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Cannabis and Mental Health in Middle-aged and Older Adults

A Dissertation submitted in partial satisfaction of the requirements
for the degree Doctor of Philosophy

in

Interdisciplinary Research on Substance Use

by

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The dissertation of Makaya Funk- White is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

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University of California San Diego

San Diego State University

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DEDICATION

This dissertation is dedicated to my mom, my husband, my best friend, and my PhD

partner in crime, Garland. Without you all this would not have been possible.

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LIST OF ABBREVIATIONS

CUD   Cannabis Use Disorder

NESARC-III National Epidemiologic Survey on Alcohol and Related Conditions-III

THC   Tetrahydrocannabinol

CBD   Cannabidiol

DSM-V The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

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PUBLICATIONS

1. **Funk-White, M**., Moore, A. A., McEvoy, L. K., Bondi, M. W., Bergstrom, J., Chen, Y. C., ... & Kaufmann, C. N. (2020). Alcohol use patterns and cognitive impairment: A cross-country comparison: Epidemiology/Risk and protective factors in MCI and dementia. *Alzheimer's & Dementia*, *16*, e046074.

2.   **Funk-White, M.,** Moore, A. A., McEvoy, L. K., Bondi, M. W., Bergstrom, J., & Kaufmann, C. N. (2021). Alcohol use and cognitive performance: a comparison between Greece and the United States. *Aging & Mental Health*, 1-7.

3. Han BH, **Funk- White M**, Ko R, Al-Rousan T, Palamar JJ. Decreasing perceived risk associated with regular cannabis use among older adults in the United States from 2015 to 2019. J Am Geriatr Soc. 2021; 1–7. https://doi.org/10.1111/jgs.17213.

4. Han, B. H., Le, A., **Funk-White, M**., & Palamar, J. J. (2021). Cannabis and Prescription Drug Use Among Older Adults with Functional Impairment. *American Journal of Preventive Medicine*.

5. **Funk-White, M.** & Han, B. H. How Do COVID-19 and Drug ODs Intersect with Aging? Accessed August 16, 2021. http://generations.asaging.org/how-do-covid-19-and-drug-ods-intersect-aging

6. **Funk-White M,** Wing D, Eyler LT, Moore AA, Reas ET, McEvoy L. Neuroimaging-Derived Predicted Brain Age and Alcohol Use Among Community-Dwelling Older Adults. Am J Geriatr Psychiatry. 2023 Feb 20:S1064-7481(23)00217-8. doi: 10.1016/j.jagp.2023.02.043. Epub ahead of print. PMID: 36925380.

ABSTRACT OF THE DISSERTATION

Cannabis and Mental Health in Middle-Aged and Older Adults

by

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Doctor of Philosophy in Interdisciplinary Research on Substance Use

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Background: Cannabis use and cannabis use disorder (CUD) have become increasingly prevalent, with a notable rise in the United States due to legalization and greater accessibility. Moreover, there is a growing interest in cannabis use among older adults, who often turn to it form medicinal purposes. However, the association between cannabis use and mental health in older adults remains complex and requires further investigation to better understand if cannabis could have potential therapeutic benefits. Understanding these dynamics is crucial for informing policy and clinical interventions, including formulating guidelines for use and early interventions. The goal of this dissertation is to better understand the relationship between

cannabis and mental health in middle-aged and older adults via the following three aims (chapters).

Methods: Chapter 1- A scoping review was conducted on the existing literature to synthesize current research on cannabis use and depression or anxiety in middle-aged and older adults. Secondary analyses were conducted in chapters 2 and 3 with data from the National Epidemiological Survey on Alcohol and Related Conditions-III (NESARC-III) to investigate the relationship between cannabis use and mental health in middle-aged and older adults. Chapter 2- A logistic regression analyses was run to examine the association between a diagnosis of mood or anxiety disorder and cannabis use disorder controlling for sex, race/ethnicity, education, physical health, heavy alcohol use, tobacco use, and other drug use. Chapter 3- A zero inflated negative binomial regression model was run including interaction terms for sex, heavy alcohol use, other drug use, and tobacco use. All analyses use an alpha of .05.

Results: Our scoping review revealed an unclear association between cannabis use and depression or anxiety in middle-aged and older adults, with a multitude of articles reporting different associations. Findings from our two analytical aims found a positive association between lifetime diagnosis of depression or anxiety and cannabis use disorder, as well as cannabis use frequency. This relationship was also shown to be partially moderated by sex, alcohol use, other drug use, and tobacco use.

Conclusions: Our results have potential to inform clinicians and the need to be vigilant in screening older adults for cannabis use and mental health disorders and make attempts to understand the different dynamics of cannabis use.

INTRODUCTION

Cannabis and Cannabis Use Disorder

In 2018 the United Nations estimated that 192 million people, or 3.9% of the global population[1] had used cannabis in the past year. Cannabis is the most widely used substance, other than alcohol, in all age groups across the United States[2]. In fact, among adults aged over 18 years old, data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) shows that from the years 2001-2002 to 2012-2013, that past year cannabis use rates had more than doubled across all demographic subgroups[2]. Not only are the number of people who are using cannabis increasing, but use frequency is increasing as well. Approximately 9.9% of individuals who reported using cannabis in the past year used daily or near daily[1]. Cannabis refers to all products derived from the plant Cannabis sativa, including THC and CBD. The word marijuana refers to products from this plant that contain substantial amounts of THC. The word cannabis will be used primarily throughout this dissertation unless reporting on a piece of literature that specifically uses the word marijuana. They are used interchangeably in this dissertation.

The increase in prevalence of cannabis in the US is likely related to its increasing legalization across the US in recent years. Prior experience with alcohol legalization, in which individuals had increased access to alcohol and cheaper products, suggests that increasing access to cheaper and more potent cannabis products will increase the prevalence of regular cannabis use[1]. The potency of cannabis products since legalization have dramatically increased with many products containing 70% or more of THC[3]. The legalization of cannabis coincides with heightened acceptance, reduced perception of risk, and an increased risk for the development of cannabis use disorder in both adolescents and adults [1,4].

The two most common cannabinoids found in Cannabis products are, CBD and THC. They are similar in structure; however, the main difference is that THC is psychoactive while CBD will not[1]. The unhealthy related properties of cannabis are due to tetrahydrocannabinol (THC)[1]. The primary target of THC is the cannabinoid CB1 receptor, followed by the CB2 receptor. THC is a partial agonist of the CB1 and CB2 receptors meaning that when THC binds to these receptors it is able to activate them but only at partial efficacy[5]. The stimulation of the CB1 receptor can indirectly activate the dopaminergic system which mediates the rewarding effects of many different drugs[1].

Cannabis use disorder (CUD) is broadly defined as the inability to stop consuming cannabis even when it is causing physical or psychological harm[1]. CUD is much more prevalent than it once was, impacting approximately 10% of the 192 million cannabis users worldwide[1]. In 1992, the lifetime risk of dependence among those who had previously tried cannabis was estimated to be 9%, which was substantially lower than the risks for tobacco, heroin, cocaine and alcohol (32%, 23%, 17%, and 15% respectively)[1]. However, more recent data now suggests that approximately 30% of those who try cannabis may develop CUD[1]. Not only is there an increase in those developing CUD but transition from first use to dependence occurs faster among marijuana users than it does among nicotine and alcohol users (5 years compared to 27 and 13 years respectively)[6]. However, it should be noted that although this transition occurs faster, the probability of the transition to dependence occurring is estimated to be lower among individuals who use marijuana than for individuals who use nicotine, alcohol and cocaine (5.9% of users compared to 15.6% of users, 11% of users and 14.8% of users respectively)[6].

This research may suggest that in some ways cannabis is less dangerous than other substances that have addiction potential however, although the individual and public health

burden is much lower than other types of drug use, CUD still accounts for a large proportion of individuals who are seeking treatment for substance use disorders[1]. In fact, according to the Substance Abuse and Mental Health Services Treatment Episode Data, marijuana was the primary substance of "abuse" for 16.8% of all admissions in 2013 and those who were 50 years or older were 3.4% of those admissions [6]. It stands to reason that as the prevalence of cannabis use has increased since 2013, the number of individuals seeking treatment today would be even higher.

Furthermore, individuals who do develop a CUD have a higher risk of also experiencing poorer mental health[1]. In a national stratified Australian sample of persons aged 18 years and older, 7 in 10 persons with CUD had an additional psychiatric disorder, compared with 1.5 in 10 individuals who did not use cannabis[1]. When discussing cannabis use and cannabis policy there are often two distinct claims that appear. The first is that cannabis use can be a contributory cause of CUD, schizophreniform psychosis, anxiety and depressive disorders, cognitive impairment, and changes in brain pathways[3]. The other claim is that cannabis has neuroprotective properties that can be used to treat anxiety, depression, sleep disorders, pain, neurological disorders, and dependence on various drugs[3]. Ultimately, the legalization of cannabis has allowed for so many different THC/CBD combinations and forms of administration to become available that both claims may be true. This research study will work to add literature to this subject by testing the association between cannabis use and mental health in older adults.

Cannabis Use in Older Adults

As the interest in the potential health benefits of cannabis grows and legalization spreads across more states, cannabis use is becoming substantially more frequent in older adult populations[7]. Recent studies have shown that cannabis use has increased significantly across all

demographic subgroups, but most notably across middle aged and older adults [8]. A study based on the 2012-2013 NESARC data found that 3.9% of the 50+ age group reported past year marijuana use[8], and another study noted that one third to more than one half of registered medical marijuana participants were 50 years or older [8]. More recent studies have shown an increase in cannabis use from 2.4% in 2015 to 4.2% in 2018 among adults aged 65 or older[7]. While there is growing attention surrounding the increase of cannabis use among older adults, compared to adolescents and young adults, systematic research on older adult use is rare[2].

Older adults (defined here as aged 50+) have shown the sharpest growth in consumption compared to all other age groups[9], with more than a quarter of users being new users and a majority of these users indicating that they use for medicinal purposes[9]. This is an issue as the steady increase in THC potency could cause older adults to be even more susceptible to adverse effects than other populations [8,9]. One study conducted by Yang et al.[7], found that 61% of cannabis users had used for the first time as adults aged 61 years or older, and that more than half reported daily or weekly use. While marijuana has been shown to have both potential risks and benefits, more risks have been reported to date and evidence of the effects of medical marijuana use among older adults is lacking[2].

The increasing rate of cannabis use among older adults is often attributed to the aging of the baby boomer population (born between years 1946-64) [6,8,10]. The baby boomer population has had a greater exposure to marijuana than previous generations, and they tend to have more lenient attitudes toward recreational and medicinal use[8]. In a qualitative study looking at motivations for use, baby boomers described their motivations as relaxation/stress reduction, social/recreational, enhancement/expansion, and symptom relief [8]. Many baby boomers see cannabis as a safer alternative to other illicit drugs, some prescription drugs and alcohol that may

have less side effects, low risk for addiction, and a greater effectiveness in relieving common symptoms such as pain and anxiety [6]. The perception is that cannabis has no to only slight risk even during frequent or weekly use[8]. However, there are chronic health risks associated with marijuana use in this population as well as interactions with prescribed medications that older adults may not be aware of[10]. Part of this may be due to the baby boomer population having prior experience with much less potent forms of marijuana than what is currently available. It is important that we acknowledge the increase in potency as aging is already associated with many physiological changes that increase and alter effects of substances and, when coupled with marijuana with a higher potency, it could pose a higher risk to older adults [10].

Reports suggest that older adults may be interested in cannabis use as a means to eliminate or treat symptoms of chronic medical health conditions [10,11]. Generally, older adults tend to experience an increase in chronic medical and mental health conditions such as chronic pain, insomnia, and cognitive disorders[11]. Older adults also experience lifestyle changes such as retirement, loss of spouse, social isolation, and increased leisure time, which may also lead to increased cannabis use[11]. Older adults who are using cannabis either to treat these conditions or those who are using recreationally due to changes in lifestyle may be unaware of changes that occur with age that may lead to potentially harmful effects of cannabis use that were less common when using at a younger age[11].

In the Yang et al.[7] study, looking at cannabis use in a geriatric clinic setting, 80% of older adults who reported using cannabis reported using it for medical reasons. The most common conditions that older adults were using cannabis for were pain/arthritis, sleep disturbance, and anxiety. Over three quarters of these patients reported cannabis being 'somewhat' or 'extremely' helpful in managing these conditions. Furthermore, 40% also reported using cannabis for more

than one condition, the most common of which were pain/arthritis and sleep, depression and anxiety, and pain/arthritis, sleep, depression and anxiety. Another study conducted by Lum et al.[7], found that older adults were more likely to report using cannabis for both recreational and medicinal purposes and they generally felt cannabis had a positive impact on their lives.

Given that results are showing that cannabis is used primarily for medical conditions and that polypharmacy is common among older adults with medical conditions [7] it is important to determine the ways in which cannabis can interact with common medications used by this population. For example, increased doses of cannabinoids have the potential to affect the metabolism of various medications[7]. While further research in drug interactions is needed, it is important to mention that cannabis use in this population could also be leading to deprescribing efforts of potentially unneeded and harmful medications for older adults[7]. Indeed, one survey showed that of 486 respondents who reported ever using cannabis and opioids in the past year, 41% reported a decrease or elimination of opioid use due to cannabis[7]. And another survey indicated that cannabis is also being used as a substitute for benzodiazepines and antidepressant medications [7].

One of the significant challenges that is discussed less often surrounding medical cannabis is the effects of cannabis on mental disorders, both in terms of individual use and the societal acceptance of cannabis and its perceived benefits on mental health [12]. While preliminary findings suggest that low-dose, short term medical cannabis use does not carry significant risk of serious mental or physical effects in older adults without prior psychiatric history[9], epidemiological studies have found a correlation between past year cannabis use and poor mental health outcomes in community dwelling older adults [9]. Studies have suggested that older cannabis users endorse higher rates of mental disorders compared to those who do not use

cannabis. In fact, in one study conducted by Vacaflor et al.[9] past year cannabis users aged 50 and older presented with significantly higher rates of past year mental disorders (33.32% vs 18.86%) and lifetime mental disorders (48.78% vs 27.26%) compared to never users. The growing body of research looking at older adults and cannabis use highlights the importance of health care providers to screen older adults for marijuana and other substance use disorder and provide education surrounding the potential differences in effects when using as an older adult compared to the younger population. This research study will seek to fill this gap by focusing on older adults.

Cannabis and Mental Health Concerns

As many cannabis users may begin using cannabis to treat mood disorders[4], it is important that they understand the inherent risks of those decisions. Indeed, individuals who are already experiencing a mental health disorder are already a high-risk population for addiction vulnerability and roughly half of individuals who initially reported using cannabis for anxiety or depression, do not report the same reasons for continued use that they report when they first begin using[4]. In a study conducted by Choi et al.[6] over 40% of ex cannabis users and 50% of past year cannabis users had one or more mental disorders in their lifetime. Furthermore, compared to 27.3% of never users, 42.9% of ex users and 48.8% of past year users had a lifetime mental disorder, classified in this case as major depressive disorder, dysthymia, anxiety disorder, PTSD, and bipolar disorder. Even more concerning, in another study conducted by Choi et al.[6] looking at past year suicidal ideation, the highest rates were found among those using cannabis combined with other drugs followed by cannabis only users (13.64% and 5% respectively).

Research examining the relationship between cannabis use and depression has yielded mixed results. For example, in nationally representative US survey, both depression and anxiety

were shown to be strong predictors for whether or not regular cannabis use will turn into a CUD and the presence of CUD in the past 12 months was shown to be significantly associated with a high risk of mood disorders, anxiety disorder, PTSD, and personality disorders [1,4]. Multiple other studies have found an association between cannabis use and depression across all age groups [1,2,4,13]. However, much about these associations is unclear. While it is possible that CUD can be associated with an increase in individuals' odds of experiencing major depressive disorder or any form of depression, it is unclear if frequency of use moderates this association, and less use may not be associated with major depressive disorder.

Furthermore, there is potential that these associations may be due to confounding factors, specifically that of alcohol use[17-20]. Other studies have found no association between depression and cannabis once controlled for heavy alcohol use [4,13]. Furthermore, to this point there have been no randomized control trials for cannabis as a treatment for depression and there are only secondary analyses of cannabis potentially having therapeutic effects on depressive symptoms.

Current literature is similarly mixed when it comes to anxiety and cannabis use. In a cannabis survey conducted in Canada in 2017 over 50% of respondents reported a positive outcome when using cannabis to treat anxiety, however the current literature does not support this association[4]. A variety of studies have found an association between cannabis use and anxiety [4,9,12,14] however this association is not always present once controlling for common confounders such as cigarette use and childhood factors[4]. Other studies have found a strong association between anxiety and cannabis use but only among individuals with CUD. For example, in an Australian household survey, 40.5% of individuals who were diagnosed with CUD in the past year also met criteria for an anxiety disorder, this number was much lower in individuals without a CUD (20.8%) and lowest in those who do not use cannabis at all (11.2%)[1].

