Research Article



The association between cannabis use and subjective memory complaints in older adults in the United States

Kyler Mulhauser¹ (), Benjamin M. Hampstead^{1,2}, Lara N. Coughlin³ and Mark A. Ilgen^{2,3}

¹Department of Psychiatry, University of Michigan, 2101 Commonwealth Blvd, Ann Arbor, MI, 48105, USA, ²Department of Veterans Affairs, Center for Clinical Management Research (CCMR), Veterans Affairs Ann Arbor Healthcare System, 2800 Plymouth Rd., Bldg. 16, Ann Arbor, MI, 48109-2800, USA and ³Department of Psychiatry and Addiction Center, University of Michigan, 2800 Plymouth Rd., Bldg. 16, Ann Arbor, MI, 48109-2800, USA

Abstract

Objective: The U.S. population is aging and increasing numbers of older adults are using cannabis. Cognitive decline is common in older age and subjective memory complaints (SMC) have been associated with increased risk for dementia. While residual cognitive effects of cannabis use at younger ages are well understood, the links between cannabis use and cognition in older adults is less clear. The present study represents the first population-level analysis of cannabis use and SMC in older adults in the U.S. **Method:** We used the National Survey of Drug Use and Health (NSDUH) dataset to evaluate SMC in respondents over age 50 (N = 26,399) according to past-year cannabis use. **Results:** Results revealed that 13.2% (95%CI: 11.5%–15.0%) of those who reported cannabis use also reported SMC, compared to 6.4% (95%CI: 6.1%-6.8%) among individuals with no cannabis use. Logistic regression revealed a two-fold increase (OR = 2.21, 95%CI: 1.88-2.60) of reporting SMC in respondents who had used cannabis in the past year, which was attenuated (OR = 1.38, 95%CI: 1.10-1.72) when controlling for additional factors. Other covariates, including physical health conditions, misuse of other substances, and mental illness also significantly contributed to SMC outcomes. **Conclusions:** Cannabis use represents a modifiable lifestyle factor that has potential for both risk and protective properties that may impact the trajectory of cognitive decline in older age. These hypothesis generating results are important for characterizing and contextualizing population-level trends related to cannabis use and SMC in older age.

Keywords: cognition; marijuana; representative survey; aging; dementia; substance use

(Received 6 April 2022; final revision 6 December 2022; accepted 28 December 2022; First Published online 20 February 2023)

Introduction

The US population is aging, with over 35.4% of adults now over 50 compared to 27.3% just two decades ago (US Census Bureau, 2001, 2019). Cannabis use among older adults in the US is also increasing. Between 2016 and 2018, cannabis use in adults aged 55 and older increased by 40%, with twice as many men reporting use compared to women; for adults aged 65-69, past-year use increased from 4.3% to 8.2% in men and from 2.1% to 3.8% in women (Maxwell et al., 2021). This increasing use of cannabis is likely due to multiple factors, including expanded legalization of cannabis for medical use, legalization of cannabis for recreational use, and/or decriminalization of cannabis in multiple states (Kaskie et al., 2017). Among older adults currently using cannabis, about half initiated use after the age of 30, most reported infrequent use (less than once every 10 days) over the past year (Blazer & Wu, 2009), and 90% denied current emotional or functional problems (Black & Joseph, 2014), despite roughly 20% reporting a history of treatment-seeking for a non-cannabis substance use disorder (SUD) (Kaskie et al., 2017; Wu & Blazer, 2011).

Cognitive decline is well-established with normal aging, and subjective memory complaints (SMC) among older adults are associated with a two-fold increase in dementia risk (Mitchell et al., 2014).

However, the potential mechanisms of this association are not well understood and may reflect an array of factors, including increased health anxiety, mood symptoms, white matter lesions, temporal atrophy, cerebral hypometabolism, and neurodegenerative biomarkers (for a review of findings, see Mitchell et al., 2014). Although some older adults maintain strong memory abilities into very old age, almost half of those over age 85 will experience dementia, and 1 in 3 older adults will die with dementia. Age, family history, and genetic factors (e.g., apolipoprotein E ϵ 4 allele) represent the greatest predictors of dementia, each of which is nonmodifiable (Baumgart et al., 2015). However, several health and lifestyle factors (e.g., cardiovascular health, obesity, smoking status, physical activity, diet, alcohol use, social and cognitive engagement, education, sleep, and mental health) have also been linked to cognitive decline and overall risk for dementia and are potentially modifiable (Baumgart et al., 2015). Cannabis use is one such modifiable lifestyle factor; however, the links between cannabis use and cognitive functioning in older adulthood are not well understood.

