

Medicine & Science IN Sports & Exercise

The Official Journal of the American College of Sports Medicine
www.acsm-msse.org

. . . Published ahead of Print

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Accepted for Publication: 5 February 2018

Medicine & Science in Sports & Exercise® **Published ahead of Print** contains articles in unedited manuscript form that have been peer reviewed and accepted for publication. This manuscript will undergo copyediting, page composition, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered that could affect the content.

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This research was supported by the Sao Paulo Research Foundation (FAPESP, grants 2012/16700-9 and 2012/16134-3) and by Conselho Nacional de Pesquisa (CNPq, grants 485065/2012-6). The authors declare that they have no competing interests. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The authors declare that they have no conflicts of interest to disclose.

ABSTRACT

Introduction: Obese adults with asthma have an increased number of comorbidities and reduced daily life physical activity (DLPA), which may worsen asthma symptoms. Exercise is recommended to improve asthma outcomes; however, the benefits of exercise for psychosocial comorbidities and physical activity levels in obese adults with asthma have been poorly investigated. **Objective:** To assess the effects of exercise on DLPA, asthma symptoms and psychosocial comorbidities in obese adults with asthma. **Methods:** Fifty-five grade II obese adults with asthma were randomly assigned to either a weight-loss program+exercise program (WL+E group, n=28) or a weight-loss program+sham (WL+S group, n=27). The WL+E group incorporated aerobic and resistance muscle training into the weight-loss program (nutrition and psychological therapies), while the WL+S group performed breathing and stretching exercises. DLPA, asthma symptoms, sleep quality and anxiety and depression symptoms were quantified before and after treatment. **Results:** After 3 months, the WL+E group presented a significant increase in daily step counts ($3,068 \pm 2,325$ vs. $729 \pm 1,118$ steps/day) and the number of asthma-symptom-free days (14.5 ± 9.6 vs. 8.6 ± 11.4 d/mo) compared with the WL+S group. The proportion of participants with improvements in depression symptoms (76.4 vs. 16.6 %) and a lower risk of developing obstructive sleep apnea (56.5 vs. 16.3%) was greater in the WL+E group than in the WL+S group ($P < 0.05$). Significant improvements in sleep efficiency (6.6 ± 5.1 vs. $1.3 \pm 4.7\%$) and latency (-3.7 ± 5.9 vs. 0.2 ± 5.6 min) were also observed in the WL+E group. **Conclusions:** Our results strongly suggest that exercise training plus a weight loss program improves DLPA, sleep efficiency and depression and asthma symptoms in obese adults with asthma.

Key words: obesity, sleep, weight-loss, depression, physical training

INTRODUCTION

There is substantial evidence that obesity and asthma are associated diseases. Obesity-related asthma is considered a distinct asthma phenotype characterized by decreased lung volume, more pronounced symptoms, increased work of breathing, a less favorable response to controller medication and increased airway inflammation (1-3). Several mechanisms have been suggested to explain the association between asthma and obesity, including low-grade systemic inflammation, comorbidities, reduced lung function and lifestyle factors (1). Comorbidities and physical inactivity seem especially important in the management of asthma because they have been shown to contribute to worse asthma control and consequent increases in symptoms, exacerbation risk and airway inflammation (1, 4, 5). Additionally, comorbidities increase the health care costs associated with the treatment of severe asthma (4).

Asthma is a heterogeneous disease (1), and some comorbidities related to obesity, such as sleep disturbances, sedentary lifestyle and anxiety and depression symptoms, may be more common in a specific obesity-asthma phenotype. Several studies have demonstrated a high prevalence of anxiety and depression symptoms in adults with asthma (3) and obesity (6). There is also evidence suggesting that adults with asthma who suffer from psychological distress present more sleep disturbances and are less physically active, which contributes to weight gain and reduced asthma control (7). Sleep-disordered breathing has also been suggested as a possible mechanism underlying the obesity-asthma association (8). The increased prevalence of obstructive sleep apnea (OSA) in obese adults with asthma can be explained by the fact that both asthma and obesity can reduce the upper airway caliber (8). In addition, obesity may worsen asthma symptoms through its effects on other disease processes, such as gastroesophageal reflux, and on

a variety of inflammatory cytokines, mediators and hormones (9). Therefore, greater importance should be placed on tailoring management plans to focus on the comorbidities of obese adults with asthma, specifically those related to psychosocial symptoms, sleep disturbances and a sedentary lifestyle.

Physical inactivity might also explain the association between asthma and obesity. For instance, obese adults with asthma have an increased likelihood of having reduced physical activity (PA) (5). In addition, there is evidence suggesting that lower PA levels predispose adults with asthma to long-term deconditioning, thereby sustaining the vicious cycle of inactivity, obesity and worse asthma control (9). As a result, participants who have difficulty performing daily activities feel irritated or frustrated and report limitations in their social life and deteriorations in psychological well-being and sleep quality, including symptoms such as delayed sleep onset, insomnia and disrupted sleep (7, 10). Based on these findings, progressive changes toward an active lifestyle with a daily balance of sleep, sedentary behaviors and physical activities is recommended for optimal health benefits (11).

Lifestyle interventions, including dietary changes, PA and/or behavioral therapy, are the most appropriate first line of defense for all obese people with asthma (5). Increased PA plays a key role in weight loss and has been associated with a decrease in the prevalence of sleep-disordered breathing disturbances (12). In addition, evidence indicates that exercise is recommended to improve asthma outcomes, including anxiety and depression symptoms, in adults with asthma (1, 13). However, to the best of our knowledge, no previous study has reported the effect of exercise training on daily life physical activity (DLPA), psychosocial comorbidities and sleep quality in

obese adults with asthma. Therefore, we hypothesized that exercise training would improve PA and reduce comorbidities in obese adults with asthma, leading to improvements in asthma symptoms.

