# Can Exercise Improve Cognitive Symptoms of Alzheimer's Disease? A Meta-Analysis

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**OBJECTIVES:** To examine the effects of exercise training on cognitive function in individuals at risk of or diagnosed with Alzheimer's disease (AD).

**DESIGN:** Meta-analysis.

**SETTING:** PubMed, Scopus, ClinicalTrials.gov, and ProQuest were searched from inception until August 1, 2017.

**PARTICIPANTS:** Nineteen studies with 23 interventions including 1,145 subjects with a mean age of 77.0 ± 7.5 were included. Most subjects were at risk of AD because they had mild cognitive impairment (64%) or a parent diagnosed with AD (1%), and 35% presented with AD.

**INTERVENTION:** Controlled studies that included an exercise-only intervention and a nondiet, nonexercise control group and reported pre- and post-intervention cognitive function measurements.

**MEASUREMENTS:** Cognitive function before and after the intervention and features of the exercise intervention.

**RESULTS:** Exercise interventions were performed 3.4 ± 1.4 days per week at moderate intensity (3.7 ± 0.6 metabolic equivalents) for 45.2 ± 17.0 minutes per session for 18.6 ± 10.0 weeks and consisted primarily of aerobic exercise (65%). Overall, there was a modest favorable effect of exercise on cognitive function ($d_+ = 0.47$, 95% confidence interval (CI) = 0.26–0.68). Within-group analyses revealed that exercise improved cognitive function ($d_{+w} = 0.20$, 95% CI = 0.11–0.28), whereas cognitive function declined in the control group ($d_{+w} = -0.18$, 95% CI = −0.36 to 0.00). Aerobic exercise had a moderate favorable effect on cognitive function ($d_{+w} = 0.65$, 95% CI = 0.35–0.95), but other exercise types did not ($d_{+w} = 0.19$, 95% CI = −0.06–0.43).

**CONCLUSION:** Our findings suggest that exercise training may delay the decline in cognitive function that occurs in individuals who are at risk of or have AD, with aerobic exercise possibly having the most favorable effect. Additional randomized controlled clinical trials that include objective measurements of cognitive function are needed to confirm our findings. **J Am Geriatr Soc 2018.**

**Key words: cognition; brain; older adults; physical activity; aging**

Approximately 5.3 million Americans are living with Alzheimer's disease (AD), the sixth leading cause of death in the United States.[1] The incidence of AD will more than double by 2050. AD-related medical costs in the United States are estimated to exceed $1.1 trillion by 2050 unless effective methods to prevent and treat AD are identified.[1]

Exercise training is recommended as a cost-effective lifestyle therapeutic option to improve brain health in older adults, with improvements in cognitive function mediated by positive neurophysiological changes.[2] Consequently, the World Health Organization (WHO)[3] recommends that older adults (aged ≥65) perform at least 150 minutes per week of moderate-intensity aerobic exercise training (e.g., brisk walking), 75 minutes per week of vigorous-intensity aerobic exercise training, or a combination of the two supplemented by muscle strengthening activities (e.g., dynamic resistance training) on 2 or more days per week. The WHO recommendations are based upon expert opinion regarding the use of exercise as prevention and treatment for AD because there are few meta-analyses,[4–10] and they have produced mixed results.

One reason for the inconsistencies among these meta-analyses may be a lack of adherence to the high-quality contemporary methodological standards outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[11] and the Assessment

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of Multiple SysTemAtic Reviews (AMSTAR) Methodological Quality Scale,[12,13] although there may be other factors contributing to the inconsistencies among previous meta-analyses, such as unexplored moderators (e.g., age, sex) and inclusion of subjects with multiple types of dementia[5–8,10] or with a diagnosis of cognitive impairment.[9] For these reasons, it remains unclear whether exercise training attenuates the decline or improves cognitive function in individuals at risk of or diagnosed with AD. Therefore, the purposes of our meta-analysis were to evaluate the effect of exercise training on cognitive function and identify potential moderators of the exercise-induced effects on cognitive function to provide insight into an effective exercise prescription to preserve cognitive health in adults at risk of or diagnosed with AD.

## METHODS

This study followed the standards outlined in the PRISMA Statement[11] and AMSTAR Methodological Quality Scale.[12,13] Institutional review board approval was not required because this was secondary research. The methods used for data extraction and coding are outlined in Data S1, those used to assess methodological quality of the primary level studies in our sample in Data S2, and those used to assess methodological quality of the current and previously conducted meta-analyses[4–10] in Data S3.

