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Effects Of Exercise Training On Resting Testosterone Concentrations In Sedentary Men: A Systematic Review And Meta-Analysis

Nolan James Potter

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EFFECTS OF EXERCISE TRAINING ON RESTING TESTOSTERONE
CONCENTRATIONS IN SEDENTARY MEN: A SYSTEMATIC REVIEW AND
META-ANALYSIS

by

Nolan James Potter

Bachelor of Science in Athletic Training, Shawnee State University, 2016

A Thesis

Submitted to the Graduate Faculty

of the

University of North Dakota

in partial fulfillment of the requirements

for the degree of

Master of Science in Kinesiology

Grand Forks, North Dakota

May

2020

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This thesis _____, submitted by Nolan Potter _____ in partial fulfillment of the requirements for the Degree of Master of Science in Kinesiology from the University of North Dakota, has been read by the Faculty Advisory Committee under whom the work has been done and is hereby approved.

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Table of Contents

List of Figures	vii
List of Tables	viii
Acknowledgments.....	ix
Abstract.....	x
Introduction	12
Methods.....	15
Protocols and registration	15
Eligibility criteria	15
Information sources.....	15
Search	16
Study Selection	16
Data Collection Process	17
Data Items.....	17
Quality assessment	17
Summary measures and synthesis of results.....	18
Results.....	19
Study selection.....	19
Study characteristics	20
Methodological quality	22
Synthesis of results	22
Overall.....	22

Resistance vs. Aerobic training	23
Old vs. Young.....	24
Weight Status.....	25
Discussion	27
References	32
Appendices.....	37
Appendix 1.	37
Appendix 2.	37

List of Figures

Figure	Page
1. Prisma flow chart outlining the flow of studies through the review.....	19
2. Forrest plot of overall effect.....	22
3. Forrest plot of resistance training effect.....	23
4. Forrest plot of aerobic training effect.....	23
5. Forrest plot of young age training effect.....	24
6. Forrest plot of old age training effect.....	25
7. Forrest plot of obese training effect.....	26
8. Forrest plot of non-obese training effect.....	26

List of Tables

Table	Page
1. Description of training for included studies.....	20

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I want to express my appreciation to all my advisory committee members for their support and guidance throughout my time in the master's program at the University of North Dakota.

Abstract

Background: The anabolic hormone testosterone plays a pivotal role in the healthy aging of men and tends to decline with age.

Objective: The aims of this systematic review and meta-analysis were twofold: 1) to evaluate the effect of exercise training on resting total testosterone concentration in men; and 2) to determine if the effects of exercise training differed by training type, age or weight status.

Methods: Electronic databases (MEDLINE, Scopus, CINAHL, and SPORTDiscus) were systematically searched (up to and including 19 September 2019) for peer-reviewed randomized controlled trials (RCTs) meeting the following criteria: apparently healthy, previously sedentary men (aged ≥ 18 years) participating in exercise training (any modality and ≥ 4 metabolic equivalents) lasting a minimum of 4 weeks, and reporting the effect of exercise training, in comparison to a sedentary controls, on resting total testosterone concentration. Intervention effects, weighted by the inverse of the pooled variance, were calculated relative to the control group as standardized mean differences.

Results: Ten RCTs were identified and descriptive data were extracted. Data from 389 men aged 20–70 years across 14 intervention groups participating in aerobic, resistance, or combined training lasting a median of 12 weeks, were included in the analysis. Overall, exercise training had a negligible effect on resting total testosterone

concentration (mean SMD [95% CI]: 0.02 [-0.22 to 0.18]). Subgroup analyses indicated that the effect of exercise training was not significantly influenced by training type age, or weight status.

Conclusions: Exercise training does not appear to affect resting total testosterone concentration in previously sedentary, eugonadal men.

Introduction

Testosterone, an anabolic-androgen hormone, plays a pivotal role in the healthy aging of men. Serum testosterone concentration in men tends to decline with age, and by the age of 45 years, roughly one-third of United States men meet the initial criterion for hypogonadism (total testosterone concentration <300 ng/dL) (Bhasin et al., 2018). Low serum testosterone concentration in men is associated with all-cause mortality (Araujo et al., 2011), cardiovascular disease (Traish, Saad, Feeley et al., 2009), type II diabetes (Traish, Saad & Guay, 2009), sarcopenia (Ottenbacher et al., 2006), depression and other cognitive impairments (Zarrouf et al., 2009). Low serum testosterone concentration in men has also been associated with physical changes (e.g., reduced muscle mass, reduced muscle function [Emmelot-Vonk et al., 2008; Ottenbacher et al., 2006], increased fat deposition [Kelly & Jones., 2013]), which may negatively impact physical function. It was estimated that the United States spent \$190–525 billion in direct costs over a 20-year period treating patients with health conditions attributed to hypogonadism in men (Moskovic et al., 2013), with costs of testosterone replacement therapy near US\$5 billion per year (Braun, 2013).

Findings from randomized controlled trials (RCTs) indicate testosterone replacement therapy — administering exogenous testosterone (e.g., Testosterone enanthate) to return resting serum testosterone to within the physiologic range (i.e., 303 to 852 ng/dL; Bhasin et al., 2018) in hypogonadal men has positive effects on libido, erectile function, sexual

activity, mood (i.e., decreased negative and increased positive aspects), body composition (i.e., decreased fat mass and increased fat-free mass), muscle strength, and bone mineral density and strength (Bhasin et al., 2018). Possible side effects of testosterone replacement include infertility, polycythemia (Chin-Yee et al., 2017), gynecomastia (Rhoden & Morgentaler, 2004), sleep apnea, liver toxicity, and prostate hypertrophy (Bassil et al., 2009). In addition, there is apprehension about the effect of testosterone replacement on cancer and cardiovascular disease risk (Braun, 2013; Schwartz & Woloshin, 2013); however, the longitudinal evidence needed to evaluate these relationships is currently insufficient (Bhasin et al., 2018). It is possible that side effects associated with testosterone replacement may, in part, be due to altered patterns of blood testosterone concentrations resulting from alterations in pulsatile secretion and usual diurnal variation. Compared to pharmacological intervention, maintaining or achieving a physiologic resting serum testosterone concentration through lifestyle changes (e.g., diet and exercise) is preferable as it would preserve natural hormone kinetics, decrease patient risk and reduce treatment costs.