Another US population survey found that among individuals with a CUD, 8.9% had generalized anxiety disorder, 8.4% social anxiety, 7.7% panic disorder, and 16.4% specific phobias[1]. However, other studies have found an association between cannabis and an improvement in anxiety symptoms. For example, one study found that a single dose of 600 mg CBD in individuals with social anxiety disorder was associated with improved scores on a visual analogue scale measuring social anxiety disorder after a public speaking test[4]. Again, these results need further investigation in regard to frequency of use, THC to CBD ratio, confounding factors and dosing.

These mixed findings are apparent in studies on younger adults as well. However, there is much more consistency regarding the relationship between cannabis and mental health. For example, one systematic review conducted by Moore et al., (2007)[23] felt there was enough evidence available to confidently determine that young people who use cannabis could be at an increased risk for developing a psychotic illness later in their life. Although it should be noted that an additional systematic review of longitudinal studies found no evidence to strongly support a causal relationship in either direction between cannabis and mental health in younger adults.[24] There are also more longitudinal studies available on cannabis and mental health in younger adults. For example, one longitudinal study found that having a mental health disorder at age 15 lead to a significant elevated risk of cannabis use at age 18.[25] The same study found that cannabis use at age 18 lead to an elevated risk of having a mental health disorder at age 21.[25] There is further research that suggests that THC may impact learning, processing speed and memory in adolescents and younger adults due to their frontal lobe not being fully developed however THC does not impact middle-aged and older adults in this same way.[26] Furthermore, prevalence of cannabis use is much higher in younger adults which may further demonstrate why

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there is stronger evidence of the association between cannabis and adverse mental health in this population.[27]

The possibility that cannabis use and psychiatric disorders are significantly associated is concerning as psychiatric symptoms have also been shown to predict both problematic cannabis use and the perception that cannabis use is harmless[4]. For example, in a study examining Veterans experiencing PTSD and using cannabis, there was an expectation that as PTSD symptoms increased, increased cannabis use would address the symptom severity[4]. This perception that cannabis may provide relief from symptoms of psychiatric disorders has been found to potentially lead to a lack of help-seeking behavior from individuals experiencing problematic cannabis use[4]. A study examining medical marijuana users in Canada found that 85% of those with depression or anxiety reported that they substituted cannabis for prescription drugs based on the belief that cannabis would address these conditions with less adverse side effects and better symptom management [15]. Furthermore, the rates of anxiety and mood disorders are also higher among medical users than nonmedical users. For example, in a study conducted by Choi et al.[6] it was shown that 32.88% of medical users had past year marijuana use disorder whereas only 25.25% of nonmedical users had marijuana use disorder. More research is needed to better understand this association. Our study will seek to fill this gap by gathering existing literature and systematically mapping it in our scoping study, and then going on to test the association between cannabis use and mental health using both logistic and linear regressions.

The bidirectional relationship between cannabis and mental health

There is an emerging paradox in cannabis use research in which a multitude of individuals report using cannabis to treat symptoms of a mental health disorder[15]; however, research thus far has shown that having a using cannabis may lead to an increased chance of

individuals developing a mental health disorder[13]. Individuals who are experiencing mental health disorder are more likely to also be experiencing a cannabis use disorder[15]. In fact, in one nationally representative study the presence of cannabis use disorder in the past 12 months was significantly associated with a high-risk mood disorder, anxiety disorder, post-traumatic stress disorder, and personality disorder[13]. Conversely studies have also shown that individuals who are experiencing CUD are more likely to be experiencing a mental health disorder[13]. Indeed, there are several factors that could potentially lead to a person developing CUD and these could be the same factors that also could lead to an individual developing a mental health disorder. This is demonstrated well in the addiction vulnerability hypothesis which states that there are preexisting vulnerabilities that lead to an individual developing an addiction[1]. For example, certain factors that could lead to a person developing any substance use disorder including CUD may include impulsivity, genetics, epigenetic states, and neurobiology[1]. In turn these are the same factors that could lead to an individual developing a mental health disorder. Certain genetic studies have confirmed vulnerability models where there are shared genetic predispositions for CUD and major depression[13]. Not only are there shared vulnerabilities but experiencing a mental health disorder is in and of itself a vulnerability for potential addiction[15].

The possible health benefits of cannabis

There is a high amount of interest across the US in the possible health benefits of cannabis[7]. Thus far research has found some evidence suggesting that cannabis has therapeutic benefits, specifically in cancer patients and those with chronic medical conditions[7]. In 2017, the National Academies of the Sciences, Engineering and Medicine published a review on the health effects of cannabis, ultimately finding evidence to suggest that cannabis can reduce symptoms including pain, spasticity, tremors, nausea and insomnia[16]. In another study done across 18

different countries, participants reported using cannabis medically rather than recreationally with the primary use reasons being for pain, anxiety, and depression (61.2%, 58.1% and 50.3% respectively)[4]. Indeed, a significant proportion of medical marijuana users report that not only is cannabis effective for symptom relief, but they also consider it a safer alternative to prescription medication[6].

In fact, so many individuals have begun reporting using cannabis as a way to self-treat symptoms of mental illness that some clinicians have begun to prescribe it for anxiety and depression[4]. Furthermore, an increase in legalization of medical marijuana laws have been shown to be associated with a decrease in opioid prescribing in older adults, suggesting that cannabis could assist in decreasing the risk of opioid use disorder in this otherwise high risk population[10]. Certain studies have just begun to investigate dosing recommendations for THC and CBD in cannabis and further research is needed prior to definitive treatment recommendations can be made.

Cannabis use can not necessarily be put into a box of purely good or bad as it comes in many different forms and concentrations. While current literature suggests that cannabis use in highly THC potent forms may be harmful, it is possible that smaller doses or pure CBD may have therapeutic effects. Understanding that cannabis does not fit into one category, or another will help in filling research gaps and addressing policy. While there is evidence to suggest that cannabis use in populations experiencing a mental health disorder is extremely prevalent, there is not enough literature to confidently say that cannabis use has therapeutic benefits. In the interest of both policy and clinical interventions it is important that we better understand this relationship and its potential harms and benefits.

References

1. Connor JP, Stjepanović D, Le Foll B, Hoch E, Budney AJ, Hall WD. Cannabis use and cannabis use disorder. *Nat Rev Dis Primer*. 2021;7(1):16. doi:10.1038/s41572-021-00247-4

2. Choi NG, DiNitto DM, Marti CN. Older-adult marijuana users and ex-users: Comparisons of sociodemographic characteristics and mental and substance use disorders. *Drug Alcohol Depend*. 2016; 165:94-102. doi: 10.1016/j.drugalcdep.2016.05.023

3. Hall W, Hoch E, Lorenzetti V. Cannabis use and mental health: risks and benefits. *Eur Arch Psychiatry Clin Neurosci*. 2019;269(1):1-3. doi:10.1007/s00406-019-00986-2

4. Lowe DJE, Sasiadek JD, Coles AS, George TP. Cannabis and mental illness: a review. *Eur Arch Psychiatry Clin Neurosci*. 2019;269(1):107-120. doi:10.1007/s00406-018-0970-7

5. Partial Agonist - an overview | ScienceDirect Topics. Accessed September 2, 2022. https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/partial-agonist

6. Choi NG, DiNitto DM, Marti CN. Older adults who use or have used marijuana: Help-seeking for marijuana and other substance use problems. *J Subst Abuse Treat*. 2017; 77:185-192. doi: 10.1016/j.jsat.2017.02.005

7. Yang KH, Kaufmann CN, Nafsu R, et al. Cannabis: An Emerging Treatment for Common Symptoms in Older Adults. *J Am Geriatr Soc*. 2021;69(1):91-97. doi:10.1111/jgs.16833

8. Choi NG, Marti CN, DiNitto DM, Choi BY. Older adults' marijuana use, injuries, and emergency department visits. *Am J Drug Alcohol Abuse*. 2018;44(2):215-223. doi:10.1080/00952990.2017.1318891

9. Vacaflor BE, Beauchet O, Jarvis GE, Schavietto A, Rej S. Mental Health, and Cognition in Older Cannabis Users: A Review. *Can Geriatr J CGJ*. 2020;23(3):242-249. doi:10.5770/cgj.23.399

10. Han BH, Palamar JJ. Marijuana use by middle-aged and older adults in the United States, 2015–2016. *Drug Alcohol Depend*. 2018; 191:374-381. doi:10.1016/j.drugalcdep.2018.07.006

11. Wolfe D, Corace K, Rice D, et al. Effects of medical and non-medical cannabis use in older adults: protocol for a scoping review. *BMJ Open*. 2020;10(2):e034301. doi:10.1136/bmjopen-2019-034301

12. Newton-Howes G. The challenges of "medical cannabis" and mental health: a clinical perspective. *Br J Clin Pharmacol*. 2018;84(11):2499-2501. doi:10.1111/bcp.13687

13. Pacek LR, Martins SS, Crum RM. The Bidirectional Relationships Between Alcohol, Cannabis, Co-occurring Alcohol and Cannabis Use Disorders with Major Depressive Disorder: Results from a National Sample. *J Affect Disord*. 2013;148(0):188-195. doi:

10.1016/j.jad.2012.11.059

14. Haines-Saah R. Cannabis and Mental Health: Insights from Canadian Research. *Can J Psychiatry Rev Can Psychiatr*. 2019;64(5):302-303. doi:10.1177/0706743719835844

15. Corroon JM, Mischley LK, Sexton M. Cannabis as a substitute for prescription drugs – a cross-sectional study. *J Pain Res*. 2017; 10:989-998. doi:10.2147/JPR.S134330

16. National Academies of Sciences E. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*.; 2017. doi:10.17226/24625

17. Thompson K, Holley M, Sturgess C, Leadbeater B. Co-use of alcohol and cannabis: longitudinal associations with mental health outcomes in young adulthood. International journal of environmental research and public health. 2021 Mar 31;18(7):3652.

18. Hellemans KG, Wilcox J, Nino JN, Young M, McQuaid RJ. Cannabis use, anxiety, and perceptions of risk among Canadian undergraduates: the moderating role of gender. Canadian Journal of Addiction. 2019 Sep 1;10(3):22-9.

19. Daros AR, Pereira BJ, Khan D, Ruocco AC, Quilty LC, Wardell JD. Daily associations between cannabis use and alcohol use in young adults: The moderating role of self-report and behavioral measures of impulsivity. Addiction Research & Theory. 2022 Mar 4;30(2):79-88.

20. Yurasek AM, Aston ER, Metrik J. Co-use of alcohol and cannabis: A review. Current Addiction Reports. 2017 Jun;4(2):184-93.

21. NIAAA Publications. Accessed September 19, 2022. https://pubs.niaaa.nih.gov/publications/arh29-2/107-120.htm

22. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology*. 2005;8(1):19-32. doi:10.1080/1364557032000119616

23. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *The Lancet*. 2007;370(9584):319-328. doi:10.1016/S0140-6736(07)61162-3

24. Macleod J, Oakes R, Copello A, et al. Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *The Lancet*. 2004;363(9421):1579-1588. doi:10.1016/S0140-6736(04)16200-4

25. McGee R, Williams S, Poulton R, Moffitt T. A longitudinal study of cannabis use and mental health from adolescence to early adulthood. *Addiction*. 2000;95(4):491-503. doi:10.1046/j.1360 0443.2000.9544912.x

26. Mueller RL, Ellingson JM, Bidwell LC, Bryan AD, Hutchison KE. Are the Acute Effects of

THC Different in Aging Adults? *Brain Sci*. 2021;11(5):590. doi:10.3390/brainsci11050590

27. National Academies of Sciences E, Division H and M, Practice B on PH and PH, Agenda C on the HE of MAER and R. Cannabis: Prevalence of Use, Regulation, and Current Policy Landscape. In: *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. National Academies Press (US); 2017. Accessed August 24, 2023. https://www.ncbi.nlm.nih.gov/books/NBK425763/

Chapter 1: THE RELATIONSHIP BETWEEN CANNABIS AND MENTAL HEALTH IN MIDDLE-AGED AND OLDER ADULTS: A SCOPING REVIEW

Background

Cannabis, the most widely used federally illegal drug in the United States[1], has garnered limited research attention regarding its health impacts. This knowledge gap is concerning, as recent legislative changes have expanded access to cannabis and led to a substantial increase in its usage across all age groups.[2] Of particular significance is the steep rise in cannabis use among older adults, whose experiences may be influenced by the effects of the aging process.[3] Moreover, older adults exhibit a higher propensity for using cannabis for medical purposes, compared to the recreational use more commonly observed in younger generations.[4] Indeed, one of the reasons for the increase in use in this population could be due to the aging of the baby boomer generation, who possess higher historical usage rates of cannabis, as well as more positive attitudes towards cannabis.[5]

The relationship between cannabis and mental health has been the subject of research previously, however this relationship has been scarcely studied in older adults. Consequently, the implications of cannabis use as a potential treatment for depression or anxiety in this population are still inadequately understood. Factors such as differences in comorbidity, motivation for use, patterns of use, and modes of use could contribute to distinct outcomes among older adults.[3] Notably this demographic is more likely to experience chronic medical and mental health conditions, including chronic pain, insomnia, mood disorders and cognitive impairment.[6]

Preliminary investigations suggest that older adults may express interest in using cannabis to alleviate the symptoms of these chronic conditions.[7] However, their understanding of age-related physiological changes that may impact the effects of cannabis remains limited. Thus,

there is a pressing need to conduct systematic research focusing specifically on older adults to better understand the relationship between cannabis use and mental health outcomes.

Although systematic and scoping reviews have been conducted on cannabis use in younger age groups, the unique age-related changes and increased use in the older adult population necessitates a dedicated exploration of the effects of cannabis in this specific demographic. A scoping review presents an opportunity to collate and map the available research on cannabis and depression or anxiety specifically in middle-aged and older adults, therefore identifying topic areas that require further research and those that already possess sufficient evidence for future reviews. Furthermore, this review will contribute to the consolidation and mapping of relevant research in this area, aiming to inform care practices, develop policy guidelines, and direct future research endeavors. The objective of this scoping review is to provide a comprehensive synthesis of the literature concerning the relationship between cannabis use and depression or anxiety in middle-aged and older adults.

Methods

This scoping review forms part of a larger dissertation investigating the association between mental health and cannabis use in older adults. We ultimately decided to pursue a scoping review instead of a systematic review because scoping reviews are more exploratory whereas systematic reviews seek to answer a more precise question. Furthermore, the state of the current research is rather heterogeneous, which also suggests a scoping review. Scoping reviews have been defined as 'exploratory projects that systematically map the literature available on a topic, identifying key concepts, theories, sources of evidence, and gaps in the research. We used the DistillerSR software to conduct our scoping review. Three reviewers took part in this scoping review (MF, KJ, RA).

We followed the participant-concept-context inclusion criteria as set forth by Arksey and O'Malley.

Participants: Inclusion criteria for participants included any studies that included middle-aged or older adults (i.e., 40 and older). We also included studies that had analyses stratified by age or birth cohorts. We included participants of any sex/gender/race/ethnicity and included both current and past cannabis users. As well as those who used cannabis both with and without additional substances. Inclusion criteria also included any mode of cannabis use (i.e., smoking, eating, topical, etc.).

Concept: The concept of relevance was based on the outcomes of interest. Both beneficial and harmful effects of cannabis use were considered outcomes of interest. Studies looking at both cannabis use and mental health outcomes were considered.

Context: The context of the studies included was both current and past cannabis use in any geographical areas, any timeline, and any follow up period.

Types of Evidence: We included systematic reviews, cross-sectional and longitudinal research studies. We made the choice to exclude editorials, letters, commentaries, abstracts, and case reports. Only publications in English were considered due to the cost and time restrictions of the study.

The framework proposed by Arksey, and O'Malley identifies five stages for conducting a scoping review; (i) Identify the research question (ii) Identify relevant studies (iii) Study selection (iv) Chart the data (v) Collate summarize and report the results. The five different stages are described in more detail below.

Identify the research question

We began our project by conducting a preliminary review of the literature and reviewing the main objectives of scoping reviews. We identified the main objective of this review as that of mapping the available evidence on the association between depression and anxiety and cannabis use in middle-aged and older adults. To address this main objective, we developed the following research question; what does the literature show about the association between depression/anxiety and cannabis use among middle-aged and older adults?

Identify relevant studies

The current scoping review identified, selected, and evaluated evidence from peer-reviewed articles that examined the association between depression or anxiety and cannabis use in the middle-aged and older adult population. Following the Joanna Briggs Institute manual for conducting scoping reviews, we first conducted a broad unstructured search to identify key literature and search terms. We also reviewed prior systematic reviews on similar topics and used those to identify additional search terms. In the structured search we focused on papers published in the past 10 years (2013 to 2023) and published in the English language. These parameters were set based on similar scoping reviews which set a 10 year period for currency.[15] Furthermore, in 2006 only 0.4% of older adults had used cannabis and by 2013 older adult use had only grown 3% to 7.1%. However, after 2013 cannabis use among older adults rapidly increased, rising to 9% in 2015 and growing from there.[16] Any key literature identified outside of the past ten years was still made note of to include in the introduction section, to capture a broad view of past literature.

