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Let's Move! Benefits of Exercise Compared to SSRIs (escitalopram) for the Management of Depression: Research from 2020 and Beyond

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Table of Contents

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Abstract

The purpose of this literature review is to determine the effectiveness of exercise as either monotherapy or in combination with SSRIs (selective serotonin reuptake inhibitors) for the management of major depressive disorder. Studies gathered for this review came from the following databases: PubMed, SpringerLink, Academic Search Ultimate, Academic Search Complete, and CINAHL. Current research completed between the years 2020-2023 that consisted of either clinical trials, RCTs, or meta-analysis were included. A total of eleven studies were reviewed that addressed either the benefits of exercise, SSRIs, or a combination for the management of depression. Upon completion of the literature review, it was determined that exercise can be equivocal to SSRIs and considered a treatment option. While this is a significant finding, the benefits of exercises are more consistent in those that adhere to a program and are more effective if prescribed in combination with SSRIs. While exercise has the potential to be considered as a treatment option for patients with major depressive disorder, it would require providers to have the knowledge and awareness of appropriate exercise modalities and resources available to the patients. It is also vital that providers offer continued support to patients and encourage compliance with their programs to yield optimal outcomes.

Keywords: depression, depressive disorders, antidepressives, escitalopram, exercise, exercise movements/techniques, exercise therapy, running, at-home exercise, Pilates, application-based exercise, antidepressive agents, Lexapro

Introduction

Statement of the problem

Major depressive disorder is a continued health care concern that impacts many individuals across the age spectrum. Most providers will encounter an individual on their schedule that has a history, or a current diagnosis of depression and should be equipped with multiple treatment strategies to assist in reducing this growing problem. Use of antidepressants has been one of mainstay treatments for managing symptoms associated with depression, however any time a pharmacological option introduced, as is the possibility of adverse effects. With this understanding, it would be beneficial to consider other options, such as exercise and movement to not only reduce the psychological symptoms associated with depression, but also physiological effects. Exercise and physical activity should be considered as part of the treatment plan for individuals suffering from depression and concomitant comorbidities.

According to the World Health Organization (WHO), there are approximately 264 million people in the world that are affected by major depressive disorder (Wang et al., 2021). Due to the significant impact this number has on the health care system, it is essential that providers consider an array of different treatment options. Symptoms of depression are highly variable amongst patients; therefore, it is important that treatment must also be adaptable based on clinical presentation. Historically, many providers may have relied on pharmacological management, such as selective serotonin reuptake inhibitors (SSRIs), for their patients with depression. However more recently, the research is supporting different approaches to

management. This includes exercise and movement, either in addition to medication, or as monotherapy.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (2013), major depressive disorder is diagnosed based on the presence of five or more of the following symptoms during the same 2-week time period: depressed mood most of the day (nearly every day), diminished interest or pleasure in activities, significant unintentional weight loss or gain, insomnia or hypersomnia, fatigue or loss of energy, feelings of worthlessness or excessive guilt nearly every day, decreased ability to concentrate, or recurrent thoughts of death. The symptoms cause clinical distress and are not attributable to other medical conditions. As used throughout the literature, the term remission describes patients who experienced a period of two or more months without symptoms, or only one to two mild symptoms.

The purpose of this literature review is to analyze research published in the year 2020 or after that investigated the effects of using active modalities, such as exercise, Pilates, or running, compared to use of an SSRI, such as Escitalopram, for the management of subjects that had a diagnosis of major depressive disorder according to the DSM-V or DSM IV, depending on the resource.

Research Question

In patients with depression, does prescribed exercise or SSRIs (Escitalopram) reduce symptoms more effectively?

Methods

For the literature review different online search databases provided through the University of North Dakota were utilized. The primary online databases included PubMed,

SpringerLink, Academic Search Ultimate, Academic Search Complete, and CINAHL. The emphasis of this literature review was to analyze current research that was completed between the years 2020-2023 that consisted of either clinical trials, RCTs, or meta-analysis. The timeframe was the initial inclusion criterion when starting the search. The other inclusion criteria included any gender and age, major depressive disorder as defined by the DSM-IV or DSM-V (depending on the source), performance of any exercise modality, and antidepressant use/escitalopram. Studies were excluded if they included limiting co-morbidities, other psychiatric diagnoses, polypharmacy, postpartum, published prior to 2020, systematic reviews, and incomplete studies. In order to narrow down the search, MeSh terms included depression, depressive disorders, antidepressives, escitalopram, exercise, exercise movements/techniques, exercise therapy, and running. Other key terms included at-home exercise, Pilates, application-based exercise, antidepressive agents, Lexapro, and various forms of depression. This search strategy yielded 103 studies on PubMed, and from there those that met the inclusion criteria were considered for the literature review. When searching SpringerLink and CINAHL the results were similar. The search strategy was established with the assistance of University of North Dakota's reference librarian, Megan Denis.

Literature Review

Benefits of Escitalopram (Lexapro) for Management of Depression

Major depressive disorder (MDD) may become the second most common cause of disability and burden of disease by the year 2030, according to WHO (Wang et al., 2021). To address this, providers prescribe different antidepressants based on patient history and current complaints. In a multicenter, double blinded, placebo-controlled study performed by Wang et al.

(2021) they specifically looked at the effectiveness of generic escitalopram on the management of depression compared to placebo, and whether it is as effective as the brand name escitalopram (Lexapro). Because escitalopram has been found to have two times greater potency for inhibition of serotonin reuptake compared to citalopram, it was chosen as the intervention. The study was performed over the course of eight weeks, and it randomized 390 participants that were diagnosed with MDD into the three groups (130 per group): generic escitalopram (intervention), Lexapro (control), or placebo. Individuals included in the study were 18-65 years old, that had been diagnosed with depression based on DSM-IV criteria and had no recent history of drug abuse or suicidal ideation. Exclusion criteria included any allergic reactions, lack of response to either medication, or history of epilepsy.

Throughout the study, the intervention group was provided with 10 mg of generic escitalopram per day for two weeks. If that was found to be ineffective, then they increased the dose to 20 mg per day for the remaining six weeks. The Lexapro group was given a consistent dose of 10 mg per day for the entire eight weeks. The efficacy of treatment was determined based on improvements of Montgomery-Asberg Depression Rating Score (MADRS), Hamilton Anxiety Rating Scale (HAM-A), and Hamilton rating scale for depression-17 (HAM-D17) (Wang et al., 2021). Outcomes were assessed on the full analysis set, and subjects that were analyzed had received at least one dose of either medication, and also one post-baseline assessment of their MADRS score. Intervention was considered effective if two parameters were met including a >50% decrease in MADRS total score, and a >50% reduction in HAM-D17 score (Wang et al., 2021).

