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Anxiety, Depression, Immunity, Quality of Life, and Cannabis in Appalachia

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Abstract

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MA, Radford University, 2015

BS, Western Carolina University, 2013

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of Doctor of Philosophy

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Abstract

As decriminalization of cannabis in the United States increases, understanding how cannabis use may alter physical and mental health is important. The Appalachian Mountain region is an area with poor support systems, stigma against mental health, and historic drug use problems, resulting in residents being more vulnerable to societal change. The theoretical framework for this quantitative research was psychoneuroimmunology (PNI), which is the study of the interconnections between psychology, neurology, and immunology as a holistic approach to health. Via SurveyMonkey, 160 participants completed the study, and data were based on self-reporting of cannabis use patterns in relation to anxiety, depression, immunity, and quality of life. This quantitative research study involved using multiple regression analysis to determine if relationships exist between longevity and frequency of cannabis use and anxiety, depression, immune function, and quality of life. Findings revealed that longer histories of cannabis use reduced anxiety and depression levels, while frequency of use had a non-linear relationship with anxiety where low and high frequency of use reduced scores compared to intermittent use. Cannabis was found to worsen immune function scores. Quality of life was unaffected by cannabis use frequency or longevity, but perceived quality of life improved. The data set was created to capture a baseline for future research involving the Appalachian Mountain region to improve the livelihood and quality of life of residents and protect them from further exploitation thus leading to positive social change.

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Dedication

This study would not be possible without the inspiration of my master's thesis advisor, Dr. Pamela Jackson of Radford University. I was perhaps not the best student that you could have worked with, but I am eternally grateful that you took the time to educate and advise a young, reckless student and gave me direction to help mold and improve my life.

I also want to dedicate this work to my wife, Moira, who as both a teacher and student of our life together has helped me to stay grounded and consider things from perspectives that I would have never been able to articulate or empathize with. It is through my exploration of the Tennessee mountains with you that I have been able to further understand and appreciate these smokey hills enough to find a drive to help those around, even if we do not agree with many of our community members' lifestyles or beliefs, because it is the proper Appalachian thing to do.

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I want to give an acknowledgment to my dissertation advisor, Dr. Jay Greiner, who has kept me on task while being understanding of the delicate balance of work, mental well-being, and quality of life. We have had many great conversations and I hope to continue doing so for many years. As well, Dr. Craig Marker, I have enjoyed our time working together and look forward to working together further towards publication.

I also want to acknowledge Equilibar, a company of people with amazing leaders who saw potential in this author and treated me far kinder than I could have imagined. It is through your encouragement and respect that I believe I found the drive to pursue a PhD after nearly giving up many times. Thank you so much, especially to David, Sam, and Jeff.

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Chapter 1: Introduction to the Study

The recent legalization of cannabis in states but not nationwide has created an unusual scenario in which a substance previously deemed to be illicit is legal for individuals to consume, but not capable of being properly researched due to federally enforced laws complicating the investigation of cannabis for human studies. While research is not illegal for schedule 1 substances, the barriers to entry are numerous, including legality issues, substance use/abuse stigma, and funding concerns (Andreae et al., 2016). With recent legislation proposed to decriminalize cannabis in the United States, social change will occur with or without an informed understanding of how the usage of cannabis will alter overall health. More thorough research regarding cannabis is not only imperative, but essential for the wellbeing of individuals who currently use the substance to ensure their prolonged safety.

Background

Until recently, research on cannabis has included unfounded negative biases against cannabis, products of the reefer madness craze of the 1930's and 40's (Hirliman, 1936). Public opinion has altered significantly, with an increase in support from Democratic and independent adults in the U.S., while Republican support has increased in recent years, though not as significantly (Swift, 2016). Due to historic research stigma, recent studies are having to develop against the existing negative perception of cannabis use perpetuated by poor quality research. Simultaneously, society has allowed general

access to cannabis faster than scientists can measure cannabis health effects to ensure safety of use.

When observing social and health effects of people in the U.S., specific regions are often overlooked in terms of resources and healthcare. The Appalachian Mountain region, consisting of 420 counties from Mississippi to New York (Appalachian Regional Commission, 2011) has a population of highly vulnerable citizens due to the increased frequency of economic and mental health issues (Lao et al., 2017; Grunberg et al., 2015; Post et al., 2013). Further, while many regions have regular access to food, portions of the Appalachian region are part of a food desert where many individuals consume less healthy diets due to economic struggle and poor food availability (Wattick et al., 2018). With a population that lives with consistently underreported and underserved mental health facilities, the people of Appalachia are vulnerable and may be affected more significantly by federal legalization and decriminalization.

As Appalachia has a history of stigma in terms of mental health treatment (Gore et al., 2016), they are often not offered or sought due to cultural or geographic conflicts. Cannabis is illegal in most Appalachian states (West Virginia, Virginia, and New York are in the legal processes of decriminalization and/or legalization), despite being the historical center of most domestic marijuana farming (Stone, 2019). Illegal cannabis use is not uncommon, and 15% of Americans use the drug despite being illegal (Substance Abuse and Mental Health Services Administration [SAMHSA], 2018). With 25 million people living in the Appalachian region, despite a lack of scientific understanding

regarding safety or the complexities of use, roughly 3.75 million Appalachian people are assumed to be using or have used cannabis regularly (Appalachian Regional Commission, 2011).

While I hoped to find some beneficial outcomes of cannabis use, the safety of individuals in terms of federal legalization is a concern. By measuring overall quality of life for individuals who already consume cannabis, more careful approaches to protecting and assisting the people of Appalachia were addressed. While there may be evidence of beneficial outcomes of cannabis use, safety in terms of how cannabis is used must be addressed.

Problem Statement

Quality of life and psychological conditions of individuals living in the Appalachian Mountain region may be altered via cannabis use. Recent calls for research have elicited studies seeking to expand our understanding of cannabis use and its effect on our mental and physical well-being (Anderson, 2017; Meier et al., 2016). The natural form of cannabis, flower marijuana, is in the process of investigations for the first time on humans, however self-reports express that cannabis is helpful for psychological wellbeing (Anderson, 2017; Grunberg et al., 2015; Lao et al., 2017). How cannabis affects overall quality of life (no effect seen in Aspis et al., 2015; reduced QoL as seen in Liao et al., 2019) and immune function (increased pro-inflammatory effects as seen in Bayazit et al., 2017) are two factors now associated with mental wellbeing. Cannabis use is undergoing a research paradigm shift and expanding research will be vital to

understanding how cannabis may alter mental health and quality of life for individuals. Currently, mixed evidence has shown both positive effects (such as reduced pain, improved sleep, and reduction of nausea) and negative effects (lung and heart damage, cancer risk, increased anxiety) on overall health of individuals using cannabis and have come under scrutiny for some claims in past research (LaMarine, 2012).

Cannabis has recently become legal in half of the U.S. for both medicinal and/or recreational use. Federally, this leads to issues in terms of funding for studies to ensure safety and investigate long-term effects of cannabis use on individuals (Yeager, 2019). By collecting survey data from current users in Appalachia, a data set was developed to help predict anxiety, depression, immunity, and quality of life scores related to different longevities and frequencies of cannabis use. From this data, an understanding of self-reported cannabis use gave insight into predictability of anxiety, depression, immune function, and quality of life scores. By predicting these relationships, a more considerate understanding of cannabis use in Appalachia can help promote the appropriate action in future safety decisions for the region.

With cannabis likely to be legalized for various uses nationwide in the next decade, understanding use and patterns of use among self-treating and recreational users is important to curtail a future health crisis like nicotine use in the 1990s (United States v. Philip Morris, 2006). By collecting information on consumers' self-reported longevity and frequency of use and scores on measures of anxiety, depression, immunity, and quality of life, the data set can help when comparing methodical approaches to cannabis

use over time. Use patterns are measures of longevity of use compared across individuals to determine any long-term relationships, while frequency of use (days per month) helped to determine how frequent use could predict any relationships with scores on measures of anxiety, depression, quality of life, and immunity.

Immunity in relation to use of cannabis is a more recent idea in the field with limited research. When observing the direct effect of cannabis consumed by smoking, measures of increased inflammation markers (interleukin-6, interleukin-8, and tumor necrosis factor- α) were found in individuals with cannabis use disorder (Bayazit et al., 2017). Conversely, when observing individuals with HIV undergoing retroviral treatments with cannabis use disorder, tumor necrosis factor-α, as well as $CD4^+$ and $CD8^+$ T-cells, all inflammatory markers, were significantly reduced compared to controls (Manuzak et al., 2018). Connections between the endocannabinoid system, use of cannabis, and the immune system are still being investigated, indicating a need to understand how cannabis use patterns and immunity possibly relate.

Purpose of the Study

The purpose of this study was to examine the relationship between frequency and longevity of cannabis use across four dependent measures: depression, anxiety, immunity, and quality of life. A series of eight multiple linear regressions (MLRs) were used to examine individual and combined relative effects of longevity and frequency of cannabis use for each variable. By understanding relationships between usage and overall

health, future programs and healthcare may use the data accordingly to aid decision-making and care options upon increased cannabis use specific to the Appalachian region.

Research Questions and Hypotheses

RQ-1: Do relationships exist between the frequency and longevity of cannabis use and anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959)?

H_{01}- No relationship exists between cannabis use frequency, longevity, and anxiety scores on the HAM-A.

H_{1}-A relationship exists between cannabis use frequency, longevity, and anxiety scores on the HAM-A.

RQ-2: Do relationships exist between the frequency and longevity of cannabis use and depression as measured by the PHQ-9 (Kroenke et al., 2001)?

H_{02}- No relationship exists between cannabis use frequency, longevity, and depression scores on the PHQ-9.

H_{2}-A relationship exists between cannabis use frequency, longevity, and depression scores on the PHQ-9.

RQ-3: Do relationships exist between the frequency and longevity of cannabis use and quality of life as measured by the Center for Disease Control's Health-related Quality of Life scale (HRQOL; Center for Disease Control, 2000)?

H_{03}- No relationship exists between cannabis use frequency, longevity, and quality of life on the HRQOL.

H_3-A relationship exists between cannabis use frequency, longevity, and quality of life on the HRQOL.

RQ-4: Do relationships exist between cannabis use frequency, longevity, and self-reported immunity as measured by the Immune Status Questionnaire (ISQ; Versprille et al., 2019)?

H_{04}- No relationship exists between cannabis use frequency, longevity, and self-reported immunity on the ISQ.

H_4-A relationship exists between cannabis use frequency, longevity, and self-reported immunity on the ISQ.

Theoretical Framework

Psychoneuroimmunology (PNI) is a multidimensional paradigm that involves observing the separate functions of psychology, neurology, and immunology and how changes in each construct affects patient/participant holistic well-beings (Ader, 2001). Unique to PNI is how the immune system is thought to change based on the central nervous system, and vice versa, integrating into a holistic view of health. By observing the paradigm in other applications, such as cancer and HIV, a structure of research thought has been established to establish parameters necessary to explore how PNI's holistic view of health can benefit both research and people's well-beings (McCain et al., 2005; Halaris et al., 2019).

Physiological and psychological stress is the major factor involved in observing questions related to PNI, as stress in any part of the body alters the body's functionality.

A prime example can be seen in cancer patients, where psychological wellbeing has a tremendous effect on recovery. Disease progression is significantly faster in individuals with negative moods (McCain et al., 2005). Anxiety and depression can have a direct influence on the physical health and immune function of individuals (Ader et al., 1995). By investigating through PNI, data were used to observe changes in overall wellbeing and quality of life created by patterns of cannabis use.

Nature of the Study

The nature of this study was quantitative and involved using multiple regressions to determine if relationships existed between cannabis use longevity and frequency and scores on measures of anxiety, depression, immune function, and quality of life. All outcome variables were preestablished measures of peer-reviewed, validated constructs, while predictor variables were self-reported measures of cannabis use patterns. Participants' responses provided data involving evidence of relationships between frequency and length of cannabis use with depression, anxiety, quality of life, and immunity. Expectations for the study were to determine how different cannabis use patterns altered or correlated with participants' scores on a PNI-style battery of health scales measuring anxiety, depression, immune function, and quality of life.

Within the PNI paradigm, an understanding of the overall well-being of the individual gives a more holistic understanding, as cannabis has a wide array of potential applications and dangers that to this point have a poor history of evidence. The neurological function of cannabis is the more established area of research with more

concrete evidence of the effects at a chemical level. Predictor variables of length of cannabis consumption and frequency of consumption were chosen due to the variability of use possible. These two variables allow for understanding possible alterations in individuals, but were not specific enough for measuring dosage levels due to study procedures and legalities involved.

Criterion variables were chosen specifically to allow for a varied understanding of overall health without becoming encumbering. Anxiety, depression, and quality of life were chosen as measures of subjective experience that may change due to the use of cannabis, while immunity measures were included to determine if cannabis use could be influencing the immune system, as well as a potential mediating factor for the other three criterion variables. Demographic information was observed involving age, regional location in Appalachia, and gender.

To collect data from participants, online formats were used. SurveyMonkey allowed for quick access to a diverse population of participants throughout the region. Participants were compensated by SurveyMonkey at undisclosed amounts but were only recruited into the study if they lived in one of 420 counties in the Appalachian Region. Data from this study were analyzed via logistic regression to determine if the predictor variable of cannabis use had any relationship to the criterion variables.

Definitions

Anxiety: "An emotion characterized by feelings of tension, worried thoughts and physical changes like increased blood pressure" (American Psychological Association

[APA], 2020). Anxiety disorders are diagnoses given to individuals who experience these symptoms regularly.

Cannabis Use: Consumption of cannabis measured in terms of length and frequency of use. Due to difficulties in measuring dosage due to variable strengths of different cannabinoids, a broader viewpoint is necessary until further studies can achieve dosage measurements.

Depression-"is more than just sadness. People with depression may experience a lack of interest and pleasure in daily activities, significant weight loss or gain, insomnia or excessive sleeping, lack of energy, inability to concentrate, feelings of worthlessness or excessive guilt and recurrent thoughts of death or suicide." (American Psychological Association, 2020b).

Immunity: A measure of the state of the immune system within the body. Reduced immune systems are more likely to allow infection and disease.

Legalization (of cannabis): The potential political decision to remove cannabis from schedule I to a substance that is legal to use. As of the COVID-19 pandemic of 2020, half of the U.S. has legalized medicinal or recreational cannabis use; however, only Virginia, West Virginia, Pennsylvania, and New York have explored the use of medicinal cannabis, while North Carolina and Georgia have reduced punishments for small quantity possession.

Psychoneuroimmunology (PNI): "An integrating paradigm for advancing both theoretical and empirical knowledge of physiological patterns that contribute to the

dynamics of health" (McCain et al., 2005, p. 1). The paradigm of PNI involves observing psychological, neurological, and immunological factors of humans as a collective force in human health.

Quality of Life: A measurement of human health contrary to the mechanical nature of medicine, the measurement of quality of life is designed to determine the effect of disease and sickness on individuals at an emotional and humanistic level, rather than focusing in a binary fashion on sickness or wellness (Centers for Disease Control [CDC], 2000).

Assumptions

Assumptions of the study existed in the method of cannabis measurement, as the definition of the usage was intentionally vague. Due to the unknown and difficult to measure factors of individual cannabis sources, especially in areas where the product is being purchased illegally from non-regulated sources, the relationships that were observed between frequency and longevity of cannabis use did not consider route of administration or dosages.

Due to a lack of online survey tools, assumptions of the neurological portion of the PNI framework were made to fit the overall discussion of the study. The literature reinforcing the connections in PNI between the three constructs imply that if the psychological and immunological factors collected in the study were significant that there could be assumptions made that the neurological would also have some relationships when measured. In future studies where direct communication with participants is

available, neurological construct data should be collected to improve understanding of cannabis use.

Scope and Delimitations

Stratified sampling was chosen to determine how cannabis use over time as well as frequency of use influenced Appalachian adults. By observing behavior patterns rather than immediate effects of use, I sought to address whether cannabis could create problems or relief. Further, all participants were over the age of 21, without a maximum age cap. Adolescent marijuana use was not observed, as previous research conducted by the author has indicated adolescent exposure in rats had known dire effects on brain development (Ostrander, 2015).

While my expectation was that healthy patterns of cannabis use would improve measures, there was clearly a lack of information regarding lung health that could not be addressed based on the methodology of this study. In future research where participants' vitals and health traits could be collected in tandem with these measures, the use of spirometry, a test of lung function that measures the strength of inhaling and exhaling that often is used to help diagnose breathing problems (Mayo Clinic, 2017), would be highly recommended.

Observing the region of Appalachia was a decision made due to its exclusion from research that often troubles the region. By using PNI, perspectives regarding patterns of use could be observed in a population with major losses in terms of industry, resources, and historic exploitation. While the neurology function of this new paradigm is

not directly observed in this study, literature on neurological functions in Chapter 2 supports current research on the topic.

Limitations

Due to the illicit nature of cannabis in much of the region, individuals are more likely to have issues with disclosure of activities if they are not anonymous. To further protect participants' anonymity, demographic information was intentionally less specific than many studies to avoid potential of identification (e.g. race information, exact zip codes, specific ages rather than ranges, etc.) in the event of a catastrophic data leak.

The virtual structure of survey data collection online created issues by preventing collection of lab result-driven measures of immune and neurological functions, such as cortisol testing or electroencephalography. For this study, immune function was collected using a verified scale of measure, the Immune Status Questionnaire (ISQ), that allowed for survey collection of immune function data. Finding a test of neurological functions that did not require direct human interaction was nearly impossible; therefore, neurological function was not measured for this study, leaving the neuro- portion of PNI out of the data.

A major limitation of the study existed in the severe difficulty in measuring cannabis products and dosages by participants. Due to the illicit nature of cannabis, most participants likely purchased their products from an unreliable/inconsistent source that would include products with widely varying cannabis quality and cannabinoid profiles. Further, route of administration (ROA) was not measured due to the size of the study, and

assumptions were made that most products being used by the participants were likely inhalants/smoked as “smoking combusted cannabis materials (e.g., by way of a joint, spliff, pipe, blunt, water-pipe/bong) remains the most predominant ROA among users in North America” (Russell et al., 2018, p. 88).

Significance

I examined relationships between cannabis use patterns and anxiety, depression, immune function, and quality of life among Appalachian users. By creating a quantitative data set, data may also serve as a basis for future investigation into patterns of use. The data set can help promote understanding real cannabis use patterns for future research, rather than rely on a history of studies involving artificial isolates and lab-created alternatives.

Quality of life has recently become a more relevant topic, especially in how it relates to patients with terminal or serious diseases. Cannabis has reportedly led to improved quality of life among patients with severe symptomology and pain that cause distress and degradation of health. When given to patients in a study of head and neck cancers, cannabis was found to improve quality of life, anxiety, and depression scores when compared to controls (Zhang et al., 2018).

Summary

The study involved understanding how anxiety, depression, quality of life, and immunity related to differing patterns of cannabis use within the Appalachian Mountain region, a region that is often overlooked research and resources. Historically, the region

has issues, including mental health neglect, stigma, and lower quality of life compared to surrounding regions. By looking at variables involving mental and immune health, as well as perceived quality of life, using the theoretical framework of PNI, a more robust understanding of current cannabis use capable of being measured. In Chapter 2, a review of literature was used to understand relationships between variables.

Chapter 2: Literature Review

Introduction

Appalachian residents live within a region that is often overlooked for resources that include structures for food safety and mental health treatment. With potential legalization of cannabis, many in the region may believe it may help provide relief. Until the 2010s, anxiety and depressive disorders were not part of considerations for medicinal cannabis (Grunberg et al., 2015; Lao et al., 2017; Zuardi et al., 2017). Informed decision-making has been complicated by historic studies contributing data with negative bias leaving modern researchers the task of learning how to research cannabis. The use of marijuana as antianxiety and antidepressant, as well as the effect different use patterns have on quality of life and immunity were explored in this chapter via the lens of PNI.

Through new interest fueled by state legalizations, the field of research has begun to expand to show that the number of potential uses of cannabis products can be wide-ranging. It may be possible that use of cannabis and cannabinoids could be beneficial or detrimental to those suffering from mental health distress in terms of direct neurological changes or altered quality of life. I observed theories, measures, and concepts related to the research questions and how that altered within the Appalachian region.

Literature Search Strategy

In this study, I used the following library databases: PsycInfo, PsycTests, and SAGE Journals, and Google Scholar. The following key terms were used: *cannabis, tetrohydrocannabidiol (THC), marijuana, cannabidiol (CBD), pot, depression,*

depressive symptoms, *anxiety*, *anxiety disorders*, *Appalachia*, *quality of life*, and *immunity*. Of the research collected, most articles were published between 2016 and 2021; however, older studies were included due to their relevance. Further, older studies on cannabis, especially prior to 2000, often held flawed or biased views against cannabis. Several sources were taken from national or regional databases, as well as some historic sources for the theoretical framework, scales, and paradigms involved. No academic studies were used that were not peer-reviewed or published articles.

Theoretical Foundation

PNI is the study of the interconnected nature of psychology, neurology, and immunology of individuals as a holistic approach to health. The predominant notion involved in this theory is how the mind, immune system, and brain function together, and how stress interacts with all three domains differently. By observing behavioral responses in relation to conditions within disease models, studies of observation began making connections between psychological well-being to disease outcomes (Solomon & Moos, 1964).

PNI helps in terms of explaining relationships between inflammation, stress, immune function, and psychological states (McCain et al., 2005). By observing how cannabis use patterns relate to health across a variety of measures via the lens of PNI, information regarding potential effects of cannabis on the Appalachian region can help prevent harm in advance of regional legalization. Further, observing quality of life in

relation to holistic health show affect users may help create an understanding of perceptions of effects as opposed to actual effects.

When conducting an open-label clinical trial between PNI-based interventions and psychoeducation, Chacin-Fernández et al. (2019) observed a positive correlation between quality of life and immunity among children with leukemia. After receiving comparable interventions, with one group receiving additional education on PNI, Significant improvements of quality of life and measures of immunological markers were seen between groups. By including extended psychological intervention and education on how mood affects the body, calls for further support for education in treatment models using PNI paradigms continue to increase.

Conceptual Framework

The framework of PNI creates the ability to observe connections between previously unrelated fields, allowing for insight regarding psychology's effect on overall health of individuals. PNI further allows understanding how stress is interrelated with these paradigms by assessing each construct with well-established psychological measurement tools. By exploring the connection between inflammation, stress, and quality of life, determination if cannabis use's relationship alters with any of these concepts can help determine to what extent access to cannabis may affect Appalachian residents.

Literature Review

PNI

Origin

The PNI theory started with Robert Ader and Nicholas Cohen (1975), as connections between classical behavioral conditioning and immunology were observed during a taste aversion study. By conditioning rodents with paired saccharin and immunosuppressing agents, differences in immune function were measurable in an experimental group compared to control and nonpaired conditioned rats. When given injections and saccharin without the immunosuppressing agent, the experimental group of rodents expressed a significantly reduced antibody response as measured by immunoglobulin levels. The conditioned response of immunosuppression from an introduction of saccharin without the paired cyclophosphamide immunosuppression agent provided the foundation to address connections between psychology and immunology.

Research in the field of PNI has often presented with rodent models, especially early on (Ader & Cohen, 1993). Researchers used negative stimuli and stressors such as electric foot shocks or physical restraints, that are now considered unethical in human studies. While studies have begun looking at stress in humans using the paradigm of PNI, the research field is full of studies that use both animal and human populations, this literature review will include both.

Stress

"Stress is the physiological or psychological response to internal or external stressors. Stress involves changes affecting nearly every system of the body, influencing how people feel and behave." (APA, n.d.). Stress as an influence on immune function has been explored throughout the world, with studies finding a plethora of connections between the function of stress on disease models. Examples of such can be seen in Laudenslager (1987), where identification of a change in symptomology, or lack thereof, from sickness could be attributed to familial stress for strep throat and pneumonia cases. Considerations for the cause of this difference could be attributed to illness behaviors, such as a failure to maintain a schedule of treatment due to stress, leading to an unnecessary progression of the disease (Cohen & Williams, 1991). Further, if the stressors are high enough in frequency, it is likely that individuals will put off seeking medical care due to the stresses, leading to diminished health from neglect. By considering stress and its effects on the entire body, immune system, and otherwise, a more holistic approach to overall health can be ascertained.

Stress affects different parts of the body in ways that alter the likelihood of disease vulnerability (Kendall-Tackett, 2010). Directly or indirectly, stress can have marked effects on an individuals' immune system or behavior in relation to their own health, such as an increase in negative or unhealthy behaviors like coping by binge drinking or loss of sleep. Within the brain, two different systems are affected by stress: the sympathetic adrenomedullary system and the hypothalamic-pituitary-adrenal system

(HPA axis). Further, exterior to the brain inflammatory changes that occur with stress can further alter immune system function.

Sympathetic Adrenomedullary and Parasympathetic Systems

The sympathetic and parasympathetic nervous systems, the two parts of the autonomic nervous system, respond to stress in different ways by design. For living creatures, acute levels of stress in situations of survival are beneficial in helping fuel and protect the self, however chronic stress holds only deleterious effects on well-being, even going as far as to promote cancer development (Dai et al., 2020; McCarty et al., 1988). When observed in animal models, measures of chronic stress are seen in several markers, such as the dopamine-beta-hydroxylase (DBH) process, where chronic stress increases the activity levels of DBH that lead to increased norepinephrine production in the body. From here, the process of converting norepinephrine into epinephrine becomes more frequent, leading to a system designed to adapt to stress more readily. While this may sound like a positive thing, chronic stress begins to cause the parasympathetic system that counters it to begin falling behind, leaving the being in a state of heightened alert that taxes health and likely contributes to depression (Won & Kim, 2016).

In addition to taxing health, when presented with more stress over time, novel forms of stress were seen to cause more powerful increases of sympathetic activity (McCarty et al., 1998). This change in reaction, where chronic stress numbs to familiar stresses, is called habituation (McCathy, 2016). While this habituation makes common place stressors less burdensome, a process called dishabituation occurs where a novel

stressor may cause a stronger reaction from the novel source, but also alter the original habituated stressor to create a more deleterious effect than usual. An example of dishabituation may be seen in an individual who has overcome a fear of heights spontaneously having an acute response to heights again when presented with a more intense stimulus, like skydiving. With chronic stress, the sympathetic adrenomedullary system begins to downregulate, leading to a fatigue where a stressor is present, but the system does not respond to address the stimuli. Conversely, the upregulation to novel stressors can lead to responses that exacerbate the health of the individual and increase the sensitization, or response of magnitude, to stimuli. This atypical adjustment to stressors creates a consistent vulnerability that further exacerbates issues as time persists.

HPA Axis

In tandem with the sympathetic adrenomedullary and parasympathetic systems, the HPA axis also reacts uniquely during stress imposed on individuals. The hypothalamic-pituitary-adrenal axis operates by releasing corticotropin-releasing hormone, beginning a process that leads to adrenocorticotropic hormone (ACTH) and glucocorticoids, important proteins in the stress response cycle that acts as a catecholamine agonist. The most important glucocorticoid is cortisol, which is released during times of stress to help convert glucose to energy and increase food intake and reduces other less-necessary to survival drives, i.e., reproduction (Kendall-Tackett, 2010). The reduction of drive response allows the body to more efficiently distribute energy to respond to acute stresses by increasing the activity of the limbic system

(Herman, et al., 2016). Like the autonomic nervous system, chronic activation of the HPA axis can be problematic.

Cortisol in excess or deprivation can cause several issues, including damaging neural constructs, and confusing the responses that are fundamental to the HPA axis' function. One example of this can be seen in the drive to eat when measured against perceived acute stress. In a study of life stress, women were compared between the highest and lowest quartile participants on measures of life stress. When compared, the high perceived life stress group expressed a diminished appetite over time, when compared to the low perceived life stress group (Kaltzkin et al., 2019). The differentiating factor being the length of the stress on the individual, as chronic stress can cause changes in the reactivity of the HPA axis.

Changes to the HPA axis' efficacy occur when chronic stress is implemented on an individual. Cortisol, the anti-inflammatory and immunosuppressive glucocorticoid responsible for preventing inflammation from damaging the body can be habituated by the body over time causing decreased efficacy (Kendall-Tackett, 2010). When cortisol is measured in individuals with motor function neurological disabilities against their own perceived stress levels, levels of background cortisol are found to be higher, regardless of the perceived stress levels of the individual than control participants (Apazoglou et al., 2017). When introduced to an acute stressor, both parties were found to have similar response levels of cortisol, but conditioned participants were found to report higher

perceived stress during the acute event, while cortisol took longer to diminish post-stress for those with disabilities.

When completing a test on stress, the Trier Social Stress Test (TSST), individuals who were rated as having a higher level of lifetime stress (measured by frequency, not severity) often had diminished, blunted reactions to cortisol activity (Lam et al., 2019). Further, when tested using acute psychosocial stress on the TSST, individuals were found to have diminished cortisol responses from almost every form of major stressor, sans pregnancy, in a laboratory setting (Foley & Kirschbaum, 2010). The stunted response allows more inflammation to occur in the body over time, as the natural control mechanisms become less efficient.

Inflammation

Inflammation is a process that occurs as a defense mechanism to threats to the body, whether that be psychosocial stress, physical injury, or imminent danger (Kendall-Tackett, 2010). While inflammation is helpful in protecting the body from the detrimental effects of viruses, bacteria, and injury, excess or prolonged inflammation can become problematic. Commonly, excess inflammation has been seen in individuals suffering from depression and have been linked to early life stresses, as measured by inflammation markers interleukin (IL-6) and C-reactive protein (CRP; Tannous et al., 2020). The excess inflammation has the potential to become cyclical and is likely a major contributing factor of the difficulty surrounding treating depression.

Lifestyles of western society are often plagued with stressors that remain constant, such as poor nutritional diet. With the added stressors of poor nutrition, a study on the effects of dietary changes in patients suffering from chronic inflammation diseases (diabetes, metabolic syndrome, dyslipidemia, etc.) while measuring for inflammatory markers presents evidence of a direct connection of chronic inflammation to diet (Margină et al., 2020). Further, weight did not express a significant effect on inflammation, but increased dietary fiber and periods of fasting were both found to correlate with reduced inflammation compared to baseline.

Thoughts about how inflammation interacts with nutrition have been chronicled by Dr. Moss (2018), who argues that evidence of nutrition's effect on the body and how it interacts with inflammation can be challenging. Chronic inflammation, a condition that causes long term damage to cells, is often linked directly with a condition called "insulin resistance". Along with an allostatic load (overall deterioration due to stress), the increased frequency and duration of stress over time will decrease the effects of the immune system, catalyzed by aging. By surviving with the effects of insulin resistance and chronic stress, individuals are found with resistance to anti-inflammatory effects, creating another cyclical issue of inflammation perpetuated by inflammation.

Cannabis and Cannabinoids

Cannabis is a cultivated plant originally native to Central Asia that contains an unknown number of cannabinoids as products of their natural growth. Tetrahydrocannabinol (THC) is one of the more understood cannabinoids that are found

in the cannabis plant with psychoactive effects. Often paired with cannabidiol (CBD), the two cannabinoids are frequently the focus of studies, with many inadvertently ignoring the numerous other cannabinoids in cannabis flowers that may have major influences on individuals ingesting them. One example of this can be seen with cannabichromene, an anti-inflammatory, pain-relieving cannabinoid found naturally in cannabis that has very little research on it to date (PubChem, 2020). While other countries have begun to explore the potential of uses that cannabis may hold for the future, the United States has created a paradox of federally listing cannabis as a schedule I substance (classified as having no medical or safe use, on par with heroine and psilocybin), while simultaneously allowing legal medical cannabis in more than half of states. Until the legality of cannabis across the board for research can occur, the information presented regarding its use is a subject rife with the potential for bias and issues with validity that may complicate validating data. The effects of cannabis on the psychology, neurology, and immunology of individuals to follow from here were presented with the understanding of the current bias in the field, as the two are impossible to separate until the availability and funding for research becomes readily available.

History

Cannabis is a plant with an unprecedently long history of various uses that have been used medicinally in records dating back as far as around 2700 BCE during the era of Chinese Emperor Shen-Nung (Zuardi, 2006). The cannabis/hemp plant has been commonly used throughout human history for many things, such as rope and paper.

Indications of medicinal use during this period were varied, including uses for “rheumatic pain,” digestive issues, female reproductive issues, malaria. Additionally, cannabis use has been seen in a variety of forms, including smoking, ingestion of flower, ingestion of seeds, use in teas, and more. An early record of cannabis use, the *Shen-nung Pen-ts’ao ching* recorded information of overuse of cannabis causing hallucinations, despite a lack of evidence of others experiencing hallucinations in other references throughout history. While unique, this fallacy may have been an influential component in the more modern reefer madness craze which falsely indicated hallucinations as a common symptom of cannabis use.

Outside of ancient China, the history of cannabis use is pervasive across the globe, with cultures of all sorts having references to cannabis use, such as in India from 1000 BCE on (Zuardi, 2006). Common usages of cannabis through history have included use indications such as “analgesic, anticonvulsant, hypnotic, tranquilizer, anesthetic, anti-inflammatory, antibiotic, anti-parasitic, antispasmodic, digestive, appetite stimulant, diuretic, aphrodisiac or anaphrodisiac, antitussive and expectorant” effects (Zuardi, 2006, p.154). Historic uses of cannabis have a rich history with legalities not becoming an issue until racism led to its schedule I status due to its connection with Mexican immigrants during World War II (PBS, 2014).

Following the legal change of cannabis into a schedule 1 substance, consistent racism has been present in tandem with the law’s existence. Where many individuals continued to use marijuana, the intentions of government officials were often opposed to

people of color and anti-war “hippies”, which led to the creation of the Controlled Substance Act to disproportionally bully minority communities during the Nixon era (Solomon, 2020). Senior advisor to Nixon, John Erlichman, stated that during the time, they fully understood they were lying about the danger of the substance as a manner to subjugate communities politically opposing him. Erlichman further acknowledged that cannabis was not as dangerous as other schedule one substances (e.g. heroine) and later spent a portion of his career calling for cannabis’ decriminalization to no avail (Lopez, 2016).

Effects of Use

Cannabis has been used for thousands of years for an assortment of reasons including medicinal, mood-altering, euphoric, etc. (Maule, 2015). Modern use is commonly related medically to chronic pain and nausea/appetite stimulation associated with chemotherapy treatment, but there are reports of aide for ALS, Alzheimer’s, Glaucoma, Multiple Sclerosis, etc. Reports of cannabis’ role in relief from anxiety and depression brought calls to research to investigate the relationship (Anderson, 2017).

Cannabinoids are not equivalent of each other. The two major cannabinoids most often studied are Δ9-tetrahydrocannabinol (THC), known for its intoxicating effects, and cannabidiol (CBD), known for its therapeutic effects (Russo & Guy, 2006). Between the two, contradictory effects can be seen on changes to the cardiovascular, central nervous, and immune systems, as seen in Table 1. Further, due to the complexity of the

interactions between cannabinoids, calls for whole cannabis and cannabinoid isolate studies propagate.