To date, most of the literature investigating the effectiveness of therapeutic lifestyle changes on resting serum testosterone concentration has focused on weight loss, though experimental trials employing exercise training interventions are starting to accumulate. In a meta-analysis of dietary restriction and bariatric surgery trials, Corona et al. (2013) reported small-to-moderate benefits of weight loss on resting serum testosterone concentration. Although studies have reported increases in serum testosterone concentration during, or immediately after, high-intensity exercise in men (O'Leary &

Hackney, 2014; McMurray & Hackney, 2005), Hayes and Elliot (2019) found small, albeit inconsistent, increases after chronic exercise training on resting serum testosterone concentration in a recent meta-analysis of older men. It is not known, however, whether the results from Hayes and Elliot (2019) are generalizable to younger and middle-age men (i.e., <60 years). Furthermore, most studies included in the Hayes and Elliot (2019) meta-analysis were uncontrolled trials, with resting serum total testosterone, free testosterone, and bioavailable testosterone included in the analyses, which cloud the interpretation of the effects of exercise on testosterone. The clinical guidelines set forth by the Endocrine Society (Bhasin et al., 2018) recommend measurement of serum total testosterone and/or free testosterone, depending on certain patient characteristics (e.g., obesity, aging, diabetes), for the diagnosis of hypogonadism. However, few RCTs evaluating the effects of exercise training report serum free testosterone and large inter-assay variation complicates its interpretation (Bhasin et al., 2018). RCTs provide the best evidence for causality as they are less prone to bias and confounding, and meta-analyses of RCTs best guide recommendations to practitioners. Therefore, the aim of this systematic review and meta-analysis was to evaluate the effect of exercise training on resting serum total testosterone concentration in previously sedentary, apparently healthy men when including only RCTs. The secondary aim of this study was to determine whether the effects of exercise training on resting serum total testosterone concentration differed by training type, age or weight status.

Methods

Protocols and registration

The review protocol was prospectively registered with the International Prospective Register of Systematic Review (PROSPERO; 131461). This review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009).

Eligibility criteria

Studies were eligible for inclusion if they reported on the effects of exercise training (e.g., aerobic, resistance) on resting total testosterone concentration in previously sedentary, apparently healthy men (aged ≥ 18 years). Studies were not excluded on the basis of recruiting men with low testosterone concentration or exhibiting signs and symptoms of hypogonadism. Only RCTs lasting a minimum of four weeks and reporting pre- and post-intervention resting total testosterone concentration assessed from serum or changes in such concentration, were included. It was a requirement that the control group maintained sedentary behavior throughout the study period. Studies were excluded if the training intervention was below moderate intensity (4 Metabolic Equivalents of Task [METs]) (Garber et al., 2011), or was conducted in special interest groups (e.g., elite athletes). Only studies published in peer-review journals were considered. While systematic reviews were not included, the reference lists of topical reviews were searched for candidate RCTs.

Information sources

A systematic search of the literature was performed on the 27th of January 2019 in Medline, Cumulative Nursing and Allied Health Literature (CINAHL), Scopus, and SPORTDiscus, without date restrictions. A secondary search was performed on the 19th of September 2019 with date restrictions of from the 1st of January to the 19th of September 2019. All the sources were limited to the English language. An academic librarian experienced in systematic reviews was consulted during the search strategy development, with the search strategy piloted by two researchers to identify the combination of search terms most likely to yield relevant articles.

Search

The systematic search was limited to the abstract, title and keywords. Search terms that were included in a group were combined by the Boolean OR, and entered before being combined by the Boolean AND. For some search terms, proximity operators were used to search for the root word. Selection of search terms was informed by the PICO method. First group of search terms identified exercise training intervention (exercise training, aerobic training, resistance training, high intensity interval training, and sprint training); the second group identified the outcome (testosterone, hormone*, and androgen*); and the third group identified the participants (men, males). RCT's were then screened at the full text level. Appendix 1 shows the full search strategies for each database.

Study selection

One researcher executed the database search strategy and imported all results into RefWorks. At the first level, two researchers independently screened all studies by title

and abstract. At the second level, two researchers independently screened all studies at the full-text level. Consensus (at both levels) was required between both researchers for final inclusion; if not, then a third researcher resolved any discrepancies. The reference lists of included studies were also examined. Two experts were also contacted to locate additional studies, with such studies were evaluated against inclusion criteria.

Data collection process

Descriptive data from included studies were extracted and imported into a study-specific template created in Excel (Microsoft Corp.; Redmond, WA, USA). Data were extracted independently by two reviewers and examined for errors.

Data items

The following descriptive data were extracted: study title, training exposure (exercise modality, training volume, and sessional intensity, frequency, and duration) age, height, mass, body mass index (BMI), serum testosterone assay, pre-test, post-test and/or change measures for testosterone concentration (sample sizes, means, and standard deviations), and effect size data. Serum free-testosterone concentration data were extracted if available. For each study, exercise intensity (METs) and volume (MET minutes per week) were estimated from reported descriptive data using intensity classifications described by Garber et al. (2011).

