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The Protective Effects of Exercise on Depression: Analysis from the NHLBI CARDIA
Study

by

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Thesis submitted to the Faculty of the
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ABSTRACT

Title of Thesis: The Protective Effects of Exercise on Depression: Analysis from the NHLBI CARDIA Study

Nicholas R. Moorehead, Master of Science, 2020

Thesis directed by: David S. Krantz, Ph.D., Professor of Medical and Clinical Psychology, Department of Medical and Clinical Psychology

Introduction: Previous studies have established that physical activity and exercise levels as well as depression change across the lifespan, and exercise has been used as a treatment intervention for depression. However, little is known about developmental changes in physical activity and depression from young adulthood to middle age.

Objectives: To determine the cross-sectional and longitudinal relation between usual physical activity levels and depression among young adults, and whether developmental increases in physical activity are associated with reduced levels of depression across a 25-year period.

Methods: This was a reanalysis of 25-year follow-up data from the NHLBI CARDIA study, a prospective cohort study of a diverse sample of young adults age 18-30 (N=5113; mean age= 24.76 SD = 3.628; 45% male) who were tested between 1985 and 2010. Participants reported intensity and frequency of usual physical activity (PA) at 5-year intervals using a validated CARDIA Physical Activity Questionnaire. Depression

was also measured at each time point using the Center for Epidemiological Studies Depression Scale (CES-D). Analyses examined associations between overall PA and CES-D at each time point, as well as relationships between PA and CES-D changes over a 25-year time period using multiple linear regression. Relationships between PA and CES-D changes over time were determined using multiple regression using the slope of PA over time and the slope of CES-D over time. All analyses controlled for age, sex, smoking habits, BMI, and baseline levels of depression and/or physical activity where appropriate.

Results: Consistent with previous studies, both PA and depression were relatively stable, but declined over time with an increasing negative correlation between PA and depression, which became increasingly statistically significant at each 5-year time point between Year 5 and Year 25 (r 's between 0.057 to -0.091, all p 's < 0.001). There was a small but significant relationship between the rate of change in PA over time and the rate of change in CES-D over time (partial r = -0.068, p < 0.001). For each 1 standard deviation increase in PA Slope, there was a predicted decrease of 0.07 standard deviations in CES-D Slope, when controlling for all other variables in the model.

Conclusion: Physical activity is consistently associated with reduced levels of depression at different points in the lifespan, and appears to have a modest protective effect against depression over a 25-year time period. These findings suggest not only that physical activity earlier in life predicts subsequent depression, but that both physical activity and depression demonstrate plasticity and variability across the lifespan and also are negatively related to one another.

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CHAPTER 1: Introduction to Physical Activity and Depression

HEALTH, EXERCISE, AND FITNESS

Considerable research indicates that physical fitness and regular exercise are major factors affecting both physical and mental health (Harvey et al., 2010; Lee et al., 2011; Strohle, 2009), and may lead to a longer life and increased well-being (Myers, 2003). Research also indicates that physical exercise may improve cardiovascular health and reduce cardiovascular risk factors. While both the terms physical activity and physical exercise are used in current research, the terms are often used interchangeably. A lifestyle without physical activity and/or a sedentary living style also is one of five major modifiable risk factors for coronary heart disease, together with other factors such as smoking, obesity, elevated blood lipids, and increased blood pressure (Myers, 2003). Thus, cardiorespiratory fitness as a major indicator in health (Lee et al., 2011).

In addition to the consequences of exercise and fitness for physical health outcomes, exercise is also associated with better mental health and well-being Harvey, Hotopf, & Overland, 2010; Lee et al., 2011; Strohle, 2009). In particular, studies indicate that exercise can be used as an intervention to treat major depressive disorder (Blumenthal, Smith, & Hoffman, 2012; Blumenthal et al., 2007; Schuch et al., 2016), and that better fitness has been associated with decreased levels of depression in a several cross-sectional studies (Deslandes et al., 2009; Mikkelsen et al., 2017; Strohle, 2009).

The purpose of this proposed study is to determine whether fitness and/or exercise has a protective effect against depression across the lifespan. The study Introduction will include a review of the differences between fitness and exercise, the physical and mental

health benefits of each. Next, the prevalence of depression across the lifespan will be reviewed, followed by a review of what is known about how fitness and exercise practices change across the lifespan, and how exercise and fitness are related to depression across the lifespan.

Short- and Long-term Physiological Effects of Aerobic Exercise

Although evidence indicates that exercising leads to a healthy lifestyle (Adamu, Sani, & Abdu, 2006; Penedo & Dahn, 2005), and exercise can lead to increased physical fitness, exercising and fitness are not identical to one another. Physical exercise refers to bodily movement by skeletal muscle which requires the consumption of energy mainly designed to improve or maintain a component of fitness (Martínez-Vizcaíno & Sánchez-López, 2008). Physical fitness can be interpreted as a measure of the capacity to perform physical exercise (Martínez-Vizcaíno & Sánchez-López, 2008). Furthermore, repeated bouts of high-intensity exercise have been shown to improve aerobic response. In addition, regular exercise leads to increased fitness as measured by faster recovery rates from exercise, increased aerobic capacity, and greater strength/capabilities during exercise (Tomlin & Wenger, 2012).

Not all forms of exercise are the same, and doing different forms may hold different benefits (Gunn et al., 2006; Mekary et al., 2014). Two broad forms of exercise will be described here, aerobic exercise and strength-training, also known as resistance training. Aerobic exercise includes exercises such as running, swimming, and cycling and is typically seen as endurance-based. It is known aerobic exercise improves abilities in peak oxygen consumption, improving more with increasing intensity (Helgerud et al., 2007). Furthermore, aerobic training has improved abilities in autonomic control, vagal

control on the heart and sympathetic control on peripheral vessels, and reductions in basal heart rate and blood pressure (Radelli et al., 1996). Both aerobic exercise and strength training are associated with weight loss (Mekary et al., 2014). However, current literature shows it must be done consistently for a long period of time (6-12 months) for modest effects (Thorogood et al., 2011). Strength or resistance training is described as more power-based, involving short bursts of energy rather than longer smaller bursts of energy seen in aerobic exercise. Strength exercises are typically seen as resistance-based or done with weight-training. Strength training's benefits are not limited to healthy populations. It is also known to be beneficial in heart failure patients improving peak oxygen consumption, increasing autonomic control, reducing basal heart rate and blood pressure, and helping with weight loss, but not to the same extent or benefit of aerobic exercise (Gunn et al., 2006). Strength training is better known for its sustainment of muscle mass, muscle strength, and muscle ability, even in old age (Beavers, et al., 2017). Strength training was also associated with a greater retention of lean muscle mass if done for at least 20 minutes a day in a population followed for 12 years (Mekary et al., 2014). Both forms of exercise are effective at keeping individuals healthy, and often it is recommended to do both forms of exercise to receive the most health benefits (Kaushal et al., 2019; Villareal et al., 2017). Ideally, future studies would be able to differentiate between the two forms of exercise to better define their separate or converging benefits on health. However, for the purposes of this study, both forms of exercise will be considered plainly as physical exercise as the pathway through which they improve fitness is the same. Furthermore, as will be explained further in the methods section, data

collection parameters used in this study do not differentiate between strength training exercises and aerobic exercises.

Both forms of exercise are able to increase fitness by causing an increase in heart rate for an extended period of time while recruiting more muscle fibers pushing the body to a new metabolic limit. Doing so regularly will result in the body and utilized muscles recovering and improving over time, resulting in improvements in the exercises done. Doing so also results in many of the aforementioned physical health benefits which altogether form better fitness (Gunn et al., 2006; Helgerud et al., 2007; Mekary et al., 2014).