Cannabis use has well characterized acute effects on cognition, including impairments to attention, executive functioning, learning, and memory (Campeny et al., 2020; Crane et al., 2013;

Copyright © INS. Published by Cambridge University Press, 2023. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (https:// creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

Corresponding author: Kyler Mulhauser, email: mulhause@med.umich.edu

Cite this article: 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**: 870–877, https://doi.org/10.1017/S1355617723000061

Crean et al., 2011; Ranganathan & D'Souza, 2006; Volkow et al., 2016). However, many of these effects resolve with abstinence and the residual effects of cannabis use on cognition remain an area of ongoing debate (Crean et al., 2011; Meier et al., 2018; Ross et al., 2020). The most heavily researched cannabinoids contained in cannabis (Δ 9-tetrahydrocannabinol [THC] and cannabidiol [CBD]) function as exogenous ligands for CB1 and CB2 receptors in the central and peripheral nervous systems and have been associated with differential and interacting neuropsychological effects (Abate et al., 2021; Aso & Ferrer, 2014; Chayasirisobhon, 2019; Englund et al., 2013; Scott et al., 2019; Weinstein & Sznitman, 2020). THC has notable psychoactive properties, including deficits in cognition, increased anxiety, and inducing psychotic experiences in vulnerable individuals (Cohen et al., 2019; Englund et al., 2013; Scott et al., 2019), while also possessing neuroprotective properties such as enhancing cholinergic transmission and inhibiting amyloid-beta aggregation (Abate et al., 2021; Aso & Ferrer, 2014; Weinstein & Sznitman, 2020). In contrast, CBD has been associated with enhanced learning, reduced anxiety, and inhibition of psychotic processes, while also providing anti-inflammatory and anti-oxidative properties (Chayasirisobhon, 2019; Lucas et al., 2018; Vacaflor et al., 2020). Most of the existing research on cannabis use and cognition has focused on adolescents and young adult participants (Abate et al., 2021; Lisdahl et al., 2021) and considerably less is known about cannabis use in later life stages. Furthermore, existing studies with adults are often limited by a lack of representation for older adults and comparisons between those with heavy chronic use and those without use, thus failing to account for differential effects associated with milder cannabis use in older adults (Scott et al., 2019; Volkow et al., 2016; Weinstein & Sznitman, 2020).

Despite these limitations, three reviews have summarized findings on cannabis use and cognition in samples that include older adults. One recent review of cannabis use in older adults (Vacaflor et al., 2020) found that 17.5% of participants across seven studies (three prospective observational studies, one retrospective survey, and three double-blind randomized controlled trials) reported SMC, although study authors concluded that low-dose, short-term medical cannabis use was generally well tolerated in older adults and did not confer significant risk for adverse cognitive outcomes. These findings were similar to a review of recreational and medical cannabis use in middle to older adulthood (Scott et al., 2019) that found modest reductions in cognitive performance associated with higher doses and heavier lifetime use of cannabis, although negative cognitive effects were less evident in older adults using medical cannabis. Another review (Weinstein & Sznitman, 2020) acknowledged potential risks for cognitive decline in older adults who use cannabis, but the authors concluded that the animal literature and a small number of experimental studies in older adults using medical cannabis indicate that cannabis use may be associated with better cognition. Research continues to investigate the potential therapeutic application of cannabis for neurological disorders in older adults, including Alzheimer's disease, although the beneficial and adverse effects in human trials is not clear (Abate et al., 2021; Aso & Ferrer, 2014; Bosnjak Kuharic et al., 2021; Cohen et al., 2019). To better understand the associations between cannabis use and cognitive deficits in older adults, representative population-based analyses of SMC and cannabis use patterns are needed. To our knowledge, no population-level analyses of cannabis use and SMC in older adults have been conducted.

To address this gap in the literature, we used the National Survey of Drug Use and Health (NSDUH) dataset to evaluate rates of SMC in older adult respondents (age 50+) according to pastyear use of cannabis. The NSDUH, a nationally representative cross-sectional survey in the U.S. that assesses drug use and related health concerns, uses a multistage area probability sampling design covering all 50 states, surveying non-institutionalized individuals ages 12 years and older.

Method

Participants and procedures

The present study used data from the 2017–2019 NSDUH surveys and included adults ages 50 years and older (n = 26,399). Interviewers administered study questions using computerassisted personal interviewing and audio computer-assisted selfinterviewing, which provides respondents with privacy to answer potentially sensitive questions such as those related to substance use. Respondents were compensated with \$30. Further information regarding survey methods have been reported elsewhere (Substance Abuse and Mental Health Services Administration, 2014). The RTI Institutional Review Board (IRB) approved the data collection procedures in compliance with the Helsinki Declaration, and this secondary data analysis was considered exempt by the University of Michigan IRB.

