Does Exercise Decrease the Level of Anxiety in Adults?

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not "Does exercise decrease the level of anxiety in adults?"

Study Design: A systematic review of three randomized controlled trials (RCTs) that were peer reviewed and published between 2016 and 2020.

Data Sources: All articles were published in peer-reviewed journals. Two of the RCTs were researched using Pubmed and one RCT was found using Academic Search Premier, AMED. All studies were selected based on applicability to the clinical question presented in the objective, and if the researched outcomes were patient oriented.

Outcome Measured: A reduction in anxiety level was the outcome measured in all three studies. The outcomes were measured using three different scales: Hamilton Inventories for Anxiety (Ham-A), Anxiety-DASS-21 subscale, and Chinese Mandarin Version of the State-Trait Anxiety Inventory Form (CMSTAI-Y) scores.

Results: In the RCT lead by Plag et al., high intensity interval training (HIIT) and low intensity training (LIT) were statistically significant for anxiety reduction ($p<0.01$) when comparing the mean (standard deviation) Ham-A scores from baseline to post-test to follow-up. The effect size was large ($F=65.56$) and about double in HIIT compared to LIT. De Manincor et al. produced results that were not clinically significant in reducing anxiety when yoga was implemented for exercise. The study was found to have a p-value of .16, an adjusted mean difference (AMD) of -1.91, and a confidence interval (CI) of -4.58 to .76. Ma et al. had a significant reduction in state anxiety ($F=9.35$, $p=.000$) and trait anxiety ($F= 6.18$, $p= .003$).

Conclusion: The evidence of this systematic review is inconclusive. Plag et al. and Ma et al. both yielded significant data (p-value $<.01$) supporting that their exercise interventions, six 20-minute HIIT sessions and a 6 week home-based exercise program respectively, helped reduce anxiety in adults. De Manincor et al. did not have significant data ($p=.16$) to prove that their exercise intervention, yoga, reduced anxiety levels. Future studies should be conducted to investigate other exercise alternatives and repeat studies with a larger treatment population.

Key words: Exercise, generalized anxiety, randomized control trial, yoga, anxiety, reducing, exercise program

INTRODUCTION

Anxiety disorders are the most prevalent psychiatric disorders.[1] Among anxiety disorders, specific phobias are the most common (10.3% prevalence), then panic disorder (8% prevalence), followed by generalized anxiety disorder (GAD; 2.2% prevalence).[1] GAD is classified as excessive anxiety and worry out of proportion to events or activities most days for at least 6 months.[2] Typically, it is accompanied by symptoms that can affect every part of the body: muscle tension, irritability, disturbed sleep, etc.[2] About 7% of women and 4% of men will meet criteria for GAD at least once in their lifetime.[3] Patients with GAD typically present with excessive anxiety about everyday situations.[4] The anxiety they experience causes them distress across multiple domains of life and is often associated with physical symptoms including sleep disturbance, gastrointestinal symptoms, and muscle tension.[4] The etiology of anxiety disorders is multifactorial and stems from an interaction of psychosocial factors and genetic vulnerability.[1]

Anxiety is one of the leading causes of disability worldwide.[5] 4.7% of the world population suffer from anxiety; however, only 43.2% are receiving treatment.[5] Anxiety disorders are associated with high healthcare costs, and represent an economic burden estimated to be between $42.3 and $46.6 billion annually in the United States.[6] Patients with anxiety have higher healthcare use and costs.[6] There is not one total number of healthcare visits each year; however, there are an estimated 1,247,000 anxiety-related ED visits annually.[7] Most of the patients who sought out care from the ED had a follow up appointment scheduled with their primary care provider or a mental health specialist upon discharge.[5] However, if they were in imminent danger, admission to the hospital or transfer to a psychiatric facility was necessary.[7]