Physical health benefits of exercise

Regular exercise improves cardiovascular health and reduces cardiovascular risk factors, improves muscular and cardiorespiratory fitness, improve bone/functional health, reduce the risk of hypertension, coronary heart disease, stroke, diabetes, various types of cancer, reduce risk of falls/ fractures, and reduce chance of obesity/ help with maintaining a healthy weight (Alford, 2010; Kokkinos, 2012; Mora et al., 2007; World Health Organization, 2018).

While the precise mechanisms through which physical activity/ exercise is able to improve or prevent various medical conditions remains unclear, it is clear there is strong evidence towards a causal relationship with numerous health benefits (Kokkinos, 2012; Mora et al., 2007).

Relationship Between Exercise and Fitness

Because of the causal relation of exercise improving fitness and greater fitness allowing greater capacity to exercise, there is the general belief that all individuals who

exercise are fit and all fit individuals exercise. However, multiple factors affect the impact of exercise on physical fitness.

With regard to the effects of regular exercise on physical fitness, other factors (e.g., genetics, diet, age, current conditions such as illnesses, and recovery tactics such as getting appropriate amounts of rest and not exercising too often) affect the ability of regular exercise to increase fitness (Zadro et al., 2017). With regard to genetic factors, certain individuals are predisposed to having a greater or lesser response to physical exercise. That is, certain people will increase in fitness after exercise more quickly than others (Zadro et al., 2017). Furthermore, twin studies have shown there are large heritable effects on muscular endurance and strength, meaning some individuals could retain higher levels of fitness with less required exercise (Costa et al., 2012). Therefore, it is possible that an individual could engage in physical exercise every day and be less fit than an individual that exercises more infrequently (Costa et al., 2012; Zadro et al., 2017).

With regards to factors that are more controllable than genetics, such as post-exercise recovery, modifications can lead to more improvements in fitness. Post-exercise recovery includes factors such as diet, stress level, and sleep where in a good diet, lack of chronic stress, and good quality sleep improve fitness faster while a bad diet, high stress, or low amounts of sleep may result in fewer fitness gains (Hoffman et al., 2009). For example, to improve muscle building following strength-based exercise it is recommended to consume more protein while improvements from aerobic exercise are likely to improve from a mix of proteins and carbohydrates (Hoffman et al., 2009). Sleep may be even more important. Good quality sleep, that is sleep that feels restful and

restorative, is associated with more fitness gains while low quality or low amounts of sleep are associated with a reduction in fitness even with controlled diet and exercise plans (Guillermo, Gal, & Mair, 2006).

Finally, and of great interest in this study is how age may affect fitness gains from exercise. Sarcopenia, the decline of skeletal muscle tissue with increased age, is a known issue in populations over the age 50 (Walston, 2012). As a result, it is more difficult for those above the age of 50 to see fitness gains from exercise. It often takes individuals more effort and more frequent exercise to maintain the fitness compared to their younger counterparts (Holviala et al., 2012). In older individuals due to declining metabolic processes in the body it becomes more difficult to maintain muscle and fitness (Ichimura et al., 2006). However, ability to recover from exercise also begins to decline making increasing the frequency or intensity of exercise to compensate difficult as well. The result is older individuals generally becoming less fit; though it is not inevitable as many studies have exercise programs uniquely made to help older adults maintain and improve fitness (Holviala et al., 2012; Ichimura et al., 2006). This is ideal as fitness is increasingly an important factor in older populations for improving quality of life.

Thus, while physical exercise does improve fitness, it is possible to exercise often and not necessarily be fit; it is also possible to exercise sparingly and remain fit (Costa et al., 2012; Zadro et al., 2017). Therefore, when looking into the effects fitness and exercise may have on human health, it is necessary to clarify if fitness or exercise is making the significant effects occur (Weening-Dijksterhuis, 2010).

Exercise and Fitness Throughout the Lifespan

Exercise causes increased fitness but is still limited by the genetic and environmental factors of each individual. This means as a result both exercise and fitness can change throughout the lifespan as genetic and environmental factors also change throughout the lifespan. Exercise has been shown to continue to improve health and fitness throughout life, but the level at which exercise is performed changes for each person as they age (Troiano et al., 2008). According to Troiano et al. (2008), children ages 6-11 were more likely to obtain the recommended amount of physical activity whereas only 8% of adolescents achieved this goal. The recommended amount of physical activity when this study was conducted was approximately 30 minutes of physical activity per day for at least 5 or more days out of the week. This is consistent with current CDC guidelines of about 150 minutes physical activity per week (CDC, 2020). More distressingly, the adherence of adults to this exercise recommendation, which is half that of the children's recommendation, is less than 5% (Troiano et al., 2008). Additionally, exercise habits are more likely to persist throughout the lifespan (Camhi et al., 2013). Biological factors such as sarcopenia (age-related degenerative use of skeletal muscle) result in less fitness gained through exercise as well as a decreased ability to exercise as individuals get older (Walston, 2012). Additionally, apart from biological factors that accompany aging, there are also environmental factors that affect individuals' ability to exercise. These include exercise interfering with social/family activities, having no one to exercise with, lack of facilities, being too tired, having a lack of motivation, and plainly not having enough time to do so (Justine et al., 2013). These factors seem to increase with age following adolescence into middle and older adulthood. In addition, social and cultural factors such as ethnicity, educational level, and

socioeconomic status might also affect fitness and exercise habits (Jimenez-Pavon et al., 2010; O'Donoghue et al., 2018; Ombrellaro et al., 2018; Parks, Housemann, & Brownson, 2003). These differences are likely due to a number of different variables including access to means of activity, time available, cultural norms, availability of time due to socioeconomic stability, and choice of what is being reported as “exercise” or “activity” (Stalsberg & Pedersen, 2018).

While there is some decline in exercise habits from childhood to adolescence, to adulthood, habits formed in adolescence/ early adulthood are likely to stay to relatively stable throughout life (Ortega et al., 2008; Friedman et al., 2008; Picavet et al., 2011). This decline in exercise habits is thought to correspond and account for the decline in fitness as well (Camhi et al., 2013). This means that individuals who engage in exercise early in their life more frequently are likely to continue to do so later in life as well (Camhi et al., 2013). Even though the best way to maintain exercise habits and fitness is to start at a young age and build consistent, healthy habits as individuals are likely to keep habits built early on, interventions later in life can also be effective (Daniels, Pratt, & Hayman, 2011). In addition, exercise interventions tailored to the needs and abilities of individual adults have been shown to improve cardiorespiratory, musculoskeletal, and neuromotor fitness in adults regardless of previous fitness status (Garber et al., 2011).

In summary, improved exercise leads to improved fitness consistent with genetic and environmental constraints. Exercise and fitness tend to decline slightly throughout the lifespan, that is from childhood to adulthood, but stay relatively consistent from adolescence/early adulthood onward (Camhi et al., 2013). Therefore, it is important to

build healthy habits in childhood; however, interventions to improve exercise habits in its have also been proven to be effective (Bullard et al., 2019).

MENTAL HEALTH, DEPRESSION, AND EXERCISE

Many studies demonstrate that fitness and exercise are not only beneficial to physical health, but are also associated with emotional and cognitive improvements such as including elevated moods, increased concentration, increased sense of well-being, and improvement in academic performance (Bezold et al., 2014; Deslandes et al., 2009 Garber et al., 2011). Fitness and physical exercise appear to play such a large role in academic performance, there may be long-reaching consequences in terms of academic success and socioeconomic class later on (Bezold et al., 2014). These studies demonstrate physical activity and fitness can have longitudinal effects on health and well-being both in terms of physical health, overall success in academics, and subsequently in careers.