Quality assessment

The Physiotherapy Evidence Database (PEDro) tool for RCTs was used to assess the quality of included studies. The PEDro tool assesses a studies methodological quality and completeness in reporting using an 11-criteria scale. Scores range from 0–10 points as the first criterion is not scored. Scores of 0–3, 4–5, and 6–10 were interpreted as poor, moderate, and high quality, respectively. The PEDro tool exhibits good reliability (Maher et al., 2003). Quality assessment was independently conducted by two reviewers. The intraclass correlation coefficient determined the test-retest agreement between raters.

Summary measures and synthesis of results

Meta-analyses were performed in RevMan 5 (v5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The primary analysis was conducted to determine the overall effect of exercise training on resting serum total testosterone concentrations in previously sedentary, apparently healthy men, with secondary subgroup analyses conducted to determine whether the overall training effect was influenced by age, training type, age or weight status. Standardized mean differences (SMDs) weighted by the inverse of the pooled variance, and corresponding 95% confidence intervals, were calculated for each intervention group using a random effects model. Experimental effects were calculated relative to the control group using the weighted mean-difference method. Positive mean differences indicated favorable experimental effects and negative mean indicated unfavorable experimental effects. SMDs were interpreted using Cohen's (1988) thresholds of 0.2, 0.5 and 0.8 for small, medium and large, respectively, with SMDs <0.2 considered to be negligible. Statistical heterogeneity was quantified using the I^2 statistic, with values of 25%, 50% and 75% used as thresholds for small, medium, and

large, respectively (Higgins & Greene, 2011). Funnel plot asymmetry analysis was used to assess the risk of publication bias for only the primary analysis, because the power of this test to distinguish chance from real asymmetry is too low when there are fewer than 10 comparison groups (note, all subgroup analyses comprised fewer than 10 comparison groups) (Higgins & Green, 2011).

Results

Study selection

A total of 3354 unique articles were located through the online database search, with 68 studies retained after the first level of screening (title and abstract), and 7 studies retained after the second level of screening (full-text). Three additional studies were located from reference list searching (n=1) and consultation with experts (n=2), resulting in a total of 10 included studies. Figure 1 shows the identification of included studies.

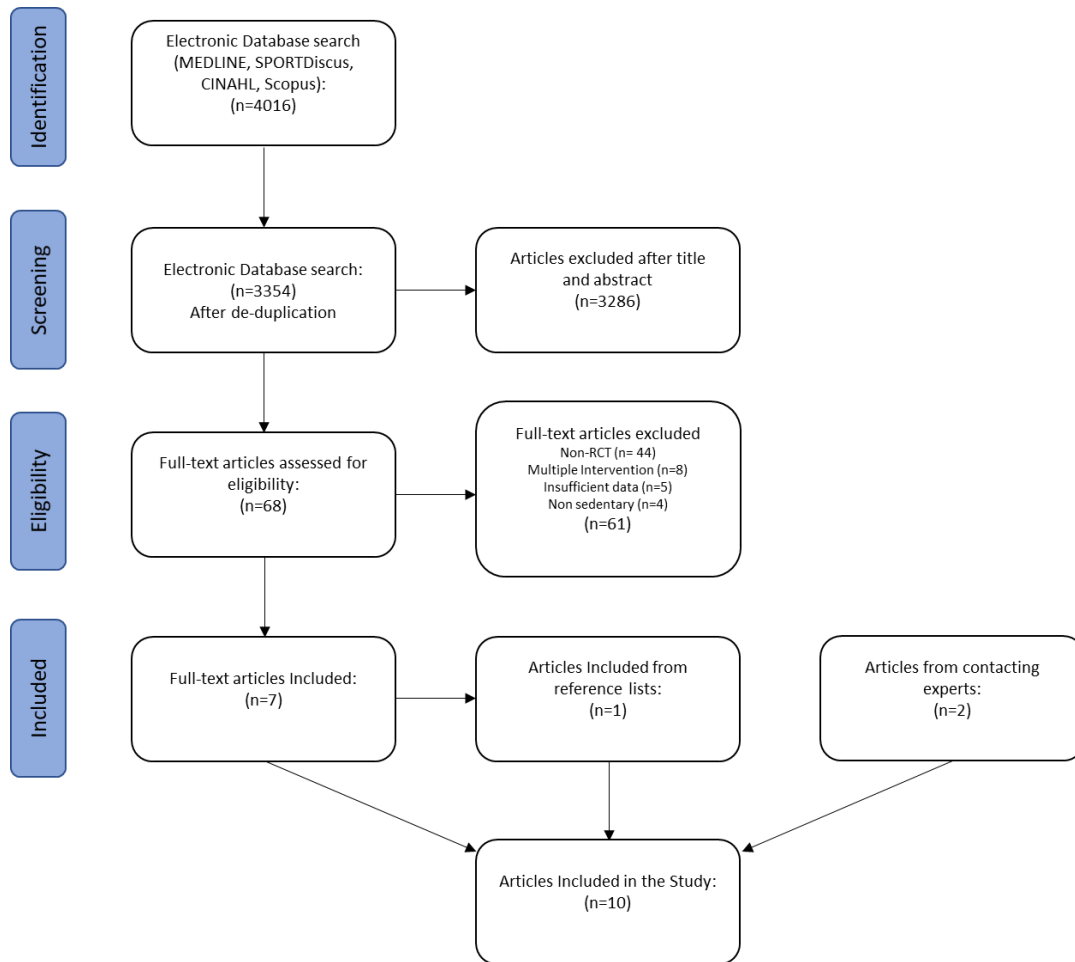


Figure 1. Prisma diagram showing flow of studies through the systematic review

Study characteristics

All RCTs were published in English between 2004 and 2018, collectively represented 389 previously sedentary, apparently healthy men with a mean±SD age range from 20±1 to 75.2±3.0 years. Overall, there were 14 intervention groups utilizing three types of exercise training (resistance [n=9], aerobic [n=3], and a combination of resistance and aerobic [n=2]) lasting between 8 and 52 weeks in duration. Study characteristics are presented in Table 1.