Currently, pharmacotherapy and psychotherapy are effective in treating anxiety disorders as monotherapy or adjunctive therapy. Antidepressants are efficacious for acute and chronic

management of anxiety disorders. Anxiety disorders are often multifactorial contributing to a complex treatment.[1] First line medications include venlafaxine, duloxetine, paroxetine, escitalopram, and sertraline (SSRIs and SNRIs). Second line medications include imipramine (TCA), buspirone, and pregabalin. Alternative medications include hydroxyzine and quetiapine. Benzodiazepines can be used for short-term, initial, and acute management; but should not be used for long-term control. Psychotherapy can be implemented as monotherapy or adjunctive to medications. Examples of psychotherapy include, but are not limited to, cognitive behavioral therapy (CBT) and eye movement desensitization and reprocessing (EMDR).

The usual treatment options mentioned above can all be effective in managing anxiety but do not come without side effects. The barriers of pharmacologic treatment due to side effects displays the value and necessity of alternate therapies. The first line treatment, SSRIs and SNRIs, cause sexual dysfunction, making many patients noncompliant. They also have additional side effects such as nausea, diarrhea, and weight gain.

Implementing various forms of exercise as a treatment option for patients may be used as a nonpharmacologic approach to reduce anxiety levels with less or no medication at all. Anxiety is due to a decrease of serotonin in the brain which is why the first line treatment is typically with an SSRI or SNRI in practice. Studies show that serotonin levels increase following exercise which is why it is being experimented as a possible treatment for decreasing anxiety levels.[5]

This paper evaluates three randomized controlled trials (RCTs), assessing the efficacy of exercise in the treatment of anxiety.

OBJECTIVE

The objective of this selective EBM review is to determine whether or not "Does exercise decrease the level of anxiety in adults?"

METHODS

The scholarly literature selected was based on their relevance and ability to answer the clinical question: Does exercise decrease the amount of anxiety in adults? Further, articles were selected based on their ability to discuss a newer treatment intervention, exercise, and evaluate patient-oriented outcomes (POEMS) of anxiety based on this intervention. Articles were chosen only if they had the appropriate population, intervention, comparison, and outcome-measured criteria. Studies were researched via PubMed, Academic Search Premier, and AMED. The first study referenced in this review, Plag et al., was found on Academic Search Premier, AMED using key words "exercise", "generalized anxiety" and "randomized control trial". The second study referenced in this review, de Manincor et al., was found on Pubmed using keywords "yoga", "anxiety", and "reducing". The third study referenced in this review, Ma et al., was also found on Pubmed using keywords "exercise program" and "anxiety". All three studies implemented randomization, were published in peer-reviewed journals, and were in the English language. Inclusion criteria consisted of randomized controlled trials that were published in or after 2010 that utilized subjects 18 years old or older. Studies published before 2010, studies that involved subjects less than 18 years old, and studies that were published in languages other than English were excluded. Statistical analyses utilized in these studies include mean change (SD) in the baseline of Hamilton Inventories for Anxiety (Ham-A), Depression, Anxiety and Stress Scale (DASS-21), and Chinese Mandarin Version of the State-Trait Anxiety Inventory Form (CMSTAI-Y) scores, as well as the statistical significance of their p-value. Plag et al. also utilizes 95% confidence intervals (CI) and an F-score, de Manincor et al. utilizes AMD and 95% CI, and Ma et al. uses an F-score to analyze results. The population studied in this selective EBM review were adults diagnosed with an anxiety disorder. The demographics and characteristics of

each study can be found in Table 1. The intervention used throughout each study was exercise.

Plag et al. compared two types of exercise: high intensity interval training (HIIT) vs low

intensity interval training (LIT).[8] De Manincor et al. compared 6 week yoga plus treatment-as-

usual (TAU) vs waitlist plus TAU.[5] Ma et al. compared a home-based exercise program (in

addition to traditional care) vs traditional care.[9] The outcome measured that is discussed is a

reduction in anxiety.