### Inclusion Criteria

Studies were included if they met the following a priori criteria: involved an exercise-only intervention; included a nondiet, nonexercise control group; included human subjects aged 19 and older at risk of or diagnosed with AD; and reported pre- and post-intervention cognitive function measurements (e.g., Mini-Mental State Examination (MMSE)[14] for the exercise and control groups. Study populations were considered to be at risk if they had mild cognitive impairment (MCI), a genetic risk (e.g., apolipoprotein E $\varepsilon$4 allele), or biological parents diagnosed with AD. Study populations were determined to have MCI based on clinical diagnosis of MCI reported in each trial (Data S4). Studies that were qualitative or investigated the effects of exercise on cognitive function in combination with another intervention (e.g., medication, cognition therapy) were excluded.

### Search Strategy

Boolean searches in PubMed and Scopus were run in consultation with a medical librarian (JL) for trials related to AD that examined the effect of an exercise intervention on cognitive function. Databases were searched from inception until August 1, 2017, using key words (dementia, Alzheimer's disease, exercise, cognition) in combination with Medical Subject Heading descriptors (e.g., physical activity, brain function). Our search permitted studies conducted in any country and reported in any language, but only English-language reports were identified. (The full search strategy is outlined in Data S5.) Two investigators (GAP, ALZ) screened the search results for inclusion with duplication of effort to determine and code eligible articles. To identify gray literature, additional searches were conducted using Clinicaltrials.gov, the International Federation of Pharmaceutical Manufacturers and Associations clinical trials results portal, and ProQuest for dissertations and theses. Manual searches of reference lists of included studies, reviews, and other meta-analyses were used to supplement electronic database searching.

### Effect Size Calculation and Moderator Analyses

The standardized mean difference effect size ($d$) was used to quantify the influence of exercise on cognitive function in adults at risk of or diagnosed with AD and has been described previously.[15,16] Briefly, d values were calculated for exercise and control within-group comparisons and exercise versus control between-group comparisons,[15,16] correcting for small sample size bias and, for the between-group comparisons only, baseline differences.[17] Multiple d values were calculated for 4 studies[18–21] that involved more than 1 exercise intervention group (e.g., aerobic exercise training vs resistance training) and analyzed as independent studies.[22] To determine whether multiple intervention studies influenced our weighted mean estimates, we performed alternative analyses in R[23] using the metafor package[24] (rma.mv function). Positive d values were set to represent an increase in cognitive function over time or better cognitive function in the intervention than the control group. Studies that reported better cognitive function with a negative value, such as shorter response time, were changed so that d values were directionally consistent. The magnitude of d values was interpreted as 0.20 to 0.49 for small improvement in cognitive function, 0.50 to 0.79 for medium improvement, and 0.80 or greater for large improvement.[25]

The homogeneity Q statistic,[26] and the $I^2$ statistic and its 95% confidence intervals (CIs)[27] were used to estimate inconsistencies with d values among the included studies. $I^2$ values range from 0% (homogeneity) to 100% (maximal heterogeneity); a CI that does not include 0% indicates that the hypothesis of homogeneity is rejected and an inference of heterogeneity is merited.[27,28] The potential for publication or other selection bias was evaluated using the Begg strategy[29] and Egger test.[30] We also performed sensitivity analyses to reduce the heterogeneity of our sample (e.g., winsorizing large effects).[31]

Weighted regression models (meta-regressions) using random-effects assumptions were used to explain the variability in d's. In total, 15 theoretically driven, a priori study-level moderators including study quality, sample (age, baseline cognitive scores, sex, education, body mass index, diagnosis, type of control group, type of cognitive function assessment, duration of follow-up) and exercise intervention (exercise frequency, intensity, time, type, adherence) characteristics were examined to determine which combinations led to the greatest improvements in cognitive function. Baseline cognitive function scores were used to capture AD severity because six studies with populations diagnosed with AD did not report AD severity. In addition, 2 studies that reported AD severity reported mild to severe AD, indicating a range of AD severity in their sample, and only 4 studies clearly indicated a sample with mild to moderate (k = 3) or severe (k = 1) AD. The

moving constant technique[32] was applied to estimate the magnitude of weighted mean effect sizes ($d_+$) and their CIs at different levels of interest for individual study–level moderators, including extreme values and other observations, within that range (see references[15,16] for greater detail). Effects of continuous variables were held constant at their sample means by mean-centering them and for categorical variables using contrast codes.[32]

Studies included in our meta-analysis used a variety of measures to assess change in cognitive function. The questionnaires used to assess cognitive function varied with respect to content of questions, scoring, and cut-points used for clinical judgment. Therefore, our results focused on the standardized mean difference effect size (d) and the statistical interpretation of the association between exercise training and cognitive function.

