Short title: Aging, Sex and Cannabis Use

Understanding Cannabis Use Disorder in Midlife and Older Adults: The **Role of Age and Sex**

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Abstract

Background: The primary psychoactive ingredient in cannabis interacts with the endocannabinoid system (eCB), which declines with age, potentially reducing its ability to regulate homeostasis and altering responses to cannabis. Indeed, animal studies suggest age-related differences in response to cannabis that result in mixed effects in older individuals. Importantly, biological sex modifies the eCB system, which complicates interpreting these effects. *Objective*: The goal of this study was to understand how individual variation in human endocannabinoid system function due to age and sex influences cannabis's effects in middle-aged and older adults. Methods: Self-reported measures of cannabis use behaviors, memory, mental and physical health, cannabis use disorder (CUD) symptom severity, and sleep quality were collected from 107 adults (age range= 35-78, 54 females) who use cannabis. Partial correlations examined associations between age and outcomes controlling for years of use. Biological sex was assessed as a moderator. Results: Regression analyses revealed a significant age × sex interaction for CUD symptoms and mental health scores. Specifically, CUD symptom severity decreased, and mental health scores improved with age in females but not in males. Sensitivity analysis suggested that participants who reported medical-only use exhibited a steeper decline in CUD symptom severity with age than recreational-only or hybrid-use participants. Conclusions: This study contributes to the growing body of literature on cannabis use in aging populations and underscores the need to consider age, sex, and reason for use when evaluating cannabis-related outcomes such as CUD risk in the emerging demographic of middle-aged and older adults who use cannabis.

Keywords

Cannabis Use Disorder; Aging; Sex Differences; Cognitive Health; Memory; CUDIT-R; Moderation

1. Introduction

Cannabis use has risen significantly among middle-aged (35 to 64 years old) and older adults (65 years or older), with those >65 years old being the fastest-growing demographic for use (Han & Palamar, 2020a; Mattingly et al., 2024; Salas-Wright et al., 2017). Factors such as decreases in perceived risk of harm, promise of cannabis as a therapeutic substance, and loosening legality of cannabis all contribute to this trend (Carliner et al., 2017; Compton et al., 2016; Han et al., 2021; Hasin, 2018; Hasin et al., 2016; Yang et al., 2021). Despite these trends, research evaluating the effects of cannabis in older populations remains limited. Previous research on cannabis has predominantly focused on younger populations, given their higher rates of use, greater vulnerability to abuse, and pronounced developmental consequences (Lawn et al., 2022; Mattingly et al., 2024; Silins et al., 2014). This discordance between the current state of the literature and evolving cannabis use trends highlights the necessity for research across the entire lifespan.

The main psychoactive compound in cannabis is tetrahydrocannabinol or "THC", which binds to cannabinoid receptors in the brain's endocannabinoid system (eCB) system. The eCB system declines with age through changes in receptor expression, eCB levels, and signaling efficacy (Berrendero et al., 1998; Romero et al., 1998; Wang et al., 2003). These eCB alterations may diminish its ability to regulate homeostasis and respond to cannabinoids. Indeed, emerging evidence demonstrates these distinct age effects of cannabis across the lifespan. For example, despite the surge in cannabis use in those aged >65 years, rates of cannabis use disorder (CUD) have not risen proportionally in this group relative to younger groups (Substance Abuse and Mental Health Services Administration, 2024). While prior work has generally found that CUD symptom severity decreases with age (Livne et al., 2025;

Pravosud et al., 2025), the growing number of new users among older adults (Mattingly et al., 2024; Yang et al., 2021) may alter this historically low prevalence of symptom severity in this population.

Biological sex further modulates cannabis effects. Sex hormones interact with eCB function, potentially producing differential vulnerabilities to CUD (Farquhar et al., 2019; Fattore et al., 2007, 2010; Marusich et al., 2015; Struik et al., 2018). Epidemiological studies show that males use cannabis more frequently and have higher rates of CUD across the lifespan (Gutkind et al., 2023; Stinson et al., 2006), whereas females tend to progress more rapidly from initial use to problematic use, a phenomenon known as the telescoping effect (Hernandez-Avila et al., 2004; Kerridge et al., 2018; Schepis et al., 2011). Sex differences are also found for motivations for use, routes of administration, and quantity consumed (Niklason et al., 2022; Sexton et al., 2016). Age-related declines in sex hormones—such as late-onset hypogonadism in men and peri- to post-menopause in women—may further influence cannabis responses (Hägg & Jylhävä, 2021; Broekmans et al., 2009; Tajar et al., 2012). Notably, 78% of women using medical cannabis in a recent study reported using it for a menopause-related symptom (Dahlgren et al., 2022), suggesting interactions between sex, aging, and cannabis use.

Given these considerations, examining cannabis use and its effects in middle-aged and older adults is critical. The present study investigated how age relates to self-reported physical health, mental health, memory, sleep, and CUD symptom severity, and whether biological sex moderates these relationships. We hypothesized that younger participants would report greater CUD symptom severity and poorer health- and memory-related outcomes than older participants. Furthermore, we

expected sex to moderate the association between age and CUD symptoms, with females exhibiting lower CUD symptom severity scores with age compared to males.

2. Methods

2.1 Participants

One hundred and seven adults (54 females), aged 35 to 78 years, from the general population in Texas, completed an anonymous online survey between 2021 and 2022 examining cannabis use patterns and related health outcomes. Participants voluntarily responded to advertisements posted on social media, flyers in the Dallas-Fort Worth area, or were recruited through research participant databases (ListServ and researchmatch.org). The eligibility criteria included (1) current residence in Texas to control for any potential differences in cannabis legislation across regions, (2) previous cannabis use by indicating at least one lifetime use, and (3) aged 35 years of age or older to detect early aging-related vulnerability that includes eCB declines (Nidadavolu et al., 2022) and perimenopausal changes (Hughes et al., 2018; Lyndaker & Hulton, 2004; Parker et al., 2019). One hundred fifty participants with missing informed consent and/or incomplete assessment were excluded from the study. All participants were entered into a raffle for a \$100 gift card for their participation in the study. Ethics approval was obtained from the University of Texas at Dallas Institutional Review Board.