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Plag[8] (2020)	RCT	33	Adults $\geq$ 18 years old (mean age 41.03)	A primary diagnosis of GAD; a minimum age of 18; sufficient German language skills; Preexisting treatment with antidepressants or pregabalin was allowed if the daily dosage was stable for at least four weeks before the trial and throughout	People who suffered from distinct mental or somatic comorbidities and in case of current psychotherapy	4	High intensity interval training (HIIT) vs. low intensity exercise (LIT)
De Manincor[5] (2016)	RCT	107	18-65	Ability to give informed Consent; Age 18–65; Ability to speak, read and write English; General health and ability to be involved in a yoga program; Medication and professional mental health assistance unchanged for 3 months; DASS-21 scores showing mild, moderate or severe anxiety	Serious injury, medical or psychological disorder likely to preclude the end of the trial; recent surgery; acute or chronic pain; alcohol or drug use; already in a personal yoga practice; DASS-21 scores in the normal or extremely severe range	10	6-week yoga plus treatment-as-usual (TAU) vs waitlist plus TAU
Ma[9] (2017)	RCT	86	Mean age 39.76 - 40.45	Patients diagnosed with anxiety disorders that were at psychiatric clinics	Individuals with schizophrenia, mood disorders, dementia, or physical disability	3	Home-based exercise program + traditional care vs traditional care

OUTCOME MEASURED

The outcome measured in this review is a reduction in anxiety level as measured by Ham-A, Anxiety-DASS-21 subscale, and CMSTAI-Y. Ham-A is a clinician-based questionnaire consisting of 14 symptom-defined psychological and somatic elements correlated with an anxious mood.[10] Each item is scored on a scale of 0 (not present) to 4 (severe) and results are added which indicate the following: >17 is mild anxiety and 25-30 is moderate to severe anxiety.[10] DASS-21 is a set of three self-reported subscales to measure emotional states of depression, anxiety, and stress. Each of the three scales has 7 items on it. Scores on this test rank anxiety as follows: 0-7 is normal, 8-9 is mild, 10-14 is moderate, 15-19 is severe, and 20+ is extremely severe.[5] The DASS-21 scoring scale is proven to be reliable in clinical populations and is recommended as a measure of change in intervention trials.[5] CMSTAI-Y is a self-report form incorporating 20 items to measure state anxiety and 20 items to measure trait anxiety on a 4 point scale.[9] It has a high correlation with the Hamilton Anxiety Rating scale.[9] Higher scores indicate higher levels of anxiety.[9]

RESULTS

All three studies in this review enrolled individuals diagnosed with anxiety disorders and evaluated the efficacy of exercise in reduction of anxiety. Plag et al. conducted a parallel-group, assessor-blinded RCT over 30 days to compare the effect of HIIT vs LIT on anxiety levels using Ham-A.[8] The authors enrolled subjects who were a minimum age of 18 years old and had a primary diagnosis of GAD.[8] The cohort was comprised of 33 individuals who were allocated to the intervention or control group by biased coin minimization using MinimPy, a randomization software.[8] In total, 17 subjects received HIIT and 16 subjects received LIT.[8] Participants were blinded to the hypotheses of the trial but not to the intervention as they were told that the goal of the study was to investigate the treatment effects of two different forms of exercise.[8]

Investigators were also not blinded to the treatment as they supervised the training that was instructed by trained staff.[8] The LIT group received six 30-minute sessions, and the HIIT group received six 20-minute sessions.[8] A heart rate monitor was used in the LIT group patients to ensure that they did not endure high physical strain and were continuously below 70% HR_{max}.[8] In the HIIT group, three patients discontinued the exercise intervention: one was no longer interested and two left due to personal reasons.[8] In the LIT group, one patient left the exercise due to disinterest.[8] An intention-to-treat analysis was performed and a worse-case analysis was done.[8]

