



Effect of exercise training on sleep apnea: A systematic review and meta-analysis



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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is difficult to manage for those who are intolerant or non-compliant with standard facial mask treatment options. Current treatment options do not address the underlying cause of OSA. Exercise as a treatment option has been found to improve OSA indices.

Study objectives: To assess the efficacy of exercise on apnea/hypopnea index (AHI) in adult patients with OSA via a systematic review and meta-analysis. Additional objectives included evaluation of other indices of OSA and well-being in patients after completing an exercise regimen.

Measurements and results: Web of Science, MEDLINE, CINAHL, and Cochrane Central Register of Controlled Trials were searched based on a priori criteria of all studies evaluating the effect of an exercise program on various sleep apnea indices. Both PRISMA statement and MOOSE consensus statement were adhered to. Eight Articles (182 participants) were included: a meta-analysis using a random effects model showed, a decrease in AHI (unstandardized mean difference [USMD], -0.536 , 95% confidence interval [CI], -0.865 to -0.206 , I^2 , 20%), reduced Epworth sleepiness scale (ESS) (USMD, -1.246 , 95% CI, -2.397 to -0.0953 , I^2 , 0%), and lower body mass index (BMI) (USMD, -0.0473 , 95% CI, -0.0375 to 0.280 , I^2 , 0%), in patients receiving exercise as treatment. Relative risks (RR) and odds ratios (OR) showed decreases in AHI (OR: 72.33, 95% CI, 27.906 to 187.491, RR: 7.294, 95% CI, 4.072 to 13.065) in patients receiving exercise as treatment.

Conclusion: Among adult patients with OSA, exercise as the sole intervention was associated with improved clinical outcomes.

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1. Introduction

Obstructive sleep apnea (OSA) is commonly characterized by recurring upper airway obstruction during sleep [1]. Common predisposing factors for OSA include gender (male), craniofacial anomalies [2], and obesity [3]. Many health consequences are associated with OSA, including lethargy, memory loss, problems with thinking and judgment [4], disruption of normal metabolic functions [5], and cardiovascular disorders [6,7].

The measure of the severity of OSA is based on the number of apnea or hypopnea events per hour of sleep represented as apnea

hypopnea index (AHI). Previous literature has established parameters for OSA; none/minimal OSA diagnosed as AHI <5 per hour, mild OSA diagnosed as AHI ≥ 5 and AHI <15, moderate OSA diagnosed as AHI ≥ 15 and AHI <30, and severe OSA diagnosed as AHI ≥ 30 [2]. The exact etiology of OSA is unknown and has led to multiple treatment and management options [8]. Previous studies have evaluated treating OSA symptoms via continuous positive airway pressure (CPAP) [9], mandibular adjustment [10,11], weight loss via diet [4,12], bariatric surgery [13–15], pharmacotherapy [16–18], and upper airway surgery [19–21]. However, long-term studies have shown that the therapeutic efficacy of these treatments do not address the underlying cause of OSA, evident by the AHI reduction then resurgence in AHI of participants who underwent treatment by CPAP [9], weight loss via reduced calorie intake [22,23], bariatric surgery [14], and mandibular adjustment [10,11,24].

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Exercise programs to treat and manage OSA in patients have displayed promising results in reducing AHI and Epworth Sleepiness Scale (ESS) [25–29]. Further, exercise has been shown to reduce the severity of other disorders and/or diseases associated with OSA including diabetes [30], cardiovascular disease [31], hypertension [32], and obesity [33]. It is not fully understood how exercise reduces OSA symptoms, but previous reviews have indicated that the impact of exercise on OSA is not related to reduction of body weight or body mass index (BMI) in both epidemiologic [34] and experimental studies [35–37].

Previous reviews and meta-analyses evaluated different treatments on OSA patients: diet and lifestyle [38], supervised exercise [36], diet or diet and exercise [39], diet and/or supervised exercise [8], and intensive lifestyle intervention (low calorie or very low calorie diet, mandibular advancement) [40]. Additionally, in the literature we found studies that were excluded from previous reviews because the exercise programs were initially led by professionals and study personnel (supervised exercise programs), but ended as unsupervised exercise programs where the participants were solely responsible for their treatment [8].