METHODS

Participants

Participants with moderate or severe persistent asthma (1) who were between 30 and 60 years old and had grade II obesity ($\text{BMI} \geq 35$ and $< 40 \text{ kg/m}^2$) were recruited from a university hospital that provides specialized treatment for adults with asthma. The participants has been receiving optimal medical treatment for at least 6 months, were clinically stable (i.e., no crises or changes in medication for ≥ 30 days) and performed < 60 minutes of structured or planned PA per week (14). Individuals with cardiovascular, musculoskeletal or other chronic pulmonary diseases or uncontrolled hypertension or diabetes; those who had experienced a $> 5\%$ change in body weight or who had taken anti-obesity drugs within the last 6 months; those who had undergone bariatric surgery; those who had reported regular use of oral corticosteroids; were smokers or ex-smokers (≥ 10 pack years); or were pregnant were excluded from the study.

Experimental design

The study was conducted between two regular medical visits to avoid changes in the asthma pharmacotherapy. The participants were randomly assigned (via computer-generated randomization) using concealed allocation into 2 groups: the weight-loss program with exercise program (WL+E) group or the weight-loss program with a sham exercise treatment (WL+S) group. Both groups completed a 6-h education program after the baseline evaluations. Before

and after the interventions, DLPA, clinical asthma symptoms, levels of anxiety and depression symptoms and quality of sleep were blindly assessed. The study was approved by the Hospital Research Ethics Committee (07137512.9.0000.0068) and registered with ClinicalTrials.gov as NCT02188940. Written informed consent was provided by all the participants. This study is linked with previously published studies where the methods have been reported in detail (15, 16).

Treatment groups

Both groups completed an educational program (4 classes twice a week, each lasting 90 minutes) that included information regarding asthma pathophysiology, medication and peak flow meter skills, self-monitoring techniques, environmental control, avoidance strategies (1, 13), and the current international PA recommendations and the benefits thereof (14). The WL+S group was assigned to the weight-loss program which was provided by a nutritionist and psychologist in 12 individual hypocaloric diet counselling sessions and was supported by behavioral techniques based on the transtheoretical model (17) combined with sham exercises (stretching and breathing) (2 sessions/week for 3 months). The breathing program was based on yoga's pranayama breathing exercises without intensity progression, which have previously been shown to have a sham effect (13). The stretching program consisted of two sets of exercises for each of the following major muscle groups: trapezius, pectoralis, gluteus, hamstrings, quadriceps femoris, paraspinal, latissimus dorsi and pubis adductors. Each exercise lasted 10 seconds, with no progression.

The WL+E group incorporated an exercise program into the same weight-loss intervention used for the WL+S group. The exercise program included 2 sessions of supervised aerobic and

resistance exercises (2 sessions/week for 3 months) plus PA recommendations. The exercise sessions were conducted in an outpatient pulmonary rehabilitation clinic at a university hospital, and all sessions were supervised by a physiotherapist. Aerobic training was performed on a treadmill interspersed with either bike or elliptical machine workouts to avoid overloading the participant's joints. The exercise intensity was based on 50-75% of peak oxygen consumption (VO_2) (14) and was monitored using the target heart rate (THR). Participants received an accelerometer (*Power Walker-610 YAMAX, Japan*) to encourage walking aiming to reach the international PA recommendations. The accelerometer was given in the 1st, 6th and 12th weeks. During these weeks, participants also received advises to walk at least twice a week for 30 minutes per day and to complete a daily PA diary. Resistance training targeted the following major muscle groups: pectoral, deltoid, quadriceps and hamstrings. The training consisted of 2 sets of 10 repetitions for each exercise (50%-70% of the one-maximal resistance test, 1-RM) (18) and progressed in number and load. Salbutamol (200 μg) was used before exercise if the peak expiratory flow (PEF) was <70% of the participant's best value. PEF, blood pressure and asthma symptoms were monitored before and after every exercise session.

Outcomes

DLPA was objectively quantified using a movement sensor (ActiGraph GT3X, ActiGraph, Pensacola, FL, USA). All units were initialized via a computer interface to collect data in 60-s epochs on the 3 axes using specific software (ActiLife 6.9.5 Firmware version). Each participant was instructed to wear the movement sensor for 7 consecutive days one week before and after the interventions on the hip (non-dominant side) using an elastic belt (19). Data are presented as the average number of steps per day (steps/day), the time spent performing moderate and

vigorous activities (MVPA, minutes/day), light-intensity PA and sedentary time. The cardiopulmonary exercise test (CPET) was used to assess physical fitness; the test took place on an electrical cycle ergometer using a ramp-symptom-limited protocol consisting of 2 min of rest, 2 min of warm-up and incremental work periods (10-20 W/min) (16). The predicted values for CPET set from the Brazilian population were used (20). The peripheral muscle strength was assessed via a one-repetition-maximum resistance test (1-RM) as described previously (15). The participants' heights and weights (Filizola®, Brazil) were measured using a standardized protocol (21) and the BMI was calculated by dividing each participant's weight in kilograms by their height in meters squared (kg/m^2) (22).

Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) (23), which consists of 14 items divided into 2 subscales (7 for anxiety and 7 for depression). Each item was scored from 0 to 3, with a maximum score of 21 points for each subscale. The HADS uses a cut-off score to classify participants as having or not having symptoms of anxiety or depression (score > 9 each). The HADS results does not have a score to detect clinically meaningful change (24).

Clinical asthma symptoms were quantified using a daily diary that included questions regarding episodes and symptoms (coughing, wheezing, shortness of breath, nocturnal awakenings and the use of relief medication), as previously reported (13) and as recommended by the GINA guidelines (1). A day was considered "asthma-symptom-free" when the participant did not report any symptoms, and the number of asthma-symptom-free days was quantified one month before

and after the interventions and monthly during the interventions. The number of asthma-symptom-free days was expressed as the sum during a 30-day period.

The risk of OSA was estimated using the Berlin questionnaire (25). The questionnaire has been translated into and validated for Portuguese and consists of 3 categories: snoring, daytime somnolence and history of hypertension and obesity. The Berlin Questionnaire includes only a cut-off score for estimating the risk of OSA in terms of the number of positive categories and does not have a score to detect clinically meaningful change. Each category was classified as positive if the score was ≥ 2 points, and participants were considered to have a high risk for developing OSA if they had at least 2 positive categories. Sleep quality was evaluated using an ActiSleep monitor (Pensacola, FL, USA), which the participants wore on their non-dominant wrist for 7 consecutive nights before and after interventions. The outcomes derived from the monitor were sleep latency (the amount of time needed to fall asleep) and sleep efficiency (number of sleep minutes divided by the total number of minutes the participant was in bed). The device is a valid and reliable method for detecting sleep/wake diurnal patterns compared with polysomnography (26).

