DIETARY INTAKES OF SATURATED, POLYUNSATURATED, MONOUNSATURATED,OMEGA-6, AND OMEGA-3 FATTY ACIDS IN RELATION TO SELF-REPORTED ANXIETY, SELF-REPORTED DEPRESSION, AND RISK FOR CLINICAL DEPRESSION IN THE CIVILIAN, NON-INSTITUTIONALIZED ADULT POPULATION IN THE UNITED STATES

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DEDICATION

This paper is dedicated to Mango, who loved coffee and the outdoors.

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ABBREVIATIONS

ALA	Alpha Linoleic Acid
EPA	Eicosapentaenoic Acid
DHA	Docosahexaenoic Acid
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
NHANES	National Health and Nutrition Examination Survey
PHQ-9	Patient Health Questionnaire - Nine
SFA	Saturated Fatty Acid
MFA	Monounsaturated Fatty Acid
PFA	Polyunsaturated Fatty Acid
EFA	Essential Fatty Acid
TFA	Trans Fatty Acid
HEI	Healthy Eating Index
NCI	National Cancer Institute
SAS	Statistical Analysis System
USDA	United States Department of Agriculture

ABSTRACT

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DIETARY INTAKES OF SATURATED, POLYUNSATURATED, MONOUNSATURATED, OMEGA-6, AND OMEGA-3 FATTY ACIDS IN RELATION TO SELF-REPORTED ANXIETY, SELF-REPORTED DEPRESSION, AND RISK FOR CLINICAL DEPRESSION IN THE CIVILIAN, NON-INSTITUTIONALIZED ADULT POPULATION IN THE UNITED STATES

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The primary aim of this study was to elucidate any relationships between various fatty acid intakes and self-reported anxiety, self-reported depression, and risk for clinical depression in a nationally-representative sample of US adults. Other study aims were to examine usual intakes of designated fatty acids and diet quality across levels of self-reported anxiety, self-reported depression, and risk for clinical depression in the same sample. Participants (n = 5139) in this cross-sectional study were adults ($\geq$ 20 years) in the US who participated in the 2015–2016 survey cycle of the National Health and Nutrition Examination Survey (NHANES). There were no significant differences in fatty acid intakes among frequencies of self-reported anxiety. Intakes of monounsaturated fatty acids (MFA), saturated fatty acids (SFA), palmitic acid, polyunsaturated fatty acids (PFA), omega 6 fatty acids, omega 3 fatty acids, and eicosapentaenoic acid (EPA) decreased as frequency of self-reported feelings of depression increased and risk for clinical depression increased. Additionally, intake of docosahexaenoic acid (DHA)

decreased as risk for clinical depression increased. Overall Healthy Eating Index scores (HEI-scores), or diet quality, were suboptimal for all subjects. No significant differences were found for diet quality across frequencies of self-reported anxiety. There was a moderate negative correlation between self-reported depression frequency and diet quality ($p = 0.0002$). Subjects with minimal risk for clinical depression had significantly greater diet quality (measured by HEI-scores) compared to subjects with mild to severe risk for clinical depression ($p = 0.0003$). Palmitic acid was positively correlated with self-reported frequency of anxiety ($p = 0.0075$), but no other fatty acids were significant predictors of self-reported anxiety or depression, or risk for clinical depression. This study demonstrates distinct differences in how anxiety and depressive disorders impact US adults' diet quality, and that both disorders do not hold the same risks for various dietary deficiencies.

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CHAPTER I

INTRODUCTION

Although the comorbidity of anxiety and depression disorders in all reported cases is as high as 58%, the two are distinctly separate mental disorders.[1] Anxiety disorders are classified into five general categories: posttraumatic stress disorder, general anxiety disorder, obsessive compulsive disorder, panic disorder, and phobia.[1] In developed countries, anxiety disorders can affect between 15–30% of all people; with approximately 40 million adults in America alone suffering from anxiety.[2] Anxiety prevalence is high worldwide, and the chemistry behind the disorder is multifactorial and complex (lifestyle factors, dietary deficiency, hormonal imbalances, life stressors, genetics, and traumatic experiences can all contribute to anxiety).[1] Similarly, depression prevalence is high worldwide—with more than 264 million people affected.[3] Depressive disorders are also complex—resulting from a variety of social, psychological, and biological causes.[3] At its worst, depression can lead to suicide—close to 800 000 people die due to suicide each year.[3]

Fat is a major fuel source for mammals that exists in many forms and exerts various physiological effects.[4] Fatty acids are hydrocarbon chains that contains a methyl end (CH_3) and a carboxyl end (COOH).[4] Fatty acids vary in carbon chain length and degree of unsaturation, or number of double bonds within the carbon chain.[4] Fatty acids are classified into the following categories: saturated fatty acids (SFA), cis monounsaturated fatty acids (MFA), cis polyunsaturated fatty acids (PFA), and trans fatty

acids (TFA).[4] SFA contain no double bonds within the carbon chain, and the major dietary SFA range from eight to eighteen carbon atoms in chain length.[4] SFA are a source of energy and are also structural components of cell membranes.[4] MFA contain one double bond within their carbon chain, and those found in foods mainly have a double bond located seven (n-7) or nine (n-9) carbon atoms from the methyl end.[4] MFA are important in membrane structural lipids, particularly in myelin nervous tissue.[4]

PFA are fatty acids that contain more than one double bond within their carbon chain; PFA are further classified as omega-6 fatty acids, where the last double bond is six (n-6) carbon atoms from the methyl end, and omega-3 fatty acids, where the last double bond is three (n-3) carbon atoms from the methyl end.[4] PFA are components of membrane structural lipids, assist in cell signaling pathways, help maintain epithelial cell function, regulate gene expression, and select PFA are eicosanoid precusors.[4] TFA are unsaturated fatty acids that contain at least one double bond in the trans configuration; a trans double-bond configuration results in a larger bond angle than a cis configuration, resulting in an extended fatty acid carbon chain more similar to SFA rather than those of cis PFA.[4] TFA are found naturally in dairy fat and meat and are also artificially produced in food products via partial hydrogenation.[4]

The major dietary SFA include caprylic acid (8:0), caproic acid (10:0), lauric acid (12:0), myristic acid (14:0), palmitic acid (16:0), and stearic acid (18:0).[4] Since SFA can be synthesized de novo, SFA are not considered essential fatty acids.[4] The major dietary MFA include oleic acid (18:1 n-9), myristoleic acid (14:1 n-7), palmitoleic acid (16:1 n-7), vaccenic acid (18:1 n-7), eicosenoic acid (20:1 n-9), and erucic acid (22:1 n-9);

however, oleic acid accounts for about 92% of dietary MFA.[4] The primary n-6 PFA include linoleic acid (18:2), arachidonic acid (20:4), and docosapentaenoic acid (22:5).[4] Linoleic acid, which is the precursor to arachidonic acid, cannot by synthesized by the human body and therefore is an essential fatty acid.[4] The primary n-3 PFA include alpha-linolenic acid (18:3), eicosapentaenoic acid (20:5, EPA), docosapentaenoic acid (22:5, DPA), and docosahexaenoic acid (22:6, DHA).[4] Alpha-linolenic acid, which is the precursor for fatty acids EPA and DHA, also cannot be synthesized by humans and therefore is an essential fatty acid.[4]

Since their discovery in 1929, omega-3 fatty acids have been studied for their possible effects on inflammation, cognitive decline, and certain psychiatric disorders.[5] Omega-3 fatty acids include the short-chain alpha linoleic acid (ALA, 18:3), which is found in oils from flaxseed, soybean, rapeseed, and various nuts. The primary long-chain omega-3 fatty acids, EPA and DHA, can be found in fatty fish like salmon, tuna, and sardines.[5] Omega-3 fatty acids in the serum and brain have been inversely associated with the prevalence of unipolar depression, seasonal winter affective disorder, and major depressive disorder.[5-8]

Although both depressive and anxiety disorders can be impacted by inflammation in the brain, there has been a dearth of research that has explored the correlation between anxiety disorders and the intake of omega-3 fatty acids in humans and there is a scarce amount of research on the relationships between omega-6, saturated, and trans fatty-acids and the occurrence of anxiety disorders.[5,9-11] While there are studies indicating an inverse association between omega-3 fatty acids in the brain and prevalence of depressive

disorders, there has been limited research that has explored the correlation between other fatty acids (such as omega-6, omega-6: omega-3 ratio, trans fatty acids, etc.) and incidence of both anxiety and depressive disorders in humans.[5-8,11] This study aimed to explore any relationships between various fatty acid intakes and prevalence of both anxiety and depressive disorders in a nationally-representative sample of US adults. Additionally, this study examined usual intake of these fatty acids in this sample, as well as diet quality among subjects in this sample.

CHAPTER II

REVIEW OF LITERATURE

PREVALENCE OF ANXIETY AND DEPRESSION

The prevalence of anxiety and depression have shifted slightly over the years. In 2008, approximately 46.4% of respondents in a nationally representative US household survey had a history of at least one of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) disorders assessed in the survey (mood disorders, anxiety disorders, substance disorders, and impulse control disorders).[12] The most prevalent class of disorders found in this survey was anxiety disorders (28.8%), followed by impulse-control disorders (24.8%), mood disorders (20.8%), and substance use disorders (14.6%).[12] In 2019, the National Center for Health Statistics estimated that 4.7% of adults aged 18 and over had regular feelings of depression and there were 47 511 suicide deaths in the US in 2019.[13] More recently, the Centers for Disease Control and Prevention (CDC) conducted a survey to examine the COVID-19 pandemic's effect on mental health.[14] Consequently, the CDC found that the prevalence of symptoms of anxiety disorder was approximately three times those that had been recorded in 2019 (25.5% versus 8.1%) and prevalence of depressive disorder was approximately four times those that had been reported in 2019 (24.3% versus 6.5%).[14]

The Anxiety and Depression Association of America (ADAA) reports that anxiety disorders are the most common mental illness in the US, affecting 40 million adults in the US age 18 and older, or 18.1% of the population every year.[15] The ADAA also reports

that nearly one-half of those diagnosed with depression are also diagnosed with an anxiety disorder.[15] A recent 2020 study examined the 2005–2016 National Health and Nutrition Examination Survey (NHANES) to examine depression trends in US adults and estimated the prevalence of depression was 22.7%, including 15.1% for mild depression, 4.8% for moderate depression and 2.8% for severe depression.[16] In the 2015–2016 cycle alone, it was found that the estimated prevalence of depression was 19.8%, including 14.4% for mild depression, 3.7% for moderate depression and 1.8% for severe depression.[16] Although the prevalence of the US suffering with anxiety and depressive disorders has shifted throughout the years, both continue to be prominent disorders that have lasting impacts on the US population.

