

Exercise and Pharmacotherapy for the Treatment of Eating Disorders: A Meta-Analysis

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Abstract: Eating disorders, including anorexia nervosa, bulimia nervosa, and binge eating disorders, can severely impact people's physical and mental health. Among all psychological treatments, exercise has been examined lately as one of the novel methods. Multiple literature has proved its benefits on physical health, including improving cardiovascular function and growing skeletal musculature. Moreover, studies have demonstrated its benefits on treating depression and anxiety. However, exercise may be deemed inappropriate in treating eating disorders since patients usually engage in compulsive exercise. In addition to exercise treatment, medications have been broadly applied in eating disorder treatments. Major medications include Selective Serotonin Reuptake Inhibitors (SSRI) and anti-psychotics. This meta-analysis aims to determine whether exercise intervention or pharmacological therapy is more effective in treating eating disorders. The result shows little difference in overall effectiveness, but different treatments may impact different symptoms of patients. Future researchers should continuously investigate the effect of exercise intervention and various types of pharmaceuticals to determine their practical application in eating disorder treatment according to the characteristics of specific patients

Keywords: eating disorders, exercise intervention, pharmacotherapy

1. Introduction

Eating disorders (ED) are a collection of conditions include anorexia nervosa (AN), bulimia nervosa (BN), and binge-eating disorder (BED), and other Specified Feeding and Eating Disorders are described fully in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders [1]. While ED share common features related to eating, they also involve specific characteristics. A meta-analysis was performed to determine whether exercise intervention or pharmacological therapy are differentially effective in treating eating disorders.

1.1. Anorexia Nervosa

AN usually involves self-starvation. Also, patients with AN are usually significantly underweight. Defined by DSM-5, adults with AN have a body mass index (BMI) of less than 18.5 kg/m². Furthermore, individuals with AN are fear of gaining weight or becoming fat, a phenomenon that is usually explicitly expressed by patients themselves or by other observers. Individuals with AN also experience a disturbance in body image, which may include misconception of the body or body parts

as being overweight despite being underweight; the significant influence of weight or shape in self-evaluation; lacking the recognition of the danger associated with maintaining a low weight. Although AN is characterized by restriction of caloric intake, individuals with AN can have binge-eating episodes. Binge-eating episodes are defined by consuming a large amount of food in a short period and experiencing a loss of control when eating. AN patient may also use purging behaviors, such as self-induced vomiting or diuretics to compensate for binges to achieve weight control goals. [1].

1.2. Bulimia Nervosa

BN consists of binge-eating episodes and compensatory behaviors such as self-induced vomiting, diuretics abuse. Also, similar to AN patient, BN patients frequently engage in compulsive exercise as a compensation for weight gain. Also, BN patients usually have significantly concern on their body shapes and weights, which impairs their ability to accurately evaluate themselves. The severity of BN is specified by weekly binge eating episodes, with 1-3 episodes per week being Mild, 4-7 episodes being moderate, 8-13 episodes being severe, and more than 14 episodes being extreme [1].

1.3. Binge Eating Disorder

BED consists of binge eating episodes but without compensatory behaviors. Binges are represented by characteristics including eating when not hungry, eating to the point of feeling uncomfortably full, eating alone because of embarrassment, eating more rapidly than usual, and feeling disgusted or depressed or guilty after the binge episode. Most patients with BED are significantly overweight or obese, but this is not part of the diagnostic criteria [2].

Eating disorders significantly impact people's health, especially for females. For the population in the US, at any given point in time, between 0.3-0.4% of young women and 0.1% of young men will suffer from anorexia nervosa [3], 1.0% of young women and 0.1% of young men will meet diagnostic criteria for bulimia nervosa [4], and 3.5% of women and 2.0% of men had binge eating disorder during their life [5]. Researcher has found the reason of female having higher prevalence of eating disorder is that more females are dieting and losing weight. Also, they have more severe degree of body dysmorphia, poorer self-image, and more profound role confusion during adolescent [6]. Furthermore, mental health related conditions are often comorbid with ED. Two-thirds of people with anorexia also showed signs of an anxiety disorder several years before the start of their eating disorder, and approximately one in four people with an eating disorder have symptoms of post-traumatic stress disorder (PTSD) [7]. Other mood disorders also frequently appear with the incidence of ED, such as depression and Obsessive-Compulsive Disorder (OCD) [8,9]. Apart from the range of psychiatric disorders, ED can lead to a high mortality rate in the US population. Eating disorders have the second-highest mortality rate of all mental health disorders, surpassed by opioid addiction [10]. Specifically, anorexia has an estimated mortality rate of around 10% [11].