Exercise, Depression, and Anxiety

In addition to other psychological and behavioral benefits, it has been demonstrated that that exercise may play a role in reducing the incidence of depression and anxiety disorders (Strohle, 2009; Deslandes et al., 2009; Mikkelsen et al., 2017). While individuals who are considered to be active or in good-shape can still experience anxiety and depression, evidence shows there seems to be a trend of depression and anxiety occurring with lower incidence in such populations (Strohle, 2009; Deslandes et al., 2009; Mikkelsen et al., 2017). Furthermore, fit individuals with depression and anxiety show correlations of having less severe depression and anxiety when compared to their less fit counterparts (DeBoer et al., 2012; Paluska & Schwenk, 2000; Strohle, 2009; Wipfli et al., 2011). Strohle (2009) notes despite these findings, attempting to prescribe

exercise as a treatment may prove more difficult. However, prescribing exercise is gaining more traction due to an increasing amount of studies suggesting subjects who are exercising have reduced incidence rates of depression suggesting more causation rather than just modest correlations (Harvey et al., 2018). The present study will expand on these existing data.

In clinical trials, exercise has shown to be effective at reducing symptoms of major depression in clinical populations (Blumenthal, Smith, & Hoffman, 2012; Blumenthal et al., 2007; Schuch et al., 2016). Blumenthal, Smith, and Hoffman (2012) assert that while there are many effective treatment modalities, certain treatments such as psychopharmacology and psychotherapy will not prove effective for every patient, necessitating other forms of empirically validated treatment. One such form of treatment worth exploring was using exercise to treat depression due to the evidence that fit individuals have lower rates and less severe depression was fitness. Findings currently demonstrate that regardless of exercise intensity and whether it is strength-based or aerobic-based, exercise has been effective at preventing depression (Harvey et al., 2018) and treating depression (Blumenthal, Smith, & Hoffman, 2012). Because of this finding, current studies focus more on implementing moderate aerobic exercise as a means of treatment because of the ease at which it can be completed (Blumenthal, Smith, & Hoffman, 2012). Furthermore, while studies have advanced to the point of demonstrating exercise as a treatment for depression can be as effective as psychotherapy and psychopharmacology, it is noted the treatment may not be effective for all in the same way other treatments are not cure-alls for every patient (Blumenthal, Smith, & Hoffman, 2012). Additionally, current studies are limited to focusing on exercise's effects in

preventing and treating depression rather than looking at it aiding in treatment of other forms of mental disorders (Cooney et al., 2013; Rosenbaum et al., 2014; Schuch et al, 2016).

There are numerous working theories as to why exercise/fitness may connect to depression. The endorphin hypothesis states there may be improvement in depression due to exercise due to an increase in endorphins following exercise (Craft & Perna, 2004; Josefsson, Lindwall, & Archer, 2014). The monoamine hypothesis suggests an increase in neurotransmitter availability as a result of exercise may be the reason for the connection, but results on whether or not exercise directly increases neurotransmitter availability have been mixed (Craft & Perna, 2004; Josefsson, Lindwall, & Archer, 2014). The distraction hypothesis states exercise provides a distraction from the worries and depressing thoughts, but when compared with activities such as relaxation, health education, or social contact results have varied on efficacy (Craft & Perna, 2004; Josefsson, Lindwall, & Archer, 2014). However, exercise itself may lead to health education or increased social contact which would combine activities for added efficacy. Finally, the self-efficacy hypothesis states that in completing exercise individuals feel more confident and efficacious about themselves because of the success of attaining a positive desired outcome. Doing so then increases confidence in one's abilities while reducing self-rumination, feelings of low efficacy, and negative self-evaluations. However, this theory needs more research in order to be validated (Craft & Perna, 2004; Josefsson, Lindwall, & Archer, 2014).

Exercise, stress-reduction, and improved quality of life

Additional studies have reinforced these findings, showing that regular aerobic exercise can improve quality of life and reduced distress (Awick et al, 2017; Gill et al., 2013; Schuch et al., 2015). Awick et al. (2017) demonstrated in a randomized clinical trial that in older adults (aged 65+) an increase in exercise strongly predicted an increase in quality of life and decreased negative psychological indices including those related to depression. This provides further support for the implications of exercise improving mental well-being and psychological health, demonstrating again exercise can be used for treatment and utilized as a behavioral change which can have cognitive benefits. While both Blumenthal (2012) and Awick (2017) note it can six to eight weeks for increased exercise regiments introduced in an individual's life to have an effect, it still demonstrates there are immediate benefits to be gained from engaging in physical activity at any point in the lifespan. That is to say, it is never too late to start and begin reaping benefits.

Depression Throughout the Lifespan

Major depressive disorder (MDD) is one of the most common mental disorders with the National Institute of Mental Health (NIMH) reporting in the past year 7.1% of all U.S. adults had at least one major depressive episode (NIMH, 2019). Adult females are more likely to have depression than males with rates of 8.7% and 5.3% respectively. With regards to age, adolescents being with the lowest recorded incidence of a depressive episode at 4.8%. However, at age 13 this number jumps to 8.8% and continues to rise to 18.5% by 17 years of age representing the highest incidence of depression at in any age group. Adults aged 18-25 were the second most likely to have a major depressive episode at 13.1%. This number begins to decline more in the 26-49 age bracket with an incidence

rates of depression at 7.7%. Incidences continue to decline where at age 50+ prevalence of depression is at the lowest the NIMH reports of any age demographic at 4.7%. This illustrates the decline in depression across the lifespan. Depression is more likely to occur in adolescents and young adults than in older adults. While there are some concerns this may be due to reporting issues or expression in the psychopathology of depression, results have indicated differences are not large enough to be a cause for concern (Mezuk & Kendler, 2012).

The prevalence rate of depression at a young age is unfortunate for those who have the condition because there is a high risk for recurrence of depression later in life for those who have been previously diagnosed (Burcusa & Iacono, 2007). Burcusa and Iacono (2007) found risk for recurrence is highest in the first five years following a depressive episode. Furthermore, the average person who has had MDD will have between five and nine separate depressive episodes in their lifetime. However, there remains conflicting evidence on whether or not the initial age of onset has an effect on the rates of recurrence of depression. That being said, even though the chance of depression decreases throughout the lifespan, due to high recurrence rates examining preventative and protective measures against depression would be beneficial. This is where exercise and fitness may be able to play a role.

Effects of Exercise on Mental Health Across the Lifespan:

For those that have been exercising since an early age, the question remains of how protective exercise may be with regards to the development and/or maintenance of mental disorders such as depression. In a population study of predominantly middle-age healthy adults in Norway, self-reported exercise levels have been shown to have a

predictive relationship to depression regardless of intensity (Harvey et al., 2018). Harvey et al. (2018) found data corroborating the findings of other investigators regarding using exercise as a preventative measure for depression, finding that regardless of intensity or exercise modality, consistent exercise seemed to be the key to success in terms of exercise's protective abilities. This study showed that over the course of 11 years, those who engaged in exercise at higher levels were less likely to develop depression and depressive symptoms, implicating a protective effect for exercise. However, this study is not without limitations. Even though it was a large sample, it was a controlled sample size, consisting of individuals with a mean age of 45.2, and did not go across the lifespan.