Table 1
CBD and THC differences in Effects

Effect	THC	CBD
CNS Effects		
Anticonvulsant	+	++
Muscle Relaxant	++	+
Antinociceptive	++	+
Psychotropic	++	-
Anxiolytic	±	++
Antipsychotic	-	++
Neuroprotective Antioxidant	+	++
Antiemetic	++	+
Sedative	+	-
Analgesic	++	+
(Other) Drug withdrawal symptoms	+	+
Receptor/Non-receptor Effects		
Anti-inflammatory	+	+
Immunomodulatory	+	+
Cardiovascular Effects		
Hypertension	+	-
Hypotension	-	+
Tachycardia	+	-
Bradycardia	-	+

Anxiety

Anxiety is characterized as an increase in arousal that leads to distress or worry and can physically activate systems in your body out of turn (Psychology Today, 2021). It is estimated that one in three adults in the United States will experience out-of-control anxiety at one time in their lives, but anxiety has recently taken the position of the most common mental health issue in the world. This rise is shocking as the history of anxiety in psychology as anxiety was not recognized until as recently as the DSM-III revision in 1980 (American Psychiatric Association). Due to the rise in anxiety, both pre- and post-COVID-19, calls for treatment and understanding of the construct have increased. By understanding the mechanisms behind the recent increase in reported anxiety, how anxiety interacts with cannabis use, and how anxiety interacts with the paradigm of PNI, a more thorough understanding of what relationships cannabis have on anxiety shape the hypotheses of this study.

Prior to the Covid-19 pandemic that started in March of 2020, the prevalence of anxiety in the world had been increasing significantly. While subgroups expressed proportionately higher rates than the general population, instances of anxiety disorders have been slowly increasing since the coining of the term to a rate somewhere between 3.8 and 25% of the entire adult population of the world (Remes et al., 2016). When compared from 1990 to the year 2010, a sharp increase in prevalence can be seen while critics have largely written off these rises as changes of age across the population, despite these increases being seen globally outside of a few East Asian countries. Within the

reported subgroups, higher instances of anxiety were more prevalent in younger adults, LGBT+ adults, individuals living with chronic diseases, addiction sufferers, and individuals suffering from respiratory diseases and diabetes (Remes et al., 2016).

After the Covid-19 pandemic began, the proportions of the population that have suffered or are suffering anxiety have increased exponentially (Salari et al., 2020). In a meta-analysis of modern COVID studies, reports of prevalence have increased to 31.9% of the world general population with no Appalachian region specific study to be found to date. With the increase in anxiety worldwide and the decriminalization of cannabis in Virginia (Possession of marijuana unlawful, code of Virginia § 18.2-250.1, 2021), assumption of an increase in cannabis use is expected in the region as availability increases. To predict the relationship between increased cannabis use and anxiety, an understanding of cannabis' effect on anxiety was needed.

Cannabinoids and Anxiety

Cannabinoids are known to have different effects on anxiety based on the specific cannabinoid. Δ9-tetrahydrocannabinol (THC) is thought to decrease anxiety until cannabis intoxication occurs, subsequently changing magnitude and direction to increasing anxiety (Crippa et al., 2009). Conversely, cannabidiol (CBD) has been shown to decrease anxiety across species at nearly every dose (Russo, 2017; Campos et al., 2013). CBD has shown such a strong anxiolytic effect that it has past been proposed as a treatment for anxiety disorders as early as 2015 in medical literature (Blessing et al.,

2015). Further, CBD heavy products are not illegal in most of the United States, which has led to an increase in use of CBD as an anxiolytic.

Individuals in legalized states or states with allowed medicinal use have reported up to 58.1% of users that state they use cannabis to help curb anxiety (Sexton et al., 2016), the second most prominent indication only surpassed by uses for pain relief reporting at 61.2%. Additionally, CBD specific use has been reported for anxiety relief among 42.6% of respondents in an international survey (Moltke & Hindocha, 2021). Perceptions of cannabis users indicate their belief that cannabis can help reduce anxiety, which may explain trends of increased recent cannabis use by individuals who score higher on anxiety (Kedzior & Laeber, 2014). While perceptions of users do not constitute scientific truth, the overwhelming consistency of reporting does raise questions as to the potential reality of the relationship and the potential for uses as an anxiolytic.

PNI and Anxiety

Anxiety affects the whole body through activation of anxiolytic responses that release a substantial amount of stress on the nervous system. When comorbid with other diseases, anxiety has been found to significantly increase several pro-inflammatory markers (IL-17, TNF-α, and IL-6) and markedly decrease T-cell proliferation when compared to controls (Furtado & Katzman, 2015). These alterations of increased activation of the HPA axis can lead to increased stress on the immune system, where high anxiety creates stress on the psyche. Pharmacological treatment often looks to directly

treat anxiety with alterations to the HPA axis with SSRIs, reducing the activity of corticotrophin releasing factor in the brain (Tafet & Nemeroff, 2020).

SSRI treatments of anxiety show reduction in proinflammatory cytokines (Hou et al., 2019). After a treatment of twelve weeks, individuals diagnosed with generalized anxiety disorder (GAD) showed marked reductions across cytokines IL-1α, IL-6, IL-8, IL-12, IFN-γ and CRP measures when compared to their baselines, in tandem with reductions in anxiety measure scores. If treatment helps to treat the comorbidity of anxiety and inflammation, reason stands to believe that the two are related in a way that may be more than simply correlational in nature.

Depression

Depression is the most common mental health disorder that is commonly misinterpreted or incorrectly defined. Depression is defined as "a negative affective state, ranging from unhappiness and discontent to an extreme feeling of sadness, pessimism, and despondency, that interferes with daily life" (American Psychological Association, 2020b). Estimates of the U.S. population that is depressed pre-COVID 19 averaged around 4.7% of the population (National Center for Health Statistics, 2019). Post the COVID-19 pandemic, the estimates of depressive symptomology have thought to have nearly tripled in frequency (Ettman et al., 2020).

Amongst Appalachians, depression is more prevalent than the rest of the United States (Marshall et al., 2017). With increased levels of depression, and in turn suicidality rates, maintain 17% higher than the rest of the country. As well, consideration must be

taken as to the cost of depression, not only on the individuals suffering from it, but the community involved. With reductions in life span and increased healthcare requirements, depression taxes individuals' well-being and fiscal health by presenting difficulties in life that hinder growth and health.

Cannabinoids and Depression

THC and CBD are both thought to have anti-depressant qualities at different doses, based on animal studies currently available (El-Alfy et al., 2010). Conversely, cannabis withdrawal syndrome is thought to mirror many symptoms of depression, such as reduced dopamine release in the brain and increased negative mood biases (Stoner, 2017). The endocannabinoid system appears to benefit from the proposed "monoamine effect" provided by cannabis use (Micale et al., 2014), but without further research into the topic, more questions were present than were answers.

A common concern that many have brought up has been the occurrence of "marijuana-induced psychosis", an unknown mechanism of cannabis in which users exposed to tremendously high doses of THC may cause individuals already predisposed to psychosis to trigger a temporary psychosis (Bloomfield, et al., 2014). Further investigation into the psychosis has not led to much understanding of how this functions, as increases in dopamine synthesis and release are typical in individuals experiencing psychosis, but chronic users of cannabis see a reduction in their dopamine synthesis. Many of the articles implying this effect as causation rather than correlation are using an increase in "marijuana-related emergency department visits" as an indicator of the

psychosis without adequate evidence (Grewal & George, 2017). While this should remain on the radar, evidence must be developed to better understand the likelihood, implications, and severity of cannabis-induced psychosis.

Another common problem presented by anti-cannabis proponents, amotivational syndrome is a theory proposed by McGlothlin and West (1968) that claims that frequent cannabis use will cause difficulty in higher functioning and introduce apathy that may parallel depression. To this point, research has not been capable of proving or disproving this theory, however data does indicate that college students who use cannabis often do not engage as frequently (Lac & Luk, 2017). While there may be potential for this issue to be problematic, argument over perspective may be the defining line between the two states, as "amotivational syndrome" being related to cannabis use, and depression being related to cannabis use are not inherently equal despite common parallels. Further, as the relationship between depression, cannabis use, and a lack of motivation are correlational without an agreed upon direction or causation, the claims of an amotivational syndrome that exists solely in tandem with cannabis use evokes suspicion.

PNI and Depression

The interaction of depression with the HPA axis lends to a question of whether depression is an inflammatory disease in nature as well as a mental health concern. Changes in the concentration of pro-inflammatory cytokines that occur in chronic stress, additionally occur in depression (Leonard & Myint, 2009). Further, changes in the HPA axis caused by external stimuli often express changes in the parts of the brain directly

related to depression: the amygdala, hippocampus, and prefrontal cortex. These changes and the lack of a full explanation of how depression perpetuates itself into a cycle have led to several new hypotheses on depression as an inflammatory disease relating fluctuations to the kynurenine pathway, a pathway identified in other neurodegenerative diseases (Moss, 2019; Won & Kim, 2016).

The connection to other neurodegenerative diseases is not insignificant. Several commonly comorbid diseases with depression (asthma, obesity, cancer, rheumatoid arthritis, cardiovascular disease, etc.) often have shared inflammatory markers and pathways activation (Yan, 2016). Further, the common hypotheses of depression being a response to a serotonergic imbalance falls directly in line with increases in inflammation creating a cyclical pattern of serotonin reduction from chronic stress and chronic inflammation (Moss, 2019). By looking at the same problem from multiple fields, PNI helps to clarify the connections of the whole-body system onto the mind and body.

Quality of Life

Quality of life as a general concept is not one defined within the realms of a single field, rather a pervasive, wide-ranging concept. To help narrow the idea for this study, health-related quality of life (HRQoL) looked specifically only at social, physical, and emotional well-being (Fallowfield, 2009). While the concept of quality of life remains somewhat uncertain, researchers have put together a few validated measures of the concept, such as the CDC's HR-QoL measure, that was used to observe quality of life in this study. While the concept of quality of life has been leading to new scales, quality of

life measures have been tremendously beneficial to individuals in helping to determine courses of treatment and need for intervention options for a plethora of conditions and issues.

The region of Appalachia overall has not fared well on most measures of quality of life. When investigating two rural towns in central Appalachia, five common themes were major components frequently associated with the region and quality of life: socioeconomic status, economic opportunity, access to healthcare/insurance, social/mental health difficulties, and food vulnerability (Hege et al., 2018). Further, age seems to be related to the quality of life in Appalachia, with adolescents expressing higher quality of life, but a sharp decline occurs in the late twenties that continues plummeting until end of life (Roberts, et al., 2019). The consistent reduction of quality of life indicates a much larger problem in health, as quality of life has a direct correlation with the likelihood of a positive prognosis for individuals fighting illness (Fallowfield, 2009).

The HRQoL (Center for Disease Control, 2000) measure itself does something that many measures have difficulty doing: measuring one concept across multiple dimensions well. A factor analysis of the HRQoL supports the use of the measure as a single-factor score for measurement of quality of life, indicating that despite differences in the portions of the measure, the overall measurement of quality of life can be utilized for a large variety of applications (Yin et al., 2016). Further beneficial to the study was that the HRQoL is a patient-reported measure of well-being that may be answered with a

questionnaire, rather than a lengthier interview process (Fallowfield, 2009). Where quality of life is an indicator of well-being, Appalachia has not fared well in studies due to the regions' history of economic and social struggles (Roberts, 2017).

Cannabinoids and Quality of Life

Cannabinoids have a complicated relationship with quality of life. For some individuals suffering from chronic conditions, the use of cannabis appears to improve overall quality of life by removing factors that otherwise create detriment, such as pain in fibromyalgia patients (van de Donk et al., 2018) or spiked anxiety responses in PTSD (Yarnell, 2015). When observing a general population however, improvements made by a reduction in cannabis use can be seen in anxiety, depression, sleep quality, but not quality of life (Hser et al., 2017). This anomaly in a lack of change of quality of life from heavy smokers creates more questions than it answers.

Frequency of use finds its first major factor here with cannabinoids, as a study of individuals suffering from chronic depression or major depressive disorder, found significant differences between occasional, frequent, and non-cannabis smokers lending positive remarks towards occasional smokers (Aspis et al., 2015). When measured on several factors of quality of life, frequent depressed smokers, especially women, had significantly worse QoL scores than other groups. Assumptions could be made that cannabinoids have variable relationships with quality of life that are contingent on external factors, but a consistent trend of a reduction of QoL is consistent with frequent, heavy use of cannabis (Goldenberg et al., 2016).

PNI and Quality of Life

PNI and quality of life have overlap in their objective goal of what was measured. Psychosocial factors involved in disease progression are often associated with inflammation and immune response, a trend consistent with quality of life measures in the same disease progressions (Fagundes et al., 2013). Further, there are reasons to believe that high psychosocial stresses measured by QoL may be associated with a higher likelihood of incidence of some diseases, such as breast cancer in women (Lillberg et al., 2003). PNI-based interventions have been shown to improve outcomes on depression and quality of life measures (Moraes et al., 2018), which is consistent with the central concept of PNI as proposed by Ader and Cohen (1993).

Immunity

Immunity is based on the measure of functionality of the immune system. This study's structure to be capable of incorporating immunity required a self-reported measure of immune function that could be observed without the use of expensive lab equipment or cortisol testing. The ISQ was created as an 11-item health screening questionnaire intended to measure individuals' responses and determine whether help is needed based on their lifestyle. While a newer test, reliability has been reinforced, and applications in studies have shown validity to the concept of self-reported immune function (Abdulahad et al., 2019; Baars et al., 2019).

The effects of stress on immunology can be observed at a cellular level, as shown in Ader and Cohen's conditioned taste aversion study (1975). When pairing the saccharin

with an immunosuppressing agent, direct measurements of hemagglutinating antibodies were shown to decrease in conditioned, experimental subjects after being exposed to only saccharin. Behavioral manipulation of the immune system due to conditioned and unconditioned stressors indicates the connection between the psychology and the immune system in an early measurement structure.

Cannabis and Immunity

Inflammation in relation to cannabis use is still a field of uncertainty as studies are finding contradictions to each other on every aspect, despite known cannabinoids (such as cannabichromene; CBC) having captured data indicating anti-inflammatory effects on the body (PubChem, 2020). Salivatory cortisol measurements were shown to have no difference between users and controls (Cloak et al., 2015). Further, no tremendous increases in cortisol levels for cannabis users compared to controls (King et al., 2011) or significantly decreased cortisol levels in regular users (Cuttler et al., 2017) have been recorded to date. When observing each study, major confounds in their data were found to make conclusions ill-advised or marred with inaccuracy. Due to the consistency in poor reporting of cortisol, cannabis use, and what effect the drug has on common measurements, inflammation and cannabis has been an under-developed topic. While inflammation has been found to have inconsistent data, the anomaly of contradiction has not been exclusive to inflammation when discussing cannabis, and as such, all data and findings should be considered with a grain of salt, due to the frequent contradictory findings across all measurements.

For the purposes of this study, the hypothesis of the relationship between immunity and cannabis was uncertain. As the ISQ was a newer scale, the use of the scale was intentionally to create a new bridge between immunity and cannabis use, a gap in the research that was certain to be developed across the field in several fashions as both cannabis science and research in immunity continue to grow.

Summary and Conclusions

Cannabis, a substance that has been regularly used and predominantly legal globally until the past century, has been historically investigated with negative biases that modern research has not replicated, possibly due to the severe systematic limitations of investigation. As more information has been discovered and distributed about cannabis, new products and methodologies have appeared and promoted the calling for more thorough understandings of cannabis use. With digital communication and research access available, a literature review helped to frame the relationships between the criterion and predictor variables.

Much of the research currently available was either published during early stages of understanding cannabis or has seen recent movement with the changes in public perception. Individuals have reported positive improvements towards their depression and anxiety with use, a relationship that in historic research implied the opposite going as far as to create a diagnosable syndrome that modern research has not really addressed yet. In immunity, mixed research has presented uncertainty to the effects, short- and long-term, of cannabis on immune function, complicated further by the differing effects of

separate cannabinoids being found to be both pro- and anti-inflammatory at various doses. Lastly, in quality of life, relationships were seen of significant decreases in heavy cannabis use but improvements in occasional use, while facing a backdrop of research showing no definitive understanding of direction or magnitude.

By understanding the background of how data regarding cannabis has had a rocky history and has left a significant gap in research to be filled with modern methodology, the framework of PNI stitches the fields together. By looking at the individuals through a more holistic view, these variables were better defined, and their relationships may help understand more tangibly what relationship cannabis may have with life across concepts.

Chapter 3: Research Methods

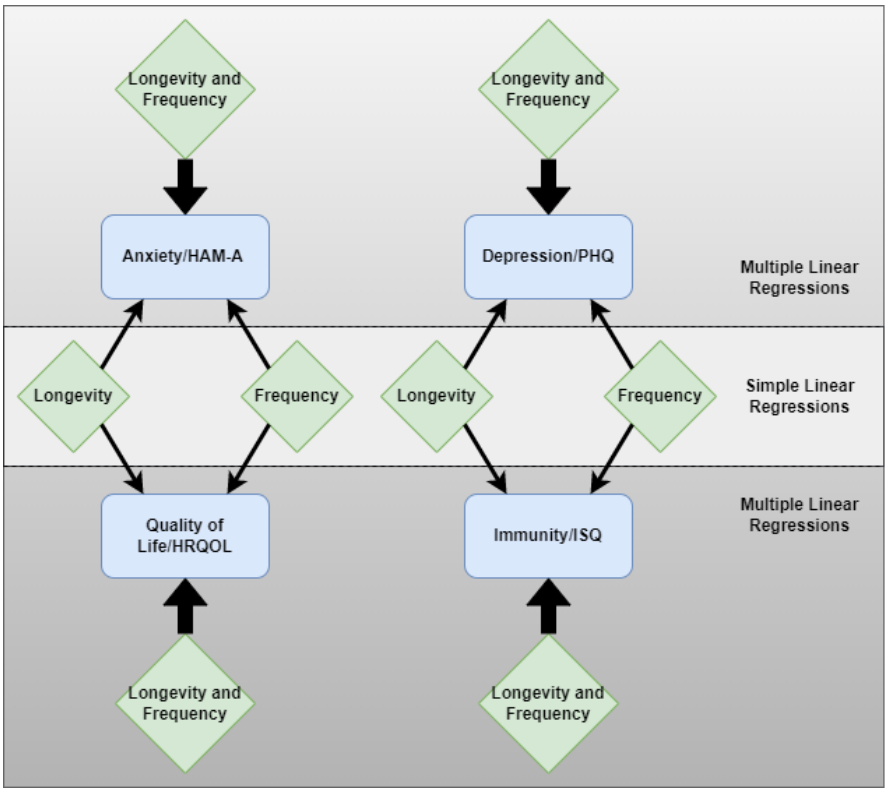
This study was designed to evaluate differences among individuals who have been using cannabis for differing lengths of time and with different frequencies of use, which allowed for a comparison of depression, anxiety, quality of life, and immunity in their everyday lives. Using the PNI paradigm of multi-faceted effects on the overall well-being looked to help predictions of relationships between variables by looking to approach the relationships from a more gestalt lens.

Research Design and Rationale

The purpose of this quantitative study was to understand through survey collection of individuals living within Appalachia how cannabis usage patterns affect their lives on multiple facets. Anxiety and depression measures of individuals using cannabis for different lengths of time and at different frequencies were used to determine if correlative connections between usage and self-perceived evaluations of anxiety and depression symptoms were altered with increased usage.

Figure 1

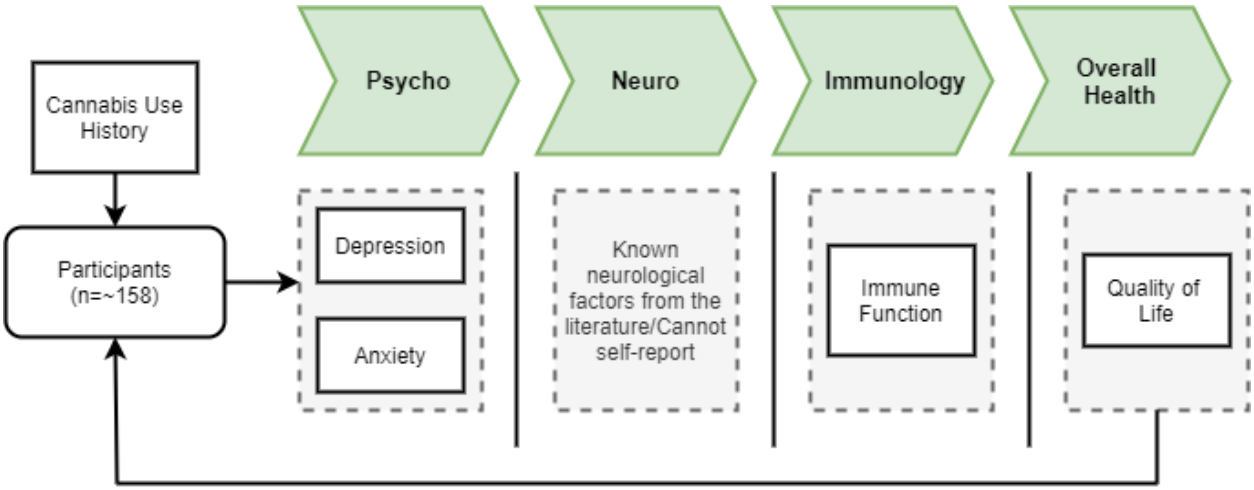
2x4 Multiple Regression Design



A 2x4 design was used to compare predictor variables of frequency and longevity of use with the criterion variables of anxiety, depression, immunity, and quality of life. By observing using the framework of PNI, observations regarding immune health and quality of life were used to help to understand the overall effects that cannabis has, especially for individuals suffering from mental health issues in a region where mental health treatment is often rare. The research plan in this chapter includes the methodology, sampling and population procedures, recruitment and data collection, instruments and constructs, data analysis plan, threats to validity, and ethical considerations.

Figure 1

Functions of the Test in Relation to the PNI Paradigm



Research Questions

I sought to observe these research questions to determine the effects of cannabis usage patterns:

RQ-1: Do relationships exist between the frequency and longevity of cannabis use and anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959)?

H_{01}- No relationship exists between cannabis use frequency, longevity, and anxiety scores on the HAM-A.

H_1-A relationship exists between cannabis use frequency, longevity, and anxiety scores on the HAM-A.

RQ-2: Do relationships exist between the frequency and longevity of cannabis use and depression as measured by the PHQ-9 (Kroenke et al., 2001)?

H_{02}- No relationship exists between cannabis use frequency, longevity, and depression scores on the PHQ-9.

H_{2}-A relationship exists between cannabis use frequency, longevity, and depression scores on the PHQ-9.

RQ-3: Do relationships exist between the frequency and longevity of cannabis use and quality of life as measured by the Center for Disease Control's Health-related Quality of Life scale (HRQOL; Center for Disease Control, 2000)?

H_{03}- No relationship exists between cannabis use frequency, longevity, and quality of life on the HRQOL.

H_{3}-A relationship exists between cannabis use frequency, longevity, and quality of life on the HRQOL.

RQ-4: Do relationships exist between cannabis use frequency, longevity, and self-reported immunity as measured by the Immune Status Questionnaire (ISQ; Versprille et al., 2019)?

H_{04}- No relationship exists between cannabis use frequency, longevity, and self-reported immunity on the ISQ.

H_{4}-A relationship exists between cannabis use frequency, longevity, and self-reported immunity on the ISQ.

Methodology

Quantitative methods were used to help address lengths of usage among users as well as frequency of usage on how they present differently when compared with

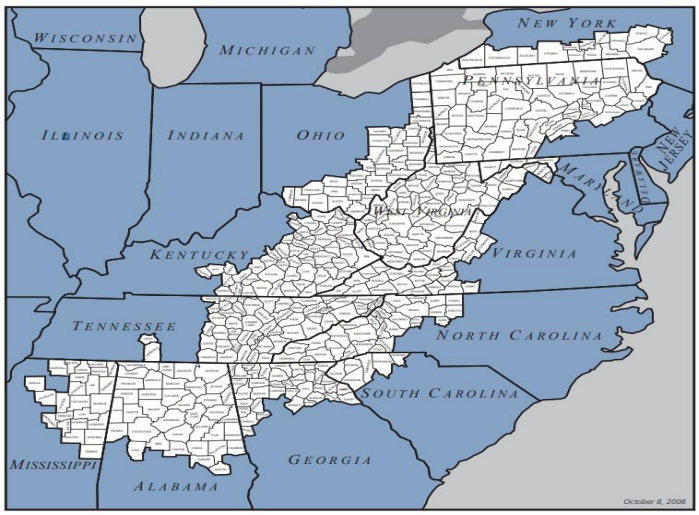
measures of anxiety, depression, immunity, and quality of life among individuals living in Appalachia. While a qualitative design was considered, the quantitative method was determined to be more appropriate in terms of understanding and collecting broader data trends regarding cannabis consumption behaviors.

Population

The target population was comprised of individuals living in the Appalachian region, meaning one of 420 counties that are quantified as Appalachia by the Appalachian Regional Commission as seen in Figure 2 (see Appendix A).

Figure 2

Map of Counties within the Appalachian Region in 2020



Sampling and Sampling Procedures

Participants for this study were recruited via SurveyMonkey, and individuals were recruited based on inclusion and exclusion criteria. Three major factors that were central to the study for inclusion include the residential location of the participants, which was

collected as county and state identification, participants' use of cannabis, and age group membership of the participants, as the research between adult and adolescent use of cannabis has shown significant differences (Gorey et al., 2019). With the ethical difficulties of including adolescent participants, participants surveyed were all adults eighteen or older to help ensure validity of measures and safety of participants.

Sample sizing was determined based on the percentage of Americans that have used cannabis per the most recent National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration, 2018), resulting in an estimate of 15% of the population based on sampling from their study. Comparing this to the population of Appalachia, roughly 25 million people (Appalachian Regional Commission, 2011), of which 22.5% are under the age of 18, giving 21.8 million after basic inclusion criteria, and an assumed 4.9 million individuals who use or have used cannabis. After applying standard sample size calculations, a sample size is needed of 158 participants for a confidence interval of 95%, which will be increased to 160 participants to account for potential errors in survey results.

To help find samples of only Appalachian participants, two groups of participants based on their location were created separately to conform to the SurveyMonkey recruiting structure. The groups were separated by states, but not subregions, to promote appropriate random selection. The first group encompasses Alabama, Georgia, Kentucky, Mississippi, Maryland, New York, North Carolina, and West Virginia; the second group covers Ohio, Pennsylvania, South Carolina, Tennessee, and Virginia.

Instruments and Constructs

Demographic information was collected from all participants with consideration for participant privacy by collecting only information that is necessary for relevance of the study. The measures that were collected included participants' sex, age (by grouped ranges), county and state of residence, and whether the participant had access to health insurance. The use of less specific location and age demographic information was used to protect the privacy of individuals living in the region, as most regions in Appalachia are comparatively small and sparsely populated, which could allow variables to make identifying potential participants easier. The lack of collection of race demographic information was also intentional, as individuals living in the region are overwhelmingly majority white, and as such any individuals identifying as any other race were more likely to be identified easier in the event of a catastrophic data leak issue.

Cannabis Use

For measurement of cannabis usage, the length of time in which individuals have partaken in cannabis use was measured across the length of months and years that a participant had used cannabis. The difference in usage length allowed for chronic effect comparisons when compared against shorter lengths of usage within the sample size. Frequency of use was also measured by the number of days in a month that a participant consumed cannabis and was compared across scales separately from longevity of use.

Anxiety-Hamilton Anxiety Rating Scale

For this study, the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959) was utilized to measure anxiety, but not expressly anxiety disorders. As a brief battery of 14 Likert-style items, the Hamilton Anxiety Rating Scale has been utilized as one of the most frequently used scales for measuring states of general anxiety, rather than focusing specifically on disorders (Bech, 2011). While the HAM-A has been criticized for its lack of specificity of anxiety disorders, the focus of this study was not to seek anxiety disorders, but instead understand anxiety states.

The reliability of the HAM-A was favorable with a few exceptions to specific questions; measuring at an interrater reliability of 0.74 overall, well over recommendation of .70 for early research studies (Nunnally & Bernstein, 1994), and reported validity of the scale at a Spearman coefficient of 0.63, with less validity in somatic anxiety measures over psychic anxiety measures (Maier et al., 1988). The review of reliability and validity does not create a strong case for the choice of this scale, but without the intention to diagnose anxiety disorders, using the HAM-A was complicated largely by one flaw, difficulty in pre-/post-test differentiation between anxiolytic and anti-depressant effects (Maier et al., 1988). For the purposes of this study, the difficulty in identification of changes in anxiety states between testing does not pose a problem due to the singular instance of data collection structure.

Scoring for the HAM-A was simple, as the test was designed to use total scores with each question scoring on a 0-4 scale based on the Likert-style 5-choice responses.

All 14 questions were similar scored, with no need for reverse coding any variable. Subtypes for the scores were not investigated in this study due to uncertainty of validity between the subtypes brought up due to overlap (Bech, 2011). The scales' group scoring was clear with <17 being mild, 18-24 being mild to moderate, and 25-30 being moderate to severe (Hamilton, 1959). There was not a mention of what a score over 30 indicated in the original scale manual, but more recent versions list the range as severe anxiety (Bech, 2011).

Depression-Patient Health Questionnaire

The PHQ-9, patient health questionnaire, is a self-administered scale that was utilized to measure rates of depression (Kroenke et al., 2001). The scale is a 9-item questionnaire that like the HAM-A (Hamilton, 1959) is all positive-loaded and did not require any reverse coding to score. Scores on the PHQ were grouped by the total scores clearly from 0-4 (minimal), 5-9 (mild), 10-14 (moderate), 15-19 (moderately severe), and >20 (severe).

While a very short form survey with only nine items, the test has been utilized in health care clinics, with an overwhelmingly positive reliability, measuring at a Cronbach's alpha of .89 and .86 in two studies upon the establishment of the PHQ-9 in 2001. Further, the reliability of this scale was supported on one-dimensional measurements at a Cronbach's alpha of .87 in recent research (Villarreal-Zegarra et al., 2019). Validity was reinforced using likelihood ratios that consistently improved as

scores increased, between 6 and 13.6 times as likely to correctly identify major depression in tandem with the score ranges (Kroenke et al., 2001).

Quality of Life-CDC's Health-related Quality of Life

The Center for Disease Control's health-related quality of life (HRQOL; Center for Disease Control, 2000 is a commonly used measure for determining quality of life of participants. A 14-item measure, the CDC has used the HRQOL frequently since its inception with some critics of the scale arguing of subjectivity versus objectivity (Lin et al., 2013). While the scale has historic use in pieces, by design the scale are three modules: Healthy days core module, healthy days symptoms module, and activity limitations module. For both the limitations of the SurveyMonkey structure and qualitative nature of the "activity limitations module", the module was removed from data collection, but their removal does not reduce validity of the measure, as even the HRQOL-4 (consisting of only the Healthy Days core module) has been used in medical practice with success.

The methodology in which the HRQOL is designed to be scored for summary scores does not allow for use in linear regression models, additionally the scale was not designed to utilize summary scores, but summary scores have been validated to be used when removing the same module (Horner-Johnson et al., 2009). For measurement of the 30 days measures, questions #2 - #8 were combined (with one question reverse-coded) so that every question was in the same direction as the "unhealthy days" structure discussed in the HRQOL manual. When scoring for unhealthy days in the manual however, the

intention for scoring limits the number at 30 when combining scores, and due to concern of summary scores all nearing 30 when combining across items, scores were not capped for measurement. Given the nature of the study being predominantly self-reported measures and the construct validity of the questions being used, the HRQOL scale should be sufficiently consistent for the purpose of this measurement but staying cognizant that summary scores were not the original intention of the scale.

Immunity-Immune Status Questionnaire

Measuring self-reported immune function created a different level of complication, as typical measurements of immune function are done with in-person lab tests by measuring blood concentrations of immunoassays, including cytokines and antibody concentrations. A battery of measurement of perceived immune function, called the Immune Status Questionnaire (ISQ; Versprille, et al., 2019) has recently been published that upon release had attained appropriate reliability ($r = .80$) and predictive validity (85%), after psychometric reductions of the number of items in the scale from 21 to 7.

In scoring the seven questions, a summary score is used and then reverse-coded with some numbers being combined to reduce a scale of 0-15 possible answers to a 0-10 scale. By including this measure, comparisons were made between the use of cannabis, measures of depression and anxiety, quality of life, and immune function. These relationships were compared and predicted with linear regression analyses. While not the

most ideal choice for measurement of immunology, the ISQ was likely the most efficacious given the structure of online survey methodology.

Operationalization

By recruiting individuals online, measures of the relationships of cannabis use were discerned by responses to surveys. Where the individuals report their own use over a span of months and years, rather than dosages, the directive of this study was to observe the effects of patterns of use whilst dealing with the issues of self-reporting that has been proven to be very poor in cannabis studies of humans (National Academies of Sciences, Engineering and Medicine, 2017). By observing long-term use and frequency of use, the introduction of variability did exist. Without a standardized manner to measure the dosages, especially with multiple forms of delivery methods and tolerance differences between individuals, the variability was an ever-present artifact amongst any non-manipulation study of cannabis that until legalization, and subsequent standardized research design, were always going to be present across studies.

The study was conducted digitally, with surveys presented as separate pages of a multi-page interface. With a small, undisclosed reward from the listing facilities as reward, participants should have completed the test in 30 to 60 minutes, but on average less than 15 minutes was spent, as the interface involved was simple.

The survey included a brief cannabis use question as an inclusion/exclusion criteria question to help avoid participants who had no history of cannabis use, however due to some errors in the study conducting through SurveyMonkey, an additional subsect

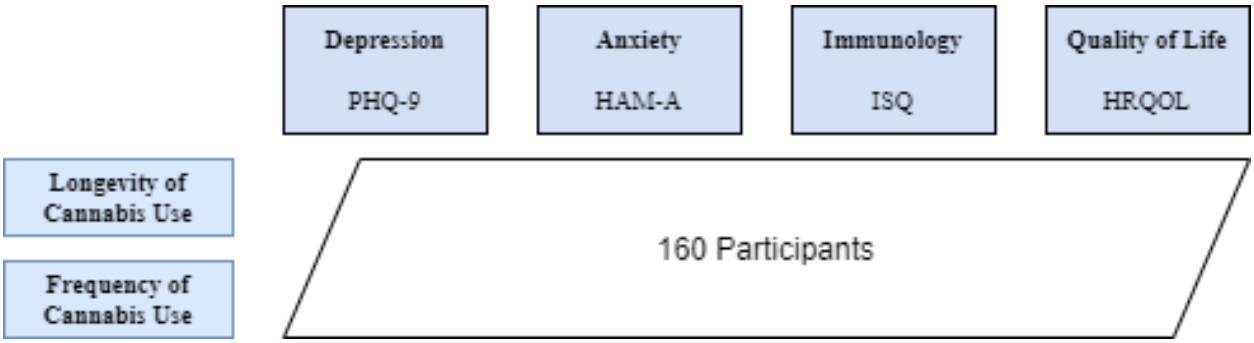
of non-users was collected in addition to the 160 participants sought. Participants aged 18-25 years old in West Virginia, the only state entirely in the Appalachian Mountain region, showed an average of 30.66% of individuals having used cannabis before, while 12.40% of participants expressed having used cannabis for greater than 10 years (National Survey on Drug Use and Health, 2018). As the comparative incidence reduced over time, the collection of participant data was expected to show a larger population of individuals having shorter histories of use on average in the region. This assumption was not true, as the spread of longevity data was not heavily weighted, rather only marginally higher frequency in short-term use.

