

ABSTRACT

Title of Thesis: EXERCISE AND PREVALENCE AND FIRST ONSET DEPRESSION IN WOMEN OF CHILDBEARING AGE

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Background: Major depressive disorder is the leading cause of disability disproportionately affecting women of reproductive age. Prior research suggests that exercise may be an effective preventative measure. Objective: To examine the association between exercise and current and first onset major depressive episodes (MDE) among women 20-45 years (n=8175) participating in National Epidemiologic Study of Alcohol and Related Conditions II (2004-2005). Methods: Logistic regression models were used to examine the relationship between exercise and MDE prevalence and incidence. Results: Some exercise was associated with elevated odds of first onset MDE, compared to no exercise, but this association was not significant after controlling for covariates (adjusted odds ratio = 0.87, 95% confidence interval:0.75-1.01). No other associations were observed. Conclusion: This study did not find evidence of an association between exercise and prevalence or incidence of MDE in reproductive-aged women. Future research with prospective study designs and objective exercise measures needed.

**EXERCISE AND PREVALENCE AND FIRST ONSET OF DEPRESSION IN
WOMEN OF CHILD BEARING AGE: A CROSS-SECTIONAL ANALYSIS**

by

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List of Abbreviations

MDD: Major Depressive Disorder

MDE: Major Depressive Episode

NESARC: National Epidemiologic Survey on Alcohol and Related Conditions

DSM-IV: The Diagnostic and Statistics Manual of Mental Disorders 5th edition

NHANES: National Health and Nutrition Examination Survey

SES: Socioeconomic Status

PPD: Post-Partum Depression

HHS: Health and Human Services

RCT: Randomized Controlled Trial

AUDADIS-IV: Alcohol Use Disorder & Associated Disabilities Interview Schedule

NIAAA: National Institution on Alcohol Abuse and Alcoholism

BMI: Body Mass Index

aOR: Adjusted Odds Ratio

CI: Confidence Interval

NPHS: National Population Health Survey

LTPA: Leisure Time Physical Activity

Chapter 1: Introduction

According to the World Health Organization, depression is the leading cause of disability, affecting 121 million people worldwide.¹ Compared to men, women are disproportionately affected by on, reporting a lifetime history of major depressive episodes (MDE) twice as often as men.² It is estimated that 8-16% of women of reproductive age (15-45)³, are affected by MDE, which is associated with negative outcomes such as increased substance abuse, adverse reproductive outcomes, unfavorable pregnancy outcomes and reduced maternal functioning and bonding.² MDE is a mood disorder that impacts a person's ability to experience normal mood states and is characterized by five or more of the following symptoms for a period of two weeks⁴: depressed mood, loss of interest or pleasure, significant weight loss when not dieting or exercising, or weight gain, insomnia, psychomotor agitation or delay, fatigue, feeling worthless or inappropriate guilt, inability to concentrate or make decisions and recurring thoughts of death or suicide. Exercise is considered one protective measure against mental illness through promotion of neural plasticity and releasing positive endorphins, but there have been limited studies examining the associations between exercise and current MDE and first onset of MDE. Drawing on large nationally-representative sample with detailed measure of lifetime history of MDE, this project seeks to examine self-report of past-year exercise habits in relation to prevalence and incidence of MDE in women of childbearing age.

Public Health Significance of Depression among Reproductive-Aged Women

Research has shown that a history of MDE prior to pregnancy is a significant risk factor for the development of maternal depression which carries long term health consequences.⁵

Maternal depression—including antepartum (before giving birth) and postpartum (immediately after given birth) depression—is associated with negative health outcomes in both the infant and mother such as unhealthy coping mechanisms, low birth weight, and poor adherence to prenatal and postnatal care.⁶ Given these damaging health effects for mothers and their children, the prevention of MDE prior to pregnancy and postpartum is a critical public health issue.

Chapter 2: Research Question and Specific Aims

Using data on women of child-bearing age from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) waves I (2001-2002) and II (2004-2005), we investigated the hypothesis that the recommended amount of exercise is associated with a lower prevalence and incidence of DSM-IV MDE.

Specifically, this study had two main aims:

Aim 1. To evaluate the association between self-reported past-year exercise and DSM-IV MDE in women of childbearing age. *Hypothesis: Women who meet the recommended levels of exercise will have lower odds of MDE compared to those with no exercise.*

Aim 2. To examine the association between self-reported past-year exercise and first onset MDE in women of childbearing age. *Hypothesis: Exercise will be associated with lower odds of first onset MDE compared to no exercise.*

Observational studies have shown that regular exercise is associated with lower rates of MDE in women.⁷ For example, in a prospective study of 26,913 women there was an inverse dose- response association between exercise and future symptoms of mental illness.⁷ Similarly, experimental studies have shown that in some circumstance exercise can be an effective treatment for active cases of MDE.⁸ To my knowledge, this research is the first to evaluate if exercise is associated with lower prevalence and incidence of DSM-IV MDE in women of

childbearing age utilizing the NESARC II dataset. NESARC data is advantageous relative to other comparable studies (e.g., NHANES) because NESARC included a clinically-validated questionnaire to assess mental disorders according to DSM-IV diagnostic criteria.⁹ Further, NESARC is a large nationally-representative population-based sample, which allows our results to be generalized to reproductive-aged women in the U.S. Understanding the role of exercise and its effect on MDE has the potential to inform prevention strategies to protect women from MDE in the antepartum and postpartum periods.