A similar study from Sweden showed corroborating evidence that in middle age and elderly women, populations that continued to report regular exercise over a lifespan appear to be protective against depression (Gudmundsson et al., 2015). Again, demonstrating strong evidence for the protective effects of exercise against depression. While this study has a collection of available data from across the lifespan, its findings correspond until to women in Sweden born before 1930, potentially limiting its generalizability. Still, the implications of the potential for protective effects of exercise on depression suggests the need for further research in this area.

Since the aforementioned studies of Harvey et al. (2018) and Gudmundsson et al. (2015) are unique and were based on Scandinavian populations, these findings need to be replicated in other populations in order to confirm the findings in other populations. The present study, based on the NHLBI CARDIA study data set, will examine the relationship between regular exercise, fitness, and depression in a young adult population

of Caucasian and African Americans in differing areas of the U.S. across the lifespan. A growing body of evidence demonstrates that different forms of physical activity are effective in reducing and preventing symptoms of depression and providing potentially protective effects from depression. That is to say they are less likely to develop depression or having less severe depression symptomology. However, research has not established the stability of the relationship between exercise and depression over the lifespan, and how it may differ between populations, regions, and countries. This study will begin to close those research gaps.

SUMMARY AND OVERVIEW

In sum, this review has described the health benefits of, and differences between, fitness and exercise, and how fitness and exercise are thought to change throughout the lifespan. In addition, studies have demonstrated that there are physical and mental health benefits of regular exercise. A growing body of evidence indicates that exercise habits and fitness are associated with depression, and that exercise appears to have an effect on depression and can be used as a form of treatment for depression and a form a preventative measure which protects against depression. Although the relationships between depression and exercise have been widely demonstrated, the relationships between exercise, fitness, and depression across the lifespan are poorly understood. Therefore, the present study will examine the time course of depression across the lifespan and its correspondence to both fitness and depression.

CHAPTER 2: The Present Study

THE PRESENT STUDY

The Cardiovascular Risk Factors in Young Adults (CARDIA) is a study “examining the development and determinants of clinical and subclinical cardiovascular disease and their risk factors” beginning with identifying these risk factors in young adulthood, which is typically two to three decades prior to the development of cardiovascular disease (NIH, 2019). CARDIA began in 1985 with follow-ups during 1987 (Year 2), 1990 (Year 5), 1992 (Year 7), 1995 (Year 10), 2000 (Year 15), 2005 (Year 20), 2010 (Year 25), and 2015 (Year 30).

Using publicly accessible data from the NHLBI CARDIA study of young adults aged 18-30 at intake, the aims of the proposed study are to: (1) determine the cross-sectional and longitudinal relationships of measured fitness and reported exercise levels to depression in youth and middle-aged individuals; (2) the relationship of stability and change of fitness and reported exercise to depression from youth to middle-age.

SPECIFIC AIMS AND HYPOTHESES

The specific aims of the study are as follows:

Specific Aim 1

- (1) To determine the stability and change of fitness, reported exercise, and depression from young adulthood to middle-age;

Hypothesis 1a.

Fitness and reported exercise will decline from young adulthood to middle age, but remain relatively stable.

Hypothesis 1b.

Depression will on average decrease from young adulthood to middle age.

Specific Aim 2

- (2) To determine the cross-sectional relationships of measured fitness and reported exercise levels to depression in youth and middle-aged individuals;

Hypothesis 2.

Depression will be related to both fitness and reported exercise levels in both young adults and middle age individuals wherein increased levels of depression will be related to lower levels of fitness and exercise.

Specific Aim 3

- (3) To determine the longitudinal relationship of fitness, reported exercise, and depression from youth to middle age.

Hypothesis 3a.

Changes in fitness from young adulthood to middle age will be related to changes in depression wherein increased levels of depression will be related to lower levels of fitness.

Hypothesis 3b.

Changes in reported exercise from young adulthood to middle age will be related to changes in depression wherein increased levels of depression will be related to lower levels of exercise.

CHAPTER 3: Methods

PRESENT STUDY

This study utilized data from the NHLBI limited access dataset from CARDIA study (NIH, 2019), a study of a diverse population of young adults age 18-30 at intake who have been followed up for 30 years between 1985 and 2015. The study was designed to “examine the factors that contribute to the development of cardiovascular disease, as well as to better understand the natural history of cardiovascular disease over the entire adult life,” (NHLBI, 2019, para. 1).

Subjects were 5115 black and white men and women age 18-30 at intake who were re-tested at follow-ups during 1987 (Year 2), 1990 (Year 5), 1992 (Year 7), 1995 (Year 10), 2000 (Year 15), 2005 (Year 20), 2010 (Year 25), and most recently 2015 (Year 30). Due to the low number of individuals identifying as Hispanic (14), which was identified as a race rather than ethnicity at baseline, they were excluded from analyses. The present analyses will utilize follow-ups at 1990 (Year 5), 1995 (Year 10), 2000 (Year 15), 2005 (Year 20), and 2010 (Year 25). Using publicly accessible data from the NHLBI CARDIA study we will examine the variables collected to look for potential protective effects against mental disorders throughout the lifespan.

The Center for Epidemiological Studies Scale (CES-D; see description below), a measure of depression (Radloff, 1977) was administered at the 5, 10, 15, 20 and 25-year follow-ups). To measure physical activity, we plan to utilize physical activity and fitness measures in the CARDIA Study including the treadmill test results, heart rate test measures, and self-report physical activity history were measured at each CARDIA examination. In order to provide further insight to potential moderating factors demographic variables including age at baseline and sex will be taken into account.

MEASURES

Demographic and Clinical Data

At baseline and every follow-up in CARDIA, medical and demographic measures were collected. Study coordinators intended to get a collection of data which may be relevant to analyses at later dates. These variables of interest to this study include anthropomorphic and sociodemographic variables such as body mass index, age, race, sex, smoking status. Medical and physiologic variables including: resting heart rate, max heart rate, and recovery heart rate.

Physical Activity Related Indices

Treadmill Test:

The treadmill test was done for individuals as a part of the CARDIA study. It is intended as a measure of current level of physical fitness with several objective measures. Participants went on the treadmill which began to increase in difficulty every 2 minutes until they cannot continue. Data collected from this measure included:

- Total duration (seconds) seconds on treadmill test
- Number of 2-minute periods completed on treadmill
- Time (seconds) to reach a HR of 130 on treadmill
- Time (seconds) to reach HR of 160 on treadmill

Each of these is considered an objective measure which can be combined to identify each participant's level of physical fitness. Each of these measures is collected via the treadmill test was done at baseline and every data collecting interval to the present day.

Physical Activity (PA) Questionnaire:

A physical activity questionnaire (Jacobs et al., 1989) was administered in CARDIA to measure recall of the type and intensity of physical activity participants engage in during everyday life. Questions pertain to the types of physical activity, perceived level of difficulty/ rigor, and the total amount in hours/ minutes at either daily or weekly intervals. Participants are asked to recall the type and intensity of physical activities participant has engaged in since the last data collection interval. Total physical activity units are derived from the physical activity history. Total hours per week of moderate, hard, very hard activity are also derived from the physical activity recall. Furthermore, Kilocalories/Kilogram/Day expended as estimated from physical activity are calculated as well.

This physical activity questionnaire measure was developed specifically for use in the CARDIA study to provide a suitable reliable, brief yet comprehensive questionnaire to measure different types of physical activity. Answers on the questionnaire are used to calculate a physical activity score based on the time, intensity, and frequency of each documented activity. The measure has been shown to be valid and reliable within the study (Jacobs et al., 1989, Camhi et. al, 2013). Jacobs et al. (1989). Specifically, test-retest reliability of the questionnaire was established and correlated with skinfolds measures, caloric intake, duration of the treadmill test, levels of high-density lipoprotein cholesterol. It also had a moderate correlation with given objective fitness measures.

