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# Exercise Compared to SSRIs in the Treatment of Major Depressive Disorder

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## Abstract

Major Depressive Disorder (MDD) is a common disease seen every day by primary care providers across the United States. According to the Centers for Disease Control and Prevention (CDC, 2018), eight percent of all adults over the age of 20 suffer from depression, and a study by the American Psychological Association found depressive disorders to cost roughly \$71 billion annually. Today, psychotherapy is the recommended first-line therapy for treating MDD, but pharmacotherapy is more commonly used. Alternative forms of therapy are also being researched in order to avoid the use of medication while adequately treating the symptoms of MDD. For this review, seven databases were searched including PubMed, Cochrane Database of Systematic Reviews, PsycInfo, Cinahl, DynaMed, ClinicalKey, and ScienceDirect from September 1 to November 21, 2018. Works chosen for review were published after the year 2000 and included randomized controlled trials (RCTs), systematic reviews, and meta analyses. This review found several benefits of using exercise to treat MDD while reducing risks, but exercise alone is not superior in effectiveness to psychotherapy or pharmacotherapy. Overall, exercise offers the greatest benefit in reducing MDD symptoms when used as an augmented therapy to either psychotherapy or pharmacotherapy. Limitations of this literature review include lack of studies with longevity or large sample sizes.

Keywords: pathophysiology, exercise, depression, SSRIs, selective serotonin reuptake inhibitors, Major Depressive Disorder, MDD

## Introduction

- 8% of all adults over the age of 20 suffer from depression
  - Women are twice as likely to be affected (CDC, 2018)
- Depression is the 6<sup>th</sup> most costly health condition overall with \$71 billion spent annually (Winerman, 2017)
- Diagnosis is clinical with the use of screening tools such as the PHQ-9
- Psychotherapy is the recommended first-line treatment, but pharmacotherapy is more commonly used due to availability and convenience (DynaMed, 2018)
- Recent research shows alternative therapies, including exercise, may be just as beneficial as traditional therapies while avoiding side effects and limiting the use of medication

## Statement of the Problem

- With the increasing cost of medications and potential for high risk side effects, some providers are recommending alternative therapies to SSRIs for adult patients diagnosed with mild MDD in hopes of providing an option that is safer and more cost effective while providing the same benefit. Further research is needed to show if exercise and SSRIs are equal in efficacy in the reduction of symptoms associated with mild MDD in adults.

## Research Question

- In adult patients diagnosed with mild MDD in a primary care setting, does treating with exercise as a stand-alone therapy compared to treating with SSRIs adequately improve symptoms while minimizing side effects?

## Literature Review

- Pathophysiology of MDD**
  - Exact pathophysiology remains unknown, but many hypotheses exist
  - Two common theories:
    - Biogenic monoamine theory: basis for pharmacologic treatment, developed after medications unexpectedly increased monoamine neurotransmitters in the brain by blocking MAOI or reuptake of neurotransmitters such as serotonin (Fekadu, Shibeshi & Engidawork, 2016)
    - Combined source of pathogenesis: Environmental stress combined with genetic factors act on immunologic and endocrine responses to cause structural and functional changes in the brain leading to dysfunction of neurogenesis and neurotransmitters which ultimately causes symptoms of depression (Jesulola et al., 2018)
- Exercise in the Treatment of MDD**
  - SMILE study assigned groups to supervised exercise, home exercise, sertraline, or placebo pill (Blumenthal et al., 2007):
    - 41% of participants achieved remission based on HAM-D at the completion of the study including:
      - 45% of supervised exercise participants
      - 40% home exercise
      - 47% medication
      - 31% placebo pill
  - Cochrane review compared exercise versus control and pharmacological treatments (Cooney et al., 2013):
    - Exercise was moderately more effective than control
      - Resistance or resistance + aerobic exercise at a vigorous intensity was the most effective
    - No statistical difference between pharmacologic treatment and exercise
  - Systematic review of RCTs by Danielsson, Noras, Waern, and Carlsson (2013):
    - No statistical difference between exercise and antidepressants
    - No statistical difference between exercise versus physical activity
    - Small effect of augmenting exercise to traditional treatment versus traditional therapy alone
  - RCT by Dunn, Trivedi, Kampert, Clark, and Chambliss (2005):
    - Exercise at a higher energy expenditure of 17.5kcal/kg/week is superior to lower energy expenditure
  - RCT by Bartholomew, Morrison, and Ciccolo (2005):
    - Single episode of exercise compared to 30 minutes of rest resulted in no improvement in depressive symptoms, but exercise produced an acute change in positive well-being
- SSRIs in the Treatment of MDD**

