Vigorous Intensity Exercise Training Improved Severity of Obstructive Sleep Apnea in a Prediabetic Individual

Trent A. Hargens, PhD, ACSM-CES[1], Nicole Gilbertson, MS[1], Joan A. Mandelson, MS[2], Elizabeth S. Edwards, PhD[1], Jeremy D. Akers, PhD, RD[2], David L. Wenos, PED[2]

ABSTRACT

Obstructive sleep apnea (OSA) is a prevalent form of sleep disordered breathing that increases ones risk for numerous chronic health conditions such as cardiovascular disease and diabetes mellitus. A limited number of studies have suggested that exercise training, mostly focusing on light-to-moderate intensities, may positively impact OSA severity and other health outcomes. This case study describes a moderately active man who was diagnosed as pre-diabetic through his physician and found to likely have moderate severity OSA through at-home screening device. He underwent eight of aerobic training at vigorous intensity. *Journal of Clinical Exercise Physiology*. 2017;6(2):36–41.

Keywords: sleep disordered breathing, polysomnography, apnea-hypopnea index, cardiorespiratory fitness

BACKGROUND

Mr. MT, a 64-year-old man who was previously diagnosed with prediabetes (glycated hemoglobin [HbA1c] between 5.7% and 6.4%) by his physician, was recruited, and subsequently volunteered for, the James Madison University prediabetes training study (PDTS). The purpose of this study was to examine how aerobic exercise training benefits physiological and psychosocial outcomes for persons participating in the National Diabetes Prevention Program developed by the Centers for Disease Control and Prevention (1).

As part of the study procedures, Mr. MT underwent baseline testing that included maximal oxygen consumption measurement, body composition assessment, blood lipid and glucose status measurement, assessment of self-reported lifestyle behaviors through questionnaire, and sleep screening for the presence of obstructive sleep apnea (OSA) through unattended home sleep evaluation. Mr. MT underwent a fasting blood draw on a separate day from other baseline testing, which included a complete lipid panel and measurements of glycated hemoglobin and insulin.

Baseline and Follow-up Testing Procedures

After signing the informed consent document, Mr. MT completed several questionnaires. Self-reported physical activity was assessed using the International Physical Activity Questionnaire (2). Height, weight, and waist and hip circumference were all measured using standardized procedures according to the American College of Sports Medicine's *Guidelines for Exercise Testing and Prescription*, 9th edition (3). Dietary habits were assessed through a 4-day food intake record administered by a registered dietitian. Total and regional body fat were measured via dual-energy x-ray absorptiometry (DEXA; Lunar iDXA, GE Healthcare, Chicago, IL).

Mr. MT completed a maximal graded exercise test on a treadmill, for which (after a 2-min warm-up) he self-selected

[1]Department of Kinesiology, James Madison University, Harrisonburg, Virginia
[2]Department of Health Sciences, James Madison University, Harrisonburg, Virginia

Address for correspondence: Trent A. Hargens, PhD, ACSM-CES. Department of Kinesiology - MSC 2302, 261 Bluestone Drive, Harrisonburg, VA 22807; (540) 568 5844; e-mail: hargenta@jmu.edu

Conflict of Interest: The authors have no conflicts of interest to report.

Source of Funding: This study was supported by grants from the James Madison University College of Health and Behavioral Studies Interprofessional Research Grant Program and Sentara Rockingham Memorial Hospital.