Measures

Respondents reported their use of cannabis, including (a) any use in the past year, (b) any use in the past month, (c) number of days using cannabis in the past year, and (d) number of days using cannabis in the past month. Respondents reported their use of alcohol, tobacco, cocaine, heroin, hallucinogens, inhalants, methamphetamine, pain relievers, tranquilizers, stimulants, and sedatives; substances used as prescribed by a medical provider were not included in these counts. Alcohol and tobacco were evaluated individually as binary variables. Use of the remaining substances was combined as a new binary variable (Other Substance Use) given the very low base rate (0.9%) of respondents endorsing use of more than one of these substances. Respondents were asked about select health conditions experienced in the past year (i.e., asthma, cancer, heart condition, and hypertension) and these were included as a binary variable (Health Conditions). To control for mental health factors that may impact cognition, we used the NSDUH Mental Health Module, which is a predictive classification variable based on responses to a 12-item questionnaire of past-year and past-month psychiatric symptoms derived from the NSDUH 2012 dataset. Respondents were classified in the NSDUH dataset as having no mental illness, mild mental illness, and moderate to severe mental illness. Regarding SMC, respondents were asked, "Because of a physical, mental or emotional condition, do you have serious difficulty concentrating, remembering, or making decisions?" and responses were recorded a binary variable. Demographic characteristics included age grouping (50-64, 65+), sex (male, female), race/ethnicity (non-Hispanic white, all others), domestic status (married, all others), education (greater than 12 years of education, 12 years or less), and population density (greater than one million persons, less than one million persons, others). Categorization of variables reflected NSDUH-suggested categories to allow for comparison with other publications using NSDUH data. See Supplementary Table 1 for a list of variable names. Further information about NSDUH measures and coding are available online (Center for Behavioral Health Statistics and Quality, 2021).

Data analyses

NSDUH-derived variables were utilized for stratification, clustering, and weighting to ensure that findings are representative of the general non-institutionalized U.S. population. Reported percentages represent weighted statistics to reflect U.S. population estimates. The sample was divided according to use of cannabis over the past year. Bivariate comparisons of demographic and clinical characteristics were assessed utilizing likelihood ratio chi-square tests for categorical variables and t-tests for continuous variables. Multivariable logistic regression was used to examine the association of demographic (age, sex, race/ethnicity, domestic status, education, and population density) and clinical characteristics (alcohol, tobacco, other substance use, physical health conditions, and mental illness) in people who used cannabis compared to those who did not. All data analysis was performed using SAS v 13.1 (SAS Institute, n.d.).

Results

Between 2017 and 2019, 26,399 respondents aged 50 and older completed the survey, 45.2% (95%CI: 44.4%-45.9%) of whom were over age 65. Approximately 8.2% (95%CI: 7.9%-8.6%) of the total sample over age 50 reported using cannabis in the past year. Differences by sex revealed that 60.5% (95%CI: 57.9%-63.1%) of cannabis users were male and that, overall, 10.7% of male and 6.1% of female respondents used cannabis in the past year. See Table 1 for additional data on respondent demographics and clinical characteristics. The average person who used cannabis consumed cannabis 2.26 (95%CI: 2.11-2.40) days per week over the past year. Overall, 7.0% (95%CI: 6.7%-7.3%) of survey respondents reported SMC. Among respondents, 13.2% (95%CI: 11.5% -15.0%) of those who reported cannabis use in the past year also reported SMC, compared to 6.4% (95%CI: 6.1%-6.8%) among those individuals with no cannabis use. Directionally consistent effects were obtained when evaluating associations with pastmonth cannabis use (see Table 2).

The association between cannabis use and SMC was further evaluated using a logistic regression, which revealed an unadjusted model odds ratio (OR) of 2.21 (95%CI: 1.88-2.60), indicating greater odds of SMC in those with past-year cannabis use compared to those with no cannabis use. An adjusted model controlling for age, sex, race, domestic status, education, population density, alcohol use, tobacco use, other substance use, health conditions, and mental illness, yielded an adjusted OR of 1.38 (95% CI: 1.10-1.72), indicating greater likelihood of SMC associated with past-year cannabis use (see Table 3). Other measured variables significantly contributed to the likelihood of SMC, including reduced risk of SMC associated with higher levels of education (OR = 0.58, 95%CI: 0.51-0.67), being married (OR = 0.76, 95% CI: 0.68–0.86), and use of alcohol in the past year (OR = 0.65, 95%CI: 0.56-0.75). Risk of SMC increased with having a physical health condition (OR = 1.29, 95%CI: 1.12-1.48), use of other substances in the past year (OR = 1.52, 95%CI: 1.21–1.92), or mental illness (OR = 6.05, 95%CI: 5.03-7.28 for mild severity; OR=20.6, 95%CI: 17.8-23.9 for moderate or severe severity).

When a parallel set of analyses were conducted using pastmonth cannabis use, the unadjusted model revealed significant OR of 2.08 (95%CI: 1.69–2.56) and the adjusted model revealed directionally consistent but nonsignificant effects (OR=1.15, 95%CI: 0.90–1.49). ORs across covariates were otherwise highly similar to those previously presented, although tobacco use became a significant finding (OR = 1.16, 95%CI: 1.01–1.34). See Table 4 for details. We also conducted a dose-response analysis among respondents reporting past-year cannabis use (n = 2,286) according to frequency of past-year cannabis use predicting SMC. These results were nonsignificant, with OR of 1.001 (95% CI: 0.999–1.002).