We searched multiple databases including PubMed, PsycINFO, MEDLINE, SDSU library, and UCSD library. The structured search took place between December and January of 2022 and 2023. An example of the search strategy used on the PubMed database is included in

Appendix 1. Based on recommendation by the Joanna Briggs Institute, we used this search strategy for all 5 databases. In addition to this systematic search strategy, the primary researcher identified relevant literature through hand searches of references lists in key articles and updated the search terms when necessary.

Select studies

Inclusion criteria included participants that were in middle or older adults (i.e., 40+), any sex/gender/race/ethnicity and both current and past cannabis users. We also included those who use cannabis both with and without additional substances. Studies that looked at multiple modes of cannabis use were also included. We excluded editorials, letters, commentaries, abstracts, case reports, and narrative reviews. We underwent three different stages of study selection. We began with a title screening, we then moved on to an abstract screening and finally a full text screening. For the title screening we began by asking the question; does this study appear as if it could be POTENTIALLY relevant to our study? Screeners were given the response options of 'yes', 'no', or 'can't tell'. For this level of screening any article with 'can't tell' selected was included in the next level of screening. During abstract screening we asked the following questions and excluded any study that did not meet the following criteria (i) does the abstract indicate this study was published in or after 2013? (ii) does the abstract indicate that the study is published in English? (iii) does the abstract indicate that the analysis was run in adults aged 40 or older OR that there is an age stratified analysis? (iv) does the abstract indicate that cannabis use, in any mode, was studied? (v) does the abstract indicate that anxiety or depression was studied? Screeners were again given the response options of 'yes', 'no', or 'can't tell'. Once again, if 'can't tell' was selected it was included in the next level of screening; assuming it met all other requirements. Any abstracts that elicited different responses from reviews were flagged as a "conflict".

Reviewers then met and discussed all conflicts, with a third reviewer breaking any ties that appeared. Once abstract screenings were completed the reviewers moved on to full text screenings. Reviewers were asked to collect various information during full text screening including title of article, author, year of publication, study design, population studied, size of sample, cannabis measures, anxiety/depression measures, and primary outcomes. A small sample of studies were reviewed using these questions, all three reviewers then met to discuss and give feedback on the form. Once all three reviewers felt comfortable proceeding all further texts were screened.

Chart the data

Figure 1 summarizes the selection process. The initial number of references uploaded to the DistillerSR software after duplicate deletion was 1,626. After title screening, 1,051 of these were excluded due to not potentially fitting into the scope of the study, leaving 575 for abstract screening. During abstract screening 152 articles were excluded due to not being published after 2013, 270 articles were excluded due to not being conducted in a population of adults aged 40 or older or having an age stratified analysis, 4 abstracts were excluded because they did not study cannabis, and 38 articles were excluded because they did not study anxiety or depression. An additional 71 articles were excluded after being flagged as 'conflicted', meaning that reviewers initially disagreed about their inclusion in the scoping review but after discussion they were excluded. After abstract screenings were complete, reviewers were left with 40 articles to review for full text screening. At the completion of all screening levels, 18 articles were selected for inclusion in the scoping review.

Data Extraction

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All three reviewers (MF, KJ, RA) extracted data independently from all 18 journal articles using an excel extraction form designed by the lead author (MF). Conflicts were discussed amongst all three reviewers until consensus was met.

Data Synthesis

A systematic narrative framework was followed. Results were classified upon their findings regarding primary outcomes, cannabis measures, and depression and anxiety measures. To contextualize the findings methodological and reporting practices, descriptive characteristics of the studies were also included.

Results

See figure 1 for the PRISMA flow diagram of articles selected. Following the removal of duplicates 1,626 titles and abstracts were independently reviewed. Ultimately, 40 full-text articles were reviewed for inclusion during the full-text screening, with 18 articles selected for data extraction. See Tables 1.1, 1.2, 1.3 and 1.4 for summaries of study characteristics.

Study Characteristics

Of the 18 articles selected for inclusion in the scoping review, they ranged from years 2014 to 2022. Two articles were published in 2014 (11%), one article was published in 2016 (6%), two articles were published in 2017 (11%), two articles were published in 2018 (11%), three articles were published in 2019 (17%), two articles were published in 2020 (11%), four articles were published in 2021 (22%), and two articles were published in 2022 (11%). Fifteen of the articles were conducted in the United States (83%), two articles (11%) utilized data from Canada, and one study used data from Sweden (6%). Thirteen (72%) studies were cross-sectional, two were cohort (11%), one was a trend study (6%) and two were longitudinal (11%). Cannabis use and/or dependence was assessed via a multitude of questions and many studies

asked a range of different questions when assessing for cannabis use. Six (33%) studies asked about ever use, six (33%) asked about adverse effects of cannabis, five (28%) studies asked about age first used cannabis, five (28%) studies asked about methods of use, four (22%) studies asked what symptoms participants targeted by using cannabis, three (17%) studies asked about THC/CBD combination, and three (17%) studies asked about the benefit or helpfulness of cannabis while addressing symptoms. Various other cannabis use questions were asked throughout the studies including current use, products used, quantity of use, acquisition of cannabis, and past month use. For a full list of the questions asked about cannabis, see Table 2. Of all 18 studies selected for inclusion, only five (28%) of them asked about cannabis use disorder (CUD). Of those five that asked about CUD, only two (11%) used a validated scale to assess use disorder. The two validated scales used were WMH-CDI 3.0 to measure ICD-10 criteria for CUD and the marijuana dependence scale. Fifteen (83%) articles asked about depression and ten (56%) articles asked about anxiety. Ten (56%) of these articles used self-report for depression and anxiety and the remaining eight (44%) articles used validated scales. These validated scales included the PHQ-9, the K-9 psychological distress scale, the 15-item geriatric scale, and the beck depression inventory and the beck anxiety inventory. A majority of studies that used validated scales used DSM diagnosis criteria to determine depression or anxiety.

Sample Characteristics

The sample sizes of the included articles ranged from 38 to 76,018. Study population age was measured in a variety of ways. For studies where older adults were just a subset of the population, age was measured using stratified age breakdowns, as well as birth cohorts. Age ranges for studies that focused wholly on middle-aged to older adults included adults aged 40+

(6%), adults aged 50+ (28%), adults aged 55+ (6%), adults aged 60+ (6%), and adults aged 65+ (22%). Populations ranged from psychiatry patients in Southern Almeda to those living in housing units in South Los Angeles and nine (50%) studies used primary data collection. Six (33%) studies used nationally representative data of US adults. The studies primarily had a mix of gender and races, however one (6%) study focused solely on African Americans and another study focused solely on women in Sweden (6%).

Primary Outcomes

The outcomes of the included studies had a wide variety. The first longitudinal study recruited participants from Kaiser Permanente in the Southern Alameda Center Department of Psychiatry and had a sample size of 307. The objective of the study was to examine marijuana use in a population of psychiatry patients and investigate if it contributes to barriers of recovery. Findings ultimately showed that patients 50+ were at risk for increased marijuana use and that higher depressive symptoms placed patients at risk for continued marijuana use across ages. Furthermore, ongoing marijuana use led to poorer symptoms and mental health functioning. The second longitudinal study used data from the 2007 Australian National Survey of Mental Health and Wellbeing to perform a secondary data analysis investigating the predictors of both initiation of cannabis use and the transition to CUD. Older adults were just a subset of this sample which stratified its analysis based on birth cohorts (1942-51, 1952-61, 1962-71, 1972-81, 1983-91). It had a sample size of 6,935. Ultimately, it was found that the oldest cohort had lower cannabis use than the younger cohort, however they also initiated use at an older age, suggesting that older adults who previously had not tried cannabis are now attempting to use it. Relevant to this scoping review, depression was found to associated with significantly elevated risk of cannabis use and CUD in women but not in men.

Two studies used cohort design. The first used birth cohorts from the Women and Alcohol in Gothenburg dataset in Sweden and had a sample size of 1,100. The objective of this study was to examine changes in cannabis use over time in relation to anxiety and depression. The study found that cannabis use was associated with anxiety in the older cohort but no association between depression and cannabis use was found in this age group. The study speculates that period of cannabis use seems to influence the association between cannabis use and depression, they offer two possible explanations for this finding which are changes in THC concentration and decreased risk perception in the younger cohort. The other cohort study is the only study thus far to look at solely older adults. Participants were collected by a commercial medical cannabis provider in Canada. At intake they were received a prescription for use of medical cannabis. The objective of this study was to assess the characteristics of older medical cannabis users and it had a sample size of 9,766. Findings indicate that among older adults using cannabis, 52.8% reported better mood after use. One trend study examined the most recent national trends in cannabis use to determine whether cannabis use has continued to increase in older adults. Participants for this study were pulled from the National Survey on Drug Use and Health and results are therefore nationally representative. Sample size for this study was 14,896. This study ultimately found that older adults with mental health problems experienced increases in cannabis use.

The remaining studies are cross-sectional and also found a variety of results. Of the cross-sectional studies, five (28%) studies used data from a nationally representative survey of US adults. These nationally representative datasets included the NSDUH and the National Epidemiological Survey on Alcohol and Related Conditions (NESARC-III). It is worth noting that five studies (four cross-sectional and one trend study) used data from the NSDUH. We chose

to move forward with including all these studies as no two studies looked at the same variables. Furthermore, all five studies had different sample sizes. Three of the five studies were conducted in adults aged 50 or older but they still all differed in sample size as one study only looked at participants who used pain medication, one study only looked at participants who had a major depressive episode in the last year, and one study only looked at those who had experienced suicidal thoughts. The remaining two NSDUH studies were both conducted in the population 65 and older however they used data from different years, limiting concern about counting participants multiple times. Based on guidance from Hussein et al. (2022) we examined the difference in sample, sample sizes, and outcome variables during our consideration about including all five articles. Ultimately, as all five NSDUH studies looked at different samples, had different sample sizes, and did not overlap in any outcome variables we chose to include all five studies in our scoping review. Sample sizes for these studies ranged from 6,454 to 76,018. Results were similar across these studies, finding a positive association between cannabis use and depression or anxiety so that as cannabis use increased in middle-aged and older adults, depression and anxiety increased as well. Remaining cross-sectional studies included a secondary analysis of data pulled from the Canadian Tobacco, Alcohol and Drugs Survey, included participants 40 and older and had a sample size of 4,789. Results ultimately found that females who experienced poorer self-rated mental health were more likely to be cannabis users as compared to those who reported very good or excellent mental health. The study goes on to discuss that medical marijuana is more commonly seen in men, however the trend of heightened mental health disorder among women may be cause for increased uptake in medical marijuana in women and as cannabis has been portrayed as a tool to improve mental health, middle-aged to older adults could be over-acknowledging its potential benefits.

Other cross sectional studies included studies that recruited participants from geriatric care clinics in Colorado, primary data collected in Washington State, primary data collected from participants applying for re-certification of medical use in Hawaii, participants recruited from a geriatric clinic at UCSD, participants collected from an economically challenged area of south Los Angeles, participants collected using advertisements in Colorado, and a convenience sample of athletes recruited through social media, emails and flyers. Sample sizes for these studies were much smaller, ranging from 38 to 2,905. Results from these studies varied. Many studies reported that two of the most common symptoms targeted by older medical users is anxiety and depression and that a majority of cannabis users find cannabis helpful in treating these symptoms. One interesting pattern to highlight is that studies seemed to find that older participants tend to report less adverse effects than younger participants, with two different studies finding that younger participants reported adverse effects of anxiety with cannabis use but that older participants did not report these same effects. Older participants also reported withdrawal effects at a lower rate than their younger counterparts. Furthermore, in one study where participants were allowed to write-in responses related to their cannabis use, several patients reported that cannabis had helped them decrease or discontinue medications for pain, anxiety and insomnia. Some quotes included, "I do not need Xanax anymore" and "In the last two years I have been able to drop meds for anxiety, sleep and depression". Three (17%) of the remaining cross-sectional studies found no association between cannabis and depression or anxiety.

Discussion

The current scoping review synthesized the recent literature examining potential associations between anxiety and/or depression and cannabis use in older adults. The studies that

met inclusion criteria were from multiple countries, the studies included cross-sectional and longitudinal data, and ranged in sample sizes from 38 to 76,018. High variability was present in terms of methodological approaches including the assessment of anxiety and/ or depression and cannabis use to collecting and reporting demographic characteristics. Crucially to this review, studies indicated mixed findings regarding the relationship between cannabis use and anxiety/ depression in older adults. Indeed, both longitudinal studies found that individuals with depression or anxiety were more likely to have continued marijuana use, higher use frequency and higher rates of CUD (although these last two relationships were only found in women; not in men). However, findings of the two cohort studies are not in line with this association, with the one cohort studying reporting the older adults had improved mood after cannabis use and the other cohort study finding no association between cannabis and depression, although they did find an association of cannabis use and anxiety in the oldest cohort. Furthermore, a group of cross-sectional studies reported that anxiety and depression were two of the most common symptoms targeted with marijuana use and that a majority of cannabis users found cannabis to be helpful in its treatment of these symptoms. Additionally, a small portion of studies found no association between cannabis and anxiety or depression.

The clinical implications of this research are vast. Research has shown that a majority of older adults use cannabis for medicinal purposes[7] and more clinicians are beginning to prescribe cannabis for a variety of conditions.[14] With the legalization of cannabis occurring in multiple states the rates of cannabis use in older adults and the accessibility of cannabis to older adults will only continue to grow. Clinicians need to be vigilant in screening older adults for cannabis use and mental health disorders and make attempts to understand the different dynamics of cannabis use.

There is a substantial need for additional research in this area. In particular, there is a need to conduct large, longitudinal studies that are able to track the onset of anxiety and depression in relation to cannabis use. In addition, future research should focus on examining different confounding factors that may be impacting the relationship between cannabis use and depression or anxiety such as sex, race, or alcohol use. The use of more consistent methodological approaches when assessing for cannabis use outcomes would increase the generalizability of results.

There are several limitations to the current review. First, it was focused on specifically depression and anxiety and cannabis use which excludes many other domains of psychiatric variables and substance use conditions. The degree of comorbidity for both anxiety, depression and cannabis use may intersect with other phenomena that may not be well reflected in this review. This review also focused on research that was published in English. There is a possibility that some important literature may have been excluded as anxiety, depression, and cannabis are all global experiences. And finally, several studies used limited sampling, heterogeneous definitions, and a range of sample sizes that may reduce generalizability.

Cannabis use is increasing at a rapid rate in older adults.[3] Furthermore, many older adults experience anxiety and depression.[6] The rising acceptance of cannabis among this population is bound to continue to grow and further expand the presence and use of cannabis. In this scoping review of the literature, 18 studies were identified that examined the relationship between anxiety and/or depression and cannabis use. Of these studies, twelve found a positive association between cannabis and anxiety/ depression, five found a negative association between cannabis and anxiety/ depression and three found no association between cannabis and anxiety/ depression. When fully reviewing this literature, these findings present a mixed picture with

unclear outcomes regarding the relationship between cannabis use and anxiety or depression. There is a significant need to conduct more research examining this association in the older adult population.

Acknowledgements

Chapter 1, in full, is currently being prepared for submission for publication of the material. Funk-White, M; Jones, K; Membreno, R. The dissertation author was the primary researcher and author of this material.