The efficacy of exercise in the improvement of anxiety was measured by Ham-A score.[8] The patients rated their anxiety using the Ham-A score which was performed blind to the treatment allocation.[8] The authors used mean scores calculated from the patients' Ham-A assessments to measure and compare the anxiety level rated at baseline, 12 days after the training, and 30 days after baseline.[8] The Ham-A scores showed a baseline mean score of 31.29 (CI 27.42–34.50) for the HIIT group which dropped to a mean score of 17.04 (CI 12.81–21.81) after the 12 day HIIT treatment, and then decreased further to 15.82 (CI 12.01–19.98) with the follow-up Ham-A score 30 days after baseline.[8] The baseline mean score of Ham-A for the LIT group was 28.75 (CI 24.12–33.37) which decreased to a mean score of 20.83 (CI 15.50–26.17) after the 12 day LIT treatment, and then further dropped to 18.98 (CI 13.71–24.26) 30 days after baseline.[8] The mean scores of Ham-A from baseline to post-treatment to follow up were statistically significant for anxiety reduction ($p<0.01$) for both HIIT and LIT interventions.[8] However, the effect sizes from baseline to post-treatment to follow-up were about double the size in HIIT compared to LIT. The mean Ham-A score decreased by 14 from baseline to post-treatment compared to a decrease of 8 in the LIT group.[8] Additionally, the mean Ham-A score

decreased by 16 from follow-up to baseline in the HIIT group, but only by 10 in the LIT group.[8]

The statistical analysis between these two showed a large treatment effect size of F=5.33

indicating a stronger reduction in anxiety when patients participated in HIIT compared to LIT.[8]

Table 2. Means and post-hoc tests for secondary clinical outcomes/endurance-related variables at all points of measurement (N = 33)[8]

	Baseline: Mean (95%-CI)	Post-treatment	Follow-up
HIIT	31.29 (27.42–34.50)	**17.04**** (12.81–21.81)	**15.82****(12.01–19.98)
LIT	28.75 (24.12–33.37)	**20.83**** (15.50–26.17)	**18.98**** (13.71–24.26)

**significant at .01-level (two-tailed)

Table 3. Results from ANOVAs from baseline to post (n = 33) for clinical outcomes[8]

Clinical Measure	ANOVA	F(df)	P value
HAM-A	Group x time	5.33	.03

**significant at .05-level (two-tailed)

De Manincor et al. conducted a two-group RCT to compare a decrease in anxiety levels

between a 6 week yoga plus TAU group vs a waitlist plus TAU control group.[5] If subjects were

on medication for their anxiety and/or utilizing professional mental health assistance, it had to be

unchanged for 3 months prior to the study.[5] The study recruited people ages 18-65 with DASS-

21 scores demonstrating at least mild, moderate or severe anxiety (score between 8 and 19).[5] The

study was conducted over a 6 week period and enrolled 107 participants.[5] The randomization of

patients was conducted using a computer-generated randomization of numbered allocation.[5]

Participants were unaware of the study design and blinded to group allocations, but they were

aware that completion of outcome measure self-report scales occurred pre- and post-

intervention.[5] Overall, 53 patients received yoga plus TAU, and 54 patients received TAU.[5] The

yoga intervention included four individual 1 hour consultations/lessons over a 6 week period

where an individualized plan was developed for subjects to continue at home.[5] The TAU group

continued their regular care including medications, therapy, and other mental health services for

the six weeks.[5] Six participants discontinued the yoga plus TAU intervention, and five

participants discontinued the TAU group.[5] The primary analysis for the yoga intervention excluded 6 subjects from their analyses.[5] All 54 in the control group were analyzed in the primary analysis, and there was a worst-case analysis performed.[5] Therefore, 101 participants were included in the primary outcome analysis of change in anxiety level at the end of week six.[5]

Assessments for efficacy and improvement of anxiety using DASS-21 scores were measured 6 weeks after treatment using postintervention means, AMD between groups, and associated 95% CI and p-values.[5] The reduction of DASS-21 anxiety scores with yoga relative to waitlist was not statistically significant (p=0.16).[5] The mean (SD) DASS-21 scores for the yoga group was 12.98 (7.38) at baseline and 9.62 (6.97) after treatment.[5] The mean (SD) DASS-21 score for the TAU group was 14.65 (9.45) at baseline and 12.56 (9.65) after treatment.[5] The AMD was -1.91 showing a small treatment effect.[5] The 95% CI was -4.58, 0.76.[5] The results are summarized in Table 3 below. Overall, this data was not clinically significant to indicate that yoga decreases anxiety levels.