### Statistical Computing

Continuous variables are summarized as means ± standard deviations unless otherwise stated, and categorical variables are presented as absolute values and percentages. Analyses used Stata version 14.0 (Stata Corp., College Station, TX) with macros for meta-analysis,[22,33] incorporating fixed- and random-effects assumptions. Fixed- and random-effects analyses did not yield different results, so we report only the results from the random-effects analyses. Two-sided statistical significance was set at $P < .05$.

## RESULTS

### Description of Studies

Nineteen controlled studies were included, yielding 23 total interventions (Figure 1). The 1 study that involved only a resistance training intervention[21] was combined with the interventions that consisted of aerobic and resistance exercise training for moderator analyses. Data S4 provides a detailed description of the sample and intervention characteristics of the included studies, which were published between 2002 and 2015. Eighty-nine percent of studies were randomized controlled trials (RCTs), and 5.5% was a non-RCT, and 5.5% was a cross-over study. Overall, included studies had good methodological quality (81%), with scores ranging from 62% to 92% on the Downs and Black Checklist.[15,16] The MMSE[14] was the most common assessment used to measure cognitive function (57%), followed by the Trail-Making Test (13%), Symbol Digit Modalities, (9%), Montreal Cognitive Assessment (4%), AD Assessment Scale Cognition score (4%), Matching Sample (4%), London Psychogeriatric Rating Scale (4%), and Rapid Evaluations of Cognitive Functions (4%).

The exercise training (total N = 612) and control (N = 538) groups consisted of older (77.0 ± 7.5) adults (71.1% female) who had 9.2 ± 4.3 years of education. Most of the studies included samples of individuals who were at risk of AD because they had MCI (64%; n = 732); another 1% were at risk because they had a parent diagnosed with AD (n = 17), and 35% had AD (n = 396). Exercise training was performed 3.4 ± 1.4 days per week at moderate intensity for older adults (3.7 ± 0.6 metabolic equivalents), 45.2 ± 17.0 minutes per session for 18.6 ± 10.0 weeks. Most interventions consisted of aerobic exercise training (65%), with a smaller proportion consisting of a combination of aerobic and resistance training (35%). Ninety-six percent of interventions involved an active-content control group in which a majority of study participants were assigned to usual care (63%) for AD, followed by low-intensity stretching (15%), range-of-motion routines (4%), planned social visits (10%), or educational information materials on health (4%), with the remaining 4% including a nonexercise wait-list control.

### Effect of Exercise Training on Cognitive Function

There was a favorable between-group effect of exercise training on cognitive function ($d_+ = 0.47$, 95% CI = 0.26–0.68; Figure 2), although effect sizes were heterogeneous ($I^2 = 59.6\%$; 95% CI = 36.2–74.5). Sensitivity analyses revealed a similar effect ($d_+ = 0.50$, 95% CI = 0.27–0.73) and heterogeneity ($I^2 = 60.1\%$; 95% CI = 36.9–74.7) when we tested whether nonindependent treatment effects (multiple comparisons) influenced our mean estimates. Within-group analysis revealed that exercise training had a small positive effect on cognitive function ($d_{+w} = 0.20$, 95% CI = 0.11–0.28; $I^2 = 0\%$), whereas the control group experienced a decline in cognitive function ($d_{+w} = -0.18$, 95% CI = −0.36 to −0.00; $I^2 = 65.1\%$). The Egger ($t = 4.38$, $P < .001$) and Begg ($z = 3.49$, $P < .001$) tests suggested that the effect size distribution was skewed. The control group effect size from one study[48] was determined to be an outlier (>3 standard deviations from the mean). To reduce the influence of this study on our results, we winsorized its effect size (d),[31] but our original findings did not significantly change for the control group sample ($d_+ = -0.16$, 95% CI = −0.33 to −0.02), the overall effect of exercise on cognitive function relative to control ($d_+ = 0.39$, 95% CI = 0.18–0.59), or the altered presence or level of heterogeneity in the control group ($I^2 = 56.3\%$) or overall ($I^2 = 50.7\%$) sample.