Table 1.1: Characteristics of Articles Included in Scoping Review

Article Name	Author/Year	Study Setting/ Dataset Used	Sample Age	N	Objective	Research Design
Patterns of marijuana use among psychiatry patients with depression and its impact on recovery	Bahorik et al., 2017	Kaiser Permanente Southern Alameda Center Department of Psychiatry Patients	Stratified age analysis (30-39, 40-49, 50+)	307	Examine marijuana use in a population of psychiatry patients and investigate if it contributes to barriers of recovery	Longitudinal
Factors associated with the timing and onset of cannabis use and cannabis use disorder: results from the 2007 Australian National Survey of Mental Health and Well-Being	Butterworth et al., 2014	Australian National Survey of Mental Health and Wellbeing	Birth Cohorts (1942-51, 1952-61, 1962-71, 1972-81, 1983-91)	6935	To investigate the predictors of both initiation of cannabis use and transition to cannabis use disorder (CUD)	Longitudinal
Relationship between marijuana and other illicit drug use and depression/suicidal thoughts among late middle-aged and older adults	Choi et al., 2016	National Survey on Drug Use and Health	50+	29,634	Examine the relationship between marijuana and/or other illicit drug use and major depressive episode and serious suicidal thoughts among those aged 50+	Cross-sectional
Is cannabis use associated with prescription psychotropic and pain reliever medication and other substance use among individuals aged 50+ with mental illness?	Choi et al., 2021	National Survey on Drug Use and Health	50+	6,454	Provide insights into cannabis users' use of prescription medications and other substances	Cross-sectional
Cannabis and binge alcohol use among older individuals with major depressive episode	Choi et al., 2022	National Survey on Drug Use and Health	50+	44,007	Examine the associations among depression, cannabis use and problematic alcohol use in late life	Cross-sectional,
Trends in Cannabis Use Among Older Adults in the United States, 2015-2018	Han and Palamar, 2020	National Survey on Drug Use and Health	65+	14,896	Examine the most recent national trends in cannabis use to determine whether cannabis use has continued to increase among older adults	Trend Study
Cannabis use and patterns among middle and older aged Canadians prior to legalization: a sex-specific analysis of the Canadian Tobacco, Alcohol, and Drugs Survey	Keethakumar et al., 2021	Canadian Tobacco, Alcohol and Drugs Survey	40+	4,789	Identify the prevalence, characteristics, and patterns of past-year cannabis use among older Canadians	Cross-sectional
The association between lifetime cannabis use and dysthymia across six birth decades	Livne et al., 2018	National Epidemiological Survey for Alcohol and Related Conditions-III	Birth Decades	36,309	Explore clinical correlations of cannabis use among individuals with dysthymia	Cross-sectional

Table 1.1: Characteristics of Articles Included in Scoping Review continued

Article Name	Author/ Year	Study Setting/ Dataset Used	Sample Age	N	Objective	Research Design
Cannabis use and the risk of anxiety and depression in women: A comparison of three Swedish cohorts	Rabiee et al., 2020	Women and Alcohol in Gothenburg Cohorts	Birth Cohorts	1,100	Examine changes in cannabis use over time in relation to anxiety and depression	Cohort
Trends and correlates of marijuana use among late middle-aged and older adults in the United States, 2002-2014	Salas-Wright et al., 2017	National Survey on Drug Use and Health	50+	76,018	Provide a systematic examination of the trends and correlates of marijuana use among late middle-aged and older adults in the US	Cross-sectional
Characteristics and patterns of marijuana use in community-dwelling older adults	Reynolds et al., 2018	Academic geriatric primary care clinics in Colorado	65+	345	Better understand patterns of marijuana use in community-dwelling older adults in Colorado	Cross-sectional
A Survey of Cannabis Acute Effects and Withdrawal Symptoms: Differential Responses Across User Types and Age	Sexton et al., 2019	Washington State	Stratified age analysis (18-29, 30-49, 50+)	2,905	Describe the acute effects of cannabis, subjective experiences of withdrawal, and beliefs about the addictiveness of cannabis	Cross-sectional
Medical Cannabis Use Among Older Adults in Canada: Self-Reported Data on Types and Amount Used, and Perceived Effects	Tumati et al., 2021	Commercial medical cannabis provided in Canada	65+	9,766	Assess the characteristics of older medical cannabis users	Cohort study
Therapeutic Benefits of Cannabis: A Patient Survey	Webb et al., 2014	Patients applying for re-certification for medical cannabis use in Hawaii	Mean age 50	100	Discover perceived benefits and adverse effects of medical cannabis	Cross sectional
Cannabis: An Emerging Treatment for Common Symptoms in Older Adults	Yang et al., 2021	Geriatrics clinic at UCSD	65+	568	Investigate what reasons cannabis is used in the older adult population	Cross sectional
Marijuana Use among African American Older Adults in Economically Challenged Areas of South Los Angeles	Cobb et al., 2019	Economically challenged area of south LA, sampled primarily from housing units and senior centers	55+	340	Explore demographic, social, behavioral, and health factors associated with current marijuana use	Cross-sectional
Long-term recreational cannabis use is associated with lower executive function and processing speed in a pilot sample of older adults	Stypulkowski et al., 2022	Online advertisements and direct mail flyers were used to recruit, in Colorado	60+	38	Explore cannabis use measures, cognitive performance on a brief computerized battery, and self-reported depression, anxiety, and emotion regulation	Cross-sectional
Age related differences in cannabis use and subjective effects in a large population-based survey of adult athletes	Zeiger et al., 2019	Adult Athletes, convenience sample recruited through social media, email, and flyers posted in specialty sports stores in Boulder and Baltimore	21 to >60	301	Determine whether age related differences exist in patterns of cannabis use and subjective effects to cannabis in adult athletes	Cross-sectional

Table 1.2: Cannabis and Mental Health Measures of Articles Included in Scoping Review

Author/Year	Cannabis Use or Cannabis Use Disorder	Mental Health Symptoms or Mental Health Disorder
Bahorik et al., 2017	Patients were asked how many days they used marijuana during the past 30 days, how often they used marijuana during the past 3 to 6 months, patients endorsing marijuana were asked if use in the past 30 days was always used for medical purposes	Depression was measured 2 weeks prior to each interview using the PHQ-9
Butterworth et al., 2014	Participants were asked about prior cannabis use, age first used cannabis, and the WMH-CIDI 3.0 was used to estimate if participants met ICD-10 criteria for cannabis use disorder	Depression, bipolar disorder, agoraphobia, social phobia, panic disorder, generalized anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder
Choi et al., 2016	Ever use, age of first use, time since last used, frequency of use	DSM-IV diagnosis of past year major depressive episode and DSM-IV diagnosis of lifetime major depressive episode, past year suicidal thoughts,
Choi et al., 2021	Past-month cannabis use, use frequency, medical cannabis measured by asking if all past year use was recommended by a healthcare professional, Past year CUD, cannabis initiation age	K-6 psychological distress scale, thoughts of suicide, major depressive disorder, World Health Organization Disability Assessment Schedule score, past-year mental health treatment
Choi et al., 2022	Past month use, past year use, CUD, medical use categorized by asking if any or all past year use was recommended by a healthcare professional	Major depressive disorder- as classified by the DSM-IV, categorized for this study as no history of MDE, prior to past year MDE, and past year MDE
Han and Palmer, 2020	Asked if participants smoked or ingested marijuana, hashish, pot, grass, and hash oil	Mental health treatment
Keethakumar et al., 2021	Past-year cannabis use; measured by the question "During the past 12 months have you used marijuana?"	Self-reported mental health
Livne et al., 2018	Ever use, frequency of use, Cannabis use disorder diagnosis	DSM-V criteria for persistent depressive disorder
Rabiee et al., 2020	Lifetime cannabis use, measured using composite international diagnostic interview	Lifetime diagnosis of depression or anxiety. Diagnoses were assessed during interviews by trained clinicians using DSM-III or DSM-IV
Salas-Wright et al., 2017	Self-report of past 12-month use of marijuana	Self-report of diagnoses of anxiety/depression by a doctor
Reynolds et al., 2018	Lifetime marijuana use, use of marijuana products since legalization of recreational marijuana, including frequency of use, sour of marijuana acquisition, method of use, symptoms targeted for marijuana use, those using for medical purposes were asked to rate perceived benefit, comment on adverse effects	Self-report anxiety and depression
Sexton et al., 2019	Participants were asked if they used cannabis for recreational or medicinal purposes, method of administration, frequency of use, quantity of cannabis used per week, age first used cannabis, what factors they considered when picking cannabis (i.e., high THC content, high CDB content etc.), acute effects of cannabis, participants were asked to rate yes/no on 13 withdrawal symptoms (from DSM-V)	Self-report anxiety, motivation, mood, feeling calm/ peaceful
Tumati et al., 2021	Self- report of cannabis products used, symptoms, and adverse effects	Self-report of mood and self-report adverse effect of anxiety
Webb et al., 2014	Participants were certified for the medical use of cannabis for a minimum of one year and were re-applying for certification	Asked if there were any adverse effects from using medical cannabis, asked if medical cannabis helps with a condition; what?
Yang et al., 2021	Ever used cannabis or cannabis products, what ages in their life they used cannabis, most recent time cannabis was used, primary cannabinoid used, reasons for use, source of cannabis acquisition, frequency of use, method of use, and others who are aware of patients use	Self-report of negative adverse effects of cannabis, what conditions or symptoms they used cannabis to treat, and the helpfulness of cannabis or each condition
Cobb et al., 2019	Current marijuana use	15-item geriatric depression scale
Stypulkowski et al., 2022	Years of regular cannabis use, Timeline follow back used to report cannabis use and amount used per day for 90 days prior to participation, preferred potency, method of consumption, marijuana dependence scale, marijuana motives measure	Beck depression inventory and Beck anxiety inventory, emotional regulation questionnaire
Zeiger et al., 2019	Used marijuana in the past two weeks, primary use of THC, CBD, or both, positive and adverse effects, routes of administration	Self- reported anxiety

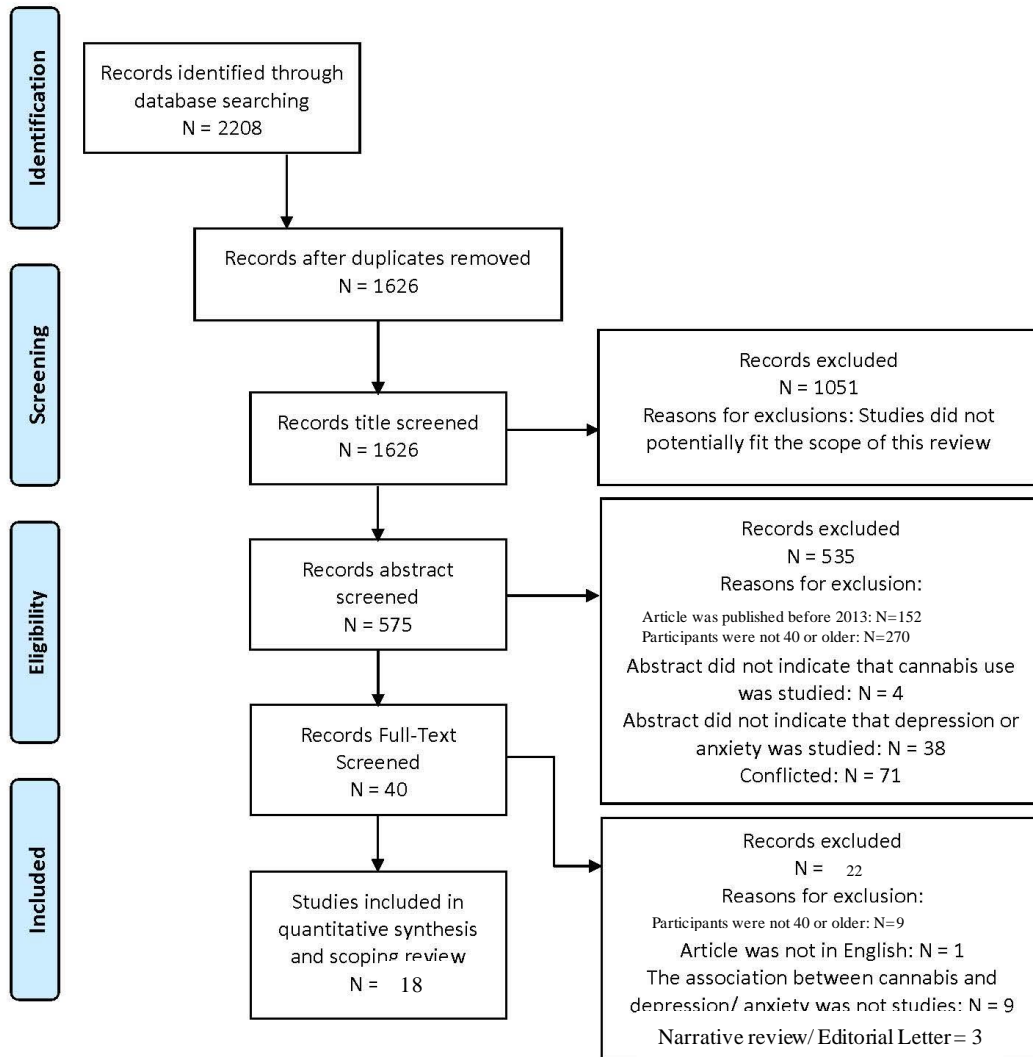Table 1.3: Primary Findings of Included Articles in Scoping Review

Article Author/Year	Primary Findings
Bahorik et al., 2017	Higher depressive symptoms placed patients at risk for continued marijuana use, and patients aged 50+ were at high risk for increased marijuana use
Butterworth et al., 2014	The oldest cohort had lower cannabis use than younger cohort, however they also initiated use at an older age. Social phobia was directly associated with increased risk of cannabis use, depression was associated with significantly elevated risk of cannabis use in women but not men, PTSD was associated with decreased risk of cannabis use in women but an increased risk of cannabis in men, for female users depression was associated with elevated risk of CUD but associated with a lower risk for men, social phobia and panic disorder were both associated with increased risk of transitions from cannabis to CUD
Choi et al., 2016	Past year marijuana and/or other drug use was associated with increased odds of both lifetime and past year major depressive episode. Only marijuana and illicit drug user group had increased odds of suicidal thoughts, marijuana use frequency was not associated with the likelihood of MDE, those who used marijuana and other drugs had higher rates of SUD, MDE and suicidal thoughts, among marijuana users with MDE, higher frequency of marijuana use was linearly associated with increased odds of suicidal ideation. Cannot deduce time-order and previous longitudinal research provides ambiguous findings on the time/order between marijuana and MDE and suicidal ideation, the current study suggests that more frequency marijuana use may contribute to a higher likelihood of MDE and suicidal thoughts, also suggest that older adults with MDE may be using marijuana as a coping mechanism or for symptom relief
Choi et al., 2021	Nearly one in ten individuals with past-year mental illness, compared to one in 25 individuals without mental illness, reported past-month cannabis use.
Choi et al., 2022	Cannabis use rate was highest among those with past year MDE, followed by prior to past year MDE and then those with no MDE history. Past use cannabis use was 1.7-1.8 times higher among those with prior to past year or past year major depressive disorder
Han and Palmer, 2020	Older adults with mental health problems experienced increases in cannabis use
Keethakumar et al., 2021	Females who experienced poorer self-reported mental health were more likely to be cannabis users as compared to those who reported very good or excellent mental health. Previous studies have identified that medical marijuana is more commonly seen in men, the trend of heightened mental health disorders among women may be the cause for increased uptake of medical marijuana in women. As cannabis has been portrayed as a tool to improve mental health, middle-older adults could be over-acknowledging potential benefits
Livne et al., 2018	Significantly higher rates of several psychiatric disorders among individuals with dysthymia who use cannabis compared to those who do not. Findings indicate a significant decline in the strength of the association between cannabis use, but not cannabis use disorders, and dysthymia across six birth decades.
Rabiee et al., 2020	Cannabis use was associated with anxiety in the older cohort. Association between depression and cannabis use was not found in the oldest cohort. Found that period of cannabis use seems to influence the association between cannabis use and depression, two possible explanations are increased THC concentration and decreased risk perception
Salas-Wright et al., 2017	Middle-aged and older adults who use marijuana are more likely to experience anxiety and depression. Late middle-aged marijuana users were significantly more likely to report diagnoses of anxiety and depression
Reynolds et al., 2018	The most common symptom targeted was pain, followed by sleep, anxiety (24%) depression (22%), and appetite stimulation. Only 16% of respondents reported adverse effects, of that 16% only 5 respondents elaborated on adverse effects and of those 5 only 1 described "anxiety" as an adverse effect, respondents reported that marijuana was most helpful when used for anxiety (100%), depression (92%), sleep, pain and appetite stimulation.
Sexton et al., 2019	Older and middle-aged individuals reported fewer undesirable psychological effects including anxiety and loss of motivation. Older individuals were significantly less likely than middle-aged and younger individuals to endorse withdrawal symptoms including anxiety. Older individuals were significantly less likely to report increased anxiety, paranoia, apathy, and decreased motivation. High rates of participants (78-82%) report feeling more calm and peaceful after cannabis use across all age groups
Tumati et al., 2021	Among older adults using cannabis 52.8% reported better mood after use. Among older adults a large proportion reported a significant improvement in mood
Webb et al., 2014	50% of respondents reported relief from anxiety and 7% reported relief from depression. Several patients wrote notes that cannabis helped them to decrease or discontinue medications for pain, anxiety, and insomnia. "I do not need Xanax anymore" "In the last two years I have been able to drop meds for anxiety, sleep, and depression"
Yang et al., 2021	24% of respondents used cannabis to treat anxiety, over three quarters of patients deemed cannabis somewhat or extremely helpful in managing this condition. Only 3 participants reported an adverse effect of anxiety after using cannabis
Cobb et al., 2019	Did not find an association between marijuana use and depression. Authors speculate that this suggests that African American older adults in economically challenged areas of LA do not use marijuana to self-medicate. Could also be due to age as depression and marijuana in African Americans has been primarily explored among adolescents.
Stypulkowski et al., 2022	Across measures of depression and anxiety participants did not differ by cannabis use group
Zeiger et al., 2019	The positive effect items including sleep, calm, decreased anxiety, euphoria, decreased nausea, and increased energy were found to have a significant trend towards younger athletes. The reason for this association in younger athletes but not older may be due to CBD/THC combination or quantity of use

Table 1.4: Study Characteristics of Included Articles in Scoping Review

Year	
2014	2 (11%)
2016	1 (6%)
2017	2 (11%)
2018	2 (11%)
2019	3 (17%)
2020	2 (11%)
2021	4 (22%)
2022	2 (11%)
Sample Ages	
40+	1 (6%)
50+	5 (28%)
55+	1 (6%)
60+	1 (6%)
65+	4 (22%)
Stratified age breakdowns	3 (17%)
Birth cohorts	3 (17%)
Research Design	
Cross-Sectional	13 (72%)
Cohort	2 (11%)
Longitudinal	2 (11%)
Trend Study	1 (6%)
Cannabis Measures	
Recreational or Medical use?	2 (11%)
Years of regular use	1 (6%)
Ever use	6 (33%)
Current use	2 (11%)
Products used	3 (17%)
Age first used	5 (28%)
Time since last used	2 (11%)
THC/CBD	3 (17%)
Frequency of use	6 (33%)
Quantity of use	3 (17%)
Acquisition	2 (11%)
Method of use	5 (28%)
Are others aware of your use?	1 (6%)
Symptoms targeted	4 (22%)
Benefit/ Helpfulness	3 (17%)
Adverse effects	6 (33%)
Withdrawal	1 (6%)
Past month use	3 (17%)
Past year use	3 (17%)
Used in the past 2 weeks	1 (6%)
How often used in the past 3-6 months?	1 (6%)
Was some or all use in the past 30 days recommended by a healthcare professional?	3 (17%)
Lifetime cannabis measured by composite international diagnostic interview	1 (6%)
Cannabis Use Disorder (CUD)	5 (28%)
Did the studies look at cannabis use/ characteristics or CUD?	
Characteristics	13 (72%)
CUD	0 (0%)
Both	5 (28%)
Mental Health	
Depression	15 (83%)
Anxiety	10 (56%)
Self-Report	10 (56%)
Was a validated mental health measure used?	
Yes	8 (44%)
No	10 (56%)

PRISMA Flow Diagram

Identification

Records identified through database searching
N = 2208

Screening

Records after duplicates removed
N = 1626

Records title screened
N = 1626

Records excluded
N = 1051
Reasons for exclusions: Studies did not potentially fit the scope of this review

Eligibility

Records abstract screened
N = 575

Records excluded
N = 535
Reasons for exclusion:

Article was published before 2013: N=152
Participants were not 40 or older: N=270
Abstract did not indicate that cannabis use was studied: N = 4
Abstract did not indicate that depression or anxiety was studied: N = 38
Conflicted: N = 71

Records Full-Text Screened
N = 40

Included

Studies included in quantitative synthesis and scoping review
N = 18

Records excluded
N = 22
Reasons for exclusion:

Participants were not 40 or older: N=9
Article was not in English: N = 1
The association between cannabis and depression/ anxiety was not studies: N = 9
Narrative review/ Editorial Letter = 3

Figure 1.1: PRISMA Flow Diagram of Article Selection.