Previous research and reviews indicate that multiple psychological and pharmacological treatments are effective for ED, primarily Cognitive Behavior Therapy (CBT) [12], Interpersonal Therapy (IPT) [13], Pharmacotherapy, and their combinations [14]. For pharmacotherapy, research has indicated that antidepressants, such as SSRI and Tricyclics, significantly decrease the core symptoms of ED in the short term [15]. Among antidepressants, fluoxetine is the only drug that is only drug authorized by the US Food and Drug Administration (FDA) for the treatment of BN (at a dose of 60 mg/day). One random controlled trial (RCT) has confirmed that fluoxetine not only reduces the binge eating episodes in patients with BN or BED but also reduces the incidence of relapse [16]. Antipsychotics (AP) are also used in treating ED, especially for AN. However, AP was not widely proved to be effective in contributing to the weight gain of AN patients but alleviates other cognitive symptoms, such as the distortion of the body image, hyper-arousal and psychomotor

agitation [17]. There is limited evidence on the efficacy of AP in treating BN or BED particularly, and the side effect might limit their usefulness [18]. Studies have shown that antipsychotics contribute to the weight gain of individuals with severe mental illness such as schizophrenia or bipolar disorder. The cause of the weight gain is that the pharmacodynamic action of AP is mainly focused on the modulation of dopaminergic and serotonergic systems, which can induce increased appetite [19].

Nonpharmacological interventions such as exercise has been suggested to have a wide range of benefits to an individual's health and has been one of the behavioral methods for treating predominantly mood disorders, such as anxiety and depression and also have the potential to moderate weight. Studies have shown that if the prescribed dose of exercise is adequate and adhered to, exercise may mediate moderate to severe Major Depressive Disorder [20]. Since individuals with ED might also experience similar emotional symptoms, doing exercise can help them to alleviate the emotional aspect of the eating disorders. However, some scholars have focused on compulsive exercise in ED and elicited controversial opinions on utilizing exercise treatment [21]. Several articles have investigated the exercise treatment in an eating disorder and have shown positive results. Exercise intervention is a behavior therapy that is considered more economical and is not being proved to have weight gain or other unpleasant cognitive side effects as pharmacological treatments do. Also, exercise intervention offers patients internally managed behavior that may support agency and self-control in a manner that drug therapies may be less inclined to function. Thus, in this work, I aim to collect and analyze the evidence from the research base to yield a complete result on whether the exercise intervention is superior to pharmacotherapy in treating individuals with ED. Successfully investigation could offer insights on the future development of treating strategies on ED and offer comparable treatment selections that would satisfy individual needs. Moreover, this study would help resolve the historical confusion on utilizing exercise in treating eating disorders and offer empirically testable recommendations for using exercise as a tool for treating ED.

2. Method

2.1. Literature Search

Research was selected via databases Psycinfo, PsycText, Wiley Library, and Pubmed. The searching key words and procedures include Eating Disorders or Anorexia or Bulimia or Binge Eating Disorders with Exercise Intervention or Pharmacotherapy or Drug Treatment. The publication time frame chosen was 1980 (introduction of DSM-III) to 2021, and restricted to English language, peer-reviewed journals.