Discussion

Among a representative sample of U.S. adults over age 50, our results reveal that approximately 8.2% have used cannabis at least once in the past year, and that cannabis use is associated with increased risk of SMC. This base rate of cannabis use reflects a continued increase among older adult respondents from the NSDUH studies since 2006 (Han et al., 2017) and is comparable to other recent surveys (Maxwell et al., 2021) that reported 8.3% of men and 3.9% of women used cannabis in the past month. Thirteen percent of those who used cannabis in our sample reported SMC, slightly lower than the 17.5% reported in the review by Vacaflor et al. (2020). We found a two-fold increase (OR = 2.21) in likelihood of reporting SMC in respondents who had used cannabis in the past year, which was attenuated (OR = 1.38) when controlling for demographic, health conditions, and psychiatric factors. However, this association between cannabis use and SMC became nonsignificant when evaluating respondents who had used cannabis in the past month, when acute and post-acute cognitive effects would be more likely to emerge, and a doseresponse relationship between cannabis use and SMC was also nonsignificant. To the best of our knowledge, this is the first population-level analysis of associations between cannabis use and SMC in older adults.

While cannabis use and acute cognitive deficits in samples of adolescents and young adults is well-established, residual effects are mixed and few studies have examined these associations in older adults. Studies including middle and older adult participants have lacked well controlled, longitudinal, performance-based assessment of cognition and have been limited by small sample sizes and wide age bands that are not specific to older adults, thus diluting potential differential effects of cannabis use in older adulthood specifically (Scott et al., 2019; Vacaflor et al., 2020; Volkow et al., 2016; Weinstein & Sznitman, 2020). Despite these limitations, results of available studies tend to show improved executive functioning with medical cannabis (Bar-Sela et al., 2019; Gruber et al., 2016; Sagar et al., 2021; Scott et al., 2019) and more mixed findings for those who use cannabis recreationally (i.e., lower verbal memory and processing speed in individuals who use recreational cannabis compared to those who do not, but between-group differences in change over time or dose-dependent associations were not evident) (Auer et al., 2016; Dregan & Gulliford, 2012; McKetin et al., 2016; Weinstein & Sznitman, 2020).

The present analyses reveal a relationship between past-year cannabis use and SMC, but this association is complicated by several considerations, and the potential mechanisms underlying this relationship remain unclear. In our analyses, the increased risk of SMC in those who used cannabis in the past year was comparable to the contributions made by comorbid health conditions, such as asthma, cancer, heart conditions, or hypertension, each independent risk factors for SMC. Similarly, misuse of other substances (e.g., cocaine, heroin, inhalants, methamphetamine, etc.) also conferred comparable levels of risk for SMC. However, mental illness revealed a notably stronger effect on SMC, with the greatest risk observed in moderate to severe mental illness,

Table 1.	Respondent	demographics	and clinical	characteristics	in adults aged 50+.
----------	------------	--------------	--------------	-----------------	---------------------