Table 1. Description of training for included studies

Study	Exercise Group Resting Testosterone Change Mean(SD)	Control Group Resting Testosterone Change Mean(SD)	Sample Size E (n)	Sample Size C (n)	Age (years) Mean(SD)	Country	Training Duration (weeks)	Frequency (per week)	Training Type	Training Program	PEDro score
Ahtianinen et al., 2011 (young)	8.7(100)	49(162)	7	10	E: 28(5) C: 25(3)	Finland	21	2	Resistance	3 leg exercises and 4–5 upper body, 3 7week phases. P: 1: multiple sets, 10–20 reps,40–60% 1 RM, P: 2: multiple sets 8–12 reps, 60–80% 1RM. P:3: multiple sets 5–8reps, 70–90% 1RM	6
	(old)	23(138)	10	8	E: 61(5) C: 64(8)						
Harber et al., 2004	-32(253)	5.8(254)	8	4	E: 24(1.8) C: 21(1.0)	USA	10	3	Resistance	10 exercises 1–3 sets 12–20 reps at 40–60% 1RM	6
Hawkins et al., 2008	-16(169)	-12(192)	50	51	E: 56(6.7) C: 56(7.6)	USA	52	6	Aerobic	60 min sessions at 60–85% HRmax (e.g., treadmill, rowers, stationary bike)	7
Hiruntrkul et al., 2010	23(162)	47(124)	19	18	E: 21(2) C: 20(1)	Thailand	14	1	Aerobic	5 min warm up followed by 50 min biking at 60% VO _{2max} and 5 min cool down	6
Katznelson et al., 2006	15(189)	14(125)	16	16	E: 72(5.4) C: 72(5.2)	USA	12	3-4	Resistance	11 extremity and trunk resistance strengthening exercises using therabands	6
Lovell et al., 2012	RT: 17(100) AT: 32(134)	32(172)	RT: 10 AT: 11	11	RT: 74(2.1) AT: 75(3.0) C: 74(3.3)	Australia	16	3	Resistance	Incline squat 3 sets of 8 at 50% 1RM increased to 6–10 reps at 70– 90% 1RM Cycling at 50% VO _{2max} 30 min increasing to 70% VO _{2max} for 45 min.	6
					Aerobic						
Moradi et al., 2015	130(240)	-30(190)	10	11	E: 27(2.8) C: 27(2.9)	Iran	12	3	Resistance	10 exercises at 3 sets of 8–12 reps at 60–80% 1RM. 20–40 min per session.	6
Roberts et al., 2012	-20(118)	3.3(121)	28	8	E: 22 C: 22	USA	12	3	Resistance	8 upper and lower body exercises. Phase 1-2 weeks, 2 sets 12–15 reps at 100% effort; Phase 2–4 weeks, 3 sets 8–12 reps at 100% effort; Phase 3–4 weeks, 2 sets 6–8 reps at 100% effort	5
Sedliak et al., 2018	M: -66(276) A: 28(91)	97(201)	M:11 A: 7	7	ME: 23(2) AE: 24(4) C: 24(3)	Slovakia	11	2	Resistance	3 Leg exercises and 5 core and upper body exercises. First 5 weeks at 40–60% 1RM 10–15 reps for 3 sets; Second 6 weeks increased to 50–80% 1RM 8–12 reps in 4 sets.	4
Sheikholeslami et al., 2015	CRE: 30(120) CER: 10(160)	-20(130)	CRE: 10 CER: 10	10	23(1.4)	Iran	8	3	Concurrent	Running at 70–75% HRmax or 10 min increase to 80% for 21.5 min then 5 resistance exercises 3 sets of 8 at 80% 1RM	4

Note: RT = resistance training; AT = aerobic training; E = exercise group; C = control group; M = morning group; A = afternoon group, CRE= concurrent-resistance-endurance group, CER= concurrent endurance-resistance group, RM= repetition max, VO_{2max} = maximal oxygen uptake, Change mean data in ng·dL⁻¹, Heart Rate= HR.

Methodological quality

There was perfect agreement (ICC=1.00) between the two reviewers who assessed methodological quality using the PEDro scale. Included studies were moderate-to-high in quality, with scores ranging from 4/10 (n=2) to 7/10 (n=1) and most scoring 6/10 (n=6). None of the studies scored positive for blinding of subjects and therapists. One study did have blinding of assessors. All studies scored positively for similar baseline, random allocated to groups, point measures and comparison between groups.

Synthesis of results

Overall

Serum testosterone concentration change data were collected from 10 studies (14 interventions) representing 389 previously sedentary, apparently healthy men. Mean testosterone concentration for the exercise training group was 496 ± 72 ng·dL⁻¹ at the start of the study. Exercise training had a negligible effect on testosterone concentration (mean SMD [95% CI]: 0.02 [-0.22 to 0.18]).

The heterogeneity for exercise training on testosterone concentration was negligible ($I^2=0\%$) and the funnel plot showed no evidence of asymmetry.