CHARACTERISTICS OF THOSE WITH ANXIETY AND DEPRESSION

Varying demographics appear to be more likely to experience anxiety and depressive disorders based on current research and data. Lorant et al found in 2003 that depression disproportionately affects people with lower socioeconomic status.[17] In 2017 the National Institute of Mental Health (NIH) analyzed the prevalence of major depressive episodes among US adults across varying demographics.[18] The NIH found that the prevalence of major depressive episode was higher among adult females (8.7%) compared to males (5.3%), was highest among individuals aged 18–25 (13.1%), and was highest among adults reporting two or more races (11.3%).[18] Yu et al found in 2020 that adults between the ages of 40–64 years exhibited the highest depression rates as compared to adults between the ages of 20–39 years and $\geq$ 65 years (21.4% prevalence,as compared to 19.6% and 16.2%, respectively).[16] Taken together, these studies show that

people who are female, have lower socioeconomic status, identify as two or more races, or are either 18–25 or 40–64 years of age have the highest prevalence of depression.

Physiological characteristics may contribute to risk for mental health disorders. A recent study of adults in the US reported that subjects' body mass index (BMI) was positively correlated with higher depression scores ($P < 0.001$) and higher perceived stress scores ($P < 0.001$), but not with anxiety scores.[19] This study also noted that depression and perceived stress were strongly associated with increased serum levels of pro-inflammatory markers, such as C-reactive protein (CRP); however, no association was found with anxiety scores.[19] Kodjebacheva et al in 2015 found that depressive symptoms were more strongly associated with BMI among African Americans and women than among non-Latino Whites and men.[20] Multiple studies have also found that substance use disorders (SUD) and drug use disorders (DUD) are positively correlated with levels of anxiety and depression.[21-24] Specifically, in 2016, Grant et al found significant associations between any 12-month DUD and major depressive disorder, bipolar I disorder, posttraumatic stress disorder, borderline personality disorders, generalized anxiety disorder, panic disorder, and social phobia.[24]

SCREENING TOOLS

While anxiety and depressive disorders need to be diagnosed by a healthcare professional, there are validated instruments that have been developed to assess risk for clinical risk for anxiety and depression. The Primary Care Evaluation of Mental Disorders (PRIME-ED), a rapid procedure developed for primary care physicians to diagnose mental disorders, was the first instrument designed for use in primary care that

actually diagnosed specific disorders using diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* (*DSM-III-R*) and *DSM-IV*.[25,26] The PRIME-ED is a two-stage system in which the patient initially completes a 26-item self-administered questionnaire that screens for five of the most common groups of disorders in primary care: depressive, anxiety, alcohol, somatoform, and eating disorders.[25] This was then followed by time spent by the physician administering the clinical evaluation guide to patients who scored positively on the patient questionnaire.[25] The PRIME-ED was initially validated in a 1994 study by Spitzer et al; however, despite being widely used in clinical research, its use in clinical settings had been found to be limited due to the time needed by physicians to administer the clinical evaluation guide.[25,26]

A study that validated a new self-administered version of the PRIME-MD Patient Health Questionnaire (PHQ) was released by Spitzer et al in 1999.[25] The new version combined the PRIME-ED information into a single, three page questionnaire that can be entirely self-administered by the patient (it can also be read to the patient, if necessary).[25] While the PRIME-ED assessed 18 mental disorders in total, the new PHQ assessed eight mental disorders in total by way of grouping several specific mood, anxiety, and somatoform categories into larger rubrics.[25] A marked change that was made was that, in the original PRIME-MD, response categories for depressive and somatoform symptoms were dichotomous (yes/no), while in the new PHQ response categories were expanded.[25] Patients indicate for each of the nine depressive symptoms whether, during the previous two weeks, the symptom has bothered them *not at all*, *several days*, *more than half the*

days, or *nearly every day*.[25] This expanded version of the PHQ allows it to not only be a diagnostic instrument, but it also enables physicians to measure depression severity and monitor outcomes over time.[25,27,28]

Most recently, a study conducted in 2017 assessed various screening tools for behavioral health conditions. Through systematic review Mulvaney-Day et al found that screening tools originating from the PHQ had the most testing and application within a primary care setting.[29] The modern PHQ screeners assess multiple mental and substance use disorders, such as depression in the 9-item PHQ (PHQ-9), somatoform disorders in the 15-item PHQ (PHQ-15), and anxiety disorders in the 7-item General Anxiety Disorder (GAD-7).[27,30,31] The PHQ also screens for alcohol use and eating disorders, but these scales are not promoted by the distributor for individual administration.[29,32] The PHQ-9, PHQ-15, and GAD-7 are appropriate for administering either separately or together.[29] Testing of the psychometrics for the PHQ-9, PHQ-15, and GAD-7 demonstrated good to excellent sensitivity and specificity across most relevant DSM-5 disorders with a few exceptions.[29] The GAD-7 only has fair sensitivity for panic and social phobia and low sensitivity for posttraumatic stress disorder and the PHQ-15 has only fair specificity.[29] Patel et al demonstrated, through a measurement invariance analysis of subjects from the 2005–2016 NHANES cohorts, that the PHQ-9 is acceptable to use in major US sociodemographic groups and allows for meaningful comparisons in total, cognitive/affective, and somatic depressive symptoms across these groups, extending its use to the community.[33] The PHQ-9 is the validated survey used in NHANES to assess risk for clinical depression.[34]

PREVALENCE OF PERCEIVED FEELINGS VERSUS CLINICAL SYMPTOMS OF DEPRESSION

A study by Cao et al in 2020 looked at the prevalence and misperceptions of depression in the United States utilizing NHANES. In this study, it was found that the prevalence of depressive symptoms using the PHQ-9 (significant score is ≥ 10) were 8.0% from 2015 to 2018 in the US, while 11.3% of adults reported feelings of depression weekly.[35] Depressive experience was largely misperceived in the US (Kappa agreement = 50.98%, Cohen's Kappa = 0.16, $p < 0.001$).[35] Among those categorized in the "non-depression" group based on the PHQ-9 assessment (0–4), 55.7% self-reported never felt depressed; among the mildly depressed (PHQ-9: 5–9), 37.5% reported that they had felt depressed a few times a year; among moderately depressed individuals (PHQ-9: 10–14), 15.7% reported having felt depressed monthly; among moderately severe depressed individuals (PHQ-9: 15–19), 19.9% reported having experienced depression weekly and among severely depressed individuals (PHQ-9: 20–27), 68.4% reported having felt depressed daily.[35]

Particularly, an estimated 1.1 million US adults had depressive symptoms but never felt being depressed, whereas an estimated 1.3 million US adults had no depressive symptoms but felt being depressed daily.[35] For self-reported depression, the estimated prevalence of feeling depressed at least monthly and feeling depressed at least weekly was 19.7% (95% CI, 18.5% to 20.9%) and 11.3% (95% CI, 10.3 to 12.3), respectively.[35] This study found that it is likely that self-reported depressive experience is measuring a different construct than that measured by a clinical tool.[35] This study demonstrates the

variability in responses based on whether a study is measuring self-reported feelings of depression or clinically depressive symptoms as based on a validated depression screening tool. The resulting difference between measuring depression based on self-reported or validated tools highlights the importance of indicating in a study which responses to depression will be analyzed.

RECOMMENDED DIETARY ALLOWANCES FOR FATTY ACIDS

The Institute of Medicine (IOM) released a collective report from 2002–2005 of recommended Daily Reference Intakes (DRIs) for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids.[4] The IOM lists no Adequate Intake (AI), Recommended Dietary Allowance (RDI), or Tolerable Upper Intake Level (UL) for total fat; however, there is an Acceptable Macronutrient Distribution Range (AMDR), which is set at 20–35% of total energy intake.[4] Saturated fatty acids and trans fatty acids have no AI or RDA, as there is a positive linear trend between total saturated and trans fatty acid intake and increased risk of coronary heart disease.[4] The American Heart Association's (AHA) Strategic Impact Goal Through 2020 and Beyond, a paper outlining evidence-based recommendations to improve the cardiovascular health of all Americans, provides further recommendations for saturated fatty acid intake.[36] The most recent AHA recommendations are that Americans keep their saturated fat intake to less than 7% of their total energy intake.[36] The AHA also recommends overall avoidance of trans fats (particularly hydrogenated fats); however, the AHA is unable to provide more specific recommendations due to current lack of means for monitoring consumption in nationally representative samples.[36]

There are currently no RDA, AI, or UL for total monounsaturated fat intake, total polyunsaturated fat intake, total omega-6 or omega-3 polyunsaturated fat intake, or intake of specific saturated fatty acids set by the IOM.[4] There are, however, set recommendations for essential omega-6 polyunsaturated fatty acid linoleic acid and essential omega-3 polyunsaturated fatty acid alpha-linolenic acid.[4] The IOM has AI of linoleic acid set at 17 g/day for young men and 12 g/day for young women, or an AMDR of 5–10% of energy for omega-6 polyunsaturated fatty acids (linoleic acid).[4] While it is noted that intake levels lower than the AI for linoleic acid occur in the United States without the presence of a deficiency, the IOM states the AI can provide beneficial health effects associated with the consumption of linoleic acid.[4] Similarly, the AI for alpha-linolenic acid is set by the IOM at 1.6 g/day for men and 1.1 g/day for women, or an AMDR of 0.6–1.2% of energy, for similar reasons of providing beneficial health effects and preventing deficiency.[4]

Furthermore, for omega-6:omega-3 fatty acid ratio recommendations, the FAO (Food and Agriculture Organization of the United Nations) and the WHO (World Health Organization) in 1994 recommended a general linoleic: alpha-linolenic acid ratio between 5:1 to 10:1 for adults, based on limited studies in animals, children, and adults.[4] In regards to intake of essential fatty acids EPA and DHA, the IOM proposes that approximately 10% of the AMDR for alpha-linolenic acid can be consumed as EPA and/or DHA (approximately 160 mg per day total).[4,37] As more research has been conducted on the health benefits of EPA and DHA consumption, various organizations worldwide are suggesting increasing intakes of EPA and DHA.[37] The 2015–2020 Dietary

Guidelines for Americans (DGA), as well as the more recent 2020-2025 DGA, recommend, for the general population, consumption of about 8 ounces per week of a variety of seafood, which would provide an average of 250 mg per day combined of EPA and DHA.[38,39] Both the 2015–2020 and 2020–2025 DGA recommend, for women who are pregnant or breastfeeding, increasing consumption of a variety of seafood to at least 8 and up to 12 ounces per week, which correlates with increased EPA and DHA consumption.[38,39] Also recommended by both the 2015–2020 and 2020–2025 DGA is limiting saturated fat intake to less than 10% of daily calories by replacing them with unsaturated fats, particularly polyunsaturated fats.[38,39]

DIETARY GUIDELINES FOR AMERICANS AND THE HEALTHY EATING INDEX

In 1990, Congress passed the National Nutrition and Monitoring Act, which mandated that the USDA and Health and Human Services (HHS) jointly publish the DGA every 5 years.[40] The DGA provides food-based recommendations to help prevent diet-related chronic diseases, and is an important contributor to federal nutrition programs.[40] The Healthy Eating Index (HEI), a collaboration between the USDA and the National Cancer Institute (NCI), is a measure of diet quality that assesses how well a set of foods aligns with the DGA recommendations.[41,42] The HEI was originally developed in 1995 as a tool to discern the extent to which Americans are adhering to the DGA.[41] The HEI was first revised in 2005, and has since been revised twice to conform to the most updated DGA.[41] The HEI-2015 is the most current version of the HEI in regards to

aligning with the 2015–2020 DGA.[41] At the time of this study, there was no published HEI that aligned with the most recently released 2020–2025 DGA.