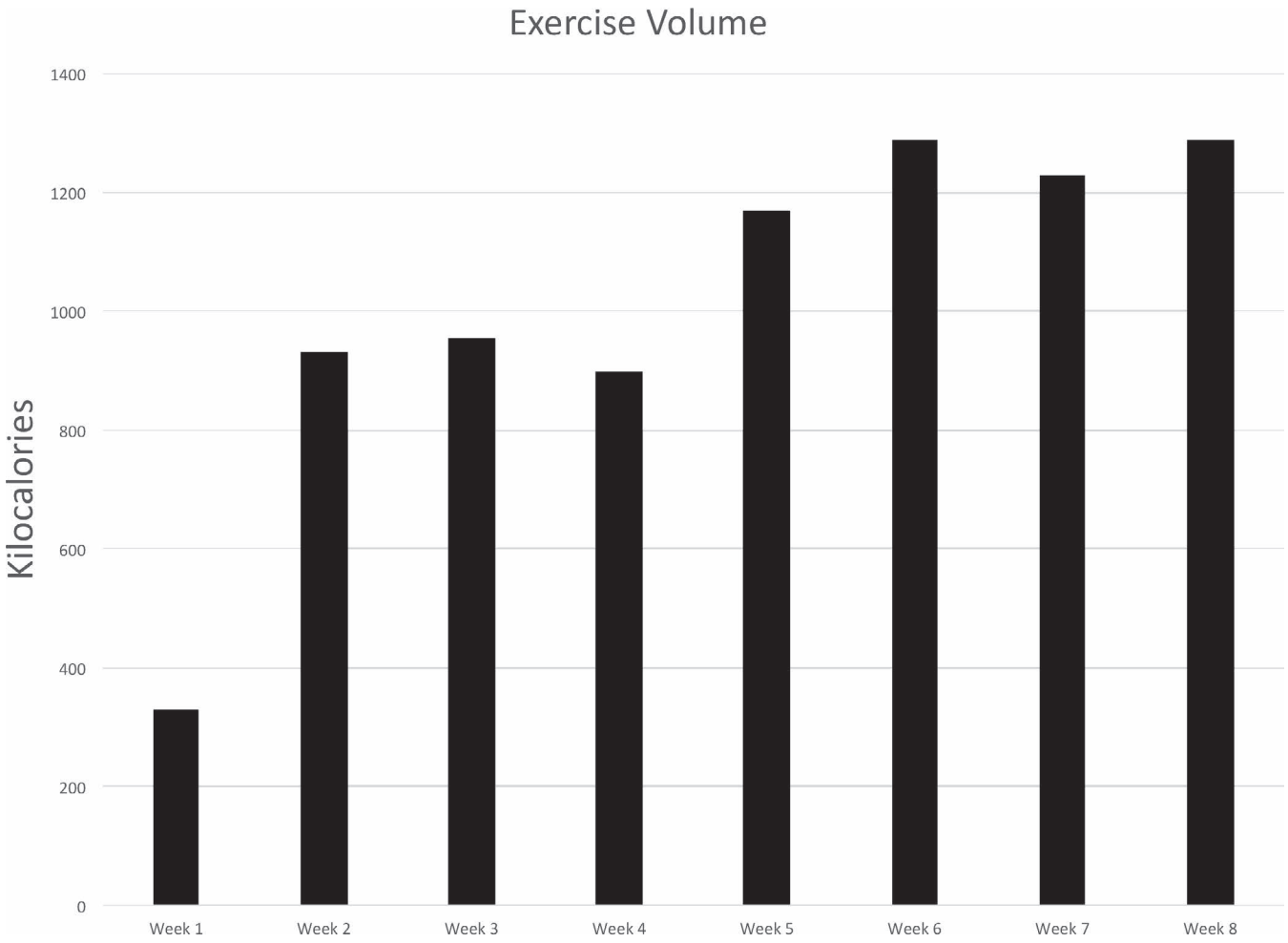

FIGURE 1. Exercise volume, expressed as total kilocalorie expenditure, for 8 weeks of vigorous intensity aerobic training

a walking speed that remained constant throughout the test. Grade increased by 2.5% every 3 minutes until volitional fatigue. Oxygen consumption was measured continuously using metabolic measurement system (Parvo TruOne 2400, Parvo Medics, Sandy, UT). Heart rate was measured continuously via a Polar heart rate device (Polar FT1, Polar Electro Inc., Lake Success, NY), and blood pressure was measured during every stage.