2.2. Eligibility Criteria

To determine the eligible literature, this article refers to the modified Participants, Interventions, Comparator/Control group, Outcomes, Study design (PICOS) criteria [22]. Eligible literature on exercise intervention in treating ED should use treatment methods that have exercise components, but not limited to the type of exercise (e.g., yoga, walking). The disorders needed to be among the three major subtypes of ED: Anorexia Nervosa (AN), Bulimia Nervosa (BN), and Binge Eating Disorder (BED). Literature on using pharmacotherapy to treat ED should be about using certain medications; the numbers and types of medications are not restricted. The symptoms should also be among the three major subtypes of ED mentioned above. Both exercise intervention and pharmacological intervention should last for at least one month. The psychological variables is represented by depression symptom measured by the end of the treatment using the Beck Depression Inventory [23] or Hamilton Depression Scale [24]; the ED symptom variable is represented by binge frequency or the score on Eating Disorder Inventory [25]; BMI values of patients represent the physiological variable after the treatment. Other fundamental numeric values, including sample size

(n), standard deviation (sd), and effect size (d), are extracted from the eligible literature. For literature that does not directly show effect size, the formula of Cohen's d ($d=(M1-M2)/sd$) or Hedges' g is used for calculation [26].

2.3. Data Extraction

First, the articles were screened based on the inclusion and exclusion criteria. Then, the author reviewed the full text of each article. Individual data, including the total sample size, the sample size of treatment and control groups, and the mean and standard deviation of treatment and control groups are extracted after the review.

2.4. Integration of the Result

Since most eligible literature did not report effect size and confidence interval, the author utilized excel and constructed algorithm on specific calculations after the data extraction [27]. Most paper reported post treatment result, including treatment groups' (TG) and control groups' (CG) sample size, mean, and standard deviation, so the author measure the mean difference between TG and CG as the main effect. Individual effect size and 95% confidence interval are calculated using the constructed calculator.

3. Result

3.1. Characteristics of Included Studies

Among 44 searched articles, 14 of them satisfied the inclusion criteria, and 6 of which were exercise intervention's effects on EDs, while 8 of them investigated the medications' effects. Regarding the design of each experiment, all of them randomized controlled trials (RCTs). The studies used different diagnostic criteria for EDs (see Table 1), but all of the subjects are suffered from AN, BN, or BED. Eight articles only contained female participants [28-35], while n equals to reported both male and female. The details of the exercise interventions varied, including walking, yoga, strength, and cardiovascular training. Regarding pharmacological treatment, the medications include Topiramate, Lithium Carbonate, Fluoxetine, Olanzapine, phenelzine, and imipramine. Multiple results within one study [29, 31, 36] were used, because they treated the same group of patients with different time frames, or different medications, or treated different groups of people with the same methods.

3.2. Physical Outcome

Four studies in the exercise intervention measured the BMI changes of patients. Figure 1 illustrates the overall effect size comparing exercise treatment and control groups (ES) was 0.14 (95% CI -0.25 to 0.52). Only one study demonstrated the medication's effect on BMI change (ES=1, 95% CI -0.85 to 1.06;), which also showed no significant effect. Comparing exercise interventions and medication's effect on BMI change, medication has a stronger effect on BMI change, though the study number is limited.