Figure 2: Adverse effects associated with escitalopram

| Adverse effects                   | n  | Incidence, % |
|-----------------------------------|----|--------------|
| Nausea                            | 77 | 11.9%        |
| Dry mouth                         | 44 | 6.8%         |
| Somnolence                        | 39 | 6.0%         |
| Dizziness                         | 35 | 5.4%         |
| Fatigue                           | 26 | 4.0%         |
| Dyspepsia                         | 22 | 3.4%         |
| Headache                          | 16 | 2.5%         |
| Liver dysfunction                 | 14 | 2.2%         |
| Loss of appetite                  | 13 | 2.0%         |
| Insomnia                          | 11 | 1.7%         |
| Nervousness                       | 11 | 1.7%         |
| Constipation                      | 10 | 1.5%         |
| Upper respiratory tract infection | 10 | 1.5%         |

Li, G., Shen, Y., Lou, J., & Li, H. (2017). Efficacy of escitalopram monotherapy in the treatment of major depressive disorder: A pooled analysis of 4 Chinese clinical trials. *Medicine*, 96(39), e8142. <https://doi.org/10.1097/md.00000000000008142>

## Literature Review

- Review on escitalopram: more effective than placebo at decreasing antidepressant effects and preventing relapse
  - Side effects mostly mild to moderate in severity and generally well-tolerated (Garnock-Jones & McCormack, 2010)
- Meta-analysis pooled studies on effectiveness of escitalopram: significantly reduced depressive symptoms
  - Response rate 76.9% and remission rate 64%
  - Side effects mild to moderate in severity, considered generally safe (Li, Shen, Lou, & Li, 2017)
- Cochrane review: benefits associated with SSRIs significantly greater than that of placebo (Arroll et al., 2009)

## Discussion

- Exercise in the Treatment of MDD**
  - Exercise alone is effective at improving depressive symptoms (Dunn et al., 2005 & Bartholomew et al., 2005)
  - Higher dose and intensity of exercise produced greater effects (Dunn et al., 2005)
    - Exercising at energy expenditure of 17 kcal/kg/wk 3 or more times per week is just as effective as traditional therapy (Dunn et al., 2005)
  - Exercise also improved positive well-being for a short period of time (Bartholomew et al., 2005)
  - Exercise provided benefits over medication or CBT including: reduction of risk of mortality from diseases such as cardiovascular disease and obesity (Dunn et al., 2005)
  - Weaknesses of the current research include:
    - Lack of blind due to nature of exercise as treatment
    - Small sample sizes
    - Studies lack longevity
- SSRIs in the Treatment of MDD**
  - SSRIs effective at treating mild MDD (Garnock-Jones & McCormack, 2010, Li et al., 2017, & Arroll et al., 2009)
    - SSRIs more effective than placebo (Garnock-Jones & McCormack, 2010 & Arroll et al., 2009)
    - SSRIs more effective at preventing relapse than placebo (Garnock-Jones and McCormack, 2010)
  - Relatively safe with only mild to moderate intensity side effect noted with increased incidence at higher dosages (Garnock-Jones & McCormack, 2010)
  - Weaknesses of the current research include:
    - Small sample sizes
    - Studies lack longevity
    - No specific recommendations regarding dose and duration
- Exercise Compared to SSRIs in the Treatment of MDD**
  - Results varied based on the study:
    - Blumenthal et al. (2007) found exercise to be comparable to antidepressant medication in achieving remission
    - Cooney et al. (2013) found exercise to be less effective than antidepressants or psychological therapy and only moderately more effective than control
    - Danielsson et al. (2013) concluded exercise is beneficial as an augmentation to medication
  - Weaknesses of the current research include:
    - Studies lack longevity
    - Small sample sizes

## Applicability to Clinical Practice

- Depression is one of the most common illnesses seen by primary care providers today
- CBT is the recommended first-line treatment, but the convenience of pharmacotherapy has appealed to many causing SSRIs to become first-line
- SSRIs come with risks, however, and providers should be educated on alternative forms of therapy that may be of equal benefit without the added risks of medication
- Benefits of using exercise to treat MDD include minimizing medication use, avoiding side effects, reducing cost, improving self-confidence, aiding in weight loss, and improving overall health
- Research on this topic is becoming very popular but current research includes more women than men and lacks longevity
- At this point in the research, exercise is noted to have a moderate effect on depression, but after correcting for bias, the effect may only be small (Cooney et al., 2013)
- Future research should be completed to correct for weaknesses noted throughout the studies
- Overall, exercise at this point cannot be reported as a superior therapy over traditional options such as pharmacotherapy or psychotherapy, but it can be recommended as a beneficial augmented therapy in addition to traditional treatments for all patients with MDD

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