After completing these tests, Mr. MT was provided instructions on how to set up and wear the device used to screen for the presence of OSA (ApneaLink Air, ResMed Corp, San Diego, CA). Presence of OSA was determined through an unattended, limited home sleep evaluation over a single night utilizing a validated device (4,5). The evaluation consisted of snoring and airflow detection, heart rate and oxygen saturation measurement, and thoracic breathing effort. Data from the sleep assessment were downloaded and scored by ApneaLink software. The apnea hypopnea index (AHI) score derived from the ApneaLink device was 20 events per hour of sleep, placing Mr. MT as having a high likelihood of OSA. Were this AHI derived by full polysomnography (PSG), in a sleep clinic, Mr. MT would have been diagnosed with moderate severity OSA. Mr. MT was informed of these findings and encouraged to seek further evaluation through his primary care physician and a local sleep clinic. Upon completion of his time with the PDTS, full diagnosis and treatment had yet to occur.

Aerobic Training Program

Upon completion of baseline testing, Mr. MT was randomly assigned to perform continuous exercise vs interval-based exercise. His training target was a frequency of 3 days per week, progressing from 30 minutes per session up to 40 minutes per session.

Prior to initiating the exercise training regimen, Mr. MT reported that in the previous 7 days he had performed 15.8 MET-hr^{-1} of physical activity. This included 90 minutes of moderate intensity physical activity (housework and maintenance activities), 50 minutes of moderate intensity intentional exercise (walking on 5 of the previous 7 days), and no vigorous intensity physical activity. Based on this assessment, Mr. MT achieved the recommended amount of physical activity as outlined in the Physical Activity Guidelines for Americans (6).

The heart rate–based training intensity for Mr. MT was between 63% and 73% of heart rate reserve for the duration of his training program. By PDTS study design, the goal for exercise attendance was ≥85%. Mr. MT achieved 92%

TABLE 1. Body composition and blood values

	Baseline	8-Week
Body weight (kg)	103.5	93.0
Waist circumference (cm)	116.0	101.3
Hip circumference (cm)	104.5	102.0
Body fat (%)	37.6	34.3
Lean mass (kg)	62.4	59.2
Visceral fat (kg)	2.6	2.0
Body mass index	33.1	29.6
HbA1c (%)	5.7	5.3
Glucose (mg/dL)	9.2×10^1	9.3×10^1
Total cholesterol (mg/dL)	1.47×10^2	1.47×10^2
Low-density lipoprotein cholesterol (mg/dL)	8.2×10^1	7.14×10^1
High-density lipoprotein cholesterol (mg/dL)	5.0×10^1	5.6×10^1
Triglycerides (mg/dL)	8.4×10^1	9.8×10^1
Insulin (μU/L)	1.52×10^1	1.12×10^1

attendance of his exercise sessions, only missing two sessions, both in week 1. The duration of exercise for the initial 4 weeks was 30 minutes, which was increased to 40 minutes for the final 4 weeks. Resting blood pressure was obtained prior to each exercise session, while exercise heart rate and ratings of perceived exertion (Borg 6-20 scale) were monitored continuously throughout each session. Figure 1 depicts Mr. MT's exercise volume, expressed as kilocalorie expenditure, for each week of training. Energy expenditure values were calculated based on documented heart rate values at each 5-minute interval throughout each session.

Training Outcomes

Results of Mr. MT's training are highlighted in Tables 1 and 2. After 8 weeks of vigorous intensity aerobic exercise, Mr. MT decreased his body weight by 10%. His resulting body mass index change meant that at baseline he was classified as obese, whereas after 8 weeks of exercise training he was classified as overweight. His percent body fat was reduced by 3.3% (9% relative decrease), waist circumference was reduced by 12%, and estimated visceral fat decreased 23%. (Table 1).

