

# Association of Efficacy of Resistance Exercise Training With Depressive Symptoms

## Meta-analysis and Meta-regression Analysis of Randomized Clinical Trials

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**IMPORTANCE** The physical benefits of resistance exercise training (RET) are well documented, but less is known regarding the association of RET with mental health outcomes. To date, no quantitative synthesis of the antidepressant effects of RET has been conducted.

**OBJECTIVES** To estimate the association of efficacy of RET with depressive symptoms and determine the extent to which logical, theoretical, and/or prior empirical variables are associated with depressive symptoms and whether the association of efficacy of RET with depressive symptoms accounts for variability in the overall effect size.

**DATA SOURCES** Articles published before August 2017, located using Google Scholar, MEDLINE, PsycINFO, PubMed, and Web of Science.

**STUDY SELECTION** Randomized clinical trials included randomization to RET (n = 947) or a nonactive control condition (n = 930).

**DATA EXTRACTION AND SYNTHESIS** Hedges *d* effect sizes were computed and random-effects models were used for all analyses. Meta-regression was conducted to quantify the potential moderating influence of participant and trial characteristics.

**MAIN OUTCOMES AND MEASURES** Randomized clinical trials used validated measures of depressive symptoms assessed at baseline and midintervention and/or postintervention. Four primary moderators were selected a priori to provide focused research hypotheses about variation in effect size: total volume of prescribed RET, whether participants were healthy or physically or mentally ill, whether or not allocation and/or assessment were blinded, and whether or not the RET intervention resulted in a significant improvement in strength.

**RESULTS** Fifty-four effects were derived from 33 randomized clinical trials involving 1877 participants. Resistance exercise training was associated with a significant reduction in depressive symptoms with a moderate-sized mean effect  $\Delta$  of 0.66 (95% CI, 0.48-0.83;  $z = 7.35$ ;  $P < .001$ ). Significant heterogeneity was indicated (total  $Q = 216.92$ ,  $df = 53$ ;  $P < .001$ ;  $I^2 = 76.0\%$  [95% CI, 72.7%-79.0%]), and sampling error accounted for 32.9% of observed variance. The number needed to treat was 4. Total volume of prescribed RET, participant health status, and strength improvements were not significantly associated with the antidepressant effect of RET. However, smaller reductions in depressive symptoms were derived from randomized clinical trials with blinded allocation and/or assessment.

**CONCLUSIONS AND RELEVANCE** Resistance exercise training significantly reduced depressive symptoms among adults regardless of health status, total prescribed volume of RET, or significant improvements in strength. Better-quality randomized clinical trials blinding both allocation and assessment and comparing RET with other empirically supported treatments for depressive symptoms are needed.

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Depression is a highly prevalent global burden, affecting more than 300 million people worldwide<sup>1</sup>; is a significant source of absenteeism and disability in the work force<sup>2</sup>; has an economic burden of approximately \$118 billion annually<sup>3</sup>; and is the most costly mental health disorder in Europe, accounting for 1% of the total gross domestic product.<sup>4</sup> Depressive symptoms are highly comorbid and significantly associated with poor health,<sup>5</sup> including an increased risk of cardiovascular diseases,<sup>6,7</sup> Alzheimer disease,<sup>8</sup> type 2 diabetes,<sup>9</sup> mortality,<sup>10</sup> and noncompliance with medical treatment.<sup>11</sup>

Current frontline treatments for depression include medication and psychotherapy. However, for individuals with mild to moderate or severe depression, medication can be expensive, with limited efficacy ( $d < 0.20$ ).<sup>12,13</sup> Psychotherapy can be expensive and inaccessible, and previously reported effects may be overestimated owing to publication bias.<sup>14</sup> Moreover, among individuals with depression who are seeking treatment, depressive symptoms persist for approximately 67% after first-line treatment of up to 14 weeks, and at least 30% remain depressed after 4 rounds of distinct 12-week treatments.<sup>15</sup> Thus, there is continued interest in alternative treatments for depression and continued need to compare potential alternative treatments with established treatments.

Exercise interventions are promising treatments for depressive symptoms, and these interventions are free from the adverse effects and high costs associated with antidepressant medications and psychotherapy.<sup>16,17</sup> Exercise interventions also have established benefits for cardiovascular diseases, the leading cause of death among individuals with major depressive disorder.<sup>6</sup> Exercise training improves depressive symptoms among otherwise healthy adults,<sup>18</sup> chronically ill adults,<sup>19</sup> and adults with a depressive disorder.<sup>17</sup> However, the magnitude of the effect remains unclear, as publication bias and flawed inclusion criteria may have resulted in underestimations of the magnitude of exercise effects.<sup>17,20</sup> The benefits of acute aerobic exercise and aerobic exercise training (AET) for depressive symptoms among otherwise healthy adults and chronically ill adults are well established,<sup>18,19,21,22</sup> but less is known regarding the associations of resistance exercise training (RET) with depressive symptoms. In addition, few trials have included both an RET and an AET arm in the same investigation, limiting direct comparisons between the modalities.

