

## EVIDENCE BASED PRACTICE: AEROBIC EXERCISE AND MAJOR DEPRESSIVE DISORDER

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### Introduction

Mental health problems are international challenges that have a significant contribution in illness burden over the entire world (Blake, 2012). Major Depressive Disorder (MDD) is one of the common health problems, and is estimated to affect 121 million adults worldwide (World Health Organization [WHO], 2012). Projections for the year 2030 indicate that MDD will rank second only to coronary heart disease as a cause of illness burden over the entire world (WHO, 2012). Furthermore, WHO, 2012 reported that MDD currently represents a second health problem regarding disability caused by illness in the world.

MDD is associated with significant morbidity, mortality, and disability that burden the individual and his family, and contribute to impaired cognitive skills and deterioration of the individual life aspects (Blake, 2012; Nahas & Sheikh, 2011). Many risk factors are associated with incidence of MDD as genetic factors, life events, sleeping disturbance, alcohol, and some drugs (Townsend, 2011). Symptoms of depression include feeling of hopelessness and helplessness, loss energy, anhedonia, agitation, fatigue, withdrawn, weight loss or gain, fatigue and inappropriate thinking (Townsend, 2011).

MDD is a recurrent illness, with high incidence of returning, and the risk of relapse increases as the number of previous episodes increase (Solomon, Keller, Leon, Mueller, & Lvori, 2000). Hence the choice of treatment is important to improve the quality of life and to prevent or minimize recurrent episodes. For instance, the majority of western guidelines published since 2000 have similar recommendations about all stages of treatment of depression, that is first line treatment is usually serotonin reuptake inhibitor, psychotherapy, or combination of psychotherapy and pharmacotherapy (Gelenberg, 2010). Indeed, no single

### Abstract

Major Depressive Disorder (MDD) is one of the common health problems, and is estimated to affect 121 million adults worldwide. MDD is a recurrent illness, with high incidence of returning, and the risk of relapse that increases as the number of previous episodes increase. Hence, the choice of treatment is important to improve the quality of life and to prevent or minimize recurrent episodes. Physical exercise is an example of alternative and complementary therapy that has received considerable and significant attention in the treatment of MDD. The efficacy of aerobic exercise approaches is considered and has a place in mental health practice. According to many studies aerobic exercise is the preferred form of exercise for patients with MDD. Moreover, Aerobic exercise has been proven as an effective treatment for MDD, and there are sufficient studies to help health care providers to prescribe aerobic exercise as a treatment choice for MDD patients. It is recommended that patients participate in three to five exercise sessions per week, for 30 to 45 minutes per session. Within the range of intensity for aerobic exercise, that achieves a level of heart rate of 70 to 85 % of the heart rate reserve. Furthermore, the majority of research emphasizes that the exercise regimen should be continued for at least 10 to 16 weeks to achieve the greatest antidepressant effect.

**Key words:** Aerobic Exercise; Major Depression.

treatment for MDD is effective for every patient (Nahas & Sheikh, 2011). Almost half of depressed patients who are treated do not attain full remission of their symptoms of MDD and they remain under risk of residual symptoms and relapse (Solomon et al., 2000). Allopathic therapies could be undesirable options for MDD management illustrated by antidepressant medications having unpleasant side effect, and psychotherapy could be time consuming and expensive (Demyttenaere et al., 2001). Many depressed patients choose complementary alternative medicine instead of allopathic (Solomon et al., 2000). Hence, there is a great interest in development of alternative and complementary therapies to enhance and promote treatment options of MDD (Blake, 2012).

Physical exercise is an example of alternative and complementary therapy that has received considerable and significant attention in treatment of MDD (Blake, 2012). Physical exercise may be a viable treatment because it can be recommended for any patient at any time without suffering a negative social stigma (Nahas & Sheikh, 2011). In general, physical exercise has a significant and clear positive effect on physical health and psychological process in the human body (Blake, 2012). Normal physical health conditions may play a significant role in mental health balance, and maintain biopsychological aspect in the human body (Helmich et al., 2010). A number of studies indicated a consistent association between improving mental health and regular physical exercise (Hassmen, Koivula, & Uutela, 2000). In addition, many studies reported that physical exercise might reduce depressive symptoms in the nonclinical population and in patients diagnosed with MDD (Nahas & Sheikh, 2011). At the same time, an association between physical inactivity and higher levels of depressive symptoms in patients with MDD is observed (Helmich et al., 2010).