			Used cannabis in the past year		
5		Overall	Yes	No	
Raw N, weighted %	26399		2286 (8.2%)	24113 (91.8%)	
Age	Raw N	Weighted % (95CI)	Raw N / Weighted % (95CI)	Raw N / Weighted % (95C	
50-64	14815	54.8% (54.1% - 55.6%)	1764	13051	
65+	11584	45.2% (44.4% - 45.9%)	76.4% (74.1% - 78.7%) ^a 522	52.9% (52.1% - 53.7%) 11062	
Sex			23.6% (21.3% - 25.9%)	47.1% (46.3% - 47.9%)	
Male	12097	46.7% (46.1% - 47.3%)	1361	10736	
Female	14302	53.3% (52.6% - 53.9%)	60.5% (57.9% - 63.1%) ^A 925	45.5% (44.8% - 46.1%) 13377	
Race/Ethnicity			39.5% (36.9% - 42.1%)	54.5% (53.8% - 55.2%)	
Non-Hispanic White	19167	71.8% (70.9% - 72.8%)	1751	17416	
All others	7232	28.1% (27.2% - 29.1%)	77.6% (75.4% - 79.8%) ^A 535	71.3% (70.4% - 72.3%) 6697	
		х, <i>,</i> , , , , , , , , , , , , , , , , ,	22.4% (20.2% - 24.6%)	28.7% (27.7% - 29.6%)	
Domestic status Married	15649	61.2% (60.1% - 62.2%)	1064	14585	
All others	10750	38.8% (37.8% - 39.9%)	48.9% (46.1% - 51.6%) ^A 1222	62.3% (61.2% - 63.4%) 9528	
	10150	30.070 (31.070 - 33.370)	51.1% (48.4% - 53.9%)	37.7% (36.6% - 38.8%)	
Education Any post-H.S./GED	15734	61.1% (60.3% - 62.0%)	1439	14295	
			65.0% (62.4% - 67.5%) ^A	60.8% (59.5% - 61.7%)	
H.S./GED or less	10665	38.9% (38.0% - 39.7%)	847 35.0% (32.5% - 37.6%)	9818 39.2% (38.3% - 40.1%)	
Population Density ≥1 million persons	10518	51.1% (50.1% - 52.0%)	959	9559	
			53.1% (49.8% - 56.3%) ^{NS}	50.9% (49.9% - 51.9%)	
<1million persons	13159	41.9% (40.9% - 42.9%)	113 41.1% (38.3% - 43.9%)	12026 42.0% (40.8% - 43.1%)	
segment not a CBSA	2722	7.0% (6.5% - 7.6%)	114	2528	
Alcohol use (past year)			5.8% (4.5% - 7.1%)	7.2% (6.6% - 7.7%)	
Yes	16449	62.9% (62.2% - 63.4%)	1943 86.1% (84.4% - 87.9%) ^A	14506 60.8% (60.0% - 61.5%)	
No	9950	37.1% (36.4% - 37.8%)	343	9607	
Tobacco use (past year)			13.9% (12.1% - 15.6%)	39.2% (38.5% - 40.0%)	
Yes	5776	20.7% (20.0% - 21.4%)	1161	4615	
No	20623	79.3% (78.6% - 80.0%)	50.6% (46.7% - 53.3%) 1125	18.1% (17.5% - 18.8%) 19498	
			49.4% (47.9% - 52.1%) ^A	81.8% (81.2% - 82.5%)	
Other substance use (past year) Yes	1132	4.3% (3.9% - 4.7%)	442	690	
No	25267	95.7% (95.3% - 96.1%)	19.3% (17.1% - 21.5%) 1844	2.9% (2.6% - 3.2%) 23423	
	23201	55.170 (55.570 56.170)	80.7% (78.4% - 82.9%) ^A	97.1% (96.8% - 97.4%)	
Physical health conditions (past year) Yes	10307	39.2% (38.6% - 39.8%)	753	9554	
			34.2% (31.7% - 36.6%) ^A	39.7% (39.0% - 40.3%)	
No	16092	60.8% (60.2% - 61.4%)	1533 65.8% (63.4% - 68.2%)	14559 60.3% (59.7% - 61.0%)	
Mental Illness (past year) None	22534	85.9% (85.4% - 86.4%)	1661	20873	
			71.9% (69.2% - 74.6%)	87.2% (86.7% - 87.6%)	
Mild	2086	7.7% (7.3% - 8.1%)	271 12.6% (10.4% - 14.8%) ^A	1815 7.3% (6.9% - 7.7%)	
Mod/Sev	1779	6.3% (5.9% - 6.7%)	354 15 506 (12 206 17 706)A	1425	
Subjective Memory Complaint			15.5% (13.3% - 17.7%) ^A	5.5% (5.2% - 5.9%)	
Yes	1933	7.0% (6.7% - 7.3%)	308 13.2% (11.5% - 15.0%) ^A	1625 6.4% (6.1% - 6.8%)	
No	24344	93.0% (92.6% - 93.3%)	1966	22378	
Cannabis use (past month)			86.8% (85.0% - 88.5%)	93.6% (93.2% - 93.9%)	
Yes	1528	5.3% (5.0% - 5.6%)	1528 64 8% (62 4% - 67 2%)*	NA	
No	24871	94.7% (94.3% - 95.0%)	64.8% (62.4% - 67.2%)* 758	NA	
			35.2% (32.8% - 37.5%)		

Note: A p < 0.005; Ns not significant at 0.05; *not tested; Physical health conditions include asthma, cancer, heart condition, and hypertension; Mental illness in the past year according to NSDUH designations.

Table 2.	Cannabis	s use in the	past year a	nd past m	onth accordir	ng to report of
subjectiv	e memory	/ complaint	s (SMC) in a	adults age	d 50+.	

	SI	МС
	Yes	No
Cannabis u	se in past year	
Yes	308	1966
	15.6% (13.7% - 17.5%)	7.8% (7.3% - 8.1%)
No	1625	22378
	84.4% (82.5% - 86.3%)	92.3% (91.9% - 92.7%)
Cannabis i	n past month	
Yes	211	1308
	9.8% (8.4% - 11.4%)	5.0% (4.6% - 5.4%)
No	1722	23036
	90.1% (88.6% - 91.6%)	95.0% (94.6% - 95.3%)

Note. SMC=subjective memory complaints.

Table 3. Logistic regression of past-year cannabis use on subjective memory complaints (SMC) in adults aged 50+.