Resistance exercise training interventions are generally designed to increase strength, skeletal muscle mass, endurance, and/or power.<sup>23</sup> Evidence has supported significant anxiolytic effects of RET among adults, regardless of their health status,<sup>24</sup> and a previous narrative review supported the antidepressant effects of RET.<sup>25</sup> However, no quantitative synthesis of randomized clinical trials (RCTs) of the antidepressant effect of RET has been conducted. Furthermore, there is a need to identify potential sources of variability in the antidepressant effect of RET, particularly modifiable participant and trial characteristics, to better inform the prescription of RET and future RET interventions.

The key objectives of this meta-analysis and meta-regression analysis were to estimate the overall association of

## Key Points

**Question** What is the overall association of efficacy of resistance exercise training with depressive symptoms, and which logical, theoretical, and/or prior empirical variables are associated with depressive symptoms?

**Findings** In this meta-analysis of 33 clinical trials including 1877 participants, resistance exercise training was associated with a significant reduction in depressive symptoms, with a moderate-sized mean effect. Total volume of resistance exercise training, health status, and strength improvements were not associated with the antidepressant effect; however, smaller reductions in depressive symptoms were derived from trials with blinded allocation and/or assessment.

**Meaning** The available empirical evidence supports resistance exercise training as an alternative and/or adjuvant therapy for depressive symptoms.

efficacy of RET with depressive symptoms; determine the extent to which the overall effect varies based on variables of logical, theoretical, and/or prior empirical variables associated with depressive symptoms; and compare the effect of different exercise modes derived from RCTs in which participants were randomized to RET, AET, or a nonactive control condition.

## Methods

### Data Sources and Searches

This systematic review was conducted in accordance with the PRISMA guidelines.<sup>26</sup> Articles published before August 2017 were identified using Google Scholar, MEDLINE, PsycINFO, PubMed, and Web of Science. Key words used included combinations of *strength training*, *resistance training*, and *weight training*, along with *depress\**. Supplementary searches of relevant systematic reviews<sup>17,18,24,25,27</sup> and references within included articles were performed manually.

### Study Selection and Inclusion Criteria

Inclusion criteria were peer-reviewed publication, clinical trials, randomized allocation to either an RET intervention or a nonactive control condition, and a validated self-report or clinician-rated measure of depressive symptoms assessed at baseline and at midintervention and/or postintervention. Investigations were excluded that included exercise as part of a multicomponent intervention but did not include the additional component in comparison conditions, and/or compared RET only with an active treatment for depression, including cognitive therapy, pharmacotherapy, relaxation or meditation, and flexibility training. One article<sup>28</sup> was excluded because the depressive outcomes were reported in an earlier included article.<sup>29</sup> eFigure 1 in the [Supplement](#) provides a flowchart of article inclusion and exclusion.

### Data Extraction

Data were extracted from the included RCTs into an SPSS (SPSS Inc) file by 3 of us (B.R.G., C.P.M., and M.P.H.). The data extracted included the characteristics of the participants and the

trials and the associations of exercise with outcomes of logical, theoretical, and/or prior empirical relation to depressive symptoms and/or the associations of RET with depressive symptoms; these included age, sex, physical and mental health status, type of control condition, whether allocation and/or assessment were blinded, duration of exercise program, frequency, session duration, RET intensity, whether or not RET sessions were supervised, whether or not the primary outcome of the trial was depressive symptoms, depressive symptom measure used, and whether or not there was a significant improvement in strength. To calculate total volume of RET prescribed, intervention duration (weeks), weekly frequency (days), and session duration (minutes) were multiplied together.

### Study Quality Assessment

Two of us (B.R.G. and M.P.H.) independently assessed trial quality (scored 0-13) using the Detsky scale.<sup>30</sup> This scale was amended to include research design, control condition, randomization and blinding methods, outcome measures, adherence, and characteristics of the exercise intervention. Higher scores indicated better study quality. The individual scores of each included RCT are presented in eTable 1 in the Supplement.

### Effect Size Calculation

To calculate Hedges *d* effect sizes, the mean change for the control was subtracted from the mean change for RET, and the difference was divided by the pooled baseline SD.<sup>31</sup> Larger reductions in depressive symptoms for RET resulted in positive effect sizes. eTable 2 in the Supplement presents the values used to calculate Hedges *d* and primary moderator values. Interrater reliability for effect size calculations was examined by calculating 2-way (effects × raters) intraclass correlation coefficients for absolute agreement. The initial intraclass correlation coefficients were greater than 0.90. When means and SDs were not reported, the authors were contacted. When these values could not be provided (*k* = 5), they were estimated from exact *P* values reported in the trial,<sup>32</sup> included graphs,<sup>33,34</sup> or from the largest other study of the same population sample that used the same measure of depressive symptoms,<sup>35,36</sup> in accordance with common meta-analytic protocols.<sup>37</sup> Discrepancies (eg, values of SDs estimated from included graphs) were resolved by consensus among the investigators involved in the data extraction (B.R.G., C.P.M., and M.P.H.).