Data Analysis Plan

By observing the differences in cannabis use patterns, differences in the overall health of the individuals were compared to determine if differences in relationships existed across users. By conducting regressions in both linear (1 predictor x 1 outcome) and multiple regressions (2 predictors x 1 outcome) using SPSS (IBM Corp., 2020), patterns of differing usage were observed across four interval-measure scales of overall well-being: depression, anxiety, quality of life, and immunity. Each of the scales was measured as raw data numbers, with the exceptions of the ISQ, that required one variable to be reverse-coded to find the summary scores, and the HRQOL, which gave a summary score across the 30 day variables and had one reverse-scored variable in the measure.

Figure 3

Research Design and Participant Pool Structure Across Variables



Threats to Validity

Validity for this study was based on multiple constructs that to this point have had very little overlap with the field of observing behavior in relation to cannabis, as much of the research is still being called for. While the instruments that have been chosen were all reviewed for their own validity of measuring their respective constructs, there were reasonable arguments that the construct measurements directly related to anxiety, depression, immunity, quality of life, and drug use were not going to be remarkably powerful. With these instruments having high degrees of validity and reliability, the resulting assumptions from data analysis was relevant and realistic for the study design and constructs being measured. Until the time of legalization loosens the restrictions on research, the validity in the field of cannabis cannot be improved more than marginally.

External Validity

Comparing mental health criteria (depression and anxiety) of cannabis users without directly seeking individuals with confirmed diagnoses is an area that is largely

undeveloped at the time of this study. Many research organizations are still constrained from investigating cannabis use, for scientific purposes or otherwise, as the substance is federally illegal. While the validity of measurements is strong, the generalizability of the construct has some issues, particularly when discussing the method of measuring cannabis use and the usage methodologies in which individuals pursue when consuming.

For this study, measurements of long-term use and frequency of use (but not dosage or methodology) were applied. As research has shown, dosage of the cannabis used can greatly alter the effects of cannabis on the brain (Bolla et al., 2002), but dosages and even physical forms of cannabis can create variability. For example, by ingesting different strains of cannabis (indica v. sativa) differences can be seen in resulting behavioral changes, such as increased energy and appetite found when consuming indica-prominent strains, rather than lethargic and euphoric effects from sativa-prominent strains (Corral, 2001). Due to variability of cannabis that is unable to be measured or controlled based on availability, focus on the patterns use was necessary to be capable of measuring cannabis use at all.

Internal Validity

Of the utilized measures of this study, all scales have been reinforced and defended for their ability to measure the constructs they have been chosen for. While the use of cannabis as a predictor variable cannot be determined to be the sole variable involved in changes to the criterion variables inter-personal differences, survey-based measures of illicit activities consistently have lower comparative internal validity against

a true experimental design with active manipulation. With a large enough sample size and comparability across use patterns, internal validity showed the direct relationships with external variables that were compared in post-hoc comparisons. While internal validity in this study may raise some speculation, the study itself was not looking for direct cause and effect, but rather relationships in the patterns of use and how changes in criterion variables appeared in vivo without manipulation.

Ethical Procedures

Given the stigma of mental health treatment in the region and the illicit nature of cannabis use, anonymity of the individuals participating in the study was of the utmost importance. As such, collection of demographic information was limited to avoid any potential for a data leak that could make identifying the participants possible. By collecting the name of the county that the individual lives in, rather than zip code or city/state, confirmation of residence in Appalachia was enough to qualify for the study, with gender and age group membership being key measures that allowed for analysis without excessive identifying potential.

Due to the survey nature of the study, as well as a complete lack of use of troubling or new measures outside of a demographic question, the ethical ramifications from this study were minimal. By administering this procedure online as well, further anonymity and a lack of potential manipulation of the data via researchers was promoted. The illicit nature of cannabis use being an open, anonymous admission of criminal activity means that three-quarters of the potential participants could be charged if the

demographic information was specific enough to be able to identify individuals (such as someone of a minority race in a region that is overwhelmingly Caucasian). The IRB approved this methodology without exception on August 24th, 2021, two days before data collection began. IRB approval #: 08-24-21-0762207.

Data collected in this study was stored securely on an external hard drive and kept in a locked, fire-proof safe at the researcher's home, and will be kept safe for seven years. The dataset has had all specific identifiable information removed, and as such the data set may be requested and distributed to researchers upon request, but safety for the participants has been ensured due to anonymous data collection practices.

Summary

Designing a quantitative measure of the relationships between cannabis use and the criteria variables, the structure of the study utilized four variables to help answer the four hypotheses. While unable to measure neurological factors, the four variables measured were chosen to encompass much of the PNI lens. For both the ability to reach more participants throughout the region and for safety during the COVID-19 pandemic, utilizing online surveys was ideal to find a sample of 160 participants within the 420 counties that reported using cannabis. While validity and reliability have some room for errors, the interactions and relationships between variables and ethical handling practices were approved for data collection, which was analyzed and presented in Chapter 4.

Chapter 4: Data Analysis

Observations of cannabis use behaviors of Appalachian individuals were conducted digitally to investigate relationships between predictor and criterion variables. Cannabis use behaviors in terms of both frequency and longevity of use were used to determine if predictions could be made about scores on one of several scales being used in PNI to observe well-being. The hypotheses of the study being that there were some predictable relationships that could be drawn between well-being (mental, physical, and immune health, as well as QoL) and cannabis based on data collected. In this chapter, research questions were addressed individually to understand relationships and determine if specific behaviors were more prevalent than others.

Data Collection

Data were collected from SurveyMonkey's interface on August 26, 2021 and completed within 24 hours of posting the study. Study participants were broken into two groups of states to allow for demographic selection to only recruit Appalachian participants. The two groups were:

- Group A: Alabama, Georgia, Kentucky, Maryland, Mississippi, New York, North Carolina, and West Virginia
- Group B: Ohio, Pennsylvania, South Carolina, Tennessee, and Virginia

Table 2

Recruiting Insights: Group Separation

	Total Responses	Complete Responses	% Complete	Qualified	% Qualified
Group A	204	122	59.8%	84	41.2%
Group B	149	108	72.5%	81	54.4%

Discrepancies occurred during data collection due to a logic loop in the survey structure that allowed participants to disqualify and still proceed to completion. Due to this error, the study was open at two separate times: 9 a.m. to 12 p.m. and 3:30 p.m. to 7 p.m. The logic loop was caught by the SurveyMonkey engineering team after I noticed that disqualified participants were being counted in the final count of participants. Due to this error, roughly 65 completed participants who do not use cannabis' data were collected.

Of the reporting data, 230 participants' full responses were collected, of which 165 participants qualified fully. Participant response was moderately high, with 86% of qualified participants who began the survey completing it. On average, the survey took participants just over 5 minutes from start to completion.

Overall, the population involved was representative of the region; however, it should be noted that West Virginia, the only state to be entirely within the boundaries of Appalachia, had only one participant in this survey. Lack of representation of West Virginia aside, participants were well-balanced in terms of age and region of residence. While some representation issues may cause concerns in terms of external validity, this

was a data collection anomaly that may have been avoidable with more expensive survey collection methods that were outside the scope of this study.

Results

Participants' descriptive data included their state of residence, age, and gender.

Table 3

Participants by State of Residence

State	n	%
Alabama	17	10.3
Georgia	21	12.7
Kentucky	13	7.9
Maryland	4	2.4
Mississippi	6	3.6
New York	7	4.2
North Carolina	13	7.9
Ohio	13	7.9
Pennsylvania	34	20.6
South Carolina	9	5.5
Tennessee	17	10.3
Virginia	10	6.1
West Virginia	1	.6

Sizeable populations from each state appeared to be represented, apart from West Virginia (n=1). Other states all were similar in proportion to the portion of land that is part of the Appalachian Region, e.g. the portion area of Maryland that is within the Appalachian Mountain region is very small (n=4; three counties), compared to Pennsylvania where most of the state is within the region (n=34; fifty-two counties).

Table 4

Participants by Age Group

Age Group	N	%
18 to 24	22	13.3
25 to 34	38	23.0
35 to 44	46	27.9
45 to 54	30	18.2
55 to 64	15	9.1
65 to 74	11	6.7
75+	3	1.8

Age span for participants in this study was largely sufficient in terms of representing age groups across Appalachia, with the smallest group being those over the age of 75, with only three participants. While this was acceptable for data analyses and scope of this study, it was not appropriate to generalize about group behaviors with such low representation.

Table 5

Gender Breakdown of Participants

Gender	N	%
Female	108	66.7%
Male	54	33.3%

Two women participated for each man in this study. Gender was not a consideration for the study, but women were predominantly surveyed. There were

options for survey collection that did account for gender balancing; however, this was out of the scope of this study and available funding, as gender balancing would have increased the study cost exponentially. Women reported higher summary scores than men on the HAM-A, as women are historically more likely to report anxiety than men (Jalnapurkar et al., 2018).

Multiple Linear Regressions

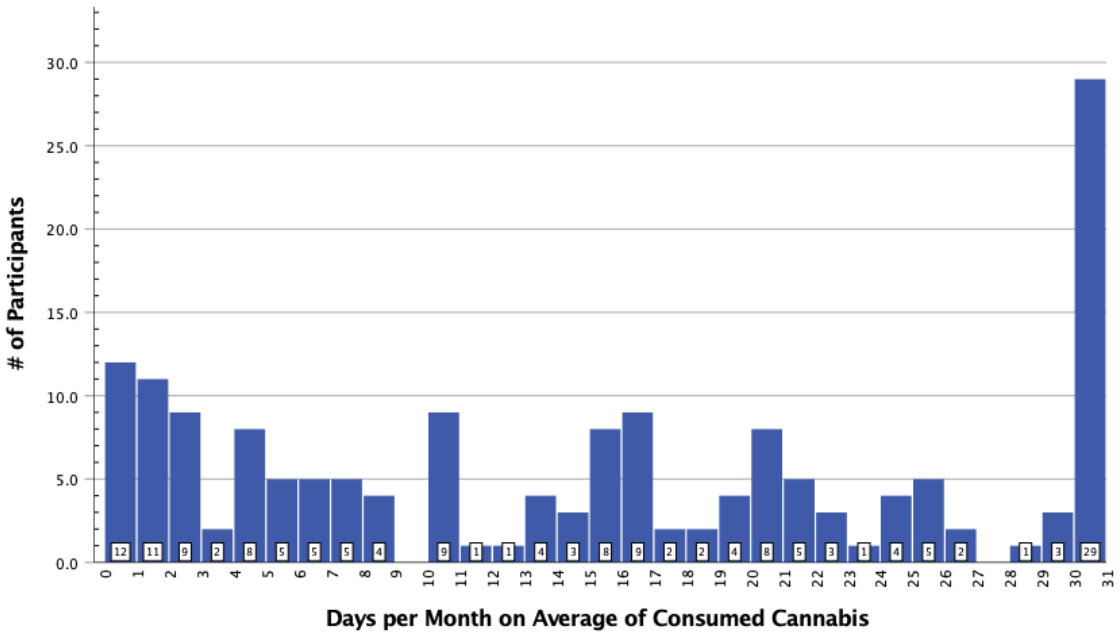
For most analyses in this study, linear regressions were used. Data in this study were visualized with the dependent variable on the y-axis, and standardized predicted values on the x-axis. The acronym MLR (multiple linear regression) was used to shorten the length of graph titles in this chapter.

Cannabis Use

Cannabis use data were robust, with longevity of cannabis use being measured in months from the data collected (months and years were combined into one variable by multiplying years by 12 and finding a sum), while frequency was measured in terms of days per month. Twenty-nine participants (roughly 18%) were daily cannabis users and 49% of participants have used cannabis for over 10 years.

Figure 4

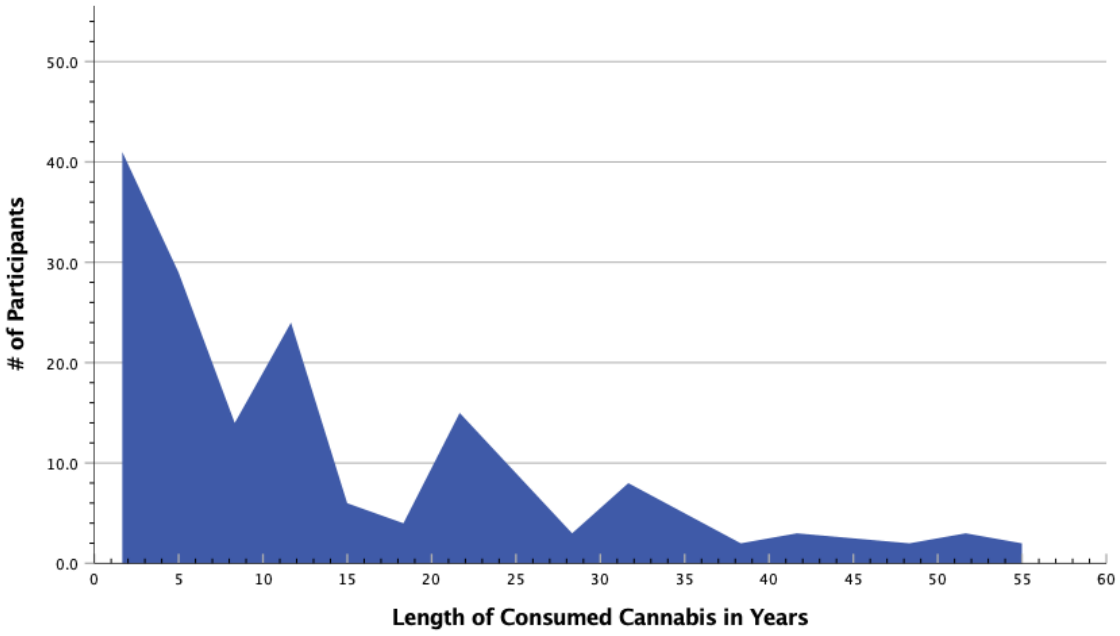
Frequency/Days Per Month of Average Cannabis Consumption



Frequency of cannabis consumption was spread from 0 (for those who use, but at a less than once monthly rate), to 30 (denoting daily users). It should also be noted in reading this graph, that the X-axis numbers for each bar are to the left of their base, there were no responses of 31 days per month.

Figure 5

Longevity of Cannabis Consumption



Longevity of cannabis consumption shows many individuals have only in the past fifteen years started to use cannabis, but history of cannabis use in the region dates back much earlier. The longest participants' history of cannabis use was just over 55 years, but a spread was obtained where roughly 50% of all participants are above 10 years, and 50% fall below.

Data Analyses

To observe many of these scales, both total scores and individual questions were investigated to determine if relationships may exist between specific factors of each of the hypothesized domains in addition to overall effects. Only significant individual

effects were reported, but data outputs for each question and their relationships to the predictor variables can be found in Appendices C & D.

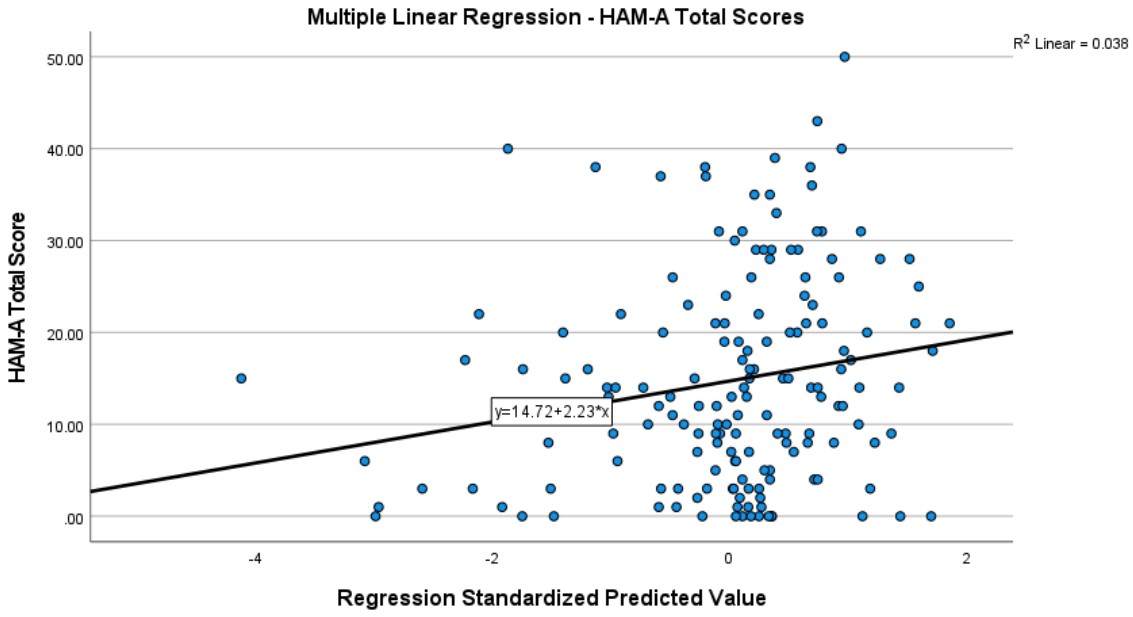
Anxiety

When investigating the participants' anxiety levels, several relationships were observable: one amongst the total scores of the HAM-A, and three statistically significant individual relationships based on specific question domains.

HAM-A Total Scores

Figure 6

MLR: Longevity and Frequency on HAM-A Total

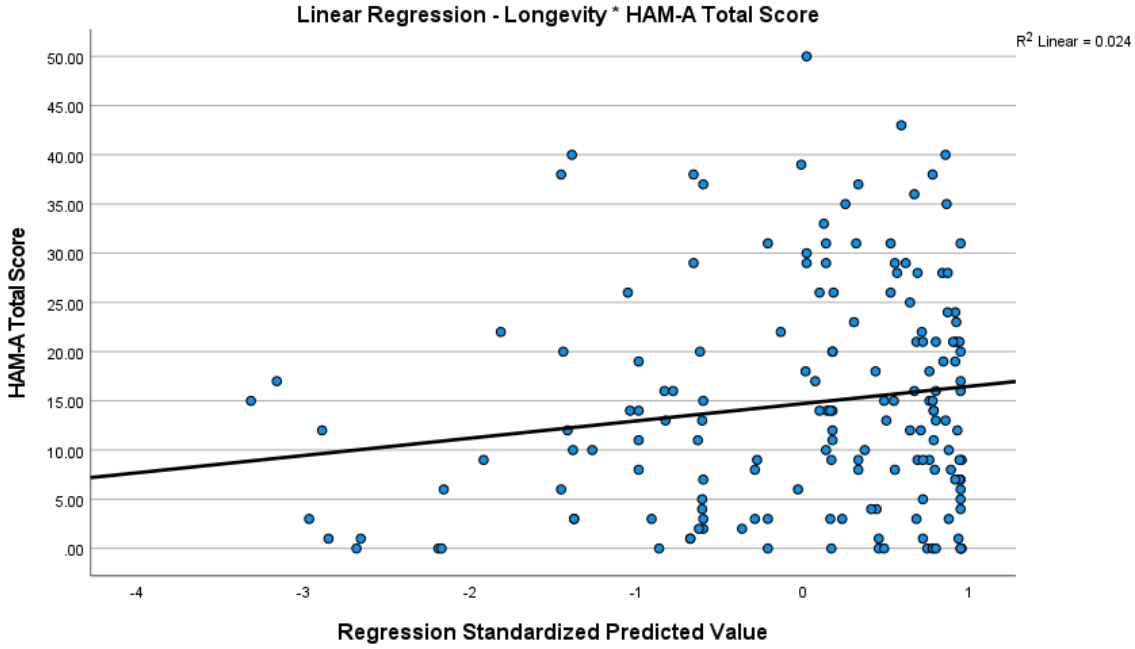


A multiple linear regression analysis using the enter method was conducted to examine whether total scores on the Hamilton Anxiety scale can be predicted by

frequency of cannabis use per month and length of time using cannabis. The model was significant, *F(2, 164) = 3.212, p = .043*, explaining 3.8% (R^2 = 0.038) of variance in predicting the total score. Longevity of use (B = -.174, t = -2.403, p = .017) contributed significantly to the model, but frequency (B = .138, t = 1.562, and p = .120) did not.

Figure 7

Longevity of Cannabis Use on HAM-A Total Scores



Observing the individual predictor variable (Longevity) against the total score for HAM-A revealed a significant relationship, *F(1,164) = 3.949, p = .049, R^2 = .024*, that explained 2.4% of variance in predicting the total score just using longevity *(B = -.136, t = -1.987, p = .049)*.

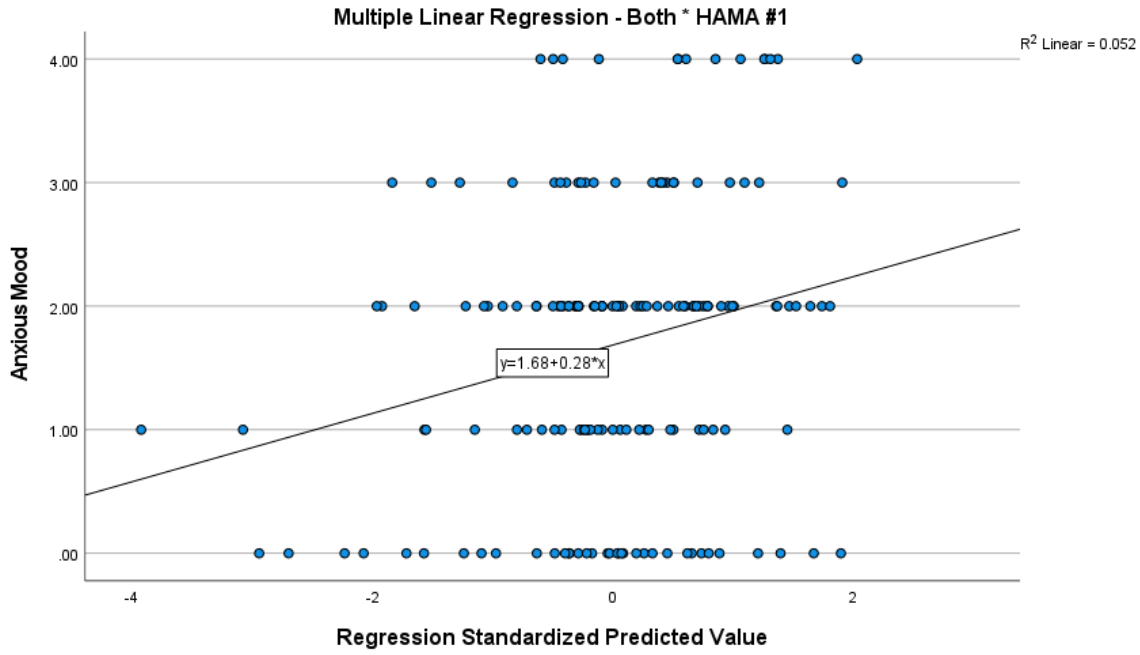
HAM-A Individual Questions

When observing relationships between predictor variables and individual questions on the scales, more understanding of how cannabis interacts with specific domains of the measures could be observed with the data. Of all the individual questions in the scale, these were statistically significant, for data outputs on other, non-significant relationships, see Appendix C.

HAM-A #1-Anxious

Figure 8

MLR: Frequency and Longevity on HAM-A #1



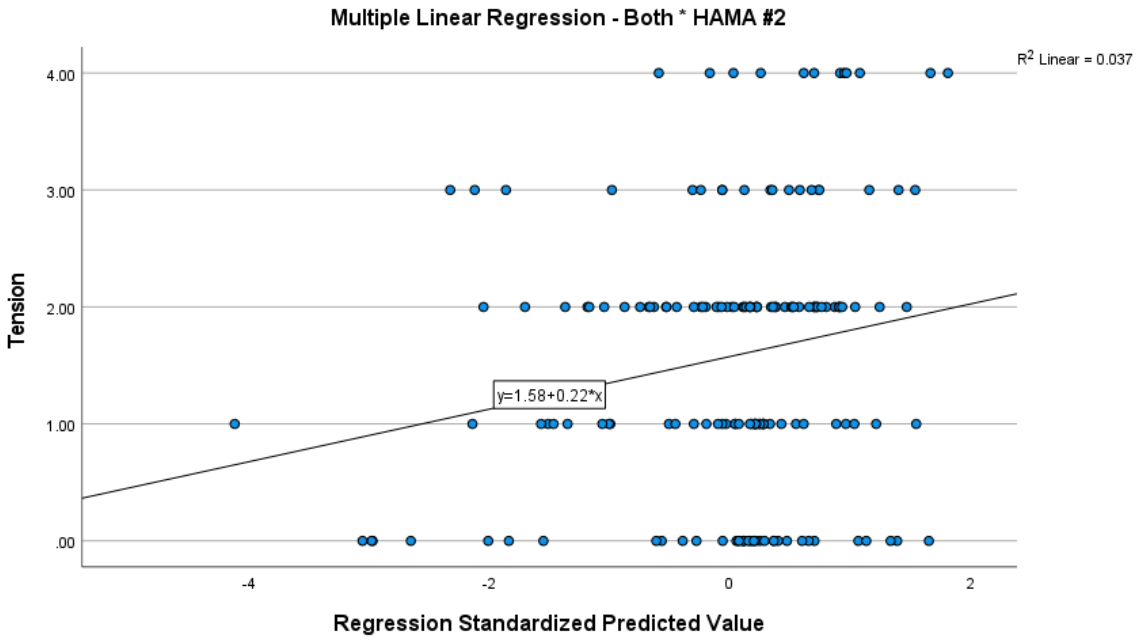
A multiple linear regression analysis using the enter method was conducted. The model was significant, *F(1, 164) = 4.477, p = .013*, explaining 5.2% (R^2 = 0.052) of

variance in predicting the summary score. Longevity of use (*B = -.002, t = -2.460, p = .015*) and frequency of use (*B = .023, t = 2.427, p = .016*) both contributed significantly to the model.

HAM-A #2-Tension

Figure 9

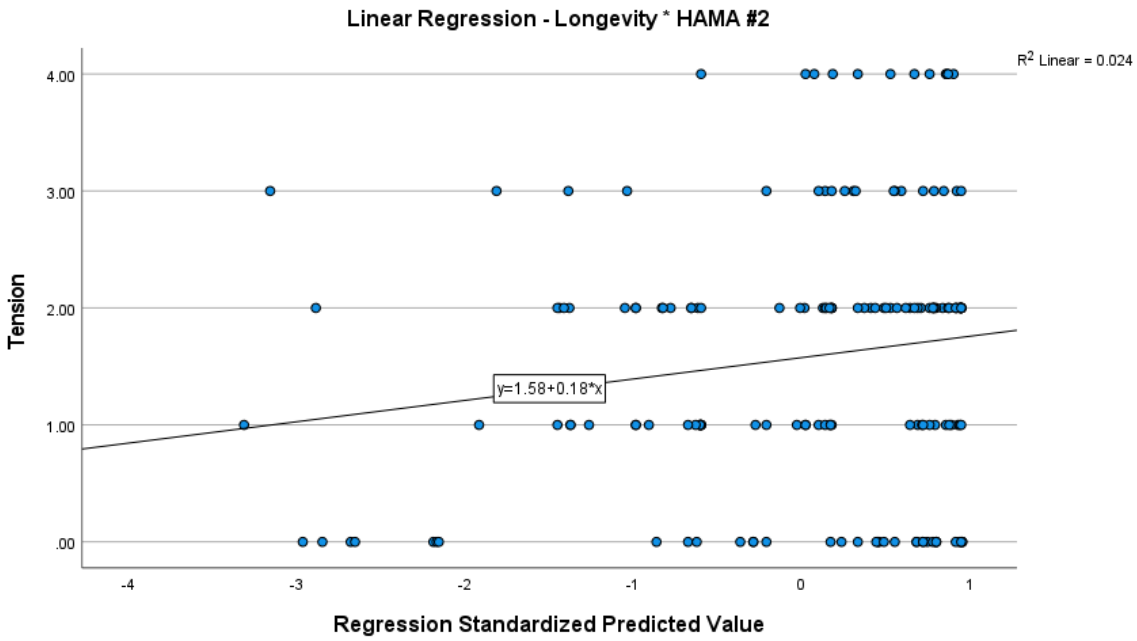
MLR: Frequency and Longevity on HAM-A #2



The enter method was used to conduct a multiple linear regression. The model was significant, *F(1, 164) = 3.103, p = .048*, explaining 3.7% (R^2 = 0.037) of variance in predicting the tension score. Longevity of use (B = -.001, t = -2.394, p = .018) contributed significantly to the model, but frequency (B = .013, t = 1.450, and p = .149) did not.

Figure 10

Linear Regression: Longevity on HAM-A #2

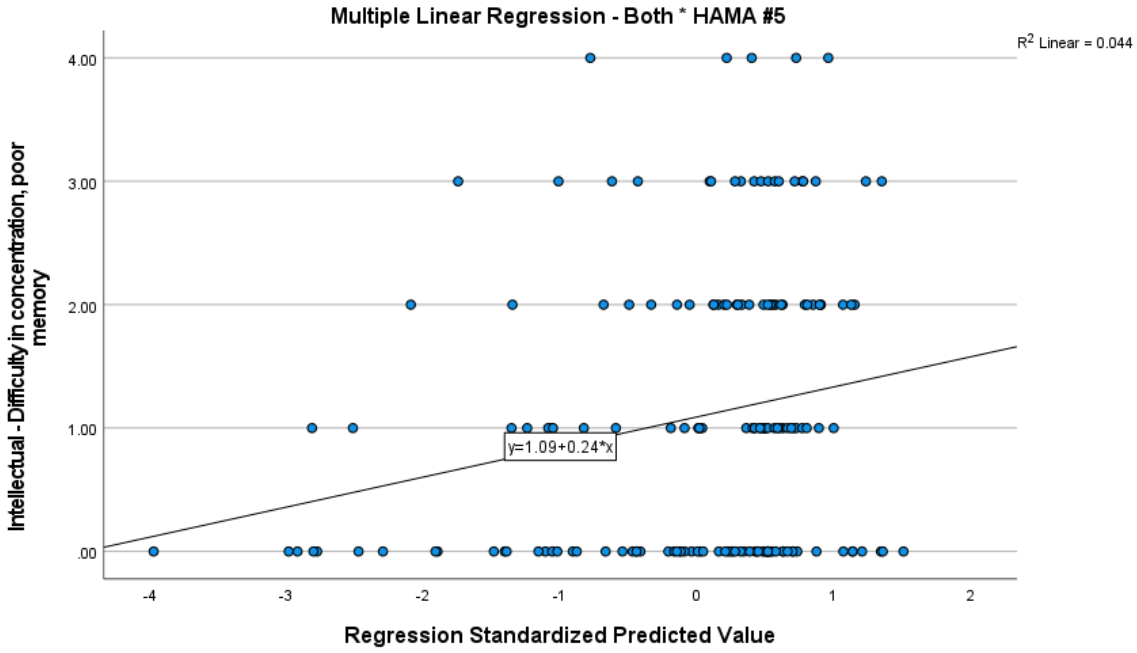


On a simple linear regression of longevity's ability to predict scores on HAMA #2, a significant model was found, $F(1,164) = 4.077$, $p = .045$, $R^2 = .024$, that stated longevity ($B = -.001$, $t = -2.019$, $p = .045$) accounted for 2.4% of the variance in scores on this question.

HAM-A #5-Intellectual

Figure 11

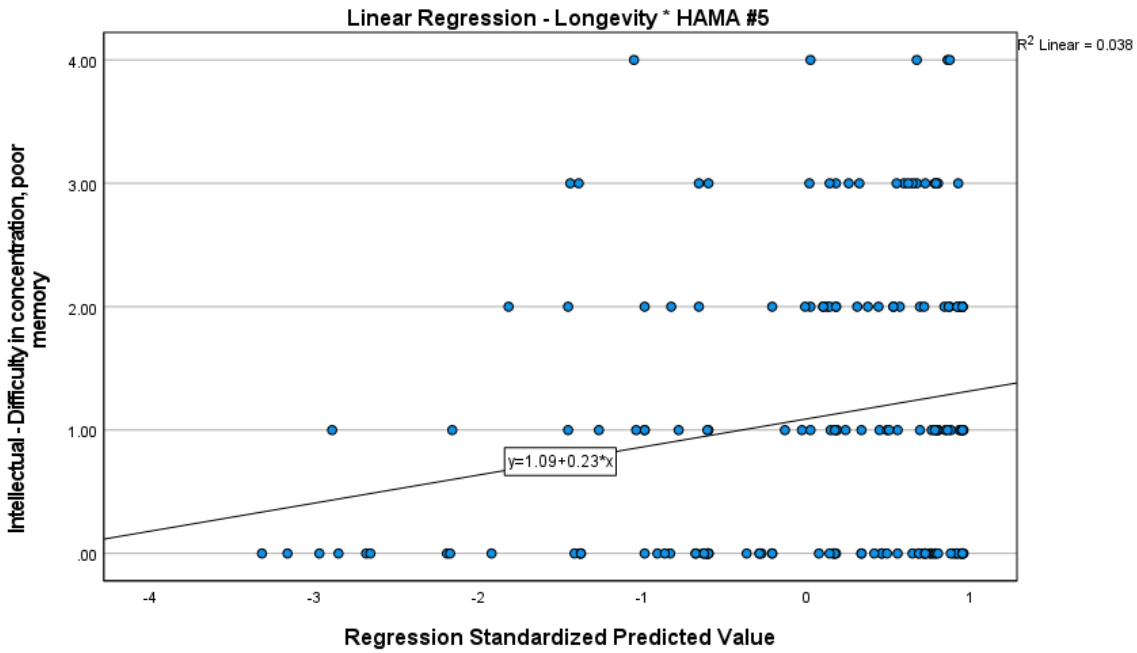
MLR: Longevity and Frequency on HAM-A #5



This model was significant, *F (1,164) = 3.728, p = .026,* and explains 4.4% (R^2 = .044) of the variance of intellectual difficulties. In an ongoing trend, longevity significantly contributed (*B = -.002, t = -2.730, p = .007*) and frequency did not (*B = .009, t = .974, p = .331*).