Concept of physical exercise indicates regular, structured, continuous, rhythmical fashion, and leisure time activity (Hassmen et al., 2010). Specifically, aerobic exercise is a kind of exercise which involves prolonged activity of large muscle groups to produce energy by metabolizing oxygen; such as running, swimming, and aerobic dancing (Reed & Buck, 2009). Unlike aerobic exercise, anaerobic exercise reflects intense, brief, and nonsustainable muscular activities that use the energy to produce activity without inhaling oxygen; such as in weight lifting, and pushing down (Reed & Buck, 2009).

In fact, the majority of healthy people prefer and use this kind of exercise in their life activities, and aerobic exercise is one of the common exercise modalities that is recommended for mental health improvement (Reed & Buck, 2009). Many studies have examined its effectiveness and viability to manage mental disorders (Kanning & Schlicht, 2010). Moreover, the efficacy of aerobic exercise approaches is considered and has a place in mental health practice, but some researchers suggested inconsistent recommendations regarding adoption of aerobic exercise as treatment choice for MDD

(Reed & Buck, 2009).

### Dose, Frequency, and Technique of Aerobic Exercise for MDD Management

The efficacy of aerobic exercise in treatment of MDD may be affected by age and severity of symptoms, but intensity of exercise programs have a substantial impact on aerobic exercise effectiveness for MDD (Silveira et al., 2013). Determining the type of exercise for people with MDD has to focus on personal interest, physical needs, risk for injury, and adverse effects for current medication. Selecting the convenient exercise is primary for continued consistent exercise intensity (Silveira et al., 2013).

In a report of 2013, American College of Sports Medicine (ACSM) defined many concepts related to intensity of aerobic exercise. In the beginning, ACSM used heart rate reserve term to reflect exercise intensity that is equivalent to the desired percentage of maximal oxygen uptake. Heart rate reserve means the difference between resting heart rate and maximum heart rate. ACSM set maximum heart rate as the highest number of beats per minute during physical exertion, and resting heart rate is the lowest number of heart beats per minute during full relaxation and without distractions. The intended increase in heart rate reserve means increase in the aerobic exercise intensity (ACSM, 2013). Additionally, ACSM articulated that exercise intensity reflects how much energy is expended when exercising. ACSM clarifies a way to optimize energy expenditure by modifying the intensity of the exercise. It is important to choose mode of exercise that can be regulated to overload the cardio respiratory system and increase the heart rate reserve level, so it will increase exercise intensity (ACSM, 2013).

ACSM (2013) classified exercise mode for MDD treatment regarding energy expenditure into three groups of exercise (a) exercises that provide a consistent intensity and energy expenditure such as walking, jogging, cycling, and stair climbing; (b) in this group the exercise will burn more calories if a person worked harder and longer such as aerobic dancing, bench stepping, and swimming; (c) large muscle contractions with prolonged activities such as basketball, racquet sports, and volleyball are high energy expenditure exercise activities. Moreover, many doses are used to determine energy expenditure in an aerobic exercise program, for instance, public health dose of aerobic exercise that is total weekly energy expenditure of 17.5 kcal/kg/week, and low dose aerobic exercise that is total weekly expenditure of 7 kcal/kg/week (ACSM, 2013). More energy expenditure means more effective exercise practice because of the biophysiological actions of muscle contractions, and hormonal excretion after intensive exercising program (Drevets, 2001).

Aerobic exercise program for MDD. In their study, Dunn et al. (2005) reported that aerobic exercise consistent with public health dose is an effective treatment for MDD, but a lower dose is comparable to no treatment intervention.

Dunn et al. also concluded that there was no difference in result between 3 days per week of aerobic exercise and 5 days per week. Hence, the distinct factor for reduction of MDD symptoms is total energy expenditure not frequency of exercise sessions. In the same way, Blumenthal, Smith, and Hoffman (2012) concluded that no differences between 3 days per week and 5 days per week of aerobic exercise as a therapeutic exercise regimen for MDD, but exercise adherence is the essential factor to profit from the exercise program.