Unadjusted Logistic Model	β (se)	Odds ratio (95% CI)
Cannabis use in past year	0.40 (0.04)	2.21 (1.88 - 2.60)
No use cannabis in past year	(referent)	
Adjusted Model*	β (se)	Odds ratio (95% CI)
Age group ^{NS}		
50-64	(referent)	_
65+	0.05 (0.03)	1.10 (0.98 - 1.25)
Sex ^{NS}	0.00 (0.00)	1110 (0100 1120)
Male	-0.05 (0.03)	0.90 (0.78 - 1.03)
Female	(referent)	
Race group ^{NS}	(101010110)	
Non-Hispanic White	0.02 (0.04)	1.03 (0.89 - 1.20)
All others	(referent)	
Domestic status ^A	(referency)	
Married	-0.13 (0.03)	0.76 (0.68 - 0.86)
All others	(referent)	-
Education ^A	(referency)	
>12 years	-0.27 (0.03)	0.58 (0.51 - 0.67)
≤ 12 years	(referent)	-
Population Density ^{NS}	(referency)	
≥ 1 million persons	(referent)	_
<1million persons	-0.04 (0.05)	1.02 (0.88 - 1.18)
segment not a CBSA	0.09 (0.07)	1.16 (0.93 - 1.44)
Alcohol use (past year) ^A	0.05 (0.01)	1.10 (0.35 1.11)
Yes	-0.22 (0.04)	0.65 (0.56 - 0.75)
No	(referent)	-
Tobacco use (past year) ^{NS}	(101010110)	
Yes	0.06 (0.03)	1.13 (0.98 - 1.30)
No	(referent)	-
Other substance use (past year) ^A	(101010110)	
Yes	0.21 (0.06)	1.52 (1.21 - 1.92)
No	(referent)	
Physical health conditions (past ye		
Yes	0.13 (0.03)	1.29 (1.12 - 1.48)
No	(referent)	-
Mental Illness (past year) ^A	(101010110)	
None	(referent)	_
Mild	0.19 (0.06)	6.05 (5.03 - 7.28)
Moderate/Severe	1.42 (0.05)	20.6 (17.8 – 23.9)
Cannabis use (past year) ^B		
Yes	0.16 (0.06)	1.38 (1.10 - 1.72)
No	(referent)	_
	(

Note. ${}^{A}\rho \leq 0.005$; ${}^{B}p \leq 0.01$; NS not significant at 0.05; SMC = subjective memory complaints; CBSA = core based statistical areas; Physical health conditions include asthma, cancer, heart condition, and hypertension; Mental illness in the past year according to NSDUH designations.

consistent with the clinical literature showing large effects of mental illness on SMC (Keefe & Fenton, 2007; McCleery & Nuechterlein, 2019; Rock et al., 2014). But even after accounting for these and other covariates, past-year cannabis use remained

 Table 4. Logistic regression of past-month cannabis use on subjective memory complaints (SMC) in adults aged 50+.

β (se) 0.37 (0.05) (referent)	Odds ratio (95% CI) 2.08 (1.69 – 2.56)
	2 (18 (169 - 256)
(referency)	2.00 (1.03 - 2.30)
β (se)	Odds ratio (95% CI)
(referent)	-
0.04 (0.03)	1.09 (0.97 - 1.23)
	. ,
-0.05 (0.03)	0.91 (0.79 - 1.05)
(referent)	-
0.02 (0.04)	1.04 (0.90 - 1.20)
(referent)	_
. ,	
-0.14 (0.03)	0.76 (0.67 - 0.85)
(referent)	_
. 7	
-0.27 (0.03)	0.58 (0.51 - 0.67)
	_
(
(referent)	_
	1.01 (0.87 - 1.18)
	1.15 (0.93 - 1.43)
-0.20 (0.04)	0.66 (0.57 - 0.77)
	_
()	
0.08 (0.04)	1.16 (1.01 - 1.34)
(
0.23 (0.06)	1.59 (1.27 - 1.99)
	-
(10101010)	
0.12 (0.03)	1.28 (1.11 - 1.47
· · ·	
(referency)	
(referent)	_
	6.11 (5.07 – 7.36)
	20.91 (17.99 - 24.29)
1.72 (0.03)	20.31 (11.33 - 24.23)
0.07 (0.06)	1.15 (0.90 - 1.49)
	1.13 (0.30 - 1.49)
	(referent) 0.04 (0.03) -0.05 (0.03) (referent) 0.02 (0.04) (referent) -0.14 (0.03)

Note: $^{A}p \le 0.005$; $^{B}p \le 0.01$; $^{C}p \le 0.05$; NS not significant at 0.05; SMC = subjective memory complaints; CBSA = core based statistical areas; Physical health conditions include asthma, cancer, heart condition, and hypertension; Mental illness in the past year according to NSDUH designations.

a significant predictor of SMC. Given the higher rates of cannabis use among individuals with chronic health conditions, polysubstance use, and mental illness, these concurrent findings are not surprising, although it is important to underscore that multiple potential causal pathways may exist across these factors and more tightly controlled experimental methods are needed to clarify causal mechanisms underlying the associations between cannabis use and SMC in older adults. Moreover, recent use of cannabis (in the past month) did not show a statistically significant association with SMC, and no dose-response relationship between cannabis and SMC could be established in our analyses. In contrast, being married, having higher levels of education, and consuming alcohol in the past year were associated with small to moderate reductions in risk for SMC, consistent the clinical literature identifying marriage (Sommerlad et al., 2018), education (Stern, 2009; Tucker, 2012), and light to moderate alcohol consumption (Mukamal et al., 2003; Ruitenberg et al., 2002; Topiwala & Ebmeier, 2018) as protective factors for cognitive aging. Taken together, these findings provide

important context for understanding the relationship between cannabis use and SMC in older adults and underscore the importance of population-level research to better understand the causal mechanisms underlying this relationship.