The HEI-2015 includes thirteen components that best represent the key recommendations from the 2015–2020 DGA.[42] There are two groupings: adequacy components and moderation components.[42] Adequacy components represent the food groups, sub groups, and dietary components that are encouraged; while moderation components represent the food groups and dietary components for which there are recommended consumption limits.[42] For adequacy components a higher score reflects higher intakes, due to higher intakes being desirable; whereas for moderation components, a higher score reflects lower intakes, due to lower intakes being more desirable.[42] The nine "adequacy" components are: total fruits (includes 100% fruit juice), whole fruits (includes all forms except juice), total vegetables (includes legumes), greens and beans (includes legumes), whole grains, dairy (includes all milk products and fortified soy beverages), total protein foods (includes legumes), seafood and plant proteins (includes seafood, nuts, seeds, non-beverage soy products, and legumes), and fatty acids (ratio of PFA and MFA to SFA).[42] The four "moderation" components are: refined grains, sodium, added sugars, and saturated fats.[42] Further details on the breakdown of scoring for each component can be found in Appendix A.

Each of the HEI-2015 components measures compliance with a different aspect of the DGA, and each of the 13 components is assigned a standard that must be met in order to attain the maximum score.[42] All HEI components are weighted equally because they are all considered equally important.[42] However some areas of the diet (fruits, vegetables,

and protein foods) are represented by two separate components.[42] In these instances, these components receive a maximum of five points each, while all other components receive a maximum of 10 points each.[42] When all 13 components are added up, the maximum attainable HEI score is 100 points.[42] The component scores, when examined together, demonstrate a pattern of diet quality; while the total HEI score is a representation of overall diet quality.[42] The HEI scoring method follows a density scoring approach, meaning that components are calculated as a food group amount per every 1000 calories in the total amount of food consumed.[42] The only exception to this method is the fatty acids component, which is scored as a ratio of unsaturated to saturated fatty acids.[42] The density scoring approach enables HEI-scores to separate diet quality from diet quantity, allowing researchers to apply the HEI in a variety of applications.[42] The HEI has been reviewed and validated to be a reliable and effective way to examine diet quality in relation to the DGA.[43-45]

RELATIONSHIP BETWEEN DIET AND MENTAL HEALTH

The central nervous system (CNS) has the second highest concentration of lipids stored in the human body; and these lipid profiles vary greatly depending on the area of the brain.[11,46] The most abundant lipids present in the brain are not limited to omega-3 fatty acids, yet most current studies on fatty acids and mental disorders look exclusively at omega-3 fatty acids.[11] The most abundant fatty acids in the brain are palmitic acid (SFA, 16:0), stearic acid (SFA, 18:0), oleic acid (MFA, 18:1 n-9), arachidonic acid (PFA, 20:4 n-6), and docosahexaenoic acid (PFA, 22:6 n-3).[11] The limbic system is the brain's emotional-processing center and contains both white and grey matter.[11,46] The white

matter in the brain contains more saturated and monounsaturated fatty acids than polyunsaturated fatty acids.[11] White matter connects the myelinated synapses to convey signals from one neuron to another. Alternatively, grey matter, where most neuronal messages are received and computed, contains mostly omega-3 polyunsaturated fatty acids.[11]

Palmitic acid (PA) and stearic acid (SA) are the most commonly consumed saturated fatty acids; however, they may have differing effects on inflammation.[47] The most common saturated fatty acid found in the human body is PA, which can be provided via the diet or synthesized endogenously via de novo lipogenesis (DNL) from other fatty acids, carbohydrates, or amino acids.[48] Typically PA tissue content is controlled around a well-defined concentration; however, in the presence of factors such as positive energy balance, excessive carbohydrate intake (particularly mono- and di-saccharides), and a sedentary lifestyle, an overaccumulation of PA can occur.[48] This overaccumulation of tissue PA can result in dyslipidemia, hyperglycemia, increased fat accumulation, and overall increased inflammation.[48] Alternatively, SA has been found to decrease low-density lipoprotein (LDL)-cholesterol (LDL-C) levels when replacing PA in the diet.[47] Elevated LDL-C levels are a well-accepted risk factor for cardiovascular disease and systemic inflammation.[47] Therefore, researchers must consider the impact of all the constituent fatty-acid types when elucidating relationships to anxiety and depressive disorders, and not solely omega-3 fatty acids.[11]

There are a few proposed mechanistic explanations for the relationship between dietary fatty acid intake and mental disorders. The brain is sensitive to oxidative stress,

and particularly to lipid peroxidation.[49] Lipid peroxidation in the brain has been associated with various psychiatric disorders, including neurodegenerative disorders and autism disorders.[49] Additionally, meta-analyses show that antioxidant levels in the brain are typically decreased in people with various psychiatric disorders such as depression and anxiety within major depressive disorder, and they also have increased free radical levels in the brain as compared to controls.[49-51] Fatty acid levels have a direct relationship to the varying levels of antioxidants and peroxidation in the central nervous system; for example, isoprostanes, byproducts of arachidonic acid that are produced without the impact of cyclooxygenase (COX) and resemble prostaglandins, are the main biomarker of oxidative stress in the human brain.[51,52]

Eicosanoids are lipid-signaling mediators derived from arachidonic acid, a byproduct of omega-6 EFA linoleic acid, and EFA's eicosapentaenoic acid and docosahexaenoic acid, derived from the desaturation and elongation of omega-3 EFA alpha-linolenic acid.[49,53] There are four families of eicosanoids: COX mediates the synthesis of prostaglandins, thromboxanes, and prostacyclins, while lipoxygenase mediates the biosynthesis of leukotrienes.[49,53] Arachidonic acid, EPA, and DHA are substrates that compete for attachment to COX and lipoxygenases which synthesize eicosanoids. Whether or not the omega-6 or omega-3 fatty acid attaches to the enzyme determines whether the synthesized eicosanoid will have a pro-inflammatory or anti-inflammatory effect.[54]

Neuroinflammation, which influences the formation of neurodegenerative disorders like Alzheimer's and Parkinson's disease, is characterized by the continuous

activation of glial cells (microglia and astrocyte cells).[55,56] Under any neuronal injury—such as oxidative stress, acute inflammation, chronic inflammation—microglial cells release large amount of prostaglandins, which can have a protective effect or a further-detrimental effect, depending on which fatty acid it was synthesized from.[56] As mentioned previously, prostaglandins are a variety of eicosanoids, which are one of the major regulators of inflammation in the central nervous system.[49] Polyunsaturated fatty acids are important constituents of the phospholipids that comprise cell membranes of all cells in the body, and eicosanoids, which are comprised of PFAs, are key mediators and regulators of inflammation.[56] Eicosanoids derived from omega-6 fatty acids have primarily pro-inflammatory roles, while eicosanoids derived from omega-3 fatty acids have primarily anti-inflammatory roles.[56]

Additionally, through the COX and lipoxygenase pathways both EPA and DHA produce anti-inflammatory resolvins and protectins.[56] Recent research has been finding that EPA and DHA are precursors to three groups of lipid mediators: protectins, resolvins, and maresins.[57] These lipid mediators are called specialized pro-resolving mediators (SPMs) due to their direct involvement in the resolution stage of inflammation.[57] Resolvins prevent inflammation from becoming chronic, thereby preventing tissue damage and reducing risk for various diseases.[57] Protectins have a similar effect as resolvins but mainly impact brain tissues by promoting resolution of neuroinflammation and stimulating nerve regeneration.[57] Protectins synthesized in the brain have been found to have protective effects against stroke and Alzheimer's disease,

while protectins synthesized in white adipose tissue have been found to have anti-inflammatory effects on obesity and diabetes.[57]

Additionally, ceramide is a form of sphingolipid, which is a sphingoid base attached to a phospholipid tail, and sphingolipids are found heavily in the CNS.[58,59] Sphingolipids are located in the cell membranes and myelin sheaths of nerve cells and dendritic cells, having a potential impact on mental health and brain signaling.[58] Increased omega-3 fatty acid intake decreases the amount of ceramide released from degraded sphingolipids as well as pro-inflammatory arachidonic-based eicosanoids present in the central nervous system, instead favoring anti-inflammatory omega-3 fatty acid-based eicosanoid release.[56]

Research on omega-3 fatty acids' impact on mental disorders began in the 1980's, although research was scarce until the early 2000's. A 2013 randomized-control study with a 52-person sample size examined the effect of omega-3 fatty acid supplementation (500 mg DHA and 500 mg EPA) versus baseline treatment only on the occurrence of depression and anxiety symptoms in acute myocardial infarction (AMI) patients with no previous mental illness history.[6] The psychological tests used were the Beck Depression Inventory (BDI), State (S)-Trait (T) Anxiety Inventory (STAI-S or STAI-T), and the Emotional State Questionnaire (ESQ, there are four classes: ESQ1 – challenge [excitement, satisfaction, enthusiasm]; ESQ2 – threat [fear, uncertainty, worry, helplessness]; ESQ3 – benefits [contentment, joy, optimism, relief]; ESQ4 – harm/loss [anger, disappointment, depression].[6] After adjusting for age, sex, BMI, coronary artery disease severity, ejection fraction, serum troponin level and the baseline tests results,

omega-3 fatty acid supplementation was associated with decreased scores for BDI (p = 0.046), STAI-S (p = 0.03) and ESQ4 (p = 0.04).[6] Although this study only examined a very specific sub-set of the overall population (status-post AMI patients receiving medical care), the results are still an important contribution to the overall conversation.