Figure 12

Linear Regression: Longevity on HAM-A #5



A simple linear regression analysis of longevity (*B = -.001, t = -2.551, p = .012)* on HAMA #5 showed a significant model, *F(1,164) = 6.509, p = .012, R^2 = .038).* This model helped predict 3.8% of the variance in scores on HAMA #5.

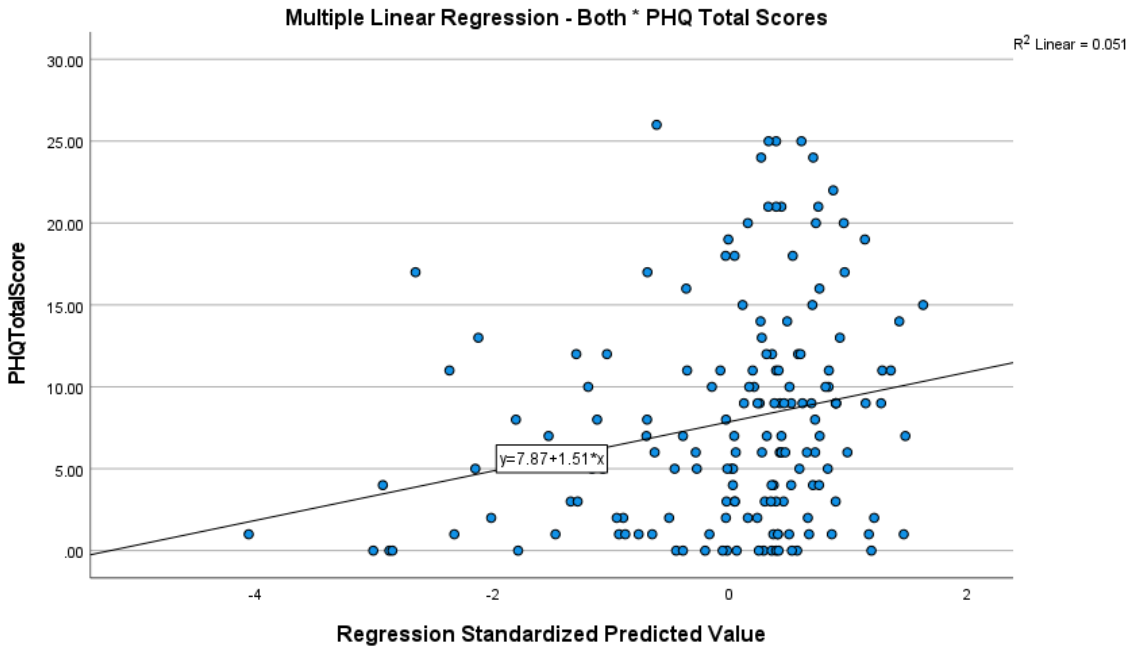
Depression

For depression, data was collected using the patient health questionnaire (PHQ; Kroenke et al., 2001). One major relationship was found, in addition to three individual domain relationships.

PHQ-9 Total Scores

Figure 13

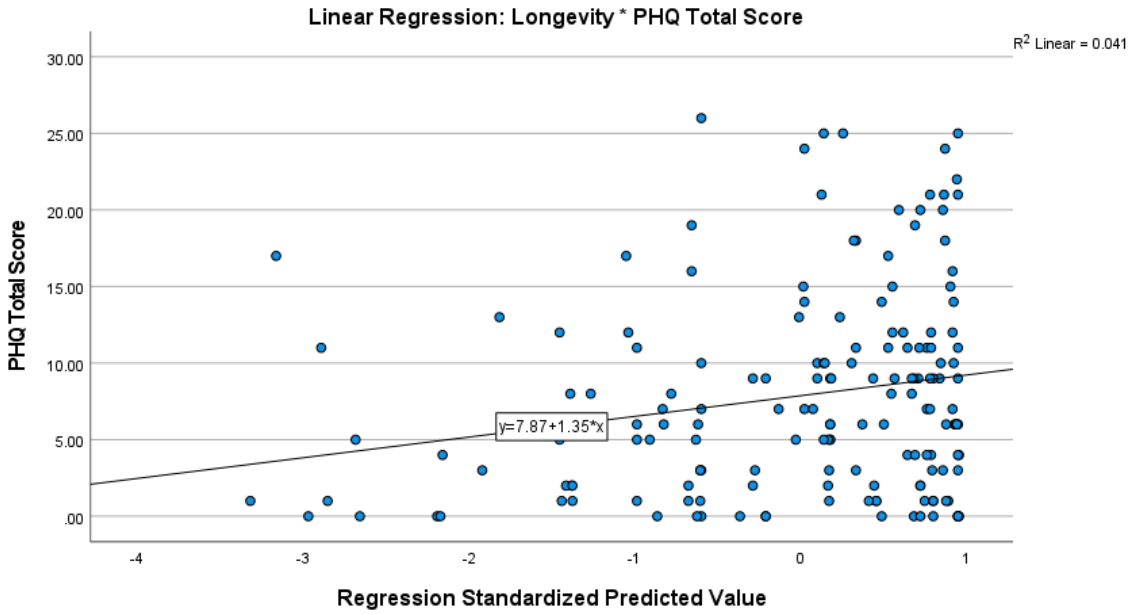
MLR: Longevity and Frequency on PHQ Total Scores



A multiple linear regression analysis using the enter method was conducted to examine whether total scores on the patient health questions could predict depression using the frequency of cannabis use per month and length of time using cannabis. The model was significant, *F(2, 164) = 4.397, p = .014*, explaining 5.1% (R^2 = 0.051) of variance in predicting the total score. Longevity of use (B = -.010, t = -2.945, p = .004) contributed significantly to the model, but frequency (B = .067, t = 1.312, and p = .191) did not.

Figure 14

Linear Regression: Longevity on PHQ Total Scores



In observing a linear regression between longevity and PHQ total scores, the model was significant, which allowed longevity of use to predict total scores on the PHQ, $F(1,164) = 7.042$, $p = .009$, $R^2 = .041$, with variance being explained by 4.1% ($B = -.009$, $t = -2.654$, $p = .009$).

PHQ-9 Individual Question Scores

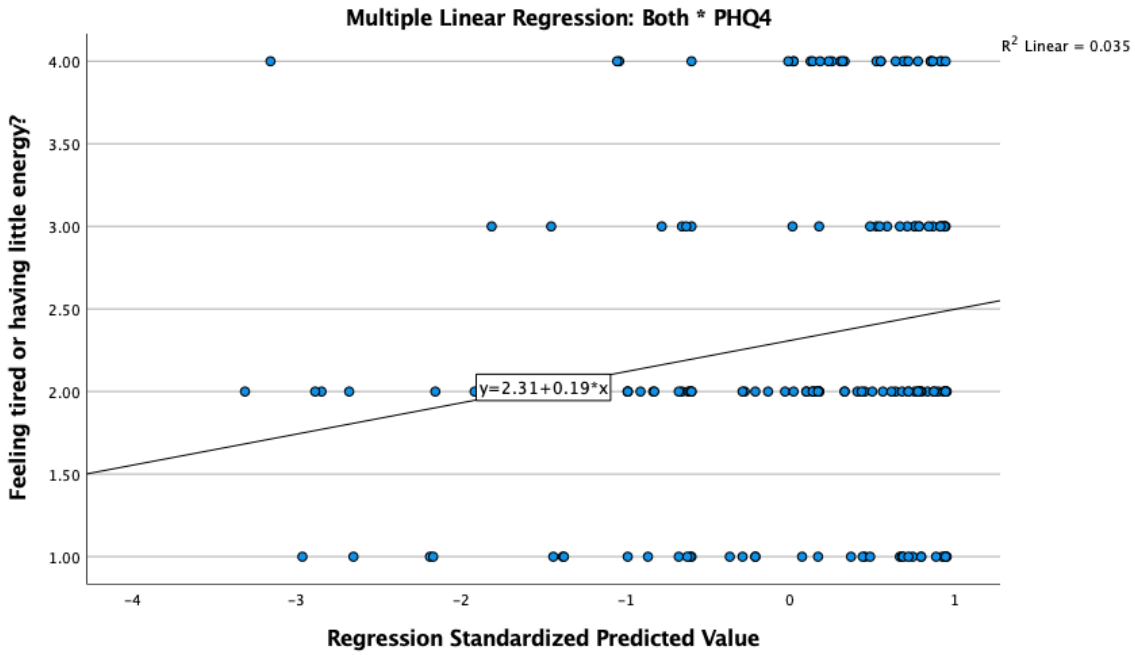
Several relationships were found among PHQ question responses, specifically on questions 4, 5, and 7.

PHQ #4-Tired

A multiple linear regression analysis using the enter method was conducted. The model was significant, *F(2, 164) = 3.198, p = .042*, explaining 3.8% (R^2 = 0.038) of variance in predicting the total score. Longevity of use (*B = -.001, t = -2.536, p = .012*) contributed significantly to this model, but frequency of use (*B = .006, t =.747, p = .456*) did not.

Figure 15

MLR: Longevity and Frequency on PHQ #4

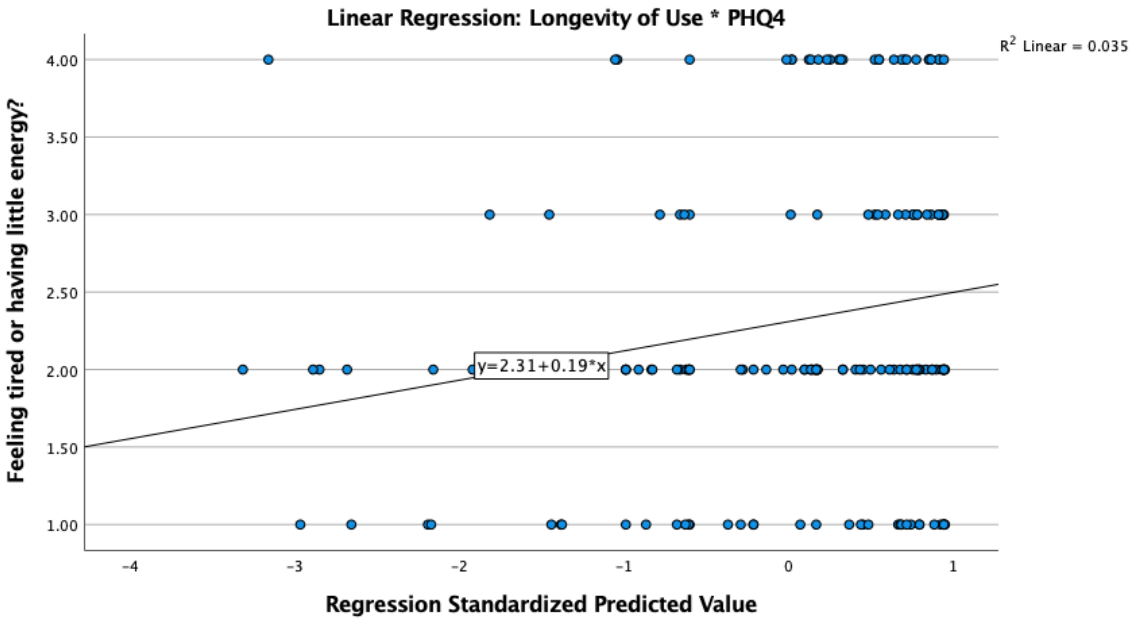


When observing the question utilizing a simple linear regression with the significant longevity variable, a significant relationship was also seen: *F(1,164) = 5.901,*

p = .016, R^2 = .035. Only accounting for 3.5% of the variance, longevity did contribute significantly to the model (*B = -.001, t = -2.429, p = .016).*

Figure 16

Linear Regression: Longevity on PHQ #4

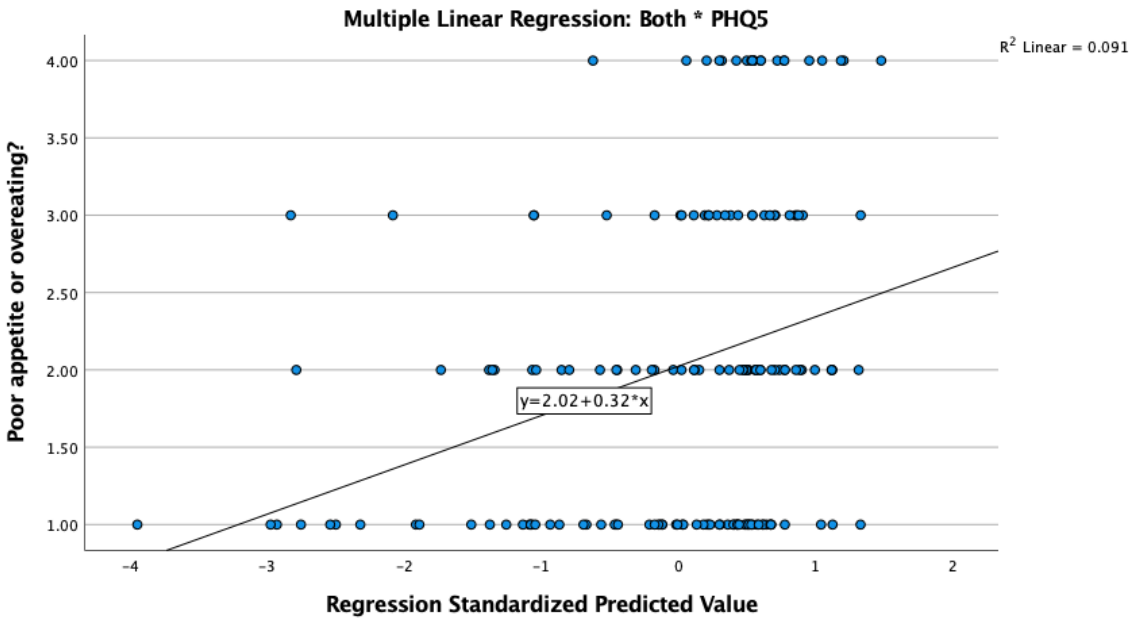


In a simple linear regression, a relationship was found between longevity of cannabis use and feelings of tiredness: *F (1, 164) = 5.901, p = .016, R^2 = .035.* 3.5% of the variance was explained by longevity *(B = -.001, t = -2.429, p = .016).*

PHQ #5-Appetite

Figure 17

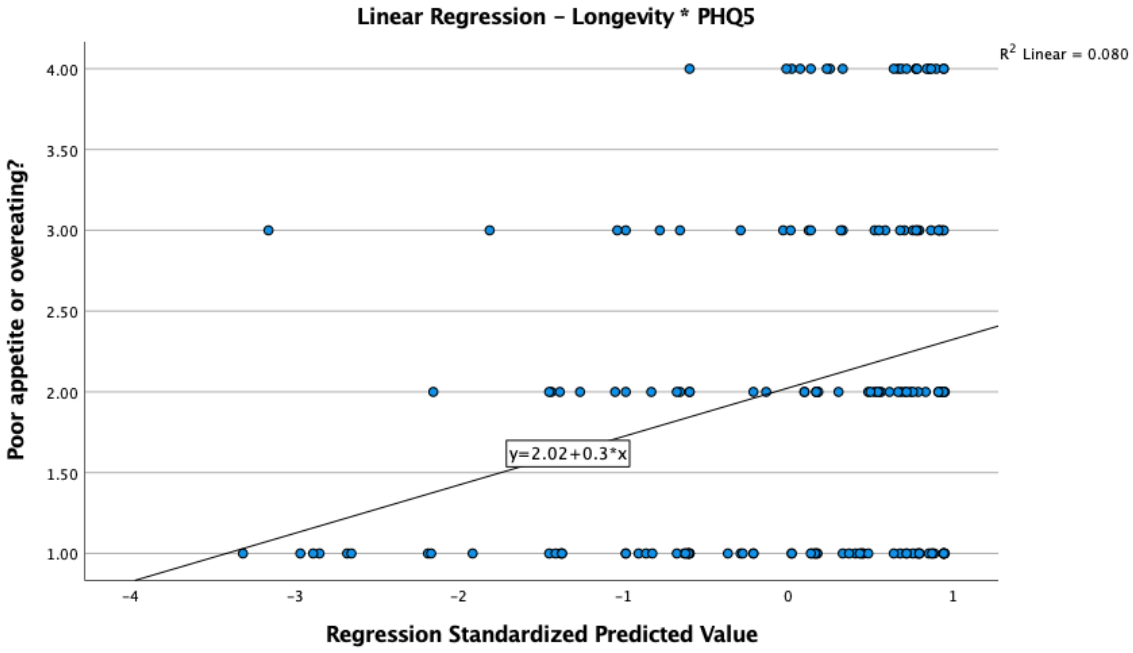
MLR: Longevity and Frequency on PHQ #5



A multiple linear regression analysis using the enter method was conducted. The model was significant, *F(2, 164) = 8.075, p < .001*, explaining 9.1% (R^2 = 0.091) of variance in predicting scores related to appetite. Longevity of use (*B = -.002, t = -4.019, p < .001*), but not frequency of use (*B = .011, t = 1.366, p = .174*), contributed significantly to the model.

Figure 18

Linear Regression: Longevity on PHQ #5

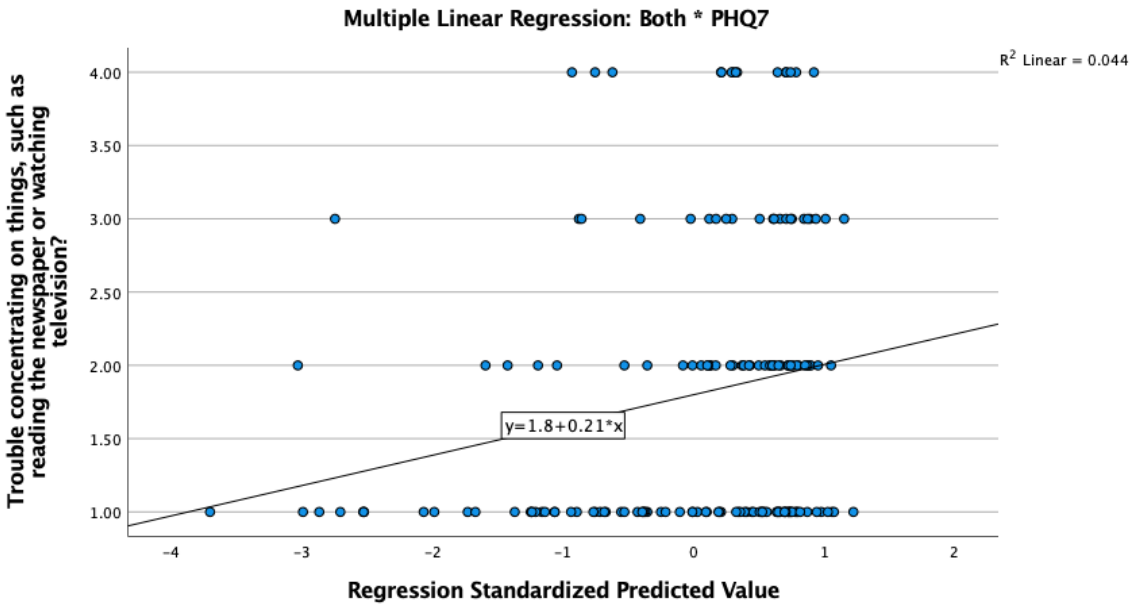


When observing longevity *(B = -.002, t = -3.769, p < .001)* directly against PHQ #5, a significant relationship was found, $F(1,164) = 14.209$, $p < .001$, $R^2 = .080$. 8% of variance in responses to PHQ #5 could be predicted by how long an individual has consumed cannabis.

PHQ #7: Trouble Concentrating

Figure 19

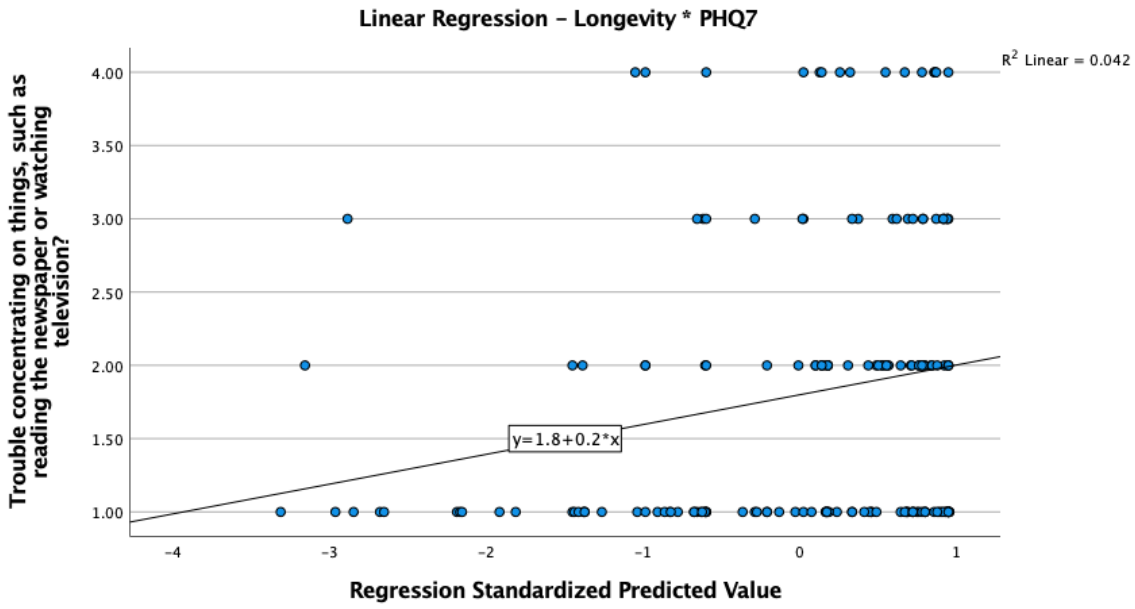
MLR: Longevity and Frequency on PHQ #7



A multiple linear regression analysis using the enter method was conducted. The model was significant, *F(2, 164) = 3.696, p = .027*, explaining 4.4% ($R^2 = 0.044$) of variance in predicting scores related to appetite. Longevity of use (*B = -.001, t = -2.685, p = .008*), but not frequency of use (*B = .004, t = .494, p = .622*), contributed significantly to the model.

Figure 20

Linear Regression: Longevity on PHQ #7



Observing longevity *(B = -.001, t = -2.680, p = .008)* in relation to PHQ #7, significance was found: *F(1,164) = 7.182, p = .008, R^2 = .042*. 4.2% of the variance was accounted for by this model.

Quality of Life

For the quality of life measure in this study, the HRQOL was utilized with a few questions being removed to fit the SurveyMonkey survey structure and allow for summary scores to be utilized. Rather than the entire HRQOL-14, the Health Days Core module (4 questions) and Healthy Days Symptom module (5 questions) were collected,

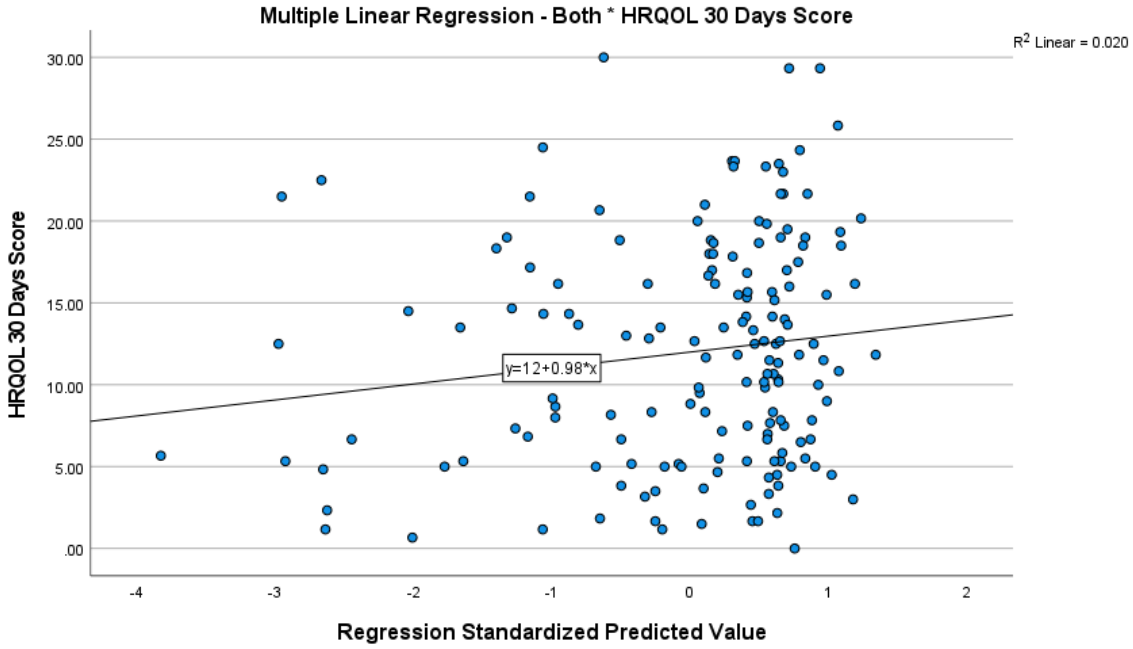
opting out of the Activity Limitations module (5 questions), as their relevance to the research question was less focal than the other scales.

HRQOL 30 Days Scores

30 Days scores for the HRQOL were scored cumulatively to include questions 2 through 9, with 9 being reverse-coded, referred to as the variable name "HRQOL 30 Days". Questions 1 and 10 were used for post-hoc analyses, as they did not directly assist in answering the research questions.

Figure 21

MLR: Longevity and Frequency on HRQOL 30 Days Score

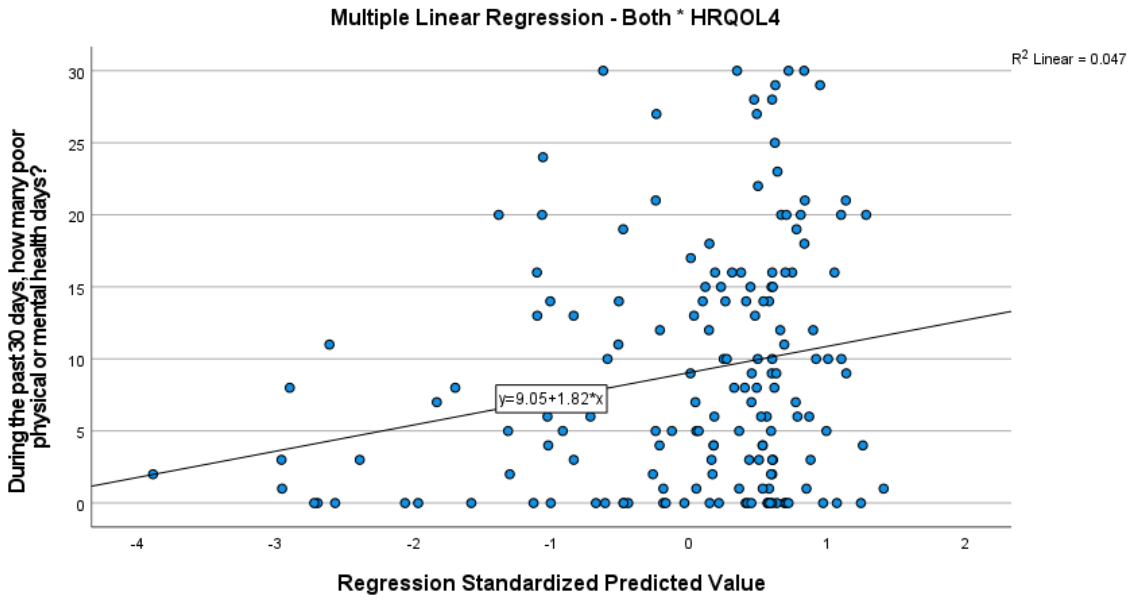


Using the enter method, no significant relationships were found when observing the total score for the HRQOL 30 Days measures. $F(2,164) = 1.675$, $p = .191$.

HRQOL Individual Question Scores

Figure 22

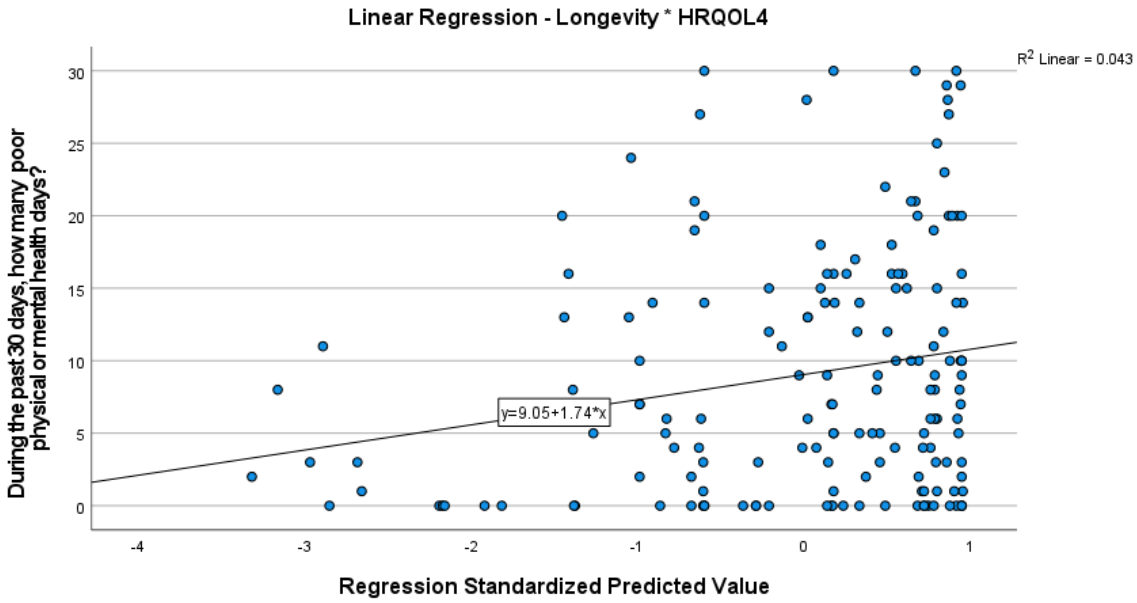
MLR: Longevity and Frequency on HRQOL #4



Using the enter method, a multiple linear regression produced a significant model, *F(2, 164) = 3.987, p = .020, R^2 = .047 (4.7% of variance).* Longevity of use *(B = -.012, t = -2.821, p = .005)* contributed significantly to the model, however frequency *(B = .054, t= .831, p = .407)* did not.

Figure 23

Linear Regression: Longevity on HRQOL #4

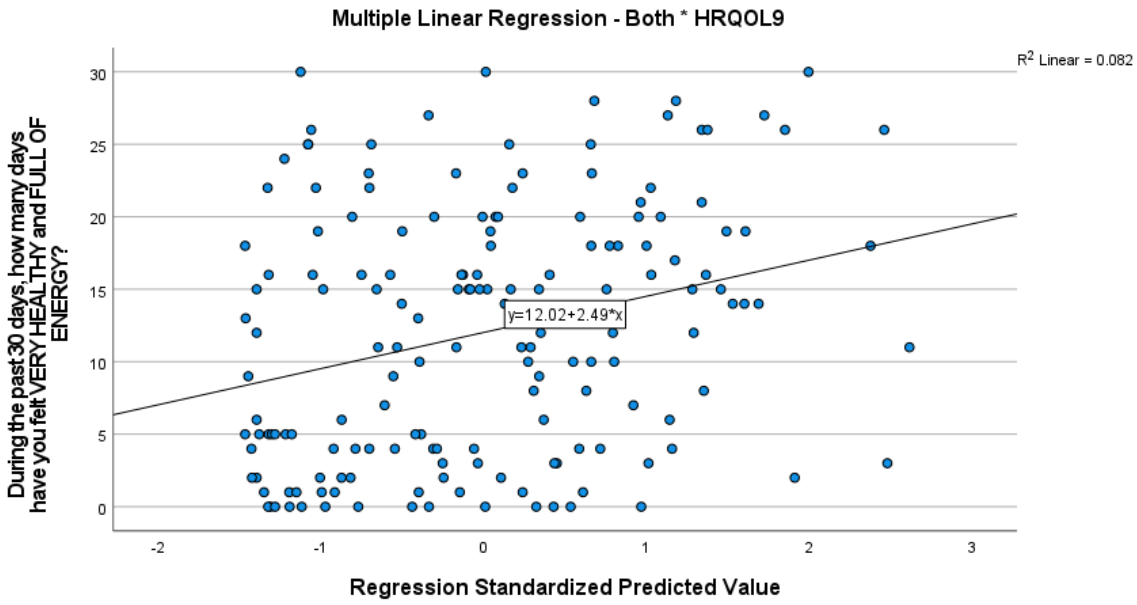


In a simple linear regression analysis, a significant model was also found, *F(1,164) = 7.299, p = .008, R^2 = .043 (4.3 % of variance explained), between l*ongevity *(B = -.011, t = -2.702, p = .008)* and the number of physical or mental health days that have prevented activity.

HRQOL #9

Figure 24

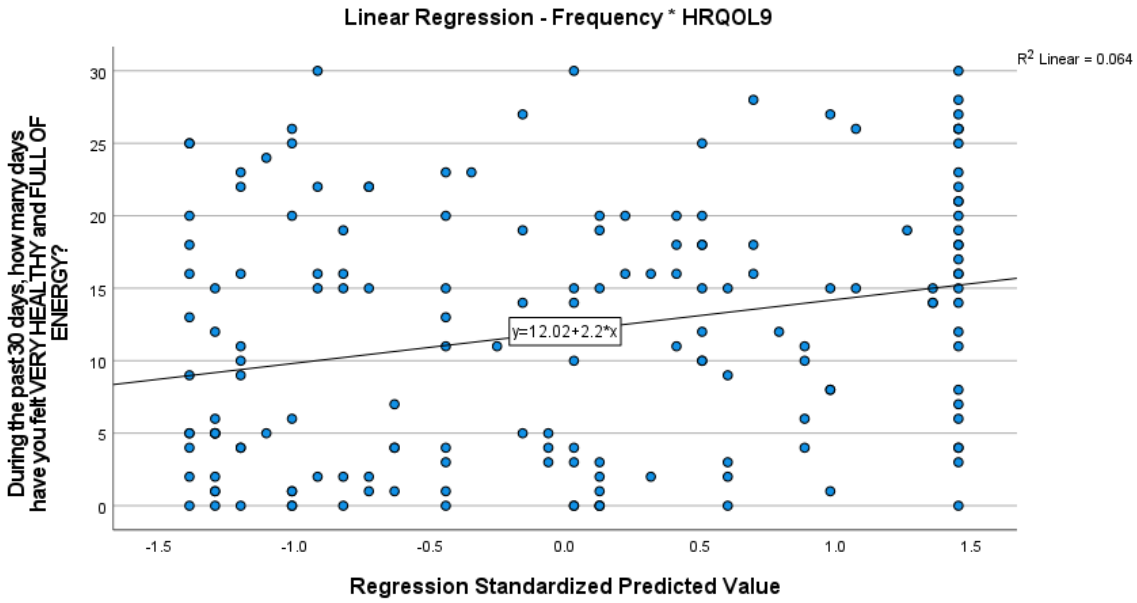
MLR: Longevity and Frequency on HRQOL #9



A multiple linear regression analysis using the enter method was conducted. The model was significant, *F(2, 164) = 7.233, p = .001*, explaining 8.2% ($R^2 = 0.082$) of variance in predicting scores related to appetite. Frequency of use (*B = .169, t = 2.563, p = .011*), but not longevity of use (*B = .008, t = 1.792, p = .075*), contributed significantly to the model.