Chapter 3: Background

3a. Existing Knowledge

i. Significance of Depression in Reproductive Years:

MDE is the primary cause of disease burden and disability in women of child bearing age, and is reported twice as likely in woman than men.^{2,10} First onset of MDE peaks during reproductive years, and the lifetime prevalence of MDE for women is about 21%.¹¹ MDE is also one of the most common reasons that a woman aged 18-44 stays in a hospital for non-obstetric reasons.¹² Some of the known risk factors for MDE include low socioeconomic status (SES), unemployment, lower levels of education, racial and ethnic discrimination, marital dissolution, loss of a child, single parenthood, abuse in childhood and adulthood including sexual and physical abuse, genetics, and a prior history of MDE.¹¹ MDE that occurs during the reproductive-years can negatively impact fertility¹³, pregnancy and neonatal outcomes^{14,15}, and maternal functioning and child rearing.¹⁶ MDE confers specific concerns during the postpartum/antepartum periods, as discussed below.

ii. Significance of Antepartum/ Postpartum Depression:

During pregnancy and the postpartum period, women have an increased vulnerability to MDE, especially if they have a history of MDE prior to pregnancy.¹⁷ For example, in a small clinical study of 4,398 women with eligible pregnancies ending in live births, about 678 had depression during at least one pregnancy phase.¹⁷ Among the women with depression prior to pregnancy (n=381), 56.4% also had a diagnosis of depression during pregnancy.¹⁷ In the U.S., 12% of

women will experience antepartum depression (i.e., depression during pregnancy), which substantially raises their risk for postpartum depression.¹⁸ After delivery, about 15% of mothers will experience postpartum depression.¹⁹ Antepartum depression has long term implications on not only maternal health but fetal health as well. There is evidence that antepartum depression is associated with unhealthy coping behaviors such as smoking^{20,21}, drug and alcohol use^{20,22}, inadequate weight gain²², and poor adherence to prenatal care²³ such as delaying seeking care, and low attendance in prenatal visits. Antepartum depression is also associated with elevated risk of adverse obstetric outcomes such as emergency cesarean sections²⁴. With regard to infant outcomes, antepartum depression in mothers is associated with low birth weight^{22,25,26}, preterm delivery^{22,25} and a small for gestational age baby^{22,27}.

Postpartum depression (PPD) is a clinical condition that presents for at least two weeks, and can occur up to six months after giving birth. Risk factors for PPD include a previous history of depression, antepartum depression, low self-esteem, marital troubles, stressful life events, diminished social support, unwanted pregnancy, low SES, and being single.²⁸ PPD is associated with negative outcomes in both mom and infant, with the potential for long term impairment. In the mother, PPD is associated with persistent depressive episodes²⁸⁻³⁰, and poor infant health practices^{28,31,32} such as not completing immunizations, low attendance to well child visits, not placing infants in proper sleeping positions, and incorrect use of car seats. In children, maternal PPD is associated with poorer language and IQ development³³, increased risk of gastrointestinal and lower respiratory tract infections³⁴, and greater stroke volume and cardiac output which is a precursor to hypertension.³⁵

3b. Exercise Recommendations

It is recommended by The Department of Health and Human Services (HHS), that women remain moderately active for at least 30 minutes per day, 5 days a week and/or engage in vigorous activity for 25 minutes a day, 3 days a week.⁶ Both resistance and cardiovascular training have been shown to be effective in lessening depressive symptoms, and currently there is no evidence to suggest one over the other.³⁶ Some examples of effective methods of exercise are walking, running, resistance training, and swimming.³⁷ For women in particular, group exercise is highly recommended in reducing depressive symptoms due to the increased feeling of belonging, connectedness, and social skills training.³⁷ With regard to depression, there is evidence that even low levels of exercise (150 min a week or less) can be beneficial.⁷ Unfortunately, while exercise promotes many long-term benefits throughout the life course, only about 50% of women follow the guidelines implemented by the HHS. In a study measuring the prevalence of physical activity in women aged 18-44 over the span of 30 days, 22.5% reported engaging in no physical activity at all.³⁸

3c. Hypothesized Mechanism Linking Exercise and Depression

While there has been extensive evidence on the utilization of exercise as an effective treatment for MDE^{39,40}, there is a lack of consensus on the biological function of exercise in preventing or reducing MDE. Some factors that researchers believe play a role are that exercise releases “feel good” chemicals in the brain (endorphins⁴¹, endocannabinoids⁴², and neurotransmitters⁴³) that are known to reduce depressive symptoms. The ‘endorphins hypothesis’

states that exercise causes the release of opioid peptides and B-endorphins, which reduce pain, and cause general euphoria which is associated with decreased MDE.⁴¹ Psychologically exercise can prevent or reduce MDE by creating a distraction and preventing rumination^{44,45}, and increasing self esteem⁴⁶ and coping efficacy⁴⁶.

3d. Analyses Performed by Others

i. The Association Between Exercise and Depression

A variety of study designs have been utilized to study the relationship between exercise and depression in women, such as randomized controlled trials (RCTs), prospective cohort, and cross sectional designs. Across study designs, there is a similar conclusion of an inverse association between physical activity and depressive symptoms.⁴⁷⁻⁵⁰ For example, considering a cross-sectional study of women aged 18-45, those who were physically active three or more times per week had a prevalence of self-reported psychological disorders (measured by a general health questionnaire and the Beck Depression Inventory) that was 15.5% lower than women who were physically inactive. Individuals who reported some exercise (i.e., participating 1-2 times per week) had a MDE prevalence that was 5.2% lower than women who were physically inactive.⁵¹ Using a prospective design, another study of 17,276 participants ages 12 and older, found that women who shift from being very physically active to inactive over a period of two years have a 51% greater probability of developing depression, compared to women who continue being active.⁵² This is of great importance because women usually decrease their physical activity once they get pregnant or have a child.⁵³ Finally, there is evidence that the benefits of exercise may be long lasting. In an experimental study of 82 depressed men and

women, who participated in a fitness program, not only did they display significant improvements in MDE, anxiety and self-concept compared to the control after 12 weeks, these gains were also maintained through the 12 month follow up.⁵⁴

3e. Gaps in Literature

Based on a comprehensive review of the literature, there is limited research on the role of exercise and its association with MDE prevalence or first onset during reproductive years.⁵⁰ In this review of 25 studies, only three exclusively focused on women and of these three studies none of them solely focused on women of reproductive age. In another study that exclusively looked at women ages 18-30, the sample size was very small (n=40), thus prohibiting generalizable conclusions.⁵⁵ There is also a gap in research on the effect of exercise on first onset of MDE in the women of childbearing age, because the majority of this research is cross-sectional and does not include psychiatric interview measures that can be used to operationalize this outcome.^{51,55} Research also reports inconsistent findings on associations between exercise and MDE. In a review of thirty studies, 25 found an association, while 5 found a null association.⁵⁶

Finally, the gold standard for diagnosing Major Depressive Episode (MDE), is the Structured Clinical Interview for the DSM-IV.⁵⁷ A major limitation within existing research is the use of a self-administered questionnaire to measure MDE, or questionnaires with low internal consistency.⁵⁰ In the NESARC, the well validated National Institute on Alcohol Abuse and Alcoholism's Alcohol Use Disorder and Associated Disabilities Interview Schedule- DSM-IV (AUDADIS-IV)⁵⁸ is used to diagnose MDE, which will help to strengthen our findings in comparison to prior research. Accordingly, we are lacking an accurate nationally representative

representation of the association between exercise and MDE prevalence and incidence among reproductive-age women.