2.2 Measures

The survey was administered online and included questions regarding demographics and cannabis use behaviors (age of first use, years of cannabis use, etc.). The survey also included the Cannabis Use Disorder Identification Test-Revised (CUDIT-R) to assess the presence and severity of CUD-related symptoms in the last six months (Adamson et al., 2010). The Multifactorial Memory Questionnaire (MMQ) to assess subjective memory across three subdomains of (1) memory satisfaction (MMQ-Sa), (2) perception of memory ability (MMQ-A), and (3) the estimated number of memory strategies that one uses in life (MMQ-St) (Troyer & Rich, 2002). The Veterans RAND 12-item Health Survey (VR-12) was collected to assess self-reported physical health (PH) and mental health (MH) (Selim et al., 2009). Sleep duration was measured on a single item, four-point Likert scale rating to the question, "During the past month, on average, how many hours of actual sleep did you get at night?". Response options included: less than 5 hours" (1), "5-6 hours" (2), "7-8 hours" (3), "9 or more hours" (4). Sleep quality was measured using a single item, four-point Likert scale rating to the question, "During the past month, how would you rate your overall sleep quality?". Response options included: "Very Good" (1), "Fairly Good" (2), "Fairly Bad" (3), and "Very Bad" (4). Finally, the survey included a single item question to assess reason for cannabis use that included the following options: "I use cannabis for medical benefits", "I use for recreational purposes", and "Other".

2.3 Data Analysis

Survey data were collected and managed using REDCap hosted by the University of Texas at Dallas. Multiple procedures were implemented to ensure data quality, including branching logic to prevent inconsistent responses, comprehension

checks during consent, reverse-coded items to identify inattentive responding, and manual review to exclude implausible or contradictory values. The VR-12 physical and mental health subscales were scored using Lewis Kazis' validated R algorithm (Boston University School of Public Health), and all analyses were performed in RStudio (v2024.4.1.1).

The primary analyses examined associations between age, outcome measures (PH, MH, MMQ-Sa, MMQ-A, MMQ-St, sleep quality, sleep duration, and CUDIT-R), and sex. First, partial correlations were performed between age and the outcome measures while controlling for years of cannabis use to remove confounding effect of duration of use. Subsequently, hierarchical multiple regression models were conducted using the PROCESS macro for R (Hayes & Little, 2018) to test the moderating effect of sex on these relationships while controlling for years of cannabis use. Two participants with missing sex data were excluded. All models were bootstrapped with 5,000 samples, and false discovery rate (FDR) correction was applied to control for Type I error.

Additionally, given the existing literature that older adults use cannabis for its therapeutic potential (Bobitt et al., 2019; Choi et al., 2022; Kaufmann et al., 2022; Yang et al., 2021), we performed sensitivity analysis to examine whether reason for cannabis use (medical, recreational, or both) moderates the relationship between age and CUD symptom severity.

3. Results

3.1 Sample characteristics

Data from all 107 survey respondents were included in the analyses. Respondents had a mean (M) age of 48.12 years old (standard deviation (SD) = 13.79) with a distribution that was slightly positively skewed (skewness = 0.65) with moderate kurtosis (kurtosis = 1.81), reflecting slightly more younger participants and more participants on the extremes of the age range (35.78 years old). Fifty-one of the respondents were male. Nearly half of the sample (49.5%) reported 16 or more years of education, 59.3% reported annual household incomes above \$50,000, and 25.2% were retired. In the past 6 months, 0.9% of participants reported never using cannabis, 6.6% reported using monthly or less, 7.5% reported 2-4 times per month, 22.6% reported 2-3 times per week, and 62.3% reported using 4 or more times per week. The average reported age of first cannabis use was 27.41 (SD = 14.80) and the mean duration of cannabis use was 16.26 years (SD = 15.15, range = .1.58 years of use).

3.2 Relationship between age and outcome measures

Partial correlations controlling for years of cannabis use revealed that increasing respondent age was associated with lower CUDIT-R score (r=-0.25). Higher CUDIT-R scores were moderately associated with worse memory scores across all three domains (MMQ-Sa = -0.55, MMQ-A = -0.57, MMQ-St = 0.40) and poorer mental health (r=-0.26) (Table 2). In addition, VR-12 mental health scores were correlated with better memory performance (MMQ-Sa = 0.43, MMQ-A = 0.40, MMQ-St = -0.27), higher sleep quality (r=-0.47), and greater sleep duration (r=0.36).

3.3 Moderating effect of sex

Moderation analyses that examined sex as a moderator of the relationship between age and outcome measures (PH, MH, MMQ-Sa, MMQ-A, MMQ-St, sleep quality, sleep duration, and CUDIT-R score) found that sex significantly moderated the relationship between age and CUDIT-R scores (b = -0.20, 95% confidence interval (CI) [-0.37, -0.04]) indicating that the negative association between age and CUDIT-R was stronger in females (Table 3). Sex also moderated the association between age and the VR-12 mental health subscale (b = 0.59, 95% CI [0.03, 1.14]) such that mental health scores were more positive in older females. Although neither moderation results survived FDR correction. No potential moderation was demonstrated with any of the other outcome measures (see Supplementary Materials).