Several limitations of our study must also be considered. First, we were limited by the variables available from the NSDUH dataset. Specifically, the item used to identify respondents with SMC is conditioned upon "a physical, mental or emotional condition" impacting cognition, and it is not possible to delineate the factors that may contribute to endorsement of SMC. Additionally, NSDUH does not have objective data regarding the patterns of cannabis use, motivation for use, cannabis strain, cannabinoid profile, or route of administration. Such variables are important factors for better understanding the impacts of cannabis use in older adults and the relative risk and protective factors associated with use patterns and cannabinoid profiles on cognition (Sagar et al., 2021; Scott et al., 2019). Finally, our study did not include objective measures of memory functioning, and SMC is not reliably related to neuropsychological test performance, especially in those with mental illness (Carter et al., 2003; Hohman et al., 2011; Richardson-Vejlgaard et al., 2009). Performance-based neuropsychological testing is older adults is essential to better understand the relationships between cannabis use and cognition in this population.

A clearer understanding of the relationship between cannabis use and cognitive functioning in older adults would aid in differential diagnosis by helping to reduce heterogeneity in clinical phenotypes (e.g., mild cognitive impairment) of dementia. Furthermore, the clinical relevance of cannabis use in older adults presenting with SMC will become increasingly prevalent as cannabis use trends in this demographic continue to expand. Interventions geared toward comprehensive management of modifiable risk factors have demonstrated promising results in reducing the incidence of dementia (e.g., Rosenberg et al., 2019), although a full appreciation of cannabis use as a risk and/or protective factor in older adults remains unclear due to a lack of research in this population. Future research should include prospective, performance-based evaluation of cognitive functioning in older adults using cannabis. Particular attention should also be given to a careful assessment of use patterns, cannabis characteristics, and dose-response relationships. As the population ages and cannabis use increases, it will be important to understand the relationship between cannabis use and objective and subjective measure of cognitive functioning.

In sum, our findings reveal an increased rate of SMC in older adults with past-year cannabis use compared to those without pastyear cannabis use. Risks of SMC associated with cannabis use were comparable to physical health problems and misuse of other substances among older adults, but notably less impactful than the presence and severity of comorbid mental illness. While the relationship between cannabis use and SMC remained significant despite accounting for multiple demographic and behavioral factors with known effects on cognition, the association between cannabis use and SMC became weaker and nonsignificant when evaluating more recent use periods (one month), and no doseresponse relationship between cannabis use and rates of SMC was detected. As the first population-level analysis of cannabis use and SMC in older adults in the US, these hypothesis generating results help to characterize and contextualize the relationship between cannabis use and SMC in this population and further research is necessary to better understand the mechanisms that may underly these findings.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1355617723000061.

Acknowledgements. We would like to acknowledge the US Department of Veterans Affairs and the National Institute on Aging for their support that made this work possible. We would like to acknowledge Mary Jannausch for her contributions to the statistical analyses and data management.

Funding support. This work was supported by the Veterans Affairs Health Services Research and Development (VA HSR&D) Research Career Scientist Award Number RCS 19-333. Support to Dr. Hampstead from NIA R35AG072262 (effort) is acknowledged. The views expressed in this report are those of the authors, and do not necessarily represent those of the Department of Veterans Affairs or the United States Government. All authors had full access to all the data, and Dr. Ilgen takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of interest. None.