### Data Synthesis and Analysis

Meta-regression was used for moderator analyses because it reduces the probability of type I error by computing concurrent estimates of independent effects by multiple moderators on the variation in effect size across trials. Random-effects models were used with macros (MeanES; MetaReg)<sup>38</sup> to aggregate the mean effect size delta ( $\Delta$ ) and test the variation in effects according to moderator variables.<sup>31,38</sup> Heterogeneity was evaluated with Cochrane *Q*, and consistency was evaluated with *I*<sup>2</sup>.<sup>37</sup> If sampling error accounted for less than 75% of the observed variance, heterogeneity was indicated.<sup>31</sup> The mean reduction in depressive symptoms among partici-

pants engaging in RET, expressed as a function of absolute risk reduction, was calculated to determine the number needed to treat.<sup>39</sup> The number of unretrieved or unpublished studies of null effect that would diminish the significance of observed effects of *P* > .05 was estimated as fail-safe *N*.<sup>40</sup>

As a sensitivity analysis, the mean effect was recalculated, extracting single effects from the included RCTs determined by the effect with the maximum dose of RET, and the effect in which the Beck Depression Inventory was used,<sup>41</sup> for homogeneity of results. There were 3 exceptions in which 2 effects remained extracted from single RCTs because these RCTs each contained 2 treatment groups and 2 control groups.<sup>33,42,43</sup>

To examine publication bias, funnel plot symmetry was examined, Egger regression<sup>44</sup> and Begg rank correlation tests were calculated,<sup>45</sup> and trim and fill analysis adjusting to the left of the mean was performed.<sup>46</sup> Potential outliers, effects substantially larger than most, were also removed, and the mean effect size  $\Delta$  was recalculated for additional sensitivity analysis.

### Primary Moderators

Four primary moderators were selected a priori to provide focused research hypotheses about variation in effect size: total volume of prescribed RET, participant's health status, whether or not allocation and/or assessment was blinded, and whether or not the RET intervention resulted in a significant improvement in strength. Definitions for each primary and secondary moderator and associated levels are presented in eTable 3 in the Supplement.

### Primary Moderator Analysis

Each of the 4 primary moderators were coded according to the planned contrasts (*P* ≤ .05) among its levels.<sup>47</sup> Primary moderators were included in the mixed-effects multiple linear regression analyses with maximum likelihood estimation, adjusting for nonindependence of multiple effects contributed by single studies, baseline depressive symptoms, and the depressive symptom measure.<sup>31,38</sup> Tests of the regression model (*Q*<sub>R</sub>) and its residual error (*Q*<sub>E</sub>) are reported.

### Univariate Meta-regression Analyses

Secondary moderators were selected for exploratory univariate analyses. Random-effects models were used to calculate the mean effect sizes ( $\Delta$ ) and 95% CIs for moderator variables.<sup>38</sup> Each secondary moderator was included in random-effects univariate meta-regression analysis with maximum likelihood estimation.<sup>31,38</sup>

## Results

### Study Characteristics

Fifty-four effects were derived from 33 RCTs of 1877 participants (RET group, 947 participants; control group, 930 participants). Table 1 presents the relevant characteristics for each of the included RCTs.<sup>28,32-36,42,43,48-72</sup> Depressive symptoms were the primary outcome in 18 RCTs (*k* = 37). The mean (SD)

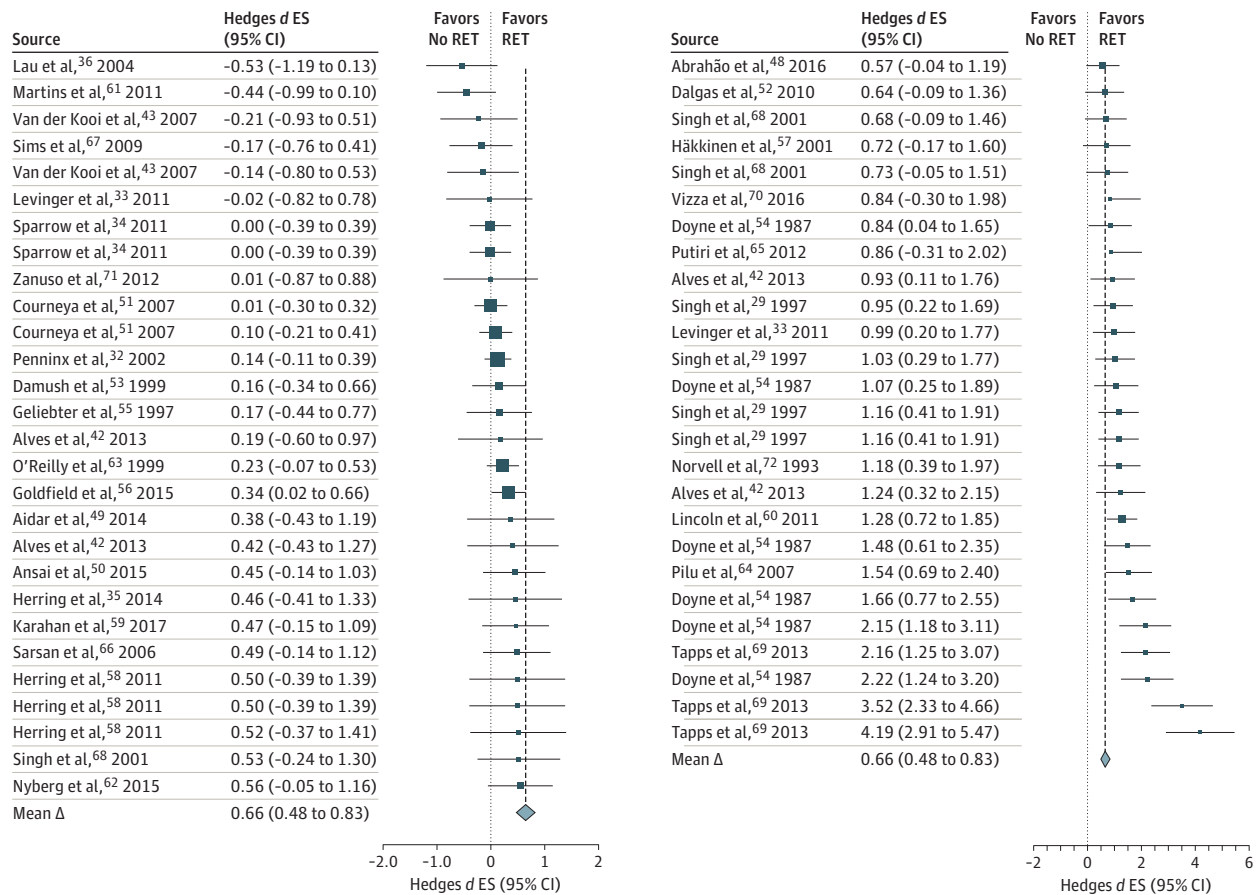
Table 1. Characteristics of Included Randomized Clinical Trials