The primary objective was to study the use of exercise (supervised and unsupervised) as management treatment for OSA by analyzing the difference in pre- and post-intervention AHI in adult patients with OSA. Secondary objectives included evaluating the effects of exercise on ESS, BMI.

2. Materials and methods

Five authors (K.A., B.N., A.S., F.M., and M.M) identified studies in Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1993–2014), Web of Science (WOS), and CINAHL. The following search strategy was used: ([text word] *exercise* OR [text word] *exercise program* OR [text word] *aerobic exercise* OR [text word] *physical activity* OR [text word] *muscle stretching exercise* OR [text word] *plyometric exercise* OR [text word] *resistance training* OR [text word] *running* OR [text word] *jogging* OR [text word] *swimming* OR [text word] *isometric exercise* OR [text word] *weightlifting* OR [text word] *weightbearing* AND [text word] *sleep apnea* OR [text word] *obstructive sleep apnea* OR [text word] *sleep disturbed breathing*). All reviewed articles and cross-referenced studies were screened for relevant data. Reference lists of included studies and previously published systematic reviews and meta-analyses on OSA and lifestyle interventions were hand searched. No language restrictions were applied. Any disagreement was resolved by consensus. All reviewed articles and cross-referenced studies were screened for relevant data. Authors also searched previously published studies, reviews, and meta-analyses on OSA and lifestyle interventions [8,36,38–41]. In the case of missing data, authors were contacted for additional unpublished data in order to complete the data set [42]. Inclusion criteria included: adult participants (age >18 years), OSA was diagnosed via polysomnography (PSG) via AHI ≥ 5 , exercise program duration ≥ 2 months, frequency of exercise ≥ 2 sessions per week, exercise session ≥ 30 min, exercise as the sole intervention, patient cohort ≥ 9 , and pre- and post-intervention changes in AHI, BMI, and ESS were reported. Randomized trials as well as observational studies were included with no restrictions on language or supervised or unsupervised exercise program.

Articles were excluded if OSA was not diagnosed via PSG, treatment was a combination of exercise and lifestyle intervention, subjects were diagnosed with heart failure (HF), neuromuscular disorders (NMD), and/or chronic pulmonary disease (COPD), were using dental sleep devices, and/or patients previously had undergone surgery. The Jadad score provides points for randomization (2), blinding (2), and patient dropouts (1), and was used to quality score and evaluate all randomized controlled trials (RCTs) (Fig. 1)

[43]. The information collected from the relevant studies included: sampling framework(s), author(s), year article was published in journal (not e-pub date), PSG data, mean of cohort age, exercise duration, exercise frequency, exercise protocol, keywords, CPAP usage, and pre- and post-intervention AHI, ESS, BMI, profile of mood states, and well-being or quality of life question. The mean differences of AHI, BMI, ESS for pre- and post-intervention for both treatment and control groups were extracted for each study and graphically represented using forest plot graphs; this data was pooled using USMD due to the uniformity of scale and analysis [44] (Fig. 2). Two authors (K.A., B.C.) conducted independent statistical analysis to confirm the results. Heterogeneity was assessed using I^2 statistics and Cochrane's Q statistic [45].

The parametric variables AHI, BMI, and ESS were represented as the mean and standard deviation despite the small sample sizes. To check for publication bias, funnel plots of effect size and standard error were constructed [46]. Funnel plots analyzed using the Begg and Mazumdar rank correlation test did not suggest significant publication bias for the analysis conducted [47]. Both the PRISMA criteria [48], and the MOOSE guidelines [49] were followed (Fig. 3). All analyses were performed using MedCalc[®] (<http://www.medcalc.org/>) and R programming language. P-values less than 0.10 were considered significant based on the literature recommended threshold [50].