3.4 Post-hoc Analysis

Because sex moderated the association between age and CUDIT-R total scores, we conducted follow-up analyses to test the idea that there may be sexspecific CUD symptoms that contributed to this effect. Bayesian logistic regression models were estimated for each of the eight CUDIT-R items, including a continuous age term and item × age interactions, to predict sex. Models were estimated in brms with four chains, 2,500 warm-up iterations, and 5,000 post-warm-up iterations.

As shown in Table 4, inability to stop use ("How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?") showed a strong and reliable main effect: females had lower scores than males (Estimate = -0.95, 95% credible interval (CrI) [-1.71, -0.30]). Additionally, hazardous use ("How often do you use cannabis in situations that could be physically hazardous, such as driving, operating machinery, or caring for children?") showed an

interaction with age (Estimate = 0.03, 95% CrI [0.00, 0.08]) such that males decreased with age, though the effect was weak. Importantly, most other items did not reliably predict sex differences, and none of the items clearly explained the age-related moderation observed at the total score level.

3.5 Sensitivity analysis: The role of medicinal vs. recreational use on effects of cannabis in aging

Thirty-three percent of the respondents reported use only for medical reasons, 38.8% for recreational reasons, and 28.2% for both. Participants who reported medical-only use were older (n = 34, M = 53.38, SD = 13.92) and predominantly female (72.7%). Participants who reported recreational-only use were younger (n = 40, M = 44.25, SD = 12.37) and more likely to be male (65.0%). There were no participants included in the study who selected "Other" for cannabis use motivation. Participants reporting both reasons fell between these groups in age (n = 29, m = 47.48, m = 13.45) and were more evenly distributed by sex (53.6% female, 46.4% male). Demographic data stratified by sex are reported in Table 1.

Because sex influenced age-related patterns of CUD symptom severity in the primary analysis and was unequally distributed across use-reason groups, sex was included as a covariate. This sensitivity analysis Bayesian multivariate regression was conducted in the brms R package with the same model specifications as the post-hoc analysis. Across all groups, predicted CUDIT-R scores declined with age. Recreational-only and combined-use participants showed nearly parallel declines of ~3 points across the age span, whereas medical-only participants showed a steeper decline of >6 points. Despite overlapping credible intervals around the interaction estimates, the predicted trajectories (Figure 1) suggest that age-related reductions

in CUD symptom severity may be more pronounced among medical-only participants. Full model estimates are reported in Table 5.

4. Discussion

Despite increasing cannabis use among middle-aged and older adults (Han & Palamar, 2020b; Mattingly et al., 2024), this demographic remains understudied, particularly with respect to how aging and biological sex interact to shape cannabis-related outcomes. This study provides novel evidence that age-related decreases in cannabis use disorder (CUD) symptom severity are more pronounced in females than in males, highlighting sex-specific trajectories of CUD symptoms across midlife and older adulthood. These findings extend epidemiological work showing overall declines in risk across the lifespan (Hasin et al., 2016; Substance Abuse and Mental Health Services Administration, 2024), but refine our understanding by suggesting that sex and reason for use may critically shape those trajectories in this emerging population of individuals using cannabis.

Our partial correlation findings are consistent with the current literature demonstrating an age-related decline in CUD symptom severity, including lower CUD symptom severity in older vs. younger adults (Livne et al., 2025; Pravosud et al., 2025). Our moderation analysis added nuance to the relationship between age and CUD symptom severity by demonstrating that sex served as a moderator such that females showed decreased symptom severity with age while males did not. Our findings highlight the important role of sex in cannabis effects on age-related outcomes.

Several explanations could account for this sex-specific pattern. Sex hormones modulate eCB system function and cannabinoid sensitivity, and agerelated endocrine changes (e.g., peri-/post-menopause) may reduce reinforcement or craving in older women, thereby contributing to lower CUD symptom severity. Preclinical studies support this interpretation, showing that sex hormones influence addiction-related effects of cannabinoids (Farquhar et al., 2019; Fattore et al., 2007, 2010; Marusich et al., 2015; Struik et al., 2018), and recent human studies have drawn associations between female sex hormones and CUD symptomology (Macatee et al., 2024; Prashad et al., 2020). Beyond biological differences, social and contextual factors may also contribute to sex-specific trajectories of cannabis use and CUD risk. For instance, being a parent, more likely in older participants, has been associated with a decreased risk for substance use disorders and this reduction may be even greater for females (Fergusson et al., 2012).

Similarly, while partial correlation analysis revealed no direct effect of age on mental health scores, moderation analysis revealed a significant age × sex interaction. Specifically, females who use cannabis exhibited improved mental health with increasing age, whereas males showed no such pattern. Biological mechanisms may again contribute; animal research suggests that estrogen regulates affective behavior via the endocannabinoid system, and cannabinoid administration can improve affective behaviors in menopausal models (Hill et al., 2007; Saberivand et al., 2010). This potential mechanism aligns with evidence that perimenopausal individuals using cannabis report higher anxiety and depression than those that are postmenopausal, underscoring the importance of considering hormonal status when evaluating the relationship between sex, age, and mental health (Dahlgren et al., 2022).

We found no relationship between age and self-reported cognition, which contradicts previous research suggesting potential adverse self-reported cognitive effects of cannabis in middle age to older adults relative to younger adults (Auer et al., 2016; Benitez et al., 2020; Mulhauser et al., 2023). However, it is important to note that the literature on differential age effects of cannabis on cognition has been mixed. Similar absence of age effects have been reported using self-reported (Dregan & Gulliford, 2012) and objective measures (McKetin et al., 2016; Thayer et al., 2019). A previous study conducted in middle-aged adults who use cannabis found that there was no association between cannabis use and cognition, but that CUD symptom severity was associated with hindered cognitive function (Livne et al., 2024). Within our own dataset CUDIT-R scores were found to correlate with worse memory and mental health scores, indicating that CUD symptom severity might be related to impaired cognition and worsened mental health. The higher rates of CUD symptom severity, rather than cannabis use generally, may therefore account for the lack of differences between younger and older participants in the study. Despite this, it is important to keep in mind that the measures employed in the current investigation may not have been sensitive enough to detect differences.