Table 4. Baseline and post-intervention mean (SD) outcomes and effect size[5]

	Baseline yoga + TAU *Mean (SD)*	**Post yoga + TAU** *Mean (SD)*	**Baseline TAU** *Mean (SD)*	**Post TAU** *Mean (SD)*	**AMD**	**95% CI**	**P-value**
Anxiety-DASS-21 Subscale	12.98 (7.38)	9.62 (6.97)	14.65 (9.45)	12.56 (9.65)	-1.91	-4.58, .76	.16

Ma et al. conducted an RCT to compare if a home-based exercise program in addition to traditional care would reduce anxiety in individuals with anxiety disorders.[9] The study recruited participants who were all above 18 years of age, with the experimental group having a mean age of 39.76 (SD 11.09) and the control group having a mean age of 40.45 (SD 11.25).[9] From 2012-2014, 86 participants were selected from psychiatric clinics in a medical center and were assigned to either the experimental or control group by selecting random numbers from a sealed

envelope.[9] Treatment for the experimental group consisted of a home-based exercise program that instructed participants to exercise 30 minutes per day, 5 days per week, for a period of 3 months.[9] Treatment for the control group only included traditional care.[9] All participants were blinded to the group assignment. [9] 43 subjects were assigned to the experimental group and 43 were assigned to the control group.[9] A total of two people did not complete the program in the experimental group: one due to lack of motivation and one due to lack of time.[9] One participant in the control group did not follow up due to disinterest in completing tests.[9] All three were not included in the analysis.[9] An intention-to-treat and a worst-case analysis was not done.[9]

The CMSTAI-Y was used after the conclusion of the study to evaluate the effect of the home-based exercise program on state and trait anxiety levels after 3 months of treatment.[9] Participants completed a pretest before the 3 month exercise program, a posttest at 1 week after the program, and a follow-up test three months after the program.[9] The change in trait anxiety from pretest to posttest to follow-up was 57.61 to 55.12 to 53.90 respectively in the experimental group and 54.79 to 54.93 to 55.69 respectively in the control group.[9] The change in state anxiety from pretest to posttest to follow up was 52.17 to 49.36 to 48.78 respectively in the experimental group and 49.57 to 49.59 to 52.21 respectively in the control group.[9] The results revealed significant decreases in state anxiety ($F=9.35$, $p=.000$) and trait anxiety ($F=6.18$, $p=.003$). [9] Although these results are statically significant, it is uncertain whether a change in 4 points on the CMSTAI-Y is clinically meaningful. The results are summarized in Table 4 and Table 5 below.

Table 5. CMSTAI-Y Change in Trait Anxiety from Pretest to Posttest to follow up[9]

	Experimental Group (Home-Based Exercise Program + Traditional Care)	Control Group (Traditional Care)
Pretest	57.61	54.79
Posttest	55.12	54.93
Follow-up Test	53.90	55.69

*p=.003 and F=6.18 in the experimental group relative to the control group from the

pretest to follow-up test[9]

Table 6. CMSTAI-Y Change in State Anxiety from Pretest to Posttest to follow up[9]

	Experimental Group (Home-Based Exercise Program + Traditional Care)	Control Group (Traditional Care)
Pretest	52.17	49.57
Posttest	49.36	49.59
Follow-up Test	48.78	52.21

*p=.000 and F=9.35 in the experimental group relative to the control group from the

pretest to follow-up test[9]

DISCUSSION

Anxiety disorders are the most prevalent psychiatric disorders.[1] Patients diagnosed with

anxiety disorders often have an associated comorbidity that increases complexity of care and

supports the need for alternative treatments. Nonpharmacologic treatment, such as exercise, is a

beneficial option as it does not carry with it the side effects of traditional medications nor the

financial expense; however, it does require patients to be adherent to an exercise routine and

physically able to participate. Additionally, different patient populations may respond differently

to various forms of exercise. This could create a challenge for medical providers, as they would

need to be knowledgeable on where to refer patients to get appropriate and quality exercise.