Blumenthal et al. (1999) applied 16 weeks exercise program of 45 minutes session per day for three days every week on MDD participants. The result showed positive outcomes after implementing this method, and the exercise program achieved therapeutic effects (Blumenthal et al., 1999). Another design, which is developed by Davidson (2010) within a guideline for MDD treatment, presented a different aerobic exercise program. Davidson's program consisted of three times weekly of regular walking and jogging sessions for 10 weeks; each exercise session consisted of 10 minutes of stretching exercise, followed by 45 minutes of continuous walking or jogging to obtain desired exercise intensity by increasing heart to 70-85% of maximum heart rate of MDD participant. A somewhat distinct aerobic exercise program performed by Babyak et al. (2000) and Blumenthal et al. (2007) suggested three exercise sessions per week for 16 consecutive weeks. Every session designate training exercise ranges equivalent to 70-85 % of heart rate reserve. Each aerobic session started with 10 minutes warm up period, next followed by 30 minutes of brisk walking or jogging at intensity consistent with assigned heart rate reserve. After that, exercise session concluded with five minutes of cool down exercise. The exercise program achieved positive results in managing symptoms of MDD (Babyak et al., 2000; Blumenthal et al., 2007). A positive outcomes study by Hoffman et al., (2011) applied similar aerobic exercise method within their randomized clinical trial study to reduce MDD symptoms. Hoffman et al. designed program of attending 45 minutes of aerobic exercise of running, jogging, and treadmill each week for four months within target heart rate of 70-85% of heart rate reserve.

Briefly, three days of aerobic exercise sessions per week for consecutive weeks range from 10 to 16 weeks; every session of jogging, running, walking, or treadmill, or any aerobic exercise that the patient is interested in, continued for 30 to 45 minutes, and maintained at 70 to 85 % of monitored heart rate reserve. Also consideration should be given to the patients' abilities for these exercise sessions in regard to their health, time, and willingness for exercise practice, could be an appropriate program for MDD management practice.

#### PICO Format

Evidence-based practice is integration of best research evidence with clinical expertise and patient values (Stuart, 2001). To implement evidence based practice strategies, we can use PICO, which is a method of putting together a search strategy that allows the health care provider to take a more evidence-based approach to the literature searching when searching bibliographic databases (Stuart, 2001).

A clinical question needs to be directly relevant to the patient or problem. It needs to be phrased in such a way as to facilitate the search for an answer. PICO makes this process easier (Stuart, 2001). It is a memorial for the important parts of a well-built clinical question. It also helps formulating the search strategy by identifying the key concepts that need to be in the article that addresses the question. A PICO question consists of four elements (a) population or patients (b) intervention (c) comparison (d) outcome.

At this level, we can clarify current clinical questions that articulate the efficacy of aerobic exercise to manage patients with MDD. Furthermore, it could compare aerobic exercise to antidepressant in managing MDD. PICO questions apply a convenient format that will ease process of answering relevant questions. PICO search strategies will consider the main elements of PICO questions. Proposed PICO questions elements are illustrated in Table 1.

**Table 1**

#### *PICO Question Framework*

PICO	Clinical Elements
1. Population	Patients with MDD
2. Intervention	Aerobic Exercise
3. Comparison	No Aerobic Exercise or Antidepressant
4. Outcome	Reducing MDD symptoms

### PICO Questions

Clinical elements are combined through PICO format to formulize PICO questions. The proposed three PICO questions are:

- 1- In patients with MDD, does aerobic exercise program reduce the symptoms of MDD?
- 2- In patients with MDD, what is the effect of aerobic exercise program on reducing symptoms of MDD compared to no aerobic exercise?
- 3- In patients with MDD, how does aerobic exercise program compared with antidepressant reduce symptoms of MDD?

### Literature Review

#### Effects of Aerobic Exercise on People with MDD

In this situation, one systematic review performed by Phillips, Kiernan and King (2003) indicated that aerobic exercise has beneficial effects on patients with MDD, and may increase social integration, successful adaptation, and self esteem of patients with MDD. In addition, Phillips et al. (2003) reported that an aerobic exercise as little as four weeks could beneficially affect people with MDD. Similarly, Lawlor and Hopker (2001) in their systematic review concluded that aerobic exercise may be efficient in reducing symptoms of depression among patients with MDD in the short term, but it is not clear for long term treatment plan due lack of follow up studies.

A number of randomized clinical trials studies examined the effects of aerobic exercise on people with MDD. For instance, Carter, Callaghan, Khalil and Morres (2012) found that sufficient intensity of aerobic exercise has effective outcome on the depressive symptoms of patients who are experiencing MDD. Equally, another randomized clinical trial conducted by Dunn, Trivedi, Kampert, Clark, and Chambliss (2005) concluded that standard aerobic exercise is an effective treatment for MDD of mild to moderate severity. The authors suggested that participants with MDD who underwent the study showed an improvement in their mental status after implementing a full aerobic exercise program (Dunn et al., 2005). In the same way, in 2007, Blumenthal et al. in their randomized clinical trial study showed that aerobic exercise program for participants with MDD is better than no treatment intervention to improve mood status. In a like manner, one randomized clinical trial reported that MDD patients positively interested in aerobic exercise, showed efficacious response after a modest exercise program (Babyak et al., 2000). Particularly, aerobic exercise is an effective and potent treatment for patients with MDD in case the patients are willing to undergo the exercise program (Babyak et al., 2000). One quasi-experimental study reported that aerobic exercise program decreased the depression scores in Hamilton rating scale among elderly women who experienced MDD (Sayyad, Nazer, ansary, & Khleghi, 2006). Furthermore, in their pilot study Dimeo, Bauer, Varahram, Proest, and Halter (2001) concluded that an improvement in mood status could

