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Community-deliverable exercise and depression in adults with arthritis: Confirmatory evidence of a meta-analysis using the IVhet model

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Abstract

Objective—Using the traditional random-effects model, a recently reported standardized effect size (*g*) reduction of −0.42 (95% CI, −0.58 to −0.27) was observed as a result of community-deliverable exercise in adults with arthritis and other rheumatic diseases (AORD). However, a recently proposed alternative model (IVhet) has been shown to have superior coverage probability to the random-effects model. The purpose of this brief report was to compare these previous random-effects results with the IVhet model.

Methods—Based on a previous meta-analysis of 35 *g*'s representing 2,449 participants, results were pooled using the IVhet model. Influence analysis, number needed-to-treat (NNT), percentile improvement, and gross estimates of the number of inactive adults with arthritis who could benefit from exercise were also calculated.

Results—The IVhet model yielded statistically significant reductions in depressive symptoms (*g* = −0.30, 95% CI, −0.49 to −0.11), a difference that was −0.12 (28.7%) smaller than the random-effects model. With each study deleted from the model once, results remained statistically significant, ranging from −0.28 to −0.34. The percentile improvement, NNT, and estimated number of people with arthritis in the United States who could improve their depressive symptoms by participating in a regular exercise program was, respectively, 11.8% (95% CI, 4.5% to 18.8%), 8 (95% CI, 5 to 23) and 2.7 million (95% CI, 1.0 to 4.4 million).

Conclusions—These findings provide more conservative and accurate evidence that community-deliverable exercise improves depressive symptoms in adults with AORD. Future meta-analyses may want to consider using the IVhet versus traditional random-effects model.

Keywords

exercise; arthritis; depression; meta-analysis; methods

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Introduction

Self-reported doctor-diagnosed arthritis is a major public health problem affecting approximately 52.5 million US adults (22.7%), with age-adjusted prevalence rates higher among women (23.9%) than men (18.6%) (1). By 2030, it is estimated that more than 67 million adults (25.0%) 18 years of age and older will have doctor-diagnosed arthritis (2). Not surprisingly, the economic costs associated with arthritis are high. Yelin et al., reported that the total costs attributable to arthritis and other rheumatic diseases (AORD) in the US in 2003 was approximately $128 billion, $80.8 billion in direct costs and $47.0 billion in indirect costs (3). A common condition among adults with AORD is depression. Murphy et al. reported that the prevalence of depression among adults with arthritis was 17.5% (6.6 million people) (4). One potential intervention for improving depression among adults with AORD is exercise, a low-cost intervention that is available to most adults. Using the traditional random-effects, method of moments model of Dersimonian and Laird (5), the investigative team recently conducted a meta-analysis of randomized controlled trials to examine the effects of exercise (aerobic, strength training or both) on depressive symptoms in adults with AORD (6). Based on a total of 35 effects sizes (*g's*) representing 2,449 adults, statistically significant improvements in depressive symptoms were observed (6). However, a recently developed inverse heterogeneity model (IVhet) has been shown to be superior to the traditional random-effects model (7). Specifically, simulation studies have shown that the IVhet model retains correct coverage probabilities as well as a lower observed variance when compared with the random-effects model, regardless of heterogeneity (7). Given the prevalence of depression in adults with AORD as well as the need to provide accurate overall estimates regarding the effects of exercise on depression in adults with AORD, the purpose of this brief report was to compare previous meta-analytic results using the random-effects model (6) with those using the recently developed IVhet model (7).

Methods

Data Source

Data for this paper were derived from a previously published meta-analysis of randomized controlled trials addressing the effects of community-deliverable exercise (aerobic, strength training or both) on depressive symptoms in adults with AORD, details of which have been described in detail elsewhere (6). Studies included those with osteoarthritis, rheumatoid arthritis, fibromyalgia, and systemic lupus erythematosus. Mean ± standard deviation (SD) length of training was 19 ±16 weeks, frequency 4 ± 2 times per week and duration 34 ± 17 minutes per session.

Data Synthesis

Effect size calculations—Effect sizes from each study were calculated as the standardized mean difference using Hedge's *g* statistic, adjusted for small-sample bias (8). This was accomplished by subtracting the change outcome difference in the exercise group minus the change outcome difference in the control group, and then dividing by the pooled standard deviation of the change outcomes for the exercise and control groups. If change score standard deviations were not available, they were calculated from either the reported change outcome or treatment effect 95% confidence intervals or pre and post standard deviation values according to procedures developed by Follmann et al. (9).

