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## **The mechanisms of resistance training and its impact on anxiety and depression: a literature review**

**Wiktoria Lewicka**

e-mail: [lewickawiktoria@gmail.com](mailto:lewickawiktoria@gmail.com)

ORCID: <https://orcid.org/0000-0002-6459-419X>

Lower Silesian Center for Oncology, Pulmonology and Hematology, Plac Ludwika Hirszfelda 12, 53-413 Wrocław, Poland

**Izabella Sośniak**

e-mail: [iza.sosniak@gmail.com](mailto:iza.sosniak@gmail.com)

ORCID: <https://orcid.org/0009-0000-9438-6175>

Brothers Hospitallers Hospital in Kraków, Trynatarska 11, 31-061 Kraków, Poland

**Konrad Szaliński**

e-mail: [konrad.szalinski.mail@gmail.com](mailto:konrad.szalinski.mail@gmail.com)

ORCID: <https://orcid.org/0009-0000-2753-5353>

Jan Mikulicz-Radecki University Clinical Hospital Borowska 213, 50-556, Wrocław, Poland

**Ewa Szczęsna**

e-mail: [szczesnae17@gmail.com](mailto:szczesnae17@gmail.com)

ORCID: <https://orcid.org/0009-0001-4767-7356>

Lower Silesian Center for Oncology, Pulmonology and Hematology, Plac Ludwika  
Hirszfelda 12, 53-413 Wrocław, Poland

## **ABSTRACT**

**Introduction:** Anxiety and depressive disorders are among the most prevalent and debilitating mental health conditions, significantly impacting global health and quality of life. Current pharmacological and psychotherapeutic treatments, while effective, face challenges such as limited accessibility, high costs, and stigma. Resistance training (RT) seems a promising non-pharmacological intervention for the prevention and management of these disorders.

**Purpose of the study:** This review evaluates the efficacy of resistance training in preventing and treating anxiety and depression, with a focus on its biological and psychological mechanisms and effectiveness across diverse populations.

**Materials and methods:** A review of studies analyzes the impact of RT on mental health outcomes. The review includes physiological and psychological adaptations, program effectiveness in various populations, and key variables such as intensity and duration.

**Results:** RT significantly alleviates symptoms of anxiety and depression across diverse populations. Biological mechanisms include improved stress regulation and reduced inflammation. Psychological benefits encompass better self-esteem, improved sleep quality and emotional well-being. Structured and supervised RT programs show the greatest efficacy, with additional benefits observed in specific groups such as older adults and individuals with chronic conditions.

**Conclusions:** Resistance training is an effective intervention to improve mental health outcomes. Future research should explore optimal RT protocols, long-term outcomes, and integration into multimodal treatments.

**Keywords:** Resistance training; anxiety; depression; neuroplasticity; inflammation; mental health interventions.

## 1. Introduction

Anxiety and depressive disorders are among the most common mental health conditions worldwide, significantly impacting global health and well-being. According to the World Health Organization (WHO), anxiety disorders affect approximately 4% of the global population, corresponding to over 300 million people, while depressive disorders impact 3.8%, or 280 million people [1][2]. These conditions disproportionately affect women and are a leading cause of disability globally, with depression ranked as the single largest contributor to non-fatal health loss. Furthermore, mental disorders contribute significantly to global economic burdens, with a projected cumulative cost of 16.3 trillion USD between 2011 and 2030, primarily due to lost productivity and increased healthcare expenditures [3]. Despite the availability of effective treatments, such as pharmacotherapy and psychotherapy, substantial barriers to care persist. Reports indicate that 76–85% of individuals with severe mental disorders in low- and middle-income countries (LMICs) receive no treatment, while in high-income countries, the treatment gap ranges from 35–50% [3]. Moreover, the quality of care is often inadequate, with institutionalized services in many regions failing to meet patients' needs, further underscoring the necessity of alternative, community-based approaches [3].