Source	Measure	Intensity	Intervention Length, wk	Age, Mean (SD), y	Control	Sex	Participant Characteristics
Abraham et al, <sup>48</sup> 2016	BDI	Low to moderate	12	39 (14)	Wait list	Mixed	Systemic lupus erythematosus
Aidar et al, <sup>49</sup> 2014	BDI	Low to moderate	12	53 (8)	No treatment	Mixed	Survivors of ischemic stroke
Alves et al, <sup>42</sup> 2013	GDS	Low to moderate	24	64 (4)	No treatment + placebo supplement	Female	Elderly
Ansai et al, <sup>50</sup> 2015	GDS	Low to moderate	16	>80	No treatment	Mixed	Elderly
Courneya et al, <sup>51</sup> 2007	CESD	Low to moderate	Duration of treatment	Range, 25-76	Wait list	Female	Breast cancer
Dalgas et al, <sup>52</sup> 2010	MDI	Low to moderate	12	48 (10)	Wait list	Mixed	Multiple sclerosis
Damush et al, <sup>53</sup> 1999	MHFI	Low to moderate	8	68 (6)	Wait list	Female	Elderly
Doynne et al, <sup>54</sup> 1987	BDI, DACL, HRSD	Low to moderate	8	28 (5)	Wait list	Female	Major or minor depressive disorder
Geliebter et al, <sup>55</sup> 1997	BDI	Low to moderate	8	35 (6)	No training	Mixed	Obesity
Goldfield et al, <sup>56</sup> 2015	BRUMS-D	Low to moderate	22	16 (2)	Wait list	Mixed	Obesity
Häkkinen et al, <sup>57</sup> 2001	BDI	Low to moderate	21	36 (6)	No treatment	Female	Fibromyalgia
Herring et al, <sup>58</sup> 2011	BDI	Low to moderate	6	24 (6)	Wait list	Female	Generalized anxiety disorder
Herring et al, <sup>35</sup> 2014	HADS	Low to moderate	6	Range, 24-68	Patient education	Mixed	Obesity
Karahan et al, <sup>59</sup> 2017	BDI	Low to moderate	8	40 (8)	Patient education	Mixed	Failed back surgery syndrome
Lau et al, <sup>36</sup> 2004	HADS	Vigorous	6	Range, 10-17	No treatment	Mixed	Obesity
Levinger et al, <sup>33</sup> 2011	CDS	Low to moderate	10	51 (7)	No treatment	Mixed	Type 2 diabetes
Lincoln et al, <sup>60</sup> 2011	GDS	Low to moderate	16	66 (8)	No treatment	Mixed	Type 2 diabetes
Martins et al, <sup>61</sup> 2011	POMS-D	Low to moderate	16	76 (8)	No treatment	Mixed	Elderly
Norvell et al, <sup>72</sup> 1993	SCL-90-D	Low to moderate	16	33 (8)	Wait list	Male	Law enforcement personnel
Nyberg et al, <sup>62</sup> 2015	HADS	Low to moderate	8	69 (5)	Patient education	Mixed	Chronic obstructive pulmonary disorder
O'Reilly et al, <sup>63</sup> 1999	HADS	Low to moderate	24	62 (10)	No treatment	Mixed	Knee osteoarthritis
Penninx et al, <sup>32</sup> 2002	CESD	Low to moderate	12	69 (6)	Patient education	Mixed	Knee osteoarthritis
Pilu et al, <sup>64</sup> 2007	HRSD	Not Reported	32	Range, 40-60	Usual care	Female	Major depressive disorder
Putiri et al, <sup>65</sup> 2012	BDI	Not Reported	12	58 (7)	Usual care	Mixed	Type 2 diabetes
Sarsan et al, <sup>66</sup> 2006	BDI	Low to moderate	12	43 (10)	No treatment	Female	Obesity
Sims et al, <sup>67</sup> 2009	CESD	Vigorous	10	68 (15)	Wait list	Mixed	Chronic poststroke patients
Singh et al, <sup>29</sup> 1997	BDI, DSM, GDS, HRSD	Vigorous	10	71 (7)	Patient education	Mixed	Major or minor depression
Singh et al, <sup>68</sup> 2001	BDI, GDS, HRSD	Vigorous	6	71 (7)	Patient education	Mixed	Major or minor depression
Sparrow et al, <sup>34</sup> 2011	BDI	Low to moderate	24	70 (8)	Patient education	Mixed	Elderly
Tapps et al, <sup>69</sup> 2013	BDI	Low to moderate	12	75 (3)	No treatment	Mixed	Elderly
Van der Kooi et al, <sup>43</sup> 2007	BDI	Low to moderate	52	38 (10)	No treatment	Mixed	Facioscapulohumeral muscular dystrophy
Vizza et al, <sup>70</sup> 2016	DASS-21	Low to moderate	12	26 (7)	Usual care	Female	Polycystic ovary syndrome
Zanuso et al, <sup>71</sup> 2012	POMS-D	Low to moderate	12	74 (4)	Wait list	Mixed	Elderly