Another recent study examined the relationship between omega-3 and vitamin E supplementation with mental health parameters in patients with polycystic ovarian syndrome (PCOS).[60] Forty subjects with PCOS (ages 20–40) were randomized into two groups: one group received a daily supplement of 1000 mg omega-3 fatty acids and 400 IU vitamin E, while the second group received a placebo supplement. After adjusting for possible confounding variables, it was found that the group consuming omega-3s and vitamin E had significantly improved BDI scores (used to assess depression, $p < 0.001$), GHQ-28 scores (used to assess anxiety and social dysfunction, $p < 0.001$), and DASS scores (used to assess depression, anxiety and stress, $p < 0.001$). These results suggest that there is an inverse relationship between increasing omega-3 and vitamin E intake and decreasing rates of anxiety, depression, and stress.[60] Although this study cannot be indicative of omega-3s independent impacts on anxiety and depression, it is still important to acknowledge.[60]

Another study examined the relationship between Atlantic salmon consumption (Vitamin D, DHA, and EPA levels) and biological markers of anxiety and self-reported anxiety.[9] Two groups received similar meals, with a set serving of either Atlantic salmon or pork/chicken/beef provided 3x/week. The findings showed that, in the group who ate salmon, there was a significant decrease in anxiety. This study had many confounding

variables that may have affected the results, including diet outside of the three set servings of protein, activity level, and other factors. Another study used data collected from the Australian Longitudinal Study on Women's Health (ALSWH) to examine the association between omega fatty acids and mental health status in women (n = 7 635).[7] They found that there was a significant association between increased alpha-linoleic acid (ALA, n-3) consumption and decreasing rates of depression and anxiety (p = 0.040 and p = 0.024, respectively).[7]

A cross-sectional study conducted in the Netherlands analyzed respondents to a survey to investigate omega-3 and omega-6 levels and rates of anxiety and depressive disorders.[8] The results showed that there were significantly higher N-6: N-3 ratios, and lower DHA levels, in participants with comorbid depression and anxiety disorders, as well as participants with only a depressive disorder, than healthy controls (p = 0.001, p = 0.015, p = 0.002).[8] Yet another study conducted in Rio de Janeiro, Brazil found that serum DHA levels < 48 micrograms/mL were associated with a 95% increased risk for having anxiety.[10]

Although artificially-derived trans fatty acids are accepted to have negative impacts on health, naturally-derived trans fatty acids (vaccenic and palmitoleic acid for example, which are produced by bacteria in the guts of ruminant animals) are more opaque in regards to their effects on human health.[61,62] Trans-vaccenic acid (18:1, n-11t) and trans-palmitoleic acid (16:1 n-7t) have been associated with reduced overall cardiovascular disease risk and improved metabolic functioning (p < 0.001).[62] Another study found that the consumption of dairy lipids (primarily SFA and TFA), when

compared to vegetable oils, resulted in a significantly increased amount of ALA and DHA fatty acids retained in brain tissue.[63] These results indicate the importance of examining various types of fatty acids and the possibility of a relation to both anxiety and depressive disorders.

Other possible dietary effects on anxiety and depression should be considered as well. Although there are mixed study results in regards to correlations between vitamin D intake and anxiety levels, there are significant studies that support the correlation between depression and vitamin D levels, indicating an impact on mood regulation.[64,65] Additionally, animal studies indicate that decreased vitamin E, or alpha-tocopherol levels, have been associated with increased anxiety in animal models.[66]

When considering the strengths and weaknesses of the current studies on this subject, most are either cross-sectional studies or randomized-control studies with relatively small sample sizes. Although cross sectional studies cannot prove cause-and-effect relationships, and a small sample may not be as representative of the overall population, cross-sectional studies are useful for hypothesis construction and indicating needs for future research. Randomized-control studies are also strong in testing and supporting, or disproving, an established hypothesis. These studies are a good start to the conversation on omega-3 fatty acids' impact on anxiety disorders.

The most recent studies suggest that omega-3 fatty acid intake, particularly EPA and DHA, may have an inverse relationship with the occurrence in adult anxiety and depression prevalence. The predominant limitations of these studies include non-generalizable samples as well as extraneous variables such as comorbid disorders or

additional nutrient supplementations. Further, there appears to be a bias towards omega-3 fatty acids, such that other fatty acids of potential significance are ignored. This cross-sectional study is the first to assess a variety of fatty acid intakes (total monounsaturated fatty acids, total saturated fatty acids, palmitic acid, total polyunsaturated fatty acids, omega 6:3 ratio, total omega 6 fatty acids, total omega 3 fatty acids, docosahexaenoic acid, and eicosapentaenoic acid) and correlations to self-reported anxiety, self-reported depression, and PHQ-9 depression scores (risk for clinical depression) in United States adults. Moreover, this study has a sample that is representative of the United States civilian, non-institutionalized adult population. This study is beneficial in providing guidance for future studies on fatty acid intake and anxiety and depressive disorders.

STUDY AIMS

Primary Aim: Elucidate any relationships between various fatty acid intakes and self- reported anxiety, self-reported depression, and risk for clinical depression in a nationally-representative sample of US adults.

Secondary Aim: Examine usual intakes of designated fatty acids in a nationally-representative sample of US adults.

Tertiary Aim: Examine HEI-scores among self-reported anxiety, self-reported depression,and risk for clinical depression in a nationally-representative sample of US adults.

HYPOTHESES

H_0: There will be no correlation between various fatty acid intakes and self-reportedanxiety, self-reported depression, and risk for clinical depression in a

nationally- representative sample of US adults.

H_a: There will be a positive correlation between saturated fatty acid intake and increased self-reported anxiety, self-reported depression, and risk for clinical depression in a nationally-representative sample of US adults. There will be a negative correlation between omega-6 and omega-3 fatty acids and increased self-reported anxiety, self- reported depression, and risk for clinical depression in a nationally-representative sampleof US adults.

H_0: There will be no variation among usual intakes of designated fatty acids in a nationally-representative sample of US adults.

H_a: There will be high usual intake of saturated fatty acid and low usual intakes of omega-6 and omega-3 fatty acids in a nationally-representative sample of US adults.H_0: There will be no correlation between HEI-scores and self-reported anxiety, self-reported depression, and risk for clinical depression in a nationally-representative sampleof US adults.

H_a: There will be a negative correlation between HEI-scores and increased self-reportedanxiety, self-reported depression, and risk for clinical depression in a nationally- representative sample of US adults.

CHAPTER III

METHODOLOGY

STUDY DESIGN

The NHANES is a national, 2-year cycle survey that uses interviews and physical examinations to assess the health and nutritional status of children and adults in America.[67] The NHANES is executed by the CDC; the data are publicly available on their website. The NHANES survey utilizes a complex, multi-stage, probability sampling design in order to produce a sample size that is both large and nationally representative of all the ages, sexes, socioeconomic classes, races and ethnicity levels, and education levels seen in the civilian, non-institutionalized population in the United States.[67] The dietary interview component is called What We Eat In America (WWEIA) and is conducted under the National Center for Health Statistics (NCHS), a partnership between the United States Department of Agriculture (USDA) and the United States Department of Health and Human Services (DHHS).[68] The Division of Health and Nutrition Examination Surveys is responsible for survey sample design and data collection, while the USDA's Food Surveys Research Group (FSRG) is responsible for collection methodology, coding, and data review and processing.[68]

PARTICIPANTS

Participants (n = 5 139) in this cross-sectional study were adults (≥ 20 years) in the United States who participated in the NHANES 2015–2016 survey cycle. Participant

demographics included age, gender, weight, BMI, ethnicity, education, family monthly poverty level index, mental health history, and dietary intake.

INSTRUMENTS

Responses from the disability survey and questionnaires were used to identify the occurrence of self-reported feelings of anxiety and depression. The disability survey includes questions related to the frequency and severity of anxious feelings and feelings of depression. Answers were obtained by trained intervewiers.[69] The survey questions on anxiety and depression are based on self-reported feelings and do not utilize *DSM-IV* verified diagnosing criteria for anxiety disorders and depression. The disability survey asks the same three questions in regards to anxiety and depression, with the first question asking: How often do you feel worried, nervous, or anxious (or depressed)? Would you say *daily*, *weekly*, *monthly*, *a few times a year*, or *never*? The second question asks if they have taken medication for these feelings. The third question asks: Thinking about the last time you felt worried, nervous, or anxious, how would you describe the level of these feelings? Would you say *a little*, *a lot*, or *somewhere in between*?

Responses to the PHQ-9 questionnaire,[34] reported interchangeably as the DPQ-I questionnaire on the NHANES website, were also utilized to identify clinical risk for depression among respondents. The PHQ-9 questionnaire utilized in the NHANES survey asks respondents to respond to these nine questions (over the last two weeks, how often have you): had little interest in doing things; been feeling down, depressed, or hopeless; had trouble sleeping or sleeping too much; been feeling tired or having little energy; had poor appetite or overeating; been feeling bad about yourself; had trouble

concentrating on things; been moving or speaking slowly or too fast; thought you would be better off dead? Each of these questions allow respondents to respond with the answers of: *not at all*, *several days*, *more than half the days*, *nearly every day*, *refused*, or *don't know*. Additionally, the PHQ-9 questionnaire also asks: How difficult have these problems made it for you to do your work, take care of things at home, or get along with people? Available responses include: *not difficult at all*, *somewhat difficult*, *very difficult*, *extremely difficult*, *refused*, and *don't know*. Response categories to the first nine questions are given a point ranging from 0 to 3, and a total score is calculated for each respondent based on the sum of points in each item—final scores can range from 0 to 27. Both self-reported and PHQ-9 assessments of depression were utilized, as previous studies have shown that both assessments measure differing outcomes.[35] NHANES does not currently include a clinical tool used to assess clinical risk for anxiety; therefore, only self-reported feelings of anxiety were analyzed.

The medication list provides data on which respondents were taking prescription medications for a comprehensive amount of anxiety manifestations: panic disorder (episodic paroxysmal anxiety) without agoraphobia, anxiety disorder (unspecified), obsessive compulsive disorder, posttraumatic stress disorder, as well as reactions to severe stress, unspecified.[70] Additionally, data is provided for participants who were taking prescription medications for both major depressive disorder and unspecified mood disorder. [70] Medication usage was utilized as a covariate, allowing for analysis to account for those who were taking prescribed medications for either anxiety or depressive disorders.