After eight weeks, participants in the generic escitalopram group and Lexapro group both had significantly reduced symptoms and improved scores compared to placebo ($p<0.001$). At baseline, the average MADRS score of the three groups was between 29-30.85, indicating moderate to severe depression. At the end of the study, individuals that were given escitalopram or Lexapro demonstrated scores between 5-10, indicating mild depression (Wang et al., 2021).

The study demonstrates that the generic form of escitalopram is as effective as proprietary escitalopram (Lexapro) in the management of MDD compared to placebo and can be considered as a cost-effective option for patients. Unfortunately, there were several participants that withdrew due to adverse effects, which the researchers did not consider. Also, the dose provided was 10 mg, which may have impacted potential outcomes, as well as the short duration of the study (eight weeks). Further research could include a longer duration, such as six months. The study did not specifically mention a baseline score for the HAM-D17, however based on graphical imaging, the baseline appeared to be 25 for all groups, with a >50% reduction in both medication groups. The study was relatively small; therefore, a larger sample size would yield more reliable clinical outcomes. Despite the sample size, the study did include a variety of demographics, which helps to generalize the results to a wider range of patients, similarly to what would be experienced in clinic.

Not only is depression becoming a common occurrence, WHO reported that nearly 23 million adults require care at some point in their diagnosis (Mandal et al., 2021). To date, there are several SSRIs available for management of depression, although few studies have assessed the efficacy of specific medications. Mandal et al. (2021), chose to evaluate the efficacy and safety of escitalopram specifically, and determine if response is different based on gender or

severity of depressive symptoms. Escitalopram was chosen due to its low side effect profile. Although it shares similar side effects with other SSRIs including insomnia, fatigue, nausea, headaches, sexual dysfunction; these tend to be mild in nature. Therefore, it often used as a first-line anti-depressant in India.

This was a 12-week, prospective, open-label observational study in Manipal, India (Mandal et al., 2021) that assessed the effectiveness of escitalopram. Subjects in this study were diagnosed with depression as verified by DSM-IV and managing symptoms with monotherapy escitalopram. Inclusion criteria included: Baseline 17-item Hamilton Depression Rating Scale (HDRS-17) of 18 or greater, south Indian ethnicity, either gender, between age 18-65, and had a first episode or recurrent episode of MDD (Mandal et al., 2021). Patients were excluded if they had other co-morbid mental illnesses within the last 12 months, had significant suicidal ideation, liver or renal impairment, pregnancy, unstable illness, or were contraindicated to take escitalopram.

Participants were treated with escitalopram at a dose of 10-20 mg daily. If they did not have a response to 10 mg, then they were able to increase the dose to 20 mg. They were not allowed to take any other psychotropic drugs, except zolpidem or clonazepam for insomnia, and any medications necessary for management of diabetes, hypertension, etc. The goal of the study was to determine efficacy based on remission and response rates. Scores of less than 12 on the Montgomery-Asberg Depression Rating Scale (MADRS), and less than eight on the HDRS-17 were considered remission and at least a 50% improvement from baseline was considered treatment response. Participants were grouped in either a moderate depression (HDRS-17 score

between 17-23) or severe depression (HDRS-17 >24) group based on their baseline score (Mandal et al., 2021).

Statistical analysis was performed using t-test and chi-square, (Mandal et al., 2021) with a p value set at <0.05. There was a total of 151 patients recruited for the study, however by the end of 12 weeks, 148 subjects had participated, with 65 (43.0%) responding and 63 of those 65 participants meeting criteria for remission. Prior to the study, 15.5% of the 148 subjects had suicidal ideation, which decreased to 6.08% by the end of 12 weeks. Of note, most of the subjects (83.78%) increased the daily dose of escitalopram from 10 mg to 20 mg.

When assessing HDRS-17 and MADRS scores, there was a significant improvement ($p<0.05$) noted starting at week four, through the duration of the study. Interestingly, those with moderate depression had an improvement in scores that was significantly higher (p value = 0.0001) compared to those with severe depression. This indicated that those with less severe symptoms at baseline experienced a better response to the medication (Mandal et al., 2021). The outcomes were similar between genders and whether this was a first episode or recurring episode. Overall, as anticipated, escitalopram was well tolerated, and no subjects were required to withdraw from the study due to adverse effects.

At the end of 12 weeks, there was a response rate of 43.9% and remission rate of 42.6% amongst participants treated for major depressive disorder with 10-20 mg of escitalopram. This was lower than response and remission rates in other studies, however there were consistencies noted, such as improved HDRS-17 and MADRS scores. Previous studies had longer durations of treatment (24 weeks), however this study demonstrated improvements starting at four weeks, which may be beneficial when predicting possible remission in MDD patients (Mandal et al.,

2021). When comparing scores of those suffering from moderate or severe depression, the findings were consistent with other studies in that the improvement in MARDS and HDRS-17 scores were higher in moderately depressed individuals (Mandal et al., 2021).

In conclusion, this study demonstrated that prescribing an SSRI such as escitalopram has proven benefits for management of major depressive disorder. The side effect profile is less significant compared to other SSRIs and has demonstrated to be a safe option for patients. The onset of effectiveness was within four weeks, which is important to consider when patients inquire about the timeline with antidepressants. Interestingly however, the benefits of this medications depended on the severity of symptoms, which had not been considered in previous studies. This study revealed escitalopram is more effective for those with moderate depression compared to severe, which then raises other questions and considerations, including the fact that those that are severely depressed may have more external stressors and situation impacting them. It would be beneficial to assess the effects of escitalopram in combination with other modalities, such as exercise for those with severe depression to determine if this would result in a decline in MADRS and HDRS-17 scores similar in those with moderate depression.

Benefits of Exercise for Management of Depression

Depression can affect the entire age spectrum, and when considering the effects of depression on the adolescent population, it is necessary to recognize how they can play a significant role in their growth, development, and adaptation to life's stresses. According to preliminary research, up to 45% of the adolescent population suffers from depression because of environmental stress. As adolescents are developing, there are several external factors that influence the level of depression including perfectionism, learning stresses, and negative events.