It is also possible that, given the study sample includes middle-aged and older adults, survivor bias may have influenced comparisons across age. Survivor bias could explain why no relationship was found between age and physical health, as older individuals with worsened health or greater CUD symptom severity may be underrepresented due to reduced lifespan (Manrique-Garcia et al., 2016; Vallée, 2024). Similarly, this bias may contribute to the lack of observed age differences in cognitive outcomes. While this possibility cannot be entirely ruled out, the results of the study indicate that biological sex was a much more relevant factor than age in

explaining the decreased CUD symptom severity across time. Further research is necessary to disentangle what factors may be important to preserving cognitive health in aging individuals who use cannabis.

It is important to note that inconsistencies between our findings and prior research may stem in large part from methodological differences, particularly the use of self-reported versus objectively measured data. Unlike objective measures, self-report data capture not only the outcomes of interest but also individual differences in introspection, self-awareness, internalized experiences, and perceived health or self-efficacy. Indeed, within our sample mental health scores correlated with self-reported CUD symptom severity, memory, and sleep, suggesting that mental health may impact subjective ratings. From this perspective, the strength of self-report lies in its ecological validity given that clinical assessments rely on selfreport and real-world functioning. Self-reported data uniquely reflects subjective experiences such as beliefs, motives, emotions, and behaviors that are often inaccessible through objective means, yet form the foundation of behavioral health. Thus, the lack of age-related effects observed in our outcomes may reflect variability in respondents' capacity for introspection that should be noted or suggest a mismatch between objective indicators and individuals' own perceptions of their health and functioning.

Our post-hoc Bayesian item analysis indicated that self-reported use in potentially hazardous situations showed a weak sex × age interaction, with evidence that hazardous use decreased in males as they aged. However, this isolated effect was outweighed by a more consistent and distributed pattern among females, who showed reductions across multiple CUDIT-R items (e.g., Hours Under the Influence, Inability to Stop, Fail Expectations, Reduction Contemplation; see Table 4).

Consequently, despite the item-level decline in hazardous use among males, females exhibited a more substantial overall decrease in CUD symptom severity with age, which drove the significant age × total CUDIT-R score interaction.

Given the rising initiation of cannabis use among older adults, partly motivated by medical purposes (Yang et al., 2021), we explored whether reason for use (medical, recreational, or both) moderated the association between age and CUD symptom severity. Some previous research has shown that reported medical cannabis use might be associated with decreased vulnerability to CUD symptoms (Lapham et al., 2023) while other research has shown that CUD symptom vulnerability may be higher in those using for medical reasons (Turna et al., 2020). In the present study, individuals using cannabis solely for medical purposes showed a steeper decline in CUD symptom severity with age compared to recreational or combined-use participants. Interpretations should be viewed cautiously due to the cross-sectional design and unequal subgroup distributions. In particular, the smaller number of older males and the higher proportion of females reporting medical-only use may have shaped the observed moderation effects, even though sex was included as a covariate. Nonetheless, these results underscore how context and purpose of use can shape risk for CUD symptoms, potentially interacting with biological sex and age-related changes in endocannabinoid and endocrine function.

5. Limitations and Conclusions

Some limitations should be considered when interpreting these findings. First, reliance on anonymous self-reported data introduces potential inaccuracies, particularly regarding cannabis use patterns (e.g., product type, potency, dosage, and frequency). Understanding these details is critical, as preclinical literature

demonstrates that variation in cannabinoid concentrations can alter the effects of cannabis in older animals (Nidadavolu et al., 2021). This study is also limited by a modest sample size (N = 107) and had a non-normal age distribution with slightly more midlife participants and more participants on the extremes of the age range. Future studies should complement self-reported data with objective measures and ensure good distribution of participants across the lifespan. Despite these limitations, this study provides novel insights regarding cannabis use in an underserved population that warrants further investigation.

Future research should further examine the role of endocrine system function and hormonal modulation (e.g. hormone-based contraception, hormone replacement therapy, age-related hypogonadism, pregnancy) on CUD symptoms. Additionally, aging-related changes across the lifespan are multidimensional and not simply biological. For example, lifespan changes in social (e.g., relationships, culture, economic status) and environmental factors (e.g., physical surroundings, access to resources) also likely contribute to these effects. Finally, future studies should prioritize longitudinal study designs using objective measures (cognitive tests, biomarkers, neuroimaging, etc.) to see changes occurring with time.

These results underscore the importance of accounting for age, sex, and motivation for use in studies of cannabis use in aging populations. This study adds to the limited human research in this area and supports the need for further investigation into how age- and sex-related changes in endocannabinoid function may influence cannabis effects across the lifespan. It also underscores the need for individualized approaches to prevention, intervention, and public health policy surrounding cannabis use across the lifespan.