Some improvement in measured biomarkers was also noted (Table 1). Although fasting glucose and total cholesterol did not change, HbA1c improved by 0.4%, moving him from prediabetic to normal glucose status. Low-density lipoprotein and high-density lipoprotein cholesterol improved by 13% and 12%, respectively, and fasting insulin improved by 26%. Additionally, there was a 17% increase of triglycerides, which is consistent with findings in people actively losing weight due to increased mobilization of fatty acids. Also, Mr. MT's Framingham Risk Score improved from 15.3% to 11.4%.

These body composition and metabolic improvements were independent of significant dietary changes. Mr. MT's pre- and postintervention daily kilocalorie and macronutrient intake per diary were 1447 vs 1472 kcal, 28 vs 24 g fat, 54 vs 60.5 g carbohydrate, and 17.5 vs 15 g protein.

Mr. MT had a 24% improvement in his peak aerobic capacity (Table 2). At baseline, Mr. MT's VO_{2peak} placed him near the 45th percentile for aerobic fitness compared with men of his age. Following training, Mr. MT increased to the 75th percentile (3).

Results before and after sleep assessment are shown in Figure 2. After participating in the PDTS, Mr. MT's AHI improved by 60%. This equated to a reduction in OSA severity classification from moderate to mild. This change is important because, moderate OSA is typically treated with continuous positive airway pressure (CPAP) device, while it is not necessary for mild OSA.

DISCUSSION

Epidemiology

OSA is the most prevalent form of sleep disorder, with estimates approaching 7% in Western populations (7). It has been established that OSA significantly, and independently, increases the risk for several adverse health conditions, including diabetes mellitus, hypertension, and cardiovascular disease (CVD) (8). An 18-year follow-up study of the Wisconsin Sleep Cohort found that severe sleep-disordered breathing, including OSA, increased the risk for all-cause mortality threefold, compared with those without sleep-disordered breathing and OSA (9). This finding was independent of age, body mass index, sex, and other confounders.

Risk factors for OSA include advancing age; male sex; craniofacial characteristics, such as crowded-appearing pharyngeal airway; retrognathia; tonsillar hypertrophy; maxillary and mandibular retroposition; and an enlarged soft palate (8,10). Large neck circumference and obesity are also risk factors for OSA (2,4). OSA is characterized by repetitive bouts of complete (apnea) or partial (hypopnea) upper airway collapse.

TABLE 2. Exercise results

	Baseline	8-Week
VO_{2peak} (mL $kg^{-1} \cdot min^{-1}$)	27.8	34.6
MET_{peak}	7.9	9.9
RER_{peak}	1.06	1.12
V_{Epeak} (L-min^{-1})	103.9	122.6
Heart rate (bpm)	Rest: 66	70
	Peak: 178	183
Systolic blood pressure (mmHg)	Rest: 124	112
	Peak: 182	178
Diastolic blood pressure (mmHg)	Rest: 72	78
	Peak: 80	70

MET = metabolic equivalent of task; RER = respiratory exchange ratio; V_E = minute ventilation; VO_2 = oxygen consumption.