Figure 25

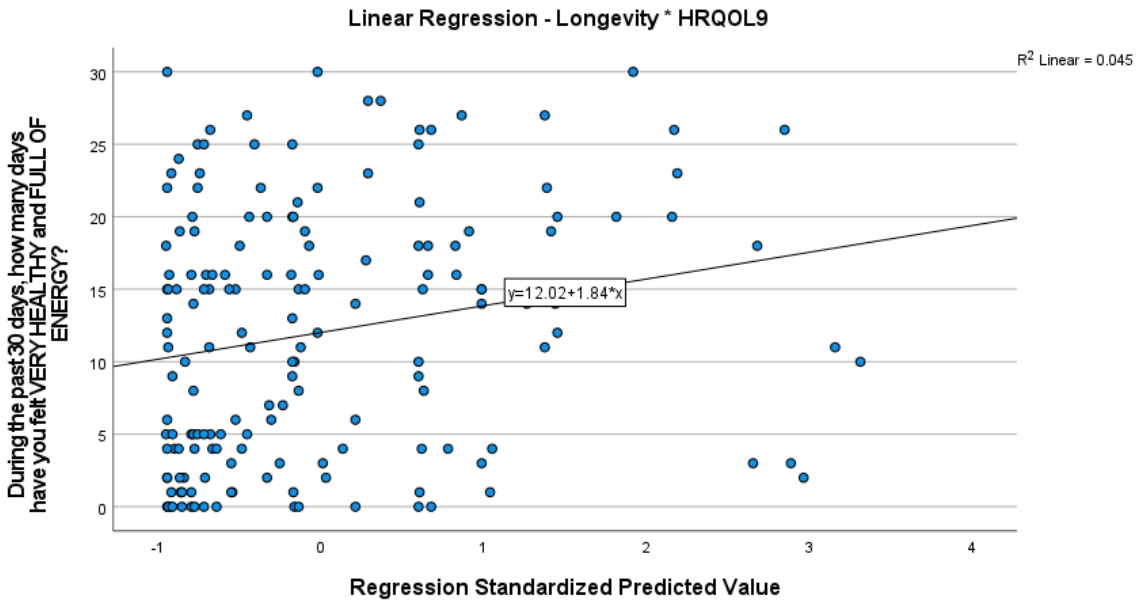
Linear Regression: Frequency on HRQOL #9



In simple linear regressions, HRQOL #9 had significant relationships with both frequency and longevity. Frequency *(B = .208, t = 3.332, p = .001)* indicated a relationship, *F(1,164) = 11.104, p = .001, R^2 = .064,* that could predict 6.4% of the variance by predicting with frequency.

Figure 26

Linear Regression: Longevity on HRQOL #9



Observing longevity *(B = -.001, t = -2.680, p = .008)* in relation to PHQ #7, significance was found: *F(1,164) = 7.182, p = .008, R^2 = .042.* 4.2% of the variance is accounted for by this model.

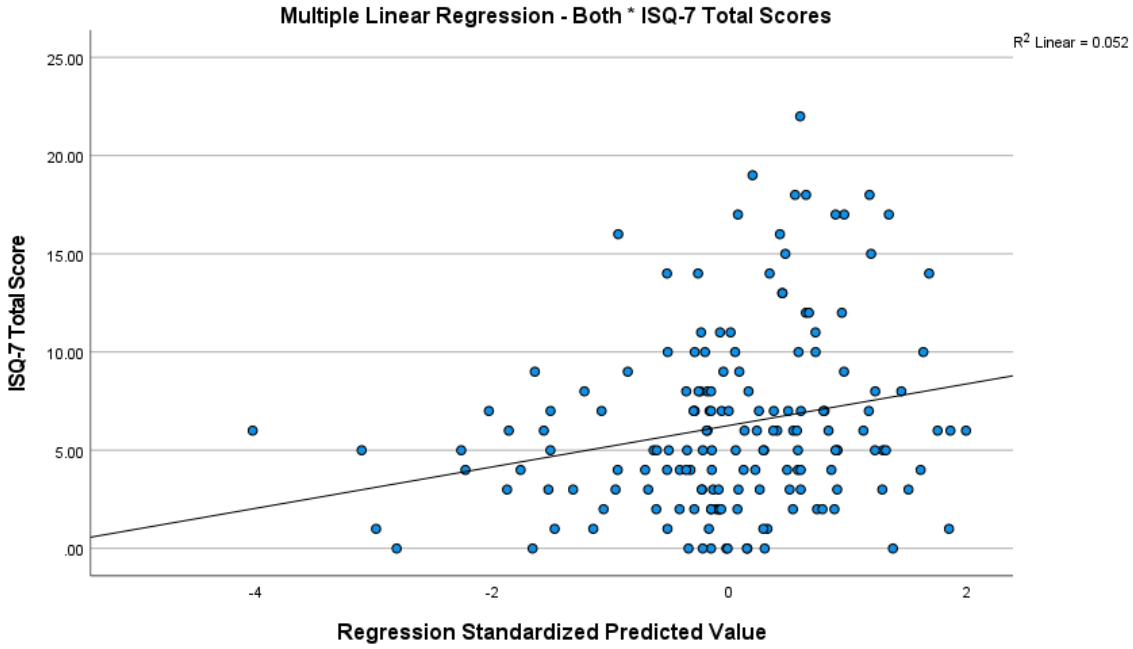
Reported Immunity

Reported immunity was measured using the ISQ. For interpretation of the ISQ scores, the first seven questions were designed to be used as cumulative scoring that is translated into a 0-10 scale. The latter two questions on the scale were qualitative in nature, and as such were not used for testing the hypotheses.

ISQ Total Scores

Figure 27

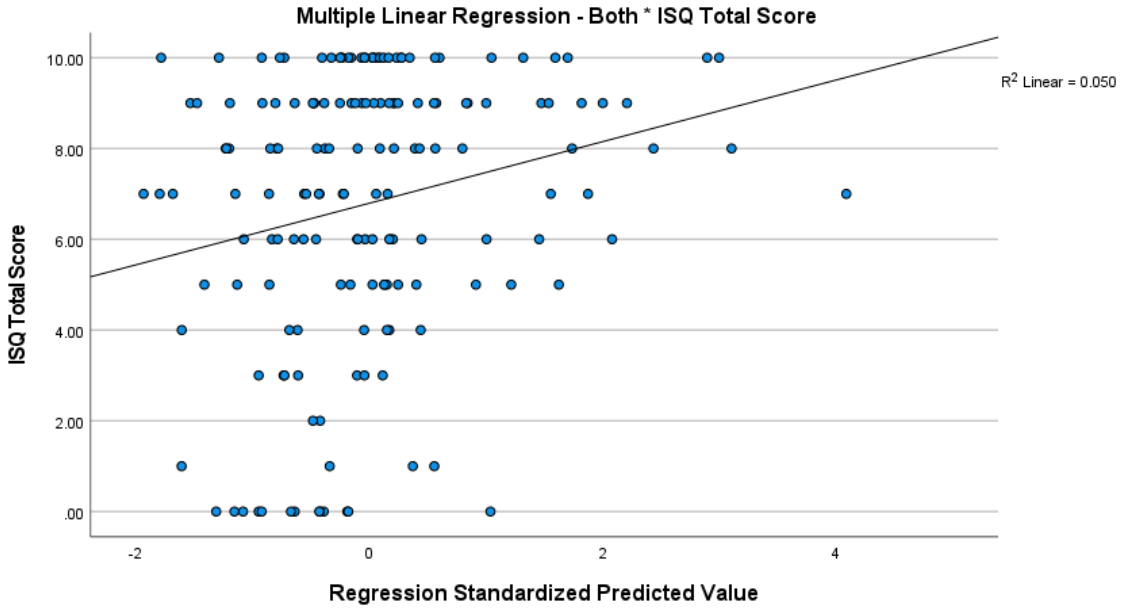
MLR: Longevity and Frequency on ISQ-7 Total Scores



Utilizing the enter method, a significant model was discovered, *F(2,164) = 4.222*, *p = .016*, R^2 *= .050*. 5% of variance was accounted for by the model, with both longevity (*B =.004*, *t = 2.653*, *p = .009*) and frequency (*B = -.047*, *t = -2.003*, *p = .047*) contributing significantly to the model.

Figure 28

Linear Regression: Longevity on ISQ-7 Total Scores



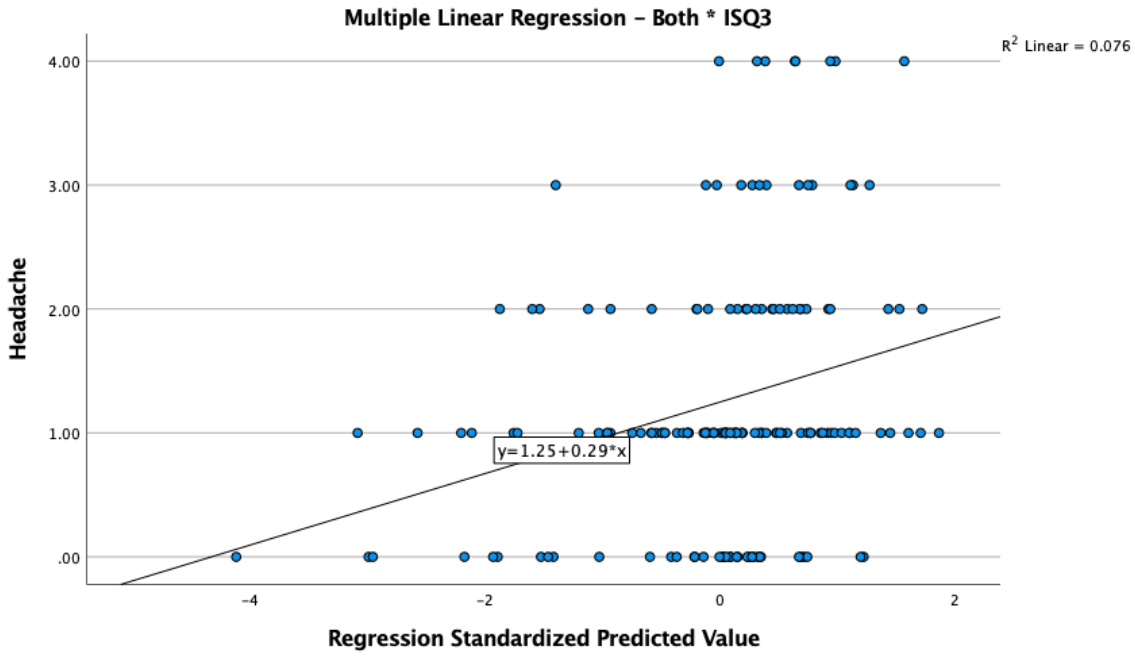
When observing the linear regression between longevity of cannabis use and ISQ-total scores, a significant model was found: $F(1,164) = 4.351$, $p = .039$, $R^2 = .026$, where longevity of cannabis use attributed to 2.6% of the variance ($B = .003$, $t = 2.086$, $p = .039$).

ISQ Individual Scores

ISQ #3: Headaches

Figure 29

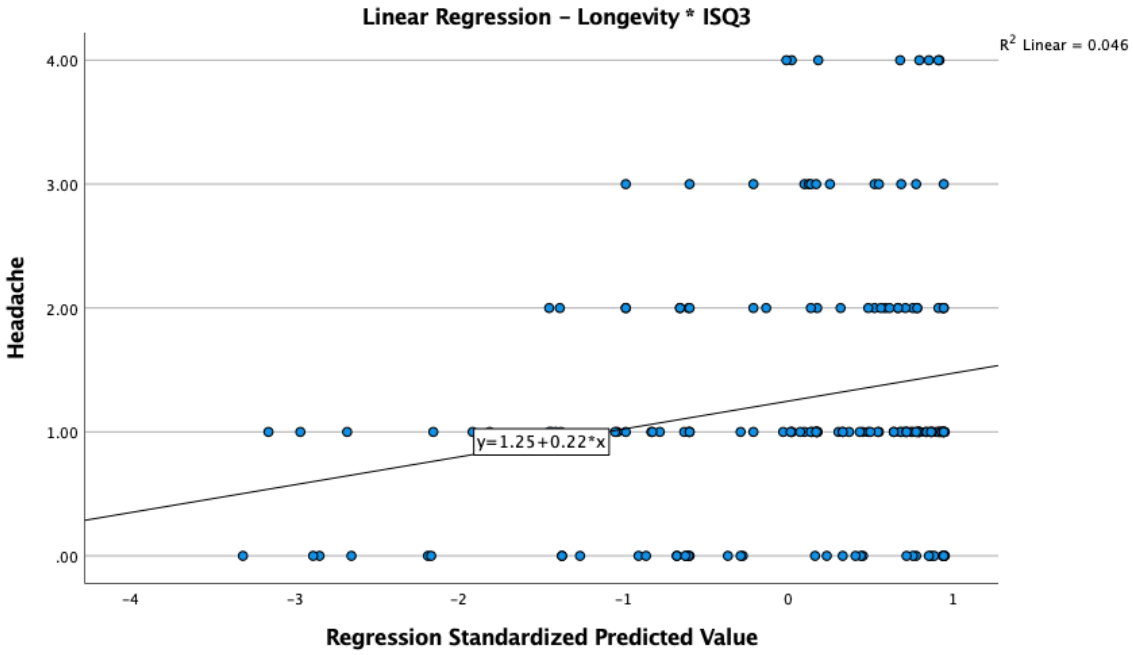
MLR: Longevity and Frequency on ISQ #3



Using an enter method multiple linear regression, a significant model, *F(2,164) = 6.696, p = .002, R^2 = .076,* was found where 7.6% of variance was explained by the predictor variables. Both longevity *(B = -.002, t = -3.454, p = .001)* and frequency *(B = .018, t = 2.293, p = .023)* contributed significantly to the model.

Figure 30

Linear Regression: Longevity on ISQ #3

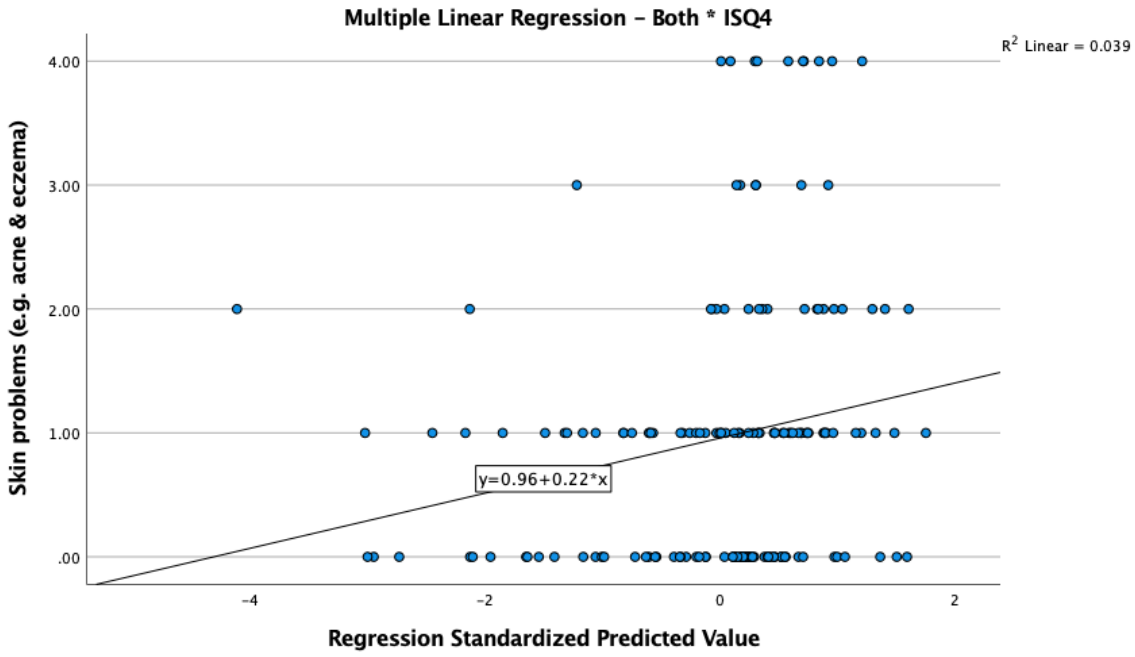


Individually, only longevity showed a significant linear regression with ISQ #3, *F(1,164) = 7.928, p = .005, R^2 = .046,* explaining 4.6% of the variance amongst responses with the predictor variable of longevity *(B = -.001, t = -2.816, p = .005).*

ISQ #4: Skin Problems (e.g., acne & eczema)

Figure 31

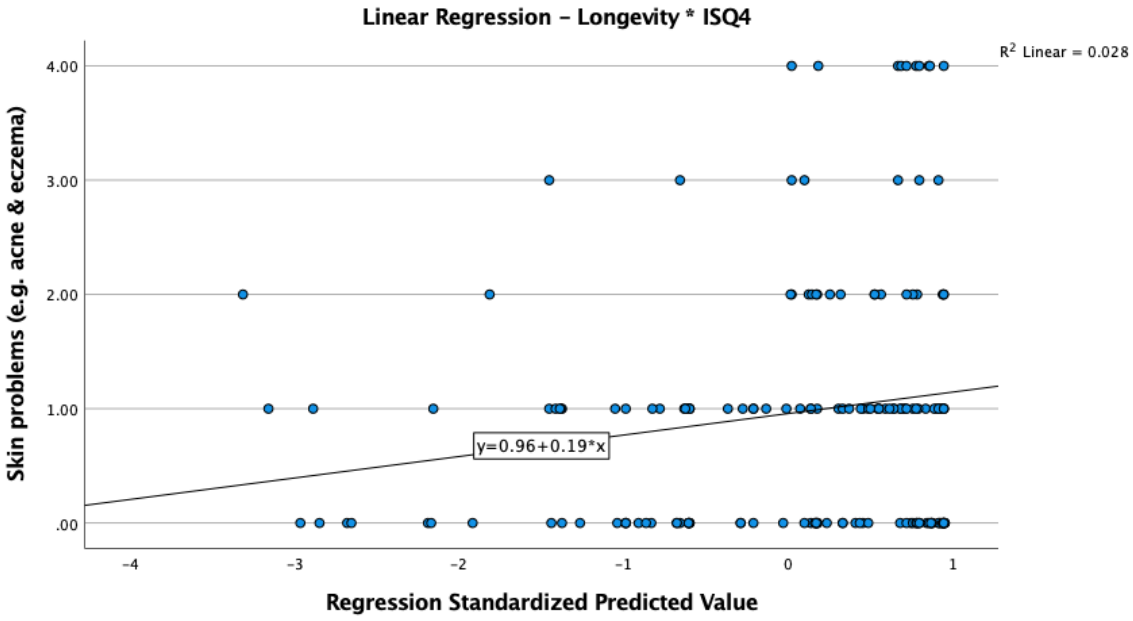
MLR: Longevity and Frequency on ISQ #4



Multiple linear regression analysis with the enter method was used to examine scores on whether skin problems could be predicted by frequency of cannabis use per month and length of time using cannabis. The model was significant, *F(2, 164) = 3.305*, *p = .039*, explaining 3.9% (R^2 = 0.039) of variance in predicting the total score. Longevity of use (B = -.001, t = -2.507, p = .013) contributed significantly to the model, but frequency (B = .012, t = 1.376, and p = .171) did not.

Figure 32

Linear Regression: Longevity on ISQ #4

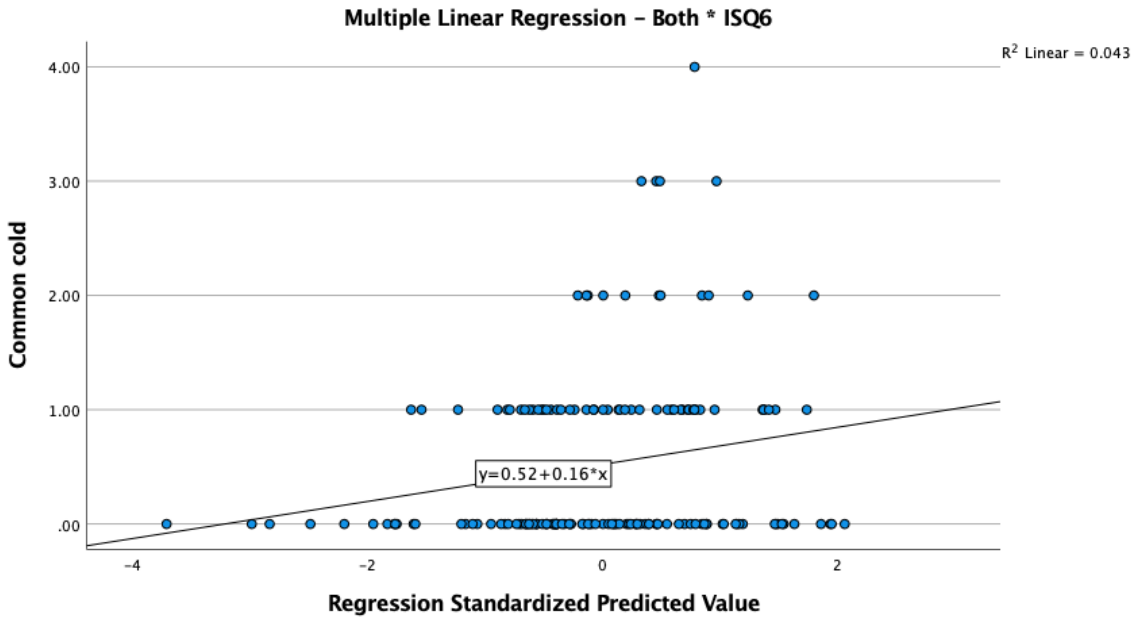


The individual linear regression model analysis between longevity and ISQ #4 showed a significant model *(F(1,164) = 4.693, p = .032, R^2 = .028)*, where longevity accounted for 2.8% of the variance found *(B = -.001, t = -2.166, p = .032).*

ISQ #6: Common Cold

Figure 33

MLR: Longevity and Frequency on ISQ #6

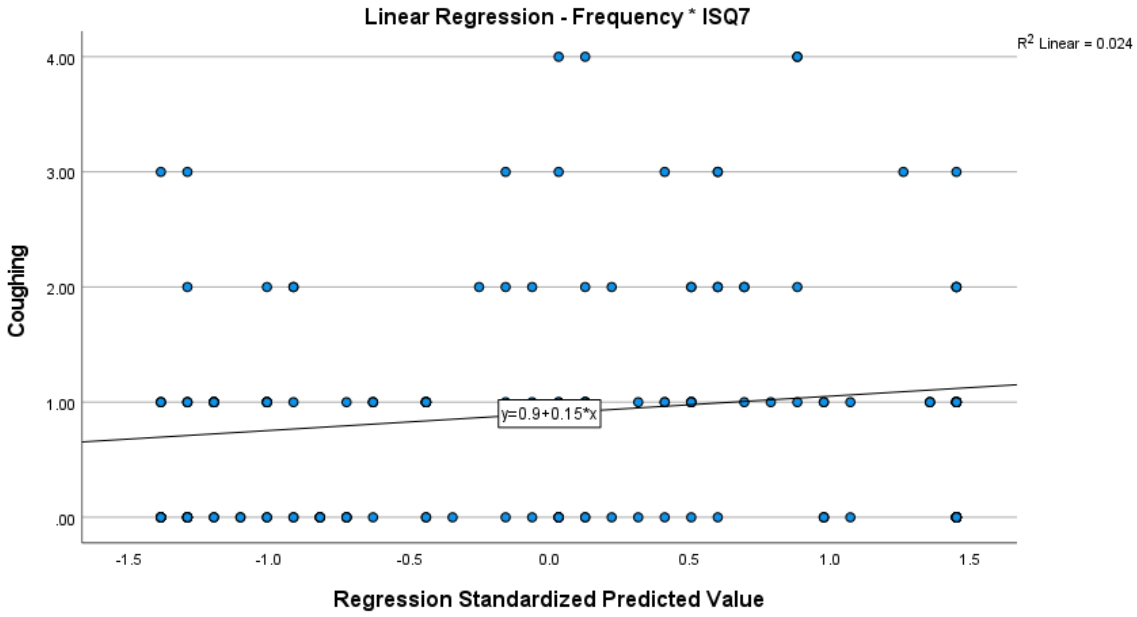


The enter method was conducted on this multiple linear regression, which produced a significant model: $F(2,164) = 3.683$, $p = .027$, $R^2 = .043$. Of the 4.3% variance explained by the predictor variables, both longevity $(B = -.001, t = -1.995, p = .048)$ and frequency $(B = .014, t = 2.401, p = .017)$ contributed significantly. When observed individually, neither simple linear regression was significant.

ISQ #7: Coughing

Figure 34

Linear Regression: Frequency on ISQ #7

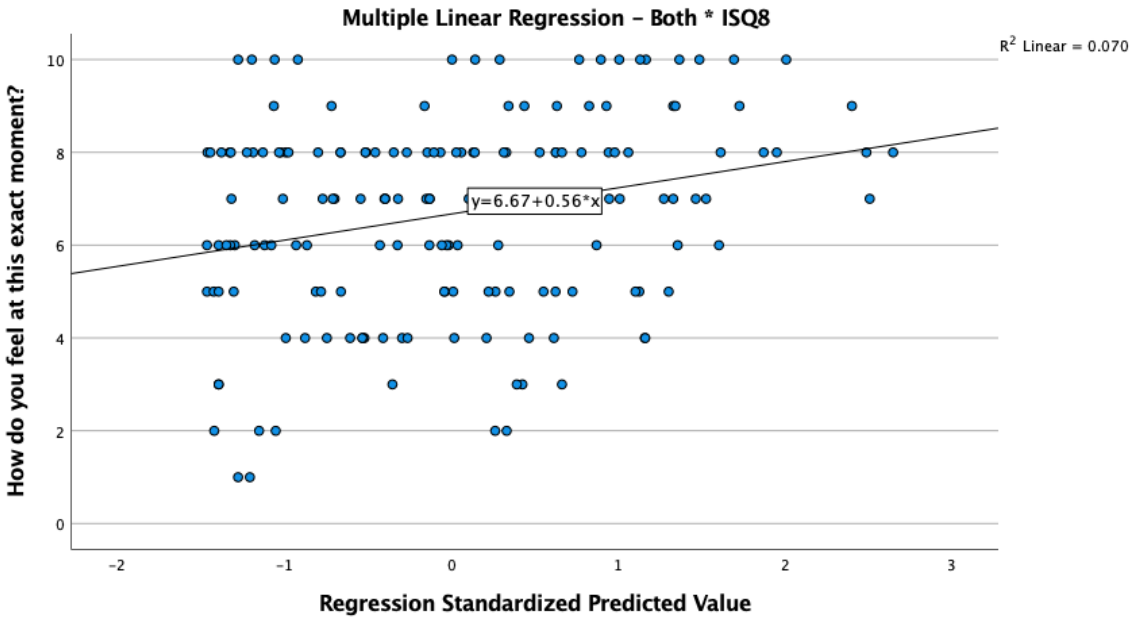


In the multiple linear regression, no significant model was found. In an individual linear regression with frequency however, a significant model, *F(1,164) = 3.937, p = .049, R^2 = .024,* was found with frequency *(B = .014, t = 1.984, p = .049)* accounting for 2.4% of the variance.

ISQ #8-"How do you feel at this exact moment?"

Figure 35

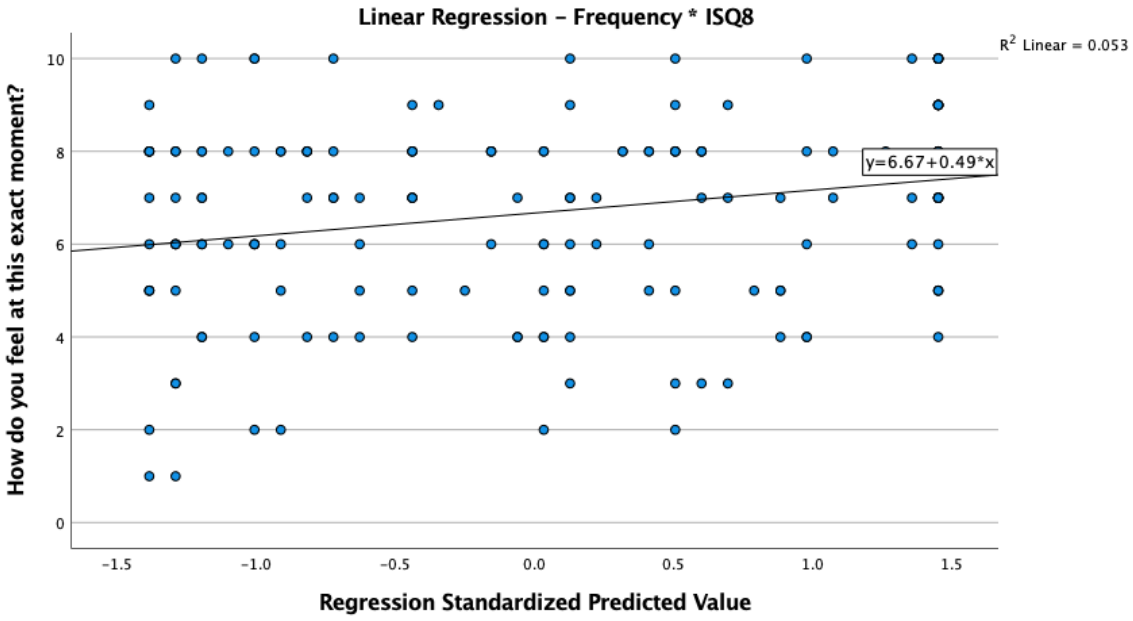
MLR: Longevity and Frequency on ISQ #8



Using an enter method for this multiple linear regression, a significant model *(F(2,164) = 6.061, p = .003, R^2 = .070)* was found with frequency *(B = .037, t = 2.302, p = .023)* contributing significantly to the model, but not longevity *(B = .002, t = 1.694, p = .092).*

Figure 36

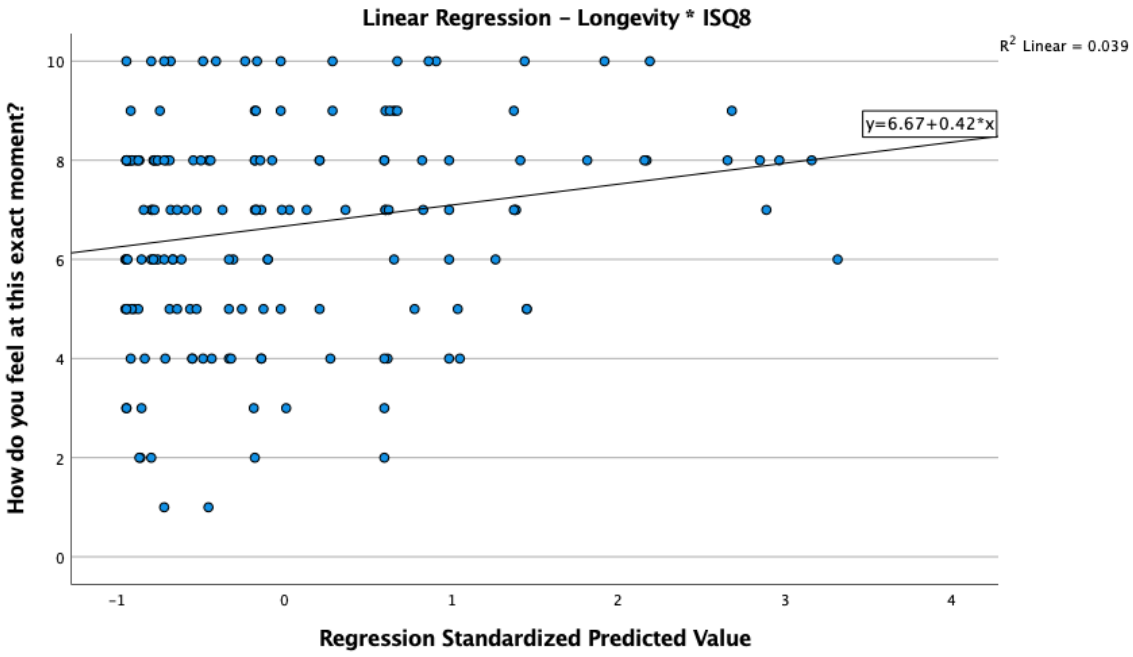
Linear Regression: Frequency on ISQ #8



When observing each predictor variables' capability to predict responses to how an individual is feeling at that current moment in time, both predictors were significant. The model presented by frequency *(B = .047, t = 3.025, p = .003)* on ISQ #8 explained 5.3% of variance in responses, $F\ (1,164) = 9.152$, $p = .003$, $R^2 = .053$.

Figure 37

Linear Regression: Longevity on ISQ #8

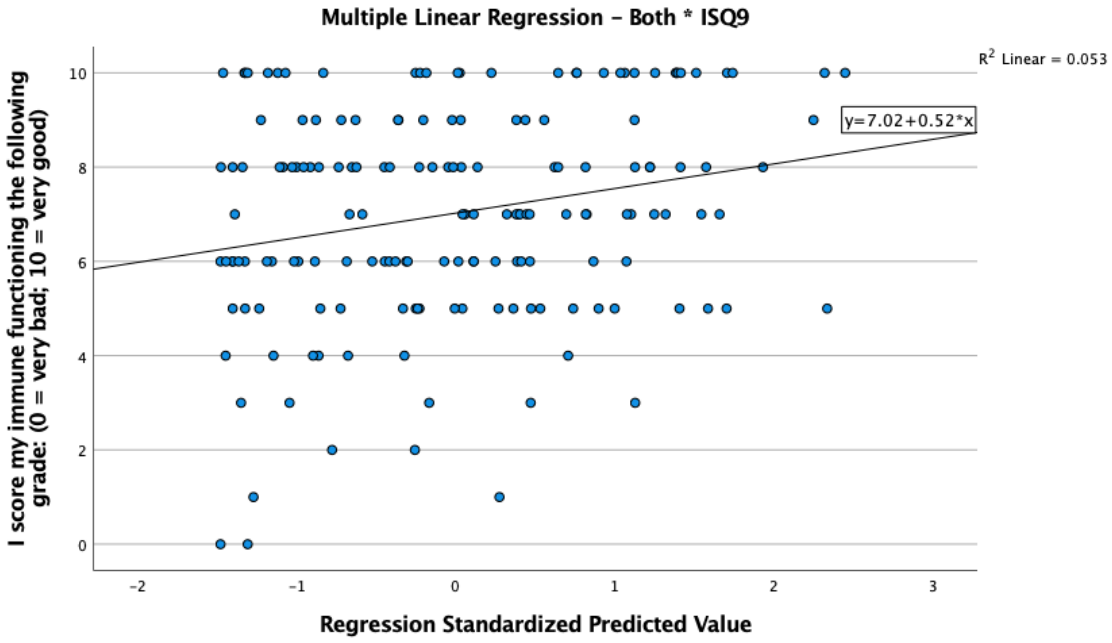


The linear regression model observing longevity in relation to the ISQ #8 found a significant model, $F\ (1,164) = 6.647$, $p = .001$, $R^2 = .039$, where longevity accounted for 3.9% of variance in responses $(B = .003, t = 2.578, p = .011)$.