Although family life and gender factors did not have as much of an influence (Bai et al., 2020). Teens experiencing depression are considered higher risk for suicide, withdrawal from society, and irritability with others (Bai et al., 2020). Current treatment recommendations include cognitive behavioral therapy, interpersonal psychotherapy, and medications such as SSRIs (Serrander et al., 2021).

In the study by Bai et al. (2020) they considered a non-pharmacological approach for management of depression in this age group, recognizing the benefits exercise can have. Not only does exercise improve respiratory and circulatory systems and digestion, but it has also been shown to have a positive effect on the nervous system and cerebral cortex excitability of younger individuals, which can assist in management of their depressive symptoms (Bai et al., 2020). Because many individuals are unfamiliar with other resources that may be available, this research aimed to introduce how a modality such as exercise can be effective.

Bai et al. (2020) recognized that adolescents are not all able to perform the same level of exercise intensity, therefore they compared three groups: control group, medium-intensity, and high-intensity, dividing 30 participants into the groups (depressed and normal), with five in each. They used electroencephalogram (EEG) to assess the adolescents under the three conditions and their ability to answer a quick answer test. Participants were given the Beck Depression Inventory and Hospital Anxiety and Depression scale, and as anticipated, those in depression group scored significantly higher than those in the control group. They were directed to train according to the intensity of their group, then they received an EEG test and responded to the same question.

Participants in the depression group that exercised at a higher intensity had quicker answer times, compared to those that did not. Conversely, those that exercised at higher intensities in the normal group demonstrated longer response times (Bai et al., 2020). This finding indicated that exercise training may help improve attention and focus which is often lacking in those suffering from depression.

While this study demonstrated that increasing exercise intensity in depressed adolescents improved correctness rate of questions and decreased the response time, it lacked supporting information. It is unknown what the type of exercise was or what was considered high versus medium intensity. They did not analyze within the groups, and the study did not specify what questions were asked. However, the study did provide general insight to the effects exercise can have on adolescents with depression and lays the foundation for more research and encouragement for non-pharmacological management of depression in the younger population.

Serrander et al. (2021) also studied adolescents, recognizing that addressing symptoms of depression at an early age could help reduce the risk of chronic depression, suicidal ideation, substance abuse, or further detachment. They interviewed 16 clinically referred adolescents and provided them with a 14-week exercise program that spanned from moderate to vigorous intensity. Unlike other studies discussed, this was a qualitative study. Individuals were included if they were between 12-17 years old with major depressive disorder per DSM-V and scored greater than a six on a clinician rated scale. Exclusion criteria included eating disorders, already participating in 150 minutes of moderate exercise or 75 minutes of vigorous a week, high risk of suicide, or recent medication changes (Serrander et al., 2021).

At baseline, the subjects scored an average of 14 per the clinician-provided Quick Inventory of Depressive Symptomology for Adolescents, which indicated moderate depressive disorder. The subjects participated in three 60-minute sessions a week under the supervision of a personal trainer. After the 14 weeks, they answered a series of questions that addressed their thoughts on exercise, how it impacted them, how they felt exercising in a group, and their motivation for exercising (Serrander et al., 2021).

Following the intervention window, they found three subjects were considered in remission, five had a 50% reduction in their baseline score, and eight were still depressed, but with milder symptoms. When interviewing the subjects, they found comments such as increased mental and physical vitality, decreased chronic pain, improved focus, better commitment to family and friends, greater joy in activities, and decreased fatigue. One of the main components was the improvement in self-esteem and empowerment. Additionally, self-deprecation was less overall, and subjects reported “feeling better than I did before,” “I have a better view of myself” and looking at themselves in a brighter light (Serrander et al., 2021).

Overall, this study demonstrated several positive outcomes from implementing exercise as a treatment modality for adolescents with depression. Limitations of this study include the small sample size and the difficulty with reproducibility. There were three interviewees, and while they had access to an interview guide, it is difficult to determine if the questions were delivered with the same tone and expression. There is also a question as to whether the age span played a role in the maturity and response to the programming. Fortunately, none of the adolescents reported negative impacts with incorporation of the exercise regimen. This study further supports adding exercise to current regimens of managing depression.

Another demographic to consider when discussing depressive symptoms, stress, and fatigue, is that of healthcare workers. During the Covid-19 pandemic, they were required to work around the clock and sacrifice their health and wellbeing to care for patients, which led to more stress, anxiety, depression, burnout, and absences from work. Unfortunately, the rate of depressive and anxiety symptoms nearly tripled, compared to pre-pandemic times (Boucher et al., 2023). To investigate management of depressive symptoms, burnout, and absenteeism, Boucher et al. (2023) designed a study that compared the impact of exercise on these concerns. To make the study more accessible to participants, they utilized an app-based exercise program and followed up after 12 weeks.

The study was a 2-group, parallel randomized control trial that separated participants into either an exercise group or a wait list group. Recognizing that not every individual has access to the same exercise equipment, those that were in the exercise group were given access to one-year subscription to the Down Dog suite of apps that included various exercises: yoga, body weight strengthening, running, and barre (Boucher et al., 2023). Meanwhile, the wait list group served as the control and those participants were given access to the app after the study had completed.

Participants were recruited from 10 different hospitals in Vancouver, BC via email communication. Inclusion criteria included: 18 years or older, accessibility to reliable internet or adequate cell phone reception for use of the app and were current employees of the hospital (Boucher et al., 2023). Those that met inclusion criteria for the study were cleared to exercise using the Physical Activity Readiness Questionnaire for everyone, or by a certified exercise physiologist. Individuals were randomly placed into the groups if they were deemed healthy enough to participate. There were 142 participants in the exercise group, and 146 in the wait list,

for a total of 288 participants. Interestingly, most of the individuals were women (85.4%). Men and nonbinary accounted for the remaining 14.6% percent. The mean (SD) age was 41 (10.8) years, and a variety of ethnicities were included. They were instructed to exercise for 20 minutes a day, doing the exercise of their choice, for four sessions a week. In total, the goal was 80 minutes of exercise a week for the duration of the 12 weeks. Those in the 'control group' were asked to maintain their current activity level (Boucher et al., 2023).