Effect size pooling—Effect sizes for the current study were pooled using the recently developed IVhet model (7). The IVhet is a quasi-likelihood model that is computed by (1) calculating weights that sum to 1 from each study, (2) pooling effects from all the studies, and (3) calculating the variance of the pooled effect sizes (*g*) as follows:

$$W_{j=}\frac{1}{v_j} \quad / \quad \sum_{j=1}^{k}\frac{1}{v_j},$$

Where, wj above are weights that sum to 1, and v_j is the variance, followed by

$$\hat{\theta}_{IVhet=}\sum_{j=1}^{k}W_j\hat{\delta}_j$$

Where $\hat{\theta}_{IVhet}$ above is the estimated pooled effect for changes in depressive symptoms, followed by

$$var\left(\hat{\theta}_{IVhet}\right)=\sum_{j=1}^{k}\left[\left(\frac{1}{v_j}/\sum_{j=1}^{k}\frac{1}{v_j}\right)^2 \quad \left(v_j+\tau^2\right)\right]$$

Where $var\left(\hat{\theta}_{IVhet}\right)$ above is the estimated variance of pooled effects and τ^2 is the between-study variance.

The IVhet model has been shown to be superior to the original random-effects, method-of-moments model of Dersimonian and Laird (7), the most common random-effects model used to pool aggregate data meta-analytic results. Specifically, simulation studies have shown that the IVhet model retains correct coverage probabilities as well as a lower observed variance than the random-effects model, regardless of heterogeneity (7).

The pooled results for depressive symptoms derived from the IVhet model at both the group and study level were then compared to those previously calculated (6) using the original random-effects method-of-moments model of Dersimonian and Laird (5). In addition, Q and I^2 statistics for heterogeneity and inconsistency were calculated as well as influence analysis with each study deleted from the model once. For I^2, inconsistency was considered to be very low (<25%), low (25% to <50%), moderate (50% to <75%) or large (≥ 75%) (10). To improve practical relevance with respect to improvements in depressive symptoms, percentile gain in the exercise groups was calculated using Cohen's U_3 index (11). In addition, the number-needed-to treat (NNT) was calculated for IVhet results using the approach recommended by the Cochrane Collaboration (12). Based on previous research, a control group risk of 30% was used to calculate the NNT (13). Derived from NNT, gross estimates were calculated for the number of adults with AORD in the United States who may benefit from exercise but were not currently meeting exercise recommendations. This was based on the reciprocal of the NNT multiplied by the number of adults in the United States with doctor-diagnosed arthritis who were not currently meeting exercise guidelines (approximately 34.8 million) (1;14). Because of the small number of effect sizes for those with osteoarthritis, rheumatoid arthritis and systemic lupus erythematosus ($n \leq 7$), results across all AORD, including fibromyalgia, were pooled as in the original investigation (6). Data were analyzed using Meta XL (version 4.0) (15).

Results

A total of 35 *g*'s from 29 studies that included 2,449 participants (1,470 exercise and 979 control) were pooled from the previous meta-analysis (6). Overall results for changes in depressive symptoms using the random-effects and IVhet models are shown in Table 1 while study level results using the IVhet model are shown in Figure 1. As can be seen, statistically significant reductions in depressive symptoms were found using both the random-effects and IVhet models. However, the IVhet model yielded a difference that was −0.12 (28.7%) smaller than the random-effects model. Statistically significant heterogeneity and a moderate to large amount of inconsistency were observed. With each study deleted from the model once, IVhet results remained statistically significant across all deletions at the group level, ranging from −0.28 to −0.34 (results not shown). Based on Cohen's U_3 index, the percentile improvement was 11.8% (95% CI, 4.5% to 18.8%) while the NNT was 8 (95% CI, 5 to 23). The estimated number of people with arthritis in the United States who could improve their depressive symptoms by participating in a regular exercise program was 2.7 million (95% CI, 1.0 to 4.4 million).