Abbreviations: BDI, Beck Depression Inventory; BRUMS-D, Brunel Mood Scale Questionnaire-Depression; CDS, Cardiac Depression Scale; CESD, Center for Epidemiologic Studies Depression Scale; DACL, Depression Adjective Checklist; DASS-21, Depression, Anxiety and Stress Scale; GDS, Geriatric Depression Scale;

HADS, Hospital Anxiety and Depression Scale; HRSD, Hamilton Rating Scale for Depression; MDI, Major Depression Inventory; MHFI, Mental Health Functioning Index-Depression; POMS-D, Profile of Mood States-Depression; SCL-90-D, Hopkins Symptom Checklist-Depression.

Figure. Forest Plot of Distribution of Hedges *d* Effect Sizes (ES)



Individual effects and overall effect of resistance exercise training on depressive symptoms. The different sizes of the data markers indicate the respective weight of the individual effects in the overall analysis. Studies are cited multiple

times because multiple effects were derived from individual trials. Each citation represents a unique effect. The dashed vertical lines show the difference between the overall effect and each individual effect.

sample age was 52 (18) years, and 67% of participants were female. The mean prescribed RET program duration was 16 weeks (range, 6-52 weeks). The frequency of RET sessions ranged from 2 to 7 days per week; the most common frequency was 3 days per week (20 RCTs; *k* = 30). Twenty-five RCTs (*k* = 39) evaluated participants with a physical or mental illness. Twenty-five RET interventions (*k* = 44) were fully supervised by various health care professionals. Seven RET interventions (*k* = 9) included a combination of supervised and unsupervised sessions, and 1 RET intervention was unsupervised. Adherence or compliance was reported in 15 of the 33 RCTs; the mean (SD) adherence rate was 78% (18%). Of the 18 remaining RCTs that did not report adherence or compliance, 2 reported attendance rates, which ranged from 87.5%<sup>53</sup> to 94%.<sup>71</sup> The Beck Depression Inventory<sup>41</sup> was the most frequently used measure of depressive symptoms (*k* = 21).

**Mean Effect Δ, Heterogeneity, and Publication Bias**

A forest plot of the distribution of effects is presented in the Figure. Forty-eight of the 54 effects (89%) were larger than zero, indicating a reduction in depressive symptoms favoring RET. Twenty effects significantly favored RET. The mean effect size

Δ was 0.66 (95% CI, 0.48-0.83; *z* = 7.35; *P* < .001). The effect was heterogeneous (total *Q* = 216.92, *df* = 53; *P* < .001; *I*<sup>2</sup> = 76.0% [95% CI, 72.7%-79.0%]), and sampling error accounted for 32.9% of observed variance. The mean quality score was 10.5 (range, 7-13). The fail-safe number of effects was 1358, indicating that 1358 null effects would be needed to diminish the overall effect to *P* > .05. Significant Begg rank correlation (Kendall *τ* = 0.45; *P* < .001) and Egger regression tests (intercept = -1.34; SE = 0.52; *P* = .01) indicated significant funnel plot asymmetry (eFigure 2 in the Supplement). Trim and fill analyses did not change the overall effect (Δ = 0.66; 95% CI, 0.48-0.83; 0 RCTs trimmed). The mean reduction in depressive symptoms among participants engaging in RET resulted in a number needed to treat of 4.

Three effects substantially larger than most were derived from 1 RCT.<sup>69</sup> The magnitude of these effects appeared to be due partly to greater depressive symptoms among participants who were randomized to the intervention group compared with controls. The mean effect was recalculated with this RCT removed, and the effect remained moderate and significant (Δ = 0.53; 95% CI, 0.38-0.68; *z* = 7.00; *P* < .001). Similarly, a nonsignificant reduction in the overall effect was ob-

Table 2. Summary of Primary Moderator Analysis

Primary Moderator	$\beta$	P Value	B (SE)	Adjusted 95% CI <sup>a</sup>
Blinded allocation and/or assessment	-0.39	.01	-0.036 (0.14)	-0.63 to -0.08
Significant improvement in strength	-0.32	.09	0.35 (0.21)	-0.76 to 0.06
Total volume of RET prescribed	-0.28	.09	-0.0002 (0.0001)	-0.0004 to 0
Participant health status	-0.23	.17	-0.19 (0.14)	-0.46 to 0.08

Abbreviation: RET, resistance exercise training.