References

- Adamson, S. J., Kay-Lambkin, F. J., Baker, A. L., Lewin, T. J., Thornton, L., Kelly, B. J., & Sellman, J. D. (2010). An improved brief measure of cannabis misuse: The Cannabis Use Disorders Identification Test-Revised (CUDIT-R). Drug and *Alcohol Dependence, 110*(1-2), 137-143. https://doi.org/10.1016/j.drugalcdep.2010.02.017
- Auer, R., Vittinghoff, E., Yaffe, K., Künzi, A., Kertesz, S. G., Levine, D. A., Albanese, E., Whitmer, R. A., Jacobs, D. R., Sidney, S., Glymour, M. M., & Pletcher, M. J. (2016). Association Between Lifetime Marijuana Use and Cognitive Function in Middle Age: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. JAMA Internal Medicine, 176(3), 352. https://doi.org/10.1001/jamainternmed.2015.7841
- Benitez, A., Lauzon, S., Nietert, P. J., McRae-Clark, A., & Sherman, B. J. (2020). Selfreported cognition and marijuana use in older adults: Results from the national epidemiologic survey on alcohol and related conditions-III. Addictive Behaviors, 108, 106437. https://doi.org/10.1016/j.addbeh.2020.106437
- Berrendero, F., Romero, J., García-Gil, L., Suarez, I., De La Cruz, P., Ramos, J. A., & Fernández-Ruiz, J. J. (1998). Changes in cannabinoid receptor binding and mRNA levels in several brain regions of aged rats. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 1407(3), 205-214. https://doi.org/10.1016/S0925-4439(98)00042-8
- Bobitt, J., Qualls, S. H., Schuchman, M., Wickersham, R., Lum, H. D., Arora, K., Milavetz, G., & Kaskie, B. (2019). Qualitative Analysis of Cannabis Use Among

- Older Adults in Colorado. *Drugs & Aging, 36*(7), 655–666. https://doi.org/10.1007/s40266-019-00665-w
- Carliner, H., Brown, Q. L., Sarvet, A. L., & Hasin, D. S. (2017). Cannabis use, attitudes, and legal status in the U.S.: A review. *Preventive Medicine*, *104*, 13–23. https://doi.org/10.1016/j.ypmed.2017.07.008
- Choi, N. G., DiNitto, D. M., Marti, C. N., & Choi, B. Y. (2022). Associations of
 Healthcare Service Utilization With Cannabis Use Status, Use Reasons, and
 Use Characteristics Among Those Age 50 and Older. *Journal of Applied Gerontology*, *41*(5), 1385–1396. https://doi.org/10.1177/07334648211069997
- Compton, W. M., Han, B., Jones, C. M., Blanco, C., & Hughes, A. (2016). Marijuana use and use disorders in adults in the USA, 2002–14: Analysis of annual cross-sectional surveys. *The Lancet Psychiatry*, *3*(10), 954–964. https://doi.org/10.1016/S2215-0366(16)30208-5
- Dahlgren, M. K., El-Abboud, C., Lambros, A. M., Sagar, K. A., Smith, R. T., & Gruber, S. A. (2022). A survey of medical cannabis use during perimenopause and postmenopause. *Menopause*, *29*(9), 1028–1036. https://doi.org/10.1097/GME.0000000000002018
- Dregan, A., & Gulliford, M. C. (2012). Is Illicit Drug Use Harmful to Cognitive

 Functioning in the Midadult Years? A Cohort-based Investigation. *American*Journal of Epidemiology, 175(3), 218–227. https://doi.org/10.1093/aje/kwr315
- Farquhar, C. E., Breivogel, C. S., Gamage, T. F., Gay, E. A., Thomas, B. F., Craft, R. M., & Wiley, J. L. (2019). Sex, THC, and hormones: Effects on density and sensitivity of CB1 cannabinoid receptors in rats. *Drug and Alcohol Dependence*, *194*, 20–27. https://doi.org/10.1016/j.drugalcdep.2018.09.018

- Fattore, L., Spano, M., Altea, S., Fadda, P., & Fratta, W. (2010). Drug- and cueinduced reinstatement of cannabinoid-seeking behaviour in male and female rats: Influence of ovarian hormones. *British Journal of Pharmacology*, *160*(3), 724–735. https://doi.org/10.1111/j.1476-5381.2010.00734.x
- Fattore, L., Spano, M. S., Altea, S., Angius, F., Fadda, P., & Fratta, W. (2007).

 Cannabinoid self-administration in rats: Sex differences and the influence of ovarian function. *British Journal of Pharmacology*, *152*(5), 795–804.

 https://doi.org/10.1038/sj.bjp.0707465
- Fergusson, D. M., Boden, J. M., & John Horwood, L. (2012). Transition to parenthood and substance use disorders: Findings from a 30-year longitudinal study. *Drug and Alcohol Dependence*, *125*(3), 295–300. https://doi.org/10.1016/j.drugalcdep.2012.03.003
- Han, B. H., Funk-White, M., Ko, R., Al-Rousan, T., & Palamar, J. J. (2021). Decreasing perceived risk associated with regular cannabis use among older adults in the United States from 2015 to 2019. *Journal of the American Geriatrics Society*, 69(9), 2591–2597. https://doi.org/10.1111/jgs.17213
- Han, B. H., & Palamar, J. J. (2020a). Trends in Cannabis Use Among Older Adults in the United States, 2015-2018. *JAMA Internal Medicine*, *180*(4), 609-611. https://doi.org/10.1001/jamainternmed.2019.7517
- Han, B. H., & Palamar, J. J. (2020b). Trends in Cannabis Use Among Older Adults in the United States, 2015-2018. *JAMA Internal Medicine*, *180*(4), 609. https://doi.org/10.1001/jamainternmed.2019.7517
- Hasin, D. S. (2018). US Epidemiology of Cannabis Use and Associated Problems.

 *Neuropsychopharmacology, 43(1), 195–212.

 https://doi.org/10.1038/npp.2017.198

- Hasin, D. S., Kerridge, B. T., Saha, T. D., Huang, B., Pickering, R., Smith, S. M., Jung, J., Zhang, H., & Grant, B. F. (2016). Prevalence and Correlates of DSM-5
 Cannabis Use Disorder, 2012-2013: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions-III. *The American Journal of Psychiatry*, 173(6), 588-599. https://doi.org/10.1176/appi.ajp.2015.15070907
- Hill, M. N., Karacabeyli, E. S., & Gorzalka, B. B. (2007). Estrogen recruits the endocannabinoid system to modulate emotionality.