### Moderator Analysis

Within-group analysis of the exercise groups revealed that aerobic exercise training interventions had a moderate favorable effect on cognitive function ($d_+ = 0.65$, 95% CI = 0.35–0.95), whereas combined aerobic and resistance exercise training had a small but nonsignificant effect ($d_+ = 0.19$, 95% CI = −0.06–0.43). Exercise type did not reach statistical significance as a moderator in our between-group analysis ($P = .11$). In addition, improvements in cognitive function were greater in samples that reported greater adherence to the exercise training interventions (more exercise sessions attended; $P = .02$; Data S6). All of these effects remained significant after controlling for diagnosis (AD vs at risk) and age ($P$s < .04). We also performed a within-group analysis according to diagnosis and found no significant difference ($P = .53$) between effects found in studies with populations at risk of AD ($d_+ = 0.27$, 95% CI = 0.05–0.50) and studies with populations diagnosed with AD ($d_+ = 0.65$, 95% CI = 0.31–0.99). No other moderators examined were significant, including sample (age, baseline cognitive scores,

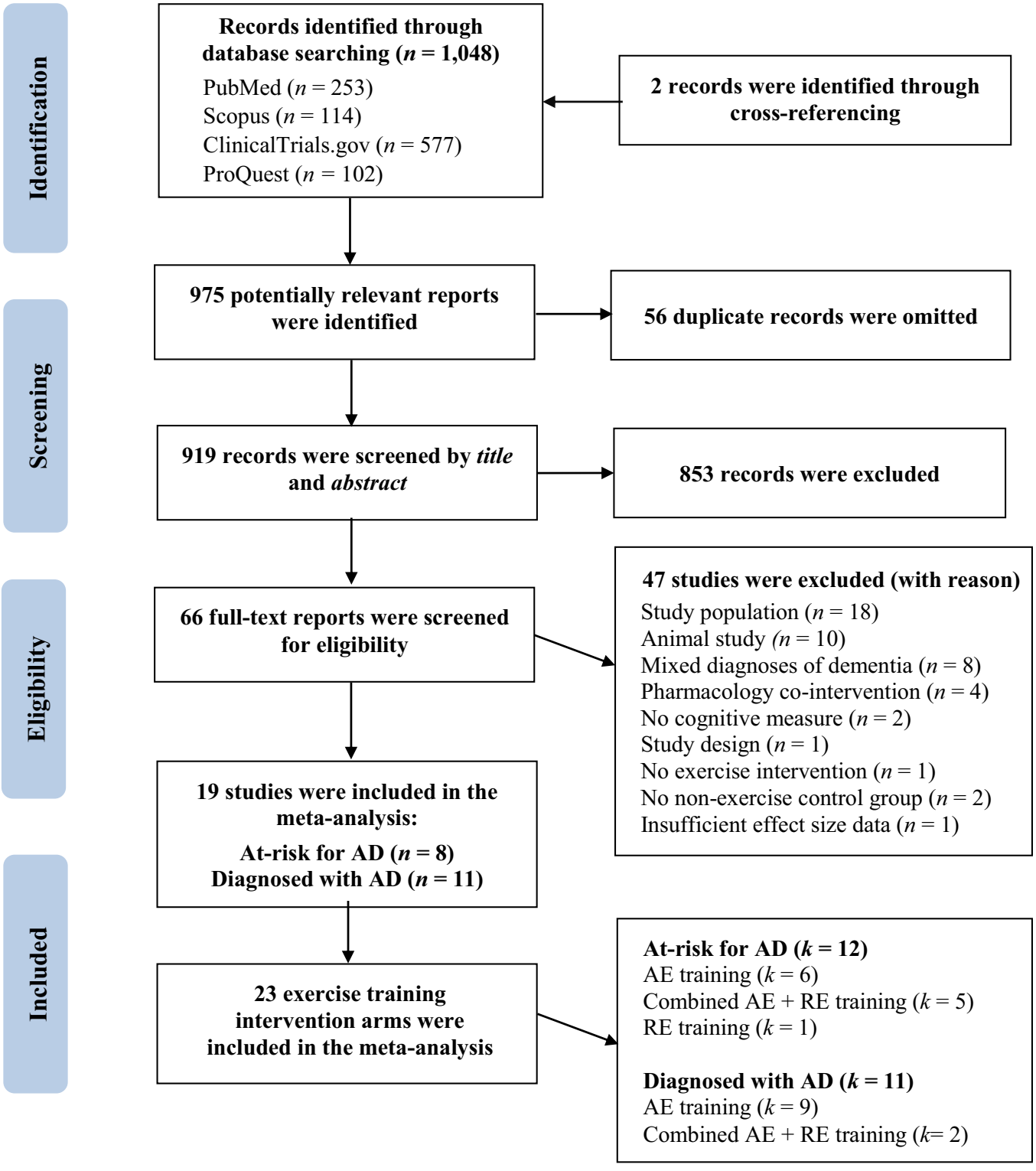


**Figure 1.** Flow chart detailing the systematic search of potential reports and selection process of included studies (n) and intervention arms (k). AD = Alzheimer's disease; IFPMA = International Federation of Pharmaceutical Manufacturers & Associations.

sex, education, body mass index, diagnosis, type of control group, type of cognitive function assessment, duration of follow-up) or exercise intervention (exercise frequency, intensity, time) characteristics or the quality of included studies.

## DISCUSSION

Our meta-analysis evaluated the effect of exercise training on cognitive function and attempted to identify potential moderators of the exercise-induced effects on cognitive