<sup>a</sup> Adjusted for nonindependence of multiple effects contributed by single studies, baseline depressive symptoms, and the depressive symptom measure.

served when calculated with single effects derived from each study ( $\Delta = 0.48$ ; 95% CI, 0.30-0.67;  $z = 5.08$ ;  $P < .001$ ).

### Primary Moderator Analyses

The overall meta-regression model was significant ( $Q_R = 17.97$ ,  $df = 7$ ;  $P = .01$ ;  $R^2 = 0.30$ ;  $Q_E = 42.57$ ,  $df = 31$ ;  $P = .08$ ;  $I^2 = 38.88\%$  [95% CI, 25.63%-49.77%]). Blinded allocation and/or assessment of outcomes accounted for significant variation in the antidepressant effects of RET ( $\beta = -0.39$ ;  $z = -2.50$ ;  $P = .01$ ). Effects were significantly smaller when outcome allocation and/or assessment was blinded ( $\Delta = 0.56$ ; 95% CI, 0.40-0.71) compared with when outcome allocation and/or assessment was not blinded ( $\Delta = 1.07$ ; 95% CI, 0.36-1.78). Total volume of prescribed exercise ( $\beta = -0.28$ ;  $P = .09$ ), significant improvements in strength ( $\beta = 0.32$ ;  $P = .09$ ), and participant's health status ( $\beta = -0.23$ ;  $P = .17$ ) were not significantly related to effect size (Table 2).

### Univariate Meta-regression Analyses

The results of univariate moderator analyses for the primary and secondary moderators are presented in Table 3.

### Subanalysis Between RET and AET

To facilitate subanalyses between RET and AET, data were extracted from 9 RCTs ( $k = 17$ ) in which participants were randomized to RET, AET, or a nonactive control condition.<sup>32,35,48,51,54-56,58,61,66</sup> Effects were not significantly different for the RET interventions ( $\Delta = 0.64$ ; 95% CI, 0.34-0.93) than for the AET interventions ( $\Delta = 0.46$ ; 95% CI, 0.22-0.70) compared with the control groups ( $P = .48$ ). When directly comparing the effects of RET with AET (positive effects favoring RET), a small, nonsignificant mean effect  $\Delta$  favoring RET was found ( $\Delta = 0.15$ ; 95% CI, -0.004 to 0.30;  $z = 1.91$ ;  $P = .06$ ).

## Discussion

To our knowledge, this is the first meta-analysis to examine RCTs to assess the efficacy of RET on depressive symptoms. Across 33 RCTs, RET was associated with a significant reduction in depressive symptoms regardless of the participants' characteristics (ie, age, sex, and health status) or the features of the RET stimulus (ie, program duration, session duration, intensity, frequency, or total prescribed volume). However, while simultaneously considering the potential variation associated with baseline depressive scores, multiple effects from single RCTs, whether or not strength was significantly improved, total prescribed RET volume, and participant's health status, blinded allocation and/or assessment was signifi-

cantly associated with the overall effect of RET, such that significantly smaller reductions in depressive symptoms were found when investigators were blinded to allocation and/or assessment.

Univariate analyses showed that significantly larger reductions in depressive symptoms were derived from RCTs of participants with scores indicative of mild to moderate depression compared with RCTs of participants without scores indicating mild to moderate depression, and from RCTs of shorter RET sessions (<45 minutes) compared with RCTs featuring longer session durations. In addition, significantly larger reductions were found in fully supervised RCTs compared with RCTs that used combinations of supervised and unsupervised RET, and in RCTs in which the primary outcome was depressive symptoms (Table 3).

The magnitude of the overall mean effect ( $\Delta = 0.66$ ; 95% CI, 0.48-0.83) is consistent with the association of diverse types of exercise training with depression (pooled standardized mean difference, -0.62; 95% CI, -0.81 to 0.42, with negative scores favoring exercise)<sup>18</sup> and is larger than the recently reported association of RET with anxiety ( $\Delta = 0.31$ ).<sup>24</sup> In addition, the magnitude of the overall mean effect and the magnitude of the effects among important subsamples are consistent with previously reported effects. Specifically, the mean effect for individuals with a physical illness ( $\Delta = 0.34$ ; 95% CI, 0.17-0.52) is consistent with previous evidence of the associations of all types of exercise training with depressive symptoms among adults with a chronic illness ( $\Delta = 0.30$ ; 95% CI, 0.25-0.36)<sup>19</sup> and adults with neurologic disorders ( $\Delta = 0.28$ ; 95% CI, 0.15-0.41).<sup>73</sup>