 *Psychoneuroendocrinology, 32(4), 350–357.

 https://doi.org/10.1016/j.psyneuen.2007.02.003
- Hughes, M. L., Agrigoroaei, S., Jeon, M., Bruzzese, M., & Lachman, M. E. (2018).
 Change in Cognitive Performance From Midlife Into Old Age: Findings from the Midlife in the United States (MIDUS) Study. *Journal of the International Neuropsychological Society*, 24(8), 805–820.
 https://doi.org/10.1017/s1355617718000425
- Karimi, I., Saberivand, A., Becker, L.A., Moghaddam, A., Azizi-Mahmoodjigh, S., Yousefi, M., & Zavareh, S. (2010). The effects of Cannabis sativa L. seed (hempseed) in theovariectomized rat model of menopause. *Methods and Findings in Experimental and Clinical Pharmacology*, *32*(7), 467. https://doi.org/10.1358/mf.2010.32.7.1487085
- Kaufmann, C. N., Kim, A., Miyoshi, M., & Han, B. H. (2022). Patterns of Medical

 Cannabis Use Among Older Adults from a Cannabis Dispensary in New York

 State. *Cannabis and Cannabinoid Research*, 7(2), 224–230.

 https://doi.org/10.1089/can.2020.0064
- Lapham, G. T., Matson, T. E., Bobb, J. F., Luce, C., Oliver, M. M., Hamilton, L. K., & Bradley, K. A. (2023). Prevalence of Cannabis Use Disorder and Reasons for

- Use Among Adults in a US State Where Recreational Cannabis Use Is Legal.

 JAMA Network Open, 6(8), e2328934.

 https://doi.org/10.1001/jamanetworkopen.2023.28934
- Lawn, W., Mokrysz, C., Lees, R., Trinci, K., Petrilli, K., Skumlien, M., Borissova, A., Ofori, S., Bird, C., Jones, G., Bloomfield, M. A., Das, R. K., Wall, M. B., Freeman, T. P., & Curran, H. V. (2022). The CannTeen Study: Cannabis use disorder, depression, anxiety, and psychotic-like symptoms in adolescent and adult cannabis users and age-matched controls. *Journal of Psychopharmacology*, *36*(12), 1350–1361. https://doi.org/10.1177/02698811221108956
- Livne, O., Borodovsky, J., Budney, A. J., Wisell, C. G., Habib, M. I., Struble, C. A., Chen, L., Liu, J., Wall, M., Aharonovich, E., & Hasin, D. S. (n.d.). *Age Differences in Cannabis Consumption Patterns and in Associations Between Delta-9-Tetrahydrocannabinol Intake and Cannabis Use Disorders Among Adults with Daily Use*.
- Livne, O., Potter, K. W., Schuster, R. M., & Gilman, J. M. (2024). Longitudinal Associations Between Cannabis Use and Cognitive Impairment in a Clinical Sample of Middle-Aged Adults Using Cannabis for Medical Symptoms.

 Cannabis and Cannabinoid Research, 9(3), e933–e938.

 https://doi.org/10.1089/can.2022.0310
- Lyndaker, C., & Hulton, L. (2004). The Influence of Age on Symptoms of

 Perimenopause. *Journal of Obstetric, Gynecologic & Neonatal Nursing*, *33*(3),

 340–347. https://doi.org/10.1177/0884217504264872
- Marusich, J. A., Craft, R. M., Lefever, T. W., & Wiley, J. L. (2015). The impact of gonadal hormones on cannabinoid dependence. *Experimental and Clinical Psychopharmacology*, *23*(4), 206–216. https://doi.org/10.1037/pha0000027

- Mattingly, D. T., Richardson, M. K., & Hart, J. L. (2024). Prevalence of and trends in current cannabis use among US youth and adults, 2013–2022. *Drug and Alcohol Dependence Reports*, *12*, 100253. https://doi.org/10.1016/j.dadr.2024.100253
- McKetin, R., Parasu, P., Cherbuin, N., Eramudugolla, R., & Anstey, K. J. (2016). A longitudinal examination of the relationship between cannabis use and cognitive function in mid-life adults. *Drug and Alcohol Dependence*, *169*, 134–140. https://doi.org/10.1016/j.drugalcdep.2016.10.022
- Mulhauser, K., Hampstead, B. M., Coughlin, L. N., & Ilgen, M. A. (2023). The association between cannabis use and subjective memory complaints in older adults in the United States. *Journal of the International Neuropsychological Society*, *29*(9), 870–877. https://doi.org/10.1017/S1355617723000061
- Nidadavolu, P., Bilkei-Gorzo, A., Effah, F., Leidmaa, E., Schürmann, B., Berger, M., Bindila, L., Schmid, M., Lutz, B., Zimmer, A., & Bailey, A. (2022). Dynamic Changes in the Endocannabinoid System during the Aging Process: Focus on the Middle-Age Crisis. *International Journal of Molecular Sciences, 23*(18), 10254. https://doi.org/10.3390/ijms231810254
- Nidadavolu, P., Bilkei-Gorzo, A., Krämer, M., Schürmann, B., Palmisano, M., Beins, E.
 C., Madea, B., & Zimmer, A. (2021). Efficacy of Δ9 -Tetrahydrocannabinol
 (THC) Alone or in Combination With a 1:1 Ratio of Cannabidiol (CBD) in
 Reversing the Spatial Learning Deficits in Old Mice. Frontiers in Aging
 Neuroscience, 13, 718850. https://doi.org/10.3389/fnagi.2021.718850
- Parker, D., Sloane, R., Pieper, C. F., Hall, K. S., Kraus, V. B., Kraus, W. E., Huebner, J. L., Ilkayeva, O. R., Bain, J. R., Newby, L. K., Cohen, H. J., & Morey, M. C. (2019).