References

1. What is the scope of cannabis (marijuana) use in the United States? National Institute on Drug Abuse. Published --. Accessed May 28, 2023. https://nida.nih.gov/publications/research-reports/marijuana/what-scope-marijuana-use-in-united-states

2. Wallace GT, Parnes JE, Prince MA, et al. Associations between marijuana use patterns and recreational legislation changes in a large Colorado college student sample. *Addiction Research & Theory*. 2020;28(3):211-221. doi:10.1080/16066359.2019.1622003

3. Han BH, Palamar JJ. Trends in Cannabis Use Among Older Adults in the United States, 2015-2018. *Archives of internal medicine (1960)*. 2020;180(4):609-611. doi:10.1001/jamainternmed.2019.7517

4. Bobitt J, Qualls SH, Schuchman M, et al. Qualitative Analysis of Cannabis Use Among Older Adults in Colorado. *Drugs Aging*. 2019;36(7):655-666. doi:10.1007/s40266-019-00665-w

5. Patterson TL, Jeste DV. The Potential Impact of the Baby-Boom Generation on Substance Abuse Among Elderly Persons. *PS*. 1999;50(9):1184-1188. doi:10.1176/ps.50.9.1184

6. Choi NG, DiNitto DM, Phillips KT. Mental health treatment use among cannabis users aged 50+: Associations with cannabis use characteristics. *Drug and alcohol dependence*. 2021;223:108705-108705. doi:10.1016/j.drugalcdep.2021.108705

7. Yang KH, Kaufmann CN, Nafsu R, et al. Cannabis: An Emerging Treatment for Common Symptoms in Older Adults. *J Am Geriatr Soc*. 2021;69(1):91-97. doi:10.1111/jgs.16833

8. Rabiee R, Lundin A, Agardh E, Hensing G, Allebeck P, Danielsson AK. Cannabis use and the risk of anxiety and depression in women: A comparison of three Swedish cohorts. *Drug and alcohol dependence*. 2020;216:108332. doi:10.1016/j.drugalcdep.2020.108332

9. Bahorik AL, Sterling SA, Campbell CI, Weisner C, Ramo D, Satre DD. Medical and non-medical marijuana use in depression: Longitudinal associations with suicidal ideation, everyday functioning, and psychiatry service utilization. *J Affect Disord*. 2018;241:8-14. doi:10.1016/j.jad.2018.05.065

10. Butterworth P, Slade T, Degenhardt L. Factors associated with the timing and onset of cannabis use and cannabis use disorder: Results from the 2007 Australian National Survey of Mental Health and Well-Being. *Drug and Alcohol Review*. 2014;33(5):555-564. doi:10.1111/dar.12183

11. Tumati S, Lanctôt KL, Wang R, Li A, Davis A, Herrmann N. Medical Cannabis Use Among Older Adults in Canada: Self-Reported Data on Types and Amount Used, and Perceived Effects. *Drugs Aging*. 2022;39(2):153-163. doi:10.1007/s40266-021-00913-y

12. Cobb S, Bazargan M, Smith J, del Pino HE, Dorrah K, Assari S. Marijuana Use among African American Older Adults in Economically Challenged Areas of South Los Angeles. *Brain Sciences*. 2019;9(7):166. doi:10.3390/brainsci9070166

13. Zeiger JS, Silvers WS, Fleegler EM, Zeiger RS. Age related differences in cannabis use and subjective effects in a large population-based survey of adult athletes. *J Cannabis Res*. 2019;1(1):7. doi:10.1186/s42238-019-0006-9

14. Kancherla N, Jeyanthi KM, Abbas R, Sathi TSCR, Upadhyay A, Garlapati SKP. Cannabis Associated Mental Health Effects: A Review. *J Pharm Bioallied Sci*. 2021;13(Suppl 2):S943-S946. doi:10.4103/jpbs.jpbs_388_21

15. O'Brien E, Clyne B, Smith SM, O'Herlihy N, Harkins V, Wallace E. A scoping review protocol of evidence-based guidance and guidelines published by general practitioner professional organisations. *HRB Open Res*. 2022;4:53. doi:10.12688/hrbopenres.13268.3

16. Abuse NI on D. Substance Use in Older Adults DrugFacts. National Institute on Drug Abuse. Published July 9, 2020. Accessed August 30, 2023. https://nida.nih.gov/publications/drugfacts/substance-use-in-older-adults-drugfacts

Chapter 2: THE RELATIONSHIP BETWEEN MENTAL HEALTH AND CANNABIS USE
DISORDER IN MIDDLE-AGED AND OLDER ADULTS

Background

Cannabis is the most widely used federally illegal drug, with approximately 48.2 million people using cannabis in 2019. About 3 in 10 individuals who use cannabis develop a cannabis use disorder (CUD),[1] which is characterized by a problematic pattern of cannabis use leading to impairment or distress.[2] The increase in cannabis use and the development of CUD may be attributed to the legalization and regulation of recreational cannabis, as well as the use of cannabis for medical purposes[3]. Interestingly, one study using data from The National Epidemiologic Survey on Alcohol and Related Conditions-III found that 41.54% of users who used cannabis both recreationally and medically met the diagnostic criteria for CUD, however only 25.25% of purely recreational users met the same criteria.[4] This suggests that individuals who use cannabis both recreationally and medically have a higher likelihood of meeting the diagnostic criteria for CUD compared to purely recreational users. Similar results were found in a study using data from the National Survey on Drug Use and Health in which 10% of individuals who used cannabis recreationally and 11% of those who used cannabis medically met criteria for CUD.[4] This suggests that the context of cannabis use (i.e. using recreationally vs medically) may influence the risk of developing a cannabis use disorder. Cannabis has been employed medicinally throughout history, however its recent legalization has led to an increase in potency and variability of products which could lead to quality control issues and a lack of education surrounding medical cannabis use, particularly among the older adult population.[5]

Middle aged and older adults have shown the greatest increase in use across both the United States and Canada[6]. A population based survey study on cannabis use among older adults conducted in 2018 indicated that 11% of adults aged 50 to 64 and 4% of adults aged 65 or older

engaged in cannabis use[6]. Furthermore, similar trends were found in a study conducted using a National Canadian dataset in which 7% of adults aged 65 and older and 15% of adults aged 45 to 64 reported using cannabis in the past three months[6]. As middle-aged adults continue to mature into older adulthood, we are likely to see an even steeper increase in cannabis use among adults aged 65 and older. It is crucial to study cannabis use and related harms in middle-aged and older adults, as this population is particularly vulnerable to drug-related harms.[6] However, research on the risk factors associated with cannabis use and the motivations for cannabis use in the older adult population is limited. Understanding these factors is essential, as many individuals report using cannabis to cope with psychiatric or medical issues. Previous studies have indicated that motives for cannabis use may differ between older and younger adult populations.[6] Therefore, it is necessary to expand research in the older adult population to examine the relationship between cannabis use and mental health.

Research regarding cannabis and mental health have yielded mixed results in all age groups. A review conducted by Degenhardt et al. in 2003 concluded that studies provided mixed evidence on the association of cannabis and depression and although heavy cannabis use may be associated with depression, this relationship could also potentially be explained by confounding factors[7]. A review conducted by Moore et al. in 2007 reported that the evidence that cannabis use leads to depression is less strong than for psychosis, however it is still concerning[7]. Results from individual studies vary between showing no significance between cannabis use and depression to showing significantly increased risk for developing depression following cannabis use[7]. One study conducted by Grant in 1995 found that people who met the criteria for cannabis use disorder within the past year had 6.4 times the odds of meeting criteria for major depression than those without a CUD[7], and another study conducted in 2021 found similar results that individuals

with CUD were about 2 to 5 times more likely to have comorbid major depression[3]. However, another study conducted by Teesson et al. in 2012 did not find any significant risk of comorbid depression with cannabis use or CUD[3]. Furthermore, another study reported a dose-response effect for cannabis use and anxiety or depression in young adults such that with more frequent cannabis use there was a greater likelihood of developing anxiety or depression. However, anxiety and depression did not predict later frequency of cannabis use suggesting a possible unidirectional association[6]. These mixed results emphasize the importance of adding to the literature surrounding cannabis and mental health, specifically in the older adult population where there is increased risk for unsafe use.

While there is a lack of research surrounding cannabis and mental health in the older adult population, based on the available literature, frequency of cannabis use does appear to be associated with certain mental health outcomes. For example, one study conducted by Choi et al., found that frequency of cannabis use increased the odds of suicidal ideation in adults aged 50 and older, however this association was only present in individuals with previous major depressive episodes[8]. However, another review conducted by Hudson and Hudson in 2021 among older adults found that, based on the available literature, frequency of cannabis use did not appear to be associated with mental health outcomes in this population[6]. Other research has suggested that older adult cannabis users and former cannabis users both have high risk of lifetime mental illness and the number of joints smoked during peak use is associated with the likelihood of experiencing a mental disorder[9]. Indeed, another study conducted by Choi et al., found that past year cannabis users aged 50 or older reported more psychological distress than those who had not used within the past year[9] and another study conducted by Blazer and Wu found significant associations between past-year major depressive episodes and past-year

cannabis use in adults aged 50 and older[6]. A meta-analysis conducted by Onaemo et al., found that cannabis, particularly heavy use or CUD increased the risk of comorbid major depression and generalized anxiety disorder[3]. The author does note that this finding may be due to the bidirectional effect of cannabis on anxiety, whereas CUD could lead to the development of anxiety symptoms but that individuals with anxiety could also experience relief from their symptoms[3].

Understanding the predictors of cannabis related harms is crucial for public health messaging and clinical interventions, especially with the increasing legalization of cannabis. Evidence of the association between cannabis and mental health can guide the clinical management of individuals with comorbid CUD and mental illness, a combination that has been associated with inadequate treatment and poor prognosis[3]. Examining the relationship between cannabis use disorder and mood or anxiety disorders can provide insights into prevention and treatment strategies and help overcome barriers in clinical management.[3] This research is particularly important in the older adult population, which experiences the highest increase in cannabis use and is more susceptible to the negative effects of cannabis.

The present study aims to investigate the relationship between mood or anxiety disorders and the likelihood of being classified as having a cannabis use disorder in middle-aged and older adults. We hypothesize that individuals who have been diagnosed with a mood disorder or anxiety disorder or have lower self-rated mental health will be more likely to have a cannabis use disorder.

Methods

Sample and Participants

The National Epidemiologic Survey on Alcohol and Related Conditions- III (NESARC-III) was designed, directed, and sponsored by the National Institute of Alcohol Abuse and Alcoholism (NIAAA). NESARC-III is based on a nationally representative sample of the civilian, noninstitutionalized population of the United States aged 18 and older and data was collected in the years 2012-13[10]. The final sample size was 36,309 participants; however, given the findings of research studies such as Choi et al., we focus only on participants aged 50 or older in this paper. In this analysis, we explored three age groups; the first age group is participants aged 50 and older (n=14,738), we then split this age group into two separate analyses in order to examine if there may be a difference between middle-aged and older adults, therefore we also ran models on participants aged 50 to 64 (n=8,932) and participants aged 65 and older (n=5,806). Because this study utilizes secondary data, the Institutional Review Board deemed this research as exempt.

Cannabis Use Disorder

Cannabis abuse and dependence were combined in the DSM-V into a single entity capturing the overall behavioral disorder that can occur with chronic cannabis use and was named Cannabis Use Disorder. It is defined by the following criteria.

1. A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
   a. Cannabis is taken in larger amounts or over a longer period of time than was intended.
   b. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.

c. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis or recover from its effects.

d. Craving or a strong desire or urge to use cannabis.

e. Recurrent cannabis use results in failure to fulfill role obligations at work, school, or home.

f. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.

g. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.

h. Recurrent cannabis uses in situations in which it is physically hazardous.

i. Cannabis use continues despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.

j. Tolerance, as defined by either: (1) a need for markedly increased cannabis to achieve intoxication or desired effect or (2) a markedly diminished effect with continued use of the same amount of the substance.

k. Withdrawal, as manifested by either (1) the characteristic withdrawal syndrome for cannabis or (2) cannabis us taken to relieve or avoid withdrawal.

Mood disorders and anxiety disorders

Mood and anxiety disorders were measured using the diagnostic manual put forth by NESARC-III. NESARC data uses the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5) to collect information on mental health disorders. This project utilized the following DSM-5 diagnoses: major depressive disorder, dysthymia, manic

episode, and hypomanic episode. We chose these diagnoses based on guidelines set forth by NESARC for measuring mood disorders.[10] Using the above diagnoses we created a variable with any individual who has been diagnosed with one or more of the above categorized as "having a mood disorder" and received a code of "1." Individuals who did not receive a diagnosis of any of the above were categorized as "not having a mood disorder" and received a code of "0." Next, we examined anxiety disorders using the following diagnoses: panic disorder, agoraphobia, social phobia, specific phobia, and generalized anxiety disorder. A new variable was also created for the measure of "anxiety disorder." If individuals had been diagnosed with one or more of the above disorders, then they were categorized as "having an anxiety disorder" and received a code of "1." If they did not receive a diagnosis of any of the above disorders, then they were categorized as "not having an anxiety disorder" and received a code of "0." We then combined these variables into a single categorical variable with response options including "no mood or anxiety disorder" (coded as "1"), "mood disorder only" (coded as "2"), "anxiety disorder only" (coded as "3"), and "both mood and anxiety disorder" (coded as "4"). This was done to address potential compounding (interaction) effects of exhibiting both mood and anxiety disorders.

Self-rated mental and physical health

The Short Form (SF) 12 scale was also used to measure self-rated mental and physical health. SF-12 is a self-report outcome measure that assesses the impact of health on an individual's everyday life. It is often used as a quality-of-life measure and has been found to be reliable and valid by prior researchers.[11] The SF-12 is a shortened version of the SF-36 and was created to lessen the burden of response. The SF-12 measures the same eight domains as the SF-36: 1) limitations in physical activities because of health problems, 2) limitations in social activities because of physical or emotional problems, 3) limitations in usual role activities

because of physical health problems, 4) bodily pain, and 5) general mental health, and limitations in usual role activities because of 6) emotional problems, 7) vitality, and 8) general health perceptions. These eight domains are used to calculate two composite scores, a physical health score (PSC) and a mental health score (MSC). Scores for both the PCS and MCS range from 0 to 100 with scores above 50 indicating higher functioning and scores under 50 indicating lower functioning. Only the PSC was used in this study.