Outcomes were assessed at baseline, then again biweekly for the duration of the study using the 10-item Center for Epidemiological Study Depression Scale. Depressive symptoms were measured between groups every two weeks. In addition to depression, the study included burnout symptoms (cynicism, emotional exhaustion, and professional efficacy) that were measured using the 16-Item Maslach Burnout Inventory (Boucher et al., 2023). Lastly, participants absenteeism was measured by inquiring if there were any absences in the last two weeks. The exercises were tracked via the app, which provided objective information regarding adherence.

All participants were included in the analyses based on intention-to-treat. A two-sided p-value <0.05 indicated significant difference when assessing effects of exercise. Because the study relied on participants to respond to surveys, there were challenges regarding missing information, and this was accounted for when analyzing the results (Boucher et al., 2023).

Adherence to the exercise program was an issue, which is a common limitation amongst studies of this nature. In the first week, a mean (SD) of 73.3 (41.5) minutes of exercise were performed, with only 78 of the 142 participants completing the subscribed 80 minutes. By week 12, only a mean of 34.7 minutes of exercise were performed and an average of 1.6 workouts per

week. Unfortunately, only 23.2% of those in the exercise group completed the 80 minutes of prescribed exercise (Boucher et al., 2023).

Despite the issues with adherence, there were significant positive effects on the depressive symptoms throughout the study. By week 12, an effect was observed (ES, -0.41 (95% CI, -0.69 to -0.13), indicating that there were significant reductions in depressive symptoms for those in the exercise group versus the waitlist (control) group (Boucher et al., 2023).

Secondary outcomes were addressed including cynicism, emotional exhaustion, professional efficacy, and sick days. Over the course of 12 weeks, each area demonstrated results that favored the exercise group. Participants reported fewer sick days and generally a more positive attitude. Overall, per-protocol analysis demonstrated improvements in depressive symptoms, as well in the secondary areas, for those that completed 80 minutes of exercise a week compared to the waitlist group. Participants completing 20 to 79 minutes a week demonstrated mild improvement regarding cynicism and emotional exhaustion, while those that completed 20 minutes or less, did not demonstrate any significant effects.

Although the results demonstrated that exercise had significant effects on depressive symptoms and burnout, cynicism, and emotional exhaustion, this was most beneficial for those completing increased minutes of exercise. As discussed, adherence was an issue, which has been a consistent limitation in studies of this kind. It is unknown what impacted individuals' ability to perform the exercises, as this was established to allow for at-home performance. The study did require individuals to have the ability to navigate the app, which may have varied throughout. Exercise was only measured through the app; therefore, it did not consider any other forms of

measurements, including walking/step counting. This study also had primarily females, which impacts the ability to generalize the findings amongst genders.

In spite of the limitations, this study revealed that exercise using little to no equipment can have a significant impact on the wellbeing of health care workers. Because of the accessibility of phone apps and online resources, it would be worthwhile to discuss this option with patients that otherwise may not have the financial or transportation means to access a gym to exercise. The findings support that exercise, which is a low-cost treatment, can have a positive effect regarding management of depressive symptoms if there is an adequate level of adherence.

According to Ravari et al. (2021) 21.5% of the global population will fall into the 'elderly' population by 2050. They noted antidepressants as management of depression may be more detrimental for these individuals, due to adverse effects, and believe utilizing a cost-effective approach such as exercise, would yield more positive outcomes. They chose to study older women and introduced them to Pilates. This is a lower intensity exercise modality that incorporates balance and core strengthening and can be performed by individuals of all capabilities (Ravari et al., 2021).

Inclusion criteria included age over 60 years, low or moderate happiness scores, ability to perform typical ADLs, lack of motor or psychological disorders, lack of drug addiction, willingness to participate, and no recent episodes of loss/grief. They were expected to attend at least three exercise sessions a week. Sixty women were chosen and divided into two groups: Pilates and control. The Pilates group participated in the exercise for eight weeks, whereas the control group did not participate in exercise. Outcomes were measured based on changes in the Oxford Happiness Inventory (OHI) and the Beck Depression Inventory (BDI) from baseline to

two months after participating in the intervention. When scoring the OHI, participants ideally would have a higher score (up to 87) which indicated very high happiness. Conversely, they would want lower scores for the BDI (<18) which is indicative of mild depression.

The study was performed over the course of eight weeks and those in the Pilates group were able to gradually increase the intensity of their exercise. While the control group did not participate in Pilates specifically, they did meet to complete the questionnaires and participated in a cancer and cardiovascular disease prevention program (Ravari et al., 2021). Data was analyzed using chi-square to compare demographics between the groups and a mixed ANOVA compared the mean scores of happiness and depression between the two groups. They also used chi-square to compare the depression levels between the two groups.

At baseline, there was no significant difference between the two groups regarding depression and happiness scores. After the study, there was a significant increase in the OHI score for those in the Pilates group compared to the control ($p<0.05$) and a significant decrease in the BDI noted as well. This indicated that those who participated in Pilates demonstrated overall improvements in their happiness and ability to manage depressive symptoms. Interestingly, this study did not have any participants in the intervention group drop and all women were happy to participate regularly in the Pilates program. As noted in previous studies, adherence has been a limiting factor, and it appears for this study, this was not the case, which may have also had a positive impact on the findings. Ravari et al. (2021) demonstrated that depression and happiness of elderly women can be altered by encouraging participation in group exercise. Fortunately, the participants in this study did not have to pay for the for the exercise classes, therefore the likelihood of attending increased. This is not necessarily realistic for the general population

because exercise classes, such as Pilates, can be costly and may be difficult to recommend for all patients that are experiencing depressive symptoms. Also, this study included only females, and most were housewives with less restrictive schedules, therefore it is difficult to assume the results would be consistent amongst all genders and demographics. It does however support the idea that exercise and physical activity can have positive effects on depressed individuals and can be a suitable recommendation.

Effectiveness of Exercise versus Pharmacological Management for Depression

When determining an appropriate treatment plan for a patient with depression, it is important to consider multiple approaches. By addressing the growing issues with depression with different modalities, it may reduce potential onset of concomitant etiologies, such as cardiovascular disease, obesity, and diabetes. The use of antidepressants should be considered in those that are physically "unhealthy," although the side effects can include increased weight gain, decreased sexual function, decreased heart rate variability, increased weight circumference, and increased triglycerides (Verhoeven et al., 2023). Unfortunately, this could result in a further increased risk of developing metabolic syndrome, cardiovascular disease, and diabetes. Because of this, many providers have tried to encourage patients to participate in an exercise of interest, rather than treat pharmacologically. Recognizing these concerns, Verhoeven et al. (2023) compared running therapy to antidepressants (escitalopram and sertraline) in the management of depression and anxiety. Because of depression and anxiety's role in one's mental and physical health, they aimed to determine if running could be as effective as antidepressants, or at the very least determine the physiological response to running and how this can impact patient outcomes, and reduce the onset of additional comorbidities.