3f. Significance of the Study

Using nationally representative data, this study examines whether exercise is associated with lower prevalence of MDE among women of childbearing age, and if it protects against first onset of MDE in this population. Our research question is of high importance because our findings could have direct implications for strategies to prevent MDE in women of child bearing age. The prevention of MDE among this subset of the population has multigenerational benefits, as the prevention of MDE in women of childbearing age can offer protective benefits against future MDE that the women may face antepartum and postpartum. Practitioners could then utilize this information to motivate women to adhere to exercise guidelines, or support policy changes in insurance companies to encourage policies that promote exercise among women of reproductive age.

Chapter 4: Research Design and Methods

I performed a secondary analysis of women aged 18-45 in the United States who participated in the NESARC waves 1 and 2 data set. NESARC is one of the largest longitudinal comorbidity studies ever conducted in the US.⁵⁹ This study was conducted by US Census Bureau under the direction of the Institute on Alcohol Abuse and Alcoholism (NIAAA). NESARC 1 (2001-2002) sample is a nationally representative sample of 43,093 noninstitutionalized, civilian Americans aged 18 years and older. For NESARC 1, possible households were stratified in each state by sociodemographic factors, and then in each stratified household one adult (18 or older) was selected at random. NESARC II (2004-2005) is a follow up of individuals from wave 1. NESARC II had a response rate of 86.7% and included 34,653 participants who completed both waves. I utilized data from NESARC I and II to construct the study outcome variable of first onset MDE, and I conducted a cross-sectional analysis to address my study aims.

4a. Study Population

I constructed two separate analytic samples to address my study aims. The first analytic sample, designed to study the association between exercise and current MDE, included all women aged 18-45, regardless of lifetime history of MDE (N=9435). The second analytic sample, designed to study the association between exercise and first onset MDE, included women aged 18-45 (similar to above), with the exclusion of:

(1) women who reported any lifetime history of MDE at NESARC I, or

(2) history of MDE during the period between NESARC I and II, other than the past year (N=6712).

We excluded women with missing data on any covariates (N=1260 missing for the full sample (13.4%), and n=874 for the restricted sample (13% missing data), which reduced our analytic samples to n=8175 and n=5838 respectively.

4b. Description of Variables

i. Dependent Variables

Major depressive episode (MDE) was assessed using a valid and reliable interview, the AUDADIS-IV.⁵⁸ Women were diagnosed with MDE if they reported at least 2 weeks of a persistent depressed mood, followed by at least 5 or more of the 9 DSM-IV symptoms of MDE when they experienced an episode.⁶⁰ The diagnoses for MDE for all participants were coded either no or yes if women met the criteria for diagnosis in the past year, or prior to it. The AUDADIS reliability for MDE is quite substantial with kappa between 0.60 and 0.65.⁶⁰ Our main outcomes include:

1. **Prevalence**, defined as a past-year diagnosis of MDE at wave 2.
2. **Incidence**, defined as no lifetime history or current disorder at wave one, and no diagnosis in the 12-month period prior to NESARC II interview, but disorder at wave 2.

ii. Independent Variable

At Wave 2, four items from the short form international physical activity questionnaire were used to measure the frequency and duration of aerobic exercise over the past twelve months. The questions focused on both vigorous activity and light to moderate activity. Following a prior

publication that examined MDE and physical activity utilizing NESARC⁶¹, we based levels of physical activity on the responses to the questions:

- “How often in the past 12 months did you USUALLY do VIGOROUS activities that caused you to sweat HEAVILY or caused LARGE increases in breathing or heart rate.”⁵⁸ Response options were 12 categories ranging from every day to never in the past year, and a response classified as unknown.
- “About how long did you USUALLY do these VIGOROUS activities each time.”⁵⁸ Response options ranged from 1-720 minutes, unknown, or not available due to not performing vigorous activities in the past year.
- “About how often in the past 12 months did you USUALLY do LIGHT or MODERATE activities that only LIGHT sweating or a SLIGHT to MODERATE increase in your breathing or heart rate.”⁵⁸ Response options were 12 categories ranging from every day to never in the past year, and a response classified as unknown
- “About how long did you USUALLY do these LIGHT or MODERATE activities each time.”⁵⁸ Response options ranged from 1-720 minutes, unknown, or not available due to not performing moderate activities in the past year.

For healthy women, the recommendations for exercise are at least 30 minutes per day/ 5 days a week of moderate-intensity aerobic exercise, or at least 25 min a day/ 3 days a week of vigorous activity.⁶² Women were categorized into three exercise categories based on their response to the above questions, women who responded “unknown” were excluded from the analysis. These categories are defined as:

- 1) *Public Health Dose*: Women who engaged in at least 30 minutes per day/ 5 days a week of moderate-intensity aerobic exercise, or at least 25 min a day/ 3 day a week of vigorous activity
- 2) *Some Exercise*: Women who were physically active but engaged in at least 30 minutes of moderate intensity activity less than 5 days a week, or engaged in at least 25 minutes of vigorous activity less than 3 days a week.
- 3) *No exercise*: Women who were not physically active in the past month

iii. Control Variables

Variables that have demonstrated associations with mental health and physical activity in prior research⁶³ will be included in our adjusted models, including age, ethnicity, education, marital status, income, household size, employment, Body Mass Index (BMI), and past year pregnancy. All of these variables were measured at NESARC II.