Statistical analysis

A sample size of 42 was estimated as the number needed to provide 90% power to detect an increase of $2,491 \pm 2,369$ steps after intervention with alpha level of 0.05 (27). Assuming up to a 20% loss during follow-up, the final sample size was set at 51 participants. An intention-to-treat analysis was used in all analyses. Normality was evaluated using the Kolmogorov-Smirnov test. Treatment-by-time interactions were analyzed via a two-way repeated-measures analysis of

variance (ANOVA) followed by Holm-Sidak corrections, and categorical outcomes were analyzed via the χ^2 test. Linear correlations were used to test the associations among changes in PA level, aerobic fitness, weight loss, depression symptoms and sleep efficiency. Multiple linear regression was used having physical fitness and DLPA as independent variables and psychosocial outcomes, asthma symptoms and sleep disturbance as dependent variables. P values <0.05 obtained using specific software (Sigmastat 3.5; Systat Software, Inc.; Chicago, IL) were considered statistically significant. The effect size (ES) was calculated using the Cohen method and was classified as small (0.21-0.49), medium (0.50-0.79), or large (> 0.80), as previously described (28).

RESULTS

Baseline characteristics

Fifty-five participants were randomly assigned to the two groups, and 4 participants (two in each group) were lost during follow-up (Figure 1). As a result, 51 participants were included in the analysis (25 in the WL+S group and 26 in the WL+E group). Of these, two participants (one in each group) did not complete all the treatment sessions (due to difficulties related to work) and were re-assessed in an intention-to-treat analysis after 3 months in the group into which they were originally randomized. Before the study, both groups had similar baseline characteristics in terms of anthropometric data, asthma medication, lung function and PA levels (Table 1).

Changes in DLPA following the intervention

At baseline, 17,4% of the participants in the WL+S group and 16.6% in the WL+E group met the international PA recommendation of 10,000 steps per day before the intervention. After 3

months of intervention, the daily step counts in the WL+E group increased ($P<0.001$), whereas they did not change significantly in the WL+S group (Figure 2A). In addition, 4.3 % of the participants in the WL+S group vs. 41.7% in the WL+E group improved the daily step counts and achieved the PA recommendation; $P=0.019$). Before the intervention, the participants in both groups spent an average of 25.6 ± 15.2 minutes/day performing MVPA. After 3 months, the participants in the WL+E group significantly increased the amount of time spent performing MVPA compared with the WL+S group (18.2 ± 17.9 vs 7.9 ± 13.8 minutes/day, respectively; $P<0.001$; Figure 2B). In addition, 65.2% of the participants in the WL+S group and 91.6% in the WL+E group met the guideline of 150 mins/week of MVPA (14) after the interventions. Neither group showed significant changes in sedentary time after 3 months (Figure 2C), but the participants in the WL+E group showed an increase in light-intensity PA compared with the WL+S group (Figure 2D). Some participants missed supervised appointments during the study, but all missing sessions were re-scheduled. The rates of adherence to the supervised and unsupervised exercise sessions were 89% and 57% at week 6, respectively, and 96% and 65% at week 12, respectively.

After intervention, participants in the WL+E group presented an average improvement of 40% in the muscle strength of the upper and lower limbs and a greater reduction in BMI than the participants in the WL+S group (respectively, -2.6 ± 1.3 vs. -1.0 ± 1.1 kg/m²) as previously described (16). In addition, 11 participants were reclassified to a lower obesity class (from the class II to class I obesity), 2 in the WL+S and 9 in the WL+E group.

Comorbidity and asthma symptom changes

Anxiety and depression symptoms: At baseline, 68.6% of the participants (score 10.0 ± 4.7) presented anxiety symptoms, and 58.8% (score 9.6 ± 4.7) presented depression symptoms, with no difference between the groups. After the intervention, there was no significant difference in the proportion of participants with improved anxiety symptoms between the groups (47.4% of the participants (score change -4.0 ± 4.6) in the WL+E group vs. 33.3% of the participants (score change -1.0 ± 3.7) in the WL+S group; $P=0.63$). However, there was a significant increase in the proportion of participants without depression symptoms in the WL+E group (76.4% of the participants (score change -4.6 ± 4.2)) compared with the WL+S group (16.6% of the participants (score change -0.4 ± 3.3)); $P<0.01$.

Asthma symptoms: The participants in the WL+S group showed a slight increase in the number of asthma-symptom-free days throughout the intervention (8.6 ± 11.4 d/mo), while the WL+E group had a greater increase in the number of asthma-symptom-free days (14.5 ± 9.6 d/mo); $P<0.05$. The interaction between time and group was significantly in favor of the WL+E group ($P<0.05$; Figure 3).

Quality of sleep: It was observed that 86.3% of the study participants (score 5.6 ± 2.4) presented a high risk of developing OSA at baseline (Figure 4A). After the intervention, the participants in the WL+E group presented a significant reduction in the risk of OSA compared with the WL+S group (56.5% of the participants (score change -2.1 ± 1.7) vs. 16.3% of the participants (score change -1.3 ± 1.2)), respectively; $P=0.03$; Figure 4A). A higher proportion of participants with an improvement in the snoring category of the Berlin questionnaire was observed in the WL+E

group compared with the WL+S group (52.9% of the participants (score change -1.0 ± 1.3) vs. 14.3% of the participants (score change -0.5 ± 1.2)), respectively; $P=0.03$; Figure 4C). Participants in both groups showed improvements in daytime somnolence, with no difference between groups ($P>0.05$, Figure 4C). There was no change in the history of hypertension and obesity in either group. The sleep actigraphy evaluation showed an improvement in sleep efficiency in the WL+E group (6.6 ± 5.1 vs. 1.3 ± 4.7 %), $P < 0.001$; Figure 4D) and a reduction in sleep latency (-3.7 ± 5.9 vs. 0.2 ± 5.6 minute; $P = 0.002$; Figure 4B) compared with the WL+S group. In addition, only the participants group who exercised achieved a sleep efficiency of 85%, which is considered the threshold for normal, healthy sleep.