The large effect of RET found among adults with depressive symptoms indicative of mild to moderate depression ( $\Delta = 0.90$ ; 95% CI, 0.68-1.11) is consistent with previously reported effects of all exercise modes among people with major depressive disorder (standardized mean difference, 1.11; 95% CI, 0.79-1.43).<sup>17</sup> Twelve RCTs ( $k = 25$ ) included samples that reported clinically significant elevations in depressive symptoms, based on cutoff scores commonly used for clinical screening.<sup>74-77</sup> The mean scores for 10 of the 25 effects (40%) suggested potential remission based on a frequently used response threshold of a 50% or greater reduction in baseline scores.<sup>78</sup> The mean percentage reduction from baseline scores for all 25 of these effects was 45%. Moreover, the mean effect for RCTs in which baseline scores were indicative of mild to moderate depression ( $\Delta = 0.90$ ; 95% CI, 0.68-1.12;  $z = 8.12$ ;  $P < .001$ ) was significantly larger than effects from RCTs in which baseline scores were below suggested clinical cutoff scores ( $\Delta = 0.45$ ; 95% CI, 0.23-0.67;  $z = 4.02$ ;  $P = .03$ ) (Table 3). The larger percentage reduction found from RCTs of participants with elevated depressive symptoms, coupled with the

Table 3. Summary of Univariate Analyses

Effect Moderator	Contrast Weights	Effects (k)	Δ (95% CI)	P Value <sup>a</sup>	
				Moderator	Contrast
Sex					
Female	1	20	0.81 (0.51 to 1.10)	<.001	.28
Mixed	-1	34	0.58 (0.36 to 0.80)	<.001	
Age, y					
<25	-0.5	2	-0.04 (-0.89 to 0.80)	.92	.63
25-54	-0.5	26	0.67 (0.43 to 0.91)	<.001	
≥55	1	26	0.72 (0.45 to 1.00)	<.001	
Health					
Healthy	1	15	0.81 (0.33 to 1.29)	<.001	.63
Physical illness	-0.5	20	0.34 (0.17 to 0.52)	<.001	
Mental illness (MDD, GAD)	-0.5	18	1.00 (0.69 to 1.31)	<.001	
Baseline depression					
Indicative of mild to moderate depression	1	25	0.90 (0.68 to 1.11)	<.001	.02
Not indicative	-1	29	0.45 (0.23 to 0.67)	<.001	
Control condition					
Attention placebo control	1	15	0.98 (0.56 to 1.41)	<.001	.09
No attention placebo control	-1	39	0.54 (0.36 to 0.73)	<.001	
Comparison type					
Wait list	NA	17	0.71 (0.39 to 1.02)	<.001	NA
Patient education	NA	13	0.51 (0.27 to 0.75)	<.001	
No treatment	NA	11	0.33 (0.02 to 0.64)	.04	
Usual care	NA	5	2.30 (1.05 to 3.55)	<.001	
Placebo or second treatment	NA	8	0.48 (0.07 to 0.88)	.02	
Program length, wk					
<12	-1	26	0.88 (0.58 to 1.18)	<.001	.70
≥12	1	26	0.51 (0.28 to 0.73)	<.001	
Session, min					
<45	-1	12	1.10 (0.49 to 1.70)	<.001	.049
≥45	1	28	0.48 (0.29 to 0.68)	<.001	
Frequency, d/wk					
2	-0.5	12	0.53 (0.25 to 0.81)	<.001	.19
3	-0.5	32	0.60 (0.37 to 0.84)	<.001	
≥4	1	10	1.00 (0.55 to 1.46)	<.001	
Intensity					
Low to moderate	-1	45	0.67 (0.49 to 0.87)	<.001	.72
Vigorous	1	9	0.59 (0.17 to 1.01)	.006	
Blinded assessment					
Yes	1	42	0.56 (0.40 to 0.71)	<.001	.15
No	-1	12	1.07 (0.36 to 1.78)	.003	
Supervision					
Combination of supervised and unsupervised	-1	9	0.14 (0 to 0.29)	.05	.02
Fully supervised	1	44	0.79 (0.57 to 1.02)	<.001	
Primary outcome depression					
Yes	1	38	0.88 (0.63 to 1.13)	<.001	.002
No	-1	16	0.19 (0.06 to 0.32)	.006	
Significant improvement in strength					
Yes	1	19	0.50 (0.32 to 0.68)	<.001	.45
No	-0.5	7	0.09 (-0.08 to 0.27)	.30	
Not reported	-0.5	28	0.94 (0.62 to 1.26)	<.001	

Abbreviations: GAD, generalized anxiety disorder; MDD, major or minor depressive disorder.

<sup>a</sup> The moderator P value indicates the P value for the mean effect of the individual moderator. The contrast P value indicates the P value of the comparison between the moderator levels.

significant difference based on initial severity of depressive symptoms, suggests that RET may be particularly helpful for reducing depressive symptoms in people with greater depressive symptoms. These findings support potentially different mechanisms of action and/or unique interactions in participants with clinical depression that may not be present in participants with subclinical depressive symptoms.