Covariates

We included the following variables as covariates in our analysis: sex, race/ethnicity, education, marital status, physical health, heavy alcohol use, ever tobacco users, and other drug use. Sex was measured by asking participants if they identified as male or female. Race/ethnicity was measured by asking participants what their race/ethnicity was with 5 different response options: White (non-Hispanic), Black (non-Hispanic), American Indian/Alaska Native (non-Hispanic), Asian/Native Hawaiian/Other Pacific Islanders (non-Hispanic), and Hispanic (Any Race). Education was measured by asking participants how many years of school they have completed, this variable was then recoded into categories 12 years or less, 13-15 years, 16 years, and 17 or more years. Marital status was measured by asking participants what their current marital status was, with response options being married, living with someone as if married, widowed, divorced, separated, and never married. This variable was then recoded into response options married or not married. Physical health was measured using the SF-12 scale described above with a mean score of 45.05 (SD= 12.18). Heavy alcohol use was measured by quantity of use and defined by the NIAAA definition of heavy alcohol use. For men, 4 or more drinks in a day or more than 14 drinks per week; for women, 3 or more drinks in a day or more than 7 drinks per week. This variable was then recoded by categorizing individuals as drinking at a heavy level

(i.e., no/yes) based on NIAAA guidelines and their sex. Tobacco use was measured by asking participants if they have ever smoked tobacco, with response options being yes or no. Multiple other drugs were asked about in NESARC-III. These other drugs include sedatives or tranquilizers, painkillers, cocaine or crack, stimulants, club drugs, hallucinogens, inhalants or solvents, and heroin. All these variables were recoded into a use variable (1=yes; 0=no). This use variable represents if these drugs were used in the past 12 months. These variables were then combined to create a scale ranging from 0 (never used any of these drugs) to 8 (used all these other drugs). This variable was then dichotomized into having used other drugs (1) or not having not used other drugs (0). In participants 50 and older, 2907 participants (19.7%) had used other drugs, with a majority of participants having only used 1 other drug (8.7%) followed by 2 other drugs and 3 other drugs (4.7% and 2.2% respectively). 29 participants aged 50 and older had used all 8 other drugs (0.2%).

Analytic Strategy

To examine if there was an association between a diagnosis of a mood or anxiety disorder and a diagnosis of cannabis use disorder, we ran a series of stepwise logistic regression analyses which provided odds ratios for CUD. Stepwise analyses allowed us to explore the changes in relationships and model fit as we added in blocks of variables. In the first block, we began with a minimally adjusted model only including our control variables, sex and race/ethnicity, and the independent variable of interest, mood, or anxiety disorder. Males served as the reference group for sex, white/non-Hispanic served as the reference group for the race/ethnicity variable, while no mood or anxiety disorder served as a reference for our independent variable. Next, we included a block of variables adjusting for potential confounding factors including education, physical health, heavy alcohol use, tobacco use, and other drug use. For education, less than 12

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years of school was used as the reference group. We considered the confounder-adjusted model to be our primary model of interest. All analyses were conducted using SPSS v.28 and used an alpha of .05.

Results

Participant demographics for the three different age groups are presented in Table 2.1. For participants aged 50 and older, a majority of these participants were female (56.6%), White/non-Hispanic (63.5%), married (45.9%), and were ever tobacco users (51.4%). Approximately 11% of the sample (1559 participants) drank at what would be considered a 'heavy' level. Within participants aged 50 and older, 493 (3.3%) were diagnosed with a lifetime cannabis use disorder 438 (3.0%) were diagnosed with a cannabis use disorder in the past year and 117 (0.8%) were diagnosed with cannabis use disorder in the past month. In participants 50 and older, 11,843 participants were not diagnosed with a mood or anxiety disorder (80.4%), 1059 participants were diagnosed with a mood disorder only (7.2%), 1168 participants were diagnosed with an anxiety disorder only (7.9%), and 668 participants were diagnosed with both a mood and anxiety disorder (4.5%).

Results for our logistic regression are reported in Table 2.2. We began by conducting assumption testing to ensure that our data were a good fit for the analysis. We conducted a Hosmer and Lemeshow goodness of fit test, which resulted in a nonsignificant result, showing our data to be a good fit for the model ($X^2 = 2.943$, $p = .816$). We also conducted a Box-Tidwell test to explore any non-linear relationships on our continuous variable, physical health scale, which yielded non-significant results as well (.138, p=.34). Once we determined this data to be a good fit for our model, we ran a stepwise logistic regression model. The first block of the logistic regressions included the variables of mood/anxiety disorder, sex, and race/ethnicity, and the

second block added education, smoking, marital status, heavy alcohol use, other drug use, and physical health. Both models were found to be a good fit (331.718, $p < .001$ and 618.931, p < .001 respectively). Across the individual coefficients, individuals diagnosed with a mood disorder only were 1.6 times as likely (i.e., a 60% increase) to have a cannabis use disorder when compared to participants with no mood or anxiety disorder ($p = .004$). Participants diagnosed with only an anxiety disorder were 1.8 times as likely (i.e., an 80% increase) to have been diagnosed with a cannabis use disorder than those with no mood or anxiety disorder ($p < .001$). Among participants with both a mood and an anxiety diagnosis, they were approximately 3 times as likely to have been diagnosed with a cannabis use disorder ($p < .001$). Heavy alcohol use ($p = .005$), ever tobacco use ($p < .001$), and other drug use ($p < .001$) were also found to be significant predictors of cannabis use disorder in the model. Individuals who drank at a heavy level were 1.4 times as likely to have a cannabis use disorder and individuals who smoked were 2.3 times as likely to have a cannabis use disorder. Participants who used other drugs were approximately 9 times as likely to be diagnosed with a cannabis use disorder.

Results were similar when participants were split into two different age groups of 50-64 and 65+. Participants in the 50 to 64 age group, who were diagnosed with only a mood disorder were 1.5 times as likely to have a cannabis use disorder and those with only an anxiety disorder were 1.6 times as likely to have a cannabis use disorder (p = .025 and p=.005 respectively). Participants were 2.6 times as likely to have a cannabis use disorder if they had both a mood and anxiety disorder ($p < .001$). Within the 65+ age group significant results were again found for those diagnosed with only an anxiety disorder and those diagnosed with both a mood and anxiety disorder. Those diagnosed with an anxiety disorder were 2.7 times as likely to have a cannabis use disorder in the 65+ age group and 3.9 times more likely to have a cannabis use disorder if

they were diagnosed with both an anxiety and mood disorder ($p = .022$ and $p = .012$, respectively). Further results for each age group are reported in Table 2.

Discussion

In this study, we examined a nationally representative sample of US middle-aged and older adults and identified a significant positive association between lifetime diagnoses of mood and anxiety disorders and the presence of cannabis use disorder.

Our findings regarding the association between mood or anxiety disorders and cannabis use disorder are consistent with some previous studies.[6,7,9] However, our results contrast with studies that reported no such association.[3,8] These discrepancies may be attributed to several factors, including the age of our study population. Previous research in this area has primarily focused on young adults, who may exhibit different patterns of cannabis use and mental health relationships.[6] Furthermore, our study used a nationally representative sample which may account for the differences in results.

The results of this study provide valuable insights into the association between mood and anxiety disorders and cannabis use disorder in middle-aged and older adults. Among participants aged 50 and older, the prevalence of CUD was relatively low, with 3.3% having a lifetime diagnosis, 3.0% with a past-year diagnosis, and 0.8% with a past-month diagnosis. The majority of this age group was female, White/non-Hispanic, married and had a history of tobacco use. Additionally, around 11% of the sample drank at a heavy level, indicating potential co-occurring substance use issues.

The logistic regression analysis revealed several significant predictors of CUD in this age group. Notably, participants diagnosed with mood disorders only and anxiety disorders only were 1.6 and 1.8 times more likely to have CUD, respectively when compared to those with no

mood or anxiety disorder. The likelihood increased even further when compared for participants with both a mood and anxiety disorder, showing a threefold increase in the likelihood of CUD. These findings highlight the strong association between mood and anxiety disorders and CUD in middle-aged and older adults.

Furthermore, heavy alcohol use, tobacco use, and other drug use were also significant predictors of CUD in this population. Heavy alcohol users were 1.4 times more likely to have CUD, while individuals who smoked were 2.3 times more likely. The strongest predictor, perhaps somewhat predictably, was other drug use, with participants who used other drugs being approximately 9 times more likely to be diagnosed with CUD. These results suggest that the presence of co-occurring substance use issues, particularly with alcohol, tobacco, and other drugs, can elevate the risk of CUD in this age group.

The consistency of these findings across the two age groups (50-64 and 65+) adds robustness to the results. Both age groups showed similar patterns, with mood and anxiety disorders being significant predictors of CUD. The specific odds ratios varied slightly between the two age groups but overall demonstrated a similar trend. These results indicate that the association between mood and anxiety disorders and CUD holds true across a broader age range of middle-aged and older adults.

Several factors could potentially explain the observed associations between mood and anxiety disorders and CUD in middle-aged and older adults. Firstly, it is essential to consider the bidirectional relationship between mental health and substance use. Individuals with mood and anxiety disorders may turn to cannabis as a form of self-medication to alleviate symptoms. However, this self-medication could potentially lead to CUD over time, especially as it becomes a coping mechanism for the individual trying to manage their mental health problems. Secondly,

the presence of mood and anxiety disorders may also be leading to a decreased risk perception of cannabis use in the older adult population, leading to higher rates of problematic use. Middle-aged and older adults may be more susceptible to using cannabis as a means of self-soothing, relaxation, or to escape from emotional challenges that may be experienced in older adulthood such as bereavement or isolation. Indeed, middle-aged and older adults may experience multiple unique stressors related to aging, retirement, loss of social support, or management of chronic health conditions. Cannabis use could begin as a way to cope with these stressors but over time it could lead to the development of CUD, particularly in vulnerable populations like those with mood or anxiety disorder.

Overall, these findings have significant implications for healthcare providers, policymakers, and public health initiatives. Healthcare providers should be aware of the elevated risk of CUD in middle-aged and older adults with mood and anxiety disorders, particularly those with co-occurring substance use issues. Screening for CUD in this population can lead to early interventions and appropriate treatment plans. Policymakers and public health initiatives should consider these findings when formulating guidelines and interventions related to cannabis use in middle-aged and older adults, with a specific focus on addressing mental health comorbidities and co-occurring substance use issues. This study addresses a critical knowledge gap in the literature concerning CUD in older adult populations. As cannabis becomes more normalized and accessible, other adults may face unique challenges related to cannabis use that differ from those experienced by younger adults. By shedding light on the associations between mood and anxiety disorders and CUD in middle-aged and older adults, this research can guide public heath initiatives aimed at promoting responsible cannabis use and preventing CUD in this age group.

The strengths of our study lie in the utilization of a nationally representative sample that was used for data analysis. Additionally, we specifically focused on middle-aged and older adults, a population that is generally understudied in relation to this topic. Furthermore, we can also assume a certain homogeneity in the dataset as it was conducted in the years 2012-13, prior to the legalization of cannabis throughout the US. Consequently, the modes of cannabis use during these years were primarily limited to smoking or eating, allowing us to infer that our findings are applicable primarily to these modes of use.

Several limitations should be acknowledged in our study. Primarily, the analysis is based on secondary data, and the variables employed were not originally collected for this specific research question. Despite this limitation, we have found that these variables align well with our research aims, and the utilization of a national dataset offers a novel opportunity to explore our questions within an older adult population of cannabis users. Although the years the data was collected can work as a strength it also could be considered a limitation in that much about the current associations between mental health and cannabis may be different in current years due to changes in legalization and modes of use. Furthermore, our study is cross-sectional and focused on lifetime diagnoses therefore we cannot determine directionality in this relationship.

The existing literature on cannabis use exhibits significant variability, particularly concerning its association with mental health. Furthermore, there has been a paucity of research in this area in the older adult population, despite this population demonstrating the most substantial increase in cannabis use compared to other demographic groups. As older adults increasingly turn to cannabis for medicinal purposes, it is crucial to develop a comprehensive understanding of the association between cannabis use and mental health, specifically within this population. This knowledge will aid in the development of targeted screening for cannabis use

and cannabis use disorder among older adults, as well as facilitate the formulation of guidelines for use. Collection and analysis of prospective data will be vital in helping to disseminate information surrounding cannabis use so that practitioners and individuals can make informed choices and foster the development of evidence-based policies. Future research should place greater emphasis on older adults aged 65 and older, as many studies combine middle-aged and older adults due to sample size, however there are certain risk factors that only impact older adults 65+ that could potentially lead to a different relationship between mental health and cannabis use disorder. Future research should also seek to utilize more current data that encompasses newer modes of use and potential changes in associations resulting from legalization.

In conclusion, this research sheds light on the complex relationship between mood and anxiety disorders and CUD in middle-aged and older adults. It provides crucial evidence to inform clinical practice and public health strategies in managing cannabis use and associated mental health issues in the growing and understudied population. Addressing the associations between mood and anxiety disorders and CUD can help improve the overall well-being and quality of life for middle-aged and older adults facing mental health challenges and substance use issues.

Acknowledgements

Table 2.1: Participant Demographics of Population 50+ separated by age group N(%)

	Age 50+ N=14,738	Age 50-64 N=8,932	Age 65+ N=5,806
Sex			
Male	6392(43.4)	4028 (45.1)	2364 (40.7)
Female	8346 (56.6)	4904 (54.9)	3442 (59.3)
Race/Ethnicity			
White, non-Hispanic	9363 (63.5)	5228 (58.5)	4135 (71.2)
Black, non-Hispanic	2782 (18.9)	1945 (21.8)	837 (14.4)
American Indian/ Alaskan, non-Hispanic	214 (1.5)	162 (1.8)	52 (0.9)
Asian/ Hawaiian/ PI, non-Hispanic	599 (4.1)	368 (4.1)	231 (4.0)
Hispanic, any race	1780 (12.1)	1229 (13.8)	551 (9.5)
Married	6759 (45.9)	4303 (48.2)	2456 (42.3)
Education			
<12	6679 (45.3)	3711 (41.5)	2968 (51.1)
13-15	4304 (29.2)	2830 (31.7)	1474 (25.4)
16	1687 (11.4)	1149 (12.9)	538 (9.3)
>17	2068 (14.0)	1242 (13.9)	826 (14.2)
Physical Health scale, mean (SD)	45.05 (12.18)	46.50 (11.92)	42.83 (12.25)
Heavy Alcohol Use	1559 (10.6)	1274 (14.3)	285 (4.9)
Ever Tobacco User	7570 (51.4)	4595 (51.4)	2975 (51.2)
Other Drug Use	2907 (19.7)	2362 (26.4)	545 (9.4)
Lifetime diagnosis CUD	493 (3.3)	444 (5.0)	49 (0.8)
Past year diagnosis CUD	117 (0.8)	105 (1.2)	12 (0.2)
Mood/Anxiety Disorder			
No mood or anxiety disorder	11843 (80.4)	6915 (77.4)	4928 (84.9)
Mood disorder only	1059 (7.2)	751 (8.4)	308 (5.3)
Anxiety disorder only	1168 (7.9)	739 (8.3)	429 (7.4)
Both mood and anxiety disorder	668 (4.5)	527 (5.9)	141 (2.4)

Table 2.2: Logistic Regression Models of Lifetime Diagnosis of Mood or Anxiety and CUD in population 50+ separated by Age Group

	Age 50+ (N=14,738)			Age 50-64 (N=8,932)			Age 65+ (N=5,806)		
	Exp(B)	SE	p	Exp(B)	SE	p	Exp(B)	SE	p
Mood Only	1.59	0.159	0.004	1.45	0.166	0.025	1.61	0.556	0.394
Anxiety Only	1.78	0.153	<.001	1.59	0.165	0.005	2.74	0.441	0.022
Both Mood and Anxiety	3.02	0.157	<.001	2.64	0.165	<.001	3.86	0.538	0.012
Female (Ref: Male)	0.44	0.105	<.001	0.47	0.111	<.001	0.26	0.357	<.001
Race (Ref: White)									
Black	0.94	0.127	0.643	0.82	0.135	0.133	1.35	0.402	0.450
American Indian	0.01	0.275	0.063	1.35	0.291	0.300	4.23	0.788	0.067
Asian/Hawaiian	0.41	0.462	0.053	0.43	0.465	0.066	0.00	0.236	0.995
Hispanic	0.34	0.239	<.001	0.28	0.258	<.001	0.64	0.642	0.483
Education (Ref: 12 years or less)									
13-15 years	1.08	0.112	0.493	1.07	0.119	0.532	0.67	0.400	0.322
16 years	1.18	0.167	0.315	1.06	0.178	0.718	1.59	0.494	0.346
17 or more years	0.84	0.169	0.264	0.81	0.187	0.272	1.19	0.422	0.682
Heavy Alcohol Use	1.41	0.120	0.005	1.24	0.125	0.080	0.15	0.476	0.421
Ever Smoker	2.32	0.129	<.001	2.37	0.138	<.001	2.39	0.405	0.031
Married (Ref: Single)	1.13	0.103	0.227	1.16	0.110	0.177	1.32	0.316	0.376
Other Drug Use	1.01	0.004	0.286	1.01	0.004	0.720	1.00	0.012	0.732
Physical Health Scale	8.59	0.110	<.001	6.31	0.119	<.001	11.19	0.012	<.001

Note: Adjusted for sex, race, education, heavy alcohol use, ever tobacco use, marital status, other drug use, and physical health.