3. Results

The initial search yielded 8394 studies (6776 from MEDLINE, 308 from CENTRAL, 291 from CINAHL, and 1019 from WOS). After removing 812 duplicates, we conducted a title and abstract search in the remaining 7582 articles, which resulted in 1142 studies. After evaluating the abstracts of each study, we excluded 1126 studies for failing to the priori inclusion/exclusion criteria. Eight articles were excluded after a close reading of the text. The final analysis consisted of 8 articles and 180 participants [42,51–57] (Fig. 4). Seven references had pre- and post-intervention data for AHI and BMI [42,51–54,56,57], 5 studies included AHI and BMI data but were missing ESS data (Fig. 1). The most complete data set was used for analysis in the instance of duplicate reports or articles [54]. Variance between studies was accounted for by using fixed and random effects methods meta-analyses [58].

Studies' baseline data including publication year, study design, total number of subjects, duration of exercise program, number of participants (% of males and females), age, and pre- and post-intervention BMI, AHI, and ESS were extracted. Six studies were RCTs [51–54,56,57] and 2 studies were single group intervention studies [42,55]. Both supervised and unsupervised exercise programs were used as treatment in the studies. Supervised exercise programs were used in 6 studies [51,52,54–57] and unsupervised exercise programs in 2 studies [42,53]. Treatment duration ranged from 2 months to 6 months. Treatment frequency ranged from 2 days a week to 7 days a week, from 30 min to 150 min each session. Exercise protocols ranged from aerobic exercise, e.g. walking/running on treadmill, stair climbing, Airdyne[®] machine, stationary bicycle, resistance training, and oropharyngeal exercises. Participants' ages ranged from 32.2 to 54.4 years.

A total of 7 studies [42,51–54,56,57] compared mean AHI scores pre- and post-intervention for a control group and experimental group. One study [59] that measured respiratory disturbance index (RDI) was not included in the AHI meta-analysis. Comparison of the 2 groups found exercise was associated with a reduction in AHI after treatment (unstandardized mean difference [USMD], -0.536 , 95% CI, -0.865 to -0.206 , I^2 , 20%). A total of 4 studies [53,54,56,57] compared mean ESS scores pre- and post-intervention for a control group and experimental group. Exercise was associated with

Author	Study Design	Number of Participants (% of males)	Age, mean (SD)	Pre-Intervention			Jadad Score
				AHI, mean (SD) RDI, mean (SD)*	BMI, mean (SD)	ESS, mean (SD)	
Ackel-D'Elia et al ⁵¹	RCT	Exercise: 13 (100%)	Exercise: 48.4 (9.2)	Exercise: 42.3 (21.6)	Exercise: 28.0 (3.1)	Exercise: 14.0 (4.1)	3
		Control: 19 (100%)	Control: 49.5 (7.7)	Control: 40.5 (22.9)	Control: 28.5 (2.2)	Control: 13.0 (4.8)	
Cavagnoli et al ⁵²	RCT	Exercise: 10 (100%)	Exercise: 40.5 (10.4)	Exercise: 3.47 (1.6)	Exercise: 26.0 (3.4)	Exercise: NA	1
		Control: 10 (100%)	Control: 32.2 (10.2)	Control: 25.71 (17.1)	Control: 27.5 (1.9)	Control: N/A	
Guimaraes et al ⁵³	RCT	Exercise: 16 (100%)	Exercise: 51.5 (6.8)	Exercise: 22.4 (4.8)	Exercise: 29.6 (3.8)	Exercise: 14 (5)	4
		Control: 15 (100%)	Control: 47.7 (9.8)	Control: 22.4 (5.4)	Control: 31.0 (2.8)	Control: 14 (7)	
Kline et al ⁵⁴	RCT	Exercise: 27 (100%)	Exercise: 47.7 (6.7)	Exercise: 32.2 (29.0)	Exercise: 35.5 (6.2)	Exercise: 11.1 (0.9)	3
		Control: 16 (100%)	Control: 45.9 (8.8)	Control: 24.4 (22.4)	Control: 33.6 (5.6)	Control: 7.3 (0.9)	
Schutz et al ⁵⁶	RCT	Exercise: 7 (100%)	Exercise: 42.3 (8.3)	Exercise: 22.8 (12.8)	Exercise: 28.1 (1.6)	Exercise: 14.1 (5.6)	3
		Control: 9 (100%)	Control: 38.6 (8.2)	Control: 25.1 (10.5)	Control: 25.9 (5.3)	Control: 9.9 (5.2)	
Sengul et al ⁵⁷	RCT	Exercise: 10 (100%)	Exercise: 54.4 (6.5)	Exercise: 15.4 (5.4)	Exercise: 29.8 (2.6)	Exercise: 8.2 (6.1)	3
		Control: 10 (100%)	Control: 48.0 (7.4)	Control: 17.9 (6.4)	Control: 28.4 (5.4)	Control: 3.4 (5.1)	
Netzer et al ⁵⁵	Single group study	10 (91%)	52.2 (6.2)	*32.8 (22.1)	27.6 (3.5)	N/A	1
Norman et al ⁴²	Single group study	8 (89%)	48.0 (9.0)	21.7 (9.0)	34.4 (3.7)	N/A	1