Verhoeven et al. (2023) revealed the benefits of utilizing exercise compared to antidepressants. Unlike most RCTs, this was a partial randomization, and they allowed some participants to choose their preferred group as this would likely improve compliance with the study. After interviewing 240 individuals, 141 were included in the study. The 16-week MOod Treatment had two arms: there were 96 in the intention-to-treat group receiving running therapy, and 45 in the intention-to-treat group receiving anti-depressants (Verhoeven et al., 2023). To be included in the trial, subjects had to have current depressive disorder or anxiety disorder, as determined by DSM-IV criteria. Exclusion criteria included the use of anti-depressants within last two weeks, current use of other psychotropic medications (except benzodiazepines with stable usage), regular exercise more than once a week, primary severe clinically diagnosed psychiatric diagnosis (other than depression or anxiety), evidence of suicidal risk, somatic contraindications to running or antidepressants (heart issues), and being pregnant (Verhoeven et al., 2023).

Subjects in the antidepressant group were given 10 mg Escitalopram initially, and if found to be ineffective they could increase the dose to 20 mg. Individuals met with psychiatry five times during the study to determine the effectiveness of current dosing. If escitalopram was found to be ineffective at its' maximum dose, then Sertraline was added starting at 50 mg and increasing to the maximum dose of 150 mg if needed. Participants in the running group were assigned two to three 45-minute outdoor running sessions that were supervised, with a goal of 70-85% heart rate reserve, based on the individual. To assess outcomes, all participants were given the Composite International Diagnostic Interview (CIDI), and severity of anxiety and depression were measured with Beck Anxiety Index (BAI) and Inventory of Depression

Symptomatology-self report (IDS-SR) at baseline and again at week 16 (Verhoeven et al., 2023). They assessed remission and response to treatment regarding management of depression and anxiety. Additionally, they also assessed physical health outcomes including weight, lung function, and hand grip strength.

A baseline was established for each participant based on their condition at the beginning of the study using ANOVA or chi-square. This helped to establish a baseline between the groups to determine similarities. As per the intention-to-treat principle, all participants were assessed regardless of if they completed the study. Change scores comparing week 16 to week 0 of both mental and physical outcomes were compared with ANCOVA analyses and within group differences were calculated with paired t-tests (Verhoeven et al., 2023).

Results revealed that at baseline, both groups were comparable, except that the IDS-SR score was higher in the antidepressant group. Remission rates were not significantly different between groups (antidepressants: 44.8%, running therapy: 43.3%). There was no significant difference between intervention groups when assessing drop-out rate, however adherence was significantly different between groups, with 82.2% of participants in the antidepressant group adhering, compared to 52.1% of participants in the running group ($p<.001$). When looking at mental health response, remission rates did not differ significantly between groups ($p=0.88$), nor did the decline in IDS-SR score ($p=0.33$) (Verhoeven et al., 2023). However, analyses of both groups demonstrated significant improvements comparing pre-post intervention. Regarding physical health, as anticipated, there was a significant difference between the two groups. Weight ($p=0.001$), waist circumference ($p<0.011$), blood pressure (systolic $=0.011$, diastolic $p=0.002$), and heart rate variability ($p=0.006$) were significantly improved in the running therapy group.

The antidepressant group demonstrated an increase in weight and decrease in heart rate variability (Verhoeven et al., 2023).

This study demonstrated significant improvements with physical health in those that participated in the running program. Although mental health outcomes did not significantly differ between the interventions, it revealed that patient remission rate and self-reported depression and anxiety levels are similar whether a patient was given antidepressants or prescribed a running program. This further supports the importance of incorporating exercise. Interestingly, allowing subjects to choose their group versus being randomized did not impact outcomes, and as expected, adherence was considerably different between groups. This is valuable to know as a provider, as this exhibits the difficulty of follow through with patients and recognizing that an emphasis on adherence is important.

Considering the number of comorbidities that often accompany depression and the number physical health improvements that running provided compared to antidepressants, it may be worth considering exercise as a first-line treatment rather than going directly to antidepressants. With that however, the exercise would have to be tailored to the patient, and this study specifically addressed running, which may not be suitable for all patients. The study also lacked complete randomization, which may have impacted the outcomes. Although it may have ultimately improved adherence, it may not validate the results completely.

In addition to multiple comorbidities that impact at a physiological level, depression in older individuals is further characterized by various complexities, including frequent somatic complaints, frailty, neurological brain changes, changes in social status and loss of loved ones, family, or friends. Depression is the most frequent psychiatric disorder among the older

population, with up to 8%-16% of community dwelling individuals presenting with depressive symptoms (Hidalgo, 2021).

As determined in previous studies, when considering treatment strategies for management of depressive symptoms in the older population, often antidepressants are recommended. However, as an individual ages, the side effects of antidepressants can be more pronounced and often undesirable. To reduce the risk of adverse side effects, clinicians can consider encouragement of physical activity. Not only will this address physical limitations and improve cardiovascular health, but it can also serve as a distraction from negative thoughts and may help in the acquisition of a new skill (Hidalgo, 2021). There are some studies that also suggest that physical activity can help with growth of new neurons, in addition to the release of proteins that can enhance the survival of current neurons (Hidalgo, 2021). With this knowledge and recognition of the adverse effects of antidepressants, this study was developed to compare the effectiveness of physical exercise to use of antidepressants as a means of reducing depressive symptoms in those aged 65 years and older over a 6-month period (Hidalgo, 2021).

The study included individuals with clinically significant depression, which was defined as anyone scoring at least 10 points on the Montgomery-Asberg Depression Rating Scale (MADRS). Exclusion criteria included: physical or mental limitation that prevented participation in the study, contraindications for physical exercise, severe depressive disorder, or use of anti-depressant drugs (Hidalgo, 2021). Physical aptitude was measured by assessing resting heart rate and submaximal heart rate on an indoor exercise bike (70-85% of maximum heart rate for six minutes) (Hidalgo, 2021). Participants were then randomly allocated into either the physical activity (PA) or antidepressant treatment (AT) group. After generation of the two groups, a total

of 313 were included in the initial study (158 in the PA group, and 155 in the AT group), however after many participants withdrew, there were 66 patients in the PA group, and 93 in the AT group that provided follow-up. (Hidalgo, 2021).

