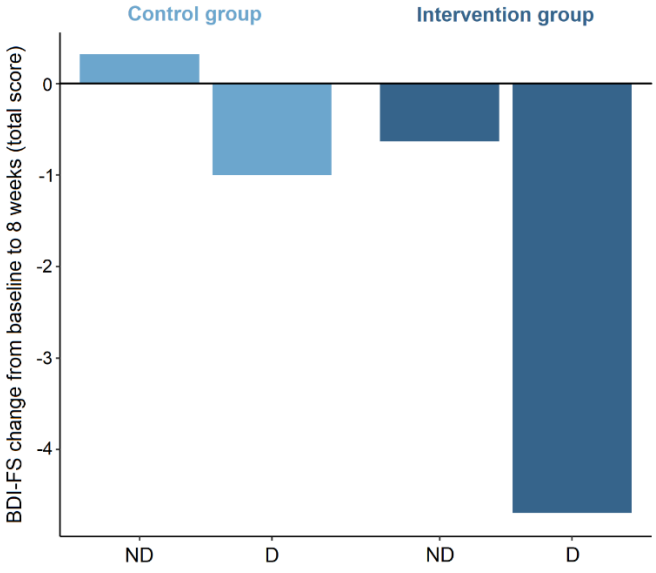
Supplementary Figure 6. Changes in the State-Trait Depression Inventory (STDI) by group and depression status at baseline



Abbreviations: A, State Depression (STDI-S); SD, participants who reported state depression at baseline; NSD, participants with no/minimal state depression reported at baseline. B, Trait Depression (STDI-T); TD, participants who reported trait depression at baseline; NTD, participants with no/minimal trait depression reported at baseline.