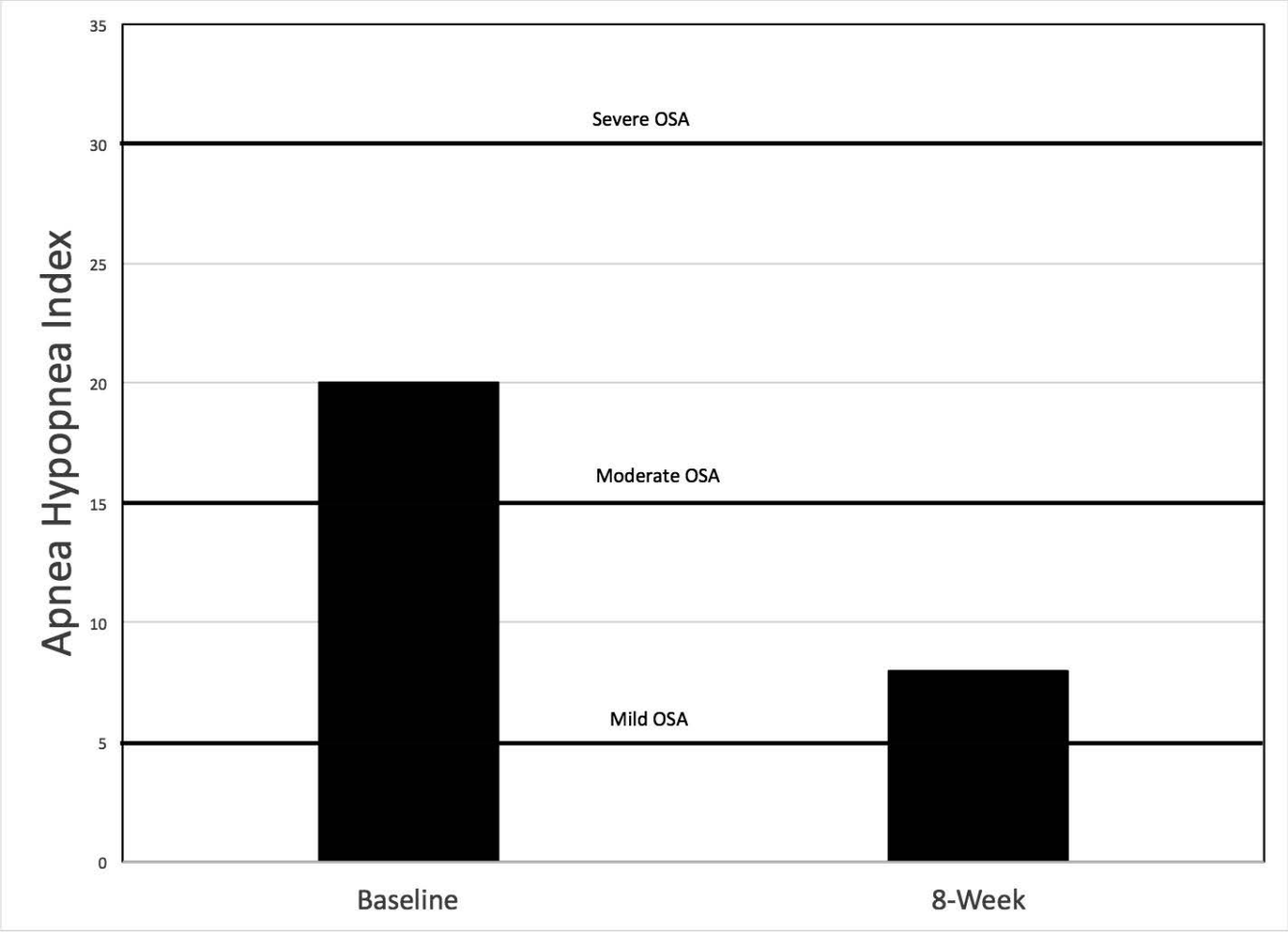

FIGURE 2. Obstructive sleep apnea severity, expressed as the apnea hypopnea index, from baseline to post 8 weeks of vigorous intensity aerobic training.

Diagnosis and Management

OSA is diagnosed using nighttime PSG at a sleep clinic. During PSG, the individual is monitored with electroencephalogram, electrooculogram, electrocardiogram, electromyogram, respiratory effort, nasal airflow, and pulse oximetry. Severity of OSA is determined by the AHI, which is the average number of apnea and hypopnea events per hour of sleep determined during PSG.

The most common treatment for OSA is a CPAP device, which is worn during sleep and prevents apneic events by keeping the airway open. If the CPAP device is not worn or used properly at night, apneas and hypopneas occur. Prevalence estimates for OSA suggest that 17% of US adults have at least mild OSA (AHI 5-14), and at least 6% suffer from moderate or severe OSA (AHI $\geq$ 15) (9). Prevalence estimates of OSA in type 2 diabetes mellitus approaches 70% (11). We present the case of a subject diagnosed with prediabetes who volunteered for an exercise training study where it was discovered that he was suffering from likely undiagnosed OSA.