Those that were in the PA group were provided with a supervised program that consisted of two 1-hour sessions per week, over the course of six months, with 10-12 people per session. Sessions included a variety of exercise modalities, including aerobic, strengthening, balance, and flexibility. The focus was to increase participants' exercise tolerance to reach a point at which they could perform at least 30 minutes of moderate intensity exercise a day. The AT group was prescribed antidepressants provided by their practitioner based on individual needs and appropriateness of a certain medication (Hidalgo, 2021).

Evaluations were done at baseline, and again at one, three, and six months. The goal of this study was a positive result which was defined as a MADRS score <10 points, which would indicate absence of a depressive disorder (Hidalgo, 2021). In addition to the main objective, other variables were also assessed, including BMI, any adverse events, level of physical activity, history of depressive disorder or use of antidepressants, smoking, alcohol consumption, sociodemographic, and overall satisfaction of the study. Another component that was monitored was attendance for the PA group, and medication adherence for the AT group.

Statistical analysis included an initial study of homogeneity of the participant characteristics and the confounding variables in both groups (Hidalgo, 2021). The goal of a score of <10 on the MADRS was compared using chi-square and T-tests were also used to determine a trend in self-perceived health status of the individuals. As with most studies, an analysis was performed on the intention-to-treat basis which included all 313 participants, with further

analysis performed specifically assessing the results of those that completed follow ups (Hidalgo, 2021).

The researchers analyzed the 313 individuals (158: PA (MADRS: 15.1) 155: AT (MADRS: 15.9)), with mean ages of 72.2 and 72.8 respectively. The PA group had an average attendance of 18.9 sessions over the six months. The AT group had a wide distribution of medications utilized, including sertraline (26.5%), trazadone (14.8%), paroxetine (12.9%), mirtazapine (9.0%), escitalopram (8.4%), venlafaxine (7.7%), duloxetine (5.8%), and other (14.8%). For this group, there was 78% compliance at one month.

Overall, the intention to treat analysis demonstrated that over the course of 6 months, the incidence of a MADRS score <10 was significantly different between the PA group and the AT group, however when assessing per-protocol analysis, there was not a significant difference (Hidalgo, 2021). Participants in both groups noted a positive perception of their health status, with significantly increased scores from baseline ($p<0.01$). Unfortunately, as with many other studies, the withdrawal from the PA group was greater than the AT group. However, there were more adverse effects reported in the AT group, including drowsiness, dizziness, and epigastric pain. Overall satisfaction was increased in both groups. When the MADRS score was the dependent variable, the PA group demonstrated a mean improvement of 4.04 points, and the AT group 5.8 points respectively with a difference of 1.76 points (95% CI, 0.39-3.13) between the groups ($p<0.05$) (Hidalgo, 2021).

Overall, the study demonstrated that both groups responded to the interventions provided with a decrease in depressive symptomology. Although the intention-to-treat analysis demonstrated significant difference after three and six months, this does underestimate the

benefits of a treatment modality when attendance is poor, which occurred in this study. When assessing the results of only those completing the study, there was not a significant difference between groups, and notably, the adverse effects were greater in the AT group.

As previously stated, the impact of physical activity on multiple systems has been greatly supported. Although this study addressed depression specifically and did not find physical activity to be superior to medication regarding reduced MADRS scores, it would be unreasonable to ignore the positive effects it has on one's health and wellbeing. Unfortunately, there were several limitations to this study. As with previous studies, adherence was a significant issue with participation, despite offering a variety of exercise modalities. It is also difficult to ascertain if the medications prescribed were equally efficient or if the choice of anti-depressant may have influenced the results in that group. Though physical exercise was the focus of this study, it may be reasonable to consider other age-appropriate activities such as crafting, arts, and music as other modalities, with potential improvement in adherences. Overall, both groups demonstrated a positive outcome, and it would be practical to utilize both treatments in combination, recognizing that it may possibly allow for lower dosed prescriptions of antidepressants to reduce risks of adverse effects. When considering the significant impact depression has on the aging population, it is vital to find a safe balance between physical and pharmacological management to improve quality of life and maintain independence.

Benefits of Combined Therapy for Management of Depression

Individually, antidepressants or exercise are viable options as monotherapy for depression. However, to investigate whether a combination of antidepressants and exercise would be effective, Imboden et al. (2020) conducted a double-blind, randomized controlled study

to determine the benefits of including aerobic exercise (AE) as an add-on to inpatient treatment of depression. To do so, they compared aerobic exercise to stretching.

Patients included in the study were between 18-60 years old with major depression, and a Hamilton Depression Rating Scale 17 score greater than 16. Patients were not eligible to participate if they were pregnant, unable to exercise, displayed acute suicidal ideation, had a BMI >35, had comorbid substance dependency or comorbid major psychiatric disorder, or had regular participation in vigorous exercise. Sixty-four patients were screened to determine if they were eligible to participate. However, after several participants withdrew for various reasons, the intention to treat analysis included 42 subjects. They were assigned to either an aerobic exercise group or a basic stretching group and participated in the activity three times a week over the course of six weeks. Baseline measurements included the HDRS-17 and BDI, which were repeated at week one and week two. Participants followed up 6 months after discharge. The outcome assessors and treating providers were blinded (Imboden et al., 2020). Results were analyzed with repeated measures analysis of variance (rANOVAs) with a between subject factor group, and within subject factor group. To look more specifically at changes in outcomes over a series of weeks, further rANOVAs were done with the main factor of time (Imboden et al., 2020).

All individuals in the study received pharmacological treatment, individual and group-based psychotherapy, and other therapies (art, music, etc). Pharmacological treatment was limited to SSRI or SNRI only. Those in the aerobic exercise groups rode on indoor bikes three times a week, at target HR 60-75% of max HR. The active control group attended a specific

stretching class that was designed for the study, with instruction to avoid over-exertion and breathlessness. There was an emphasis on avoiding an overlap in the groups.

After six weeks, symptom severity decreased significantly over the treatment period in both groups (HDRS-17: $p<0.001$, BDI: $p< 0.001$). The within-subjects single measurement timepoints revealed significant decreased HDRS-17 scores from baseline to week one, and week two to post-intervention ($p<0.05$), the same for the active control group. For BDI score, the intervention group demonstrated a decrease in score from baseline to post-intervention, compared to the active control that had improvement starting at week 1, throughout the entire trial (Imboden et al., 2020). Improvement in depression symptoms, mental toughness, cognitive responses, and BMI were still observed at the six month follow up.