Participating in regular physical activity is widely acknowledged as an effective method for enhancing mental health. Research consistently shows that individuals who maintain active lifestyles have a significantly reduced likelihood of experiencing depression compared to those who are largely sedentary. For example, achieving even half of the weekly physical activity recommended in public health guidelines—approximately 4.4 marginal MET hours—can lower the risk of depression by 18% [4]. This highlights the value of physical activity as a preventive and therapeutic tool for addressing depressive symptoms.

Among the different types of physical activity, resistance training (RT) has increasingly been recognized for its mental health benefits. Studies reveal that RT is linked to significant reductions in depressive symptoms across various demographic groups, including individuals of different ages, genders, and health statuses [8][13]. Furthermore, individuals with more severe depressive symptoms at baseline appear to achieve the most substantial improvements through RT interventions [8]. While aerobic exercise has historically been the primary focus of research, recent findings indicate that resistance training can significantly reduce depressive symptoms, particularly in individuals with more severe baseline depression [6]. Additionally, interventions that incorporate physical activity have demonstrated strong efficacy in alleviating

symptoms of anxiety and depression, underlining their potential as cost-effective and accessible strategies for mental health care [5][6].

The mental health benefits of resistance training are thought to result from its effects on both biological and psychological processes. RT is believed to enhance neuroplasticity, promote hippocampal plasticity, and stimulate the release of endorphins, all of which contribute to mood stabilization and improved emotional regulation [5][6][9][13]. Moreover, RT has been shown to reduce inflammation and regulate stress responses, while also enhancing self-esteem and improving sleep quality [5][6]. These mechanisms collectively highlight RT's role in supporting mental well-being. Furthermore, maintaining greater muscle strength through resistance training has been associated with a reduced risk of developing anxiety and depression, suggesting that physical strength may serve as a protective factor for mental health [12].

RT has also demonstrated its effectiveness in improving mental health within specific populations. In older adults, resistance training not only enhances physical functionality but also significantly improves emotional health and overall psychological well-being [10][13]. Similarly, research on individuals with Parkinson's disease shows that RT can effectively alleviate symptoms of anxiety and depression, achieving results comparable to mindfulness-based therapies, thereby highlighting its adaptability as a mental health intervention [11].

This literature review aims to examine the role of resistance training in the prevention and treatment of anxiety and depression, focusing on its underlying mechanisms and applications across diverse populations. Additionally, it seeks to identify gaps in the current literature to inform future research and establish RT as a viable intervention for improving mental health outcomes.

## **2. State of knowledge**

### **1. Biological mechanisms of RET**

Resistance training initiates a cascade of biological and psychological processes that enhance strength, endurance, and mental well-being. Most of these adaptations are cumulative, requiring consistent effort, progressive overload, and proper recovery to maximize benefits [14].

Resistance training leads to several changes in muscle tissue. One of the most visible effects is muscle hypertrophy, particularly of Type II fibers because RET induces changes in muscle fiber types, shifting some Type I (slow twitch) fibers toward Type II characteristics, enhancing strength and power [14][15].

The nervous system plays a crucial role in the early stages of resistance training. During this phase, the ability to recruit more motor units and synchronize their activity is enhanced, inhibitory signals from the central nervous system are on the other hand reduced thus leading to greater force production. The rate at which motor neurons fire action potentials can increase, allowing for faster and more powerful muscle contractions [14][16].

Strength and resistance exercises promote bone remodeling by applying mechanical stress, which stimulates osteoblast activity and increases bone mineral density, reducing the risk of osteoporosis. Those techniques are the most studied ones to increase bone mass in the elderly, working especially well when it comes to increasing bone mineral density in the neck of the femur [17].

RET also triggers the release of various hormones that play roles in adaptation like testosterone, growth hormone, and insulin-like growth factor-1 (IGF-1) and other particles like cortisol and myokines promoting muscle protein synthesis and tissue repair [18].