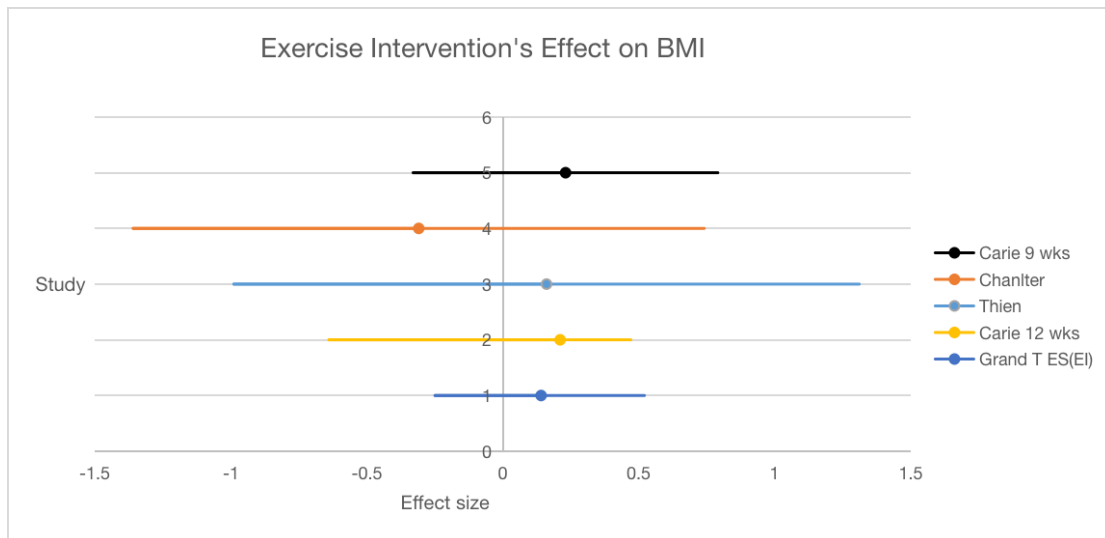


Figure 1: Exercise Intervention's Effect on BMI

3.3. Eating Disorder Symptoms

Four studies on the EI's effect measured eating disorder symptoms change shown in Figure 2. The result showed there is a significant effect between treatment and control groups. The overall effect size (ES) is -0.37 (95% CI -0.58 to -0.16). In addition, ten studies on medications' effect on patients with EDs measured eating disorder symptoms change shown in Figure 3. No significant effect appeared between treatment and control groups. The overall effect size (ES) is 0.03 (95% CI -0.11 to -0.16). Comparing the studies on exercise intervention with the ones on medications, exercise intervention has a main effect on improving patients' eating disorder symptoms.