ISQ #9: Self-Score of Immune Function

Figure 38

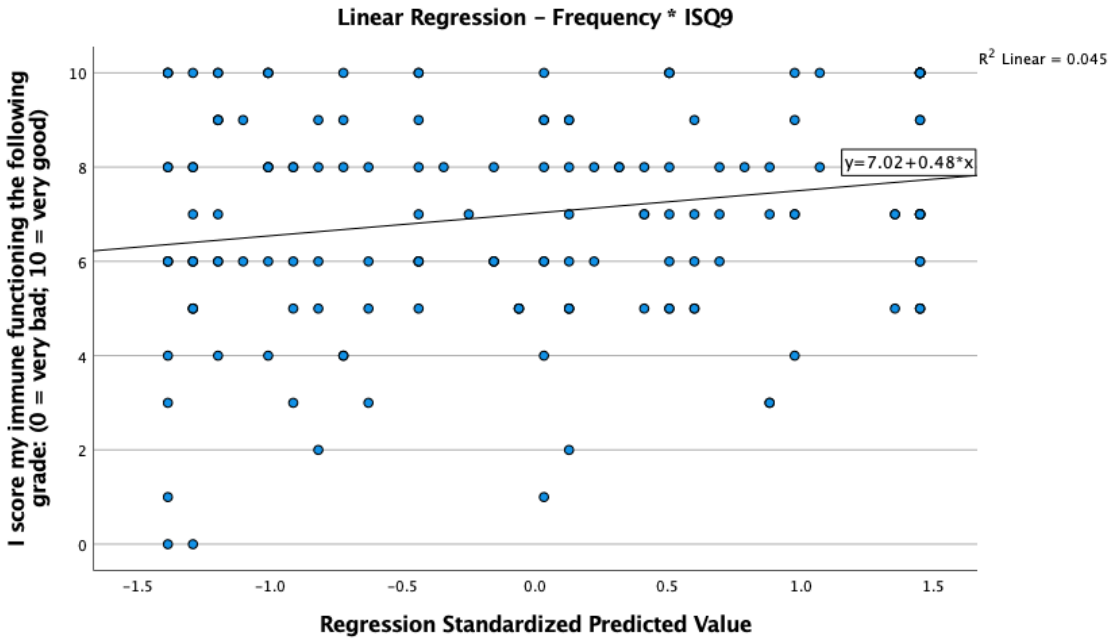
MLR: Longevity and Frequency on ISQ #9



The relationships between both predictor variables against a self-reported rating of immune function produced three significant models: one with both, and one with each predictor. The multiple linear model was found to be significant *(F(2,164) = 4.513, p = .012, R^2 = .053,* with frequency contributing significantly to the model *(B = .039, t = 2.211, p = .028),* but longevity not *(B = .001, t = 1.178, p = .248).*

Figure 39

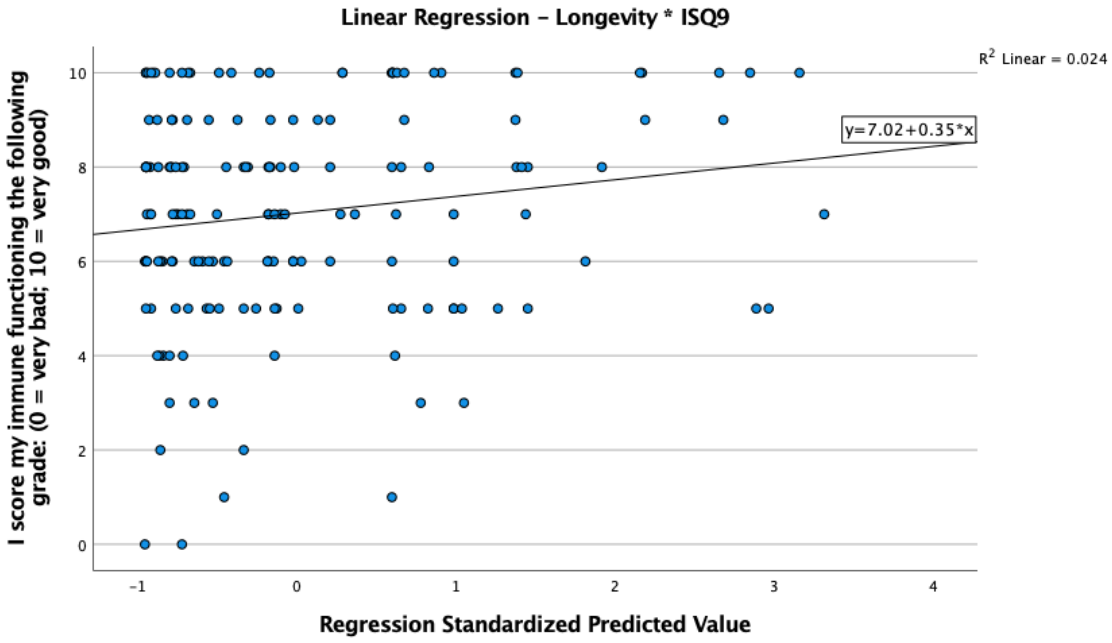
Linear Regression: Frequency on ISQ #9



In a linear regression of frequency, a significant effect was discovered, *F(1,164) = 7.620, p = .006,* R^2 *= .045,* that explained 4.5% of the variance with the predictor variable of frequency *(B = .045, t = 2.760, p = .006).*

Figure 40

Linear Regression: Longevity on ISQ #9



In a simple linear regression, a significant model *(F(1,164) = 4.040, p = .046, R^2 = .024)* was also found with longevity *(B = .002, t = 2.010, p = .046)* in predicting scores on self-reported immune function.

Research Questions

RQ-1: Do relationships exist between the frequency and longevity of cannabis use and anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A; Hamilton, 1959)?

Based on the relationships assumed by the multiple linear regressions, a relationship did exist between longevity and the total scores on the Hamilton Anxiety

rating scale. As with most of the research questions, the power of the relationship was not very strong, accounting for only 3.8% of the variance in responses when attempting to predict scores using longevity of use as a predictor.

RQ-2: Do relationships exist between the frequency and longevity of cannabis use and depression as measured by the PHQ-9 (Kroenke et al., 2001)?

Like anxiety, depression had a significant relationship with longevity of cannabis use. The power of the relationship, $R^2 = .051$, expresses that while there was a relationship is only accounted for by 5.1%.

RQ-3: Do relationships exist between the frequency and longevity of cannabis use and quality of life as measured by the Center for Disease Control's Health-related Quality of Life scale (HRQOL; Center for Disease Control, 2000)?

Based on multiple regressions, no relationship was found between either of the predictor variables and total scores on the HRQOL, indicating a need to fail to reject the null hypothesis.

RQ-4: Do relationships exist between cannabis use frequency, longevity, and self-reported immunity as measured by the Immune Status Questionnaire (ISQ; Versprille et al., 2019)?

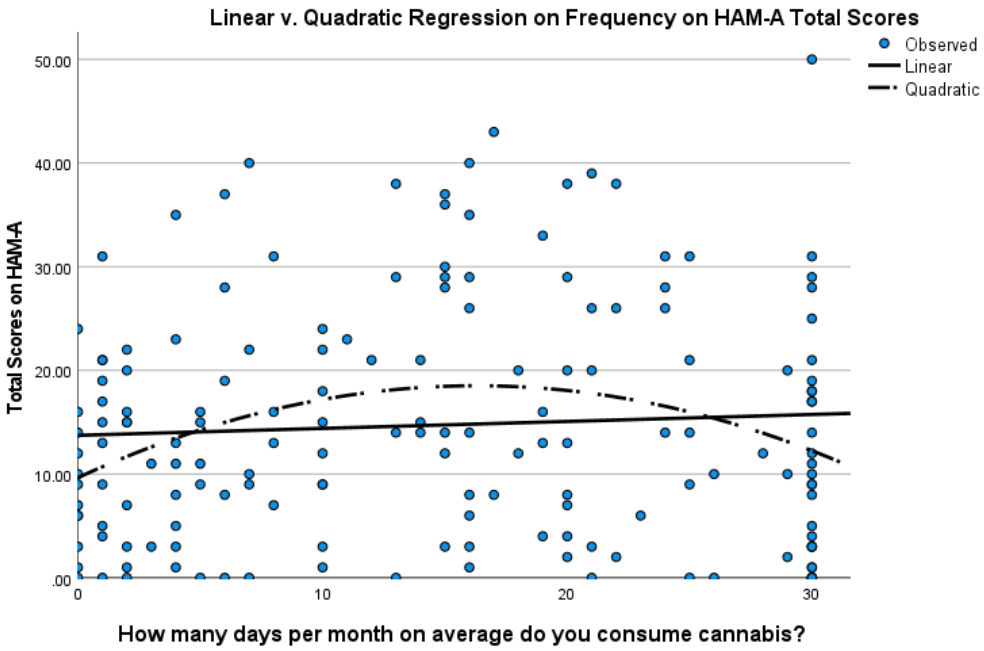
A significant relationship was found between frequency, longevity, and self-reported immunity total scores (ISQ #1-7) and individual questions (ISQ 8 & 9). While only explaining 5.2% of the variance in answers, a relationship was found to exist allowing us to reject the null hypothesis.

Post-Hoc Analyses

Due to data collection errors, a larger data set was created that allowed for further investigation into several other questions, including sex, regional differences of Appalachia, and access to healthcare. Further, variances can be compared to accidental control group participants that were allowed to complete the survey after disqualifying. The comparisons will not be optimal for the study due to differences in sample sizes (control: n = 60; condition: n = 165), but any comparisons with the control group were exploratory for future research suggestions.

Figure 41

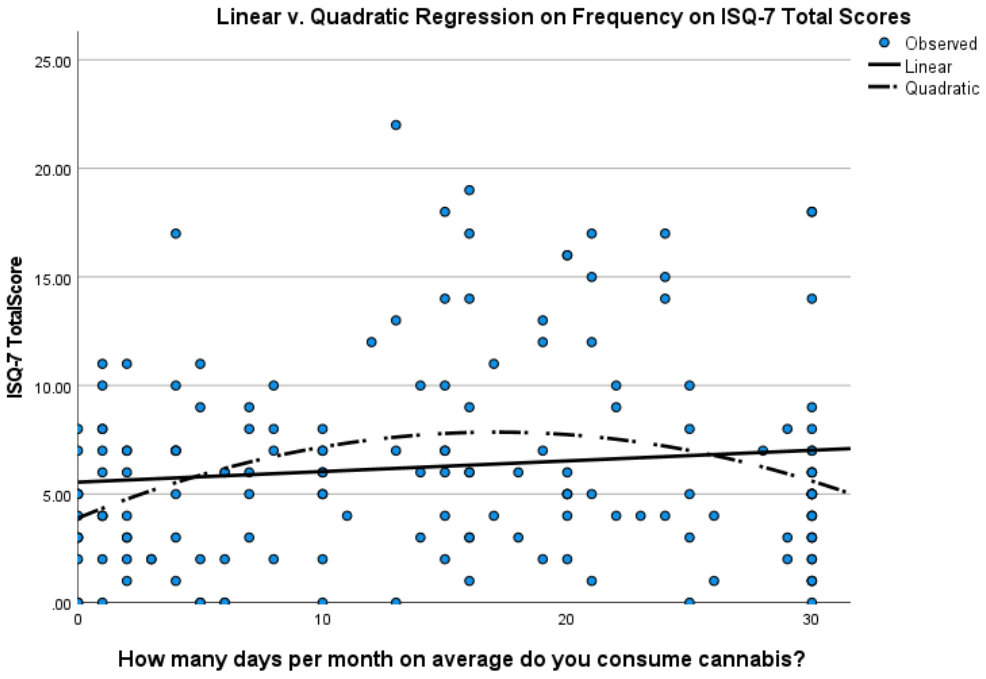
Frequency on HAM-A Total Scores: Linear Versus Quadratic



When utilizing a non-linear regression model, the quadratic model of frequency expressed a change in anxiety score predictions along a curve, *F(2,164) = 6.021, p = .003, R^2 = .069.* In contrast to the linear regression model comparison, this curve indicates a more complex relationship with anxiety score predictions in the scope of frequency of cannabis consumption *(B = 1.008, t = 3.469, p = .001; squared: B = -.003, t = -3.372, p = .001).*

Figure 42

Frequency on ISQ #7 Total Scores: Linear Versus Quadratic



This non-linear regression model was also significant, *F(2,164) = 6.828, p = .001, R^2 = .078.* The curve indicated that towards the edges of the scale, reduction in ISQ-7 total score predictions occurred in this better-fit model of the relationship with

frequency of use *(B = .463, t = 3.655, p < .001; Squared: B = -.014, t = -3.386, p = .001).*

Control Group ANOVAs

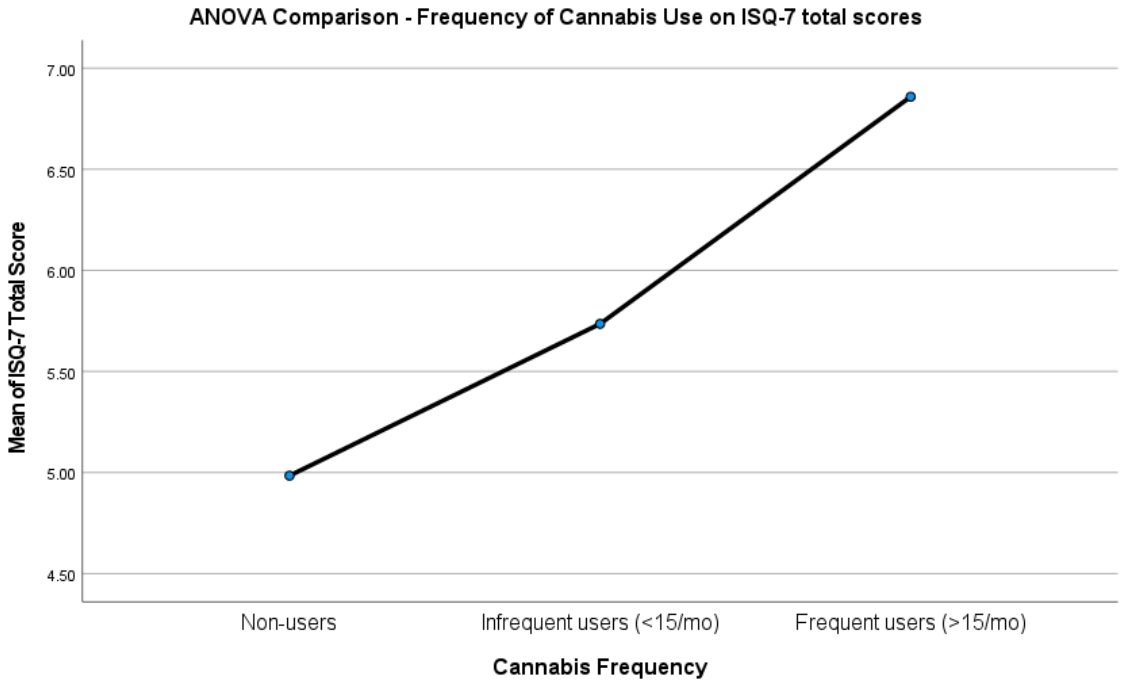
Due to the sample sizes and nature of comparisons, several ANOVAs were conducted to compare between groups means and variances, rather than regression models. to attempt to keep some consistency in group sizing for these analyses, the qualified participants were split into two groups based on the independent variable. For frequency, participants were separated into three groups: non-users (n = 65), users for 15 days or less per month (n = 87), and users who use 16 or more days per month (n = 78). For longevity, participants were separated into three groups: non-users (n = 65), users who have used cannabis for less than ten years (n = 84), and users who have more than ten years of historic use (n = 81). Of the ANOVAs conducted, a few significant relationships were seen.

Frequency

Comparisons between groups measured by frequency, when compared against controls, produced significant effects on two measures: the ISQ-7 total scores and the number of good days in a month (HRQOL #09).

Figure 43

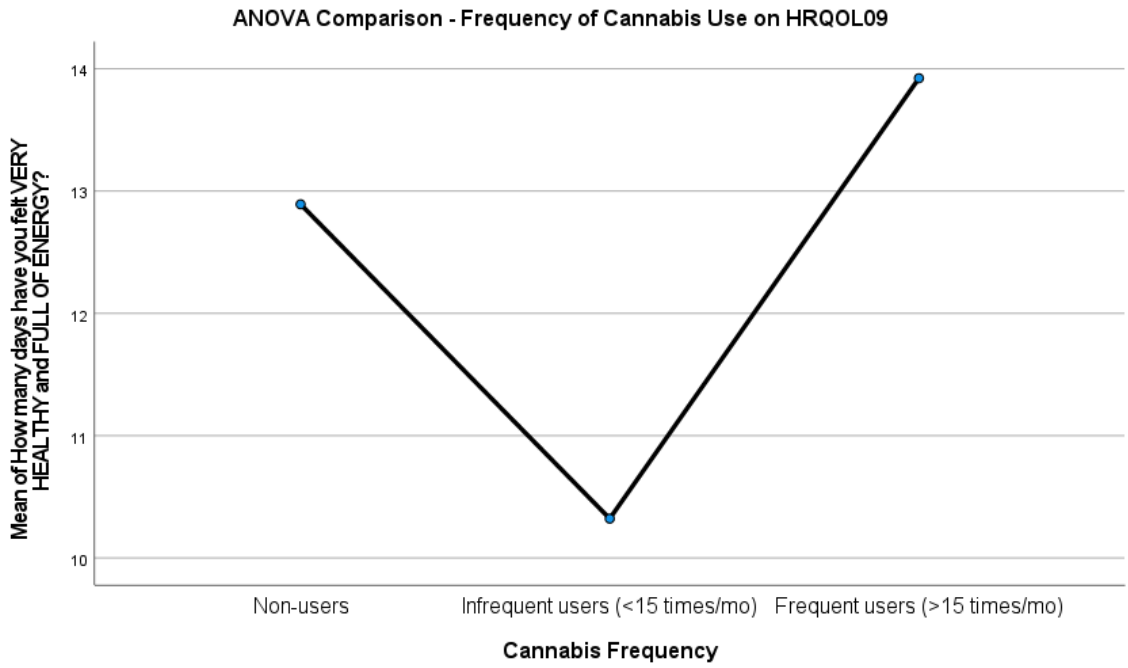
ANOVA: Frequency on ISQ-7



An observation of frequency appears to indicate that a relationship exists between cannabis use and overall immune function, with non-users (*M = 4.98, SD = 4.48)* expressing a significantly lower score on the ISQ-7 than infrequent users (*M = 5.74, SD = 4.20)* or frequent users (*M = 6.86, SD = 5.04), F(2,229) = 3.065, p = .049.*

Figure 44

ANOVA: Frequency on Good Days (HRQOL #09)

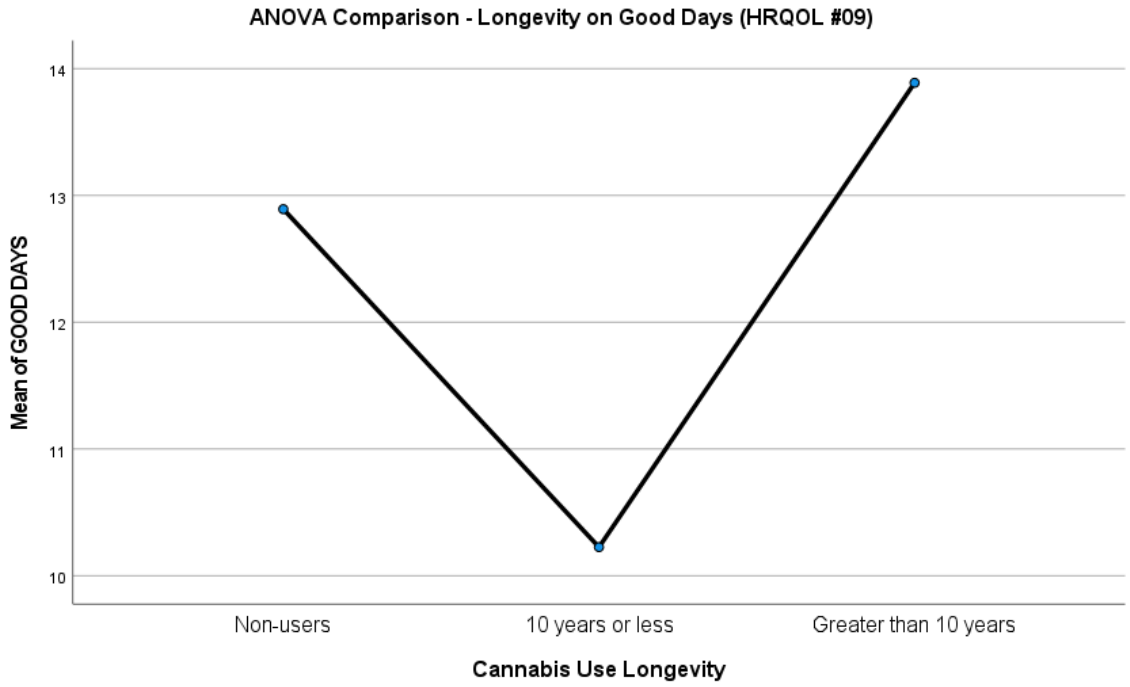


A significant effect of frequency of cannabis use, *F(2,229) = 3.386, p = .036,* indicates a unique effect between groups. Infrequent users (*M = 10.32, SD = 8.80)* reported significantly lower numbers of healthy days where they felt well than non-users (*M = 12.89, SD = 10.57)* or frequent users (*M = 13.92, SD = 8.26).*

Longevity

Figure 45

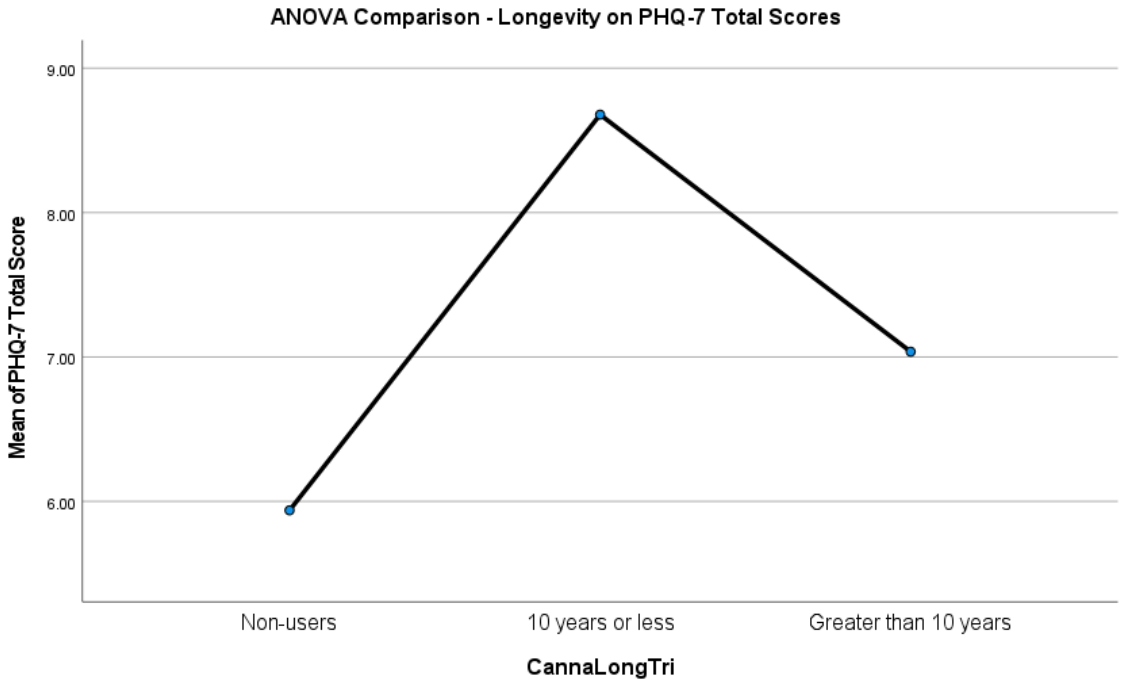
ANOVA: Longevity on Good Days (HRQOL #09)



When observing the effect of cannabis use longevity on the self-reported number of good days experienced per month, a significant effect was found: *F(2,229) = 3.508, p = .032.* Non-users *(M = 65, SD = 10.57)* and users that have consumed for over ten years (*M = 13.89, SD = 8.61)* reported significantly more positive days that users who have under ten years of consumption experience (*M = 10.23, SD = 8.47).*

Figure 46

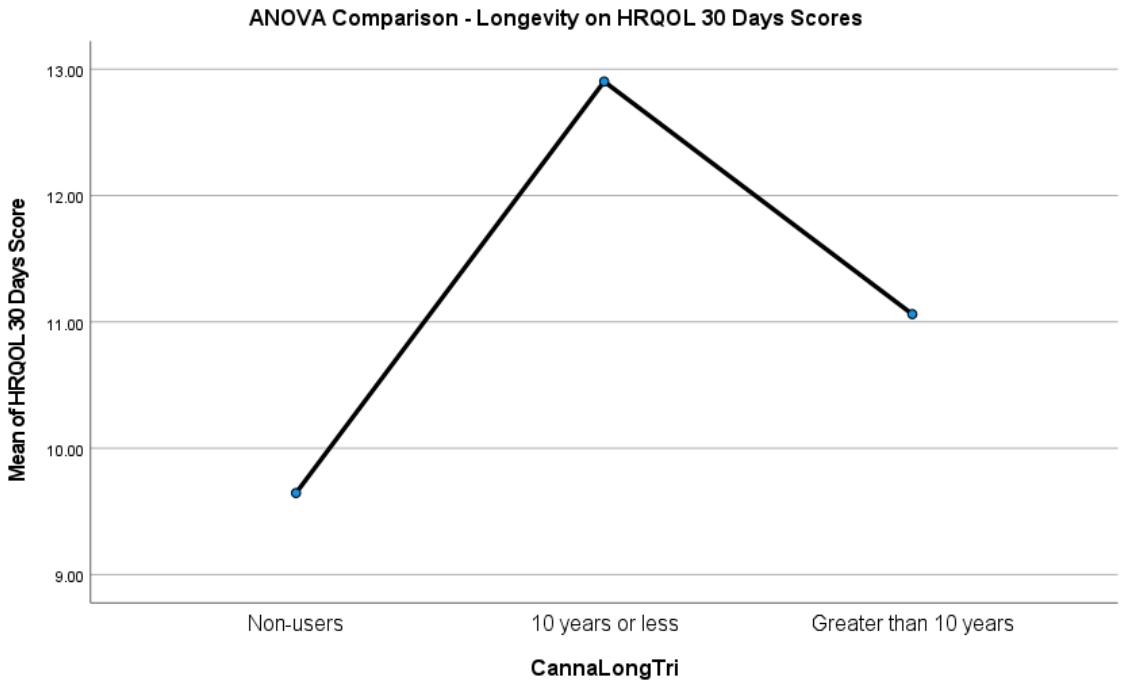
ANOVA: Longevity on PHQ Total Scores



In an ANOVA observation of longevity on depression scale PHQ total scores, a significant model was found: *F(2,229) = 3.261, p = .040.* On average, non-users *(M = 5.94, SD = 6.63)* and long-term users (>10 years of use*; M = 7.04, SD = 6.48)* were significantly lower on scores than short-term users (<10 years of use; *M = 8.68, SD = 6.74).*

Figure 47

ANOVA: Longevity on HRQOL-30 Days Scores



In an ANOVA, a significant model was found: *F(2,229) = 3.989, p = .020*, where non-users (*M = 9.65, SD = 7.66)* experienced significantly fewer bad days than short-term (<10 Years*; M = 12.90, SD = 6.99)* and long-term users (>10 year; *M = 11.06, SD = 6.63)* each month.

Gender Differences

In examining gender differences on scores, there were only two effects that appeared between the sexes, a difference in anxiety and a difference in the longevity of cannabis use.

Table 3

T-Test Results Comparing Females and Males on HAM-A Total Scores

Test	Sex	n	Mean	SD	F	df	t	p
HAM-A	**Female**	**108**	**15.685**	**11.922**	**4.779**	**160**	**-1.619**	**.030**
	Male	**54**	**12.667**	**9.542**				
PHQ-9	Female	108	8.519	6.645	.092	160	-1.811	.762
	Male	54	6.537	6.398				
ISQ-7	Female	108	6.380	4.737	.797	160	-.440	.373
	Male	54	6.037	4.527				
HRQOL	Female	108	12.694	7.105	1.050	160	-1.752	.307
30 Days	Male	54	10.691	6.340				

Within the individual questions the sex differences were only significant in two questions: gastrointestinal (*F(1,160) = 9.952, p = .002; t = -1.968, p = .051**) and behavioral fidgeting (*F(1,160) = 17.160, p < .001; t = -3.173, p = .002)*, where women experienced significantly higher scores (M_{gastro} = 1.093, SD = 1.227; M_{fidget} = 1.093, SD = 1.220) than the male participants (M_{gastro} = .722, SD = .899; M_{fidget} = .519, SD = .746).

Table 4

T-test Differences Comparing Females and Males on Longevity of Cannabis Use

Sex	n	Mean	SD	F	df	t	P
Female	**108**	**137.657**	**132.570**	**7.151**	**160**	**2.599**	**.008**
Male	**54**	**202.370**	**178.579**				

Figure 48

Population Pyramid Comparing Females and Males on Longevity of Cannabis Use

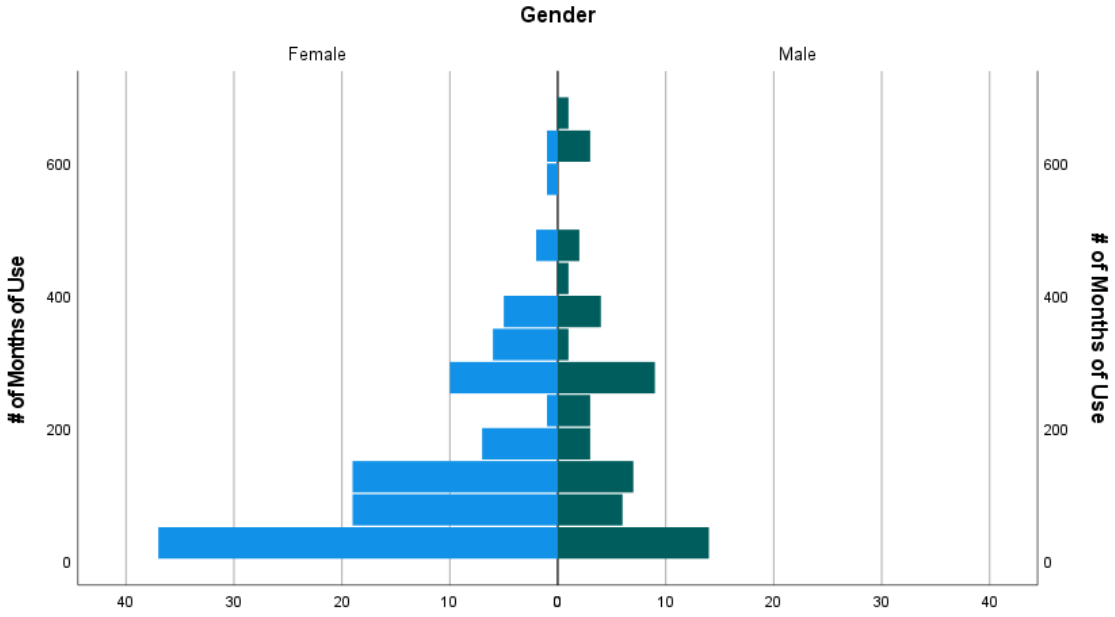


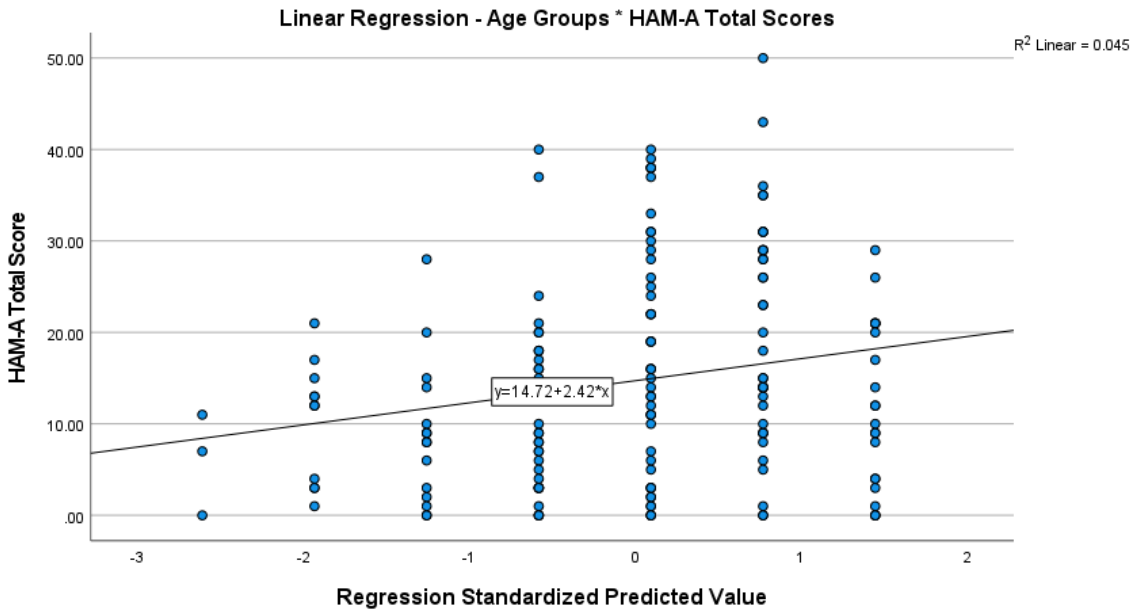
Table 4 and Figure 49 show while women outnumber men by 2:1, three times as many new users were women, while most of the high longevity participants were men.