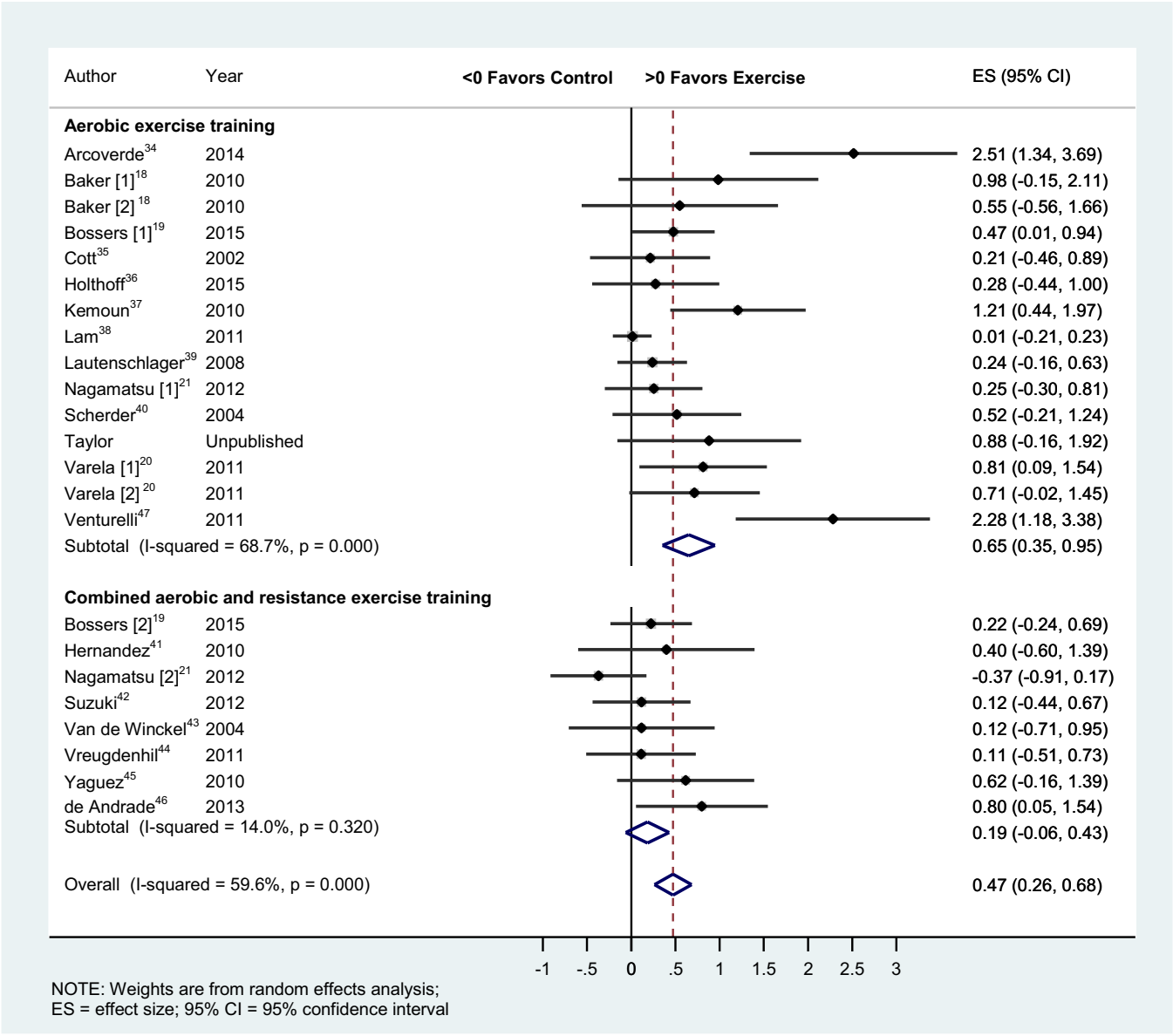


**Figure 2.** Distribution of cognitive function effect sizes from before and after the exercise intervention versus control. Baker [1], Women only; Baker [2], Men only; Bossers [1], aerobic exercise training; Bossers [2], combined aerobic and resistance exercise training; Nagamatsu [1], aerobic exercise training; Nagamatsu [2], resistance exercise training; Varela [1], aerobic exercise intensity at 40% of heart rate reserve; Varela [2], aerobic exercise intensity at 60% of heart rate reserve.

function to help identify an effective exercise prescription to preserve the cognitive health of adults at risk of or diagnosed with AD. Consistent with the WHO's exercise recommendations,[3] our overall finding was that moderate-intensity exercise training performed approximately 3 days per week for approximately 45 minutes per session resulted in modestly better ($d_+ = 0.47$, 95% CI = 0.26–0.68) cognitive function than in controls ($P < .001$). This effect size indicates that an individual in the exercise group would score higher on the cognitive function assessments than 69% of patients in the control group who had equivalent baseline cognitive scores, indicating that exercise appears to result in clinically meaningful improvements in cognitive function.[14] Most notably, ours is the first meta-analysis to find a significant within-group effect for aerobic exercise and a nonsignificant within-group effect for combined exercise training, indicating that aerobic exercise alone may be more effective than combined exercise in delaying the decline in cognitive function that occurs in older adults at risk of or who have AD. Nonetheless, these results are suggestive, and more research is needed because exercise type did not emerge