Cardiovascular and metabolic effects are among the most important results of RET. Although primarily anaerobic, resistance training has some cardiovascular and metabolic benefits. Some studies even show that it can be as effective as aerobic endurance training in reducing some major cardiovascular risk factors [19]. It promotes improved capillary density around muscle fibers, enhancing nutrient and oxygen delivery [20], improving glucose uptake in muscle cells and insulin sensitivity, and reducing the risk of metabolic disorders [21]. It also decreases resting blood pressure and improves blood lipid profiles [19].

## **2. Psychological mechanisms of RET**

### **Mood, emotional well-being, and body image**

Resistance training stimulates the release of endorphins, which are known as natural mood elevators. Additionally achieving strength or fitness goals fosters a sense of accomplishment, which can significantly enhance self-esteem and body image [22]. Study by Collins H. et al. showed that RET can reshape how individuals perceive their bodies when it comes to self-worth, promoting a positive relationship with physical appearance and functionality [23].

## **Enhanced Cognitive Function**

The structured nature of resistance training can enhance the ability to concentrate and execute tasks, benefiting attention span and mental clarity. Study by Liu-Ambrose T. et al showed task performance improved by 12.6% and 10.9% in the once-weekly and twice-weekly resistance training groups, respectively [24]. For older adults, resistance training has been associated with slower cognitive decline and improved executive functions [25].

## **Stress Regulation**

Resistance training provides a constructive outlet for stress and frustration, helping individuals manage daily challenges more effectively. It can regulate levels of stress hormones, such as cortisol and adrenaline, leading to a calmer state of mind. This physiological balance contributes to emotional stability [26].

## **Better Sleep Quality**

Resistance training enhances sleep quality and duration by reducing stress and promoting physical fatigue. Consistent training also helps synchronize the body's natural clock, improving overall sleep hygiene. Studies showed significant improvement in sleep quality when it comes to older adults [27][28], but also improvement in the condition of patients with comorbidities commonly associated with poor sleep [29].

## **Quality of life in elderly**

A systematic review and meta-analysis examined the impact of RET on health-related quality of life (HRQOL) in older adults. The findings support recommending RT for HRQOL improvement in this population [10]. Another study showed that self-efficacy and social interaction were found to be key mechanisms in perceived improvement of life in elderly participating in a resistance training program [30].

## **Reduced Symptoms of Anxiety and Depression**

Studies suggest that resistance training can reduce symptoms of mild to moderate depression, comparable to the effects of aerobic exercise. It has also been shown to lower baseline anxiety levels. Both of the above topics are explored further in this paper.

### **2.3. Resistance training and anxiety**

#### **General findings**

Resistance exercise training has been studied for its effects on anxiety, and a substantial body of research demonstrates its efficacy as a non-pharmacological intervention [31][32][33]. The following section summarizes key studies, emphasizing differences in populations, training protocols, and outcomes.

Resistance exercise training has been shown to significantly reduce anxiety symptoms, with a meta-analysis by Gordon et al. (2017) reviewing 16 clinical trials revealing small-to-moderate effects ( $\Delta = 0.31$ , 95% CI 0.17–0.44;  $p < 0.001$ ). Effects were larger among healthy participants ( $\Delta = 0.50$ ) compared to those with physical or mental illnesses ( $\Delta = 0.19$ ), though RT was effective for both groups. Moderator analyses found no significant differences based on sex, age, program features, or strength improvements, highlighting RT as a low-risk, broadly effective intervention for anxiety [31].