Exercise and OSA

Although the number of studies examining how aerobic training affects people with OSA is few, most have shown that aerobic training positively impacts OSA severity (12-18). Limitations with previous trials include small sample size, other comorbid conditions, and light to moderate exercise training intensities. An exception was a study by Kline et al. (15), who utilized a training intensity of 60% of heart rate reserve, which is the threshold of vigorous intensity training. They utilized a 12-week training protocol that gradually increased to 4 days of aerobic training per week (primarily treadmill) and 2 days of a resistance protocol per week (2 sets of 10-12 repetitions, 8 different exercises). They reported a significant reduction of OSA severity (21.7 to 15.0 events per hour from baseline to after training, respectively, $P < 0.01$), while total body weight was unchanged, suggesting exercise was a key factor in the observed OSA improvement.

The complex relationship between OSA and other comorbid conditions (e.g., obesity, diabetes, and CVD), renders it difficult to determine the physiological mechanisms responsible for the changes in OSA severity. Obesity is a major risk factor for developing OSA (8). It has been estimated that in people who are overweight or obese, the prevalence of OSA may be as high as 20% (19). In addition to improved fitness via exercise training, a likely reason Mr. MT improved was because he was able to reduce his body

weight and abdominal adiposity. Previous epidemiologic evidence has shown a relationship between body weight and OSA severity (20). Reductions in body weight and adiposity may positively impact OSA severity by several mechanisms. For instance, in persons who are obese, the upper airway is more prone to collapse. With weight loss this resolves, likely due to a decreased mechanical load on the upper airway and lungs, which restricts their ability to expand (21).

Contrary to studies showing body composition improvements leading to improvements in OSA severity, two recent meta-analyses found that exercise appears have a positive impact on OSA severity independent of body weight changes (22,23). A meta-analysis by Iftikhar et al., reported AHI was decreased by 6.3 events per hour, with no significant changes in BMI, through exercise training. (23). Further, a follow-up analysis, by Iftikhar et al. (22) noted that when independently comparing exercise training to CPAP and dietary weight loss, exercise was effective at AHI reduction, second only to CPAP. It is important to note, however, that CPAP must be worn for AHI to be reduced. While effective at eradicating apnea and hypopnea events when worn, these devices are cumbersome; many patients report that they are unable to tolerate these devices and, therefore, do not use them. Through participation in this training study, Mr. MT decreased his OSA severity to the point that CPAP treatment may not be indicated for him, sparing him the potential cost and inconvenience of the CPAP device.

Exercise training can reduce abdominal obesity independent of weight loss (24), most likely through increases in catecholamine levels, which impact lipolysis to a greater extent in visceral fat than subcutaneous fat (25). Because visceral fat can result in reductions in lung volume and can lead to an increased likelihood of pharyngeal collapse, the impact of exercise on visceral fat reduction may have a positive effect on pharyngeal collapsibility (22). While reducing total body weight significantly, Mr. MT also decreased his waist circumference and DEXA-derived visceral fat, which could be a contributor to the improvement in AHI noted. Further research is needed to better elucidate the relevant mechanisms that link exercise to improvements in OSA severity.