References

1. Data and Statistics. Published April 22, 2022. Accessed February 19, 2023 https://www.cdc.gov/marijuana/data-statistics.htm

2. Hasin DS, O'Brien CP, Auriacombe M, et al. DSM-5 Criteria for Substance Use Disorders: Recommendations and Rationale. Am J Psychiatry. 2013;170(8):834-851. doi:10.1176/appi.ajp.2013.12060782

3. Onaemo VN, Fawehinmi TO, D'Arcy C. Comorbid Cannabis Use Disorder with Major Depression and Generalized Anxiety Disorder: A Systematic Review with Meta-analysis of Nationally Representative Epidemiological Surveys. J Affect Disord. 2021;281:467-475 doi:10.1016/j.jad.2020.12.043

4. Rubin-Kahana DS, Hassan AN, Sanches M, Le Foll B. Medical Cannabis and Past-Year Cannabis Use Disorder Among Adult Recreational Users in the United States: Results From a Nationally Representative Sample. Frontiers in Psychiatry. 2022;13.

5. MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. Eur J Intern Med. 2018;49:12-19. doi:10.1016/j.ejim.2018.01.004

6. Hudson A, Hudson P. Risk Factors for Cannabis-Related Mental Health Harms in Older Adults: A Review. Clin Gerontol. 2021;44(1):3-15. doi:10.1080/07317115.2020.1808134

7. Lev-Ran S, Roerecke M, Foll BL, George TP, McKenzie K, Rehm J. The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. Psychological Medicine. 2014;44(4):797-810. doi:10.1017/S0033291713001438

8. Choi NG, DiNitto DM, Phillips KT. Mental health treatment use among cannabis users aged 50+: Associations with cannabis use characteristics. Drug and alcohol dependence. 2021;223:108705108705. doi:10.1016/j.drugalcdep.2021.108705

9. Choi NG, DiNitto DM, Marti CN. Older-adult marijuana users and ex-users: Comparisons of sociodemographic characteristics and mental and substance use disorders. Drug and Alcohol Dependence. 2016;165:94-102. doi:10.1016/j.drugalcdep.2016.05.023

10. National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III) | National Institute on Alcohol Abuse and Alcoholism (NIAAA).

11. Shah CH, Brown JD. Reliability and Validity of the Short-Form 12 Item Version 2 (SF-12v2) Health Related Quality of Life Survey and Disutilities Associated with Relevant Conditions in the U.S. Older Adult Population. J Clin Med. 2020;9(3):661. doi:10.3390/jcm9030661

Chapter 3: THE RELATIONSHIP BETWEEN MOOD AND ANXIETY DISORDERS AND CANNABIS USE FREQUENCY IN MIDDLE-AGED AND OLDER ADULTS

Background

In recent years there has been a rapid growth of the cannabis industry, accompanied by changes in public perceptions of cannabis risks, and increasing rates of cannabis use.[1] This evolving landscape necessitates research to gain a better understanding of the effects of cannabis, particularly in older adults who represent a high-risk group.[1] Conducting research in this area is crucial to inform policymakers, healthcare professionals, and individuals, including friends and family of cannabis users, about the potential risks and benefits associated with cannabis use.[2]

The baby boomer generation, born in 1946-1964, have historically exhibited higher rates of substance use, including cannabis use, than previous generations.[3] This suggests that older adults may engage in cannabis use more than ever before. Research suggests that older adults may also have different motivations for use, including using cannabis to address sleep or anxiety.[4] Furthermore, older adults also report having a lower perception of the risk cannabis poses.[4] Given the limited amount of research focusing on cannabis and mental health in older adults, it is important to investigate this relationship and contribute to the existing literature.

Previous research on the relationship between cannabis and mental health has yielded mixed findings. For example, one study by Halladay et al., found that individuals with a mental illness were twice as likely to experience a substance use disorder and almost ten times as likely to engage in weekly cannabis use compared to those without a mental illness.[5] The impact of cannabis on the risk of depression remains unclear, although it has been suggested that tetrahydrocannabinol (THC), the psychoactive ingredient in cannabis, may affect serotonin and other neurotransmitters, leading to depressive symptoms.[6] Similarly, the association between cannabis and anxiety is not well understood however, research has shown that about 20-30

percent of individuals who use cannabis show anxiety reactions after smoking cannabis as an immediate intoxication effect.[6] While other studies have reported on this association, the associations are inconsistent when controlling for covariate adjustments.[6] Other research has yielded similarly mixed results, one study by Harder et al., found that their evidence did not support a causal association between cannabis use and depression. Conversely, another study by deGraaf et al., found a modest association between early cannabis use and onset of depression. It is important to note that many of these studies were conducted in younger populations, such as adolescents and young adults. Furthermore, many of these studies were conducted prior to legalization of cannabis and focused primarily on smoking as the primary form of use.

Furthermore, studies investigating the association between cannabis and mental health have reported inconsistent findings when controlling for certain variables such as sex, childhood experiences, education, alcohol use, tobacco use, and other drug use.[1] Therefore, our study aims to shed light on the relationship between cannabis use frequency and mental health in older adults, while also examining potential moderators of this relationship. We are choosing to look at frequency of use over other cannabis use measures because it will give us a more comprehensive understanding of the dose-response relationship between cannabis use and mental health outcomes in this population. Different frequencies of use may have varying effects on mental health conditions, and healthcare providers need evidence-based guidelines to ensure safe and effective use of cannabis for symptom management. By focusing on this high-risk population that already exhibits higher cannabis use rates than previous generations, our research will contribute to the literature on cannabis use among older adults and enhance our understanding of the patterns and implications of cannabis use in this population.

In summary, there has been significant growth in the cannabis industry, changes in public perceptions, and increasing rates of cannabis use in recent years. Conducting research on the effects of cannabis in older adults is essential. The motivations for cannabis use may differ among older adults compared to younger adults, and the association between cannabis and mental health remains unclear. Our study seeks to contribute to the literature by examining the relationship between a diagnosis of a mood or anxiety disorder and cannabis use frequency in middle-aged and older adults. We also aim to understand if the variables of sex, heavy alcohol use, and tobacco use moderate this relationship. These variables were chosen based on a literature search that suggested these variables may have a moderating impact on the relationship between cannabis use and mental health.[8] We hypothesize that there is an interaction effect between mood or anxiety disorder and gender, heavy alcohol use, other drug use, and tobacco use on cannabis use frequency. Previous research has focused on moderating effects between mental health and cannabis use, however there is a lack of research surrounding moderating effects and cannabis use frequency.[8] This research will offer valuable insights into cannabis use in this high-risk population, enhancing our understanding and informing relevant stakeholders about the potential risks and benefits associated with cannabis use.

Methods

Data set and sample participants

We used data from the National Epidemiologic Survey on Alcohol and Related Conditions - III (NESARC-III). NESARC-III was designed and sponsored by the National Institute of Alcohol Abuse and Alcoholism (NIAAA). NESARC-III is based on a nationally representative sample of the civilian, noninstitutionalized population of the United States aged 18 and older and was collected in the years 2012-13. We included participants aged 50 and older

in this study with a sample size of 14,738. The institutional review board at what institution deemed this research exempt.

Frequency of Cannabis Use

Our dependent variable was frequency of cannabis use in the last 12 months. Participants were first asked if they had used marijuana in the last 12 months, and if they had, they were directed to continue to answer questions related to their use; if they had not, participants skipped to the next section. Past 12-month users were then asked how often they had used marijuana in the last 12 months. The response options included every day, nearly every day, 3 to 4 times a week, 1 to 2 times a week, 2 to 3 times a month, once a month, 7 to 11 times in the last year, 3 to 6 times in the last year, 2 times in the last year, or once in the last year. Participants who had not used marijuana in the last 12 months were coded as a "0," while the responses for marijuana use were coded in ascending categorical order by the frequency of use (e.g., 1 = "once in the last year", 2 = 2 times in the last year, 3= 3 to 6 times in the last year, etc.) Due to the large variety of response options we chose to analyze this variable as continuous instead of collapsing further into categories. The variable was normally distributed to justify its use in the model.

Mood and Anxiety Disorder

The primary independent variables of interest in this study were mood and anxiety disorders. Mood and anxiety disorders were both measured using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5). The following DSM-V diagnoses related to mood disorders were included in this study: major depressive disorder, dysthymia, manic episode, and hypomanic episode. Using these diagnoses, we created a variable for "any mood disorder," in which a participant who was diagnosed with any of the above were categorized as "having a mood disorder" and those who answered "no" to all of the above were

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categorized as "not having a mood disorder." We also examined anxiety disorders using a similar process. The diagnoses that are included in this study for anxiety include: panic disorder, agoraphobia, social phobia, specific phobia, and generalized anxiety disorder. Similar to above, any participants who were diagnosed with any of the above conditions were categorized as "having an anxiety disorder" and those without any of these disorders were categorized as "not having an anxiety disorder." We then combined the two variables of mood and anxiety disorder into a single categorical variable with response options including, no mood or anxiety disorder, mood disorder only, anxiety disorder only, and both mood and anxiety disorder.

Covariates

We included the following covariates in our analysis: sex, race/ethnicity, marital status, education, physical health, heavy alcohol use, tobacco use, and other drug use. Sex was measured by asking participants if they identify as male or female. Race/ethnicity was measured by asking participants what their race/ethnicity was with the following response options: White (non-Hispanic), Black (non-Hispanic), American Indian/Alaska Native (non-Hispanic), Asian/Native Hawaiian/ Other Pacific Islanders (non-Hispanic), and Hispanic (any race). Marital status was measured by asking participants what their current marital status was with response options of "married," "living with someone as if married," "widowed," "divorced," "separated" and "never married." This variable was then recoded dichotomously into "married" or "not married." Education was measured by asking participants how many years of school they have completed; this variable was then recoded into 12 years or less, 13-15 years, 16 years, and 17 or more years.

Physical health was measured using the short form 12 (SF-12). The SF-12 measures eight different domains; limitations in physical activities because of health problems, limitations in

social activities because of physical or emotional problems, limitations in usual role activities because of physical health problems, bodily pain, general mental health, limitations in usual role activities because of emotional problems, vitality, and general health perceptions. Two composite scores are then calculated, a physical health score (PSC) and a mental health score (MSC). Scores range from 0 to 100 with scores above 50 indicating higher functioning. Only the physical health composite score will be used in this study.

Heavy alcohol use was measured by asking participants how much they drank in an average week, guidelines set forth by the NIAAA were then used to separate participants into heavy drinkers or not heavy drinkers. Tobacco use was measured by asking participants if they had ever smoked tobacco with response options of "yes" and "no." Multiple drugs were asked about in NESARC-III, including sedatives or tranquilizers, painkillers, cocaine or crack, stimulants, club drugs, hallucinogens, inhalants or solvents, and heroin. Participants were asked if they have ever used these drugs with each question having "yes" or "no" response options. We then combined these responses into a dichotomous variable in which participants who answered "yes" to any of the above listed drugs were categorized as "having used other drugs."

Interaction Terms

Due to the possible moderating effects of multiple variables on the relationship between frequency of cannabis use and mental health in older adults, we made the decision to use interaction terms to test for potential effects. We created interaction terms for sex, heavy alcohol use, other drug use and tobacco use. These variables were chosen based on literature that suggests they could cause moderating effects.

Analysis

To examine if there was an association between a diagnosis of a mood or anxiety disorder and frequency of cannabis use in the last year, we ran a zero- inflated negative binomial regression in which we added interaction terms in later steps. A couple of systematic qualities of the data led us to use this type of model. First, given that this is a count model and the number of "zeros" in the model was inflated as a large number of participants had not used marijuana in the last 12 months (89.8%), this led us to choose a "zero-inflated" model for this analysis. Second, the data appeared to be over-dispersed, as the variance of the response variable was larger than the mean (mean = .477, variance = 2.897). A zero-inflated model generates two separate models, a logistic regression to account for the presence of excessive zeros, and the negative binomial regression to estimate the over-dispersed counts.

Results

Participant demographics are reported in Table 3.1. A majority of participants were female (56.6%), White/non-Hispanic (63.5%), not currently married (51.4%), had smoked before (51.4), and had less than 12 years of education (45.3%). Approximately 20% of participants had participated in other drug use and approximately 11% drank at a heavy level. A majority of participants had neither a mood or anxiety disorder (80.4%), followed by an anxiety disorder only, mood disorder only, then both mood and anxiety disorder (7.9%, 7.2% and 4.5% respectively).

Results for our zero-inflated negative binomial regression are reported in Table 3.2 and 3.3. The first row of results is from the logistic regression portion of the analysis. Individuals diagnosed with a mood disorder were 1.4 times *as* likely to use cannabis in the last 12 months (*p*=.008). Participants diagnosed with both a mood and anxiety disorder were almost 2 times *more* likely to use cannabis in the last 12 months (*p*<.001). Participants diagnosed with only an

anxiety disorder were not found to be more likely to use cannabis in the last 12 months (p=.131).

Sex (*p*<.001), heavy alcohol use (*p*<.001), tobacco use (*p*<.001), marital status (*p*<.001), and other drug use (*p*<.001) were also found to be significant predictors of having used cannabis use in the last 12 months.

Results were different for the negative binomial portion of the analysis (Table 3.2). Once we removed the zeros from the analysis, we were left with 691 participants who had used cannabis in the past year. Having a mood disorder, having an anxiety disorder, and having both a mood and an anxiety disorder, were not found to be significantly associated with cannabis use frequency in this sample of middle-aged and older adults. Sex was found to be significantly associated with cannabis use frequency in the main effect negative binomial model (p=.028). Furthermore, we created interaction terms for sex, heavy alcohol use, tobacco use, and other drug use (Table 3.3). None of these interaction terms were found to be significant in the model.

Discussion

Among a nationally representative sample of US middle-aged and older adults, our findings reveal a significant association between having a lifetime diagnosis of a mood or anxiety disorder and cannabis use in the past year. This aligns with certain previous studies[5,6], supporting the notion that individuals with mood or anxiety disorders are more likely to engage in cannabis use. However, it should be noted that other studies have reported no association between cannabis use and depression or anxiety, which contradicts our findings.[1,4] One plausible explanation for this discrepancy is the age and composition of our study sample. Previous research exploring the relationship between cannabis use and mental health has predominantly focused on adolescents or young adults, while our study targeted middle-aged and older adults, providing a novel perspective on this relationship.

We utilized a zero-inflated negative binomial regression analysis to provide further insights into the complex relationship between mood and anxiety disorders, cannabis use, and cannabis use frequency in middle-aged and older adults. The unique aspect of this analysis lies in its consideration of both the likelihood of cannabis use in the last 12 months and the frequency of use among those who reported using cannabis. By incorporating these two dimensions, this study offers a more comprehensive understanding of how mood and anxiety disorders related to cannabis use behaviors in this age group.

In the logistic regression portion of the analysis, individuals diagnosed with a mood disorder were found to be 1.4 times more likely to have used cannabis in the past 12 months. Moreover, participants diagnosed with both a mood and anxiety disorder exhibited an even higher likelihood, being almost 2 times more likely to have used cannabis in the past 12 months. However, participants diagnosed with only an anxiety disorder did not show a significant association with cannabis use. These findings suggest that mood disorders, especially when combined with anxiety disorders, may be more closely related to recent cannabis use in middle-aged and older adults.

The negative binomial portion of the analysis revealed no significant association between mood disorder, anxiety disorder and cannabis use frequency. Furthermore, we found no significance when testing the interaction effects of sex, heavy alcohol use, other drug use, and tobacco use. These results could be do the small sample size of those who are aged 50 and older who had used cannabis in the past year (691 participants). However, it could also suggest that the relationship between mood and anxiety disorders and cannabis is driven more by the use of cannabis than by the frequency of which it is used. This is supported by past research done in

younger adults which found that those with a mood or anxiety disorder were at elevated risk for using cannabis later in life, however no relationship was found with frequency of cannabis use.[7]

The findings in this study could be attributed to several underlying factors. Firstly, the observed positive relationships between mood disorders, anxiety disorders, and cannabis use may be partially explained by the self-medication hypothesis. Individuals with mood and anxiety disorders may turn to cannabis as a coping mechanism to alleviate symptoms. The co-occurrence of mood and anxiety disorders could exacerbate the motivation to use cannabis which could potentially contribute to the higher frequency of use among individuals with both diagnoses. Secondly, the bidirectional relationship between mental health and cannabis use needs to be considered. More frequent cannabis use could potentially be impacting areas of the brain and contributing to the development or exacerbation of mood and anxiety disorders. Furthermore, this relationship could be impacted by social and environmental factors. Older adults face unique stressors and challenges related to aging such as loss of loved ones, retirement, and isolation that could be influencing cannabis use behaviors. Additionally, the legalization of cannabis may have altered the perception of cannabis use in this age group, leading to more use.