Overall, there were benefits of aerobic exercise and active control/stretching. This study did not have a control group that did not have an active intervention; therefore, it is assumed that any physical activity can have significant antidepressant effects on inpatients. With that knowledge, it is appropriate to deduce that use of physical activity, in combination with treatment as usual (i.e., pharmacological), can have positive effects on depression.

In addition to stretching, there are many other exercise modalities that can augment antidepressant therapy in the management of depression. Moraes et al., (2020) further investigated the effectiveness of adding either aerobic exercise, strength training, or low-intensity training to a group of subjects that were currently taking a prescribed antidepressant. They recruited individuals older than 60 years old that met criteria as established according to the DSM-IV and had been sedentary for the last three months. The participants had to be on one or more antidepressants and the dosage set at a therapeutic range. Patients were excluded from

the study if they had any significant co-morbidity such as a HAM-D score >18, psychiatric disorder, recent cerebrovascular infarction, poor mobility, or balance disorders (Moraes et al., 2020). The data was collected over a 12-week time span.

Participants enrolled in the study were randomly placed into one of three groups: aerobic therapy (AT), strength training (ST), or control group. The aerobic group consisted of nine individuals that participated in aerobic exercise two times a week utilizing bikes and treadmills. The strength training group included nine participants that also participated in 30 minutes of moderate-intensity exercise twice a week that included major muscle groups: chest press, low row, leg extension, leg curl. The last group also had nine individuals that participated in low-intensity exercise for 30 minutes which incorporated level ambulation on the treadmill or cycling without resistance (Moraes et al., 2020).

Like other studies, Moraes et al. (2020) utilized the BDI and HAM-D as the primary tools to measure outcomes over the course of the 12 weeks. Remission was defined as a HAM-D <7 and BDI <10, with a positive response to treatment noted with a 50% reduction in scores. At baseline, there was no significant difference between the groups. At the conclusion, there was not a significant difference between the AT and ST groups ($p=0.991$), and remission was higher in both groups when compared to the control group. When assessing post-intervention scores of the HAM-D there was a significant difference ($p=0.005$) between aerobic therapy and control, as well as between strength training and control ($p=0.007$), with those in the strength group demonstrating more improvements overall. The BDI however did not demonstrate a significant difference despite a reduction in scores overall between the three groups ($p=0.104$). Unlike other

studies, attendance was monitored more strictly, and this study had at least a 75% attendance rate (Moreas et al., 2020).

The findings in this study aligned with results in previous studies that indicate the effectiveness of exercise on management of depression. Unique to this study however was the fact that participants were taking their antidepressant of choice**,** and the adherence was better in this study compared to most. This study also demonstrated two other considerations, one being that the more intense exercise yielded higher reduction of symptoms. Those in the aerobic or strength training group progressively increased the intensity of their programs, unlike the control group that did not have any change in intensity. The other interesting avenue that was addressed was looking at number needed to treat (NNT). They determined with this study that NNT was 1.8 for the aerobic and strength training groups, meaning for roughly every 2 patients treated, one individual would reach remission compared to the control group (Moraes et al., 2020).

Consistent with other studies, limitations include smaller sample sizes, despite significant results. Unlike other studies however, the exercise adherence was better. Another limiting factor was that individuals were on different antidepressants which makes it difficult to generalize this to a whole population. Because medications work on different receptors and yield different side effect profiles, the efficacy can vary from person to person. That, in combination with various exercise modalities would yield different outcomes. Also, this study excluded severe depression, therefore the results could only be generalized to those with mild depression. Regardless, the concept that exercise in combination with antidepressants is effective at management of depression is demonstrated.

Discussion

For decades, providers have relied on pharmacological measures to manage patients with depressive symptoms. While medication therapy remains effective, the latest research, as of 2020, continues to support that exercise may be an equivocal alternative (Bai et al., 2020; Boucher et al., 2023; Hildago, 2021; Imboden et al., 2020; Moraes et al., 2020; Ravari et al., 2021; Verhoeven, 2023). As determined in the studies reviewed, exercise has been shown to provide not only physiological benefits, but also psychological. Researchers found improvement in baseline scores utilizing a multitude of depression scales. Of note, most studies used the Montgomery-Asberg Depression Rating Scale (MADRS) and the Beck Depression Inventory (BDI). The MADRS stratifies the severity of the subjects' depression, and the highly sensitive assessment is comprised of nine subject-reported questions, and one observer-reported question for a score between 0-60, signifying the severity of depressive symptoms (Ashari, 2022). The other scale, BDI, is a 21-item self-reported rating scale that measures the individual's attitude and symptoms of depression. The BDI scoring is 0-69 and raters can interpret the results to determine the severity and is highly sensitive in identifying those with depression (Ashari, 2022). While these are both valid scoring scales, there were others that were also used throughout the studies, which is notable when assessing outcomes. Because each depression scale provides its own scoring system and is generally self-reporting, there is possibility for inconsistencies and variability in subject reporting. Although this was a limitation when comparing the studies, there was consistency regarding improvements in scores from baseline throughout most of the studies for those that participated in exercise regardless of the scale used.

A significant consideration that must be addressed is the mode of exercise chosen. Though the studies demonstrated that running, Pilates, stretching, moderate-high intensity

training, strengthening, balance, and body awareness training yield positive outcomes, each modality requires different variables that may impact an individual (Bai et al., 2020; Boucher et al., 2023; Hidalgo, 2021; Imboden et al., 2020; Moraes et al., 2020; Ravari et al., 2021; Verhoeven, 2023).When choosing an exercise modality for a patient, their functional capacity, financial resources, accessibility/transportation, and motivation must be considered. Verhoeven et al. (2023) found running to yield similar results to antidepressants. This is a considerably different modality when comparing Ravari et al. (2021) that revealed Pilates to be effective at reducing depression symptoms. Both are considered exercise modalities; however, they require entirely different physiological capacity. Ultimately, this would need to be considered for all other studies as well, which makes it difficult to ascertain which modality is most effective. This is another variable that may have impacted outcomes (i.e., compliance for running compared to Pilates). As a provider it is advantageous to know that a variety of options are available that have been proven to reduce depressive symptoms in some capacity.