NESARC measures age in years (at the time of the interview).⁵⁸

Self-reported race/ethnicity was categorized as: White, African American, Native American/Asian, and Hispanic/Latino. We had to combine Native Americans with Asian Americans and Hispanics with Latino due to the sparse data for those four racial/ethnic categories.

Education was measured as the highest grade or school year completed. I constructed a three-category variable: less than high school, High school and College/above.

NESARC II included a question about total family income in the past year, which asked respondents to report a range for their household incomes. I created a four-category measure: <\$19,000, \$20,000-\$34,000, \$35,000-\$69,000, and >\$70,000.

Household size was treated as a continuous variable and ranged from 1-15 persons. I took household size in account to account for the income variable, since income was measured as household income instead of individual income.

Marital status was coded as a binary: married or not married (which included NESARC response categories widowed, divorced, separated or never married.)

Employment was operationalized as a binary variable: Employed vs. unemployed. If participants answered yes to working full time or part time, they were considered to be employed.

Unemployed women were not working full time or part time.

BMI was created by combining variables for weight and height. The BMI variable was then created by dividing kg/m^2 . BMI was dichotomized as underweight/normal and overweight/obese due to the sparse data in the underweight and obese categories.

Pregnancy in the past year was measured by self-report and included women who were currently pregnant at the time of interview or had a pregnancy in the past year.

4c. Data Analysis

NESARC used a complex, multistage stratified design in which Black and Hispanic participants were oversampled, as well as young adults aged 18-24. The sample was also weighted to adjust for nonresponse at a household and person levels, and for the oversampling of certain populations. Due to the stratified, clustered design each data piece had a specific cluster, strata and weight variable included in the analysis to ensure the results are valid. Since I was requesting output for only a subset of the data in both the full sample and the restricted sample I created two domain statements for each. For my full sample, the domain statement isolated the NESARC sample to only include women aged 45 or less, with no missing data. For my restricted sample, the domain sample isolated the NESARC sample to again only include women aged 45 or less, with no missing data and who also didn't have a lifetime history of MDE, or MDE the year before NESARC II.

Weighted percentages and means were obtained to describe the sociodemographic and clinical characteristics of women of childbearing age stratified by level of exercise participation. Logistic regression was conducted to determine the association between physical activity and MDE. Multiple variable analysis on the association between physical activity and MDE, was sequentially adjusted for age, ethnicity, education, marital status, income, household size, employment, BMI, and past year pregnancy in four models. Model 1 adjusted for age and ethnicity. Model 2 adjusted for the covariates in Model 1, as well as education, marital status, income, household size and employment. Model 3 adjusted for all of the covariates in Models 1 and 2, as well as BMI. Finally Model 4 adjusted for all of the covariates in Model 3, and

additionally past year pregnancy status. Adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) were obtained. We also tested for an interaction between age and exercise, in case the association was specific to older or younger reproductive-aged women. This was done by including age and exercise as a cross product in Model 1. I tested for interaction with age treated as both a categorical and continuous variable. Data was analyzed using survey procedures in SAS 9.4 (SAS Institute Inc., Cary, NC).

4d. Human Subjects

IRB approval was obtained in order to conduct the secondary analysis of de-identified data.

Chapter 5: Results

5a. Descriptive Statistics

After selecting the analytic samples as defined by my inclusion criteria, descriptive statistics were calculated for the full (n=8,175) and restricted (n=5,838) analytic samples. **Table 1** displays the sociodemographic characteristics for the two analytic samples stratified by exercise category. In both the full and restricted sample, the mean age of the women across all three exercise groups was 33 to 34 years old. Across all three exercise groups, the majority of women in the overall sample were white, employed, married, and had a college education or more, and a household income of \$35,000+. In the full sample, 50-52% of women across all three exercise categories fell into the overweight/obese category. In the restricted sample 50-51% of women in the “public health dose” and “some exercise category” were in the underweight/normal BMI category. The distribution of MDE in the full and restricted samples are presented in **Table 2**. In the full sample, the overall prevalence of MDE was 12.5% with 3.2% of MDE being in the “public health” category, 5.9% in the “some exercise category” and 3.3% in the no exercise category. In the restricted sample, the incidence of MDE was 2.88% with 0.8% having first onset MDE in the “public health” category, 1.15% being in the “some exercise” category and 0.9% had first onset of MDE who did not engage in any physical activity.

5b. Exercise and its Association with Current MDE (Prevalence)

Table 3 shows the results from the multiple logistic regression models for the relationship between exercise and prevalence of MDE. Model 1 examined the association between past year self-reported exercise and current MDE, controlling for race and age. No exercise was used as a

reference and the aOR for the public health dose of exercise was 1.02 (95% CI:0.91-1.14) while the aOR for some exercise was 0.95 (95% CI:0.86-1.03). Model 2 examined this association controlling for the covariates in model one as well as education, marital status, employment, income and household number. The aOR for the public health group was 1.07 (95% CI:0.96-1.20) while the aOR for some exercise was 1.08 (95% CI:0.99-1.11) Model 3 examined this association while controlling for all of the covariates in Models 1 and 2 as well as BMI. The aORs across the exercise categories minimally changed, the aOR for the public health group was 1.06 (95% CI:0.95-1.18) while the aOR for some exercise group was 1.05 (95% CI:0.96-1.15). Finally, in Model 4 which additionally adjusted for past year pregnancy, the aORs were largely unchanged: the aORs were 1.04 (95% CI:0.93-1.16) for the public health dose of exercise, and 1.04 (95% CI:0.96-1.14) for some exercise.

In Model 4, some covariates were associated with lifetime history of MDE including marital status, employment, lower income and BMI. Compared to married women, the odds of having depressive prevalence was 1.49 (95% CI: 1.36-1.64) times higher in unmarried women. The odds of MDE were 1.30 (95% CI: 1.18-1.43) times greater in unemployed women of reproductive age compared to employed women. Women in households that earned less than \$19,000 had 2.31 (95% CI: 2.07-2.57) times the odds of MDE compared to women in households that earned >\$70,000, following the expected inverse gradient. BMI was also associated with MDE, as women who were overweight/ obese had 1.49 (95% CI: 1.40-1.59) times the odds of current MDE compared to women who not overweight.