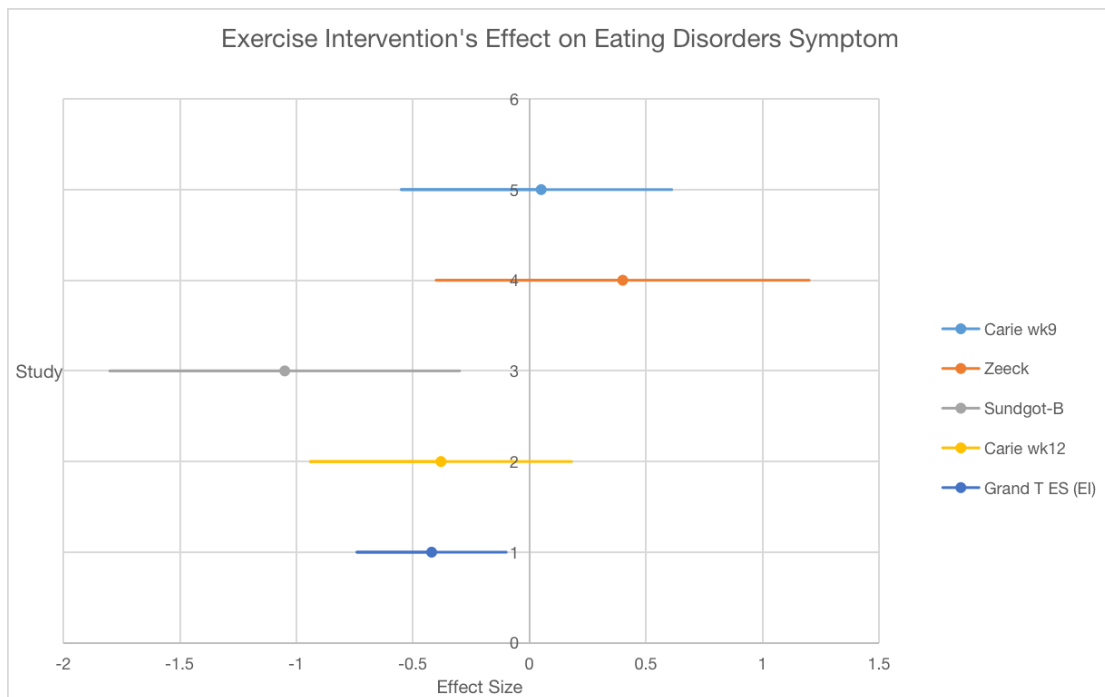


Figure 2: Exercise Intervention's Effect on Eating Disorders Symptoms

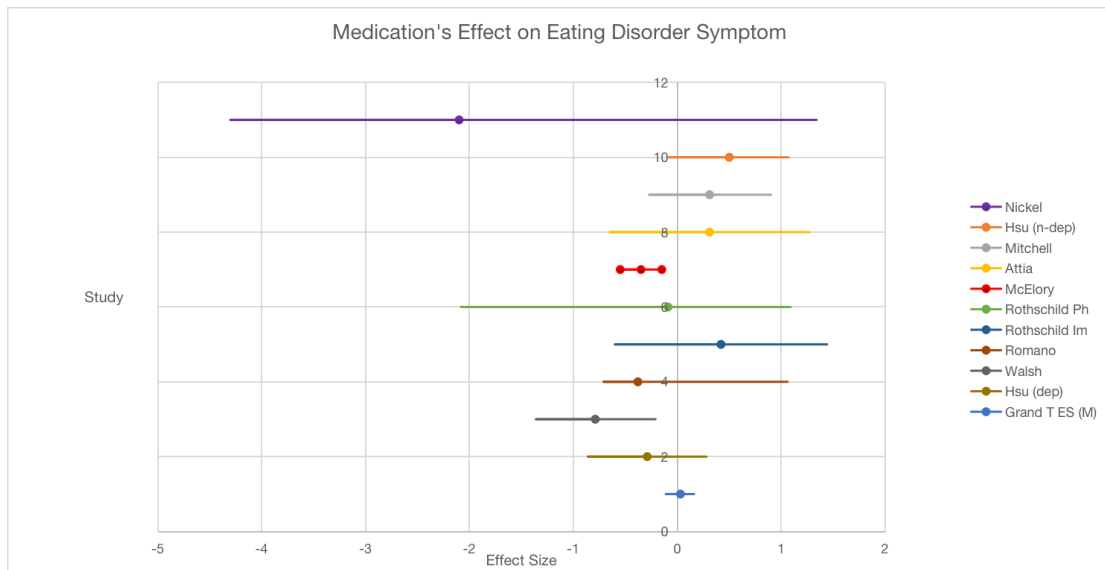


Figure 3: Medication's Effect on Eating Disorder Symptom

3.4. Depression Symptoms

There are three studies about exercise intervention's effect on depressive symptoms. No significant effect appeared between treatment and control groups, and it's indicated by the overall effect size (ES) is -0.17 (95% CI -0.5 to 0.16) (Figure 4). Regarding medication group, there are seven studies reported the effect on depression. The result showed that there is a significant effect between treatment and control groups. The overall effect size (ES) is -0.17 (95% CI -0.5 to 0.16) (Figure 5). Comparing two groups of studies, medication has a main effect on the depression symptoms of patients who had EDs.