Intervention effect size and correlation between comorbidity variables

A linear association was observed between changes in the improvement of physical fitness and the number of daily steps ($r=0.43$, $P<0.01$; Figure 5A) and the weight-loss percentage ($r=0.33$, $P=0.02$, Figure 5B). Most of the participants in the WL+E group improved by ≥ 2 mlO₂/kg/minutes and 2,000 daily steps (Figure 5A, 1st quadrant). Regardless of the treatment group, the change in depression symptoms was linearly associated with increases in both DLPA ($r=0.52$, $P<0.01$; Figure 5C) and sleep efficiency ($r=0.50$, $P<0.001$; Figure 5D). The effect size for all the analyzed variables showed that exercise training was superior to weight-loss intervention alone for improving DLPA and other comorbidities related to asthma and obesity (Figure 5E).

The multiple linear regression analysis indicate that depression symptoms was independently associated with improvements in the DPLA and in the physical fitness (VO₂) ($r=0.62$, $P<0.01$). In addition, the reduction in the risk of OSA was only associated with physical fitness ($r=0.39$,

P<0.01), while the number of asthma-symptom-free days and the improvement in sleep efficiency were only associated with the change in DLPA ($r=0.41$, $P<0.01$ and $r=0.39$, $P=0.01$; respectively).

DISCUSSION

Our data demonstrate that exercise training in association with a weight-loss lifestyle intervention improved DLPA and sleep efficiency and reduced depression symptoms and the risk of developing OSA in obese adults with asthma. In addition, we observed that these improvements in the participants who exercised were accompanied by ameliorations of self-reported asthma symptoms. These results indicate the importance to increase exercise training as a non-pharmacological therapy to reduce asthma-related comorbid conditions in obese adults with asthma.

In the present study, the participants who incorporated exercises into a weight-loss program not only presented an increase in aerobic fitness but also became physically active according to international recommendations for PA (> 10,000 steps/day) (29). Contradictory findings have been reported in the literature regarding the impact that asthma may have on PA levels. Some studies suggest that adults with asthma are equally active and in some cases, more active than those without asthma (30, 31). However, only one study used an objective monitor to evaluate levels of PA, and the authors observed that PA was significantly lower in adults with asthma and that this reduced PA was associated with worse asthma control (30). Many adults with asthma avoid exercise because they are afraid that it will exacerbate their asthma symptoms. The absence of regular physical exercise and the adoption of a sedentary lifestyle maintains a vicious

cycle of asthma-physical inactivity that leads to a loss of fitness and lowers the thresholds for exercise-induced symptoms (9). Interestingly, a lack of PA can also contribute to obesity, which is highly associated with worse asthma outcomes (10). Our findings are particularly relevant because they show that an exercise program, including supervised exercise coupled with PA recommendations, encouraged obese adults with asthma to adopt a healthier lifestyle, which increased their PA level and led to greater weight loss. These changes seemed to disrupt the cycle of asthma-inactivity-obesity and consequently resulted in improvements in sleep quality and depression and asthma symptoms.

Another highlight of the present investigation was that the participants who exercised showed improvements in MVPA (meeting the guideline of 150 mins/week) and light-intensity PA after 3 months compared with the participants who did not exercise. However, no significant change in sedentary time was observed in either group. According to a recent systematic review, interventions that target sedentary behavior (SB) were effective for reducing the time spent engaging in SB, whereas interventions that aimed to improve PA or in conjunction with time spent in SB did not change SB (32). Therefore, we hypothesized that the participants in this study did not reduce their sedentary time because the intervention was not based on a behavioral change. However, the small reduction in sedentary time observed in the participants who exercised seemed to result in an increase in light-intensity PA, which can have health benefits (33). Since the mechanisms underlying the health benefits of increased MVPA may be distinct from those associated with reducing SB, further investigations targeting behavioral intervention are warranted for this population.

Obese adults with asthma have a reduced response to asthma therapy, and it seems reasonable to incorporate non-pharmacological strategies into their medical treatment. There is evidence that weight reduction induced by bariatric surgery (34) or dietary interventions (35) leads to substantial improvements in asthma outcomes, such as airway hyperresponsiveness, lung function and systemic inflammation. However, very few studies have included exercise training as a non-pharmacological intervention for obese adults with asthma (16, 35). Scott and coworkers showed that caloric restriction alone or combined with exercise induced modest weight reductions and improved asthma control (35). In contrast, Freitas and coworkers demonstrated that the integration of exercise training and weight-loss lifestyle interventions plays an important role in improving the clinical control of asthma, health-related quality of life, lung function, airway inflammation markers and vitamin D levels (16). However, the results of the current study show for the first time that exercise training also has a positive effect on DLPA in obese adults with asthma, suggesting that the combination of physical conditioning and a weight-loss program can encourage obese adults with asthma to become physically active. These findings are particularly relevant because a sedentary lifestyle and the loss of fitness may play a key role in the development of respiratory symptoms during daily activities in these participants.

We observed a significant reduction in depression symptoms in the obese adults with asthma who exercised. Our data are supported by previous findings demonstrating that exercise may have antidepressant effects in participants with other chronic diseases (36). Depression is a common comorbidity associated with asthma and obesity (6), and it contributes to physical inactivity and loss of fitness as people with symptoms of depression often report physical fatigue and a lack of motivation. Depression symptoms seem to be multifactorial. Exercise, as part of a

healthy lifestyle, can help reduce depression symptoms by increasing physical well-being and providing positive feedback from the environment and social contact (9). The association between the improvement in daily PA and the reduction in depression symptoms observed in our study reinforces the hypothesis that exercise can modify symptoms of depression. Depression may contribute to worse asthma control in obese adults (6). Our results strongly suggest that engaging in routine PA can have an important impact on well-being by reducing psychosocial comorbidities, thus improving the management of self-reported asthma symptoms in adults with obesity.

Our data also demonstrated an improvement in sleep quality in the obese adults with asthma who exercised. This improvement was observed as a reduction in the risk of developing OSA, which appeared to be result from improvements in snoring frequency rather than in daytime sleepiness. Obese adults with uncontrolled asthma frequently present nocturnal arousal, sleep fragmentation and sleep loss that worsen upper airway collapsibility, leading to snoring episodes (37). Interestingly, our results showed that at the end of the intervention, the obese adults with asthma who exercised achieved 85% sleep efficiency, which is considered indicative of good sleep quality (38). Therefore, improving the quality of nocturnal sleep may cause a decrease in the snoring frequency and consequently positively influence the risk of OSA and the management of asthma.