5c. Exercise and its Association with First Onset MDE (Incidence):

Table 4 displays the results from the multiple logistic regression models for the relationship between self-reported past-year exercise and first onset MDE. In Model 1, which adjusted for age, and race, some exercise was associated with lower odds of first onset MDE (aOR=0.78, 95% CI: 0.67-0.91), while public health dose did not show a significant difference (aOR=1.14, 95% CI:0.92-1.41) compared to no exercise. Model 2 examined this association controlling for the covariates in Model 1 as well as education, marital status, employment, income and household number. After controlling for these covariates, there was no significant difference between some exercise and no exercise (aOR=0.87, 95% CI:0.75-1.01). The aOR for the public health dose of exercise was 1.17 (95% CI: 0.94-1.45). Model 3 examined this association while controlling for all of the covariates in Models 1 and 2 as well as BMI. The aORs across the exercise categories changed only slightly. Finally, in Model 4 which adjusted for all covariates in Model 3 in addition to past year pregnancy the aORs were largely unchanged. The public health dose of exercise was associated with 1.17 (95% CI:0.94-1.44) times the odds of first onset MDE compared to women who never exercised, and some exercise was associated with 0.87 (95% CI:0.75-1.01) times the odds of first onset MDE relative to women who never exercised.

Across all models, certain covariates were also significantly associated with first onset MDE such as marital status, and income compared to the controls. In Model 4, women who were not married, had 1.26 (95% CI: 1.02-1.55) times the odds of being diagnosed with first onset MDE compared to women who were married, and women who made \$19,000 or less had 2.83 (95%

CI: 2.24-3.57) times the odds of having new incidence of MDE compared to women who made \$70,000 or more. All other covariates did not yield statistically significant results.

Finally, our test for effect modification did not find evidence for an interaction between exercise and age.

Chapter 6: Discussion

The objective of this study was to examine the association between physical activity and MDE in women of reproductive age in NESARC 2004-2005. My findings show that the prevalence of MDE in this population of women was 12.5%, which is consistent with current literature and highlights a significant public health issue.¹² This study provides minimal data to support the study hypotheses that exercise is associated with prevalence and incidence of MDE in women of child bearing age. Contrary to our hypothesis that exercising will be associated with lower odds of current MDE, the aOR's were not significantly different across the exercise groups, in minimally- or fully-adjusted models. Our examination of exercise in relation to incident MDE found that some exercise was associated with lower odds of first onset MDE, but this finding was no longer significant after adjustment. While there is evidence that depression is effective in reducing symptoms of depression⁴⁵, our null findings suggest that it may not be as effective in protecting women against MDE.

To my knowledge, my study is one of the few to investigate the association between self-reported exercise and first onset MDE in a nationally representative sample of women of childbearing age. Prior research has often focused on the role of exercise as a treatment for MDE⁴⁵ and focuses on both males and females⁵⁶, or in smaller specialized populations such as post-menopausal women⁶⁴, pregnant/postpartum women⁶⁵⁻⁶⁹ or women suffering from cancer^{70,71}.

Our study hypotheses, of an inverse association between exercise and MDE incidence and prevalence, were based on several prior studies that examined the role of exercise and MDE in women of reproductive age. For example, in a prospective study of 496 adolescent women, exercise was associated with lower increases in depressive symptoms over time, and lower risk for incidence of major-minor depression.⁷² In another prospective study using data from the National Population Health Survey (NPHS, n=17,276), researchers found that leisure time physical activity (LTPA) was associated with a reduced risk of the development of MDE in women.⁵² Women who were active at baseline and remained active for the subsequent two years were less likely to report MDE at a four year follow up compared to inactive women.⁵² Although in this study the recommended dose of exercise was not significantly associated with reduced prevalence or incidence of MDE, the direction of the association between some exercise and first onset MDE shows a protective effect that is consistent with current research on this population of women.

Importantly, my results showing a null association between exercise and MDE are not unfounded, and are consistent with a subset of existing studies as well. In a review of thirty prospective studies, null findings were reported in five of them.⁵⁶ For example, in a prospective cohort of 2,093 adolescents aged 11-14, there was no evidence for an association between a change in exercise from baseline to follow up (2 years later) and depressive symptoms at follow-up.⁷³ Another prospective observational study of 973 midlife physicians found that self-reported MDE risk was similar for non-exercisers and exercisers.⁷⁴ Of the five studies reviewed, only one was considered to be of high methodological quality, and two only focused on elderly adults.

Four out of the five studies also only measured the frequency of physical activity and did not measure intensity which could have led to the null findings, and 3 of the five studies did not control for confounders such as BMI and SES which have been found to be associated with depression.⁵⁶ Notably, our findings are also in line with a study utilizing NESARC II dataset that examined if vigorous exercise was cross-sectionally associated with reduced prevalence and incidence of MDE in men and women of all ages. Specifically, this study found no association, and concluded that the relationship between exercise and mental illness is more complex than once thought.⁶¹

While our null findings are similar to the few aforementioned studies, a majority of the research does show an association between exercise and reduced risk of ME, albeit they are prospective in nature unlike our study. Some possible explanations for our null findings could be due to the cross-sectional measure of exercise which does not give a comprehensive look at exercise patterns month to month, and types of exercise engagement. An effect may have been obscured because of any changes in the level or type of exercise at the start of the year to the end. The measure of activity focused solely on the past year may have not been sensitive enough to changes in mental health status. This may have been too short to allow for changes in depressive symptoms, as a majority of prospective studies have followed up anywhere from 1 year to 27 years.⁵⁶ Additionally, in a similar study conducted by Dakwar who observed the relationship between exercise and depression in all adult participants of NESARC, he observed that higher levels of vigorous activity were related to alcohol dependence and bipolar disorder.⁶¹ This suggests that there could be a variance in the relationship between exercise and depression

among those with other types and severities of mental illnesses, and was a relationship that was not controlled for in our sample.