Age Differences

In observing age effects, and the effects of age and longevity together on the results on the criterion variables, several effects and relationships were seen.

Figure 49

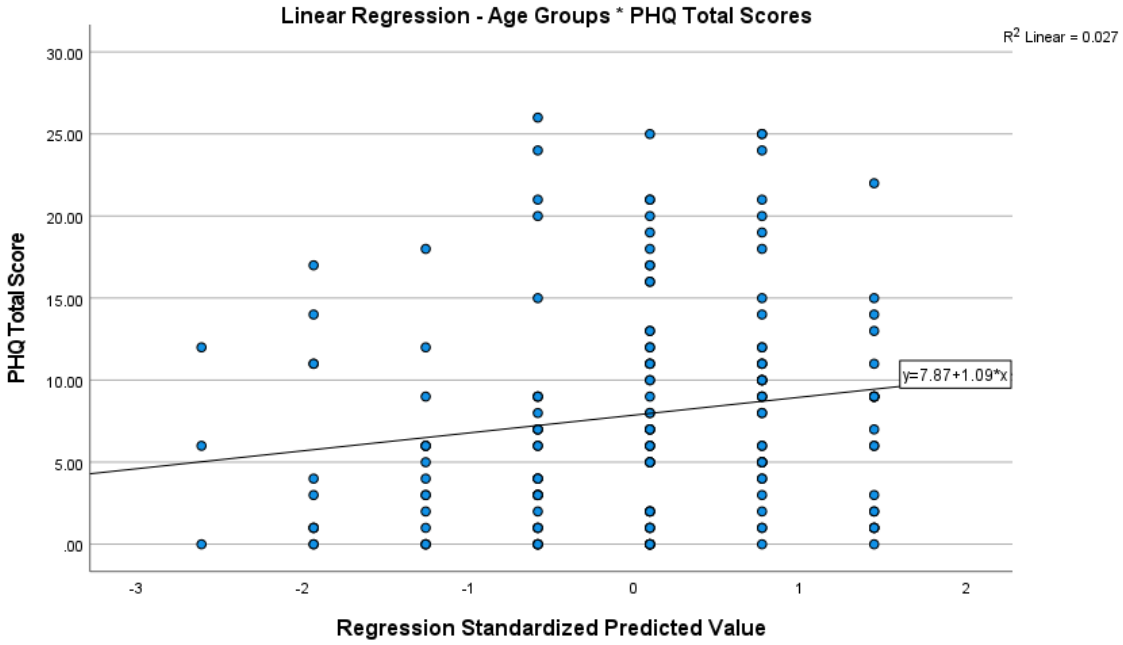
Age Differences on HAM-A Total Scores



In a simple linear regression model, a significant model was found, *F(1, 164) = 7.644, p = .006, R^2 = .045,* where age accounted for 4.5% of the variance in total scores on the HAM-A *(B = -1.633, t = -2.765, p = .006).*

Figure 50

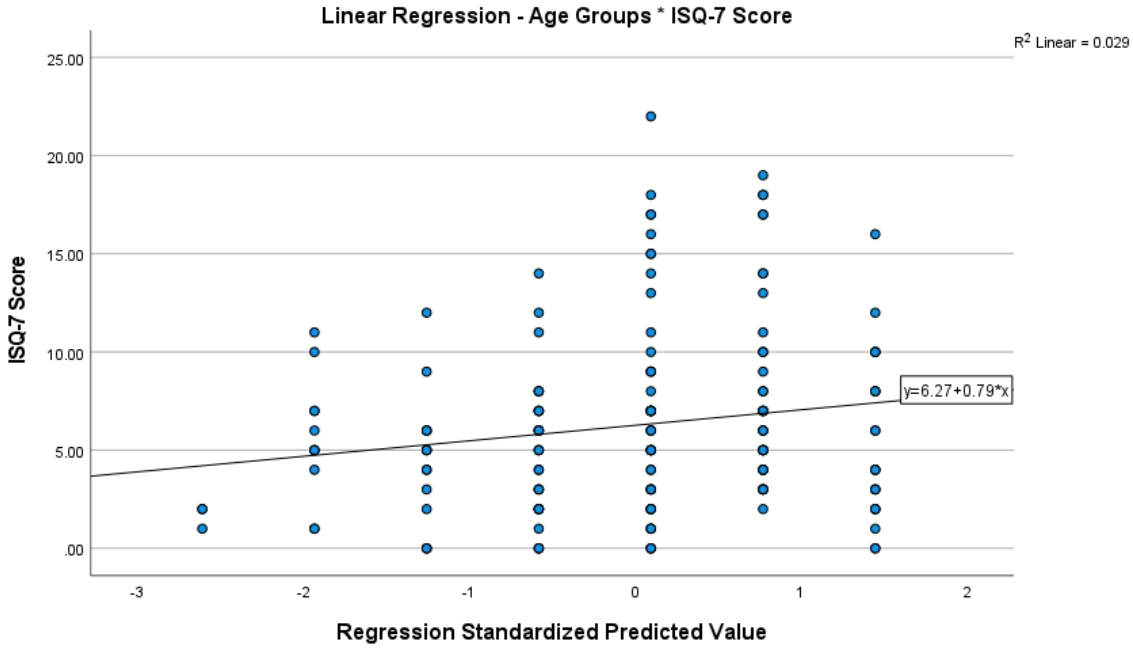
Linear Regression: Age Differences on PHQ-9 Total Scores



Observing the relationship between age groups and depression PHQ-total scores, a significant model was found, $F(1,164) = 4.520$, $p = .035$, $R^2 = .027$, where age groups accounted for 2.7% of the variance in responses ($B = -.737$, $t = -2.126$, $p = .035$).

Figure 51

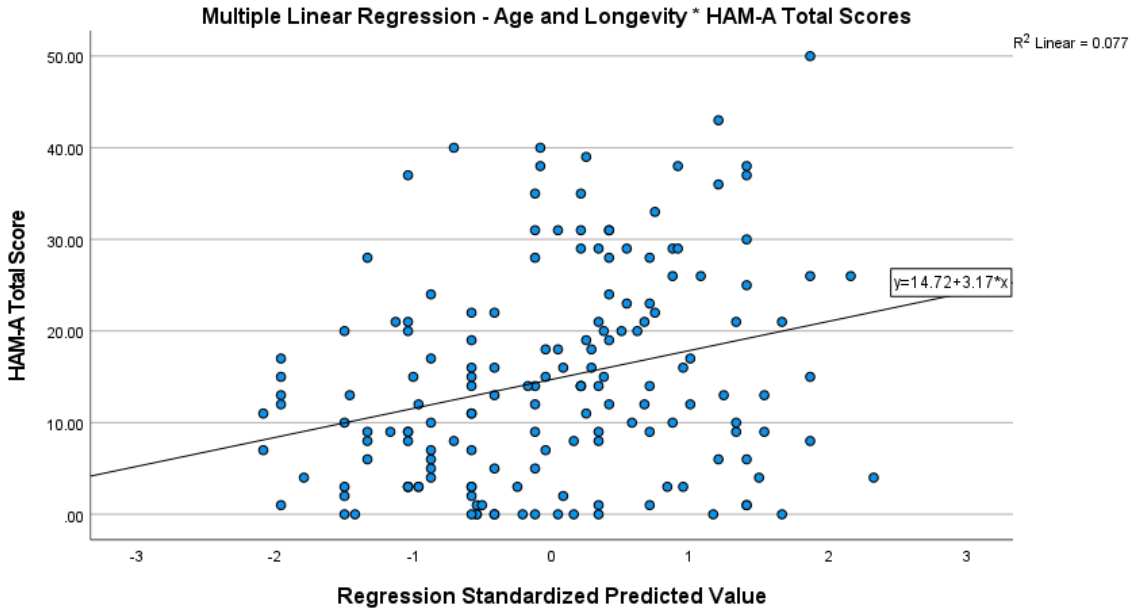
Age Differences on ISQ-7 Total Scores



In a linear regression, a significant model was found between age groups and immune scores, $F(1,164) = 4.885$, $p = .028$, $R^2 = .029$, where age groups accounted for 2.8% of the variance among responses ($B = -.534$, $t = -2.210$, $p = .028$).

Figure 52

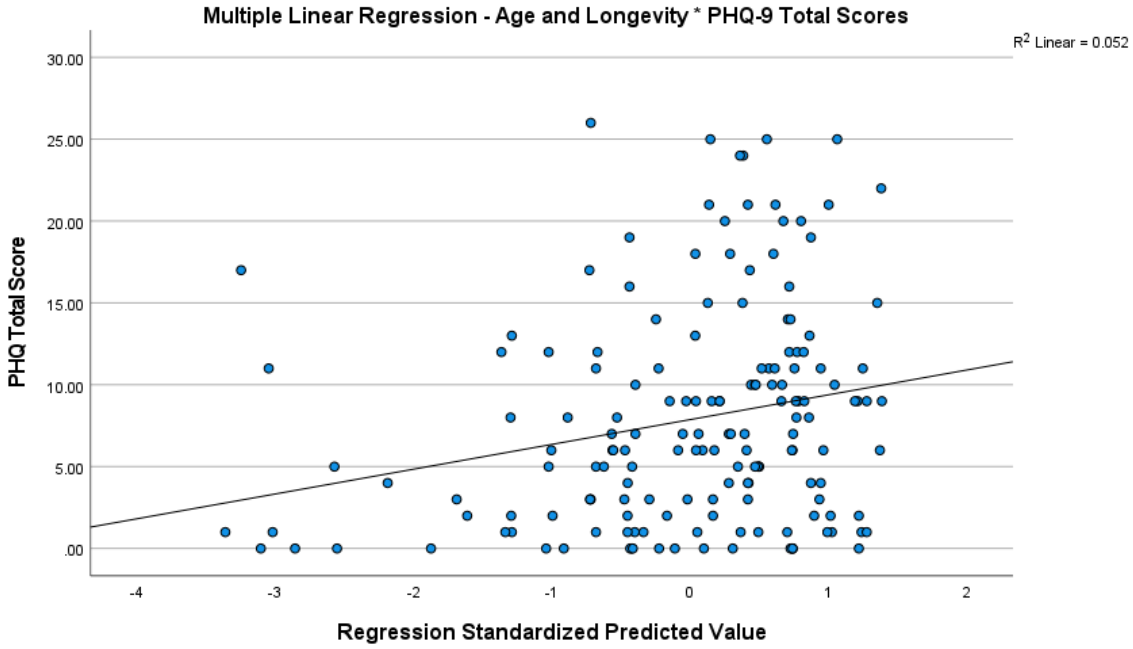
Age and Longevity on HAM-A Total Scores



Enter method multiple regression observing the relationships between age groups and longevity on the HAM-A anxiety total scores found a significant model, *F(2, 164) = 4.508, p = .012, R^2 = .053,* where age groups (*B = -1.393, t = -2.229, p = .027)*, but not longevity (*B = -.007, t = -1.164, p = .246)* contributed significantly to the model.

Figure 53

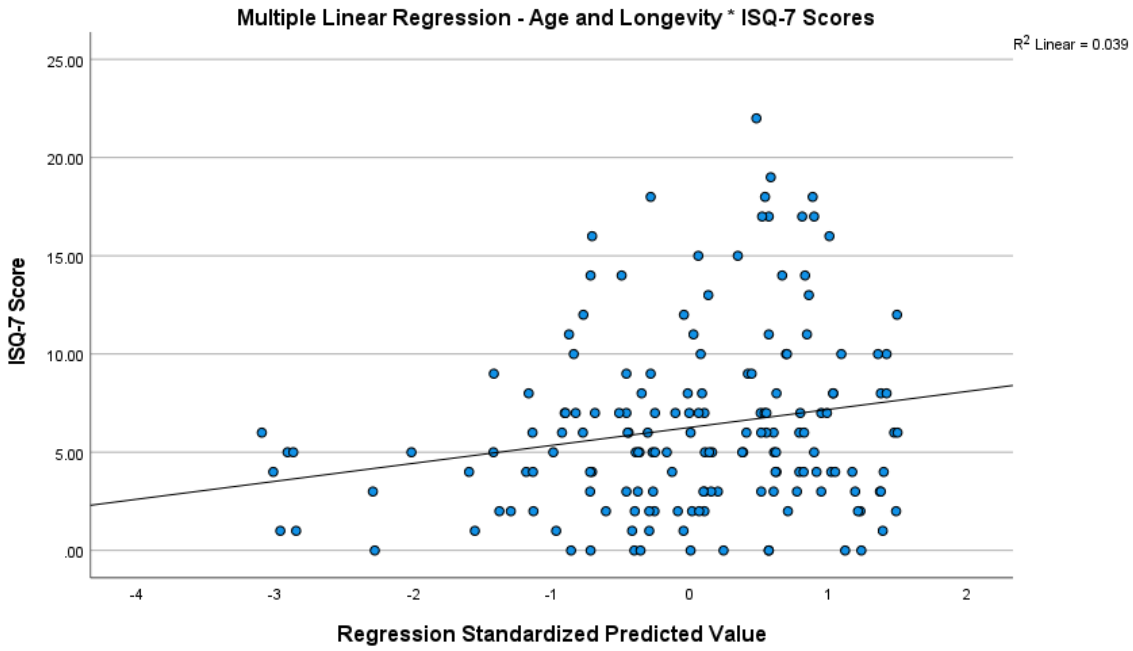
MLR-Age and Longevity on PHQ-9 Total Scores



Using the enter method, a multiple linear regression model was found to be significant, $F(2,164) = 4.444$, $p = .013$, $R^2 = .052$, where 5.2% of the variance was explained by the predictors. Longevity of use $(B = -.007, t = -2.068, p = .040)$, but not age $(B = -.489, t = -1.346, p = .180.)$ contributed significantly to this model. This difference helped to reinforce that longevity itself contributed without age being a mediating factor.

Figure 54

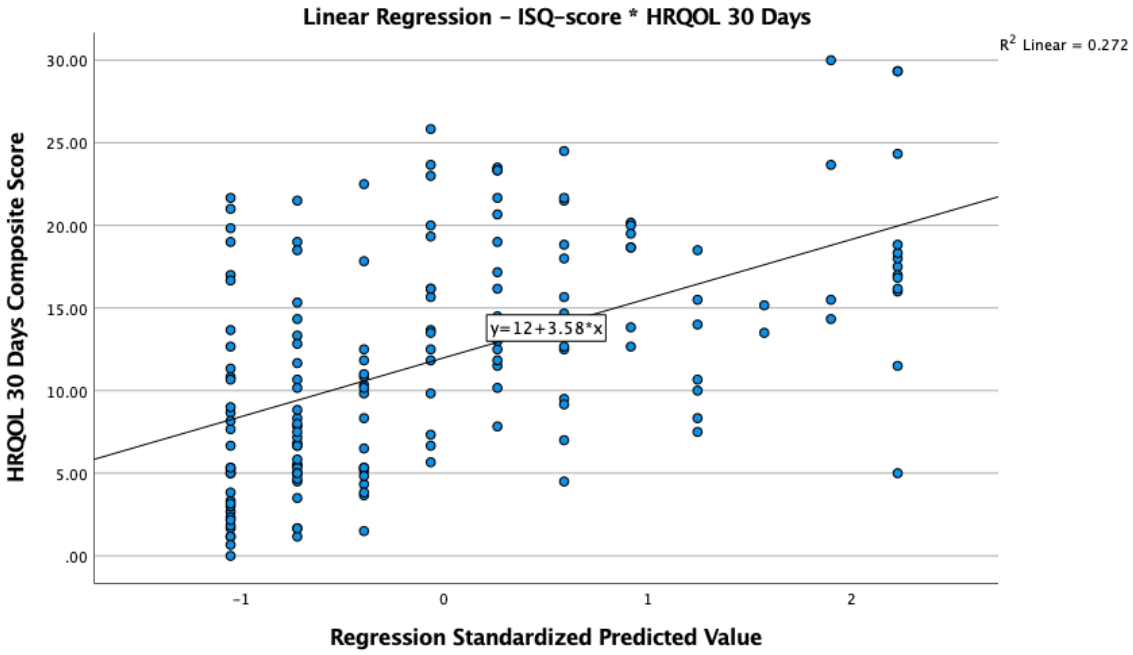
MLR: Age and Longevity on ISQ-7 Total Scores



Using the enter method, a relationship was found between cannabis use and scores on the ISQ #7 question, $F(2,164) = 3.281$, $p = .040$, $R^2 = .039$. When observed separately from each other however, neither age ($B = -.426$, $t = -1.667$, $p = .098$), nor longevity ($B = -.003$, $t = -1.287$, $p = .200$) contributed significantly independently.

Figure 55

Linear Regression: ISQ Total Scores on HRQOL-30 Days Scores



In an enter method regression, a significant relationship was found between immune scores and quality of life as measured by the HRQOL 30 days score: *F(1,164) = 60.862, p < .001, R^2 = .272*. The immune status scores were able to account for 27.2% of the variance in HRQOL 30 Day scores *(B = -1.172, t = -7.801, p < .001)*. The significant relationship in this regression implies that as immune scores increase (indicating better health with lower numbers), the number of days also increased, such that worse health meant more bad days per month.

Summary

Data analyses on 165 correct participants' responses to questions about their cannabis use, anxiety, depression, quality of life, and immunity were conducted by running multiple linear regressions. Despite a significant gender ratio of two women per one man, no relationships were seen to be affected by the sampling trend. Significant relationships were seen amongst cannabis use in relation to anxiety (complex bidirectional relationships), depression (improved with longevity), and immunity (decreased with longevity). Quality of life did not have any significant relationships, except in perceived quality of life, which increased with frequency. The results allowed for rejection of the null hypothesis on three of four research questions.

Post-hoc analyses were used to discover further perceptions and patterns of cannabis use involving intermediate use frequency, but not non- or high frequency use of cannabis for both anxiety and depression. Further, when reported immune function became worse, quality of life followed directly. Most of the significant relationship powers found were small in all analyses; however, more investigation will be needed to replicate the findings.

Chapter 5: Discussion

Appalachian residents live within a region that has often been overlooked in terms of funding, healthcare, and infrastructure, which are often spent in higher populated areas across states (Nashville, Charlotte/Durham, Philadelphia, Manhattan, etc.). This systemic neglect can encourage behaviors that, while illegal, are often unreported by neighbors for various reasons, examples can be seen in moonshining (Peine and Schafft, 2012) or methamphetamine use (Moody et al., 2017). While moonshining and methamphetamine use are significantly more dangerous than our understanding of cannabis use, the culture of silence and not reporting neighbors creates an environment where illicit activities can thrive.

Relationships were seen between measured variables in terms of how long or frequent participants have been using cannabis products. Effects and powers of relationships were relatively weak, with the highest R^2 value was .010 in terms of most relationships that included cannabis use patterns in their regression analyses. Several other relationships between the variables of anxiety, depression, and immunity were present in the data analyses that help to reinforce concepts of PNI and quality of life.

The overall goal of the study was to improve understanding of how cannabis use patterns and their relationships with difference scales of wellness were related, in order to understand the possible future for Appalachians after pending federal legalization. Results of the study involve information about cannabis and its use, with

recommendations for future research. While the study was not highly conclusive, the lack of highly significant findings was important to discuss.

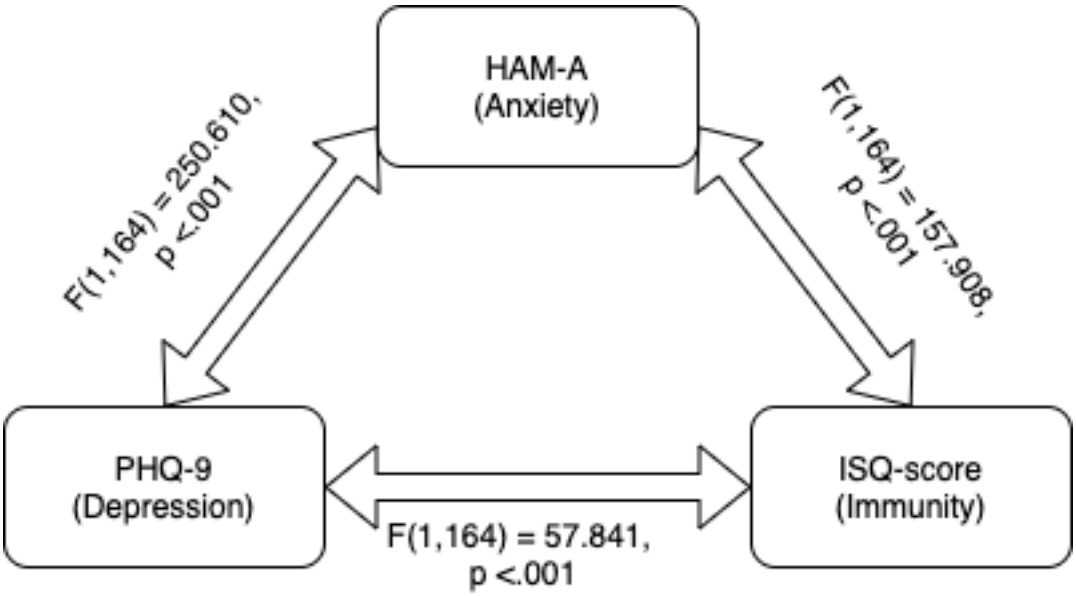
Interpretation of the Findings

Psychoneuroimmunology

PNI touts strong support to reinforce connections between mental, physical, and immune health. Data in this study helped to reinforce relationships between anxiety, depression, and immune function. These relationships were observed in this context with a known missing variable: inflammation. Inflammation is a response to threats to the body (psychosocial stress, physical injury, or imminent danger) that has a direct negative relationship to immune function, as more stress results in worse immune function (Ader & Cohen, 1975).

Figure 56

Relationships Between PHQ, HAM-A, and ISQ Total Scores



In line with expectations, as scores on the HAM-A and PHQ-9 increase, ISQ scores worsen. When allowing for the intermediate understanding of stress as a byproduct of depression and/or anxiety, this relationship appeared obvious when looking through the scope of PNI. There was a strong relationship between immune scores and quality of life measures, which was expected due to similarity in both scales measuring along disease progression (Fagundes et al., 2013).

During the early stages of this study, stress was a variable that was to be collected. After deliberation, stress was removed from the study, since it would have likely been collinear with other variables (anxiety, depression, and quality of life). This was the correct move due to the limited test capacity in SurveyMonkey, but upon

conclusion and analysis, including stress measures in the study would have been beneficial in clarifying how stress may be related to anxiety, depression, and quality of life.

Cannabinoids

Cannabis sativa, the plant used in cannabis products, can be consumed in many different forms, which have different levels of cannabinoids within each type of product. Further, during data collection, two major different types of cannabis (THC-included cannabis, and trace THC CBD-heavy cannabis) were not specified due to the complicated nature of identifying products and the illicit nature of using cannabis in research (Yeager, 2019). Without the ability to specify products being used, the study measured use of both, creating a lack of capability in attributing THC directly to any relationships found.

As seen in Tables 4 and 5, differences in cannabis use patterns existed in terms of age and gender, but there were few significant relationships between age or gender. Twice as many women responded to the study, and greater than 50% of participants had only started using cannabis products in the past 10 years, possibly as a result of societal perspective shifts regarding cannabis. Due to this, most long-term use participants (those who had consumed cannabis for longer than 10 years) were men.

Anxiety

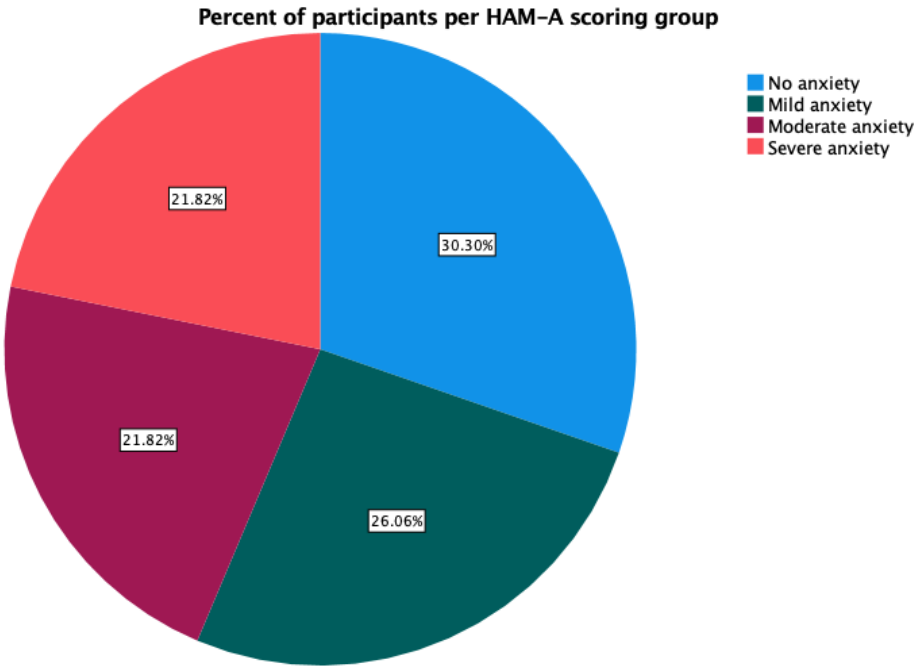
Anxiety, as measured via the HAM-A in this study was found to have multiple types of relationships in terms of longevity and frequency. For longevity, a linear relationship was found that indicated that as the number of years of cannabis use

increased, scores on the HAM-A were shown to decrease at a significant rate of .175 points per year. An investigation of age as a confounding variable was conducted and there was no significance.

Regarding frequency, a more complicated quadratic relationship was found, indicating that as individuals' use frequency neared average use numbers across the sample, their anxiety scores increased. The extremes of very infrequent and very frequent users of cannabis fell below the average score (see Figure #44), which is contrary to the original expectation of the relationship. Where I believed that intermittent use of cannabis would cause decreases in anxiety, anxiogenic effects may be possible related to intermittent use frequency, but anxiolytic effects become possible with daily or near daily use.

Figure 57

Participants per HAM-A Anxiety Scoring Groups



Overall, it was found that of the individuals who participated in this study, 42% of participants experienced moderate or severe anxiety enough to likely qualify for a diagnosis of an anxiety disorder. Compared to the previously reported prevalence post-COVID of an average of individuals who report anxiety disorders was measured at 31.9% (Salari et al., 2020), there appears to be possibility of an increased frequency amongst the Appalachian cannabis users.

Regarding the first hypothesis, a relationship between anxiety scores and cannabinoid use, a conclusion of rejecting the null hypothesis was made based on the relationships found. Making any strong claims based on the relationships would be

inappropriate, as the powers and relationships found were all small but were evidence enough to reject the null hypothesis. Additionally, the quadratic relationships found with anxiety and cannabis use frequency creates further questions of how frequent use may be anxiogenic or anxiolytic, additionally if a confounding variable of many daily non-THC CBD users reporting who have lower anxiety (Campos et al., 2013; Russo, 2017) compared to THC users experiencing more anxiety (Crippa et al., 2009). A more specified, possibly even clinical study on this subject would be recommended.

Depression

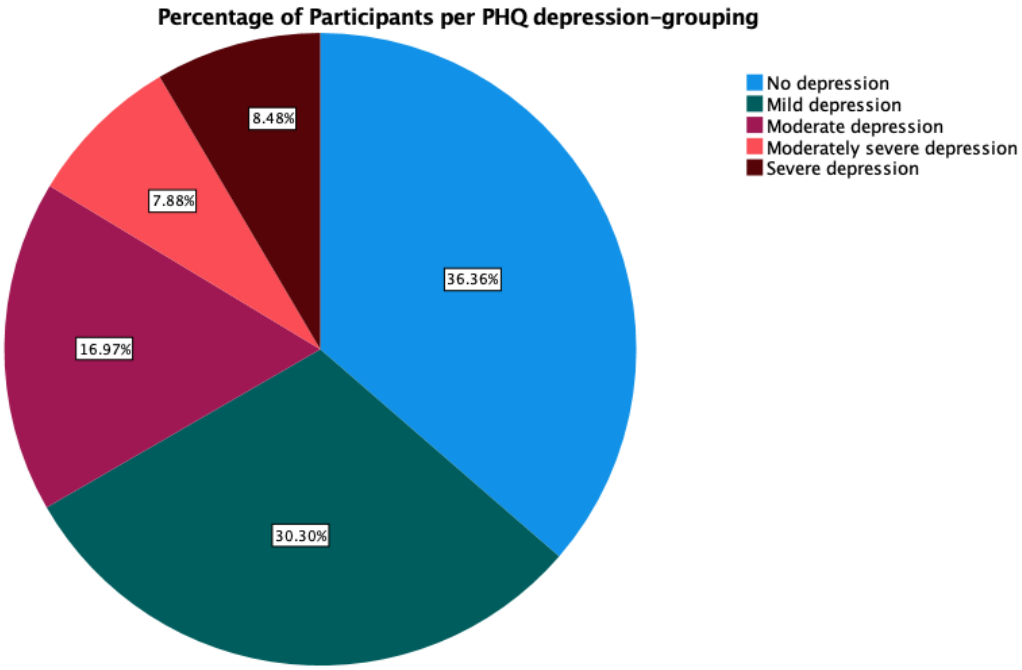
Depression, unlike anxiety, in more modern lights are thought to have anti-depressant properties (El-Alfy et al., 2010), but more concern was drawn from cannabis withdrawal related to increased depression symptoms (Stoner, 2017) or amotivational issues perpetuated further by cannabis use (Lac & Luk, 2017). Data collected showed some relationships did exist between depression, a few tenets of the depression scale, and cannabis use.

Overall, longevity had a relationship with depression total scores on the PHQ-9 (Kroenke et al., 2001) that indicated that as the amount of time using cannabis increased, the total depression scores decreased (see Fig. 16 & 17). This is consistent with some studies, however the lack of a significant relationship of frequency to depression failed to support the thread of cannabis being an anti-depressant wholesale (El-Alfy et al., 2010), but did indicate a capacity to reject the null hypothesis that no relationship exists between cannabis use and depression scores.

By investigating the individual questions, three elements of depression were seen to have relationships specifically with cannabis use. The first, “feeling tired or having little energy” was found to have a relationship to longevity of use where more overall use time decreased feelings of being tired. The second, “poor appetite or overeating?”, was found to have a relationship with longevity as well, with increased use leading to improvements in scores. Finally, “trouble concentrating on things, such as reading the newspaper or watching television?”, had a similar relationship, with more time using cannabis improving scores, but without any relationship with frequency. The overall effect was consistent with trends in total scores for the PHQ-9 lowering at a similar rate with age, however when investigating individual questions, no significant relationships were found.

Figure 58

Participants per Interpretation Group on the PHQ-9 Depression Scale



Regarding prevalence of depression in our sample, 33% of participants' PHQ-9 scores were high enough to quantify as having a depressive disorder, which included any scores in the "moderate depression", "moderately severe depression", and "severe depression" categories. Compared to the national average estimations of depression post-COVID reported at roughly 14.1% (Ettman et al., 2020), the number of participants reporting depression-symptomology were significantly higher. Where there is not enough evidence to support cannabis having a relationship that may be involved with the depression of participants, the anticipation of a significantly higher depression rate in Appalachia was consistent with expectations (Marshall et al., 2017).

Quality of Life

Following the research from the literature review, quality of life as an overarching concept did not have any significant relationships with cannabis use (Hser et al., 2017). On individual concepts, longevity once again found frequent negative relationships with quality of life, implying that with increased length of use, life measures would improve, specifically on days measured of poor physical and mental health.

One measure of interest in the HRQOL was the ninth question "During the past 30 days, for about how many days have you felt VERY HEALTHY and FULL OF ENERGY?" a significant positive relationship was found with frequency of use. An implication that more days of cannabis use in a month may relate to an increase of positive days in perception without any other trends in that direction does raise the question: "If people felt more energetic and healthier more often, what does that actually mean for their quality of life?"

A new question can be asked then based on the negative relationship of cannabis use and quality of life. Finding no effect amongst participants to point to a relationship in either direction, Goldenberg et al. (2016) and Aspis et al.'s (2015) two theories did not find support in this study. Further, if one measured perceived quality of life increases related to HRQOL #9, data would contradict Goldenberg et al. directly, as more frequency cannabis use was related to higher reported numbers of healthy and energetic days.

Another consideration for quality of life results was the lack of control for individuals who have long-term health considerations, as cannabis has been commonly paired with chronic conditions in research, such as fibromyalgia (van de Donk et al., 2018) and PTSD (Yarnell, 2015). Of the participants who answered the survey, less than 25% reported having chronic conditions on ISQ #11. When observed as a post-hoc analysis, no relationship existed amongst the small sample size (n = 39) between cannabis use and HRQOL 30-day measures. It is possible that with more focus on chronic conditions in a future study, a relationship may be present, but it was unclear from this study sample.

Immunity

The hypothesis related to immunity and cannabis was looking specifically for any relationship, as the directionality was uncertain based on the literature search. The ISQ results found interesting, albeit small relationships between longevity and frequency to ISQ total scores and individual questions within the scale. Further, when observed on two more subjective questions of immune health, relationships between cannabis also existed with headaches, skin problems, the common cold, and coughing.

Total scores were indicative of a relationship between longevity that promotes the theory of worsening scores on the ISQ with long-term cannabis use, however when total scores are observed in relation to age, the effect was similar. When age and longevity were included together in a regression predicting ISQ-7 total scores, multicollinearity was not present however (VIF = 1.122; most multicollinearity is not found until greater than

VIF = 5.000). This common trend without overlap implies that the relationship found with longevity was relevant on its own to total scores at least. Frequency alone did not have a significant relationship with the total scores.

On individual questions, relationships were found between cannabis use and headaches, skin problems, and frequency of the common cold. The relationships all implied that with increased longevity, individuals were less likely to see poor scores, but all at low rates with low powers. Several relationships stood out however in the questions of how the participant was feeling at the time of the survey and their self-rated immune functions. Individuals who utilized cannabis more frequently and who have used for longer periods of time, all reported significantly higher scores on both questions, reporting feeling better and healthier than others.

In contemplating the literature, most reports in the region of immunity and cannabis were sparse, with cortisol levels not being testing in this study to make comparisons to King et al. (2011) or Cuttler et al. (2017). Based on the data found in immunity however, it was likely that neither hypothesis correctly predicted changes in stress seen in the data here, rather finding no major effects (Cloak et al., 2015) was likely indicative that the relationship between immune function and cannabis use was more nuanced and the measures used in this study specifically for understanding immune function, stress, and the relationship with cannabis were exploratory and not optimal.

Limitations of the Study

This study fell upon some limitations that were unavoidable due to the nature of the research. As cannabis becomes more common place in society, the specificity of dosing and understanding of the products being consumed may become such that much higher quality data may be collected in the future. At the time of this study in much of Appalachia, the details surrounding the cannabis in the region are either vague or non-existent due to the legality issues, and as such even specification between THC and non-THC cannabis products was difficult to clarify.