Regardless of the treatment group, changes in sleep efficiency were linearly associated with improvements in depression symptoms. Previous findings have shown that most participants with depression symptoms reported sleeping fewer than 6 hours (39). Improvements in sleep

quality have been associated with better asthma control (39). Therefore, it seems appropriate to carefully consider sleep problems in the management of asthma control, especially when psychosocial comorbidities are involved. Our results suggest that obese adults with asthma who exercise present a better association between changes in sleep quality and depression symptoms, reinforcing the importance of exercise training for this population.

Some limitations of the current study should be considered. In the present study, most of the participants were female. Although this might suggest a selection bias, the higher number of females in our study is in agreement with the obese asthmatic phenotype in North America (40) and in Brazil (41). In addition, we included only participants with moderate and severe asthma, which may appear to reduce the external validity of our findings. However, previous evidence suggests that participants with more severe disease benefit more from exercise intervention (13, 42). The age range (from 30 to 60 years old) selected as an inclusion criterion was based on 2 factors. First, the majority of the individuals with asthma who are treated at our hospital fall within this age range (43). Second, since we were evaluating comorbidities, we excluded those with fewer comorbidities (i.e., younger participants) and higher numbers of comorbidities (i.e., elderly participants). Another limitation was the assessment of sleep quality with actigraphy instead of polysomnography, the gold standard method. However, actigraphy has been described as a valid and reliable method for evaluating sleep quality (26). Finally, the duration of our intervention may seem short for inducing behavioral changes in the participants. Nonetheless, the time frame was long enough for the participants who exercised to improve their daily PA and comorbidities related to the asthma-obesity association.

In conclusion, the addition of exercise training to a weight-loss lifestyle intervention was able to decrease depression symptoms, self-reported asthma symptoms and the risk of developing OSA and improve sleep efficiency in obese adults with asthma. These improvements in participants who exercised were accompanied by increases in PA levels and sleep efficiency. These findings have important clinical implications since asthma comorbidities related to obesity may worsen asthma symptoms and could be reversed by the effects of exercise and moderate weight loss. The results of the present study are original and provide useful information for future research on the treatment of asthma in obese adults.

ACKNOWLEDGMENTS

The authors would like to acknowledge Sonia M L Trecco for nutritional support and Clarice Tanaka, PT, for administrative support. We would like to extend special thanks to the patients and their families, who made this study possible. This research was supported by the Sao Paulo Research Foundation (FAPESP, grants 2012/16700-9 and 2012/16134-3) and by Conselho Nacional de Pesquisa (CNPq, grants 485065/2012-6).

The authors declare that they have no competing interests. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

FOOTNOTES

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

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FIGURE LEGENDS

Figure 1. Flow of participants through the study (CONSORT diagram). WL+S= weight-loss program with sham treatment; WL+E= weight-loss program with aerobic and resistance training.

Figure 2. Daily life physical activity before and after intervention in the WL+S and WL+E groups. Daily step counts **(A)**, MVPA (moderate and vigorous physical activity) **(B)**, sedentary time **(C)** and light-intensity PA **(D)**. The data are presented as the mean (SD), two-way analysis of variance (ANOVA). WL+S= weight-loss program with sham treatment; WL+E= weight-loss program with exercise training; min/day=duration of the activity in minutes per day.

Figure 3. Number of days free of asthma symptoms evaluated monthly before, during and after the intervention. The data are presented as the mean $\pm$ SD. Time points are “0” (1 month before the intervention), 1, 2 and 3 (first, second and third month of the intervention) and “4” (1 month after the intervention). WL+S= weight-loss program with sham treatment; WL+E= weight-loss program with exercise training. * $P < 0.05$ compared with baseline; + $P < 0.05$ compared with baseline and with the WL+S group (two-way analysis of variance).

Figure 4. Percentage of participants with a high risk of developing obstructive sleep apnea syndrome (OSA) **(A)**, sleep latency **(B)**, percentage of participants with improvements on the Berlin questionnaire by category **(C)**, and sleep efficiency **(D)**. The data are presented as percent (%; graphs A-C), χ^2 test, or as medians (25th-75th; graphs B-D), two-way analysis of variance.

WL+S= weight-loss program with sham treatment; WL+E= weight-loss program with exercise training.

Figure 5. Linear correlations between changes in physical activity level and aerobic fitness **(A)**, physical activity level and weight loss **(B)**, physical activity level and depression symptoms **(C)**, and depression symptoms and sleep efficiency **(D)** during follow-up. Linear correlation was evaluated using Pearson test. Effect size comparison of all outcomes between groups **(E)**. Effect size: dashed lines separate low (0.21-0.49), medium (0.50-0.79) and large (> 0.80) effect sizes. WL+S= weight-loss program with sham treatment; WL+E= weight-loss program with exercise training; MVPA= moderate and vigorous physical activity.