as a statistically significant moderator in our between-group analysis. The fact that the more heavily weighted (larger N) studies with an aerobic exercise training intervention had smaller effects may explain this nonsignificant finding for the between-group analysis. Because the effects for aerobic exercise training studies exhibited heterogeneity, the between-group model for exercise type was less likely to attain significance. Our moderator analysis also revealed that improvements in cognitive function were greater in samples that reported better adherence to the exercise training intervention, although exercise adherence was reported in only 9

studies in our sample (47%), which included participants with AD in 7 studies, participants at risk of AD in 2 studies, an aerobic exercise training intervention in 6 studies, and combined exercise training intervention in 3 studies.

The small between-group effect of exercise on cognitive function ($d_+ = 0.47$, 95% CI = 0.26–0.68) is consistent with the smaller effects found in a prior meta-analysis ($d_+ = 0.42$, 95% CI = 0.23–0.62).[6] A discrepancy between our meta-analysis and that meta-analysis was it found that combined exercise interventions ($d_+ = 0.59$, 95% CI = 0.32–0.86) had a greater positive effect on cognition than aerobic-only exercise interventions ($d_+ = 0.41$, 95% CI = 0.05–0.76). Contrary to our findings, two studies reported moderate effects of exercise on cognitive function ($d_+ = 0.57$, 95% CI = 0.43–1.17;[7] $d_+ = 0.75$, 95% CI = 0.32–1.17[4]), whereas a third study reported large effects ($d_+ = 1.17$, 95% CI = 0.75–1.59).[8] Furthermore, three meta-analyses reported no significant effect ($d_+ = 0.14$, 95% CI = −0.36–0.64)[9] or a null effect of exercise on cognitive function.[5,10]