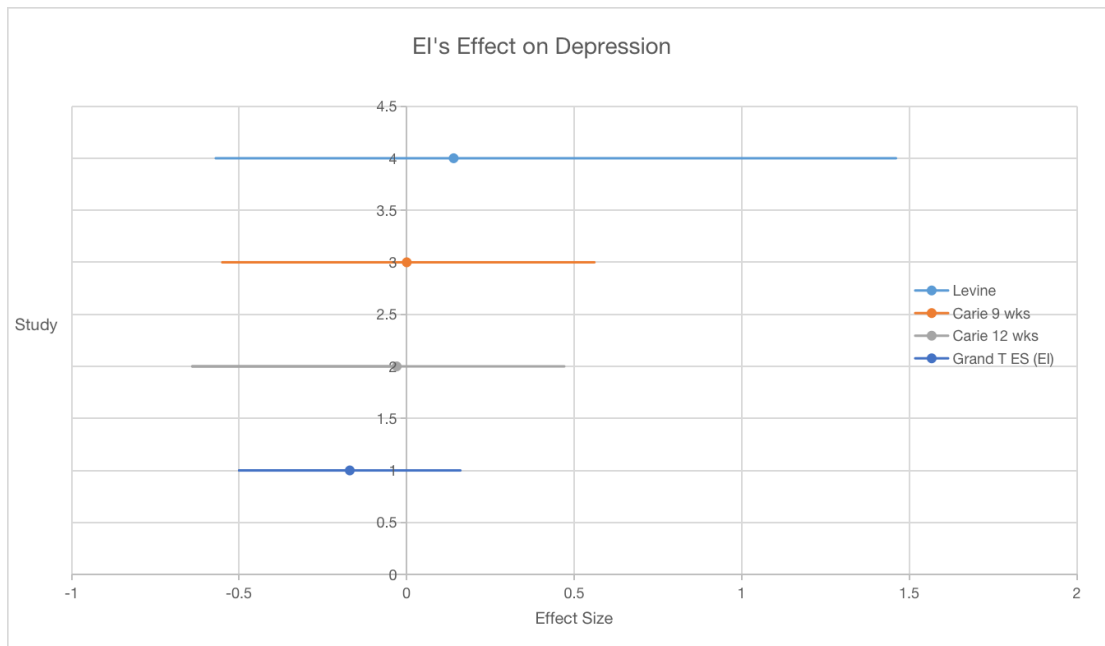


Figure 4: Exercise Intervention's Effect on Depressive Symptom

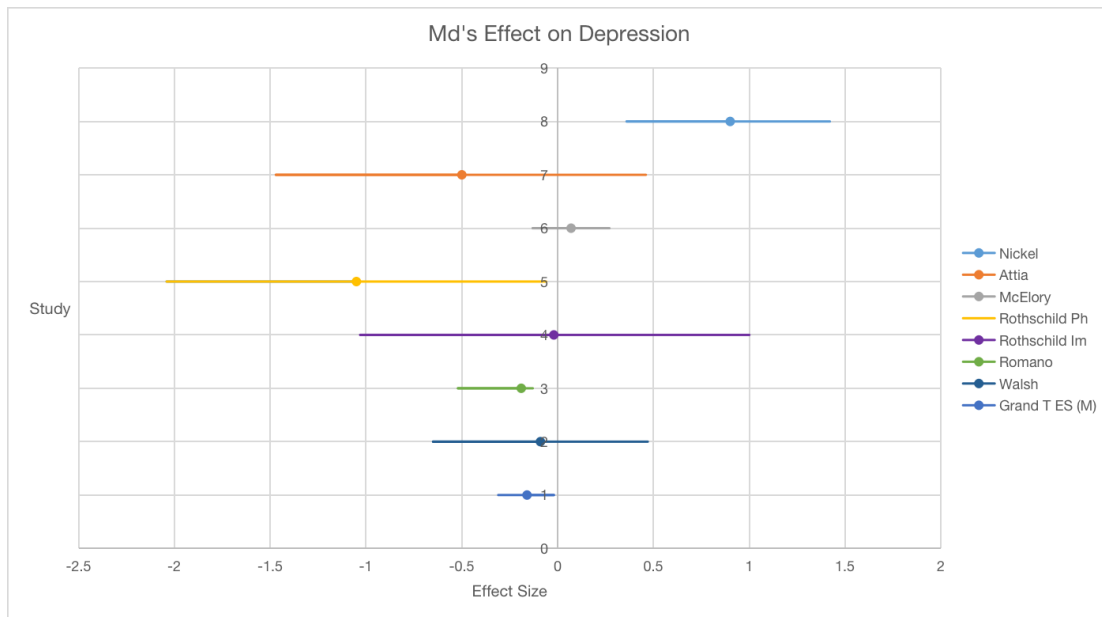


Figure 5: Medication's Effect on Depression

4. Discussion

This meta-analysis examined the efficacy of exercise intervention and pharmacological intervention on patients with eating disorders. The study also compared the effectiveness between these two groups across different outcome variables, including BMI change, eating disorder symptoms change, and depression symptom change.