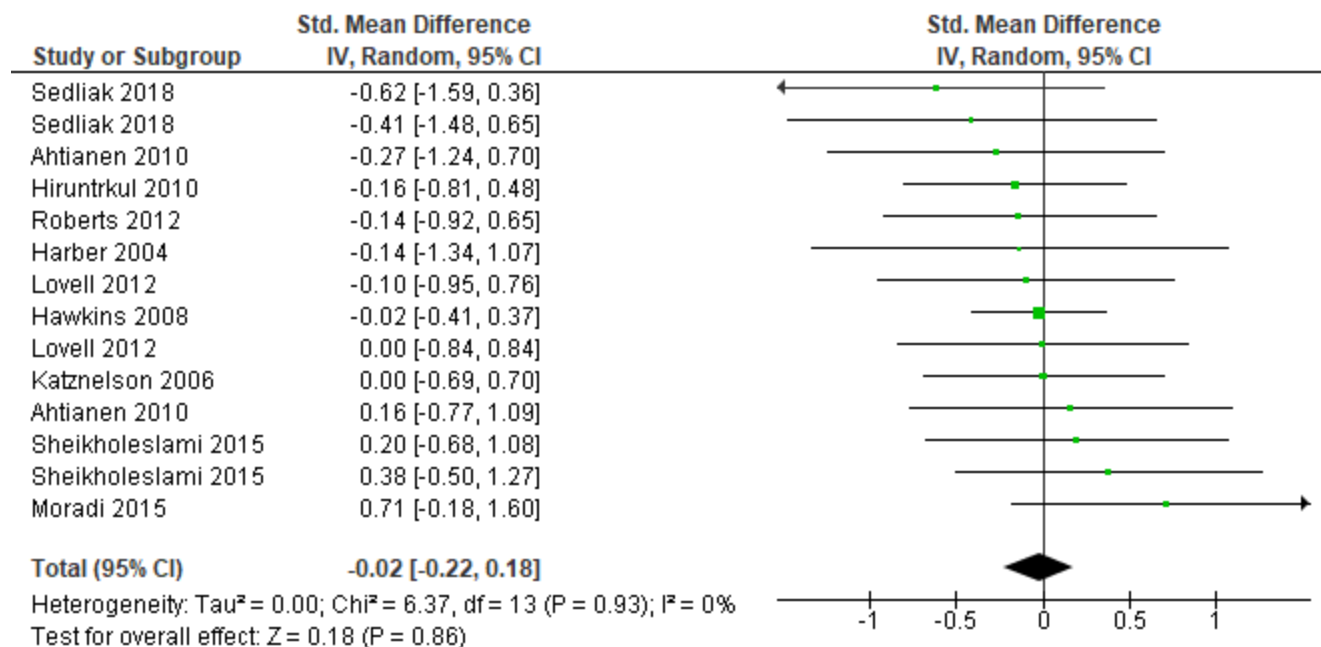


Figure 2. Forest plot of the overall exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration. The green dots represent the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represent the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

Training type

After stratifying for exercise training type (resistance [n=9] vs. aerobic [n=3]), neither the results from resistance nor aerobic training groups differed from the results of the overall analysis. Mean testosterone concentration for the resistance training group was 500 ± 87 ng·dL⁻¹ at the start of the study. Resistance training had a negligible effect on testosterone concentration (mean SMD [95% CI]: -0.06 [-0.36 to 0.24]). Mean testosterone concentration for the aerobic training group was 478 ± 47 ng·dL⁻¹ at the start of the study. Aerobic training had a negligible effect on testosterone concentration (mean SMD [95% CI]: -0.05 [-0.36 to 0.26]). The heterogeneity for both resistance and aerobic training on testosterone concentration was negligible (I²=0%).

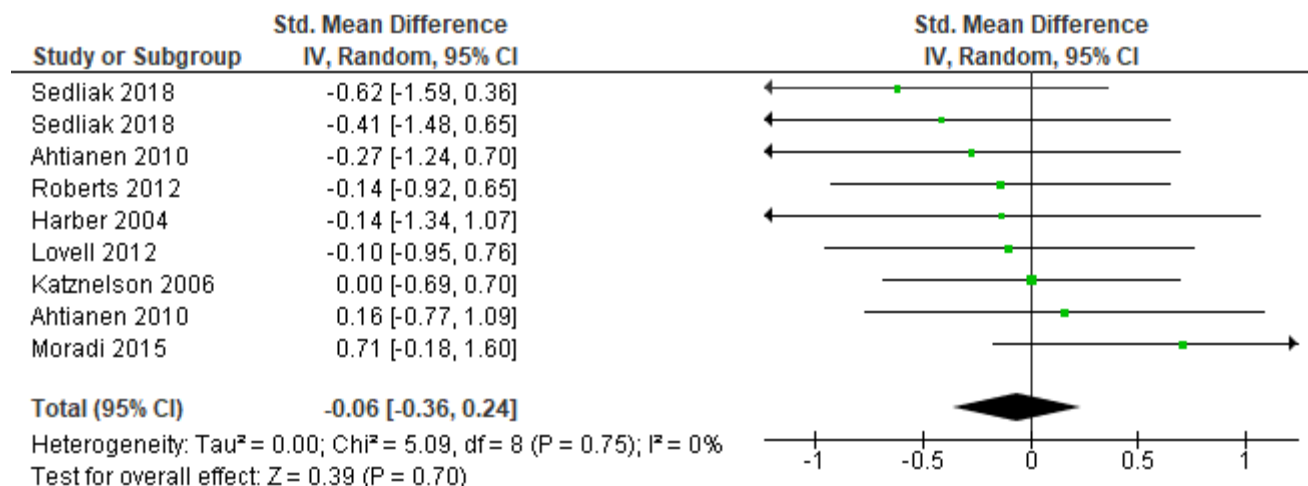


Figure 3. Forest plot of resistance exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in men. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