Dietary intake data are obtained from the individual foods and total nutrient intake lists published for the NHANES 2015–2016 data set. Individual food intakes were obtained from respondents through two, non-consecutive 24-hour dietary recalls; the first recall interviews were obtained in the Mobile Examination Center (MEC) and the second interviews were obtained three to 10 days later via telephone.[68] In-person dietary recalls were conducted by trained interviewers in either English of Spanish, with professional translators administering interviews in any other languages spoken by respondents. A set of measuring utensils were available in the MEC dietary interview room, and upon completion each respondent was provided with similar measuring tools and a food model booklet in order to assist for the consequent telephone interview.[68] Data were collected via the Automated Multiple Pass Method (AMPM), a five-step interview, computerized recall method.[71] Response values were then assigned codes and used to calculate estimated nutrient intake, energy intake, and other food component intakes for both day one and day two of acquired data.[68]

DIETARY VARIABLES

Fatty acid intakes that were analyzed include: total MFA, total SFA, SFA 16:0 (palmitic acid), total PFA, omega-6:3 ratio, total omega-6, total omega-3, PFA 22:6 (docosahexaenoic acid/DHA), and PFA 20:5 (eicosapentaenoic acid/EPA). To analyze total omega-6 FA intake, intakes of PFA 18:2 (linoleic acid) and PFA 20:4 (arachidonic acid) were combined. To analyze total omega-3 FA intake, intakes of PFA 18:3 (alpha-linolenic acid), PFA 20:5 (eicosapentaenoic acid/EPA), PFA 22:5 (docosapentaenoic

acid/DPA), and PFA 22:6 (docosahexaenoic acid/DHA) were combined. To analyze omega-6:3 ratio, the resulting totals of omega-6 and omega-3 fatty acids were utilized.

The HEI-2015 (Healthy Eating Index year 2015) is a measure of diet quality that scores 13 individual dietary components to assess how well a diet meets the DGA 2015–2020.[41] The HEI scores were compared among the varying degrees of self-reported anxiety, self-reported depression, and PHQ-9 depression scores. The purpose of including HEI-scores in analysis is that any relationship between fatty acid intake and mental health may be explained by diet quality. Therefore, examining HEI-scores in addition to usual intake of fatty acids allows for the subjects' overall diet quality to be considered in addition to the smaller scope of individual fatty acids.

DATA ANALYSIS

Usual intake was estimated using the National Cancer Institute (NCI) method.[72] In short, the MIXTRAN and DISTRIB macros in SAS 9.4, which are used in either a one-part or two-part model to estimate the usual intake distribution. Each fatty acid was examined for frequency of intake; if more than 5% report zero intake for a particular nutrient, that nutrient was considered episodically consumed. Subsequently, the BRR_PVALUE_CI macro was used to estimate standard errors, and confidence intervals of the point estimates. Independent, two-tailed *t*-tests were then conducted to assess for any significant differences between the various subgroups of self-reported anxiety, self-reported depression, and PHQ-9 depression scores. Proc SURVEYREG was used to evaluate the relationship between anxiety and depression prevalence with nutrient intake. Covariates controlled for included age, sex, race, vitamin D intake, tocopherol intake, and

medication usage. A *P*-value of < 0.01 was considered statistically significant. Data were analyzed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA.).

CHAPTER IV

RESULTS

SUBJECT CHARACTERISTICS

Total Sample

A total of 5139 US adults were examined for this cross-sectional study. These subjects had completed at least one, 24-hour dietary recall. The majority of subjects were female (52%). Overall, the majority of subjects had overweight or obesity (73%). The majority of subjects were either non-Hispanic White (34%) or non-Hispanic Black (21%). Most subjects had either completed some college or graduated college (55%), followed by subjects who had graduated high-school or had a GED equivalent (22%). Forty-nine percent of total subjects fell within the highest income category and had the lowest rates of poverty (Family Monthly Poverty Level Index [FMPLI] > 1.85).

Self-Reported Anxiety Frequency

Self-reported anxiety differed significantly across gender, ethnicity, education, and FMPLI category (see Table 1 in Appendix A). A higher proportion of women versus men reported feeling anxious at least a few times per year (85% versus 76%). Subjects who self-reported anxiety daily versus never were younger (45.3 ± 0.9 versus 51.1 ± 1.0) and had higher rates of poverty (FMPLI 2.7 ± 0.1 versus FMPLI 3.0 ± 0.1). Non-Hispanic Whites and multiracial subjects had the highest proportion of self-reported anxiety (84% for both groups), followed by other Hispanics (78%). Non-Hispanic Asians experienced the lowest proportion of self-reported anxiety (69%) out of all ethnicities,

followed by Non-Hispanic Blacks (75%). Seventy-one percent of adults with less than a ninth-grade education reported feelings of anxiety compared to 85% of those who graduated college or further. Subjects with the highest rates of poverty (FMPLI $\leq$ 1.30) had the highest prevalence of self-reported daily anxiety at 23%, while those with the lowest rates of poverty (FMPLI > 1.85) had the lowest prevalence of self-reported daily anxiety at 13%.

Self-Reported Depression Frequency

Self-reported depression frequency differed significantly across gender, ethnicity, education, and FMPLI category (see Table 2 in Appendix A). Women experienced depression more frequently than men (59% versus 48%). Subjects who were underweight and with class III obesity had the highest proportions of self-reported depression frequency (60% for both groups), followed by subjects with class I obesity (57%) and with class II obesity (56%). Subjects who were overweight had the lowest proportion of self-reported depression frequency (50%), followed by those who were within a normal weight range (51%). Multiracial subjects had the highest proportion of self-reported depression frequency (65%), followed by Non-Hispanic Whites (55%) and other Hispanics (54%). Non-Hispanic Asians reported the lowest proportion of self-reported depression frequency (43%), followed by Non-Hispanic Blacks (47%). Subjects who did not graduate high school or obtain a GED had the highest proportion of self-reported depression frequency (57%), while subjects that graduated college or further had the lowest prevalence of self-reported depression frequency (50%). Those who self-reported any frequency of depressive feelings had significantly lower incomes and higher rates of

poverty than those who reported never having depressive feelings. Subjects with the highest rates of poverty (FMPLI $\leq$ 1.30) had the highest prevalence of self-reported daily depression at 9%, while those with the lowest rates of poverty (FMPLI > 1.85) had the lowest prevalence of self-reported daily depression at 2%.

Risk for Clinical Depression

Risk for clinical depression (PHQ-9 scores) differed significantly across gender, BMI category, education, and FMPLI category (see Table 3 in Appendix A). A higher proportion of women versus men had a risk for clinical depression (scores equivalent to mild-severe; 29% versus 21%). Subjects with class III obesity had the highest risk for experiencing clinical depression (39%). Subjects who were underweight and within a normal weight range, or were overweight, had the lowest risk for experiencing clinical depression (23% for both groups). Multiracial subjects had the highest risk for experiencing clinical depression (36%), followed by other Hispanics (28%) and non-Hispanic Blacks (27%). Non-Hispanic Asians had the lowest risk for experiencing clinical depression (17%). Subjects who did not graduate high school or obtain a GED had the highest risk for experiencing clinical depression (36%), followed by subjects that had less than a ninth-grade education (32%). Subjects who had graduated college or further had the lowest risk for experiencing clinical depression (17%). Subjects who had existing risk for clinical depression based on PHQ-9 scores were found to have significantly lower incomes and higher rates of poverty than those who had PHQ-9 scores equivalent to minimal risk for depression. Subjects with the highest rates of poverty (FMPLI $\leq$ 1.30) had the highest risk for experiencing clinical depression (37%), while

those with the lowest rates of poverty (FMPLI > 1.85) had the lowest risk for experiencing clinical depression (20%).

DIETARY LIPID INTAKE

Overall, dietary lipid intake for all subjects appeared to favor saturated fatty acids while lacking in both omega-6 and omega-3 fatty acids. The total sample had a combined usual intake of DHA and EPA of 82.6 mg (63.4 mg DHA and 19.2 mg EPA). Although usual intake of DHA and EPA were lower in subjects who experienced anxiety daily and weekly, no significant differences were observed (see Table 4 in Appendix A).

Usual intakes of MFA, SFA, palmitic acid, PFA, omega-6, omega-3, and EPA were overall lower for subjects as self-reported feelings of depression increased; however, not all of the comparisons between groups were statistically significant. Specifically, the following comparisons were statistically significant: MFA never versus a few times a year, MFA never versus monthly, PA never versus a few times a year, PFA never versus a few times a year, and EPA never versus a few times a year (see Table 5 in Appendix A).

In regards to PHQ-9 scores, overall intakes of MFA, SFA, PA, PFA, omega-6, omega-3, DHA, and EPA decreased as risk for clinical depression increased; however, not all of the comparisons between groups were statistically significant (see Table 6 in Appendix A). Further details on lipid profiles and group comparisons, which were statistically significant, can be found in Tables 4–6.

DIET QUALITY

HEI scores (diet quality) were suboptimal for all subjects at 46.6 ± 0.6 (95% CI: 45.0, 48.2). Diet quality was equivalent and overall poor across all frequencies of self-reported anxiety. There was no linear trend observed for diet quality across increasing frequency of self-reported anxiety (see Table 4 in Appendix A).

Diet quality was poor across all frequencies of self-reported depression. Diet quality decreased as self-reported feelings of depression increased, and there was a significant linear trend ($p = 0.0002$) that demonstrated a negative correlation between depression frequency and diet quality (see Table 5 in Appendix A).

Subjects who had PHQ-9 scores equivalent to minimal risk for clinical depression had significantly greater diet quality compared to subjects who had PHQ-9 scores equivalent to mild risk, moderate risk, moderately severe risk, and severe risk for clinical depression (see Table 6 in Appendix A). This linear trend was statistically significant ($p = 0.0003$).

PREDICTORS OF ANXIETY AND DEPRESSION

Of all the fatty acids examined, only PA was found to be significantly correlated with either self-reported anxiety, self-reported depression, or risk for clinical depression. PA was positively correlated with self-reported frequency of anxiety (OR = 0.982, $p = 0.0075$), such that for every gram increase in palmitic acid intake, the odds of feeling less anxious decreased by approximately 2%. No other fatty acids were significant predictors of self-reported anxiety, self-reported depression, or PHQ-9 depression scores.

CHAPTER V

DISCUSSION

Mental health is complex, multi-faceted, and has potential nutritional implications. Omega-3 fatty acids in the serum and brain have been inversely associated with the prevalence of unipolar depression, seasonal winter affective disorder, and major depressive disorder.[5-8] However, there have been fewer studies to examine the benefits of omega-3 fatty acids for anxiety disorders, and there has been scarce research examining the relationships between other various fatty acids and the occurrence of anxiety and depressive disorders.[5-11] Consequently, this study aimed to identify potential relationships between various fatty acid intakes and self-reported anxiety, self-reported depression, and risk for clinical depression in a nationally-representative sample of US adults. Additionally, this study aimed to examine usual intakes of designated fatty acids and diet quality across levels of self-reported anxiety, self-reported depression, and clinical depression risk in a nationally-representative sample of US adults.