There are several possible reasons for the significant discrepancies in the literature. First, no previously published meta-analysis[4–10] fully satisfied the PRISMA contemporary methodological quality standards, as we assessed using an augmented version[29] of the AMSTAR Methodological Quality Scale;[12,13] 6 of the 7 meta-analyses conducted on the effects of exercise on cognitive function achieved only fair to moderate quality (~61% of the AMSTAR criteria were satisfied); only one other meta-analysis[5] and ours achieved a high-quality rating of 94% of the AMSTAR criteria satisfied. Second, nearly all prior meta-analyses included samples with multiple dementia diagnoses[6–10] or only cognitive impairment.[9] The heterogeneity of the levels of baseline cognitive function among the samples of these other meta-analyses[5–8,10] would clearly contribute to the mixed findings of this literature. Third, prior meta-analyses[4,7–10] rarely examined how sample features and exercise intervention characteristics modulated the effect of exercise training on cognitive function, nor did they compare cognitive changes before and after the intervention for the exercise and control groups (within-group analysis), as we did. Focusing solely on the between-group effects (exercise vs control) may be misleading because of the decline in cognitive function that is anticipated with untreated disease in the control group samples, an effect that was evident in our meta-analysis. Our within-group analyses revealed a novel and very important finding about the effects of exercise on cognitive health in that exercise training may improve cognitive function in individuals in the control group who are at risk of or have AD.

A noteworthy finding of our within-group moderator analyses is that improvement in cognitive function after aerobic exercise training was 3 times as great as the improvement after combined aerobic and resistance exercise training interventions ($d_+ = 0.65$ vs 0.19). Our finding supports the WHO recommendation that aerobic exercise training be the primary modality of exercise to maximize cognitive health for older adults (Table 1). Furthermore, the exercise intervention characteristics for the included studies support the WHO-recommended frequency, intensity, and time per session but fall slightly below the recommended exercise time per week (Table 1). The WHO recommendations are based on expert opinion. Our meta-analysis now provides evidence that the current WHO recommendations may be considered an effective exercise prescription for individuals at risk of or diagnosed with AD, although future research is necessary to determine which combinations of frequency, intensity, time, and type of exercise best preserve cognitive health of older adults at risk of or diagnosed with AD. Moreover, with only one RCT involving resistance exercise training in our sample, the results are inadequate to make any recommendations about this type of exercise, as well as about flexibility and balance, as included in the WHO recommendations.

**Table 1. Summary of Frequency, Intensity, Time, and Type Characteristics of Studies Included in Meta-Analysis and World Health Organization (WHO) Physical Activity Recommendation for Older Adults**

| Variable | Intervention, Mean ± Standard Deviation | WHO Recommendation for Older Adults (≥65) |
|---|---|---|
| Frequency | 3.4 ± 1.4 d/wk | ≥3 d/wk (aerobic); 2 d/wk (resistance) |
| Intensity | 3.7 ± 0.6 metabolic equivalents (moderate) | Moderate to vigorous |
| Time | 137.05 ± 44.95 min/wk<br>45.2 ± 17.0 min/session | ≥150 min/wk<br>≥30 min/d if Moderate<br>≥20 min/d if Vigorous |
| Type | Primary: Aerobic exercise<br>Adjuvant: Combined aerobic and resistance exercise | Primary: Aerobic exercise<br>Adjuvant 1: Resistance exercise<br>Adjuvant 2: Flexibility exercise<br>Adjuvant 3: Balance exercise |

The control group samples in our meta-analysis experienced a significant decline in cognitive function during the intervention period. Rapid declines in cognitive function are common in the literature when assessed using the MMSE, and are characterized by a loss of 3 or more points on the MMSE during a 6-month period.[49] Scores on the MMSE indicate degree of impairment and include severe (0–10), moderate (10–20), mild (20–25), and questionably significant (25–30). A mild degree of impairment indicates that the individual may require only some supervision, support, and assistance, whereas a moderate degree of impairment indicates the need for 24-hour supervision.[14] In the current meta-analysis, the average MMSE score for the control group decreased by 1.7 points, from 20.0 (mild degree of impairment) to 18.3 (moderate degree of impairment), in the total sample and 2.2 points, from 16.6 (moderate degree of impairment) to 14.4 (moderate degree of impairment), in those diagnosed with AD over 18.6 weeks. The average MMSE score for the exercise group increased by 0.6 points, from 20.4 (mild degree of impairment) to 21.0 (mild degree of impairment), in the total sample and 0.38 points, from 17.9 (moderate degree of impairment) to 18.3 (moderate degree of impairment), in those diagnosed with AD over 18.6 weeks.