According to a more recent meta-analysis by Cunha et al. (2024), resistance training is found to be an effective non-pharmacologic strategy for reducing anxiety symptoms in older adults ( $\geq 60$  years), with a mean effect of  $-1.33$  (95% CI:  $-2.10$  to  $-0.56$ ,  $p < 0.01$ ). Effects were moderate for older adults without mental disorders ( $-0.51$ , 95% CI:  $-0.67$  to  $-0.35$ ,  $p < 0.01$ ) and large for those with mental disorders ( $-2.15$ , 95% CI:  $-3.01$  to  $-1.29$ ,  $p < 0.01$ ) [32], which stays somewhat in contrast to the previously mentioned meta-analysis, where a bigger effect was found in healthy participants [31]. Additionally, it was observed that different RT characteristics (traditional vs alternative, number of exercises, frequency, duration, and sets) can influence RT effects on mental health outcomes in older adults. Engaging in resistance training three times per week, with three sets per exercise, fewer than six exercises per session, and a duration of less than 12 weeks, has been shown to be more effective in improving mental health outcomes. However, some differences between the aforementioned contradicting studies

can be highlighted: this study from 2024 analyzed just older adults, and no aerobic exercise was included in the analyses [32].

A systematic review by Strickland et al. (2014) has shown that resistance training at a low-to-moderate intensity ( $<70\%$  1 repetition maximum) produces the most reliable and robust decreases in anxiety. Significant reductions in state anxiety have been observed at intensities as low as  $10\%$  1RM, with optimal effects reported at  $50\text{--}70\%$  1RM. Higher intensities ( $>70\%$  1RM) are less effective. Factors such as longer rest intervals (90 seconds) enhance anxiolytic effects compared to shorter rests (30 seconds). [33] The findings about intensity and interval length stay in agreement with another review by Cavarretta et al. (2018), which provides evidence to support lower training volumes performed at low to moderate intensities ( $50\text{--}70\%$  1RM) with long inter-set rest intervals (90–150 s) [35].

In a population of young people, a systematic review and meta-analysis by Marinelli et al. (2024) shows that resistance training significantly reduced anxiety symptoms (Hedge's  $g = -1.02$ , 95% CI:  $-1.50$  to  $-0.54$ ,  $p < .001$ ), with a large effect size observed across educational, clinical, and community settings. Ten randomized controlled trials ( $n = 376$ ) demonstrated substantial heterogeneity ( $I^2 = 66\%$ ) and moderate certainty for anxiety outcomes according to GRADE analysis. Combined resistance and aerobic training appeared more effective than resistance training alone, particularly in interventions lasting over 12 weeks [34] (in contrast to the meta-analysis by Cuhna et al. [32]). The majority of trials in the study utilized a similar intensity ( $60\text{--}70\%$  1RM or 8–12 repetitions) across interventions [34], which is in accordance with previously mentioned research by Strickland et al. finding that optimal effects are reported at  $50\text{--}70\%$  1RM [33].

Cavarretta et al. (2018) reviewed the acute effects of resistance exercise on affect, anxiety, and mood, providing evidence that lower training volumes performed at low to moderate intensities ( $50\text{--}70\%$  1RM) with long inter-set rest intervals (90–150 s) are most effective for reducing anxiety [35].

Barahona-Fuentes et al. (2021) conducted a systematic review and meta-analysis to examine the effects of different modes of strength intervention on anxiety, stress, and depression in adolescents. The review included nine studies, with seven included in the meta-analysis, which showed a large and significant effect of strength training on anxiety (SMD =  $-1.75$ ; 95% CI:  $-3.03$ ,  $-0.48$ ;  $p = 0.007$ ). The authors concluded that different modes of strength



intervention are a suitable methodology for controlling anxiety and depression levels in adolescents, emphasizing that conventional strength training had the most benefits [36].

### **Populations with mental health conditions**

A randomized controlled trial by LeBouthillier et al. (2017) examined 48 individuals with anxiety-related disorders, comparing the effects of aerobic exercise and RET. Both exercise modalities were efficacious in improving disorder status following a 4-week intervention. The study found that while exercise enjoyment does not appear to predict the effectiveness of exercise, lower physical fitness is associated with greater reductions in specific constructs, such as general psychological distress and anxiety [41].