Supplementary Figure 7. Changes in the Beck Depression Inventory-Fast Screen (BDI-FS) by group and depression status at baseline



Abbreviations: D, participants who reported depression at baseline; ND, participants with no/minimal symptoms of depression reported at baseline.

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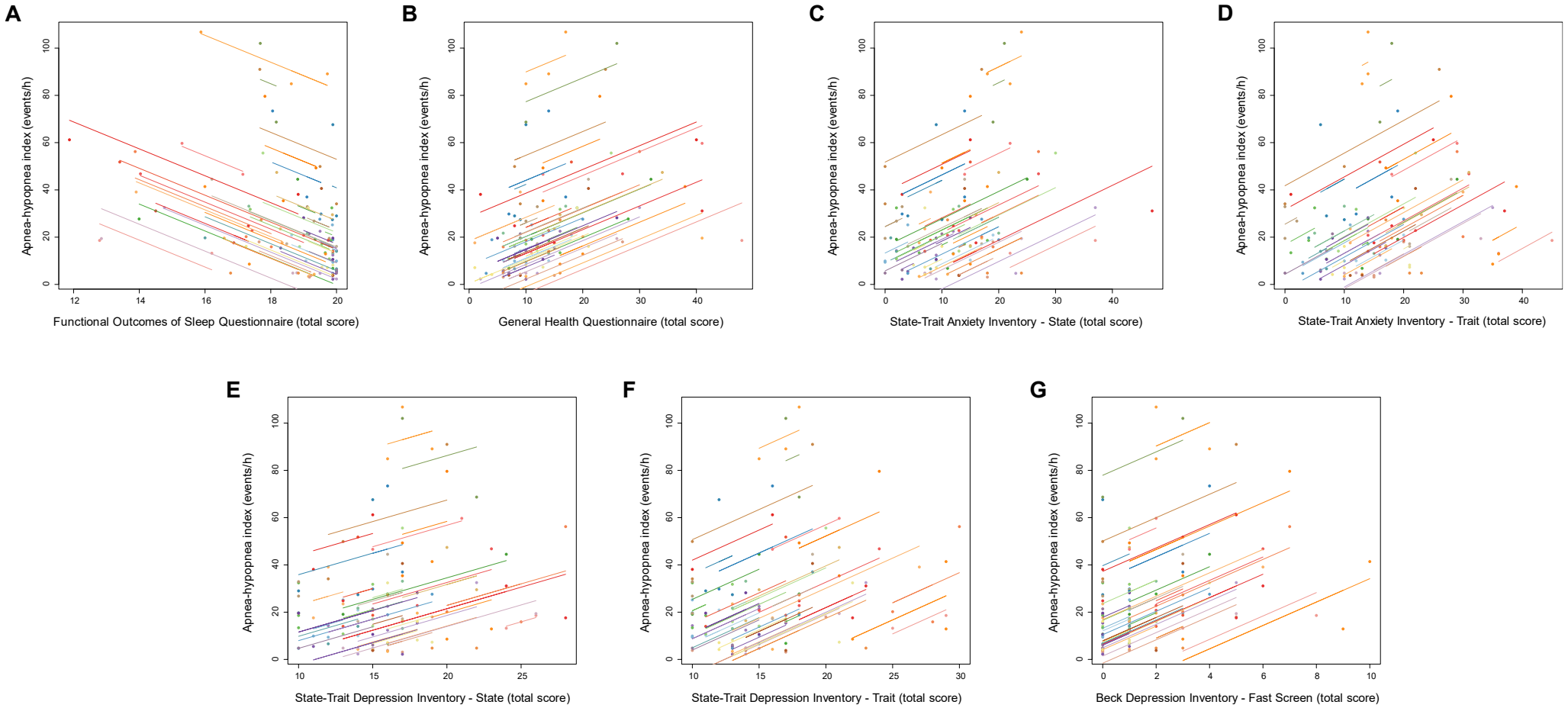
Supplementary Figure 8. Association of changes in daily functioning and psychiatric symptoms over time with changes in obstructive sleep apnea severity.[a]