REFERENCES

1. Albright AL, Gregg EW. Preventing type 2 diabetes in communities across the U.S.: the National Diabetes Prevention Program. Am J Prev Med. 2013;44(4 suppl 4):S346-51.
2. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35(8): 1381-95.
3. Pescatello LS, Arena R, Riebe D, Thompson PD, American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. 9th ed. Philadelphia: Wolters Kluwer/ Lippincott Williams & Wilkins Health; 2014.
4. Erman MK, Stewart D, Einhorn D, Gordon N, Casal E. Validation of the ApneaLink for the screening of sleep apnea: a novel and simple single-channel recording device. J Clin Sleep Med. 2007;3(4):387-92.
5. Ng SS, Chan TO, To KW, Ngai J, Tung A, Ko FW, Hui DS. Validation of a portable recording device (ApneaLink) for identifying patients with suspected obstructive sleep apnoea syndrome. Int Med J. 2009;39(11):757-62.
6. Physical Activity Guidelines Advisory Committee report, 2008. To the Secretary of Health and Human Services. Part A: executive summary. Nutr Rev. 2009;67(2):114-20.
7. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002;165(9):1217-39.
8. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, Daniels S, Floras JS, Hunt CE, Olson LJ, Pickering TG, Russell R, Woo M, Young T. Sleep apnea and cardiovascular disease: an American Heart Association/ American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council On Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health). Circulation. 2008;118(10):1080-1111.
9. Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, Stubbs R, Hla KM. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep. 2008;31(8):1071-8.
10. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):136-43.
11. Laaban JP, Daenen S, Leger D, Pascal S, Bayon V, Slama G, Elgrably F. Prevalence and predictive factors of sleep apnoea syndrome in type 2 diabetic patients. Diabetes Metab. 2009;35(5):372-7.
12. Mendelson M, Lyons OD, Yadollahi A, Inami T, Oh P, Bradley TD. Effects of exercise training on sleep apnoea in patients with coronary artery disease: a randomised trial. Eur Respir J. 2016;48(1):142-50.
13. Desplan M, Mercier J, Sabate M, Ninot G, Prefaut C, Dauvilliers Y. A comprehensive rehabilitation program improves disease severity in patients with obstructive sleep apnea syndrome: a pilot randomized controlled study. Sleep Med. 2014;15(8):906-12.
14. Sengul YS, Ozalevli S, Oztura I, Itil O, Baklan B. The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. Sleep Breath. 2011;15(1):49-56.
15. Kline CE, Crowley EP, Ewing GB, Burch JB, Blair SN, Durstine JL, Davis JM, Youngstedt SD. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. Sleep. 2011;34(12):1631-40.
16. Barnes M, Goldsworthy UR, Cary BA, Hill CJ. A diet and exercise program to improve clinical outcomes in patients with obstructive sleep apnea—a feasibility study. J Clin Sleep Med. 2009;5(5):409-15.
17. Norman JF, Von Essen SG, Fuchs RH, McElligott M. Exercise training effect on obstructive sleep apnea syndrome. Sleep Res Online. 2000;3(3):121-9.
18. Giebelhaus V, Strohl KP, Lormes W, Lehmann M, Netzer N. Physical exercise as an adjunct therapy in sleep apnea—an open trial. Sleep Breath. 2000;4(4):173-6.
19. Caples SM, Gami AS, Somers VK. Obstructive sleep apnea. Ann Intern Med. 2005;142(3):187-97.

20. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015-21.
21. Schwartz AR, Gold AR, Schubert N, Stryzak A, Wise RA, Permutt S, Smith PL. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. Am Rev Respir Dis. 1991;144(3 Pt 1):494-8.
22. Iftikhar IH, Bittencourt L, Youngstedt SD, Youngstedt SD, Ayas N, Cistulli P, Schwab R, Durkin MW, Magalang UJ. Comparative efficacy of CPAP, MADs, exercise-training, and dietary weight loss for sleep apnea: a network meta-analysis. Sleep Med. 2017;30:7-14.
23. Iftikhar IH, Kline CE, Youngstedt SD. Effects of exercise training on sleep apnea: a meta-analysis. Lung. 2014;192(1):175-84.
24. Irwin ML, Yasui Y, Ulrich CM, Bowen D, Rudolph RE, Schwartz RS, Yukawa M, Aiello E, Potter JD, McTiernan A. Effect of exercise on total and intra-abdominal body fat in postmenopausal women: a randomized controlled trial. JAMA. 2003;289(3):323-30.
25. Richelsen B, Pedersen SB, Moller-Pedersen T, Bak JF. Regional differences in triglyceride breakdown in human adipose tissue: effects of catecholamines, insulin, and prostaglandin E2. Metabolism. 1991;40(9):990-6.