### Primary Moderators of the Effect

Blinded allocation and/or assessment was independently and significantly associated with reductions in depressive symptoms; smaller reductions occurred in RCTs with blinded allocation and/or assessment ( $\Delta = 0.56$ ; 95% CI, 0.40-0.71). Blinded allocation and assessment of outcomes can limit biases associated with self-reported measures in exercise interventions.<sup>79-81</sup> Previous reports have demonstrated a reduction in the overall effect of exercise on depression after exclusion of trials that do not adequately blind allocation and/or assessment.<sup>18</sup>

Blinded allocation and/or assessment is also an indication of intervention quality.<sup>30,82</sup> Based on the study quality assessment used here, the overall quality of RCTs was high, with a mean score of 10.5 (range, 7-13) on a 13-point scale. When blinding was removed from the overall quality score, such that the maximum total score was 11, RCTs that reported blinded allocation and/or assessment had significantly higher mean (SD) quality scores (10.0 [1.0]) compared with those without blinded allocation and/or assessment (8.0 [0.9]) ( $t = 5.82$ ,  $df = 31$ ;  $P < .001$ ). Blinded allocation and/or assessment may indicate a higher-quality research design, which may have resulted in smaller effects by providing a more rigorous estimation of the “true” effect of RET on depressive symptoms.

Participant’s health status, volume of prescribed RET, and whether or not strength was significantly improved were not independently associated with the overall mean reduction in depressive symptoms. These findings are consistent with previous evidence showing that the antidepressant effects of exercise training were not dependent on a significant improvement in fitness.<sup>19</sup> These findings are also consistent with recently reported associations of RET with anxiety.<sup>24</sup>

Although RET significantly reduced depressive symptoms independent of total prescribed volume of RET, this measure of total volume (intervention length  $\times$  frequency  $\times$  session duration) could not be extracted for all RCTs because 8 RCTs ( $k = 14$ ) did not report the duration of RET sessions. In addition, this measure of total volume did not include the intensity of prescribed RET. Heterogeneous reporting of prescribed intensity did not allow differentiation between low-intensity RET and moderate-intensity RET, necessitating their merger and comparison with vigorous-intensity RET. Only 4 interventions ( $k = 9$ )<sup>28,36,70,71</sup> were of vigorous intensity. The relationship between RET intensity and strength gains is moderated by participant training status, as moderate-intensity RET improves strength most in untrained participants, and vigorous-intensity RET improves strength most in trained participants.<sup>83</sup> There is a paucity of within-study comparisons of RET dose, multiarm RCTs comparing RET and other

strictly matched exercise modalities, and investigations of the influence of exercise volume, exercise intensity, and their interaction. For example, more frequently completed vigorous RET may afford the possibility of shorter exercise sessions while meeting recommended guidelines,<sup>84</sup> potentially increasing feasibility while maintaining positive mental health benefits.

There is continued interest in the comparative effects of different exercise modes on mental health outcomes. However, with one notable exception,<sup>85,86</sup> few RCTs have directly compared the antidepressant effects of different exercise modes in a single study sample. Nine RCTs included here directly compared RET with AET and a nonactive control condition.<sup>32,35,48,51,54-56,58,61,66</sup> Although the magnitude of improvement for AET and RET did not differ significantly, consistent with recent results of the comparative associations of AET and RET with anxiety symptoms,<sup>24</sup> only 2 RCTs attempted to match AET and RET interventions in any capacity. One trial matched AET and RET based on energy expenditure,<sup>55</sup> and 1 trial more thoroughly matched AET and RET based on body region, positive work, time actively engaged in exercise, and load progression.<sup>58</sup> Future trials, matching different exercise modes on relevant features of the exercise stimulus, will allow more rigorous and controlled comparisons between exercise modalities, and the examination of interactions between factors such as frequency, intensity, duration, and exercise modality.

### Future Research

In addition, authors should report the mean session duration, the numbers of sets performed, the numbers of repetitions, the lengths of rest periods between sets, and the intensity (eg, the percentages of 1-repetition maximum and the rate of perceived exertion), to more thoroughly assess the total volume of exercise prescribed. Authors should report whether interventions were performed in groups or individually. When exercise sessions are supervised, the efforts made to control for social interaction during sessions should be reported. Future trials should blind allocation, blind assessors from group assignment, explicitly report this process, and state how missing data and dropouts were handled, including explicitly stating if intention-to-treat analyses were conducted.

Six RCTs assessed the effects of RET on depressive symptoms in participants with a clinical diagnosis of depression or anxiety, and 8 RCTs assessed depressive symptoms in participants who had scores indicative of moderate depression without an actual diagnosis. More important, individuals who display elevated subclinical depressive or anxiety symptoms are at increased risk of developing clinically significant psychopathologic features.<sup>87</sup> Because participants with baseline scores indicative of mild to moderate depression had significantly larger improvements than those who did not, investigating RET interventions among individuals at different points on the severity spectrum may be particularly interesting.

### Limitations

There was a notable lack of clear and complete reporting of intervention design, protocol, data analyses, participant infor-



mation, medication use, adherence, and compliance, which should be emphasized in future trial reporting. Medication use was insufficiently reported to allow comparisons between RCTs; 12 of the 33 RCTs (36%) did not report information regarding medication use. Twenty-one of 33 RCTs (64%) did not report adherence or compliance with the interventions. Prescribed antidepressant medication use is associated with poor adherence to exercise programs among patients,<sup>88</sup> making this omission particularly problematic.

## Conclusions

The available empirical evidence supports RET as an alternative or adjuvant therapy for depressive symptoms. Future trials should include thorough reporting of trial and RET design, specifically blinded allocation, assessment, and adherence. In addition, future trials should compare RET with other empirically supported therapies for depressive symptoms.

### ARTICLE INFORMATION

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