*Mean represented here is separated via exercise or control group and by each individual study
Abbreviations: BMI=body mass index; SD=standard deviation; ESS= Epworth Sleep Scale; AHI=apnea hypopnea index; RDI=respiratory disturbance index; RCT=randomized controlled trial

Fig. 1. Baseline Characteristics of the Studies Included in the Final Meta-Analysis. *Mean represented here is separated via exercise or control group and by each individual study. Abbreviations: BMI = body mass index; SD = standard deviation; ESS = Epworth Sleep Scale; AHI = apnea hypopnea index; RDI = respiratory disturbance index; RCT = randomized controlled trial.

having a lower decrease in the total ESS after treatment (USMD, -1.246 , 95% CI, -2.397 to -0.0953 , I^2 , 0%). A total of 4 studies [51,53,54,56,57] compared mean BMI scores pre- and post-intervention for a control group and experimental group. Exercise was not found to have statistically significant effect on BMI (USMD, -0.0473 , 95% CI, -0.0375 to 0.280 , I^2 , 0%).

Due to the results assessing AHI excluding RDI, an analysis was performed that excluded the study that measured pre- and post-intervention RDI only, fixed effects model ([USMD], -0.510 , 95% CI, -0.783 to -0.237 , I^2 , 7%, p , <0.001), random effects model ([USMD], -0.515 , 95% CI, -0.800 to -0.230 , I^2 , 7%, p , <0.001). Similar results were found when risk ratio (RR) and odds ratio (OR) were used to compare pre- and post-intervention results concerning AHI. Patients receiving exercise treatment had an AHI decrease of 4 when compared to patients not receiving exercise treatment (OR: 72.33, 95% CI, 27.906 to 187.491; RR: 7.294, 95% CI, 4.072).

4. Discussion

In this study, mean treatment outcomes of pre- and post-intervention data from 8 studies with 180 total participants were compared. The main findings highlight that exercise has an effect on reducing both AHI and ESS in patients with OSA. This conclusion remained consistent independent of different types of exercise,

durations of exercise, frequency of exercise sessions, CPAP usage, and supervised or unsupervised treatment programs. This conclusion was supported via the moderate sample size and degree of heterogeneity.

A potential explanation cited for exercise reducing AHI in mild or severe OSA focuses on the comorbidity of obesity and OSA [8,39]. Excess adipose tissue is the cause of the airway collapsing and apnea or hypopnea events occurring, and obesity is linked to increased adipose tissue in the pharyngeal airway [1–3,37,60]. Exercise can lead to weight loss and reduction in BMI [38], and studies have suggested that reduction in BMI is associated with reduction in the volume of adipose tissue in the pharyngeal airway [61]. However, our results support Iftikhar et al.'s [36] findings that exercise reduces AHI regardless of significant reduction in BMI. Previous studies have shown dramatic AHI reduction through low calorie diet [4,23,39] or diet modification [12,22,62], pharmacological treatment [16–18], exercise and lifestyle intervention [40,41], and surgery [14,15,21,61]. Though, as already mentioned, follow-up studies have shown that some of these treatments do not lead to long-term reduction in AHI [9,14,22,23].