Figure 1

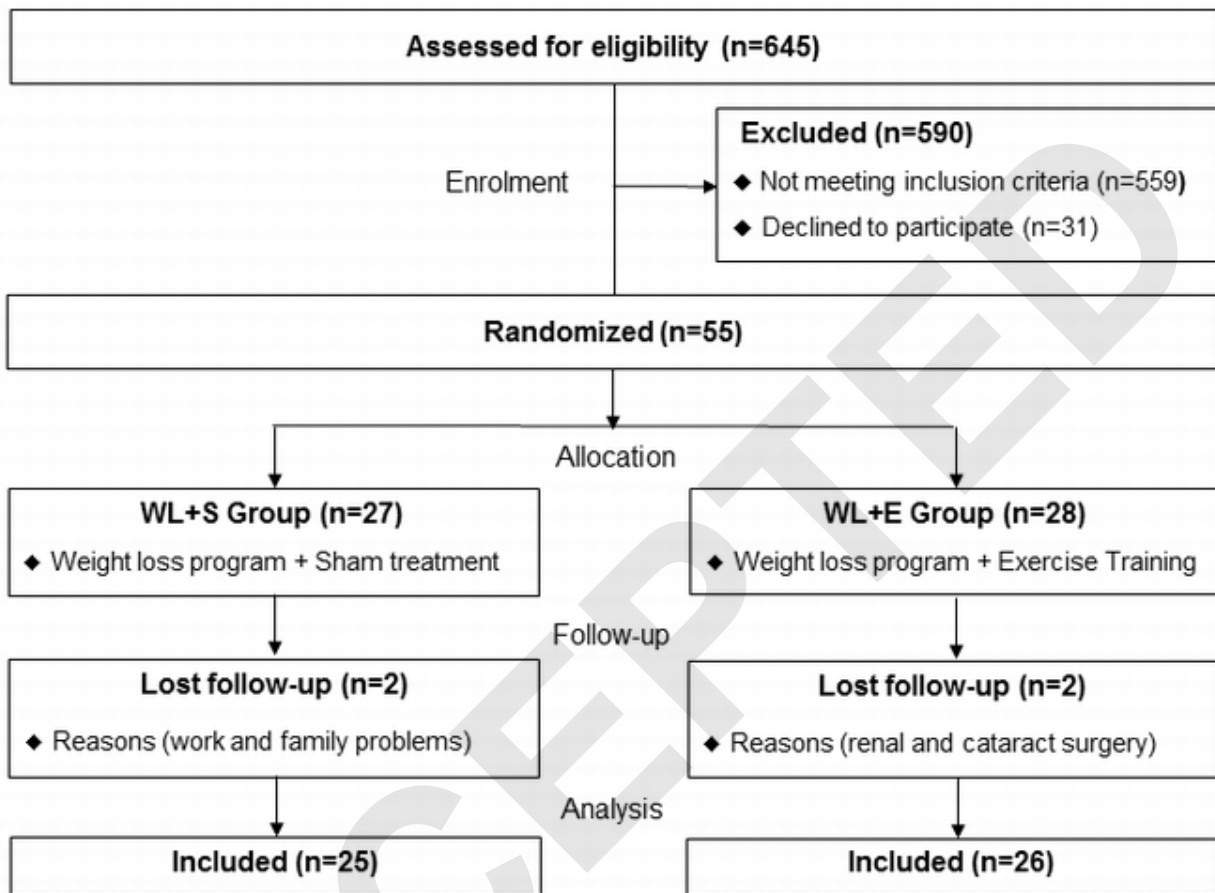


Figure 2

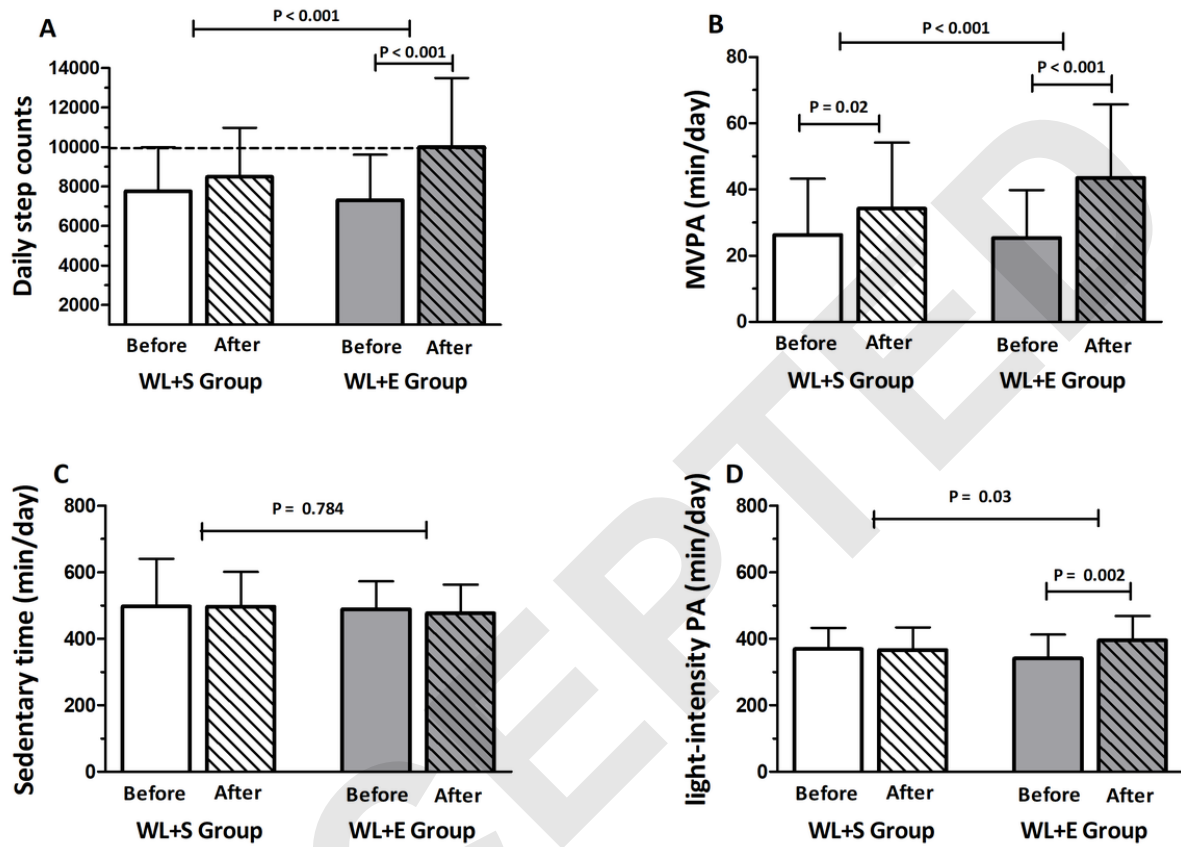


Figure 3

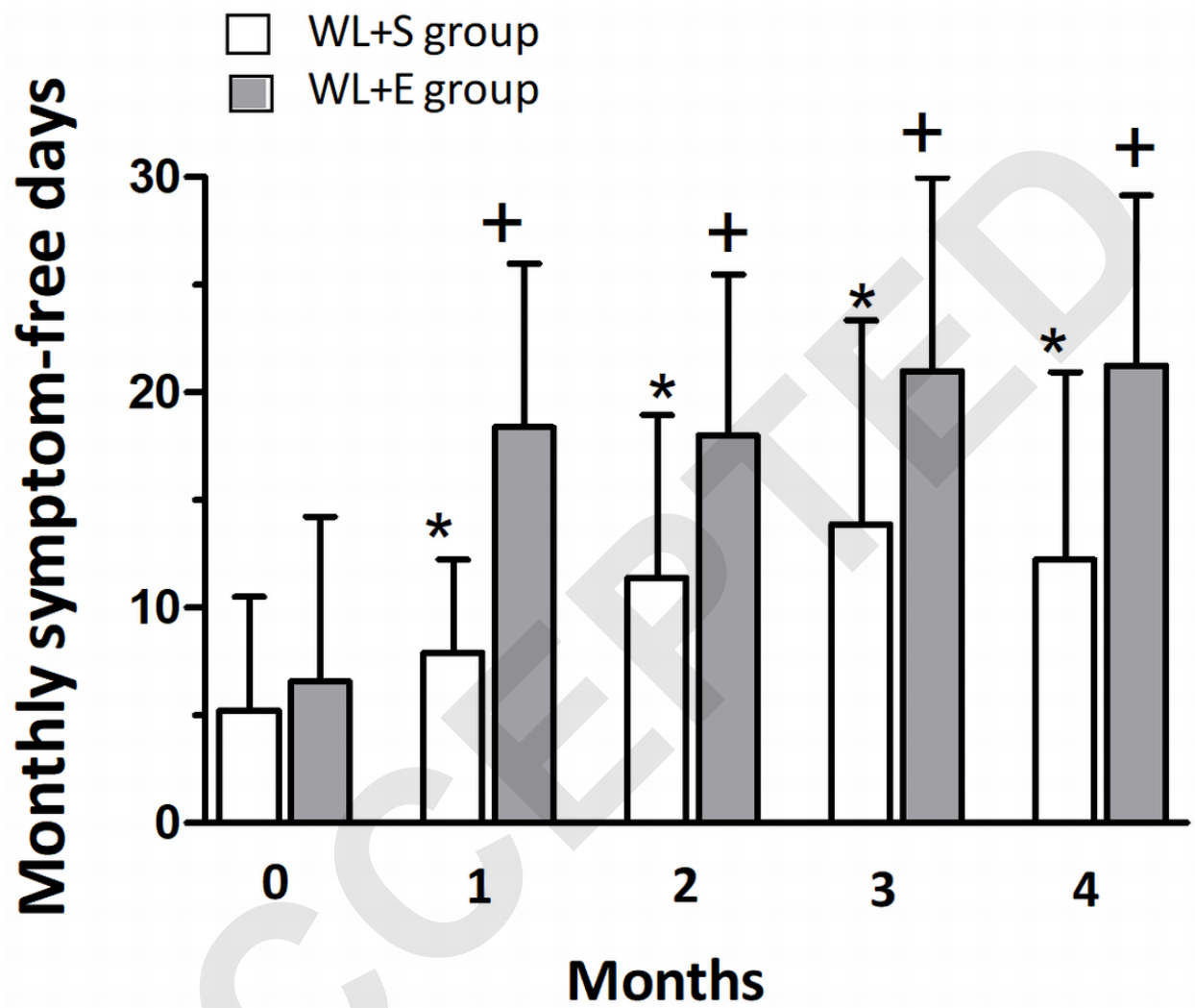


Figure 4

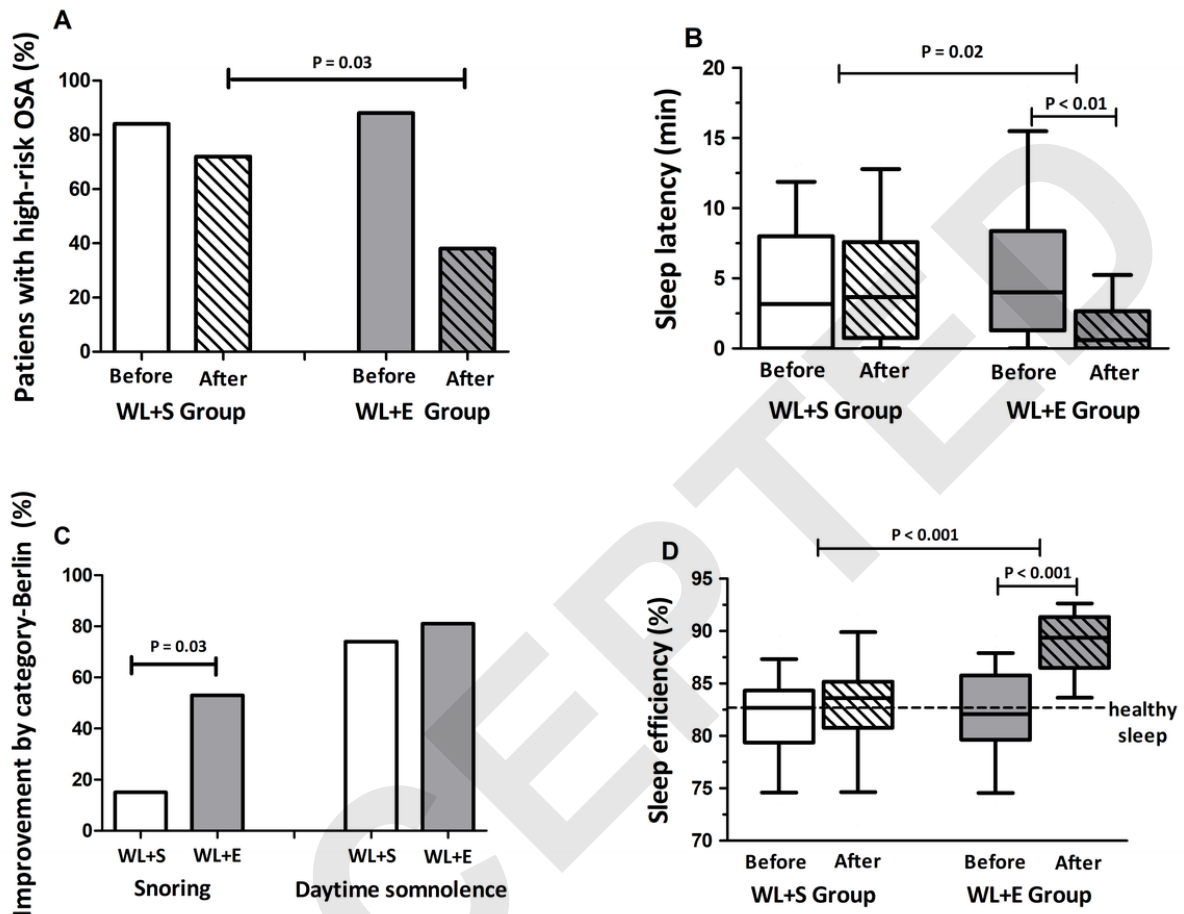


Figure 5

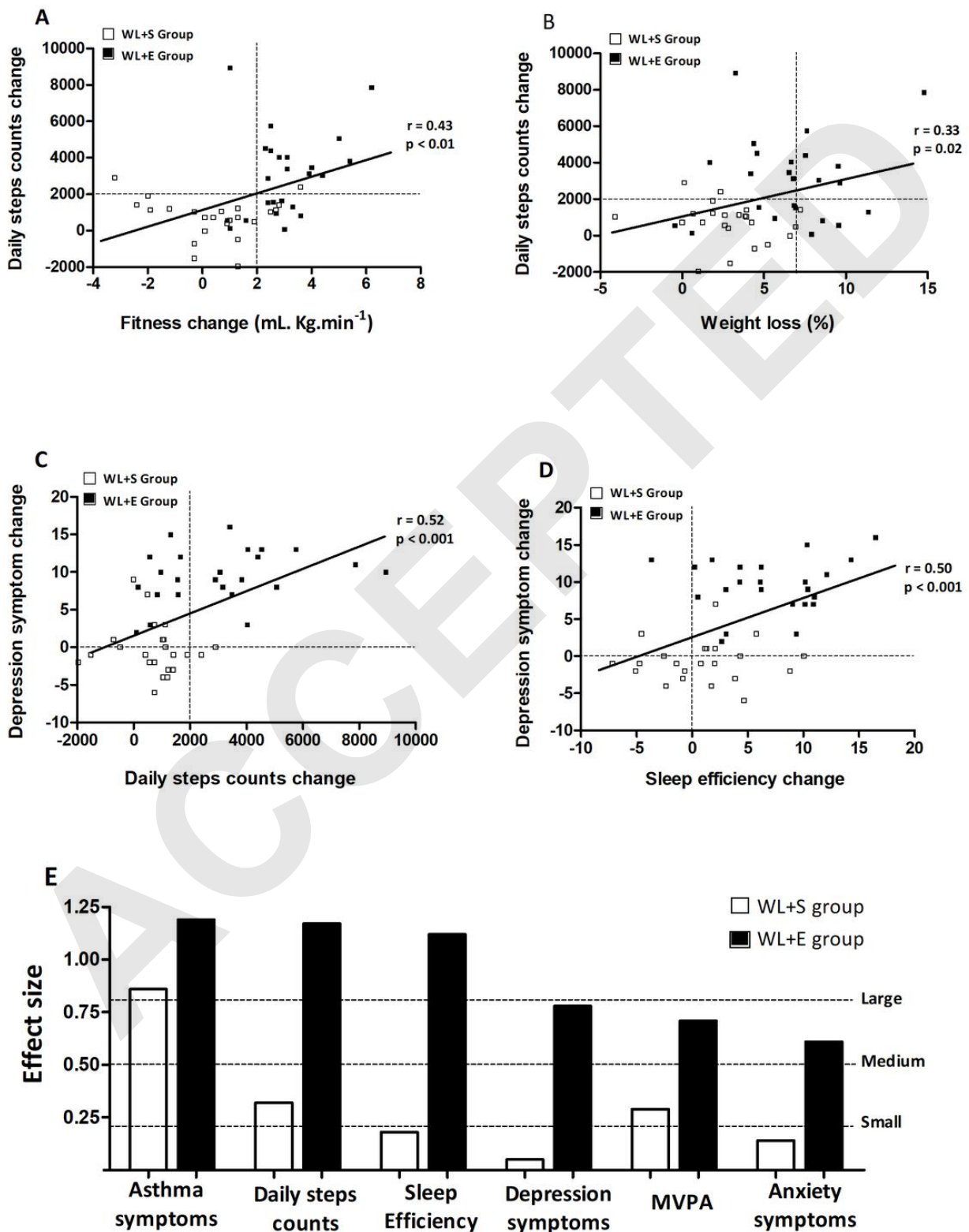


Table 1. Baseline characteristics of obese adults with asthma

Characteristic	WL+S Group (n=25)	WL+E Group (n=26)
Anthropometric data		
Female gender	25 (100)	25 (96)
Age, years	48.5 ± 9.6	45.9 ± 7.7
BMI, kg/m ²	37.2 ± 2.1	38.1 ± 2.8