Examination of data in the present data set indicated that the treadmill measures were not administered at most timepoints. For this reason, to further validate the Physical Activity Questionnaire, preliminary analyses were conducted to examine correlations between treadmill variables was compared against scores on the Physical Activity Questionnaire. We found a moderate correlations (r 's of .383, .377, .346) between total questionnaire score (Physical Activity Total) and (treadmill test total duration, number of two-minute periods with increasing intensity, and time to return to a heart rate of 130 beats per minute; r correlations of .383, .377, .346, respectively taken from the treadmill test at year 1 of the study, and corroborated using year 7 data as well where duration, number of two-minute periods completed with increasing intensity, and time to return to a heart rate of 130 beats per minute had correlations r 's of .413, .396, and .346, respectively. Every measure at both the baseline year and year 7 were significant at the $p < .0001$ level. For this reason, as well as the availability of this measure, we opted to use the physical activity questionnaire total score in the present analyses.

Center for Epidemiological Studies Depression Scale (CES-D):

This 20-item questionnaire is widely to assess depression and depressive disorder in population studies. The CES-D measures symptoms defined by the American Psychiatric Association's Diagnostic and Statistical Manual (DSM) for a major depressive episode. The CES-D Depression score is measured on a Likert scales ranging from "rarely or none of the time" to "most or all of the time," with scores ranging from 0 to 60. The scale provides cutoff scores of suspected depression

(i.e., score ≥ 16), those at risk for depression, and level of depression. While it was not intended to be used for a clinical diagnosis, the CES-D has been shown to discriminate levels of depression and changes in depression levels (Radloff, 1977). The CES-D has good sensitivity and specificity for detecting depression, is useful across the lifespan, and is reliable when compared to other depressive measures (Cosco et al., 2017; Lewinsohn et al., 1997; Radloff, 1977; Shafer, 2006). In a follow-up meta-analysis the CES-D was found to have a sensitivity of 0.87 and specificity of 0.70 (Villagut et al., 2016). Examples of questions include “I felt hopeful about the future” in which a participant would indicate how often they have felt that way during the past week choosing from “Rarely or none of the time (less than 1 day),” “some or a little of the time (1-2 days),” “occasionally or a moderate amount of time (3-4 days),” or “most or all of the time (5-7 days).” The CES-D was not given as a study measure as every CARDIA time point and is available at follow-up years 5, 10, 15, 20, and 25.

HUMAN SUBJECTS.

The CARDIA data set used in this study up to the 2015 30-year follow-up are de-identified and publicly accessible, and therefore should qualify for classification and an exempt protocol under the most recent Common Rule guidelines. The study participants themselves are from the CARDIA study which is a multi-center study of cardiovascular risk factors in a nationally representative of individuals (males, females, black, white) who were 18-30 years old when they were recruited for the study in 1985. The CARDIA study began more than 30 years ago, so the data set now includes longitudinal data from

all the CARDIA participants who were age 48-60 when the latest follow-up data were collected.

DATA ANALYSES:

Each of these measures are analyzed at available time points which includes years 5, 10, 15, 20, and 25. First, the stability and change in reported exercise and depression from young adulthood (Intake) to middle age (year 25) was analyzed using each available time period. This was done using two repeated measures ANOVAs in SPSS, one with PA as the dependent variable and the other with CES-D as the dependent variable. This ANOVA provided results at each available time point (e.g., 5,10,15,20,25).

Second, the cross-sectional relationships of reported exercise levels to depression across time were analyzed through a series of multiple linear regressions, using Physical Activity totals as independent variables, CES-D composite scores as dependent variables. Covariate adjusted cross-sectional relationships were analyzed at each available time point, e.g., years 5, 10, 15, 20, and 25. The Depression score from the CES-D was used as a continuous DV.

Third, we analyzed the longitudinal relationship of reported exercise and depression across time. First, the respective slopes for Physical Activity (PA) and CES-D over time (years 5, 10, 15, 20, and 25, were computed for each participant in order to determine the rate of change in PA and CES-D across time (time points 5, 10, 15, 20, 25 years) for subjects using a Growth Curve Model in SAS version 9.4. After a slope of the PA scores and CES-D scores across time were obtained for each subject, in order to determine the relationship between the change in CES-D over time and change in PA over time, a multiple regression was conducted using CES-D slope as the dependent

variable and PA slope as the independent variable after adjusting for the study covariates. In these analyses, the initial reference points or baselines for determining change were Year 5 (baseline) PA levels and Year 5 (baseline) CES-D, respectively. Therefore, Year 5 levels of PA and CES-D were also entered as covariates in these analyses.

Study Covariates

Study covariates used in the present analyses included sex (male/female), race (black/white), age at intake, BMI at intake, smoking habits at intake (never smoked, quit smoking, currently smoking), and physical activity levels at intake. These covariates were chosen due to their relationships with the variables of interest in available literature and their availability in the current dataset (Camhi et al, 2013; Murthy et al., 2020; Shah et al, 2016). Smoking was coded using two dummy variables. The first dummy variable was coded with 0 = Never Smoked, 1 = Not currently smoking, 0 = Smoker and the second dummy variable was coded with 0 = Never Smoked, 0 = Not currently smoking, 1=Smoker. This allow for the categorical variable of smoking status which contains three levels to be compared between each other in the regression analysis.

CHAPTER 4: Results

Demographic and clinical characteristic of the sample are presented in Table 1. The sample had an even racial split with about 51% being black and about 48% being white, a healthy average BMI of 24.44, and a fairly even age split with an average of age of 24.76 ($SD = 3.628$) as subjects were ages 18-30 at baseline. The number of participants at baseline was 5113, 4290 at year 5, 3875 at year 10, 3622 and year 15, 3477 at year 20, and 3453 at year 25. Table 2 presents descriptive statistics for Physical Activity (PA) scores and CES-D depression scores over time for all CARDIA subjects. Because of study dropouts and individuals not tested at different time points, longitudinal correlations and regression analyses will be based on the PA and CES-D data from the 2554 subjects present for all of the testing time points Table 3. Demographic differences are nonsignificant, and the number of participants stays static at $N = 2554$ at every time point in Table 3. Of note, descriptive statistics of study measures of CES-D and PA did not differ significantly from Table 2 to Table 3.

ASSOCIATIONS OF COVARIATES WITH REPORTED EXERCISE AND CES-D SCORES

Table 4 shows correlations of the covariates with the study measures at baseline. Age, sex, race, and BMI, but not smoking, were significantly correlated with reported PA at baseline. The largest correlation with PA (.279) was with sex, with women reporting less PA. For race, blacks reported less physical activity, and regardless of race reported physical activity decreased with age and with increase BMI. At baseline (year 5), CES-D depression scores were significantly correlated with age, sex, race, smoking, and BMI, with the largest correlation related to race (-.165), with blacks scoring higher on depression compared to whites.