Similarly, a pilot study by Whitworth et al. (2019) investigated the impact of high-intensity RET on 22 individuals screening positive for PTSD. Over three weeks, participants completed nine sessions of RET, leading to significant reductions in anxiety [ $F(1,17) = 5.45$ ,  $p = 0.03$ ] and improved sleep quality [42].

In another study, Broman-Fulks et al. (2015) evaluated the effects of a single session of RET on anxiety in 77 participants. Results indicated that aerobic exercise and resistance training were significantly and equally effective in reducing anxiety sensitivity compared with rest [ $(\eta^2(p) = .52)$ ]. Neither form of exercise however generated observable effects on distress tolerance, discomfort intolerance, or state anxiety (all  $ps > .10$ ) [43].

Herring et al. (2011) conducted a randomized controlled trial to compare the effects of six weeks of RET and aerobic exercise training (AET) on signs and symptoms of generalized anxiety disorder (GAD) among 30 sedentary women aged 18–37 years, diagnosed with GAD. Both RET and AET produced comparable improvements in trait anxiety, concentration, irritability, and symptoms of depression, fatigue, and vigor. RET specifically resulted in significant reductions in feelings of anxiety-tension and the frequency and intensity of irritability, with Hedges'  $d$  effect sizes of  $\geq 0.36$  for multiple outcomes, including trait anxiety, fatigue, and pain intensity. These findings suggest that short-term RET can be an effective adjuvant treatment for GAD [45].

What's more, Gordon et al. (2021) conducted a randomized controlled trial to examine the effects of an eight-week RET program on young adults with an analogue generalized anxiety disorder (AGAD). Forty-four participants were randomized to either a one-on-one, fully supervised RET intervention or a wait-list control group. RET significantly improved AGAD status, with a number needed to treat (NNT) of 3 (95% CI: 2–7). Large, clinically meaningful

reductions were observed in worry ( $d = 0.93$ , 95% CI: 0.13–1.73) and anxiety symptoms ( $d = 0.71$ , 95% CI: -0.08–1.49). Attendance (81%) and compliance (77%) rates were high, with no adverse events reported [48].

### **Populations with chronic conditions**

A review by Vilarino et al. (2021) examined seven studies on patients with fibromyalgia, with results demonstrating that the practice of RT significantly improves the mental health of patients with FM, including reduction of anxiety symptoms obtained even in a short (4-8 weeks) training period [37].

In a systematic review and meta-analysis by Ferreira et al. (2021) the effects of exercise interventions on depression and anxiety in chronic kidney disease (CKD) patients were evaluated. A total of eight studies met the eligibility criteria for the systematic review, with six included in the meta-analysis. Results revealed significant improvements in anxiety levels, favoring exercise interventions over active control groups (SMD =  $-0.78$  [ $-1.21$ ,  $-0.34$ ],  $p = 0.0004$ ) [40].

A randomized-control trial by Ferreira et al. (2018) found that among 35 elderly patients with Parkinson's disease, resistance training significantly reduced anxiety levels and improved quality of life. Authors highlighted the importance of tailored, non-pharmacological interventions such as RT in this population [38].

However, a systematic review by Abuoaf et al. (2023) of five randomized-controlled trials that investigated the effect of physical exercise, including RT, on anxiety in people with Parkinson's disease, showed different results. The review including 328 participants with early to moderate-stage PD, due to methodological limitations across studies, led to insufficient evidence to conclusively support or refute the effects of exercise on anxiety in this population [46].

A randomized-controlled trial by Moraes et al. (2021) investigated 26 breast cancer survivors, finding that a low-volume RT, performed once a week, with high supervision and control of the exercise intensity, cadence, and rest interval reduced anxiety and several fatigue aspects, and improved a number of parameters related to QOL in BCS, leading to a conclusion that once weekly RT should be recommended for this population [39].