One interesting limitation that was more notably consistent throughout the studies was that of adherence/compliance. In most of the exercise studies, compliance or follow-through was frequently lacking. Boucher et al. (2023) had requested 80 minutes of exercises per week from the volunteer subjects, and despite the easy accessibility of exercising at home, only an average of 46 minutes were completed by the end of 12 weeks. Similarly, those studied by Hidalgo et al. (2021) only completed an average of 18.9 of the 48 exercise sessions that were requested, and of those that had participated in the study performed by Verhoeven et al. (2023), only 52% of the runners complied. Conversely, subjects that were in a group that provided pharmacological treatment, the adherence was substantially better. In that same running study, 82% compliance

rate was determined for those taking medications. Likewise, elderly patients were found to be more consistent with taking an antidepressant than attending a physical activity session (Hidalgo et al., 2021). Interestingly, the one study that did not have concerns with adherence consisted of housewives that attended Pilates classes three times a week. Within this study, 100% of the participants utilized the opportunity to socialize and exercise, which resulted in no drop in subjects (Ravari et al., 2021). Unfortunately, this study is an anomaly compared to the others because Pilates as a modality may not be the most accessible depending on location, financial accessibility, and transportation.

Furthermore, because depression affects almost 300 million individuals in the world, it is alarming to witness the growing number of adolescents that contributes to this statistic. Depressive disorders are among the more common diagnoses in this population and 3% of youth are affected at any time (Walter et al., 2023). Regardless of the root cause of the depressive symptoms, it is becoming an issue that can lead into chronic major depression with significant consequences (substance abuse, suicide risk, chronic pain, etc). With this knowledge, as providers it would be a disservice to younger patients to ignore symptoms and rely solely on one modality for management. The studies provided demonstrate the benefits of discussing exercise as complimentary treatments to manage symptoms for this vulnerable demographic. Both Bai et al. (2020) and Serrander et al. (2021) found benefits of exercise in the adolescent population as another strategy for improving depressive symptoms. They both determined that higher intensity was more beneficial regarding symptom reduction overall, and furthermore, Bai et al. had determined that the reaction time and responsiveness rate improved with increased intensity. This further supports that exercise not only assists with depressive symptoms, but also improves

focus and mental stamina. Serrander et al. (2021) delved further into self-esteem, mental and physical vitality, and structure, which is meaningful considering these are areas of concern in which many adolescents are struggling. The findings support that by emphasizing consistent movement early on, major depressive symptoms may be less likely to occur later in life.

Lastly, while the emphasis of this literature review is to present the benefits of exercise for management of depression, it would be unreasonable to ignore that pharmacological management can still be an appropriate strategy. When compared to exercise, many researchers determined that while *both* exercise and antidepressants were beneficial compared to a control, exercise was not necessarily superior to antidepressants (Verhoeven et al., 2023, Hidalgo, 2021). As previously discussed, the adherence rate with antidepressants was significantly better compared to any exercise protocol prescribed. Due to the various SSRIs and SNRIs available, escitalopram was chosen secondary to its low side effect profile with mild/transient adverse reactions and relatively low toxicity (Mandal et al., 2021; Verhoeven et al., 2023; Wang et al., 2021). When compared to citalopram, *in vitro* escitalopram had a two-time greater potency for serotonin reuptake, which is necessary to consider when choosing between the two medications. Unfortunately, it would be difficult to assess effectiveness of all SSRI/SNRIs in one literature review. However, most medications in these two classes would yield the same findings when compared to exercise or a control group regarding adherence and outcomes. It is also necessary to consider the pharmacological route for those that may be deemed inappropriate to participate in a moderate-high intensity program secondary to other co-morbidities. Additionally, as providers, part of the responsibility of caring for patients is to discuss feasibility of treatment

modalities and partake in frank conversations regarding compliance. This would assist in determining which strategy would provide long-term benefits and follow-through.

Although exercise and antidepressants have both been shown to be beneficial as monotherapy, Moreas et al. (2021) and Imoben (2020), found that the combination of the two has the potential to yield positive results for both symptom reduction and adherence. Subjects in their studies utilized antidepressants of choice in addition to an exercise protocol and both studies demonstrated encouraging findings. Notably, participants were satisfied with being able to continue their preferred medication. Although this allowed for more variability regarding measuring the effects of a specific medication in conjunction with exercise, it does emphasize that regardless of a patient's preferred antidepressant, there would be benefits of adding exercise to their regimen to yield optimal outcomes on both physiological and psychological levels.

Conclusion

Based on the research provided, it is supported that there are alternative strategies for management of depression in patients across the age spectrum. Exercise is shown to be an equivocal treatment strategy if patients adhere to the treatment plan as recommended. As clinicians prescribe exercise as either monotherapy or in addition to antidepressants, they must also be prepared for potential negative feedback from patients. It is important to support and motivate patients to trust the overall benefits and encourage consistency. If they are not responding, then it would be appropriate to modify the plan. Modifications could include incorporating an SSRI or a dosage adjustment of a current medication, however continuing to encourage activity should be the forefront of treatment. As previously highlighted, there are over 260 million people affected by depression, and as a provider the goal is to assist with

management of symptoms to improve quality of life. Research supports that this can successfully be achieved with exercise and physical activity, with and without the use of medications.

Application to Clinical Practice

As providers evaluate patients and understand the resources available to them, they can now recommend other options that offer benefits to the patient as a 'whole-body' approach. While medications have been a mainstay in the management of major depressive disorder, they are not without their side effects. As previously mentioned, they do come with the risk of weight gain, sexual dysfunction, suicidal ideation, insomnia, and fatigue. In patients that are already experiencing the negative effects of depression, the risk may not be worth it.

Comparatively, while exercise is not without the possible negative side effects as discussed, including muscle strain or overuse, there is decreased likelihood of these contributing to worsening depression. Considering that exercise not only provides psychological improvements, as supported in this review, the physiological benefits are significantly more than antidepressants can offer. This demonstrates the adage "kill two birds with one stone".

When the next patient arrives for an evaluation regarding concerns of depression, it would be an excellent opportunity to discuss their current activity level, address their preferred exercise, and emphasize the benefits of engaging in either the preferred activity more consistently, or participate in a new one. There may be initial resistance to the idea, however when considering the results from recent research, it would be a disservice to patients to overlook the option, especially when considering the psychological AND physiological benefits that can be obtained.

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