HYPOTHESIS 1: DIFFERENCES IN DEPRESSION AND REPORTED EXERCISE OVER TIME

Repeated measures analysis of fitness scores across all the 6 time points controlling for age, sex, smoking, BMI, and baseline physical activity levels, indicated that fitness did decrease significantly over time $F = 4.216$, $df = 3.78$, $df_2 = 9596.328$, ($p < .003$; Partial Eta Squared = .002); see Table 3. Furthermore, the partial eta squared measure indicates that that this decrease was small. Additionally, repeated measures analysis with covariates also indicated that depression as measured by the CES-D decreased over time, but this decrease was not significant $F = 1.979$, $df = 3.852$, $df_2 = 9371.9$, ($p = .098$; Partial Eta Squared = .001). However, the repeated measures ANOVAs for hypothesis 1 were conducted using uncentered covariates, meaning the main effect of Time reflects the effect of Time when all covariates, including age, have a value of zero. Different results may be obtained if covariates were not included or were centered.

HYPOTHESIS 2: CROSS-SECTIONAL RELATIONSHIP BETWEEN REPORTED EXERCISE AND DEPRESSION

Multiple linear regressions at each measured time point controlling for age, sex, race, smoking, BMI, and baseline physical activity levels, using CES-D scores as the dependent variable and exercise levels as the independent variable are presented in Table 5. As predicted, at each time point there is a small negative correlation between depression and reported exercise. As participants aged, the negative correlation between PA and depression as measured by the CES-D tended to increase and stay statistically significant. Between Year 5 and Year 25, the correlation between PA and depression went from -0.057 to -0.091, with this relationship significant at each of these time points.

This represents a minor change over time, and a stronger relationship but no statistical significance.

HYPOTHESIS 3: LONGITUDINAL RELATIONSHIP BETWEEN REPORTED EXERCISE AND DEPRESSION

To determine the relationship between change in PA and change in CES-D over time, a slope of relationship of PA and CES-D was calculated for each participant using a Growth Curve model analysis of data at time points 5, 10, 15, 20, and 25 years. Multiple linear regressions controlling for age, sex, race, smoking, and BMI were then performed on the slope of CES-D scores as the dependent (outcome) variable and PA as independent (predictor) variable. In these analyses, Year 5 PA levels and Year 5 CES-D levels were used as baseline values, and were also entered as covariates.

Results are presented in Table 6. After adjusting for covariates, there was a small but significant relationship between the rate of change in PA over time and the rate of change in CES-D over time, partial $r = -0.068$, $p < 0.001$. For each 1 standard deviation increase in PA Slope, there was a predicted decrease of 0.07 standard deviations in CES-D Slope, when controlling for all other variables in the model. Results in Table 1 also indicate that that the slope of PA over time was a stronger predictor of slope of CES-D over time than any of the covariates with the exception of smoking status and Year 5 (baseline) PA level.

CHAPTER 5: Discussion

This study is unique in that it examines the cross-sectional and longitudinal relationships of both exercise levels and depression in a sample of black and white young adults over a 25-year period, with repeated examinations at 5-year time intervals. By examining both physical activity and depression at 5-year intervals across a 25-year time span, results of this study indicate that, both cross-sectionally and longitudinally, there are reliable negative relationships between physical activity and depression. This cross-sectional relationship was present at each of the 5 testing sessions at 5-year intervals, with depression decreasing as exercise scores increased. These relationships also persisted after controlling for demographic factors, smoking habits, and physical activity levels at baseline, and was evident as a trend at study year 5, but increased in strength over time from follow-up years 15, 20, and 25. In addition, results indicated that both reported physical activity and depression decreased over the 25-year follow-up period. Of note, decreases in physical activity were significant and decreases in depression were not significant.

Longitudinal results further indicated that rate of change in reported physical activity at 5-year intervals over a 25-year time period was significantly associated with rate of change in depression, such that as physical activity increased, depression scores decreased. Moreover, the rate of change in PA was more strongly associated with change in CES-D Depression than was age, sex, race, and BMI, and of the covariates examined, only smoking and baseline CES-D were stronger predictors of rate of change in Depression. Key strengths of the study include its longitudinal design and large sample size, racial composition, and 25-developmental data from young adulthood to middle age.

Furthermore, validated measures of physical activity and depression were used in this study.

HYPOTHESIS 1

As predicted, the data showed the hypothesized decline in both reported physical activity and depression over time, but exercise levels and depression each remained relatively stable over the 25-year time period in the sample. With regards to depression, these results corroborate data summarized by NIMH (2019) indicating that depression rates in the U.S. are lower in middle age than in young adulthood. This may be due to relative increases in emotional stability and regulation that increase normally from adolescence to adulthood (Phillips et al., 2008). With regards to the relative stability, but slight decline, in reported physical activity, this corresponds to data from previous studies which also show relative stability, but decline in physical activity across the lifespan (Ortega et al., 2008; Friedman et al., 2008; Picavet et al., 2011). Although not entirely clear, changes in physical activity across the lifespan may be due to natural degeneration of muscle and bone tissue consistent with aging (Walston, 2012), sociodemographic/access to time and resources to exercise, e.g., having career and family obligations that may reduce time to be physically active or other resources constraints (O'Donoghue et al., 2018; Jimenez-Pavon et al., 2010; Ombrellaro et al., 2018; Parks, Housemann, & Brownson, 2003).

In the CARDIA study, a variety of other factors were associated with PA levels, including BMI (Schmitz et al., 2000), smoking (Auer et al., 2014), and race (Whitaker et al., 2018). These factors also affect levels of depression (Needham et al., 2010). In the present analyses, we chose to control for baseline levels of physical activity and

depression, BMI, age, race, sex, and smoking habits. Although there are other factors that affect both physical activity and depression, such as other comorbidities or socioeconomic status, those factors are outside the scope of the present study.

HYPOTHESIS 2

The present data also indicate there were consistent, and significant relationships between reported exercise and depression cross-sectionally at each 5-year testing period, even after controlling for covariates of age, gender, race, smoking, and BMI. At each time point there was a small, but negative correlation between reported physical activity and depression which became stronger over time. By the 20 and 25-year follow-ups when participants ranged in age from 43 to 55, the relationship between reported physical activity and depression trended towards strengthening over time. In this regard, in the present CARDIA data and in other studies (Gudmundsson et al., 2015; Harvey et al., 2018), negative relationships have consistently been observed between exercise levels and depression across a variety of age groups. A contribution of the present study is not only that these relationships were replicated at different time points, but among individuals of different ages ranging from young adulthood to middle age. One exception is that for one of the follow-up periods (i.e., the 10-year follow-up) the negative relationship between PA and CES-D was not significant. This may be due to other external factors that come with the participants' age ranging from 28-40 years. This is a time of life transition where individuals may be going through personal and professional shifts in their lives; therefore, at this time point these other external factors may account for more depressive symptomology than exercise is capable of protecting far (Justine et

al., 2013). It is possible to speculate that this may demonstrate a potential limit on the protective benefits of exercise.

Additionally, it may be important to consider some research which suggests individuals may be more depressed at midlife, that is, aged at approximately 47.2 years old (Blanchflower, 2020). However, this may correspond to the results here wherein CES-D scores relatively decline, but then begin to rise slightly at the time point of 25-years. This would correspond to the age of participants being between 43 and 55 putting this cohort in the area where they would be expected to be less happy according to Blanchflower (2020). This undoubtedly will be an area for further research as this cohort continues to age.

Although it is impossible to infer causation from cross-sectional data, the increasing strength of this association may indicate that as an individual ages from young adulthood to middle age, physical activity may become a more a more important protective factor against depression. Data from CARDIA and from other studies further reveal a protective effect of exercise on such risk factors such as BMI, hypertension, diabetes, cancer, obesity, bone joint diseases, and cardiovascular disease (Warburton, Nicol, & Bredin, 2006; Shah et al., 2017; Laddu et al., 2017; Nystoriak & Bhatnagar, 2018; Murthy et al., 2020)

It is also important to note, however, that because of the retrospective nature of the study where participants are asked to recall their exercise habits then asked about their current levels of depression, it is not possible to infer causation. However, it also is possible that individuals who are more depressed may simply be inclined to be less active and engage in less frequent or less strenuous exercise.