Results of this study also show that MDE prevalence is associated with marital status, employment, income and BMI which is consistent with other studies. For example, in a study observing the relationship between obesity and MDE, women who had higher BMI had 1.57 times the odds of having increased depressive symptoms compared to women with lower BMI's.⁷⁵ Numerous cross sectional studies support our findings that low socioeconomic status is associated with an increased prevalence in MDE.^{76,77} Finally, the association we observed for unemployment is consistent with another study reporting that individuals who are unemployed have more than 3 times the odds of MDE compared to those with employment.⁷⁸ These results suggest that many factors may contribute to the current prevalence and incidence of MDE among women of child bearing age.

Study Strengths and Limitations:

Strengths:

One major strength of this study is that it consists of a nationally representative sample, with a relatively large sample size. Another strength is the validity of the MDE diagnosis based off of the AUDADIS-IV. Moreover, our analysis included an observation of not only current MDE, but first onset MDE. Our examination of prevalent and incident cases provides a more complete life course perspective of MDE and potential associations with exercise. To date there have been no

studies that examine the relationship between exercise and both of these MDE outcomes in a nationally-representative sample of women.

Limitations:

Exercise is only measured at NESARC II, which meant that we could only conduct a cross-sectional analysis, and does not allow for a comprehensive look at exercise pattern and behaviors. The cross-sectional nature of this design also limits our ability to examine causal relationships between exercise and MDE. Another limitation is that exercise is a self-reported measure, which may lead to an underestimation or overestimation of the variable, and due to the self-reported nature engagement is impossible to directly ascertain. Although it may not be feasible to objectively measure exercise in large cohorts, self-reported measures are prone to recall and social desirability bias and focuses on exercise behavior instead of energy expenditure.⁵⁶

Future studies

The role of exercise as a preventative tool is still not well understood. In light of existing studies documenting an association between exercise and lower symptoms of MDE, it makes sense from a population perspective to shift focus toward preventing depressive onset. Future studies to advance our understanding of this association require a rigorous design that includes large sample size and repeated measures of MDE and physical activity levels over time. Future studies should also utilize more precise measures of exercise such as accelerometers, as a majority of the measures are self-reported which can add bias to the study.⁵⁶ In addition, there is a need for

studies that allow careful consideration of these associations in antenatal and postpartum samples, given the public health significance of this group. Finally, future research should also consider interactions between demographic covariates and exercise. For example, in a longitudinal study among 17,276 participants, women who were divorced, separated or widowed who did not engage in physical activity had 4.2 times the risk of developing MDE compared to women who were active.⁵² This risk of MDE was not as high among women who were married/common-law/living with a partner.

Public Health Significance

The most significant public health issue facing developed nations today, is MDE, as it is predicted to make one of the most significant contributions to overall global disease burden by 2020.⁵⁶ MDE can lead to increased risk of suicide, interpersonal problems, unemployment, decline in productivity, substance abuse, and poor maternal and infant outcomes. In the U.S., the growing burden of MDE is \$210 billion per year⁷⁹ and if it has the potential to turn into antepartum and postpartum depression, can also play a significant role in the total expenditure. Antepartum depression and its association with premature births is one possible cost to take into account, as premature births cost \$51,600 per infant.⁸⁰ Children of mothers suffering from MDE may also see an increase in lifetime medical spending, and have been found to frequent doctors and the emergency more than children whose mothers do not have MDE.⁸¹

Although our study did not document an association between exercise and prevalent or incident cases of MDE in women of child bearing age, other research has found that exercise is

associated with fewer depressive symptoms in women. Findings from the present study although not significant, express a possible association between some exercise and reduced incidence of MDE, and future studies can build on this exploration to establish a more complete understanding of the potential role that exercise plays in MDE incidence in women of childbearing age. If future, larger studies are able to establish an association between exercise and first onset MDE, this will provide a foundation for prospective studies and randomized clinical trials in this population of women to establish temporality and a dose dependent relationship for policy implications. This study also features covariate information that play a role in higher depressive incidence such as race, marital status and income. This information can help support future research and aid practitioners in developing interventions to provide more support to vulnerable populations at risk for MDE, including pregnant and postpartum women.

Despite any significant findings and the limitations mentioned previously, this study is one of the first to offer a better understanding in the association between exercise and first onset of MDE in a nationally representative sample of reproductive aged women. The current findings can be interpreted to offer support that exercise may have a role in MDE onset in women of childbearing age. Prospective studies with state-of-the-art measures of exercise are needed to examine this seemingly complex relationship between exercise and first onset MDE in this population.

MPH Competencies Addressed

The table below illustrates the MPH competencies that will be addressed in this thesis

Competencies for MPH in Epidemiology	Thesis	Addressed
1) Identify vital statistics and other key sources of data for epidemiological purposes	X	Introduction section, and background to the thesis
2) Describe a public health problem in terms of magnitude, person, time and place.	X	Examine factors associated with depression in reproductive aged women
3) Discuss the principles and limitations of public health screening programs.		
4) Comprehend basic ethical and legal principles pertaining to the collection, maintenance, use and dissemination of epidemiologic data.	X	Getting IRB approval
5) Explain the importance of epidemiology for informing scientific, ethical, economic and political discussion of health issues.	X	Epidemiologic analysis of variables associated with exercise and first onset / prevalence of depression
6) Apply the basic terminology and definitions of epidemiology.	X	Data analysis and interpretation
7) Calculate basic epidemiology measures.	X	Descriptive statistics displaying socio-demographic characteristic in the sample of reproductive aged women in NESARC
8) Communicate epidemiologic information to lay and professional audiences.	X	Thesis report, oral proposal of the thesis and final presentation
9) Differentiate among the criteria for causality.	X	Discussed in limitations section
10) Draw appropriate inferences from epidemiologic data.	X	Results and discussion section of thesis
11) Describe epidemiologic study designs and assess their strengths and limitations.	X	Discussion section of the thesis
12) Evaluate the strengths and limitations of epidemiologic reports.	X	Discussion of both in the conclusion of the report
13) Calculate advanced epidemiology measures.	X	Multinomial regression models, odds ratios

14) Design, analyze, and evaluate an epidemiologic study.	X	Designed, and analyzed data for thesis
15) Demonstrate skills in public health data collection and management.	X	Managing NESARC dataset
16) Design interventions to reduce prevalence of major public health problems.	X	Examine the role of exercise as a possible intervention for depression
17) Demonstrate program administration and organizational leadership.		