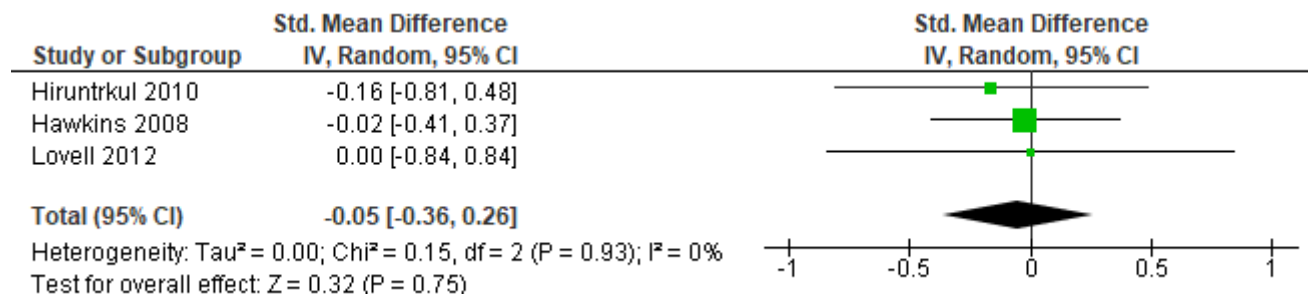


Figure 4. Forest plot of the aerobic exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in men. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

Age

After stratifying for age (younger men [<60 years; $n=10$] vs. older men [≥ 60 years; $n=4$]), neither the results from younger nor older men differed from the results of the overall analysis. Mean testosterone concentration for the younger exercise training group was 519 ± 73 ng·dL⁻¹ at the start of the study. Overall, exercise training had a negligible effect on testosterone concentration in younger men (mean SMD [95% CI]: -0.03 [-0.26 to 0.21]). Mean testosterone concentration

for the older exercise training group was $440 \pm 27 \text{ ng} \cdot \text{dL}^{-1}$ at the start of the study. Overall, exercise training had a negligible effect on testosterone concentrations in older men (mean SMD [95% CI]: 0.01 [-0.40 to 0.42]). The heterogeneity for exercise training on testosterone concentration in both younger and older men was negligible ($I^2=0\%$).

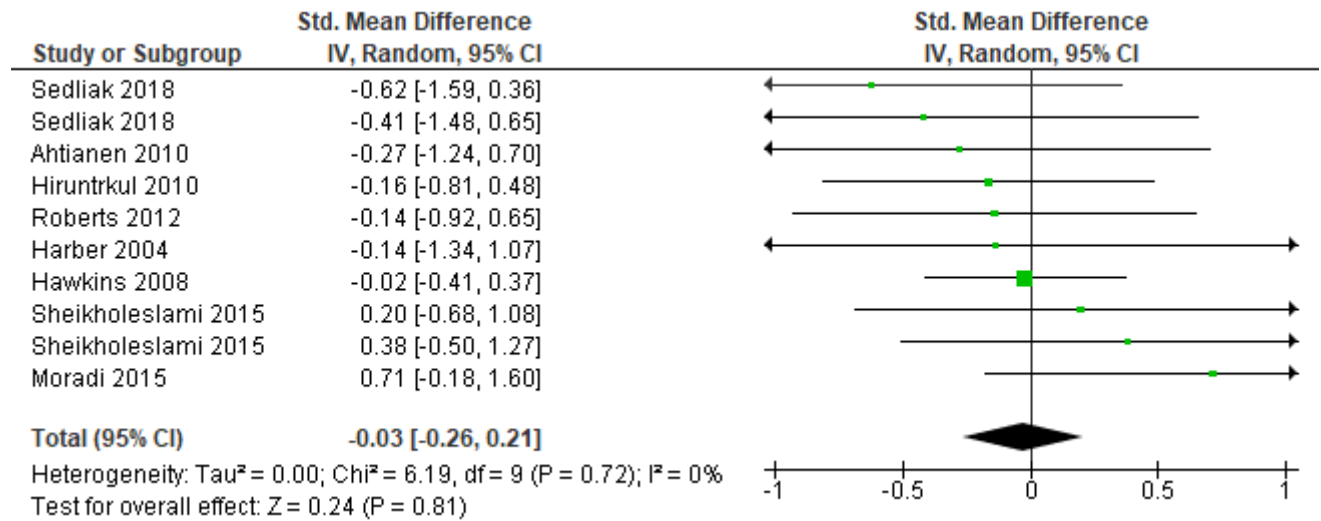


Figure 5. Forest plot of the overall exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in young men. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

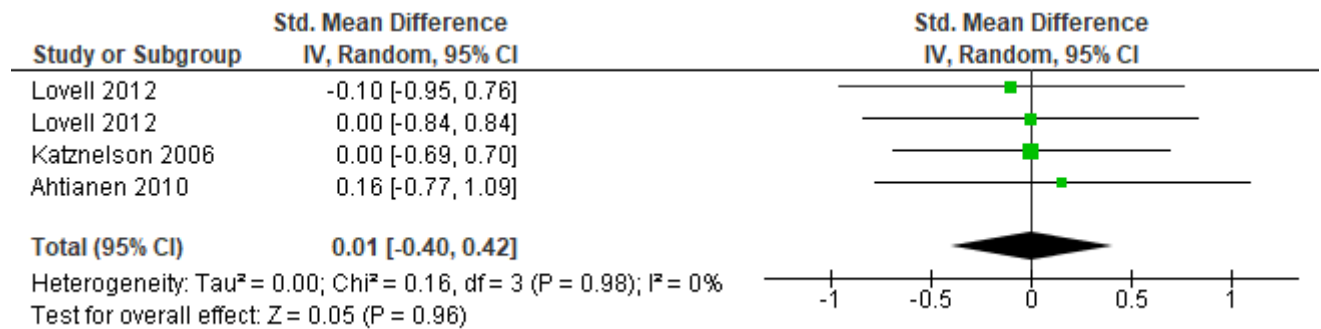


Figure 6. Forest plot of the overall exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in older men. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

Weight Status

The last subgroup analysis was stratified by weight status, with studies recruiting only obese participants (body mass index [BMI] ≥ 30) analyzed separately. Mean testosterone concentration for the obese exercise training group was 570 ± 106 ng·dL⁻¹ at the start of the study. Overall, exercise training had a small, non-significant effect on testosterone concentration in studies recruiting obese men (mean SMD [95% CI]: 0.43 [-0.08 to 0.94]). Mean testosterone concentration for the non-obese exercise training group was 476 ± 50 ng·dL⁻¹ at the start of the study. Overall, exercise training had a negligible effect on testosterone concentration in studies lacking obesity as an inclusion criteria (mean SMD [95% CI]: -0.10 [-0.33 to 0.12]). The heterogeneity for exercise training on testosterone concentration in both obese and non-obese men was negligible ($I^2=0\%$).