Limitations of our meta-analysis should be noted. First, there was significant variation in the types of measurement tools used to assess cognitive function in the included studies. Nonetheless, 57% of the studies used the MMSE as the cognitive function outcome measure, and the type of cognitive measure used was not found to be a moderator of our findings. Furthermore, the types of measurement tools used to assess cognitive function in the current meta-analysis could be confirmed as primary outcomes in only 12 of the 23 interventions, although our sensitivity analysis indicated that the effects of exercise on cognitive function were not different in studies failing to report primary versus secondary outcomes (k = 9) and studies reporting the selected cognitive measure as a secondary outcome (k = 2) versus those reporting the selected cognitive measure as a primary outcome (k = 12; $d_+ = 0.070$, 95% CI = −0.18–0.33). Second, a majority of the combined training studies (6 of 7) were included in trials with individuals diagnosed with AD, which tended to have smaller samples, although our moderator analyses indicated that diagnosis did not alter our findings, and our finding for exercise type remained significant even after controlling for diagnosis. The authors of future primary-level studies assessing the effect of exercise on cognitive function in this population should better report exercise intervention adherence and be more uniform in the tools they use to measure cognitive function. Third, because we included all types of exercise training interventions, we had to evaluate exercise intensity using metabolic equivalents, an absolute measure of intensity that some do not consider an ideal estimate of exercise intensity for older adults.[49] The difference in level of heterogeneity observed in the within-group effect size estimates between the exercise ($I^2 = 0\%$) and control (65.1%) groups was large, although the small sample in the current meta-analysis limits the complexity of the models that can be run to further evaluate how serious a threat publication bias is to our results in this domain. Finally, physical activity influences cognitive function through multiple mechanisms, and without direct measurements of these mechanistic pathways, it is impossible to discern from the current meta-analysis which mechanisms underlie our findings in individuals at risk of or diagnosed with AD.

There were important strengths of our meta-analysis. First, we adhered to the high-quality PRISMA contemporary standards as assessed using AMSTAR, resulting in the most comprehensive meta-analysis conducted on this sample to date (Data S3). Second, we used newer, more sophisticated statistical techniques than prior meta-analyses, such as the moving constant technique,[32] winsorizing,[31] and interactive modeling,[50] that allowed us to consider moderators collectively rather than individually. Third, our meta-analysis examined several a priori study-level moderators, which in turn allowed us to identify a particular modality of exercise (aerobic exercise training) that may improve cognitive function to a greater magnitude than combined aerobic and resistance exercise training in individuals at risk of or diagnosed with AD. Last, we focused on a single type of dementia (AD), whereas past meta-analyses have typically included trials of subjects with multiple types of dementia[5–8,10] or subjects with a diagnosis only of cognitive impairment.[9] Given that there are multiple neuropsychological,[51,52] electrophysiological,[53] and pathophysiological[54] differences between the various types of dementia, our results can be used to guide the development of evidence-based recommendations specifically for individuals at risk of or diagnosed with AD.

## CONCLUSIONS

Our meta-analysis adhered to high-quality PRISMA contemporary standards and provides further support for the use of exercise training as a therapeutic modality to improve cognitive function in individuals at risk of or diagnosed with AD. Our meta-analysis is the first to suggest that aerobic exercise may be more effective than other types of exercise in preserving the cognitive health of older adults at risk of or who have AD. Our findings need to be confirmed in future studies using neuropsychological measures to assess cognitive function and objective measurements of cognitive function such as pre-and post-exercise neuroimaging measures and molecular markers (e.g., inflammatory markers). Nonetheless, the current findings can serve as a framework for design of future studies examining the effects of exercise interventions on cognitive function in this population. Ultimately, studies should aim to examine physical activity and exercise in combination with other strategies (e.g., medications) to develop more targeted prevention and treatment options for AD.

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**Conflict of Interest**: The authors report no conflicts of interest.

**Author Contributions**: GAP searched, extracted, and coded all included and excluded trials; cleaned and analyzed the data; and drafted and revised the paper. He is guarantor. BAT and LSP oversaw data extraction and coding and revised the paper. HVM analyzed data and revised the draft paper. BTJ oversaw all data analysis methods and revised the draft paper. ALZ extracted and coded all included and excluded trials. JL performed the systematic literature search. PDT revised the draft paper.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Data S1** Data Extraction and Coded Variables

**Data S2** Augmented version of the Downs and Black Checklist for exercise training studies aimed at improving cognitive function

**Data S3** Characteristics of Previously Published Meta-analyses

**Data S4** Characteristics of included trials (n = 19) and intervention features (k = 23)

**Data S5** Full search strategy for the electronic databases queried

**Data S6** Bivariate meta-regression analysis: Improvements in cognitive function based on reported adherence to the exercise training intervention (k = 9)