occur after implementing 10 days of aerobic exercise for patients experiencing mild MDD.

In contrast, one randomized clinical trial conducted by Krough, Videbeck, Thomsen, Gluud, and Nordentoft (2012) indicated opposite outcomes to previous studies. Study of Krough et al. concluded that aerobic exercise has no significant effect on patients who experienced MDD. Additionally, Krough et al. reported that duration, frequency, and intensity of aerobic exercise are not substantial to potentiate aerobic exercise performance. Another randomized clinical trial showed that one year of exercise training is not effective for depressive symptoms among residents of care homes and nursing homes who are experiencing MDD (Underwood et al., 2013).

#### Aerobic Exercise versus Antidepressant Medication

Aerobic exercise may reduce negative side effects of antidepressants, such as fatigue, dizziness, and constipation, thus increasing compliance in medication use (Kruisdijk, Hendriksen, Tak, Beekman, & Rock, 2012). Aerobic exercise could be applied as a single treatment plan or complementary therapy in addition to pharmacological treatment (Kruisdijk et al., 2012). No doubt, adverse effects of aerobic exercise are less than antidepressant, and aerobic exercise is relatively safer than antidepressant with low cost charges (Kruisdijk et al., 2012).

One systematic review showed that aerobic exercise and antidepressant medication are similar regarding reduction of depressive symptoms on the Hamilton depression rating scale in patients diagnosed as MDD (Danielsson, Noras, Waern, & Carlsson, 2013). The same review recommended that people with MDD should be treated with aerobic exercise instead of antidepressant medication (Danielsson et al., 2013). Another meta-analysis concluded aerobic exercise enhances the response to antidepressant treatment for MDD patients, but it is less effective than antidepressant treatment in improving MDD symptoms (Silveira et al., 2013). On other hand, Cooney et al. (2013) concluded in their systematic review that aerobic exercise is slightly more effective than no treatment intervention to reduce depressive symptoms among MDD patients, but is less effective than pharmacological treatment in reducing depressive symptoms or improving quality of life for people with MDD.

Another clinical trial study suggested that the effect of aerobic exercise on MDD remission is similar to antidepressant, and aerobic exercise may enhance the efficacy of pharmacological treatment (Hoffman et al., 2011). This conclusion is supported by another randomized clinical trial conducted by Blumenthal et al. (2007) who found efficacy of exercise treatment similar to antidepressant medications, and both treatments are better than no treatment intervention in patients with MDD. Also, an earlier study completed by Blumenthal et

al. (1999) suggested more positive expectation regarding aerobic exercise which may be considered as alternative treatment to antidepressants to manage MDD. However, some antidepressants may provide rapid onset therapeutic response more than aerobic exercise that enhances position of antidepressant medications as the first line treatment for MDD (Blumenthal et al., 1999).

## Discussion

In general, many studies of first level of evidence concluded that aerobic exercise is effective in reducing symptoms of patients with MDD. All studies that reported positive outcomes regarding aerobic exercise efficacy in MDD are summarized in Table 2. However, as shown in Table 3, two randomized clinical trial studies showed that aerobic exercise has no effect in reducing symptoms of MDD. Hence, the clinical questions, which investigate the efficacy of aerobic exercise and compare it to no treatment approaches, could be answered after evaluating all relevant studies.

The systematic review and randomized clinical trial studies articulated a positive relation between aerobic exercise and reducing symptoms of MDD. High level of evidence in these studies affords capacity to answer the clinical questions. No doubt, number and level of evidence of former studies, that found aerobic exercise is effective in reducing symptoms of MDD, are more vigorous than studies that showed negative outcomes.

Searching of literature related to PICO questions that compare aerobic exercise to antidepressant, found high level of evidence as represented in Table 4. The studies reported that aerobic exercise may be similar or less efficient than antidepressant in reducing symptoms of MDD. However, no studies showed opposite outcomes. Similarly, aerobic exercise could not be more effective than antidepressant in reducing symptoms of MDD.