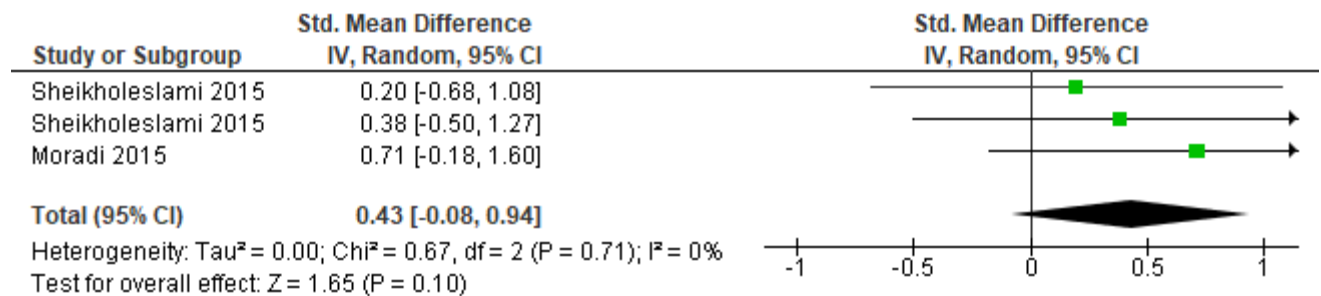


Figure 7. Forest plot of the overall exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in obese men. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

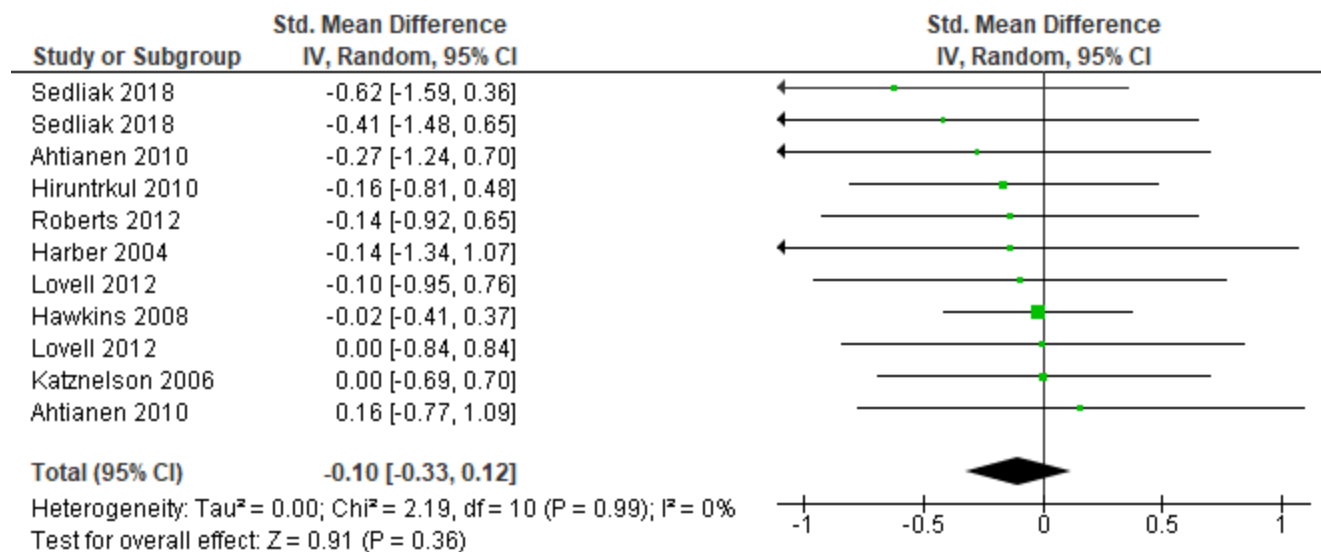


Figure 8. Forest plot of the overall exercise training effects (and 95% confidence intervals [CIs]) on resting serum testosterone concentration in non-obese participants. The green dots represented the serum testosterone concentration standardized mean differences (SMD) and the solid horizontal lines represented the 95% CIs. Positive SMDs indicated favorable experimental effects and negative SMDs indicated unfavorable experimental effects.

Discussion

The primary aim of this systematic review and meta-analysis was to evaluate the effect of exercise training on resting total testosterone concentration in previously sedentary, apparently healthy men. Overall, the effect of exercise training on total testosterone concentration was negligible, with the effect of exercise training did not differing significantly by training type, age or weight status.