Results were similar when collapsed so that only one *g* represented each study (Table 1). The IVhet model yielded a difference that was −0.17 (36.7%) smaller than the random-effects model at the study level. Statistically significant heterogeneity and a moderate to large amount of inconsistency were observed. With each study deleted from the model once, IVhet results remained statistically significant across all deletions, ranging from −0.28 to −0.37 (results not shown). Based on Cohen's U_3 index, the percentile improvement was 11.8% (95% CI, 2.3% to 20.7%) while the NNT was 8 (95% CI, 4 to 45). The estimated number of people with arthritis in the United States who could improve their depressive symptoms by participating in a regular exercise program was 2.7 million (95% CI, 0.5 to 5.5 million).

Discussion

This brief report demonstrates that changes in depressive symptoms as a result of community-deliverable exercise in adults with selected types of AORD remained statistically significant when using the recently developed, more conservative and accurate IVhet model (7). From the authors' perspective, these findings are important for at least two reasons. First, the current results reinforce previous random-effects-modeling results (6), something that is believed to be important given the tendency for overly liberal findings when a random-effects model is used (7). The former notwithstanding, the current results at the group and study levels were approximately 29% and 37% smaller, respectively, than previous findings based on the random-effects model (6). Therefore, the magnitude of effect for the current investigation using the IVhet model was smaller but probably more representative of the truth. Second, this brief communication suggests that caution may be warranted when interpreting meta-analytic results based on the random-effects model.

The results of this study should be viewed with respect to the following potential limitations. First, since these results were based on aggregate data, there is the potential for ecological fallacy. Second, the calculation of NNT and all other results derived from such may be questioned since these calculations were based on aggregate versus individual level data. Third, the results were limited to participants with osteoarthritis, rheumatoid arthritis, fibromyalgia and systemic lupus erythematosus. Therefore, the results may not be generalizable to participants with other types of AORD.

In conclusion, these findings confirm that community-deliverable exercise improves depressive symptoms in adults with selected types of AORD. Future studies may want to consider using the IVhet versus traditional random-effects model.

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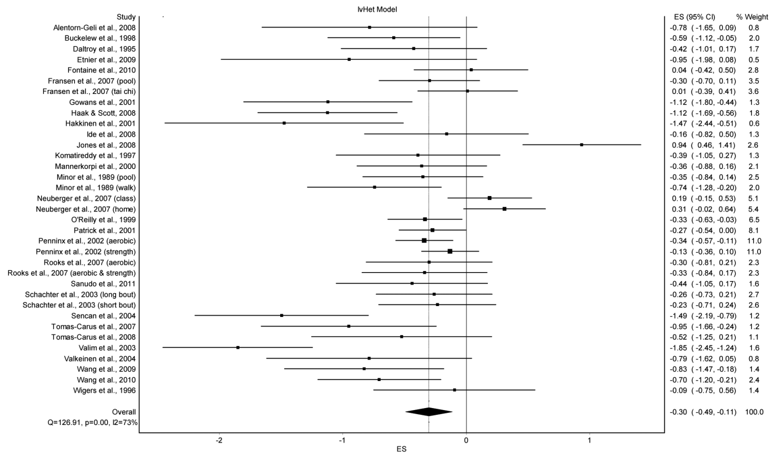

Figure 1.

Forest plot for changes in depressive symptoms in adults with arthritis and other rheumatic diseases based on the IVhet model. The black squares represent the standardized mean difference effect size (ES) while the left and right extremes of the squares representing the corresponding 95% confidence intervals. The middle of the black diamond represents the overall ES difference while the right and left extremes of the diamond represent the corresponding 95% confidence intervals.

Table 1

Changes in depressive symptoms based on IVhet and random-effects model.

Model	ES (no.)	*g* (95% CI)	Q (p)	I^2 (95% CI)
Group Level				
- IVhet	35	−0.30 (−0.49, −0.11) *	126.9 (<0.0001) **	73% (63%, 81%)
- Random-Effects	35	−0.42 (−0.58, −0.27) *	126.9 (<0.0001) **	73% (63%, 81%)
Study Level				
- IVhet	29	−0.30 (−0.54, −0.06) *	122.8 (<0.0001) **	77% (68%, 84%)
- Random-Effects	29	−0.48 (−0.65, −0.30) *	122.8 (<0.0001) **	77% (68%, 84%)

Notes: ES (no.), number of effect sizes; *g* (95% CI), Hedge's standardized effect size and 95% confidence intervals; Q (p), Cochran's Q statistic and alpha value for Q; I^2 (95% CI), *I* statistic and 95% confidence intervals

* statistically significant (non-overlapping confidence intervals)

** statistically significant (alpha value ≤ 0.10).