Despite the reliable associations between depression physical activity at different follow-up time points, the magnitude of these associations is relatively small. However, these results may partly be due to the nature of the measurement scales. The physical activity measure, created and validated specifically for use within the CARDIA study (Jacobs et al., 1989, Camhi et. al, 2013) ends up having values that range from 0 to over 2000 whereas the measure for depression, the CES-D has values that range from 0 to 60. Due to this disparity, a small change daily activity results in a very small change in the physical activity score which would account for an even smaller change on the CES-D; however, a large change in activity behaviors, such as adding in an hour of physical activity a week or meeting CDC guidelines of 150 minutes of activity per week would raise the physical activity score significantly which in turn would account for a greater drop in CES-D scores.

HYPOTHESIS 3

Most studies in the literature examine relationships between exercise levels cross-sectionally (Awick et al., 2017; Blumenthal et al., 2012). In addition, clinical trials examining the effects of exercise training on depression typically have relatively short follow-up periods (e.g., months to a year; Josefsson, Lindwall, & Archer, 2014), and do not allow the assessment of longitudinal, developmental changes across the adult lifespan. Exceptions are two studies which examined longitudinal relationships between exercise and depression over time. In a study of mid-aged adults (mean age = 45 at baseline) followed for 11 years (Harvey et al, 2018), individuals who participated in at least one hour of physical activity per week at baseline were less likely to evidence clinical levels of depression at longitudinal follow-up compared to individuals exercising

less than one hour or not at all. Another study of middle-aged individuals followed for 32 years (Gudmundsson et al., 2015), found that lower levels of physical activity at study baseline were related to higher depression scores at follow-up and individuals with decreasing physical activity showed higher depression scores at a 32-year follow-up. Results of the present study support this longitudinal relationship and provide further evidence to the studies done by Harvey et al. (2018), and Gudmundsson et al. (2015) with a longer time period and a larger age demographic starting from young adulthood into late adulthood.

However, rather than just looking at physical activity at a single predictive time point and depression at a subsequent time point, the present study also demonstrates a relationship between changes in physical activity over time and changes in depression. These findings suggest not only that physical activity earlier in life predicts subsequent depression, but that both physical activity and depression demonstrate plasticity and variability across the lifespan and also are negatively related to one another. Although the present findings are correlational, the variability and covariation of activity and depression across the lifespan suggest that interventions to increase physical activity may influence the trajectory of depression over time and reduce subsequent depression.

Another interesting result in the present study is that the change in physical activity over time demonstrated a stronger relationship to changes in the change in depression over time than age, sex, race, and BMI. Only smoking and baseline PA showed relationships of comparable magnitude and only baseline depression was more strongly related to rate of change in depression over time. Thus, regardless of

demographic factors, over time physical activity not only has a significant relationship to depression, but also accounts for more of the change in depression than these variables.

Mechanisms Linking Exercise to Depression

Although the exact mechanism causing a protective relationship between exercise and depression is not entirely clear, evidence indicates that physical exercise not only has beneficial effects on many physical conditions, but also has significant positive benefits on mental health conditions as well (Kokkinos, 2012; Mora et al., 2007). Several possible explanations have been offered to explain the pathway(s) through which physical activity may affect depression (Craft & Perna, 2004). At present, there is research to support each of these explanations, but whether one or several of these are the most convincing explanations is not entirely clear.

Most of these explanations to explain associations between physical activity and depression are physiological or psychophysiological in nature. Although these hypotheses were presented earlier, they warrant reiteration as they are potential mechanisms through which physical activity is having an effect on depressive symptoms as measured by the CES-D. One explanation offered is the thermogenic hypothesis, which states the increase in body temperature and certain brain regions induces an overall feeling of relaxation and reduction of neuromuscular tension (Craft & Perna, 2004; DeBoer et al., 2013; Mikkelsen et al., 2017). A second explanation, an endorphin hypothesis, suggests that there may be improvement in depression due to exercise due to an increase in endorphins following exercise. Endorphins, in turn, are associated with a positive mood and enhanced sense of well-being (Anderson & Shivakumar, 2013; Craft & Perna, 2004; Dishman & O'Connor, 2009). A third explanation is the monoamine hypothesis, which suggests that an increase

in neurotransmitter availability as a result of exercise may be the reason for the connection (Anderson & Shivakumar, 2013; Craft & Perna, 2004; Hirschfeld, 2000;).

Another type of explanation for the depression-reducing effects of exercise is more psychological in nature. A distraction hypothesis states exercise provides a distraction from the worries and depressing thoughts, comparable with activities such as relaxation, health education, and social contact (Anderson & Shivakumar, 2013; Craft & Perna, 2004; Roth et al., 2010). Additionally, exercise is known to increase positive affect more than other activities (Anderson & Shivakumar, 2013; Craft & Perna, 2004; Szabo, 2003). However, exercise itself may lead to health education or increased social contact which would combine activities for added efficacy. This leads to the idea that group processes such as social connection may occur through physical activity which is another potential mechanism which requires further research. Finally, a self-efficacy hypothesis states that in completing exercise individuals feel more confident and efficacious about themselves because of the success of attaining a positive desired outcome. Doing so then increases confidence in one's abilities while reducing self-rumination, feelings of low efficacy, and negative self-evaluations (Anderson & Shivakumar, 2013; Craft & Perna, 2004; Gilani & Feizabad, 2019). Although these theories are subject to further study, they provide working ideas on the connections between physical activity and depression.

STUDY LIMITATIONS

Although the present study controlled for age, gender, race, smoking, BMI, and prior exercise, it may be the case that an uncontrolled third factor (e.g., alcohol use, other comorbid illness, etc.) explains these relationships. Although some of the covariates vary

from the general populations such as current smokers at baseline being at about 30%, these variables are controlled for and thus the results are not limited by these covariates. Furthermore, due to the observational nature of the study, it is not possible to infer causation from the present findings. It is possible that exercise may reduce depression, or that less depressed individuals may exercise more. It is also possible that a third factor, such as overall health, may be associated with both depression and engaging in more physical activity. Additionally, while the physical activity measure has been well-validated by CARDIA (Jacobs et al., 1989, Camhi et. al, 2013) and correlates with objective treadmill test data (see data in the present paper), it is possible that participants may not be the best objective reporters of their exercise habits.

In this regard, it is not clear whether the present findings are due to increased fitness or to increased exercise levels, which are associated with increased fitness in the CARDIA data. As noted, the PA responses were associated with treadmill fitness levels at one testing session (Year 0 and Year 7) when both PA and treadmill tests were given. However, the treadmill test was not given at Years 5, 10, 15, or 25, and therefore we were unable to compare relationships of fitness and depression to relationships of exercise and depression.

Another issue to consider is that the relationships measured using the CES-D are more appropriately considered to be depressive symptoms and changes in depression levels, as opposed to being used for a clinical diagnosis (Radloff, 1977). While most of the literature refers to exercise having a positive benefit on clinical levels of depression, there may be a smaller effect on depressive symptomology when it is not at clinical levels due to a ceiling effect. Therefore, this study should be seen as support for the idea that

exercise can have a positive effect regardless of level of depression, even though there may be a ceiling effect on its benefits if the level of depression is less severe.