In a recent meta-analysis, Hayes and Elliot (2019) found small effects of aerobic and interval, but not resistance, training on resting testosterone concentration in older men. Consistent with Hayes and Elliot (2019), the majority of the studies identified in our systematic review evaluated the effects of resistance training and found negligible effects of resistance training on resting

testosterone concentration. Collectively, these data indicate a lack of effectiveness of short-term (median duration: 12 weeks) resistance training to increase resting testosterone concentration in younger and older eugonadal men. In contrast to Hayes and Elliot (2019), we found aerobic training to have a negligible effect on resting total testosterone concentration in men. This discrepancy may be due to differences in exclusion criteria between studies (as our study was limited to RCTs in previously sedentary, apparently healthy men) and/or outcomes included in analyses (Hayes and Elliot [2019] included multiple measures of resting testosterone [total, free, and bioavailable testosterone] in analyses). In a subgroup analysis, we did not find evidence that the effects of exercise training on testosterone concentration differed by age (younger vs. older men). Additionally, resting testosterone concentration at the start of the study does not appear to explain differences between meta-analyses as the studies recruiting participants with lower testosterone concentration were included in the resistance training analysis in Hayes and Elliot (2019). However, we did find a trend toward a difference when analyses were stratified by weight status, with studies recruiting only obese participants yielding small, albeit non-significant, effects. A plausible explanation for this trend is that exercise training led to greater weight loss in obese men (-3.0 ± 1.1 kg or 3% decrease) when compared to non-obese men (0.3 ± 1.3 kg or 0.4% increase) in the included studies. Reduced fat mass, may reduce aromatization of testosterone to estradiol and reduce leptin resistance leading to increased gonadotropin secretion promoting a small increase in resting serum testosterone concentration (Carrageta et al., 2019). The effect of weight loss on both free and total resting testosterone concentration has been reported in a meta-analysis by Corona et al. (2013). On average, they found a 9.8% weight loss during dietary interventions associated with small increases in

testosterone concentration, which is slightly greater than the weight loss observed in the studies used for the meta-analysis in our study.

The results from our systematic review and meta-analysis do not support exercise training as an effective therapeutic lifestyle intervention for low testosterone concentration in previously sedentary, apparently healthy men, especially non-obese eugonadal men. It should be noted that mean resting testosterone concentration for all analyses in this study were above the threshold for hypogonadism and it is possible that testosterone concentration at the start of the study modifies testosterone concentration change in response to exercise training. Future RCTs should recruit hypogonadal men and evaluate the effect of exercise training on testosterone concentration using effect sizes and clinical endpoints (e.g., crossing threshold for hypogonadism). Furthermore, future research should evaluate the effect of exercise-induced weightloss on free and total testosterone concentration in obese men. However, if present, the effects of exercise training interventions are likely small and may not be clinically meaningful when testosterone concentration may be well below the physiologic range (Corona et al., 2013; Carrageta et al., 2019) and adherence to lifestyle interventions may be low (Lemstra et al., 2016). Of greater interest to practitioners may be the effect of exercise training on signs and symptoms of hypogonadism (e.g., reduced sexual function and desire, decreased mental health, infertility, increased body fat, decreased muscle mass and strength, and decreased bone mineral density), which are the primary diagnostic criterion in clinical settings as evaluation of testosterone concentration is not indicated until a patient reports one or more signs or symptoms (Bhasin et al., 2018). Evidence from RCTs indicates that exercise training may improve many of the signs and symptoms of hypogonadism, for example, sexual dysfunction (Hoffman et al 2009),

infertility (Hajizadeh Maleki & Tartibian, 2017), poor mental health (Penedo & Dahn, 2005), increased in body fat (Pendo & Dahn, 2005), decreased muscle mass, low strength (Beaudart et al., 2017), and low bone mineral density (Kelley et al., 2000). Future research should evaluate the effects of lifestyle change interventions on less studied outcomes to elucidate the effects of such interventions to allow for a better understanding of the practical utility of lifestyle interventions for the treatment of hypogonadism.

This study is not without limitations. Only 10 RCTs met our inclusion criteria, with exercise training programs varying greatly across studies (e.g., mode, intensity, volume, frequency). Statistical power to detect potentially meaningful effects of exercise training on testosterone concentration was limited in subgroup analyses. Most of the studies employed an exercise training frequency of three days per week or less and exercise session duration was difficult to ascertain for some studies but appeared to vary substantially from approximately 20 to 60 minutes across studies. It is possible that increased exercise training volume is required to increase testosterone concentration in men. The majority of men in the studies analyzed were eugonadal, which limits generalizability to clinical populations. Additionally, information relevant to signs and symptoms of hypogonadism was not tracked (or was not reported), nor were both free and total testosterone concentration assessed in the vast majority of studies. Studies failed to report on population demographic descriptive data (i.e., race, ethnicity), which limits our ability to comment on this aspect. The studies identified in this review were primarily of moderate quality as assessed using the PEDro scale. Future studies should utilize more rigorous study designs.

In conclusion, this systematic review and meta-analysis found exercise training to have a negligible effect on resting testosterone concentration in previously sedentary, eugonadal men, which did not differ significantly by training type, age or weight status. Future research should examine the effect of exercise training on testosterone concentrations in obese, hypogonadal men to determine if exercise training has a favorable effect on resting testosterone concentration. The role of exercise training in addressing signs and symptoms of hypogonadism needs further evaluation.

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Appendices

Appendix 1. Search strategy for databases.

Search terms

(exercise training OR aerobic training OR resistance training OR high intensity interval training OR sprint training) AND (testosterone OR hormone* OR androgen*) AND (men, males).

Databases

Search one

CINAHL No date specific to 27 January 2019): 594 studies identified.

MEDLINE No date specific to 27 January 2019): 1825 studies identified.

SPORTDiscus No date specific to 27 January 2019): 849 studies identified.

SCOPUS No date specific to 27 January 2019): 572 studies identified.

Search two

CINAHL January 2019 to 9 September 2019): 37 studies identified.

MEDLINE January 2019 to 9 September 2019): 80 studies identified.

SPORTDiscus January 2019 to 9 September 2019): 30 studies identified.

SCOPUS January 2019 to 9 September 2019): 29 studies identified.

Appendix 2. Funnel plot for primary effect of exercise training on testosterone