Regarding exercise intervention's effect on BMI, the result shows similar BMI changes across studies, suggesting no significant effect of physical exercise interventions on patients' BMI status. It is reasonable because the exercise prescription across the investigated studies was perhaps insufficiently rigorous. Also, weight loss or BMI change usually appears with dietary pattern change, specifically requiring subjects to maintain a caloric deficit [37]. On the other side, only one study was found reporting medication's effect on eating disorder patient's BMI, and it shows no main effect. It is hard to conclude a single study. Thus, further investigation on medication's effect on the BMI of patients with eating disorders is needed. However, several studies have found that antipsychotic medications are likely to increase the BMI of patients [38,39]. Since several of the included studies investigated the effect of medications such as Olanzapine, further research on eating disorder patients' BMI is suggested.

More articles elucidated the effect of medications on eating disorders' symptoms. Although more than half of the studies in the medication group indicate a favorable outcome in treatment groups, our analysis indicates that medication has no significant effect on the eating disorder symptoms of patients. A reasonable explanation of the result is that most articles in this analysis reported anti-depressant effects, primarily treating depression and anxiety-related disorders. Despite the high comorbid rate of mood disorders and eating disorders [40], treating comorbid symptoms might not always benefit the primary disorder saliently. In stark contrast to the medication group, the result of the exercise intervention group showed a significant effect of treatment. It supports the evidence from previous literature reviews on the effect of exercise in treating eating disorders [41]. Previous analysis on the relationship between exercise and appetite among obese individuals has shown that exercise can suppress the blood concentrations of acylated ghrelin (AG), which decreases appetite [42]. In addition, King et al. conducted controlled studies and illustrated that the appetite suppression effect

occurs among lean individuals [43]. This previous evidence helped to partially explain why exercise can be effective in treating patients with eating disorders. Nevertheless, further research might aim to examine exercise's neurological and biological influence for drawing more integrated inference on exercise intervention's efficacy.

Finally, exercise intervention did not show a significant effect on improving patients' depression symptoms. The analysis is limited for concretely concluding this point because there are limited analyzed articles. A previous meta-analysis has shown the efficacy of exercises, such as Taichi and Yoga, in treating depression symptoms [44]. Further analysis should collect a larger number of studies to generate a more comprehensive result. Researchers should also conduct more controlled studies on exercise's influence on depression. Medication, on the other hand, showed a promising effect on the patients' depression symptoms. It supported the former discussion that anti-depressants are effective in treating depression. The study also helps to support the use of anti-depressants for depressive symptoms related to eating disorders.

5. Conclusion

Pharmacotherapy has been widely used as a treatment of eating disorders, while exercise intervention is a relatively novel method that raises experts' concerns and provokes debates on its safety and efficacy [21]. To bring insights into which methods is superior and offer clinicians implications of valid treatment options, this Meta-Analysis compares both treatment methods' effect on different domains of eating disorders. The result shows that both methods have no significant impact on patients' BMI. Also, the study demonstrates exercise's positive effect on treating eating disorders symptoms, while pharmacotherapy does not show a salient effect. Regarding depressive symptoms in eating disorders, pharmacotherapy shows its efficacy, while that of exercise intervention remains inconspicuous. Researchers should bring more attention into investigating exercise intervention's effect on eating disorders. Meanwhile, clinicians should bring more considerations into experimenting and prescribing exercise interventions depending on the specific symptoms of patients.

Table 1: Summary of paper relevance for disorders and Diagnostic Criteria

Paper	Disorder	Diagnostic Criteria
Levine et al	BED	DSM IV
Carie et al	AN,BN	DSM IV
Zeeck et al [45]	AN,BN	DSM V
Sundgot-Borgen et al [46]	BN	DSM IV
Thien et al [47]	AN	DSM IV
Nicket et al	BN	DSM IV
Hsu et al	BN	DSM III
Mitchell et al	BN	DSM III-R
Attia et al [48]	AN	DSM IV
McElory et al[49]	BED	DSM IV
Rothschild et al	BN	DSM III
Romano	BN	DSM IV
Walsh	BN	DSM III

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