This **s**tudy identified that women experienced more frequent feelings of anxiety and depression, and had a greater risk for clinical depression, than men. This is consistent with findings from the NIH, which found that the prevalence of major depressive episode was higher among adult females (8.7%) compared to males (5.3%).[18] Additionally, this study found that multiracial and non-Hispanic White subjects had the highest prevalence of self-reported anxiety, and multiracial subjects had the highest prevalence for both self-reported depression and risk for clinical depression. These findings are consistent with

those from the NIH, which found that the prevalence of major depressive episode was highest among adults reporting identifying as two or more races (11.3%), American Indian/Alaskan Native (8%), or non-Hispanic White (7.9%).[18] This study also found that non-Hispanic Asians had the overall lowest prevalence of self-reported anxiety and self-reported depression, and lowest risk for clinical depression. These findings are again consistent with 2017 NIH data, which found that non-Hispanic Asians had only a 4.4% prevalence of major depressive episode.[18]

Younger adults in this study experienced anxiety more frequently than older adults; however, the same trend was not found for self-reported depression or risk for clinical depression. Although the NIH[18] and others[16] showed that the prevalence of major depressive episodes was highest among younger adults, the differences between these studies and the current can be due to differences in instrumentation, sampling design, and analysis.

Furthermore, this study found that BMI was correlated with rates of self-reported depression and risk for clinical depression, such that subjects who were underweight or with class III obesity reported the highest prevalence of self-reported depression, and subjects with class III obesity had the highest risk for clinical depression. However, there were no correlations found between BMI category and frequency of anxiety feelings. These findings again correlate with previous studies, such that in 2020, Zou et al found that BMI was positively correlated with higher depression scores ($P < 0.001$) and higher perceived stress scores ($P < 0.001$), but that the same correlation was not found between BMI and anxiety scores.[19] Additionally, Zou et al found that depression was strongly

associated with increased serum levels of pro-inflammatory markers, such as CRP, among a general obese population from the United States; however, no association was found between serum levels of pro-inflammatory markers and anxiety scores.[19] However, in 2015 Kodjebacheva et al found that depressive symptoms were more strongly associated with BMI among African Americans and women than among non-Latino Whites and men, which this study did not examine.[20]

Additionally, this study found that those with higher educational attainment tended to have higher frequency of anxiety; conversely, subjects with higher educational attainment reported lower frequency of self-reported depression and lower risk for clinical depression. Interestingly, this study also found that poverty increased as frequency of self-reported anxiety, self-reported depression, and risk for clinical depression increased. This again echoes previous studies.[17,73-77] Although previous studies have not reported observations similar to those found in regards to education, previous research has found correlations between socioeconomic status and education attainment—such that education increases as socioeconomic status increases.[78,79]

Diet quality was suboptimal for the total sample (46.6 ± 0.6). This is similar to data obtained by the USDA, which found that total HEI-2015 scores for Americans were found to be 59 out of 100 for people ages 20–64 years old and 64 out of 100 for people ages 64+.[80] Per the USDA, these scores indicate that the average American's diet does not conform to dietary recommendations.[41] There were no significant differences in diet quality among subjects who experienced varying frequencies of anxiety; however, subjects who experienced feelings of depression daily were at particular risk for

experiencing lower diet quality scores. Therefore, increasing risk for various nutritional deficiencies. Similarly, subjects who had minimal risk for clinical depression had significantly better diet quality as compared to those who had substantial risk for clinical depression. Overall, this study suggests anxiety and depressive disorders cannot be treated equivalently in patient counseling when addressing diet quality.

The total sample had a combined usual intake of DHA and EPA of 82.6 mg (63.4 mg DHA and 19.2 mg EPA), which is far below both the IOM's recommendation of approximately 160 mg per day total of EPA and/or DHA and the 2015–2020 DGA's recommendation of an average of 250 mg per day combined of EPA and DHA.[4,37,38] Only usual intake of DHA and EPA were found to decrease as self-reported frequencies of anxiety increased. However, as usual intakes of MFA, SFA, PA, PFA, omega-6, omega-3, and EPA decreased, self-reported feelings of depression were found to increase. Additionally, usual intakes of MFA, SFA, palmitic acid, PFA, omega-6, omega-3, DHA, and EPA were found to decrease as risk for clinical depression increased.

Usual intakes of various fatty acids were found to decrease as self-reported anxiety, self-reported depression, and risk for clinical depression increased, which is a novel observation. Additionally, only usual intakes of DHA and EPA were found to decrease as self-reported anxiety increased; however, usual intakes of multiple FAs were found to decrease as self-reported depression increased and risk for clinical depression increased (MFA, SFA, PA, PFA, omega-6, omega-3, DHA and EPA). This is, again, a novel observation. It was also found that PA was a predictor of anxious feelings, such that for every gram increase in palmitic acid intake, the odds of feeling less anxious

decreased by approximately 2%; however, there were no such associations found between any fatty acid and depressive feelings or risk for clinical depression. These findings support the recommendations that clinicians should not treat anxiety and depressive disorders as comparable mental health disorders when considering nutritional therapy.

For future research, incorporating additional survey cycles would likely provide results that are more relevant and applicable to current conditions in the United States, as trends in population are always changing. Additionally, more survey cycles could have been incorporated to allow for further analysis of various sub-populations of the United States. Although this is not the most current cycle of NHANES, the 2015–2016 cycle was used because, at the initiation point of this study, the full data was not available for more recent cycles of NHANES. Similarly, the HEI-2015 was utilized because the HEI-2020 was not yet fully available. As this study demonstrates, people who report feeling depressed daily have lower diet quality, future research should investigate other macronutrients or micronutrients deficiencies that people who experience daily depression may have. Additionally, this study suggests that overall diet quality, and various fatty acid intakes, may be lacking in populations who experience depressive feelings and are at risk for clinical depression—not just omega-6 and omega-3 fatty acids. This raises the question of whether it is dietary intake causing increased prevalence of depression, or if experiencing depression is leading to decreased diet quality.

This study was not without its limitations. No clinical diagnoses were used within this study, and NHANES does not currently utilize a validated measuring tool for anxiety

disorders; although the PHQ-9 and self-reported anxiety/depression frequency have been useful in previous studies.[33,81-84] Additionally, this study was not able to incorporate serum lipid levels, serum vitamin D levels, serum tocopherol levels, ceramide levels, or red blood cell membrane fatty acid composition into data analysis due to lack of such data within NHANES at the time of analysis. Serum lipid levels would likely have provided more accurate results than estimation of usual intake of fatty acids based on subjects' dietary recalls. Despite this, this study was able to control for both dietary vitamin D and tocopherol intake as covariates. Although there are mixed study results in regards to correlations between vitamin D intake and anxiety levels, there are many studies that support the correlation between depression and vitamin D levels, indicating an impact on mood regulation.[64,65] Animal studies have indicated that decreased vitamin E, or alpha-tocopherol levels have been associated with increased anxiety in animal models.[66]

Additionally, dietary recalls are more susceptible to implicit bias and human error; however, the AMPM minimizes dietary recall error and the NCI method utilized provides a validated method for assessing usual intake.[71,72] It was also beyond the scope of this study to be able to differentiate between palmitic acid obtained via the diet versus that which is synthesized de novo. Furthermore, this study did not examine SA as a potential variable, which future studies may want to examine. This study also did not include additional variables, such as supplement use, as these data were not yet available at the time of study initiation. Moreover, this study did not control for drug and alcohol use, which previous studies have shown are correlated with mental health disorders.[21-24]

Additionally, this study was not equipped to evaluate environmental factors that may impact anxiety and depressive disorders, and resultantly was unable to examine possible extraneous variables that may increase the propensity for decreased intake of various fatty acids. However, this study was able to control for many covariates deemed to likely have the most impact on interpretation—including too many covariates can increase the risk of them becoming confounding variables.

Self-reported depressive experiences and responses to current validated clinical tools for depression are likely measuring differing outcomes.[35] Because of this, both self-reported feelings of depression and PHQ-9 response scores were analyzed, enabling this study to examine the dietary impacts of both self-reported depression and clinical risk for depression in subjects. Self-reported feelings may not appropriately translate to clinical rates of depression or clinical diagnosis of depression, as they are subjective and assume the subject understands how depression is classified. Despite this, self-perceived feelings may still impact subject behavior, as was shown in this study. While only the validated PHQ-9 tool measures risk for clinical depression, and neither self-reported feelings or the PHQ-9 are alone able to diagnose depression in subjects, the results of this study show that diet quality either impacts or is impacted significantly by daily feelings of depression in addition to higher scores on the PHQ-9. The significantly lower diet quality for subjects who had daily self-reported depression demonstrates that self-perceived feelings of depression are important to monitor for in addition to clinical risk for depression, as these self-perceived feelings may also impact diet quality.

This study supports the recommendations that clinicians should not treat anxiety and depressive disorders as comparable mental health disorders when considering nutritional therapy. This study demonstrates distinct differences in how anxiety and depressive disorders impact US adult's diet quality, and that both disorders do not hold the same risks for various dietary deficiencies. Therefore, clinicians and researchers should be aware that diet quality varies among patients in the clinical setting who have feelings of anxiety, feelings of depression, or risk for clinical depression, and treatment for these patients should be individualized. Additionally, although self-reported depression and clinical risk for depression appear to measure different outcomes and have differing effects on subjects, asking patients about perceived feelings of depression would appear to be adequate in regards to screening for risk of nutritional deficiencies in a clinical setting.