[a]Each dot represents one of three separate observations (baseline, 8 weeks and 6 months after intervention) of psychiatric symptoms — as measured by the Functional Outcomes of Sleep Questionnaire (A), General Health Questionnaire (B), State-Trait Anxiety Inventory (C, D), State-Trait Depression Inventory (E,F) and Beck Depression Inventory – Fast Screen (G) — and obstructive sleep apnea severity — as measured by the apnea-hypopnea index — for a participant. Observations from the same participant are given the same color, with corresponding lines to show the repeated measures correlation fit for each participant. The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

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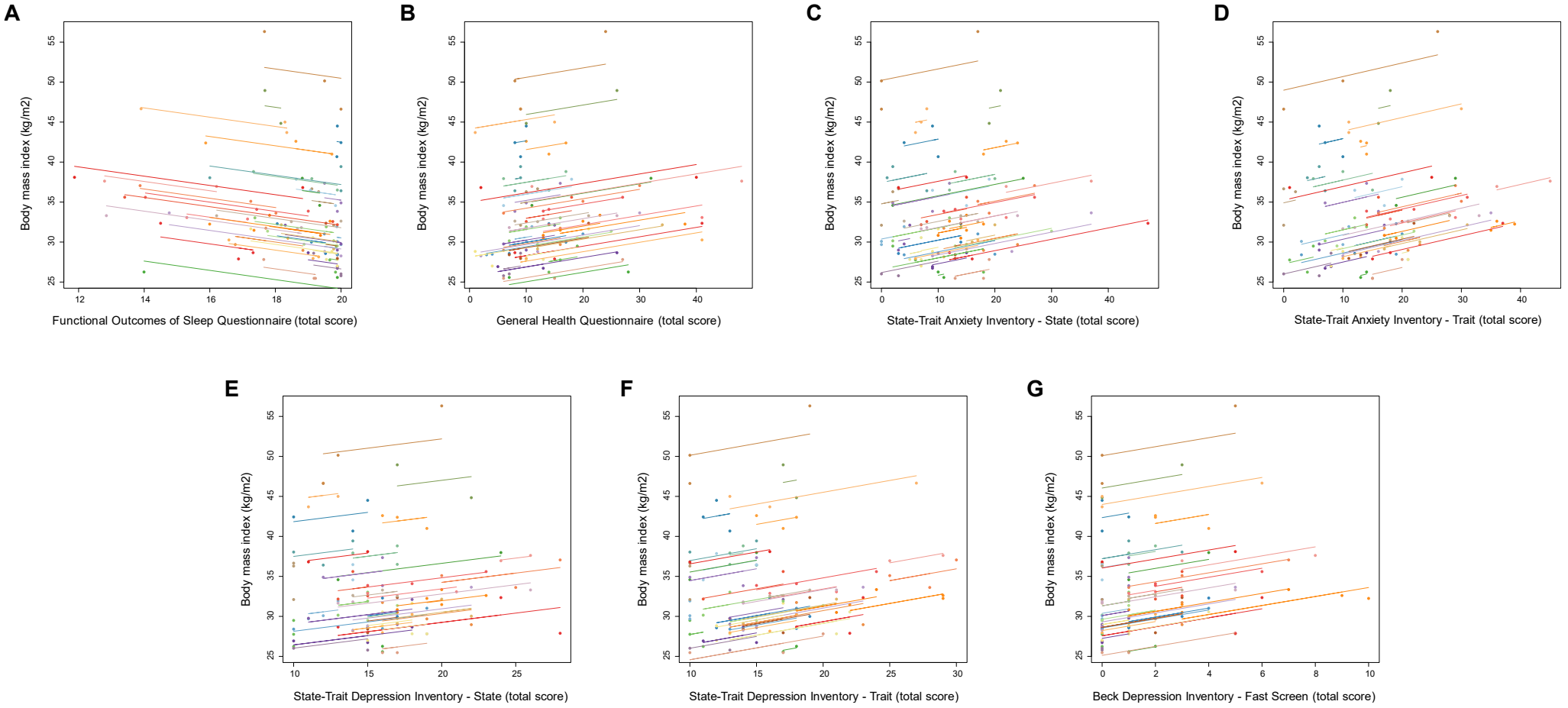
Supplementary Figure 9. Association of changes in daily functioning and psychiatric symptoms over time with changes in body mass index.[a]