To contextualize our study within the existing literature, it is important to consider the varied findings regarding the association between cannabis use and mental health. The complexity of this relationship underscores the need for further investigation, particularly within understudied populations such as older adults. As the older adult population experiences a notable increase in cannabis use, it becomes imperative to gain a comprehensive understanding of this association. This knowledge is especially relevant as healthcare providers increasingly consider advising use of cannabis as a potential treatment for symptoms of anxiety and depression. Our study contributes to the existing literature by shedding light on the association

between cannabis use and mental health in middle-aged and older adults, a population that has been relatively understudied in this regard. The long-term implications of our findings underscore the importance of screening for cannabis use in older adult populations and the need for prescribing guidelines.

This study looks at frequency of cannabis use and goes beyond simply identifying the presence of cannabis use disorder and delves into the patterns and intensity of cannabis use among individuals with mood and anxiety disorders. By considering frequency of cannabis use, this study offers a more nuanced understanding of how these mental health conditions may be associated with different levels of cannabis use, shedding light on whether the likelihood to cannabis use and its frequency vary based on specific mental health diagnoses. This highlights the importance of considering specific subgroups such as those with co-occurring mental health disorder.

It is worth noting the limitations of our study. Firstly, this study uses secondary data for analysis which means that the data was not specifically collected to address our research question. However, despite this limitation, we have found the data to be well-suited for our study objectives, The use of secondary data also means we were able to conduct the study in a nationally representative sample which increases the generalizability of the results. Additionally, our data was collected prior to the legalization of cannabis, and as such, the evolving landscape of cannabis legislation may have impacted the relationship between cannabis and mental health in recent years. Nonetheless, this aspect can also be viewed as a strength, as it allows us to assume a certain homogeneity in terms of modes of use.

In conclusion, our study contributes valuable insights to the literature surrounding the relationship between cannabis use and mental health, particularly among middle-aged and older

adults. By addressing the paucity of research in this area, we aim to bridge existing knowledge gaps and foster a comprehensive understanding of cannabis use patterns and their clinical implications. Moving forward, it is crucial for future research to focus on older adults, specifically those aged 65 and older, and employ more current data that takes into consideration the evolving landscape around cannabis legalization. Such endeavors will help to guide informed decisions making, facilitate evidence-based policies, and empower healthcare practitioners and individuals alike.

Table 3.1: Participant Demographics in population 50+ N (%)

	Age 50+ N=14,738	Have Used Cannabis in the past 12 months (N/%)	Cannabis Use Frequency (M/SD)
Sex			
Male	6392(43.4)	444 (6.9)	0.31 (1.33)
Female	8346 (56.6)	251 (3.0)	0.16 (1.07)
Race/Ethnicity			
White, non-Hispanic	9363 (63.5)	420 (4.5)	0.23 (1.22)
Black, non-Hispanic	2782 (18.9)	178 (6.4)	0.28 (1.26)
American Indian/ Alaskan, non-Hispanic	214 (1.5)	28 (13.1)	0.61 (1.85)
Asian/ Hawaiian/ PI, non-Hispanic	599 (4.1)	4 (0.7)	0.04 (0.57)
Hispanic, any race	1780 (12.1)	65 (3.7)	0.15 (0.93)
Married	6759 (45.9)	175 (2.6)	0.13 (0.91)
Education			
<12	6679 (45.3)	328 (4.9)	0.21 (1.13)
13-15	4304 (29.2)	233 (5.4)	0.26 (1.29)
16	1687 (11.4)	68 (4.0)	0.19 (1.11)
>17	2068 (14.0)	66 (3.2)	0.20 (1.24)
Physical Health scale, mean (SD)	45.05 (12.18)	--	--
Heavy Alcohol Use	1559 (10.6)	228 (14.6)	0.67 (1.96)
Ever Smoker	7570 (51.4)	554 (7.3)	0.34 (1.45)
Other Drug Use	2907 (19.7)	475 (16.3)	0.76 (2.07)
Lifetime diagnosis CUD	493 (3.3)	176 (35.7)	1.38 (2.44)
Past year diagnosis CUD	117 (0.8)	117 (100)	3.33 (2.34)
Mood/Anxiety Disorder			
No mood or anxiety disorder	11843 (80.4)	464 (3.9)	0.18 (1.07)
Mood disorder only	1059 (7.2)	81 (7.6)	0.38 (1.57)
Anxiety disorder only	1168 (7.9)	71 (6.1)	0.29 (1.36)
Both mood and anxiety disorder	668 (4.5)	79 (11.8)	0.57 (1.86)

Table 3.2: Zero-Inflated Negative Binomial predicting cannabis use and cannabis use frequency among population 50+

	Logit Portion (*n*=14738)				Negative Binomial Main Effects (*n*=691)			
	Exp(B)	SE	Lower	Upper	Exp(B)	SE	Lower	Upper
Mood Only	1.44**	0.137	1.10	1.88	1.04	0.135	0.80	1.35
Anxiety Only	1.24	0.143	0.94	1.65	0.95	0.144	0.75	1.31
Both Mood and Anxiety	1.98***	0.146	1.49	2.63	0.97	0.140	0.76	1.31
Female (Ref: Male)	0.49***	0.089	0.42	0.59	1.22*	0.090	1.02	1.46
Race (Ref: White)								
Black	1.39***	0.102	1.13	1.69	0.92	0.104	0.75	1.13
American Indian	2.39***	0.234	1.51	3.78	0.94	0.220	0.61	1.44
Asian/Hawaiian	0.28*	0.513	0.10	0.76	1.17	0.547	0.40	3.42
Hispanic	0.90	0.147	0.67	1.19	0.84	0.150	0.62	1.12
Education (Ref: 12 years or less)								
13-15 years	1.00	0.096	0.83	1.21	1.10	0.097	0.91	1.33
16 years	1.16	0.150	0.86	1.21	1.07	0.153	0.79	1.45
17 or more years	0.87	0.151	0.64	1.16	1.32	0.157	0.97	1.80
Heavy Alcohol Use	1.66***	0.095	2.20	3.20	0.97	0.092	0.81	1.16
Ever Smoker	1.91***	0.104	1.56	2.34	0.96	0.109	0.77	1.19
Married (Ref: Single)	1.98***	0.096	1.64	2.39	0.95	0.099	0.78	1.15
Other Drug Use	6.52***	0.090	5.47	7.77	0.93	0.093	0.77	1.11
Physical Health Scale	0.99*	0.003	0.99	1.00	1.00	0.003	0.99	1.01

Note: Lower and upper bounds reported for 95% Confidence interval. Adjusted for sex, race, education, heavy alcohol use, ever tobacco use, marital status, other drug use, and physical health.
*p > .05, **p > .01, ***p > .001

Table 3.3: Zero-Inflated Negative Binomial predicting cannabis use and cannabis use frequency among population 50+ with interaction terms

	Negative Binomial with Interaction (*n*=691)			
	Exp(B)	SE	Lower	Upper
Mood Only	1.21	0.347	0.61	2.38
Anxiety Only	1.09	0.505	0.40	2.92
Both Mood and Anxiety	1.02	0.456	0.42	2.48
Female (Ref: Male)	1.19	0.114	0.95	1.49
Race (Ref: White)				
Black	0.93	0.106	0.76	1.15
American Indian	0.93	0.222	0.60	1.44
Asian/Hawaiian	1.15	0.549	0.39	3.38
Hispanic	0.83	0.152	0.62	1.12
Education (Ref: 12 years or less)				
13-15 years	1.11	0.097	0.91	1.34
16 years	1.07	0.154	0.79	1.45
17 or more years	1.31	0.158	0.96	1.78
Heavy Alcohol Use	0.94	0.113	0.75	1.17
Ever Smoker	0.97	0.132	0.75	1.26
Married (Ref: Single)	0.94	0.099	0.78	1.20
Other Drug Use	0.97	0.110	0.78	1.20
Physical Health Scale	1.00	0.003	0.99	1.01
Mood Only*Female	0.95	0.293	0.53	1.68
Anxiety Only*Female	1.19	0.299	0.66	2.13
Both Mood and Anxiety*Female	1.10	0.281	0.64	1.92
Mood Only*Heavy Alcohol Use	1.26	0.324	0.67	2.38
Anxiety Only*Heavy Alcohol Use	0.94	0.300	0.52	1.69
Both Mood and Anxiety*Heavy Alcohol Use	1.18	0.279	0.68	2.04
Mood Only*Other Drug Use	0.79	0.304	0.44	1.43
Anxiety Only*Other Drug Use	1.02	0.350	0.51	2.03
Both Mood and Anxiety*Other Drug Use	0.83	0.328	0.44	1.58
Mood Only*Ever Smoker	0.97	0.309	0.53	1.77
Anxiety Only*Ever Smoker	0.82	0.396	0.38	1.79
Both Mood and Anxiety*Ever Smoker	1.00	0.379	0.47	2.09

Note: Lower and upper bounds reported for 95% Confidence interval. Adjusted for sex, race, education, heavy alcohol use, ever tobacco use, marital status, other drug use, and physical health.
*p > .05, **p > .01, ***p > .001

References

1. Degenhardt L, Hall and W. The relationship between tobacco use, substance-use disorders and mental health: results from the National Survey of Mental Health and Well-being. *Nicotine & Tobacco Research*. 2001;3(3):225-234. doi:10.1080/14622200110050457

2. Cuttler C, Mischley LK, Sexton M. Sex Differences in Cannabis Use and Effects: A Cross-Sectional Survey of Cannabis Users. *Cannabis and Cannabinoid Research*. 2016;1(1):166-175. doi:10.1089/can.2016.0010

3. Haug NA, Padula CB, Sottile JE, Vandrey R, Heinz AJ, Bonn-Miller MO. Cannabis use patterns and motives: A comparison of younger, middle-aged, and older medical cannabis dispensary patients. *Addictive behaviors*. 2016;72:14-20. doi:10.1016/j.addbeh.2017.03.006

4. Haug NA, Padula CB, Sottile JE, Vandrey R, Heinz AJ, Bonn-Miller MO. Cannabis use patterns and motives: A comparison of younger, middle-aged, and older medical cannabis dispensary patients. *Addictive Behaviors*. 2017;72:14-20. doi:10.1016/j.addbeh.2017.03.006

5. Halladay JE, Boyle MH, Munn C, Jack SM, Georgiades K. Sex Differences in the Association Between Cannabis Use and Suicidal Ideation and Attempts, Depression, and Psychological Distress Among Canadians. *Can J Psychiatry*. 2019;64(5):345-350. doi:10.1177/0706743718804542

6. Danielsson AK, Lundin A, Agardh E, Allebeck P, Forsell Y. Cannabis use, depression and anxiety: A 3-year prospective population-based study. *Journal of Affective Disorders*. 2016;193:103-108. doi:10.1016/j.jad.2015.12.045

7. McGee R, Williams S, Poulton R, Moffitt T. A longitudinal study of cannabis use and mental health from adolescence to early adulthood. *Addiction*. 2000;95(4):491-503. doi:10.1046/j.1360 0443.2000.9544912.x

8. Van der Steur SJ, Batalla A, Bossong MG. Factors Moderating the Association between Cannabis Use and Psychosis Risk: A Systematic Review. *Brain Sci*. 2020;10(2):97. doi:10.3390/brainsci10020097

CONCLUSION

In this dissertation, I investigated the relationship between cannabis use and mental health in older adults through a comprehensive analysis of existing literature, which resulted in a scoping review; as well two analytical papers that utilized a nationally representative data set to examine the association between cannabis use and mental health in middle-aged and older adults. While previous research has examined the association between mental health and cannabis use, the findings have been inconclusive and predominantly focus on younger adults. Research conducted in younger adults regarding the association between cannabis and mental health is still primarily inconclusive but it does have more consistency. Generally, findings seem to support in the younger population the existence of a positive association between cannabis and mental illness such that as cannabis use increases so does mental health disorders. One longitudinal study conducted in younger adults found a casual relationship existed between cannabis and mental health such that in adolescence having a mental health disorder lead to an elevated risk of using cannabis, however in young adulthood this causal relationship switched directions. Suggesting that young adults who use cannabis had an elevated risk of developing a mental health disorder. The lack of longitudinal studies in middle-aged and older adulthood creates a large research gap as the same determinations about causality are not able to be made in this age group. Furthermore, older adults are subject to multiple unique age-related changes such as memory problems, increase in chronic conditions, and increased bereavement that could impact their relationship with mental health and cannabis different than their younger counterparts. By conducting a scoping review, we were able to gather and analyze information that helped identify key concepts in cannabis and mental health research, particularly as they pertain to older adults, while also highlighting gaps in the existing literature. Our analytical papers aimed to

explore the relationship between mood or anxiety disorders and cannabis use, contributing to the growing body of knowledge in this area.

Our scoping review found many interesting patterns regarding the relationship between cannabis and mental health. Although the primary outcomes ultimately yielded mixed findings there are still some key takeaways from this review. The first is the need for more consistent measures across studies when looking at cannabis. The lack of a protocol or guide for measuring cannabis in research creates an issue when it comes to comparing results of studies. Furthermore, an interesting pattern emerged regarding adverse and withdrawal effects of cannabis in which younger participants seem to be reporting adverse effects and withdrawal effects of cannabis at much higher rates than their older counterparts. This was an interesting finding that supports some prior research suggesting that cannabis impacts the brain differently in younger adults than it does in older adults. Furthermore, another pattern that emerged in the scoping review and also in our analytical papers was that of the relationship between cannabis and mental health being strong in females and in males. This was shown both in articles for the scoping review only finding an association between mental health and cannabis in females, and also in the testing of gender as a moderator of this relationship in our analytical paper. These findings emphasize the need to study this relationship in subgroups of the general population such as older adults and females.

The findings of our analytical papers suggested a positive association between cannabis and mood/anxiety disorders in middle-aged and older adults however it is important to emphasize that cannabis cannot be strictly categorized as either inherently beneficial or detrimental, as it encompasses various forms (e.g. smoking, edibles) and concentrations and combinations of THC and CBD. While current literature suggests potential harm associated with

highly potent THC formulations of cannabis, it is possible that lower THC doses and/or or pure CBD may have therapeutic effects. Recognizing the complexity of cannabis will aid in addressing research gaps and informing policy decisions. Our research also highlights the growing paradox in cannabis related research where a multitude of participants report an improvement in anxiety or depression upon use of cannabis, however analytical research has yet to be able to support this finding.

Although there is evidence suggesting a high prevalence of cannabis use among populations experiencing mental health disorders, the existing literature does not provide sufficient evidence to conclusively support therapeutic benefits. Therefore, it is crucial to enhance our understanding of this relationship, including both potential benefits and harms, for the purposes of informing policy and clinical interventions.

This dissertation has several strengths. Firstly, the novel scoping review approach comprehensively gathered and systematically mapped all relevant literature on cannabis use and mental health. Secondly, our research focused on the understudied population of older adults, thereby filling a critical gap in cannabis research. Furthermore, the utilization of a nationally representative dataset allowed for a larger sample size and enhances the generalizability of our findings to a broader population.

However, it is important to consider the limitations associated with the secondary analysis in papers 2 and 3. The data being used was not collected specifically for our research question and thus limited to the variables available in the national dataset. Nonetheless, these variables were found to be well aligned with our research questions. Additionally, the data used in this study is approximately 10 years old and may not fully reflect current associations, considering the changes in cannabis legalization, use patterns and formulations over time.

The existing literature on cannabis use and mental heath is diverse, particularly regarding the association between the two. A lack of cohesive research in this area is further exacerbated when studying the older adult population. Given the increasing use of cannabis among older adults for medicinal purposes, it is imperative to deepen our understanding of the association between cannabis use and mental health, irrespective of whether it is positive or negative.

The implications of this research are substantial, especially considering that some healthcare providers have already begun advising cannabis use to manage certain symptoms. This study contributed to the literature on cannabis and mental health, emphasizing the importance of screening for cannabis use among older adult populations and the need for guidelines, including considerations of frequency of use, modes of use, and CBD/THC ratios.

Future directions should include the development of a protocol for measuring cannabis that can encourage consistency across measures. This will ensure the ability to compare and contrast findings across articles measuring cannabis use. Furthermore, there needs to be a push for large longitudinal studies that can speak more to the causality of the relationship between cannabis and mental health. The additional of longitudinal research will allow clinicians and policymakers to formulate guidelines for suggested medical use of cannabis. These guidelines should focus on unique populations as well such as older adults or those with co-occurring substance use or co-occurring mental health disorders. Finally, future research should focus on the development of early interventions for cannabis use disorder in specific subgroups such as older adults, those with mental health disorders, and women.

Appendix 1: Pubmed Search Strategy

(((((((((((cannabi*)[MeSH][Any Field] OR marijauan)[Any Field] OR Hash) [Any Field] OR CBD) [Any Field] OR THC) [Any Field] AND Depression) [Any Field] OR Anxiety) [Any Field] AND Older adults) [Any Field] OR (adults aged 50 or older)) [Any Field] OR middle-aged adults) [Any Field] OR (adults aged 65 and older) [Any Field]