**Table 2**

### *Summary of Positive Results Studies for efficacy of AE in MDD*

Level of Evidence	References	Design	Results
Level 1a	Phillips, Kiernan and King, 2003	Systematic review	Aerobic exercise (AE) has beneficial effects on patients with MDD
Level 1a	Lawlor and Hopker, 2001	Systematic review	AE may reduce symptoms of MDD in short term
Level 1b	Carter, Callaghan, Khalil and Morres, 2012	Randomized clinical trial	Sufficient intensity of AE has effective outcome symptoms MDD
Level 1b	Dunn, Trivedi, Kampert, Clark, and Chambliss, 2005	Randomized clinical trial	AE is effective treatment for MDD of mild to moderate severity
Level 1b	Blumenthal et al., 2007	Randomized clinical trial	AE for participants with MDD is better than no treatment intervention to improve mood status.
Level 1b	Babiyak et al., 2000	Randomized clinical trial	Positively interested MDD patients in AE showed efficacious response after a modest exercise program
Level 2b	Sayyad, Nazer, Ansary, & Khleghi, 2006	Quasi-experimental study	AE program decreased the depression scores in Hamilton rating scale among elderly women who experienced MDD
Level 3b	Dimeo, Bauer, Varahram, Proest, and Halter, 2001	Pilot study	Improvement in mood status could occur after implementing 10 days of aerobic exercise for patients experiencing mild MDD.

Table 3

Level of Evidence	References	Design	Results
Level 1b	Krough, Videbech, Thomsen, Gluud, and Nordentoft, 2012	Randomized clinical trial	AE has no significant effect on patients who experienced MDD.
Level 1b	Underwood et al., 2013	Randomized clinical trials	One year of exercise training is not effective for depressive symptoms among residents of care homes and nursing homes who are experiencing MDD.

Table 4

*Summary of Studies for Efficacy of AE versus Antidepressant*

Level of Evidence	References	Design	Results
Level 1a	Danielsson, Noras, Waern, & Carlsson, 2013	Systematic review	AE and antidepressant medication are similar regarding reduction of depressive symptoms in patients diagnosed as MDD.
Level 1a	Silveira et al., 2013	Meta-analysis	AE is less effective than antidepressant treatment in improving MDD symptoms.
Level 1a	Cooney et al., 2013	Systematic review	AE is less effective than pharmacological treatment in reducing depressive symptoms or improving quality of life for people with MDD.
Level 1b	Hoffman et al., 2011	Randomized clinical trials	AE on MDD remission is similar to antidepressant
Level 1b	Blumenthal et al., 2007	Randomized clinical trial	Efficacy of exercise treatment is similar to antidepressant medications in reducing symptoms of MDD.

### Summary

According to former studies aerobic exercise is the preferred form of exercise for patients with MDD. Moreover, Aerobic exercise has been proven as an effective treatment for MDD, and there are sufficient studies to help health care providers to prescribe aerobic exercise as a treatment choice for MDD patients. The results showed that patients may experience a relief in depressive symptoms in as little as four weeks after starting exercise.

Although a question whether patients with MDD could actually participate in an aerobic exercise program, the studies suggested that the majority of MDD patients

prefer the aerobic exercise rather than antidepressant medication and MDD patients drop out rate from the exercise programs is very low.

It is recommended that patients participating in three to five exercise sessions per week, for 30 to 45 minutes per session. Within the range of intensity for aerobic exercise, that achieves a level of heart rate of 70 to 85 % of the heart rate reserve. Furthermore, the majority of research emphasizes that the exercise regimen should be continued for at least 10 to 16 weeks to achieve the greatest antidepressant effect.

The recommended strategies that may help improve adherence to exercise programs, include asking patients about their favorite type of exercise, and encouraging them by using a group exercise program. In addition, it is recommended also to encourage patients to engage in at least some exercise, even if they do not exercise enough to meet current public health dose exercise, they may take a first step in this therapeutic approach.

It is also recommended more research studies should be carried out in this area with emphasis on methodological accuracy, adequate sample size, and follow up research design with long term examination methods.

## Conclusion

Aerobic exercise could be part of the treatment plan for patients with MDD even as single treatment therapy, or combined with other allopathic treatment approaches. In addition, the aerobic exercise program could be implemented as planned and structured practice according to available randomized clinical trials methods of aerobic exercise intervention, which reported that aerobic exercise is effective to treat MDD, and potentiate antidepressant medications.

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