The benefits of systematic reviews and meta-analyses lie in summarizing information and evaluating treatments; however, one of the pitfalls of meta-analyses is the assessing of information and validating methods [63]. As previously mentioned, analyses on different characteristics of participants and combination of

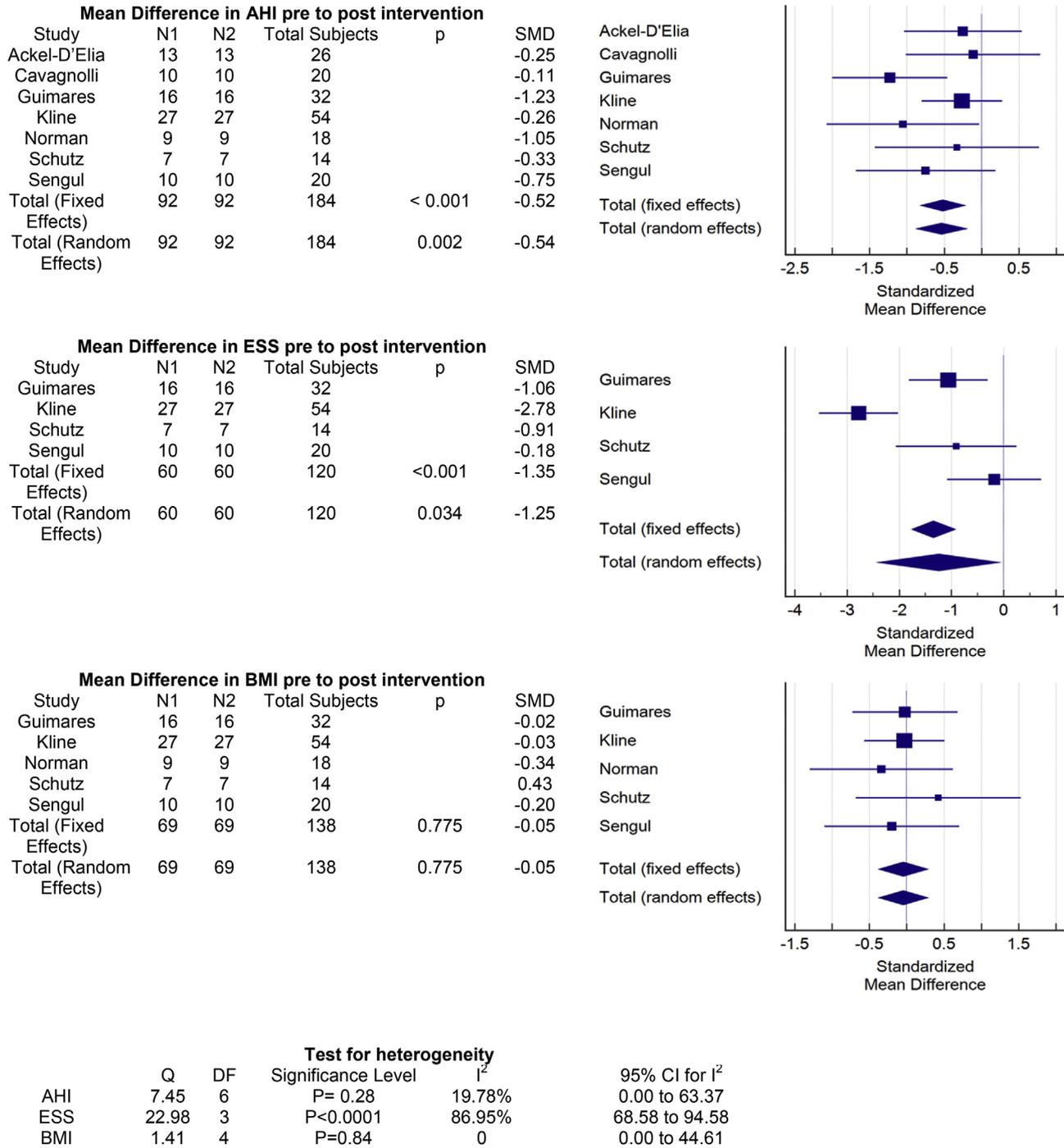


Fig. 2. Mean change in AHI, ESS, and BMI from baseline to end of treatment showing a decrease in AHI (unstandardized mean difference [USMD], -0.536 , 95% confidence interval [CI], -0.865 to -0.206 , I^2 , 20%), reduced Epworth sleepiness scale (ESS) (USMD, -1.246 , 95% CI, -2.397 to -0.0953 , I^2 , 0%), and lower body mass index (BMI) (USMD, -0.0473 , 95% CI, -0.0375 to 0.280 , I^2 , 0%), in patients receiving exercise as treatment. Abbreviations: BMI, Body Mass Index, SMD standardized mean difference, ESS, Epworth Sleep Scale, AHI, apnea hypopnea index, CI, confidence interval, N1, experimental group pre-intervention, N2, experimental group post intervention.

interventions have been performed: diet and lifestyle by Thoma-souli et al. [38]; supervised exercise as treatment was analyzed by Iftikhar et al. [36]; diet or diet and exercise as intervention was analyzed by Anadam et al. [39]; diet and/or supervised exercise was analyzed by Araghi et al. [8]; upper airway muscle tonus by Valbuza [64]; and intensive lifestyle intervention (low calorie or very low calorie diet, mandibular advancement) by Mitchell et al. [40]. In this study, we compared pre- and post-intervention standard mean difference of AHI, BMI, and ESS and found that reduction

in OSA indices were similar regardless of the exercise protocol used. Due to the similarity in results we cannot say which protocol, duration, or frequency were the best [48]; however, our results raise important questions about OSA treatment and management options. The possible implications for treatment and management of OSA from this study are: (1) exercise as the primary treatment and management option for OSA; (2) the use of unsupervised exercise or telemedicine treatment for OSA; and (3) the use of low-calorie diets and surgical interventions may not be required.

Reporting background should include	
Problem definition	Obstructive sleep apnea is a disease that reduces sleep quality.
Hypothesis statement	Exercise may be associated with decrease in AHI, ESS, and BMI.
Description	AHI outcome
Type of exposure or intervention used	Exercise
Type of study designs used	We included randomized controlled trials, and single group intervention studies.
Study population	Adults with OSA
Reporting of search strategy should include	
Qualifications of searches (e.g. librarians and investigators)	The credentials of all investigators are indicated in the author list.
Search strategy, including time period included in the synthesis and keywords	Four authors and one librarian performed the literature search for articles from 01 Jan 1993 to 01 Oct 2014.
Effort to include all available studies, including contact with authors	See PRISMA flow chart and methods section.
Databases and registries searched	PubMed, Embase, Cochrane Library, Web of Science, and Cumulative Index to Nursing & Allied Literature.