[a]Each dot represents one of three separate observations (baseline, 8 weeks and 6 months after intervention) of psychiatric symptoms — as measured by the Functional Outcomes of Sleep Questionnaire (A), General Health Questionnaire (B), State-Trait Anxiety Inventory (C, D), State-Trait Depression Inventory (E,F) and Beck Depression Inventory – Fast Screen (G) — and body mass index for a participant. Observations from the same participant are given the same color, with corresponding lines to show the repeated measures correlation fit for each participant. The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12]

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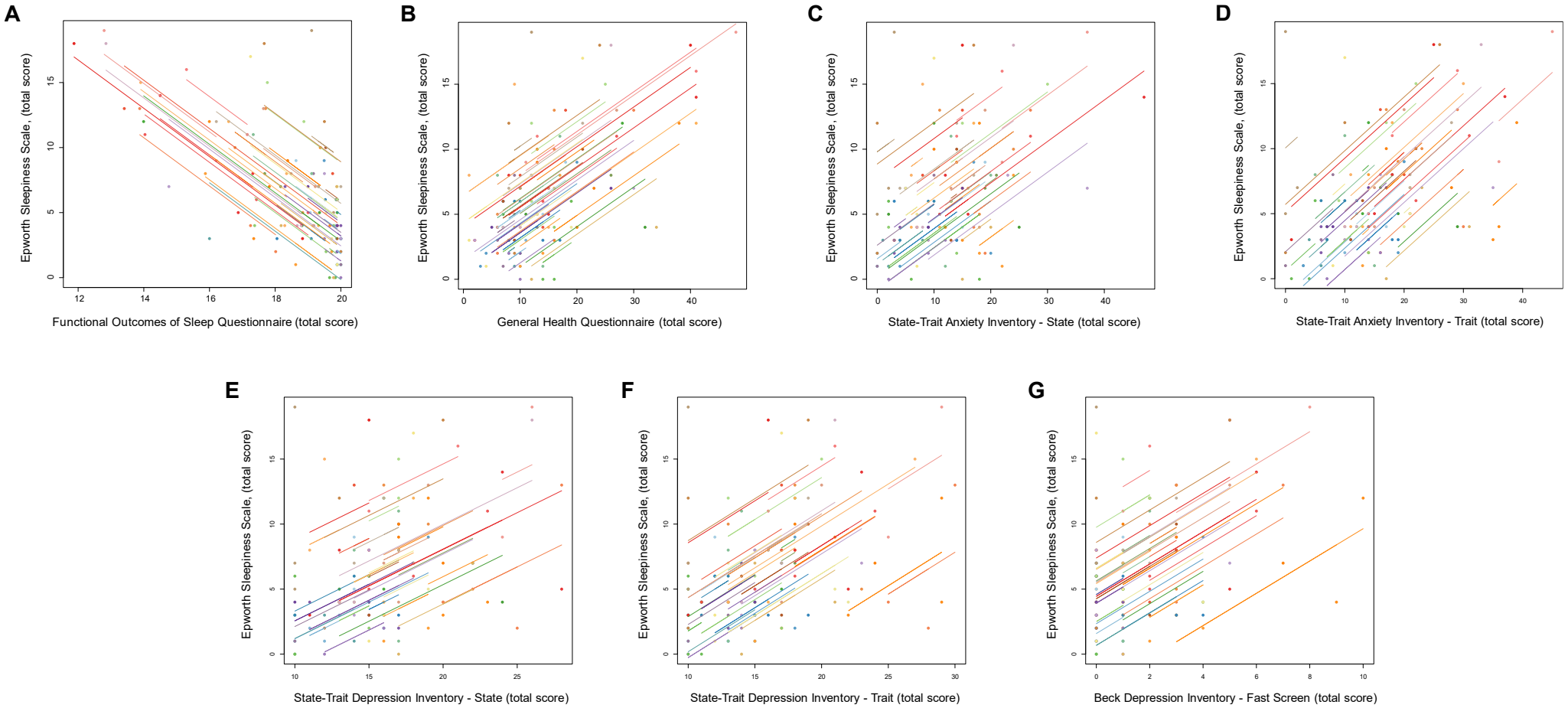
Supplementary Figure 10. Association of changes in daily functioning and psychiatric symptoms over time with changes in excessive daytime sleepiness.[a]



[a]Each dot represents one of three separate observations (baseline, 8 weeks and 6 months after intervention) of psychiatric symptoms — as measured by the Functional Outcomes of Sleep Questionnaire (A), General Health Questionnaire (B), State-Trait Anxiety Inventory (C, D), State-Trait Depression Inventory (E,F) and Beck Depression Inventory – Fast Screen (G) — and excessive daytime sleepiness — as measured by the Epworth Sleepiness Scale — for a participant. Observations from the same participant are given the same color, with corresponding lines to show the repeated measures correlation fit for each participant. The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12] The Epworth Sleepiness Scale evaluates excessive daytime sleepiness (range, 0-24; higher scores indicate more daytime sleepiness; score >10 indicates presence of hypersomnolence).[13]