Cannabis

Without the specification of what types of cannabis were being used, the entirety of this study does have some issues with validity, as measuring the product being used was impossible to determine the quality and potency of each of the cannabinoids involved. Subsequently, without having a proper measure of the products being consumed, there was no knowing which cannabinoids and in what dosages find any changes in their relationships to the study measures. Commonly, very low-THC (<.3%; commonly referred to as CBD) cannabis can be found mostly legally in many Appalachian regional areas, and even within CBD-style cannabis, vast cannabinoid profiles can be found between strains of CBD cannabis that will see varying doses of CBC, CBT, CBG, etc. Further, some forms of delta-variant THCs, such as delta-8 and delta-10 THC, have begun reaching the market in recent months that create more convolution in product choices.

Unfortunately, the varying products issue will likely continue to plague research of cannabis until federal legalization is achieved. Controlling cannabis source and quality will improve reliable measurement of the effects of specific cannabinoids and their relationships with other cannabinoids, as current research can only measure cannabis as a whole product and federal laws prevent administering cannabis in research in the United States. Studies that occur after federal legalization will have much more robust and reliable measurements of the effects of cannabis, and thus will produce much more reliable data.

Sampling

Foregoing issues with cannabis itself, the sample size used was sufficient for the study, but insufficient for a more thorough understanding of the region. Specifically in West Virginia, one of the few states in the region that has had a history of legal cannabis for medical purposes, that one only participant responded to the survey. Additionally, in studying Appalachia deeper, it became abundantly clear that there are three very different regions (northern, central, and southern) of Appalachian peoples and cultures that should likely be separated when studying any drug behaviors due to the vastly different prevalence between northern Appalachia's lower frequency to Central and Southern Appalachia (Moody et al., 2017).

Another trend in the data that may have created an interesting unseen effect in the relationships found occurred due to a lack of balancing of the participants. The gender ratio of two women for each man did not reveal any relationships when observed in the

data analysis (besides women report anxiety more often regardless of any other variables), but when considering the ratio difference and the trend of longevity scores being much higher in men and much lower in women, the possibility of reliability issues could be present. Gender and age balancing were options in the SurveyMonkey interface when selecting participants, but funding did not allow for further balancing past pulling only participants from the Appalachian region due to exponential cost increases. There was a possibility that a more complex relationship was present between gender balancing, age, and anxiety as men are less likely to express feelings of anxiety (Jalnapurkar et al., 2018), and anxiety is reported lower as age increases (Panchal et al., 2021).

Questionnaire

When inputting the measures into SurveyMonkey, a few questions were removed due to limited survey questions allowed in the study (50 questions total). Of the questions removed, all of them were qualitative in nature and were not intended to be observed in this study. While this was functional for this study, future research in the field may have benefitted from the data not collected, especially as investigations into specific conditions begin to be written.

Internet-based surveys worked functionally and promptly as seen in this study where 50 questions were collected from the entire sample size of participants in under 24 hours. What lacked in the online survey format however was that capability of a participant being able to gain clarity about questions. While the questions were attempted

to be worded clearly, there was possibility for some questions to not be completely understood by participants.

Recommendations

In future research, several factors could be improved upon to promote more dynamic results. Including stress correctly would immediately reinforce the theory behind the study. Stress was initially intended to be measured but was removed due to concerns of similarity to other measures and limited test capacity. While overlap was probably present in stress to quality of life or immunity due to their connections to PNI, non-collinear relationships may have existed between stress and the four criterion variables in this study that would have been unique to stress. Taking time to find a reliable stress measure or including cortisol saliva testing in conjunction with the surveys, would create a more thorough breakdown of the relationships between the concepts involved.

More tangible versions of this study would also allow for stronger connections to be evaluated between several measures, such as quality of life and immunity together through inflammation markers like Chacin-Fernández et al (2019). In-person evaluations/interviews would also allow for trained researchers to determine the connections of disease progression (Kendall-Tackett, 2010) in several conditions, reinforcing the PNI framework and comparing the progression to others measures as a mediating factor. While the online environment was very beneficial, especially throughout the COVID-19 pandemic during which this study was written and conducted,

in-person testing for these concepts would still improve reliability and allow for more robust data collection procedures unlimited by a maximum number of measure questions allowable.

A topic of exploration is the relationship of stress habituation (McCathy, 2016) to cannabis use behaviors. Creating a pre-post test structure to measure stress levels in relation to reported levels of cannabis use after asking participants to perform a common stressful activity could help to further understand the relationship in a manner that was not possible due to the nature of the data collection procedure in this study. By allowing collection of any relevant physical markers of immune health, future studies could improve the overall appearance of validity in these studies, especially as cannabis still faces stigma even presently (Reid, 2020).

Lastly, a comparative study between Appalachian and Non-Appalachian participants may help to highlight the differences and disparages that are present due to the cultural differences in the areas. While it is likely that post-COVID depression prevalence is higher in every region, there may be some alterations that Appalachia may not have experienced due to some areas being isolated and reducing concerns for some in the region. To better understand the nuance of cannabis use patterns amongst Appalachians, a comparison to non-Appalachians would help to determine what cultural and societal factors need to be observed in tandem with cannabis use. Through further research, particularly more detailed/controlled independent variables, more certain

relationships will be found that may either reinforce or challenge the claims of this study and should do so appropriately as new information is available.

Implications

Implications for societal change in this study often direct back towards attempting to understand how cannabis behaviors affect people, particularly people who are already living in disparaged regions. While the data created and presented for this study may become beneficial towards policy and organizational structures when organizations begin to work with individuals using cannabis, this study alone does not create a strong argument towards any specific direction, rather observing to understand and prepare. The inevitability of legalization is looming, especially as major corporations begin to promote federal legalization efforts (Palmer, 2021).

As a structure for a study, the function of looking at PNI through multiple tests in the manner this study was conducted aligns well to be a structure for future studies. Based loosely off the structure of McCain et al. (2005) and in response to Anderson (2017)'s call to research, the structure of the study is simple and could be conducted again with minor alterations to methods to explore any findings and/or discredit any relationships found in this study. By keeping the structure of the study uncomplicated, the model for the study could additionally allow some interchange for more variables to be observed in relation to cannabis use behaviors.

While superfluous, it must be stated that the data and implications made from this study should not be used in any manner to manipulate or harm others, particularly as the

reinforcement of potential anxiety fluctuations could make claims that cannabis use may induce more anxiety than it benefits at certain frequency levels. These claims are from a moderately small sample size, and as such, are not truly representative of the population to be used for decision making. The structure of this study was explorative in a manner seeking to promote and develop methods and data sets to be used in tandem with other research studies and to highlight the limitations historically of the time this study was conducted and written.

Conclusion

An explorative dive into cannabis use behaviors in Appalachia helped to determine that the research methods currently available, due to legality issues, leave specificity to be desired. While cannabis use in Appalachia was not new, legalization and societal perspectives on the substance have altered tremendously in the hundred years since it was outlawed. By observing and tracking relationships between cannabis use and scales, relationships were found with depression, anxiety, and immune function, all indicating small, but significant relationships that create more questions about the nature of cannabis use. Through more research into the field, as well as allowance for more specificity in any measures, an estimation of the future changes to Appalachian residence and their cannabis use may assist in bringing safer, more positive use patterns rather than an encore of tobacco consumption in the region (U.S. v. Philip Morris, 2006).

Quality of life stood alone as having few significant relationships with cannabis use, but stood out as perceived to strikingly improve, regardless of reporting towards the

mean. The differences between perception and reality in relation to cannabis use created further questions and discussions about the importance of perception in quality of life observations. Further, a more important question could be raised about how quality of life's perception may have altered or allowed misinterpretation of cannabis as a positive reinforcer and misled individuals into believing it may be beneficial, like Anderson's (2017) call for further research into cannabis being beneficial to mental health. While the data in this study did find some minor relationships that would imply that long-term cannabis use may coincide with some alterations in mental health, the need for more data and a more robust measure of quality of life may reveal relationships that may alter perceptions further.

Constructs of immunity, depression, and anxiety analyzed across each other reinforced the framework of PNI. As depression and anxiety scores increased, scores of immune functions directly worsened, implying a likely multi-directional relationship between constructs. This relationship is indicative of the framework and reinforces previous research (Ader et al, 1995; Solomon & Moos, 1964; McCain et al., 2005) on how the systems of the body are inter-connected. Where neurological measures were not collected, due to the nature of the data collection, further research would benefit in including some measure of neurological activity to bolster the framework in relation to cannabis use.

Measures of cannabis use against previous research found many inconsistencies against previous research. Cannabis and depression were seen to have a long-term

relationship where increased length of time was related to decreased depression scores, contrary to Stoner (2017)'s report of increased depressed moods. Without an immediate relationship of cannabis and depression, but long-term relationship, the data supported Micale (et al., 2014)'s argument for cannabis producing a monoamine effect that slowly improves in tandem with the endocannabinoid system, rather than diminishing mood.

Anxiety was found to follow some of the trends expected (Kedzior & Laeber, 2014), like perceptions of anxiety relief from cannabis would be predominantly perceived, however some relationships were seen in the data to support that there may be more tangible results, if only marginally. One question did arise from the data, what is the proportion of participants who reported using cannabis that were using THC-included product, rather than CBD-only, which is thought to be anxiolytic at every level (Russo, 2017). Was a relationship between cannabis and anxiety muddled by not separating the two products, and how much of an effect has COVID had on anxiety levels that cannabis may not be strong enough to have any notable effect? Further, how many participants who were long-term users may have stopped prior to COVID and returned to cannabis as self-prescribed anxiety relief, the second most commonly reported reason for cannabis use (Moltke & Hindocha, 2021)?

Immunity and cannabis use were related in similar ways to the studies that were observed in relation to immunity. Minor improvements in immune scores were seen with cannabis use, but without measuring cortisol in the study, difficulty in comparisons to King et al. (2011) and Cuttler et al. (2017) were not reliably valid. Immunity was not one

that a specific hypothesis had been developed, but the data supports that some cannabis use may have some positive relationship to immune function. It is noted however that relationships and causations are not the same, and as such no claims towards cannabis improving immune function should be made.

Overall, this study was designed with the intention of taking a snapshot of current Appalachian cannabis use and its relationship to several measures of life prior to any major alterations to drug laws, and to help create a structure for a quantitative measure of cannabis use that can be utilized online. With the challenges that were created by conducting this research during a worldwide pandemic, a structure was necessary to adapt the methods that inevitably allowed for a larger geographic spread in the sample population than would have been possible in vivo. Further, by observing Appalachia, the momentary study helps to create some baseline data for future research in relation to the field of cannabis in the region, as this study was one of the first to observe cannabis in Appalachia specifically. I hope that in the future, myself and other research scientists may use this data to help improve the livelihood of individuals in the region, rather than continue to allow the people of the area to be exploited.

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Table A1: Appalachian Region Counties

State	Counties that are part of the Appalachian Region (Appalachian Regional Commission, 2008)				
Alabama (37)	Bibb	Blount	Calhoun	Chambers	Cherokee
	Chilton	Clay	Cleburne	Colbert	Coosa
	Cullman	DeKalb	Elmore	Etowah	Fayette
	Franklin	Hale	Jackson	Jefferson	Lamar
	Lauderdale	Lawrence	Limestone	Macon	Madison
	Marion	Marshall	Morgan	Pickens	Randolph
	Shelby	St. Clair	Talladega	Tallapoosa	Tuscaloosa
	Walker	Winston			
Georgia (37)	Banks	Barrow	Bartow	Carroll	Catoosa
	Chattooga	Cherokee	Dade	Dawson	Douglas
	Elbert	Fannin	Floyd	Forsyth	Franklin
	Gilmer	Gordon	Gwinnett	Habersham	Hall
	Haralson	Hart	Heard	Jackson	Lumpkin
	Madison	Murray	Paulding	Pickens	Polk
	Rabun	Stephens	Towns	Union	Walker
	White	Whitfield			
Kentucky (54)	Adair	Bath	Bell	Boyd	Breathitt
	Carter	Casey	Clark	Clay	Clinton
	Cumberland	Edmonson	Elliott	Estill	Fleming
	Floyd	Garrard	Green	Greenup	Harlan
	Hart	Jackson	Johnson	Knott	Knox
	Laurel	Lawrence	Lee	Leslie	Letcher
	Lewis	Lincoln	Madison	Magoffin	Martin
	McCreary	Menifee	Metcalfe	Monroe	Montgomery
	Morgan	Nicholas	Owsley	Perry	Pike
	Powell	Pulaski	Robertson	Rockcastle	Rowan
	Russell	Wayne	Whitley	Wolfe	

State	Counties that are part of the Appalachian Region (Appalachian Regional Commission, 2008) (cont).				
Maryland (3)	Allegany	Garrett	Washington		
Mississippi (24)	Alcorn	Benton	Calhoun	Chickasaw	Choctaw
	Clay	Itawamba	Kemper	Lee	Lowndes
	Marshall	Monroe	Montgomery	Noxubee	Oktibbeha
	Panola	Pontotoc	Prentiss	Tippah	Tishomingo
	Union	Webster	Winston	Yalobusha	
New York (14)	Allegany	Broome	Cattaraugus	Chautauqua	Chemung
	Chenango	Cortland	Delaware	Otsego	Schoharie
	Schuyler	Steuben	Tioga	Tompkins	
North Carolina (29)	Alexander	Alleghany	Ashe	Avery	Buncombe
	Burke	Caldwell	Cherokee	Clay	Davie
	Forsyth	Graham	Haywood	Henderson	Jackson
	Macon	Madison	McDowell	Mitchell	Polk
	Rutherford	Stokes	Surry	Swain	Transylvania
	Watauga	Wilkes	Yadkin	Yancey	
Ohio (32)	Adams	Ashtabula	Athens	Belmont	Brown
	Carroll	Clermont	Columbiana	Coshocton	Gallia
	Guernsey	Harrison	Highland	Hocking	Holmes
	Jackson	Jefferson	Lawrence	Mahoning	Meigs
	Monroe	Morgan	Muskingum	Noble	Perry
	Pike	Ross	Scioto	Trumbull	Tuscarawas
	Vinton	Washington			

State	Counties that are part of the Appalachian Region (Appalachian Regional Commission, 2008) (cont).				
Pennsylvania (52)	Allegheny	Armstrong	Beaver	Bedford	Blair
	Bradford	Butler	Cambria	Cameron	Carbon
	Centre	Clarion	Clearfield	Clinton	Columbia
	Crawford	Elk	Erie	Fayette	Forest
	Fulton	Greene	Huntingdon	Indiana	Jefferson
	Juniata	Lackwanna	Lawrence	Luzerne	Lycoming
	McKean	Mercer	Mifflin	Monroe	Montour
	Northumberland	Perry	Pike	Potter	Schuylkill
	Snyder	Somerset	Sullivan	Susquehanna	Tioga
	Union	Venango	Warren	Washington	Wayne
	Westmoreland	Wyoming			
South Carolina (6)	Anderson	Cherokee	Greenville	Oconee	Pickens
	Spartanburg				
Tennessee (52)	Anderson	Bledsoe	Blount	Bradley	Campbell
	Cannon	Carter	Claiborne	Clay	Cocke
	Coffee	Cumberland	DeKalb	Fentress	Franklin
	Grainger	Greene	Grundy	Hamblen	Hamilton
	Hancock	Hawkins	Jackson	Jefferson	Johnson
	Knox	Lawrence	Lewis	Loudon	Macon
	Marion	McMinn	Meigs	Monroe	Morgan
	Overton	Pickett	Polk	Putnam	Rhea
	Roane	Scott	Sequatchie	Sevier	Smith
	Sullivan	Unicoi	Union	Van Buren	Warren
	Washington	White			

State	Counties that are part of the Appalachian Region (Appalachian Regional Commission, 2008) (cont).				
Virginia (25)	Alleghany	Bath	Bland	Botetourt	Buchanan
	Carroll	Craig	Dickenson	Floyd	Giles
	Grayson	Henry	Highland	Lee	Montgomery
	Patrick	Pulaski	Rockbridge	Russell	Scott
	Smyth	Tazewell	Washington	Wise	Wythe
	**includes: Covington, Galax, Martinsville, Radford, Buena Vista, Lexington, Bristol, & Norton*				
West Virginia (55)	Barbour	Berkeley	Boone	Braxton	Brooke
	Cabell	Calhoun	Clay	Doddridge	Fayette
	Gilmer	Grant	Greenbrier	Hampshire	Hancock
	Hardy	Harrison	Jackson	Jefferson	Kanawha
	Lewis	Lincoln	Logan	Marion	Marshall
	Mason	McDowell	Mercer	Mineral	Mingo
	Monongalia	Monroe	Morgan	Nicholas	Ohio
	Pendleton	Pleasants	Pocahontas	Preston	Putnam
	Raleigh	Randolph	Ritchie	Roane	Summers
	Taylor	Tucker	Tyler	Upshur	Wayne
	Webster	Wetzel	Wirt	Wood	Wyoming

Appendix B: Permission to Adapt Figure 1

Re: Request for Citation Permission

Nancy McCain <nlmccain@vcu.edu>
Wed 2/17/2021 7:57 AM
To: Matthew Ostrander <matthew.ostrander@waldenu.edu>
Cc: Nancy McCain <nlmccain@vcu.edu>

Dear Mr. Ostrander,

Thank you for your interest in the PNI model. You are welcome to use and adapt the model in support of your work.

I will appreciate your supplying me with a copy of your publication/findings when the time comes. With my best wishes for your success,

Nancy

Nancy L. McCain, PhD, RN, FAAN
Professor Emeritus

On Feb 16, 2021, at 4:21 PM, Matthew Ostrander <matthew.ostrander@waldenu.edu> wrote:

Hello Dr. McCain,

I hope that you are doing well! I wanted to reach out to you to request permission to use an adapted version of one of your figures. In your paper: "Implementing a comprehensive approach to the study of health dynamics using the psychoneuroimmunology paradigm", you have created a "generic model of the PNI-based theoretical framework" as your figure 1. This graph inspired my own diagram that I am hoping to use in my dissertation to describe the PNI paradigm with your permission.

I look forward to hearing from you and thank you for the insight that your work has brought!

M. Ian Frazier Ostrander
Walden University

Table C1: Data Tables for Multiple Regressions

Criterion Variable	**Predictor Variable(s)**	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
				HAM-A					
HAM-A	**Longevity**	**-.015**	**.006**	**-.196**	**-2.403**	**.017**	**3.212**	**.043**	**.038**
Total	Frequency	.138	.088	.128	1.562	.120			
HAM-A	**Longevity**	**-.002**	**.001**	**-.200**	**-246**	**.015**	4.477	.013	.052
#1	**Frequency**	**.023**	**.009**	**.197**	**2.427**	**.016**			
HAM-A	**Longevity**	**-.001**	**.001**	**-.196**	**-2.394**	**.018**	**3.103**	**.048**	**.037**
#2	Frequency	.013	.009	.119	1.450	.149			
HAM-A	Longevity	-.001	.001	-.158	-1.921	.056	2.648	.074	.032
#3	Frequency	.018	.010	.151	1.837	.068			
HAM-A	Longevity	-.001	.001	-.148	-1.795	.075	1.966	.143	.024
#4	Frequency	.014	.010	.115	1.394	.165			
HAM-A	**Longevity**	**-.002**	**.001**	**-.222**	**-2.730**	**.007**	**3.728**	**.026**	**.032**
#5	Frequency	.009	.009	.079	.974	.331			
HAM-A	Longevity	-.001	.001	-.133	-1.612	.109	1.614	.202	.007
#6	Frequency	.013	.010	.106	1.287	.200			
HAM-A	Longevity	-.001	.001	-.123	-1.484	.140	1.319	.270	.004
#7	Frequency	.010	.009	.093	1.119	.265			
HAM-A	Longevity	-.001	.001	-.128	-1.548	.123	1.476	.232	.006
#8	Frequency	-.002	.008	-.015	-.184	.854			
HAM-A	Longevity	.000	.001	-.006	-.799	.425	.333	.717	-.008
#9	Frequency	.003	.008	.035	.422	.674			
HAM-A	Longevity	.000	.001	-.062	-.749	.455	.317	.729	.004
#10	Frequency	.004	.008	.042	.503	.616			

Criterion Variable	Predictor Variable(s)	Slope	Std. Error	Standard Beta	t	Sig.	F	Sig.	R^2
				HAM-A (cont.)					
HAM-A #11	Longevity	-.001	.001	-.159	-1.930	.055	1.865	.158	.023
	Frequency	.006	.009	.060	.724	.470			
HAM-A #12	Longevity	.000	.001	-.076	-.915	.362	.474	.623	.006
	Frequency	.005	.008	.052	.620	.536			
HAM-A #13	Longevity	-.001	.001	-.105	-1.265	.208	.902	.408	.011
	Frequency	.007	.008	.070	.847	.398			
HAM-A #14	Longevity	-.001	.001	-.155	-1.883	.061	2.356	.098	.028
	Frequency	.015	.009	.135	1.647	.101			
				PHQ-9					
PHQ Total	**Longevity**	**-.010**	**.003**	**-.238**	**-2.945**	**.004**	**4.397**	**.014**	**.051**
	Frequency	.067	.051	.107	1.312	.191			
PHQ #1	Longevity	-.001	.001	-.142	-1.730	.086	1.920	.150	.023
	Frequency	.011	.008	.119	1.446	.150			
PHQ #2	Longevity	-.001	.001	-.120	-1.449	.149	1.143	.321	.014
	Frequency	.007	.007	.074	.891	.375			
PHQ #3	**Longevity**	**-.001**	**.001**	**-.175**	**-2.130**	**.035**	2.354	.098	.028
	Frequency	.009	.008	.091	1.103	.272			
PHQ #4	**Longevity**	**-.001**	**.001**	**-.207**	**-2.536**	**.012**	**3.221**	**.042**	**.038**
	Frequency	.006	.008	.061	.747	.456			
PHQ #5	**Longevity**	**-.002**	**.001**	**-.319**	**-4.019**	**.000**	**8.075**	**.000**	**.091**
	Frequency	.011	.008	.109	1.366	.174			
PHQ #6	Longevity	-.001	.001	-.146	-1.764	.080	1.574	.210	.019
	Frequency	.006	.008	.064	.774	.440			

Criterion Variable	Predictor Variable(s)	Slope	Std. Error	Standard Beta	t	Sig.	F	Sig.	R^2
				PHQ-9 (cont.)					
PHQ #7	**Longevity**	**-.001**	**.001**	**-.219**	**-2.685**	**.008**	**3.696**	**.027**	**.044**
	Frequency	.004	.008	.040	.494	.622			
PHQ #8	Longevity	-.001	.000	-.134	-1.617	.108	1.565	.212	.019
	Frequency	.008	.006	.100	1.216	.226			
PHQ #9	Longevity	-.001	.000	-.137	-1.662	.098	1.411	.247	.017
	Frequency	.005	.007	.065	.781	.436			
				HRQOL					
HRQOL	Longevity	-.007	.004	-.150	-1.823	.070	1.675	.191	.020
Total	Frequency	.025	.053	.038	.462	.645			
HRQOL	Longevity	.000	.000	.053	.639	.524	1.446	.238	.018
#1	Frequency	-.012	.007	-.140	-1.699	.091			
HRQOL	Longevity	-.005	.005	-.081	-.979	.329	.695	.501	.009
#2	Frequency	.070	.074	.079	.946	.345			
HRQOL	Longevity	-.006	.005	-.102	-1.243	.216	1.840	.162	.022
#3	Frequency	.122	.068	.148	1.792	.075			
HRQOL	**Longevity**	**-.012**	**.004**	**-.230**	**-2.821**	**.005**	**3.987**	**.020**	**.047**
#4	Frequency	.054	.065	.068	.831	.407			
HRQOL	Longevity	-.003	.005	-.053	-.641	.522	.608	.546	.007
#5	Frequency	.081	.076	.088	1.060	.291			
HRQOL	Longevity	-.005	.005	-.077	-.928	.355	.455	.635	.006
#6	Frequency	.039	.075	.043	.517	.606			
HRQOL	Longevity	-.005	.005	-.076	-.914	.362	1.039	.356	.013
#7	Frequency	.104	.076	.112	1.356	.177			

Criterion Variable	Predictor Variable(s)	Slope	Std. Error	Standard Beta	t	Sig.	F	Sig.	R^2
				HRQOL (cont.)					
HRQOL #8	Longevity	-.007	.005	-.102	-1.233	.219	.766	.467	.009
	Frequency	.040	.078	.042	.510	.611			
HRQOL #9*	Longevity	-.008	.004	-.143	-1.792	.075	**7.233**	**.001**	**.082**
	Frequency	**-.169**	**.066**	**-.205**	**-2.563**	**.011**			
HRQOL #10	Longevity	.000	.000	.069	.834	.405	1.961	.144	.024
	Frequency	.005	.003	.116	1.414	.159			
*Reverse coded before analysis									
				ISQ					
ISQ Total	**Longevity**	**.004**	**.002**	**.216**	**2.653**	**.009**	**4.222**	**.016**	**.050**
	Frequency	**-.047**	**.002**	**.216**	**2.653**	**.009**			
ISQ #1	Longevity	-.001	.000	-.109	-1.316	.190	1.791	.170	.022
	Frequency	.010	.006	.142	1.722	.087			
ISQ #2	Longevity	-.001	.001	-.146	-1.722	.078	1.572	.211	.019
	Frequency	.005	.008	.055	.665	.507			
ISQ #3	Longevity	-.002	.001	-.277	-3.454	.001	6.696	.002	.076
	Frequency	.018	.008	.184	2.293	.023			
ISQ #4	Longevity	-.001	.001	-.205	-2.507	.013	3.305	.039	.039
	Frequency	.012	.009	.112	1.376	.171			
ISQ #5	Longevity	-.001	.001	-.070	-.839	.403	.391	.677	.005
	Frequency	.005	.010	.045	.546	.586			
ISQ #6	Longevity	-.001	.000	-.163	-1.995	.048	3.683	.027	.043
	Frequency	.014	.006	.196	2.401	.017			

Criterion Variable	Predictor Variable(s)	Slope	Std. Error	Standard Beta	t	Sig.	F	Sig.	R^2
ISQ #7	Longevity	.000	.001	-.015	-.184	.854	1.974	.142	.024
	Frequency	.015	.008	.159	1.926	.056			
ISQ #8	Longevity	.002	.001	.136	1.693	.092	6.061	.003	.070
	Frequency	.037	.016	.185	2.302	.023			
ISQ #9	Longevity	.001	.001	.096	1.178	.241	4.513	.012	.053
	Frequency	.039	.017	.179	2.211	.028			

Table C2: Data Tables for Linear Regressions

HAM-A-Longevity-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
HAM-A Total	**-.011**	**.006**	**-.154**	**-1.987**	**.049**	**3.949**	**.049**	**.024**
HAM-A #1	-.001	.001	-.134	-1.724	.087	2.973	.087	.018
HAM-A #2	**-.001**	**.001**	**-.156**	**-2.019**	**.045**	**4.007**	**.045**	**.024**
HAM-A #3	-.001	.001	-.107	-1.377	.170	1.896	.170	.012
HAM-A #4	-.001	.001	-.109	-1.406	.162	1.976	.162	.012
HAM-A #5	**-.001**	**.001**	**-.196**	**-2.551**	**.012**	**6.509**	**.012**	**.038**
HAM-A #6	-.001	.001	-.098	-1.252	.212	1.567	.212	.010
HAM-A #7	-.001	.001	-.092	-1.177	.241	1.384	.241	.008
HAM-A #8	-.001	.001	-.133	-1.713	.089	2.935	.089	.018
HAM-A #9	.000	.001	-.005	-.700	.485	.490	.485	.003
HAM-A #10	.000	.001	-.048	-.618	.537	.382	.537	.002
HAM-A #11	-.001	.001	-.139	-1.793	.075	3.216	.075	.019
HAM-A #12	.000	.000	-.059	-.752	.453	.565	.453	.003
HAM-A #13	-.001	.001	-.081	-1.043	.298	1.008	.298	.007
HAM-A #14	-.001	.001	-.110	-1.407	.161	1.978	.161	.012
HAM-A –Frequency-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
HAM-A Total	.067	.084	.062	.794	.428	.630	.428	.004
HAM-A #1	.015	.009	.130	1.677	.095	2.813	.095	.017
HAM-A #2	.006	.009	.053	.680	.498	.462	.498	.003
HAM-A #3	.012	.009	.098	1.257	.210	1.580	.210	.010
HAM-A #4	.008	.010	.065	.837	.404	.701	.404	.004
HAM-A #5	.001	.009	.005	.064	.949	.004	.949	.000
HAM-A #6	.008	.010	.062	.790	.431	.624	.431	.004

HAM-A #7	.006	.009	.052	.659	.511	.434	.511	.003
HAM-A #8	-.006	.008	-.058	-.741	.460	.549	.460	.003
HAM-A #9	.001	.007	.013	.164	.870	.027	.870	.000
HAM-A #10	.002	.008	.021	.268	.789	.072	.789	.000
HAM-A #11	.001	.008	.007	.083	.934	.007	.934	.000
HAM-A #12	.002	.007	.026	.334	.739	.112	.739	.001
HAM-A #13	.003	.008	.035	.449	.654	.202	.654	.001
HAM-A #14	.009	.008	.084	1.072	.285	1.149	.285	.007

PHQ-9-Longevity-Linear Regressions

Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
PHQ Total	-.009	.003	-.203	-2.654	.009	7.042	.009	.041
PHQ #1	-.001	.000	-.103	-1.318	.189	1.737	.189	.011
PHQ #2	-.001	.000	-.095	-1.222	.223	1.494	.223	.009
PHQ #3	-.001	.001	-.145	-1.867	.064	3.487	.064	.021
PHQ #4	-.001	.001	-.187	-2.429	.016	5.901	.016	.035
PHQ #5	-.002	.001	-.283	-3.769	.000	14.209	.000	.080
PHQ #6	-.001	.001	-.124	-1.599	.112	2.556	.112	.015
PHQ #7	-.001	.000	-.205	-2.680	.008	7.182	.008	.042
PHQ #8	-.001	.000	-.100	-1.283	.201	1.646	.201	.010
PHQ #9	-.001	.000	-.116	-1.489	.139	2.216	.139	.013

PHQ-9-Frequency-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
PHQ Total	.017	.049	.027	.340	.734	.116	.734	.001
PHQ #1	.007	.007	.072	.915	.361	.838	.361	.005
PHQ #2	.003	.007	.034	.430	.667	.185	.667	.001
PHQ #3	.003	.008	.032	.411	.684	.169	.682	.001
PHQ #4	-.001	.007	-.008	-.105	.917	.001	.917	.000
PHQ #5	.000	.008	.002	.024	.981	.001	.981	.000
PHQ #6	.001	.008	.015	.195	.846	.038	.846	.000
PHQ #7	-.003	.007	-.033	-.420	.675	.176	.675	.001
PHQ #8	.004	.006	.056	.714	.476	.509	.476	.003
PHQ #9	.002	.006	.019	.238	.812	.057	.812	.000
HRQOL-Longevity-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
HRQOL 30 Days	-.006	.003	-.138	-1.775	.078	3.151	.078	.019
HRQOL #1	.000	.000	.006	.075	.941	.006	.941	.000
HRQOL #2	-.003	.005	-.055	-.703	.483	.494	.483	.003
HRQOL #3	-.003	.004	-.053	-.678	.498	.460	.498	.003
HRQOL #4	-.011	.004	-.207	-2.702	.008	7.299	.008	.043
HRQOL #5	-.001	.005	-.024	-.304	.761	.092	.761	.001
HRQOL #6	-.004	.005	-.063	-.803	.423	.645	.423	.004
HRQOL #7	-.002	.005	-.038	-.488	.626	.238	.626	.001
HRQOL #8	-.006	.005	-.088	-1.130	.260	1.278	.260	.008
HRQOL #9	.012	.004	.212	2.763	.006	7.636	.006	.045
HRQOL #10	.000	.000	.108	1.382	.169	1.911	.169	.012

HRQOL-Frequency-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
HRQOL 30 Days	-.008	.051	-.012	-.155	.877	.024	.877	.000
HRQOL #1	-.011	.007	-.123	-1.579	.116	2.494	.116	.015
HRQOL #2	.046	.070	.051	.657	.512	.432	.512	.003
HRQOL #3	.094	.065	.114	1.459	.147	2.128	.147	.013
HRQOL #4	-.007	.062	-.009	-.116	.907	.014	.907	.000
HRQOL #5	.065	.072	.070	.899	.370	.808	.370	.005
HRQOL #6	.016	.071	.017	.220	.826	.048	.826	.000
HRQOL #7	.080	.072	.087	1.115	.266	1.244	.266	.008
HRQOL #8	.008	.074	.008	.104	.918	.011	.918	.000
HRQOL #9	.208	.062	.253	3.332	.001	11.104	.001	.064
HRQOL #10	.006	.003	.139	1.798	.074	3.232	.074	.019
ISQ-Longevity-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
ISQ Total	.003	.002	.161	2.086	.039	4.351	.039	.026
ISQ #1	.000	.000	-.061	-.781	.436	.610	.436	.004
ISQ #2	-.001	.001	-.128	-1.647	.102	2.712	.102	.016
ISQ #3	-.001	.001	-.215	-2.816	.005	7.928	.005	.046
ISQ #4	-.001	.001	-.167	-2.166	.032	4.693	.032	.028
ISQ #5	.000	.001	-.005	-.698	.486	.487	.486	.003
ISQ #6	.000	.000	-.097	-1.247	.214	1.556	.214	.009
ISQ #7	.000	.000	.038	.483	.629	.234	.629	.001
ISQ #8	.003	.001	.198	2.578	.011	6.647	.011	.039
ISQ #9	.002	.001	.156	2.010	.046	4.040	.046	.024

ISQ-Frequency-Linear Regressions								
Criterion Variable	**Slope**	**Std. Error**	**Standard Beta**	**t**	**Sig.**	**F**	**Sig.**	**R^2**
ISQ Total	-.026	.022	-.091	-1.163	.247	1.352	.247	.008
ISQ #1	.008	.006	.106	1.357	.177	1.841	.177	.011
ISQ #2	.001	.007	.006	.077	.939	.006	.939	.000
ISQ #3	.009	.008	.091	1.169	.244	1.367	.244	.008
ISQ #4	.005	.008	.044	.562	.575	.316	.575	.002
ISQ #5	.003	.009	.022	.282	.778	.079	.778	.000
ISQ #6	.010	.006	.141	1.824	.070	3.326	.070	.020
ISQ #7	.014	.007	.154	1.984	.049	3.937	.049	.024
ISQ #8	.047	.015	.231	3.025	.003	9.152	.003	.053
ISQ #9	.045	.016	.211	2.760	.006	7.620	.006	.045