 Age-Related Adverse Inflammatory and Metabolic Changes Begin Early in

- Adulthood. *The Journals of Gerontology: Series A, 74*(3), 283–289. https://doi.org/10.1093/gerona/gly121
- Pravosud, V., Lum, E., Vali, M., Cohen, B. E., Hoggatt, K. J., Byers, A. L., Austin, P. C., Walter, L. C., Hasin, D., Zaman, T., & Keyhani, S. (2025). Cannabis Use Among Older Adults. *JAMA Network Open, 8*(5), e2510173. https://doi.org/10.1001/jamanetworkopen.2025.10173
- Romero, J., Berrendero, F., Garcia-Gil, L., De La Cruz, P., Ramos, J. A., & Fernandez-Ruiz, J. J. (1998). Loss of cannabinoid receptor binding and messenger RNA levels and cannabinoid agonist-stimulated [35s]guanylyl-5′-O-(thio)-triphosphate binding in the basal ganglia of aged rats. *Neuroscience*, *84*(4), 1075–1083. https://doi.org/10.1016/S0306-4522(97)00552-6
- Salas-Wright, C. P., Vaughn, M. G., Cummings-Vaughn, L. A., Holzer, K. J., Nelson, E. J., AbiNader, M., & Oh, S. (2017). Trends and correlates of marijuana use among late middle-aged and older adults in the United States, 2002–2014. Drug and Alcohol Dependence, 171, 97–106. https://doi.org/10.1016/j.drugalcdep.2016.11.031
- Selim, A. J., Rogers, W., Fleishman, J. A., Qian, S. X., Fincke, B. G., Rothendler, J. A., & Kazis, L. E. (2009). Updated U.S. population standard for the Veterans RAND 12-item Health Survey (VR-12). *Quality of Life Research*, *18*(1), 43–52. https://doi.org/10.1007/s11136-008-9418-2
- Silins, E., Horwood, L. J., Patton, G. C., Fergusson, D. M., Olsson, C. A., Hutchinson, D. M., Spry, E., Toumbourou, J. W., Degenhardt, L., Swift, W., Coffey, C., Tait, R. J., Letcher, P., Copeland, J., & Mattick, R. P. (2014). Young adult sequelae of adolescent cannabis use: An integrative analysis. *The Lancet Psychiatry*, 1(4), 286–293. https://doi.org/10.1016/S2215-0366(14)70307-4

- Struik, D., Sanna, F., & Fattore, L. (2018). The Modulating Role of Sex and Anabolic-Androgenic Steroid Hormones in Cannabinoid Sensitivity. *Frontiers in Behavioral Neuroscience*, *12*, 249. https://doi.org/10.3389/fnbeh.2018.00249
- Substance Abuse and Mental Health Services Administration. (2024). *Key substance use and mental health indicators in the United States: Results from the 2023 National Survey on Drug Use and Health (HHS Publication No. PEP24-07-021, NSDUH Series H-59).* Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/report/2023-nsduh-annual-national-report
- Thayer, R. E., YorkWilliams, S. L., Hutchison, K. E., & Bryan, A. D. (2019). Preliminary results from a pilot study examining brain structure in older adult cannabis users and nonusers. *Psychiatry Research: Neuroimaging*, *285*, 58–63. https://doi.org/10.1016/j.pscychresns.2019.02.001
- Troyer, A. K., & Rich, J. B. (2002). Psychometric Properties of a New Metamemory

 Questionnaire for Older Adults. *The Journals of Gerontology Series B:**Psychological Sciences and Social Sciences, 57(1), P19–P27.

 https://doi.org/10.1093/geronb/57.1.P19
- Turna, J., Balodis, I., Munn, C., Van Ameringen, M., Busse, J., & MacKillop, J. (2020).

 Overlapping patterns of recreational and medical cannabis use in a large community sample of cannabis users. *Comprehensive Psychiatry*, *102*, 152188. https://doi.org/10.1016/j.comppsych.2020.152188
- Wang, L., Liu, J., Harvey-White, J., Zimmer, A., & Kunos, G. (2003). Endocannabinoid signaling via cannabinoid receptor 1 is involved in ethanol preference and its age-dependent decline in mice. *Proceedings of the National Academy of Sciences*, *100*(3), 1393–1398. https://doi.org/10.1073/pnas.0336351100

Yang, K. H., Kaufmann, C. N., Nafsu, R., Lifset, E. T., Nguyen, K., Sexton, M., Han, B. H., Kim, A., & Moore, A. A. (2021). Cannabis: An Emerging Treatment for Common Symptoms in Older Adults. *Journal of the American Geriatrics Society*, 69(1), 91–97. https://doi.org/10.1111/jgs.16833

Figure Caption

Figure 1.

Note. Predicted CUDIT-R scores are shown across centered age for individuals reporting medical, recreational, or both reasons for cannabis use. Predictions come from a Bayesian linear model including the interaction between age and Use Reason, controlling for sex. Shaded areas represent 95% credible intervals.

Table 1. *Age and cannabis use characteristics among males and females*

Characteristic	Males	(n = 51)	Females (<i>n</i> = 54)		
	\overline{M}	SD	M	SD	
Age (years)	47.84	13.92	48.63	13.97	
Age of Onset	30.16	15.73	24.89	13.71	
YU	14.42	14.79	18.21	15.66	
Frequency of Use	3.40	0.90	3.35	1.01	
CUDIT-R Score*	15.14	6.13	11.09	6.85	

Note: YU = Years of Cannabis Use, CUDIT-R = Cannabis Use Disorder Identification Test- Revised.