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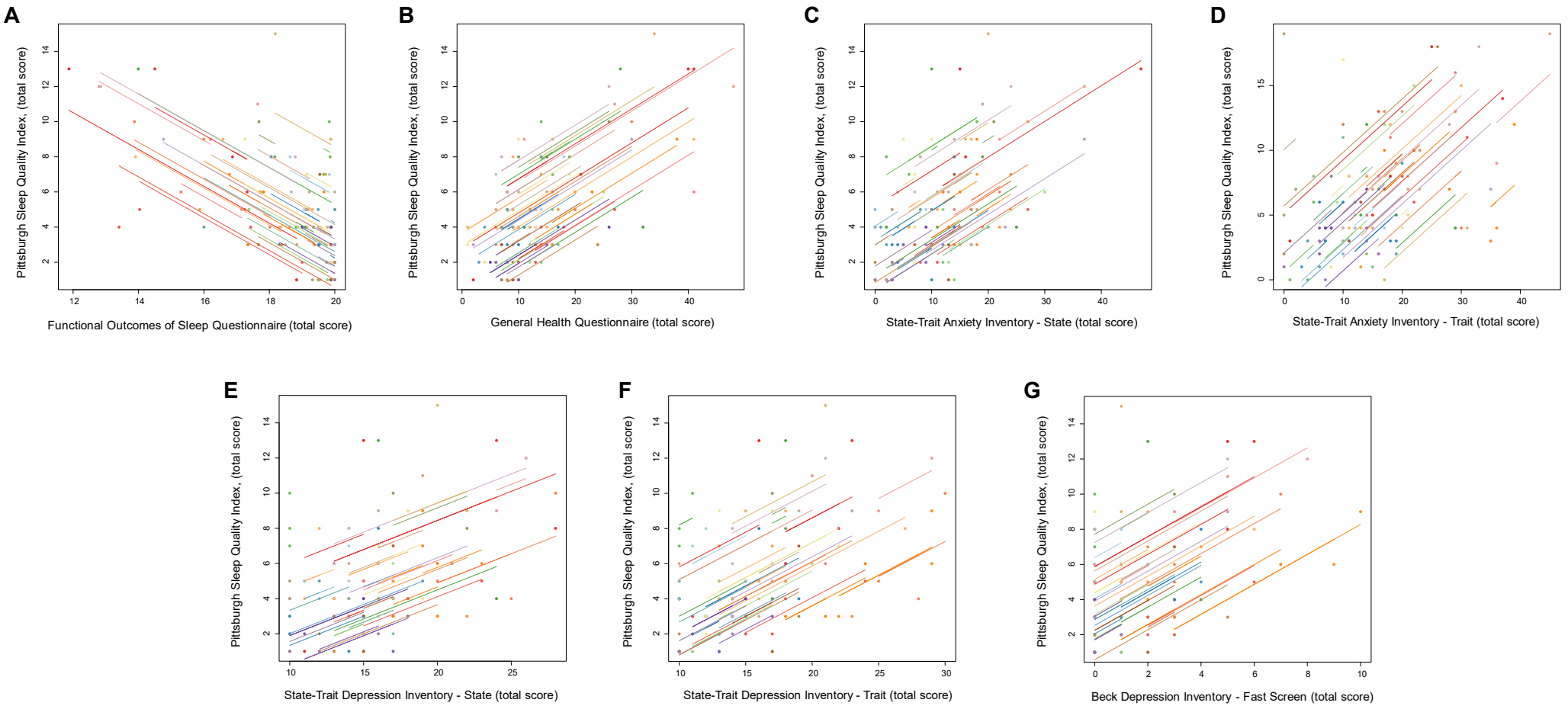
Supplementary Figure 11. Association of changes in daily functioning and psychiatric symptoms over time with changes in subjective sleep quality.[a]



[a]Each dot represents one of three separate observations (baseline, 8 weeks and 6 months after intervention) of psychiatric symptoms — as measured by the Functional Outcomes of Sleep Questionnaire (A), General Health Questionnaire (B), State-Trait Anxiety Inventory (C, D), State-Trait Depression Inventory (E,F) and Beck Depression Inventory – Fast Screen (G) — and subjective sleep quality — as measured by the Pittsburgh Sleep Quality Index — for a participant. Observations from the same participant are given the same color, with corresponding lines to show the repeated measures correlation fit for each participant. The Functional Outcomes of Sleep Questionnaire assess the impact of excessive daytime sleepiness on daily functioning (range, 5-20; higher scores indicate greater functioning; score <18 reflects negative effect of sleepiness on daily functioning).[1-4] The General Health Questionnaire evaluates psychological distress (range, 0-84; higher scores indicate greater psychological distress; score >23 indicates presence of psychological distress).[5,6] The State-Trait Anxiety Inventory measures state anxiety and trait anxiety (range, 0-60; higher scores indicate greater anxiety; score ≥21 and ≥24 suggests clinical levels of state and trait anxiety, respectively).[7-9] The State-Trait Depression Inventory measures state depression and trait depression (range, 10-40; higher scores indicate greater depression; score ≥20 and ≥21 suggests clinical levels of state and trait depression, respectively).[10] The Beck Depression Inventory-Fast Screen evaluates depression (range, 0-21; higher scores indicate greater depression; score ≥4 suggests presence of depression).[11,12] The Pittsburgh Sleep Quality Index assess subjective sleep quality (range, 0-21; higher scores indicate worse sleep quality; score >5 suggests poor sleep quality).[14]

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