This selective evidence based medicine review studied the efficacy of exercise as a

treatment to reduce anxiety levels. Plag et al. incorporated HIIT training and Ma et al.

incorporated a home-based exercise program. Both studies showed a large treatment effect with

statistically significant improvement (p<0.01) in anxiety levels after intervention with exercise.[8,9]

HIIT and LIT interventions were statistically significant for anxiety reduction (p<0.01), but the

effect sizes from baseline to post-treatment and follow-up were about double the size in HIIT

compared to LIT showing that HIIT is a more effective intervention.[8] Home-based exercise

programs were more effective than traditional care to a noteworthy extent (p=.003 and F=6.18

for trait anxiety and p=.000 and F=9.35 state anxiety).[9] The study by De Manicor, et al.

suggested that yoga was not effective in reducing anxiety levels, demonstrated by a p-value of

0.16, AMD -1.91, and CI -4.58, 0.76.[5]

All three studies had limitations. In each study, patients were unable to be blinded to

treatment, leaving participants aware of their treatment intervention. This could have led to a bias

in participants feeling a false sense of improvement. Blinded raters were also not able to be used

due to the fact that participants rated their own anxiety levels on a scale. The randomization

allocation was concealed from all of the subjects enrolling in each of the three studies, which

alleviates some concern of bias, however, the concern is not completely eliminated. Additionally

Plag et al. and Ma et al. both used a small sample size, which could lower the validity of the

results. Future studies should include more subjects to increase the power and validity of these

results. De Manincor et al. used a volunteer sample of people interested in and amenable to yoga.

Yoga may not be appealing to everyone with mental health concerns, causing the reliability of

these results to be affected.

CONCLUSION

The evidence of this systematic review is inconclusive. Plag et al. and Ma et al. both had

significant data (p-value <.01) and large treatment effects showing that their exercise

interventions, six 20-minute HIIT sessions and a 6 week home-based exercise program

respectively, helped reduce anxiety levels in adults.[8,9] However, the study that de Manincor et al.

conducted did not have significant data (p=.16) to prove that exercise in the form of yoga

reduced anxiety levels.[5] Both Plag et al. and Ma et al. had small sample sizes and shorter studies,

so additional trials should be performed with a larger sample size and longer treatment duration

to further generalize the studies. The de Manincor et al. study had 80% females with variability in the frequency, duration, and adherence to yoga practices.[5] More studies should be conducted with a broader sample group and size as well as a more consistent program. Accountability to a regimented exercise schedule would possibly help maintain more conclusive results. In addition, Plag et al. compared HIIT to LIT which are both exercises and did not have a non-exercise control group which is an added limitation of this systematic review.

This systematic review was broad and generalized as each study implemented a new form of exercise. Future research studies could be designed to implement different forms of exercise to the same group of adults with anxiety. In this instance, researchers would be able to hone in on the exercises most effective in reducing anxiety levels while looking at the same population. Further studies would need to be done to evaluate the clinical meaningfulness of the data compared to the statistical significance for reduction of anxiety symptoms.

An ongoing study being conducted by NYU Langone Health is exploring 90 adults aged 18-65 with a primary anxiety disorder.[11] They are exploring low intensity exercises vs flexible titration to high intensity exercise (HIE).[11] The participants will be assessed over the treatment at a 1 and 3 month follow up using blinded clinicians and patient rated outcomes.[11] The study started June 30, 2021 and is estimated to complete November 20, 2025.[11] If results are found significant to support that HIE reduces anxiety levels, this will further support the use of exercise for the treatment of anxiety. Hopefully, future studies can be conducted to find the best exercises to reduce anxiety levels so patients with anxiety disorders have multiple treatment options.

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