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APPENDIX A

HEI-2015 Components and Scoring Standards

HEI-2015[1] Components and Scoring Standards

Component	Maximum points	Standard for maximum score	Standard for minimum score of zero
Adequacy:			
Total Fruits[2]	5	≥0.8 cup equivalent per 1,000 kcal	No Fruit
Whole Fruits[3]	5	≥0.4 cup equivalent per 1,000 kcal	No Whole Fruit
Total Vegetables[4]	5	≥1.1 cup equivalent per 1,000 kcal	No Vegetables
Greens and Beans[4]	5	≥0.2 cup equivalent per 1,000 kcal	No Dark-Green Vegetables or Legumes
Whole Grains	10	≥1.5 ounce equivalent per 1,000 kcal	No Whole Grains
Dairy[5]	10	≥1.3 cup equivalent per 1,000 kcal	No Dairy
Total Protein Foods[4]	5	≥2.5 ounce equivalent per 1,000 kcal	No Protein Foods
Seafood and Plant Proteins[4,6]	5	≥0.8 ounce equivalent per 1,000 kcal	No Seafood or Plant Proteins
Fatty Acids[7]	10	(PUFAs + MUFAs) / SFAs ≥2.5	(PUFAs + MUFAs)/SFAs ≤1.2
Moderation:			
Refined Grains	10	≤1.8 ounce equivalent per 1,000 kcal	≥4.3 ounce equivalent per 1,000 kcal
Sodium	10	≤1.1 grams per 1,000 kcal	≥2.0 grams per 1,000 kcal
Added Sugars	10	≤6.5% of energy	≥26% of energy
Saturated Fats	10	≤8% of energy	≥16% of energy

[1] Intakes between the minimum and maximum standards are scored proportionately.

[2] Includes 100% fruit juice.

[3] Includes all forms except juice.

[4] Includes legumes (beans and peas).

[5] Includes all milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages.

[6] Includes seafood; nuts, seeds, soy products (other than beverages), and legumes (beans and peas).

[7] Ratio of poly- and mono-unsaturated fatty acids (PUFAs and MUFAs) to saturated fatty acids (SFAs).

Table 1. Participant Characteristics in Adults (≥ 20 y) Across Self-Reported Anxiety Frequency, NHANES 2015-2016 Frequency of Self-Reported Anxiety.

	Total *N* = 5139	Daily *n* = 748	Weekly *n* = 753	Monthly *n* = 662	A Few Times a Year *n* = 1784	Never *n* = 1140	*P*-value
Age (y)	47.8 ± 0.6	45.3 ± 0.9*	45.0 ± 0.9	46.2 ± 1.0	49.0 ± 0.6	51.1 ± 1.0	
Gender *n* (%)							<0.0001
Female	2629 (52)	426 (18)	434 (20)	347 (14)	960 (33)	462 (15)	
Weight (kg)	83.5 ± 0.7	84.8 ± 1.2	82.5 ± 0.9	83.9 ± 1.2	83.5 ± 0.9	83.7 ± 1.2	
BMI Category *n* (%)							0.1285
< 18.5 kg/m²	71 (1)	13 (20)	10 (17)	11 (21)	23 (25)	14 (17)	
18.5 - 24.9 kg/m²	1303 (26)	180 (16)	222 (20)	166 (14)	439 (33)	296 (17)	
25 - 29.9 kg/m²	1611 (32)	195 (15)	238 (18)	211 (12)	580 (35)	387 (20)	
30 - 34.9 kg/m²	1101 (22)	182 (17)	133 (14)	140 (15)	407 (34)	239 (20)	
35 - 39.9 kg/m²	547 (11)	80 (14)	77 (17)	86 (16)	192 (34)	112 (19)	
≥ 40 kg/m²	409 (8)	89 (20)	68 (20)	41 (12)	132 (31)	79 (17)	
Ethnicity *n* (%)							<0.0001
Mexican American	896 (18)	113 (12)	117 (15)	113 (14)	328 (36)	225 (23)	
Other Hispanic	678 (13)	107 (15)	91 (13)	87 (13)	253 (37)	140 (22)	
Non-Hispanic White	1709 (34)	327 (18)	321 (20)	234 (14)	530 (32)	297 (16)	
Non-Hispanic Black	1080 (21)	128 (12)	137 (13)	129 (12)	410 (38)	276 (25)	
Non-Hispanic Asian	533 (10)	35 (6)	53 (10)	67 (13)	209 (40)	169 (31)	
Other	191 (4)	38 (22)	34 (20)	32 (13)	54 (29)	33 (16)	
Education *n* (%)							<0.0001
Less Than 9th Grade	547 (11)	77 (15)	59 (13)	63 (12)	179 (31)	169 (29)	
9-11th Grade or 12th w/ No Diploma	577 (12)	112 (22)	57 (11)	66 (11)	189 (31)	153 (25)	
High School/GED or Equivalent	1097 (22)	161 (16)	152 (16)	143 (14)	385 (34)	256 (20)	
Some College of AA Degree	1483 (30)	240 (18)	251 (19)	196 (14)	496 (31)	300 (18)	
College Graduate or Above	1260 (25)	139 (12)	210 (21)	171 (14)	500 (38)	240 (15)	
FMPLI	3.0 ± 0.1	2.7 ± 0.1*	3.1 ± 0.1	3.1 ± 0.1	3.1 ± 0.1	3.0 ± 0.1	
FMPLI Category *n* (%)							<0.0001
FMPLI <= 1.30	1684 (36)	313 (23)	259 (16)	218 (13)	517 (30)	377 (18)	
1.30 < FMPLI <= 1.85	715 (15)	113 (18)	101 (17)	93 (14)	237 (31)	171 (20)	
FMPLI > 1.85	2322 (49)	277 (13)	346 (19)	311 (14)	907 (36)	481 (18)	

*Denotes *p*-value < 0.01 compared to reference category: Never

Table 2. Participant Characteristics in Adults (≥ 20 y) Across Self-Reported Depression Frequency, NHANES 2015-2016 Frequency of Self-Reported Depression.

	Total	Daily	Weekly	Monthly	A Few Times a Year	Never	
	N = 5139	*n* = 253	*n* = 346	*n* = 417	*n* = 1646	*n* = 2425	*P*-value
Age (y)	47.8 ± 0.6	48.2 ± 1.5	45.2 ± 1.4	44.4 ± 1.2	48.4 ± 0.7	48.1 ± 0.5	
Gender *n* (%)							<0.0001
Female	2629 (52)	141 (5)	201 (8)	235 (10)	899 (36)	1153 (41)	
Weight (kg)	83.5 ± 0.7	85.5 ± 1.5	82.4 ± 1.7	83.5 ± 1.6	84.2 ± 0.9	83.2 ± 0.9	
BMI Category *n* (%)							0.0397
< 18.5 kg/m²	71 (1)	2 (1)	8 (15)	7 (11)	22 (33)	32 (40)	
18.5 - 24.9 kg/m²	1303 (26)	62 (5)	91 (6)	113 (9)	395 (31)	642 (49)	
25 - 29.9 kg/m²	1611 (32)	63 (3)	96 (7)	142 (8)	498 (32)	812 (50)	
30 - 34.9 kg/m²	1101 (22)	57 (4)	69 (6)	78 (8)	388 (39)	509 (43)	
35 - 39.9 kg/m²	547 (11)	30 (4)	46 (9)	38 (7)	196 (36)	237 (44)	
≥ 40 kg/m²	409 (8)	34 (7)	32 (8)	36 (11)	135 (34)	172 (40)	
Ethnicity *n* (%)							<0.0001
Mexican American	896 (18)	42 (4)	50 (6)	52 (6)	319 (36)	433 (48)	
Other Hispanic	678 (13)	44 (6)	52 (7)	62 (9)	209 (32)	311 (46)	
Non-Hispanic White	1709 (34)	94 (4)	134 (7)	159 (9)	578 (35)	744 (45)	
Non-Hispanic Black	1080 (21)	53 (5)	65 (6)	68 (6)	328 (30)	566 (53)	
Non-Hispanic Asian	533 (10)	8 (1)	30 (6)	49 (10)	141 (26)	305 (57)	
Other	191 (4)	12 (5)	15 (9)	27 (13)	71 (38)	66 (35)	
Education *n* (%)							<0.0001
Less Than 9th Grade	547 (11)	44 (9)	44 (7)	35 (7)	177 (31)	247 (46)	
9-11th Grade or 12th w/ NoDiploma	577 (12)	58 (10)	42 (6)	45 (7)	187 (34)	245 (43)	
High School/GED or Equivalent	1097 (22)	63 (4)	80 (8)	103 (11)	329 (30)	522 (47)	
Some College of AA Degree	1483 (30)	68 (4)	111 (8)	119 (9)	498 (35)	687 (44)	
College Graduate or Above	1260 (25)	18 (2)	54 (5)	101 (8)	422 (35)	665 (50)	
FMPLI	3.0 ± 0.1	1.8 ± 0.2**	2.5 ± 0.1**	2.7 ± 0.1*	3.1 ± 0.1	3.2 ± 0.1	
FMPLI Category *n* (%)							<0.0001
FMPLI <= 1.30	1684 (36)	141 (9)	140 (9)	157 (11)	541 (32)	705 (39)	
1.30 < FMPLI <= 1.85	715 (15)	30 (3)	58 (9)	58 (10)	225 (35)	344 (43)	
FMPLI > 1.85	2322 (49)	56 (2)	125 (5)	179 (8)	776 (35)	1186 (50)	

*Denotes *p*-value < 0.01 compared to reference category: Never

**Denotes *p*-value < 0.001 compared to reference category: Never

Table 3. Participant Characteristics in Adults (≥ 20 y) Across PHQ-9 Scores (Risk for Clinical Depression), NHANES 2015-2016 Risk for Clinical Depression.