The present results also do not determine whether relationships are specific to the parameters of duration of exercise or intensity of exercise. Although the present study does suggest that an increase in time exercising correlates with a reduction in depressive symptoms, other studies have been able to be more specific. Harvey et al. (2018) determined that as the amount of exercise per week increased, the protective effects against depression increased up until about one hour when the effect began to level off. They were also able to find that this effect occurred regardless of intensity. Furthermore, although aerobic exercise intervention studies are more common in research, other forms of physical activity other than aerobic have also been shown to be beneficial, although there is conflicting research to show which type of exercise (e.g., aerobic, strength training, yoga, etc.) is most effective (Belvederi-Murri et al., 2018; Craft & Perna, 2004;). Similar issues come up with regard to exercise intensity. wherein studies such as the one done by Harvey et al. (2018) show that regardless of intensity, effects are seen. However, a review by Teychenne, Ball, & Salmon (2008) suggests that higher intensity exercise decreased the likelihood of depression more than lower intensities. The issue of intensity, type of exercise, and duration of exercise continues to be an area where more research is needed to determine the parameters of exercise that show a consistent effect on the prevention or treatment of depression.

Finally, another limitation is the small size of the correlations. Although larger correlations would have provided more evidence for using physical activity as both a preventative measure and intervention for depression, the small correlations also provide

information. However, due to finding relationships across a 25-year lifespan, these findings suggest further research may be needed to clarify the exact clinical relevance or lack thereof.

FUTURE RESEARCH AND CLINICAL IMPLICATIONS

Future research should focus more closely on establishing whether there is a causal relationship between physical activity and depression across the lifespan. If a causal relationship can be established, further research is warranted to determine the multi-faceted mechanism(s) through which physical activity affects depression.

Furthermore, the extent to which effects occur in different age groups, that is do the protective effects of exercise truly vary by age group, and if the age at which regular exercise is done makes a difference in preventative effects should be further investigated. Current studies such as the ones by Harvey et al. (2018) and Gudmundsson et al. (2015) establish that protective effects of exercise are significant in middle-aged (45+) and older (65+) adults, but less research has been performed on individuals in younger age groups.

Additionally, further investigations are needed to determine if the type of exercise and/or intensity of exercise have moderating effects on depression. For example, does cardiovascular vs. strength-based exercises moderate the relationship between exercise and depression, and/or does the intensity of exercise moderate the relationship between exercise and protective effects against depression. Furthermore, whether the amount of time per week spent doing different exercises at different levels of intensity and duration (i.e., mixing and matching different intensities and types of exercise) may have effects that require further investigation.

Finally, other factors which may account for or affect the relationship such as demographics, socioeconomic status, and comorbidities should be studied to discover their potential mediating and moderating effects.

The present study supports the utility of exercise interventions that, many are already used in practice. Previous research has established that exercise may be an effective intervention against depression in middle aged and older adults, and the present findings extend these relationships to young adulthood. Indeed, the present study demonstrates that, in addition to many physical health benefits (e.g., prevention of obesity and cardiovascular disease) physical activity throughout the lifespan will also benefit mental health.

For clinicians, this may provide another reason to encourage regular physical activity as a preventive measure, rather than just as a means to treat depression. Specifically, in addition to exercise-based treatment interventions, the present findings suggest that using exercise as a preventive measure in healthcare may be an important public health measure to promote better mental health. Healthcare providers encouraging patients to engage in regular exercise will provide not only a benefit to physical health, but also a preventative and protective measure against mental health conditions such as a depression. This may prove to be beneficial to those who may have a family history or genetic predisposition for depression. Furthermore, it may behoove clinicians to work on establishing treatment protocols for exercise interventions so that they may be more easily accessible and employable by their patient populations due to the many benefits of regular physical exercise.

Table 1. Baseline Characteristics of study sample N = 5113

Variable	Mean (SD) or %
Age (years)	24.76 (3.628)
Male Sex	2328 (45%)
Female Sex	2785 (55%)
BMI	24.44 (4.81)
Smoking Status	
Never Smoked	2893 (56.6%)
Not currently smoking	653 (12.8%)
Currently smoking	1566 (30.6%)
Race	
Hispanic	14 (.28%)
Black	2637 (51.57%)
White	2462 (48.15%)

Note: Row totals may not net total sample due to missing data.

Table 2. Mean (SD) of CES-D and PA measures at each time point for all study subjects
with available data

Measure	CESD (total score 0-60)	(SD)	Physical Activity (PA) (total score 0-2126)	(SD)	<i>N</i>
Baseline	Not given	--	420.14	300.76	5113
Year 5	11.24	8.14	379.42	292.55	4290
Year 10	10.7	8.22	330.9	274.93	3875
Year 15	9.16	7.85	347.28	283.58	3622
Year 20	9.33	7.87	335.87	274.13	3477
Year 25	9.47	7.74	337.79	275.64	3453

Note: Abbreviations: CES-D = Center for Epidemiological Studies Depression Scale.

Table 3. Mean (SD) of longitudinal study measures for those subjects present at every time point

Measure	CESD (total score 0-60)	(SD)	Physical Activity (PA) (total score 0-2126)	(SD)	<i>N</i>
Baseline	N/A	N/A	420.58	295.83	2554
Year 5	10.49	7.88	381.2	293.75	2554
Year 10	10.10	7.90	334.14	268.91	2554
Year 15	8.57	7.51	348.26	279.89	2554
Year 20	8.93	7.70	343.73	274.01	2554
Year 25	9.05	7.59	339.87	274.152	2554

Note: *Analyses include only those subjects who were present at every time point.

Abbreviations: CES-D = Center for Epidemiological Studies Depression Scale.

Table 4. Zero-order correlations of Covariates with PA and CES-D at Year 5

Variable	Correlation with PA	<i>p</i> -value	Correlation with CES-D	<i>p</i> -value
Age	-0.034	0.025*	-0.072	<.001*
Sex	-0.279	<.001*	0.096	<.001*
Race	0.07	<.001*	-0.165	<.001*
Smoking	-0.012	0.439	0.094	<.001*
BMI	-0.06	<.001*	0.077	<.001*
Year 5 PA	0.52	<.001*	-0.078	<.001*

Note: *Analyses marked are statistically significant. *N* = 5113

Table 5. Zero order and adjusted cross-sectional correlations between PA and CES-D at each time point

Year	Zero Order Correlation	Partial Correlation*	<i>p</i> -value*	<i>N</i>
Year 5	-0.099	-0.057	<.0001	4290
Year 10	-0.086	-0.04	0.014	3875
Year 15	-0.107	-0.065	<.00001	3622
Year 20	-0.156	-0.113	<.00001	3477
Year 25	-0.139	-0.091	<.00001	3453

Note: *Controlling for Age, Sex, Race, Smoking, BMI, Baseline PA levels.

Table 6. Zero-order and covariate-adjusted relationship between rate of rate of change in
PA to rate of change in CES-D over time

Variable	Unstandardized B	Standardized B	Zero-order correlation	Partial correlation	<i>p</i> -value
Age	0.0002	0.003	0.052	0.004	0.809
Sex	0.002	0.003	-0.042	0.003	0.834
Race	0.003	0.005	0.089	0.003	0.683
Smoking	0.024	0.066	0.009	0.08	<.001
BMI	0.001	0.019	-0.021	0.022	0.148
Year 5 PA (baseline)	-0.00009	-0.078	0.025	-0.071	<.001
Year 5 CES-D (baseline)	-0.024	-0.599	-0.584	-0.585	<.001
Slope PA	-0.002	-0.073	-0.025	-0.068	<.001

Note: *N* = 4723

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