Search software used, name and version, including special features	No search software was employed. EndNote, RefWorks, and Zotero were used to merge citations and eliminate duplicate texts.
Use of hand searching (e.g. reference lists of obtained articles)	We hand-searched bibliographies of retrieved papers for additional references.
List of citations located and those excluded including justification	Details of the literature search are in the PRISMA flow chart.
Method of addressing articles published in languages other than English	We placed no restrictions on language. If necessary, we used a combination of Google Translate™ and local scientists fluent in the original language for translation.
Method of handling abstracts and unpublished studies	We contacted authors when necessary.
Description of any contact with authors	See methods section.
Reporting methods should include	
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Specific a priori inclusion and exclusion criteria were listed in methods section.
Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Data obtained from each study were applicable to patient population characteristics, study design, treatment, outcome, and possible interactions.
Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	See methods section.
Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	Sensitivity analysis provided summary of previous reviews
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Jadad scale was used and sensitivity analysis.
Assessment of heterogeneity	The heterogeneity was evaluated by I ² and Q statistic.
Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Description of methods, sensitivity analysis, and assessment of publication bias are all detailed in the methods section.
Provision of appropriate tables and graphics	Three tables and two figures were provided.
Reporting of results should include	
Graphic summarizing individual study estimates and overall estimate	Figure 2
Table giving descriptive information for each study included	Table 2
Results of sensitivity testing (e.g., subgroup analysis)	Table 3
Indication of statistical uncertainty of findings	95% confidence intervals with all summary estimates
Reporting of discussion should include	
Quantitative assessment of bias (e.g., publication bias)	Sensitivity analysis via summary table.
Justification for exclusion (e.g., exclusion of non-English-language citations)	We excluded studies that did not diagnose OSA via PSG, participants were not adults, heart failure, chronic obstructive pulmonary disease, patients underwent previous upper airway surgery or bariatric surgery, patients had mandibular advancement, exercise was not sole treatment, and desired outcomes were not reported.
Assessment of quality of included studies	The study quality was reported in both a specific results section as well as the sensitivity analysis.
Reporting of conclusions should include	
Consideration of alternative explanations for observed results	A list of alternative explanations was discussed in discussion section.
Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)	We included studies from different countries and with different exercise protocols.
Guidelines for future research	Presented in discussion section.
Disclosure of funding source	No funding was received in support of this study.