A systematic review and meta-analysis by Lopez et al. (2021) examined 18 trials involving 1,112 men with prostate cancer to determine the minimal effective dose of resistance exercise. Resistance-based programs showed significant benefits for fatigue (effect size =  $-0.3$ ,

95% CI:  $-0.4$  to  $-0.2$ ,  $P < 0.001$ ) and quality of life (effect size =  $0.2$ , 95% CI:  $0.0$  to  $0.4$ ,  $P = 0.018$ ), although effects on depression and anxiety symptoms were positive but not statistically significant. The findings suggest that low-volume, moderate-to-high intensity resistance exercise is effective for improving fatigue and quality of life, while also potentially mitigating anxiety and depression, and may increase adherence by lowering exercise barriers [47].

An older but comprehensive systematic review by Herring et al. (2010) aimed at estimating the population effect size for anxiety outcomes of RT among patients with chronic illnesses. 75 effects were derived from 40 studies; research included patients with cardiovascular disease, fibromyalgia, multiple sclerosis, psychological disorders, cancer, COPD, chronic pain, and “other medical illnesses” (i.e. obesity, lupus, and epilepsy), with a mean effect size of  $\Delta = 0.29$  (95% CI:  $0.23$ – $0.36$ ). The review showed that exercise training significantly reduced anxiety symptoms among sedentary adults with chronic illnesses. Programs lasting 3–12 weeks showed larger effects ( $\Delta = 0.39$ ) than programs lasting more than 12 weeks ( $\Delta = 0.23$ ), and sessions exceeding 30 minutes had better effects ( $\Delta = 0.36$ ) than those of 10 to 30 minutes ( $\Delta = 0.22$ ). Longer anxiety report time frames also amplified the observed effects. While most illness categories showed significant reductions, results for patients with multiple sclerosis (MS) were not statistically significant. Adherence rates averaged 78% and were not a significant moderator of the anxiolytic effect [44].

## **2.4. Resistance training and depression**

There are many studies that indicate an antidepressant effect of physical exercise [49][50]. However not many of them focus specifically on the effect of RT on the reduction of depressive symptoms in patients suffering from such.

A meta-analysis conducted by Gordon et al. reviewed 33 clinical trials with 1877 participants. It provides a lot of data on the subject. Researchers conclude that RT has significant antidepressive effects regardless of participants' age, sex, or health. Moreover, the study suggests that even the specifics of the RT itself (for example the duration, intensity, frequency, volume) seem to play a secondary role in the anti-depressive effect. The most significant reduction in depressive symptoms was observed in participants with scores indicating mild to moderate depression in comparison to those without such scores. The study also finds that relatively shorter sessions ( $<45$  minutes in length) have a stronger antidepressant effect than longer ones. Supervision seems to play a key role in that effect. Sessions that were fully supervised have had a significantly stronger effect in the reduction of depressive

symptoms than RT that were unsupervised. The study concludes that the overall mean effect of RT in patients suffering from depressive symptoms is  $\Delta = 0.66$  which is a significant reduction and is consistent with similar studies that analyzed the effect of various types of physical activity on depressive symptoms [8][49][52].

However, a more recently published meta-analysis by Carneiro et al. reviewed four studies that focused exclusively on the impact of resistance training in people with depression. The results were heterogeneous. Out of the four studies, only two showed results that suggested a statistically significant antidepressant effect of the RT. Interventions varied in duration, training frequency, length of the sessions, and different exercise routines were utilized. This might, to some extent, explain the heterogeneity in the studies' findings [56].

Another meta-analysis focused on studies where participants aged  $\leq 26$  years participated in at least 4 weeks of RT. The total number of participants was 376 with a mean age of 19. The symptom severity in participants ranged from mild to moderate. With 2-3, 60-75 min sessions per week. Although there was significant heterogeneity between trials, the researchers report that resistance training by itself or resistance training combined with aerobic training significantly reduced depression symptoms in participants with Hedge's  $g = -1.06$ , which indicates a large antidepressant effect [34].