Tables

Table 1: Sociodemographic Characteristics of women of child bearing age with a prevalence of MDE for our full¹ (n=8,175) and restricted² (n=5,838) analytic samples, stratified by self-reported past-year exercise ; National Epidemiologic Study of Alcohol and Related Conditions, Wave 2 (2004-2005)

Full sample: all women of childbearing age, including those
with lifetime history of depression (n=8,175)

Restricted sample: only women of childbearing age eligible
for first onset of depression in past 12 months (n=5,838)

	Public health dose N=1885 (23.98%)	Some exercise N=3731 (47.97%)	No exercise N= 2559 (28.05%)	Public health dose N=1346 (23.80%)	Some exercise n=2625 (47.84%)	No exercise N=1867 (28.36%)
Characteristic						
Race % (SE)						
White	71.46(0.66)	70.61(0.35)	50.98(0.60)	69.37(0.73)	68.12(0.49)	46.59(0.72)
African American	11.68(0.42)	11.37(0.29)	18.32(0.47)	12.41(0.53)	12.62 (0.42)	19.77 (0.51)
Native American/ Asian	6.34(0.35)	6.60 (0.29)	8.85(0.23)	6.51 (0.32)	6.77 (0.23)	9.27 (0.33)
Hispanic/Latino	10.52(0.39)	11.43 (0.19)	21.85(0.34)	11.71 (0.46)	12.43 (0.25)	24.37 (0.45)
Age Mean (SE), years	33.23[0.13]	33.29[0.07]	34.26[0.08]	33.34 [0.147]	33.23[0.09]	34.05 [0.09]
Income % (SE)						
<\$19,000	19.10(0.55)	13.39(0.40)	23.07(0.46)	17.99(0.72)	12.25(0.49)	22.74(0.47)
\$20,000-\$34,000	17.99(0.45)	15.66(0.33)	22.98(0.59)	15.81(0.52)	15.58(0.33)	21.99(0.64)
\$35,000-\$69,000	34.94(0.70)	36.41(0.47)	30.95(0.59)	37.07(0.84)	36.28(0.54)	32.22(0.69)
>\$70,000	29.98(0.51)	34.53(0.39)	22.99(0.37)	29.12(0.64)	35.89(0.42)	23.05(0.46)
Marital status % (SE)						
Married	59.79(0.68)	62.42(0.45)	61.48(0.59)	61.81 (0.83)	64.08(0.62)	63.46 (0.62)
Not Married	40.21(0.68)	37.58(0.45)	38.52(0.59)	38.19 (0.83)	35.92(0.62)	36.34 (0.62)
Education % (SE)						
Less than High School	9.90(0.38)	4.93(0.24)	15.46(0.40)	10.08(0.41)	5.28 (0.33)	15.08(0.36)
High School	21.59(0.61)	20.04(0.36)	28.69(0.50)	20.86(0.73)	19.20(0.46)	30.40(0.58)
College+	68.51(0.69)	75.03(0.38)	55.85(0.53)	69.06(0.80)	75.52(0.49)	54.52(0.54)
Employment % (SE)						
Employed	72.30(0.68)	74.66(0.47)	64.87(0.55)	73.81 (0.74)	75.16(0.58)	66.35(0.62)
Unemployed	27.70(0.68)	25.34(0.47)	35.13(0.55)	26.19(0.74)	24.84 (0.58)	33.67 (0.62)
BMI % (SE)						
Underweight/ Normal	49.96(0.71)	47.91(0.41)	47.69(0.48)	51.37(0.78)	50.92(0.56)	48.73(0.58)
Overweight/ Obese	50.04(0.71)	52.09(0.41)	52.30(0.48)	48.63(0.78)	49.08(0.56)	51.27(0.58)
Pregnant past year % (SE)						

Yes	8.34(0.33)	11.83(0.35)	14.09(0.32)	7.93(0.34)	12.55(0.40)	15.04 (0.40)
No	91.66(0.33)	88.17(0.35)	85.91(0.32)	92.07 (0.33)	87.45 (0.40)	84.96 (0.40)
Number in Household Mean, [SE]	3.5[0.019]	3.36[0.02]	3.60[0.02]	3.52 [0.02]	3.40[0.02]	3.63 [0.03]

¹sample includes all women of reproductive age in the nesarc wave 2, including those with a lifetime history of depression.

²sample includes only women eligible for first onset depression at wave 2.

Table Two: Prevalence of MDE in Women of Childbearing Age, overall and by self-reported past-year exercise; National Epidemiologic Study of Alcohol and Related Conditions, Wave 2 (2004-2005)

	Full sample (N=8175) ¹		Restricted sample (n=5,838) ²	
	Major depression at wave 2		First onset major depression at wave 2	
	N	% (SE)	N	% (SE)
Study Population	1018	12.50(0.20)	180	2.88(0.11)
By Exercise Category				
Public health dose %(se)	237	3.15 (0.10)	40	0.83 (0.06)
Some exercise % (se)	473	5.89 (0.15)	72	1.15 (0.06)
No exercise %(se)	308	3.44 (0.11)	68	0.90 (0.05)

¹ sample includes all women of reproductive age in the nesarc wave 2, including those with a lifetime history of depression.

²sample includes only women eligible for first onset depression at wave 2.