Total *N* = 5139		Score 0-4 (Minimal) *n* = 3519	Score 5-9 (Mild) *n* = 838	Score 10-14 (Moderate) *n* = 280	Score 15-19 (Moderately severe) *n* = 108	Score 20-27 (Severe) *n* = 81	*P*-value
Age (y)	47.8 ± 0.6	47.8 ± 0.6	48.0 ± 0.9	45.9 ± 1.7	51.4 ± 1.7	48.0 ± 2.4	
Gender *n* (%)							<0.0001
Female	2456 (51)	1700 (71)	475 (18)	171 (7)	63 (2)	47 (2)	
Weight (kg)	83.5 ± 0.7	83.5 ± 0.7	84.5 ± 1.5	85.1 ± 1.6	87.3 ± 2.8	83.4 ± 2.4	
BMI Category *n* (%)							<0.0001
< 18.5 - 24.9 kg/m²	1293 (27)	973 (77)	202 (15)	71 (5)	30 (2)	17 (1)	
25 - 29.9 kg/m²	1527 (32)	1158 (77)	256 (17)	69 (3)	27 (2)	17 (1)	
30 - 34.9 kg/m²	1043 (22)	759 (75)	175 (16)	66 (5)	21 (2)	22 (2)	
35 - 39.9 kg/m²	529 (11)	370 (75)	102 (14)	36 (8)	8 (1)	13 (2)	
≥ 40 kg/m²	394 (8)	233 (61)	95 (24)	34 (9)	22 (5)	10 (1)	
Ethnicity *n* (%)							0.0121
Mexican American	861 (18)	640 (76)	142 (16)	43 (5)	21 (2)	15 (1)	
Other Hispanic	637 (13)	447 (72)	112 (17)	43 (7)	19 (2)	16 (2)	
Non-Hispanic White	1648 (34)	1180 (76)	289 (16)	105 (5)	42 (2)	32 (1)	
Non-Hispanic Black	1020 (21)	739 (73)	189 (18)	61 (6)	19 (2)	12 (1)	
Non-Hispanic Asian	474 (10)	391 (83)	63 (12)	15 (4)	3 (1)	2 (0)	
Other	186 (4)	122 (64)	43 (24)	13 (8)	4 (1)	4 (3)	
Education *n* (%)							<0.0001
Less Than 9th Grade	506 (11)	339 (68)	98 (18)	29 (5)	25 (5)	15 (4)	
9-11th Grade or 12th w/ No Diploma	552 (12)	352 (64)	120 (23)	49 (8)	14 (2)	17 (3)	
High School/GED or Equivalent	1047 (22)	750 (72)	192 (18)	61 (6)	23 (2)	21 (2)	
Some College of AA Degree	1419 (30)	1040 (74)	240 (17)	82 (5)	35 (3)	22 (1)	
College Graduate or Above	1182 (25)	959 (83)	163 (11)	45 (4)	9 (1)	6 (1)	
FMPLI	3.0 ± 0.1	3.2 ± 0.1	2.7 ± 0.1*	2.2 ± 0.2**	1.8 ± 0.2**	2.0 ± 0.3*	
FMPLI Category *n* (%)							<0.0001
FMPLI <= 1.30	1610 (36)	1023 (63)	337 (21)	144 (9)	55 (4)	51 (3)	
1.30 < FMPLI <= 1.85	680 (15)	504 (75)	113 (14)	40 (7)	18 (3)	5 (1)	
FMPLI > 1.85	2193 (49)	1738 (80)	333 (15)	76 (3)	25 (1)	21 (1)	

*Denotes *p*-value < 0.01 compared to reference category: Minimal Depression

**Denotes *p*-value < 0.001 compared to reference category: Minimal Depression

Table 4. Lipid Profiles and HEI Scores Across Adult (≥ 20 y) Self-Reported Anxiety Frequency, NHANES 2015-2016 Frequency of Self-Reported Anxiety.

	Total (*N* = 5087)	Daily (*n* = 748)	Weekly (*n* = 753)	Monthly(*n* = 662)	A few times a year(*n* = 1784)	Never (*n* = 1140)	*P*-value for Linear Trend
MFA (g)	30.1 ± 0.4	30.2 ± 0.5	30 ± 0.5	30 ± 0.4	30 ± 0.5	30.5 ± 0.6	0.5288
SFA (g)	28.1 ± 0.4	28.2 ± 0.5	28.1 ± 0.4	28.1 ± 0.4	28.0 ± 0.5	28.4 ± 0.4	0.5001
PA (g)	15.2 ± 0.2	15.4 ± 0.2	15.2 ± 0.2	15.2 ± 0.2	15.1 ± 0.3	15.3 ± 0.3	0.6046
PFA (g)	19.6 ± 0.3	19.7 ± 0.5	19.6 ± 0.4	19.6 ± 0.3	19.5 ± 0.3	19.7 ± 0.3	0.5744
Omega 6:3 (g)	10.1 ± 0.1	10.2 ± 0.2	10.2 ± 0.2	10.1 ± 0.1	10.1 ± 0.1	10 ± 0.1	0.0075
Omega 6 (g)	17.5 ± 0.3	17.6 ± 0.4	17.5 ± 0.4	17.4 ± 0.3	17.4 ± 0.3	17.5 ± 0.3	0.5656
Omega 3 (mg)	1950 ± 37.4	1949 ± 55.3	1942 ± 45.4	1946 ± 40.4	1950 ± 38.7	1980 ± 42.9	0.145
DHA (mg)	63.4 ± 3.8	61.7 ± 4.4	61.1 ± 4.1	62.7 ± 3.8	64 ± 3.8	66.2 ± 5.2	0.0233
EPA (mg)	19.2 ± 1.3	17.9 ± 1.4	18.3 ± 1.2	19.1 ± 1.3	19.6 ± 1.4	20.7 ± 1.6	0.0026
HEI Score	46.6 ± 0.6	45.9 ± 0.8	47.4 ± 1.0	47.0 ± 0.8	47.1 ± 0.9	45.3 ± 0.7	0.7112

MFA = monounsaturated fatty acids; SFA = saturated fatty acids; PFA: polyunsaturated fatty acids; DHA = docosahexaenoic Acid; EPA= eicosapentaenoic Acid; HEI = Healthy Eating Index

Covariates adjusted for include age, sex, race, vitamin D intake, tocopherol intake, and medication usage.

Table 5. Lipid Profiles and HEI Scores Across Adult (≥ 20 y) Self-Reported Depression Frequency, NHANES 2015-2016 Frequency of Self-Reported Depression.

	Total (*N* = 5087)	Daily (*n* = 253)	Weekly (*n* = 346)	Monthly(*n* = 417)	A few times a year(*n* = 1646)	Never (*n* = 2425)	*P*-value for Linear Trend
MFA (g)	30.1 ± 0.4	28.6 ± 0.9	29 ± 0.7	29.5 ± 0.5*	29.9 ± 0.4*	30.8 ± 0.4	0.0045
SFA (g)	28.1 ± 0.4	27.8 ± 0.6	27.9 ± 0.6	28 ± 0.5	28 ± 0.4	28.4 ± 0.4	0.0047
PA (g)	15.2 ± 0.2	14.6 ± 0.4	14.8 ± 0.3	15 ± 0.2	15.1 ± 0.2*	15.5 ± 0.2	0.0039
PFA (g)	19.6 ± 0.3	18.5 ± 0.7	18.8 ± 0.5	19.2 ± 0.4	19.4 ± 0.3*	20 ± 0.3	0.0016
Omega 6:3 (g)	10.1 ± 0.1	10.2 ± 0.3	10.2 ± 0.2	10.2 ± 0.2	10.1 ± 0.1	10.1 ± 0.1	0.0104
Omega 6 (g)	17.5 ± 0.3	16.5 ± 0.7	16.8 ± 0.5	17.1 ± 0.4	17.3 ± 0.3	17.8 ± 0.3	0.002
Omega 3 (mg)	1950 ± 37.4	1820 ± 84.5	1856 ± 65.8	1898 ± 51.4	1940 ± 37.0	2000 ± 39.6	0.0005
DHA (mg)	63.4 ± 3.8	63.7 ± 3.7	62.4 ± 3.9	62.1 ± 4.3	62.8 ± 3.7	64.2 ± 3.8	0.0098
EPA (mg)	19.2 ± 1.3	16.2 ± 1.0	17.1 ± 1.0	18 ± 1.1	18.8 ± 1.2*	20.4 ± 1.6	0.0016
HEI Score	46.6 ± 0.6	40.6 ± 1.8**	46.8 ± 1.1**	47.4 ± 0.9**	47.9 ± 0.5*	46.1 ± 0.7	0.0002

MFA = monounsaturated fatty acids; SFA = saturated fatty acids; PFA: polyunsaturated fatty acids; DHA = docosahexaenoic Acid; EPA = eicosapentaenoic Acid; HEI = Healthy Eating Index

Covariates adjusted for include age, sex, race, vitamin D intake, tocopherol intake, and medication usage.
*Denotes *p*-value < 0.01 compared to reference category: Never
**Denotes *p*-value < 0.001 compared to reference category: Never

Table 6. Lipid Profiles and HEI Scores Across Adult (≥ 20 y) PHQ-9 Scores, NHANES 2015-2016 Risk for Clinical Depression.

	Total (*N* = 4843)	Minimal Depression(*n* = 3529)	Mild Depression (*n* = 842)	Moderate Depression(*n* = 280)	Moderately Severe Depression (*n* = 108)	Severe Depression(*n* = 84)	*P*-value for Linear Trend
MFA (g)	30.1 ± 0.4	30.9 ± 0.4	28.8 ± 0.4**	26.9 ± 0.6**	25.7 ± 1.0**	25.6 ± 1.0**	0.0099
SFA (g)	28.1 ± 0.4	28.8 ± 0.4	27.1 ± 0.5*	25.6 ± 0.7*	25.0 ± 1.0**	25.3 ± 1.2**	<0.0001
PA (g)	15.2 ± 0.2	15.6 ± 0.2	14.7 ± 0.2**	13.9 ± 0.3**	13.5 ± 0.5*	13.7 ± 0.6	0.0308
PFA (g)	19.6 ± 0.3	20.1 ± 0.3	18.8 ± 0.4**	17.6 ± 0.4**	16.8 ± 0.7**	16.6 ± 0.8**	0.0049
Omega 6:3 (g)	10.1 ± 0.1	10.1 ± 0.1	10.2 ± 0.1	10.2 ± 0.2	10.3 ± 0.3	10.4 ± 0.4	0.01
Omega 6 (g)	17.5 ± 0.3	17.9 ± 0.3	16.8 ± 0.3**	15.7 ± 0.4**	15.0 ± 0.7**	14.8 ± 0.7**	0.0056
Omega 3 (mg)	1950 ± 37.4	2000 ± 37.1	1867 ± 45.6**	1733 ± 57.5**	1636 ± 82.2**	1578 ± 89.7**	0.0016
DHA (mg)	63.4 ± 3.8	64.1 ± 4.2	60.1 ± 3.7	56.5 ± 4.1	50.4 ± 4.7*	47.7 ± 6.1	0.0005
EPA (mg)	19.2 ± 1.3	19.9 ± 1.5	17.4 ± 1.2*	15.5 ± 1.2*	13.2 ± 1.3**	12.4 ± 1.5**	0.0014
HEI Score	46.6 ± 0.6	51.3 ± 0.6	49.9 ± 0.5**	48.2 ± 0.5**	46.9 ± 0.7**	44.7 ± 0.8**	0.0003

MFA = monounsaturated fatty acids; SFA = saturated fatty acids; PFA: polyunsaturated fatty acids; DHA = docosahexaenoic Acid; EPA= eicosapentaenoicAcid; HEI = Healthy Eating Index

Covariates adjusted for include age, sex, race, vitamin D intake, tocopherol intake, and medication usage.

Minimal depression = scores 0-4; mild depression = scores 5-9; moderate depression = scores 10-14; moderately severe depression = scores 15-19; severedepression = scores 20-27

*Denotes *p*-value < 0.01 compared to reference category: Minimal Depression

**Denotes *p*-value < 0.001 compared to reference category: Minimal Depression