^{*}p<.05

Table 2.Descriptive statistics and partial correlations for outcome variables controlling for years of cannabis use

Variable	n	M	SD	1	2	3	4	5	6	7	8	9
1. Age (years)	107	48.12	13.79)								
2. MMQ-Sa	a74	48.54	13.28	-0.17	_							
3. MMQ-A	71	50.56	14.58	-0.14	0.76**	_						
4. MMQ-St	66	33.12	14.00	0.11	-0.57*	*-0.78*						
5. VR12- PH	66	42.28	10.06	-0.03	0.33*	0.29*	-0.24	_				
6. VR12- MH	66	44.03	11.05	0.11	0.43**	0.40**	-0.27	*0.15	_			
7. Total Sleep	66	2.25	0.803	0.03	0.24	0.23	-0.26	*0.43**	* 0.36*	*		
8. Sleep Quality	63	2.27	0.807	-0.04	-0.22	-0.17	0.15	-0.34	*-0.47 *	*-0.66	*	
9. CUDIT-R	106	13.08	6.76	-0.25	*55**	-0.57*	0.40**	6-0.13	-0.26	*-0.16	-0.07	7 —

Note: MMQ-Sa/A/St = Multifactorial Memory Questionnaire-Satisfaction/Ability/ Strategy, VR12-P/MH = Veterans RAND 12-item Health Survey-Physical/Mental Health, CUDIT-R = Cannabis Use Disorder Identification Test- Revised

p < .05. p < .01.

Table 3.Moderation Analysis of Sex in the Relationship Between Age and Outcome

Measures While Controlling for Years of Use

Outcome/Predictor	Estima	SE	95% CI	p	FDR p
	te				
CUDIT-R Total Score					
Intercept	15.69	1.05	[13.59,	0.000^{***}	
			17.77]		
Age ^a	-0.03	0.07	[-0.16,	0.65	0.76
			0.10]		
Sex b	-4.06	1.19	[-6.43,	0.001^{***}	0.004^{**}
			-1.70]		
Years of Use	-0.02	0.04	[-0.10,	0.66	0.76
			0.07]		
Age Sex	-0.20	0.09	[-0.37,	0.03^{*}	0.10
			-0.02]		
VR-12 Mental Health (MH)					
Intercept	42.36	2.67	[37.02,	0.000***	
	42.36 2.67 47.40]		47.40]	0.000	
Age ^a	-0.27	0.24	[-0.76,	0.27	0.47
-0		0.24	0.22]		0.47
Sex ^b	4.86	2.75	[-0.63,	0.08	0.25
	4.00	2.73	10.36]	0.06	0.23
Years of Use	-0.06	0.13	[-0.31,	0.64	0.76
	-0.00	0.13	0.19]	0.04	0.70
Age × Sex	0.59	0.28	[0.03, 1.15]	0.04^{*}	0.13

Note. CUDIT-R Total Score n=99, VR-12 Mental Health n=62. CI = confidence interval; FDR p= False Discovery Rate p-value.

Table 4.Bayesian Logistic Regression: Predicting Sex from CUDIT-R Items with Age as a Moderator

CUDIT-R Items	Estimat	SE	95% CrI	
	e		LL	UL
Intercept	1.17	1.27	-1.25	3.74
Frequency of Use	0.11	0.36	-0.59	0.81
Hours Under the Influence	-0.40	0.28	-0.96	0.15
Inability to Stop	-0.95	0.36	-1.71	-0.30
Fail Expectations	-0.18	0.36	-0.89	0.53
Time Spent	0.44	0.27	-0.07	0.98
Memory/Concentration	0.51	0.32	-0.10	1.16
Hazardous Use	-0.39	0.25	-0.86	0.11
Reduction Contemplation	-0.21	0.19	-0.59	0.15
Age	0.02	0.07	-0.12	0.15
Frequency of Use \times Age	0.00	0.02	-0.04	0.04
Hours Under the Influence $ imes$				
Age	-0.01	0.02	-0.06	0.03
Inability to Stop \times Age	-0.03	0.03	-0.09	0.02
Fail Expectations × Age	-0.01	0.03	-0.07	0.05

 $^{^{\}rm a}$ Centered around grand mean. $^{\rm b}$ 0 = Male, 1 = Female.

^{*}p < .05, **p < .01, ***p < .001

Time Spent \times Age	-0.03	0.02	-0.08	0.02
Memory/Concentration \times Age	0.02	0.03	-0.03	0.08
Hazardous Use × Age	0.03	0.02	0.00	80.0
Reduction Contemplation \times				
Age	-0.01	0.01	-0.03	0.02

Note. n = 104. Estimates are on the log-odds scale. Sex is coded as 0 = 0 male and 1 = 0 female. CrI = credible interval; LL = 0 lower limit; UL = 0 upper limit.

Table 5.Moderation Analysis of Reason for Use in the Relationship Between Age and CUDIT-R Score While Controlling for Sex

Predictor	Estimat	SE	959	% CI
	е		LL	UL
Intercept (Medical Only Use)	14.50	1.53	11.52	17.47
Age ^a	-0.16	0.08	-0.32	-0.01
Recreational Only Use ^b	1.31	1.66	-1.99	4.54
Medical & Recreational Use ^b	0.62	1.72	-2.76	3.98
Recreational Only \times Age	0.09	0.11	-0.13	0.31
Medical & Recreational Use \times Age	0.08	0.12	-0.15	0.31
Sex: Female	-3.93	1.32	-6.52	-1.35

Note. CUDIT-R Total Score n = 99. CI = credible interval; LL = lower limit; UL = upper limit.

^a Centered around grand mean. ^b Medical only use used as reference category

 c 0 = Male, 1 = Female.