Abbreviations: AHI=apnea/hypopnea index; ESS=Epworth sleepiness scale; BMI=body mass index

Fig. 3. MOOSE Guidelines Checklist. Abbreviations: AHI = apnea/hypopnea index; ESS = Epworth sleepiness scale; BMI = body mass index.

These conclusions are consistent with the growing body of studies that focus on exercise as treatment for OSA is effective in reducing OSA indices [12,25–27,36,42,51–53,55–57,59]. Thus, possible future research could test exercise as treatment and management

of OSA symptoms in non-obese individuals, and continued analyses on the cause of OSA.

There has been some debate on if the size of the trial impacts treatment outcomes [65–67]. Specifically, smaller studies had

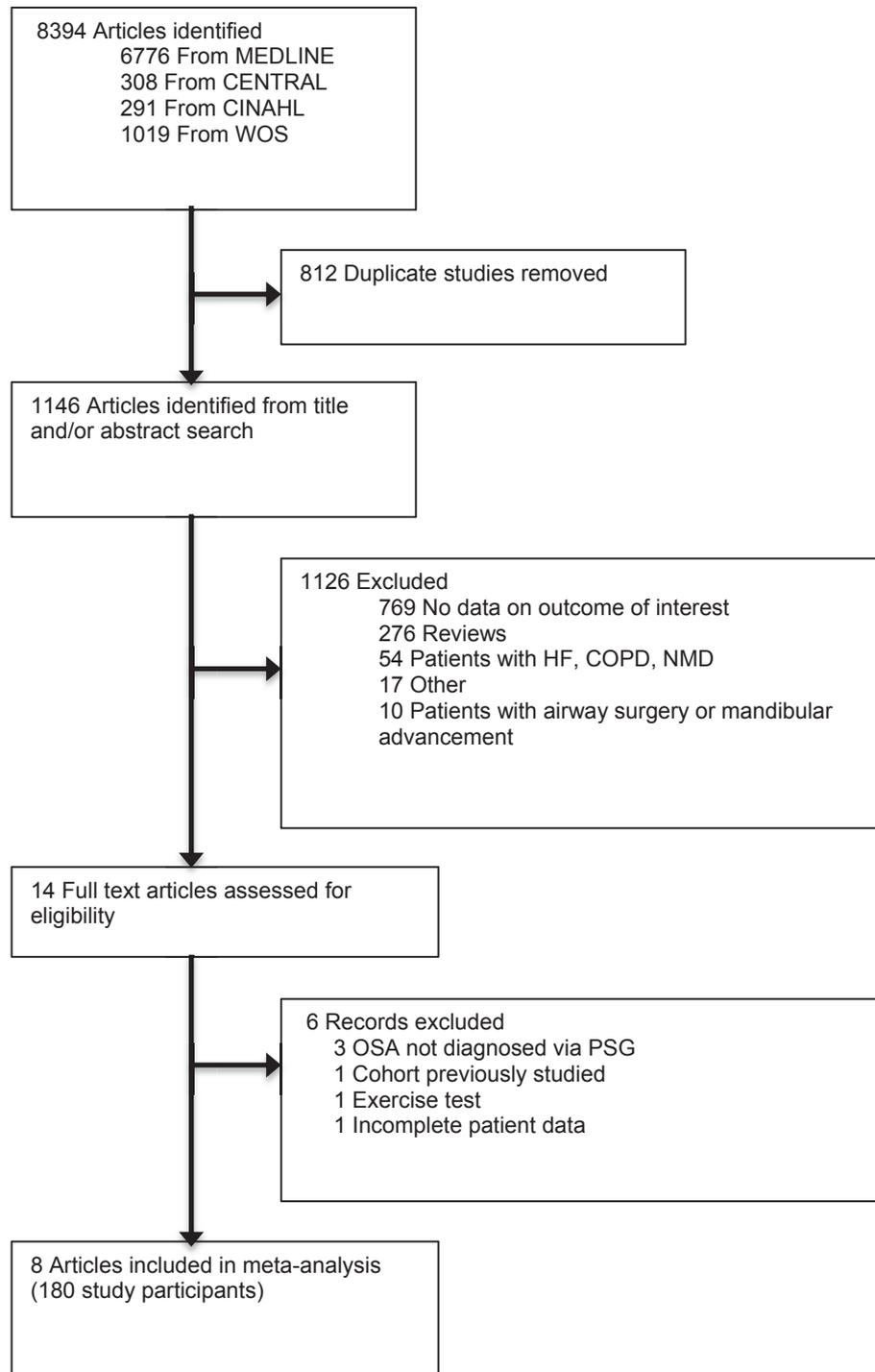


Fig. 4. Study Selection for the Effect of Exercise on Patients with Obstructive Sleep Apnea. CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature, WOS, Web of Science, HF, Heart Failure, COPD, chronic pulmonary disease, NMD, neuromuscular disorder, OSA, obstructive sleep apnea, PSG, polysomnograph.

larger treatment outcomes than similar larger more robust trials [64,65]; however, the reason for this phenomenon is unknown and some authors have proposed methods that utilize small studies for use in meta-analysis models [47,68]. Thus, future research is needed to examine if small trials are correlated with larger treatment.

It can be argued that in order to accurately determine whether exercise is associated with a reduction in OSA indices, a high

number of patients diagnosed with OSA would have to be enrolled in an RCT, have a low level of attrition, and conduct annual follow-up diagnoses. However, to enroll thousands of patients in a clinical trial of this magnitude would require years and could prove expensive to funding agencies.

Our meta-analysis represents the most recent literature on OSA and exercise; however, our study selection was restricted by our inclusion and exclusion criteria and was not exhaustively inclusive

of all articles or studies on OSA, OSA and exercise, and OSA management. However, future meta-analysis may be conducted on the efficacy of supervised compared to unsupervised exercise as treatment, and a mixed treatment comparison of the current recommendations for management of OSA by The American College of Physicians.

5. Conclusion

In this meta-analysis of exercise as the sole treatment for OSA differences in AHI between patients in exercise programs compared to those not enrolled in an exercise program were statistically significant. However, the reduction in OSA indices may need to be further explored via comparison of larger participant numbers, supervised and unsupervised exercise programs, frequency of treatment, treatment duration, and exercise protocols. Though lifestyle intervention, upper airway surgery, mandibular advancement, and CPAP have shown similar decreases in OSA indices, exercise programs as treatment reduce AHI and the underlying causes of OSA.

Disclosure statement

This was not an industry supported study. The authors have no conflict of interest or financial involvement with this manuscript.

Author contributions

Kenneth D. Aiello had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors made substantial contributions to the study and this manuscript. None were compensated for the manuscript preparation.

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