A controlled trial on effects of resistance exercise training on depressive symptoms among adults aged  $26 \pm 5$  y with Major Depressive Disorder and Generalized Anxiety Disorder. The resistance exercise training was designed based on WHO and ACSM guidelines with gradual weight progression supervised by investigators. Exercise sessions were supervised by trained investigators who could have corrected improper techniques. Results were that in comparison to the control group with participants who completed the eight-week training course showed clinically meaningful reduction in depressive symptoms ( $d = 1.01$ ). This large in magnitude antidepressant effect suggests that RT could be an alternative method to that of antidepressant medication, which had a significantly lower effectiveness in reducing depression symptoms for patients with mild to moderate depressive symptoms ( $d = 0.11$ ) [55]. Additionally, the study suggests that RT can be an effective way of preventing the onset of clinical depression. Although participants of the study have experienced a large increase in strength ( $d = 2.01$ ), changes in strength were not associated with changes in depressive symptoms, suggesting that antidepressant benefits from RT among young adults may not require an improvement in strength [51].

Different studies focus on the effect of RT in older demographics. One such study focused on the impact of resistance training in older women (age  $> 60$  years) has concluded that

a 12-week program of RT was associated with a significant reduction in depression and anxiety symptoms regardless of health status, muscular strength, and hypertrophy [53]. Another study focused on older men (between the ages of 65 and 75 years old) had similar findings, with 24 weeks of RT resulting in improved mood and reduction in anxiety levels in comparison to the control group [54].

Although many of the reviewed studies show that RT does have a positive impact in the reduction of depressive symptoms in both patients suffering from MDD and healthy patients, the results still show variability in findings. The evidence points to the effectiveness of resistance-based training routines in the reduction of depression symptoms and in preventing the onset of clinical depression [8][51]. Thus, it should be considered in multimodal treatment in patients suffering from such [57]. Future studies could further focus on the specific aspects of resistance training and how they correlate to its antidepressant effect.

### **3. Conclusions**

This review explains the mechanisms of resistance training's biological and psychological influences and examines the impact of resistance training on anxiety and depression among different populations.

RT influences a body biologically through different mechanisms, including enhancing muscle hypertrophy and promoting bone remodeling. Additionally, it triggers release of hormones important in adaptation and reduces cardio-vascular risk factors by decreasing resting blood pressure and improving blood lipid profiles.

Psychological mechanisms of RT include stimulating release of endorphins, which has a positive effect on mood, and improving emotional well-being and body image. RT boosts attention span and results in slower cognitive decline along with improved executive functions. Not only does RT regulate stress and improve sleep overall sleep quality, synchronizing the body's natural clock, but also improves health-related quality of life in elderly patients.

Resistance training is efficacious as a non-pharmacological intervention for reducing anxiety across diverse populations, with benefits observed in healthy individuals, older adults, adults with mental health conditions, and individuals managing chronic illnesses.

RT produces small-to-moderate reductions in anxiety symptoms, with meta-analyses indicating effectiveness regardless of sex, age, or training protocols. Optimal effects are achieved with low-to-moderate intensity (50–70% 1RM), longer rest intervals, and structured regimens.

Resistance training shows significant antidepressive effects regardless of participants' age, sex, or health. Moreover, while supervision appears to be crucial, the specifics of RT such as duration, intensity, frequency and volume seem to play a secondary role. Evidence points to the effectiveness of resistance-based training routines in both reduction of depression symptoms and preventing the onset of clinical depression. Researchers point out that RT should be considered in multimodal treatment in patients suffering from depressive symptoms.

While resistance training does show significant antidepressant and anxiolytic effects, there is still a need to continue exploration of the topic, so that specific modalities of resistance training can be optimized in order to incorporate RT to a multimodal therapy.

#### **4. Disclosure**

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There is no conflict of interest.

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