Asthma Medication		
ICS dose, µcg/day	1,184 ± 492	1,050 ± 337
LABA dose, µcg/day	36.7 ± 34.9	40.3 ± 36.1
Lung function variables		
FEV ₁ /FVC, % of predicted	70.2 ± 10.1	69.6 ± 9.9
% of change in FEV ₁ post-BD	22.4 ± 12.6	21.6 ± 8.4
Asthma-related variables		
Onset of asthma in childhood	15 (60)	15 (57.7)
Physical Activity		
Number of steps/day	7,764 ± 2,176	7,306 ± 2,304
Light-intensity PA, min/day	369.4 ± 63.7	395.7 ± 72.5
MVPA, min/day	26.3 ± 16.9	25.3 ± 14.5
Sedentary time, min/day	489.5 ± 143.4	488.9 ± 84.2
Peak VO ₂ , % of predicted	79.8 ± 11.9	82.6 ± 10.3

Legend: BMI= Body Mass Index; ICS= Inhaled Corticosteroids; LABA= Long-Action β_2 Agonists; FEV₁= Forced Expiratory Volume in 1 s; FVC= Forced Vital Capacity; BD= Bronchodilator; PA= physical activity; MVPA= moderate and vigorous physical activity; Peak VO₂= Peak oxygen consumption. The data are presented as the means ± SD or n (%). No differences between treatment arms were observed at baseline (P>0.05).