Table 3: Adjusted Odds Ratios and 95% Confidence Intervals for the association between self-reported past-year Exercise and Prevalence of MDE in women of childbearing age, (n=8175), National Epidemiologic Study of Alcohol and Related Conditions, Wave 2 (2004-2005). ¹

	Model 1 ⁴ aOR ² (95% CI)	Model 2 ⁵ aOR (95% CI)	Model 3 ⁶ aOR (95% CI)	Model 4 ⁷ aOR (95% CI)
Exercise				
Public Health Dose	1.02 (0.91-1.14)	1.07 (0.96-1.20)	1.06 (0.95-1.18)	1.04 (0.93-1.16)
Some Exercise	0.95 (0.86-1.03)	1.08(0.99-1.12)	1.05 (0.96-1.15)	1.04 (0.96-1.14)
No Exercise (ref)				
Race				
White (ref)				
African American	0.88 (0.77-1.01)	0.64(0.55-0.75)	0.59 (0.51-0.68)	0.59 (0.51-0.69)
Asian / Native American	1.02(0.88-1.20)	0.97 (0.83-1.13)	0.99 (0.85-1.16)	0.98 (0.84-1.16)
Hispanic/Latino	0.66 (0.61-0.72)	0.58 (0.53-0.64)	0.56 (0.51-0.61)	0.55 (0.50-0.61)
Age (years)	0.99 (0.98-1.00)	1.01 (1.00-1.01)	1.01 (1.00-1.01)	1.00 (1.00-1.01)
Education				
Less than High School		0.96(0.83-1.12)	0.93 (0.79-1.08)	0.93 (0.79-1.08)
High School		1.02 (0.90-1.14)	0.98 (0.87-1.10)	0.98 (0.87-1.10)
College+ (ref)				
Marital Status				
Married (ref)				
Not Married		1.52 (1.39-1.67)	1.54 (1.41-1.69)	1.49 (1.36-1.64)
Employment				
Employed (ref)				
Un Employed		1.27 (1.15-1.39)	1.28 (1.16-1.40)	1.30 (1.18-1.43)
Income				
<\$19,000		2.38 (2.13-2.66)	2.32 (2.08-2.59)	2.31 (2.07-2.57)
\$20,000-\$34,000		1.67 (1.50-1.86)	1.61 (1.45-1.79)	1.60 (1.44-1.78)
\$35,000-\$69,000		1.26 (1.14-1.40)	1.21 (1.09-1.34)	1.21 (1.09-1.33)
>\$70,000 (ref)				
Number in household		1.03 (1.00-1.06)	1.02 (0.99-1.05)	1.02 (1.00-1.05)
BMI³				
Underweight/Normal(ref)				
Overweight/Obese			1.48 (1.39-1.58)	1.49 (1.40-1.59)
Pregnant Past Year				
Yes				0.72 (0.65-0.81)
No (ref)				

¹ Logistic Regression

² aOR= adjusted odds ratio;

³ BMI= basal metabolic index

⁴ Model 1 adjusts for race, and age (years).

⁵ Model 2 includes covariates in Model 1 in addition to education, marital status, employment, number in household and income.

⁶ Model 3 includes covariates in Model 2 in addition to BMI

⁷ Model 4 includes covariates in Model 3 in addition to pregnant in the past year.

Table four: Adjusted Odds Ratios and 95% Confidence Intervals for the Association between self-reported past-year Exercise and First onset MDE in Women of Childbearing Age, (n=5838), National Epidemiologic Study of Alcohol and Related Conditions, Wave 2 (2004-2005).¹

	Model 1⁴ aOR ² (95% CI)	Model 2⁵ aOR (95% CI)	Model 3⁶ aOR (95% CI)	Model 4⁷ aOR (95% CI)
Exercise				
Public Health Dose	1.14 (0.92-1.41)	1.17 (0.94-1.45)	1.16 (0.94-1.44)	1.17(0.94-1.44)
Some Exercise	0.78 (0.67-0.91)	0.87 (0.75-1.01)	0.87 (0.75-1.01)	0.87 (0.75-1.01)
No Exercise (ref)				
Race				
White (ref)				
African American	1.32 (1.10-1.58)	0.99 (0.78-1.25)	0.98 (0.77-1.24)	0.977 (0.77-1.23)
Asian / Native American	1.15 (0.98-1.34)	1.07 (0.91-1.26)	1.07 (0.91-1.26)	1.07 (0.91-1.26)
Hispanic/Latino	1.26 (1.07-1.47)	1.05 (0.86-1.28)	1.04 (0.85-1.27)	1.04 (0.85-1.27)
Age (years)	0.98 (0.97-0.99)	0.99 (0.98-1.00)	0.99 (0.98-1.00)	0.99 (0.98-1.00)
Education				
Less than High School		0.89 (0.73-1.07)	0.88 (0.73-1.07)	0.88 (0.73-1.07)
High School		1.04 (0.78-1.37)	1.03 (0.78-1.36)	1.03 (0.78-1.36)
College+ (ref)				
Marital Status				
Married (ref)				
Not Married		1.26 (1.02-1.55)	1.26 (1.02-1.55)	1.26 (1.02-1.55)
Employment				
Employed (ref)				
Un Employed		1.11 (0.91-1.35)	1.11 (0.91-1.36)	1.11 (0.90-1.36)
Income				
<\$19,000		2.84 (2.25-3.58)	2.83 (2.24-3.57)	2.83 (2.24-3.57)
\$20,000-\$34,000		1.65 (1.19-2.28)	1.64 (1.18-2.29)	1.64 (1.18-2.29)
\$35,000-\$69,000		1.64 (1.37-1.97)	1.63 (1.36-1.96)	1.63 (1.36-1.96)
>\$70,000 (ref)				
Number in household		1.10 (1.05-1.15)	1.09 (1.04-1.15)	1.09 (1.04-1.15)
BMI³				
Underweight/Normal (ref)				
Overweight/Obese			1.04 (0.90-1.22)	1.04 (0.89-1.22)
Pregnant Past Year				
Yes				1.01 (0.88-1.16)
No (ref)				

¹ Logistic regression

² aOR: adjusted odds ratio; ³ BMI: Basal Metabolic Index

⁴ Model 1 adjusts for race, and age (years).

⁵ Model 2 includes covariates in Model 1 in addition to education, marital status, employment, number in household and income.

⁶ Model 3 includes covariates in Model 2 in addition to BMI

⁷ Model 4 includes covariates in Model 3 in addition to pregnant in the past year status.

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