References

- Abate, G., Uberti, D., & Tambaro, S. (2021). Potential and limits of cannabinoids in Alzheimer's disease therapy. *Biology*, 10, 542. https://doi.org/ 10.3390/biology10060542
- Aso, E., & Ferrer, I. (2014). Cannabinoids for treatment of Alzheimer's disease: Moving toward the clinic. *Frontiers in Pharmacology*, 5, 1–11. https://doi. org/10.3389/fphar.2014.00037
- 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, 352. https://doi.org/10.1001/jamainternmed.2015.7841
- Bar-Sela, G., Tauber, D., Mitnik, I., Sheinman-Yuffe, H., Bishara-Frolova, T., & Aharon-Peretz, J. (2019). Cannabis-related cognitive impairment: A prospective evaluation of possible influences on patients with cancer during chemotherapy treatment as a pilot study. *Anti-Cancer Drugs*, 30, 91–97. https://doi.org/10.1097/CAD.000000000000685
- Baumgart, M., Snyder, H. M., Carrillo, M. C., Fazio, S., Kim, H., & Johns, H. (2015). Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's & Dementia*, 11, 718–726. https://doi.org/10.1016/j.jalz.2015.05.016
- Black, P., & Joseph, L. J. (2014). Still dazed and confused: Midlife marijuana use by the baby boom generation. *Deviant Behavior*, 35, 822–841. https://doi.org/ 10.1080/01639625.2014.889994
- Blazer, D. G., & Wu, L.-T. (2009). Nonprescription use of pain relievers by middle-aged and elderly community-living adults: National survey on drug use and health: Nonprescription pain reliever use in late life. *Journal of the American Geriatrics Society*, 57, 1252–1257. https://doi.org/10.1111/j.1532-5415.2009.02306.x
- Bosnjak Kuharic, D., Markovic, D., Brkovic, T., Jeric Kegalj, M., Rubic, Z., Vuica Vukasovic, A., Jeroncic, A., & Puljak, L. (2021). Cannabinoids for the treatment of dementia. *Cochrane Database of Systematic Reviews*, 2021, 1–55. https://doi.org/10.1002/14651858.CD012820.pub2
- Campeny, E., López-Pelayo, H., Nutt, D., Blithikioti, C., Oliveras, C., Nuño, L., Maldonado, R., Florez, G., Arias, F., Fernández-Artamendi, S., Villalbí, J. R., Sellarès, J., Ballbè, M., Rehm, J., Balcells-Olivero, M. M., & Gual, A. (2020). The blind men and the elephant: Systematic review of systematic reviews of cannabis use related health harms. *European Neuropsychopharmacology*, 33, 1–35. https://doi.org/10.1016/j.euroneuro. 2020.02.003
- Carter, S. L., Rourke, S. B., Murji, S., Shore, D., & Rourke, B. P. (2003). Cognitive complaints, depression, medical symptoms, and their association with neuropsychological functioning in HIV infection: A structural equation model analysis. *Neuropsychology*, 17, 410–419. https://doi.org/10.1037/0894-4105.17.3. 410
- Center for Behavioral Health Statistics and Quality. (2021). 2020 National Survey on Drug Use and Health (NSDUH): Methodological summary and

definitions. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/

- Chayasirisobhon, S. (2019). Cannabis and neuropsychiatric disorders: An updated review. 28, 13.
- Cohen, K., Weizman, A., & Weinstein, A. (2019). Positive and negative effects of cannabis and cannabinoids on health. *Clinical Pharmacology & Therapeutics*, 105, 1139–1147. https://doi.org/10.1002/cpt.1381
- Crane, N. A., Schuster, R. M., Fusar-Poli, P., & Gonzalez, R. (2013). Effects of cannabis on neurocognitive functioning: Recent advances, neurodevelopmental influences, and sex differences. *Neuropsychology Review*, 23, 117–137. https://doi.org/10.1007/s11065-012-9222-1
- Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence-based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of Addiction Medicine*, *5*, 1–8. https://doi.org/10.1097/ADM. 0b013e31820c23fa
- 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, 218–227. https://doi.org/10.1093/ aje/kwr315
- Englund, A., Morrison, P. D., Nottage, J., Hague, D., Kane, F., Bonaccorso, S., Stone, J. M., Reichenberg, A., Brenneisen, R., Holt, D., Feilding, A., Walker, L., Murray, R. M., & Kapur, S. (2013). Cannabidiol inhibits THCelicited paranoid symptoms and hippocampal-dependent memory impairment. *Journal of Psychopharmacology*, 27, 19–27. https://doi.org/10.1177/ 0269881112460109
- Gruber, S. A., Sagar, K. A., Dahlgren, M. K., Racine, M. T., Smith, R. T., & Lukas, S. E. (2016). Splendor in the grass? A pilot study assessing the impact of medical marijuana on executive function. *Frontiers in Pharmacology*, 7, 1–12. https://doi.org/10.3389/fphar.2016.00355
- Han, B. H., Sherman, S., Mauro, P. M., Martins, S. S., Rotenberg, J., & Palamar, J. J. (2017). Demographic trends among older cannabis users in the United States, 2006–13. Addiction, 112, 516–525. https://doi.org/10.1111/add.13670
- Hohman, T. J., Beason-Held, L. L., & Resnick, S. M. (2011). Cognitive complaints, depressive symptoms, and cognitive impairment: Are they related? *Journal of the American Geriatrics Society*, 59, 1908–1912. https:// doi.org/10.1111/j.1532-5415.2011.03589.x
- Kaskie, B., Ayyagari, P., Milavetz, G., Shane, D., & Arora, K. (2017). The increasing use of cannabis among older Americans: A public health crisis or viable policy alternative? *The Gerontologist*, 57, 1166–1172. https://doi. org/10.1093/geront/gnw166
- Keefe, R. S. E., & Fenton, W. S. (2007). How should DSM-V criteria for schizophrenia include cognitive impairment? *Schizophrenia Bulletin*, 33, 912–920. https://doi.org/10.1093/schbul/sbm046
- Lisdahl, K. M., Filbey, F. M., & Gruber, S. A. (2021). Introduction to jins special issue: Clarifying the complexities of cannabis and cognition. *Journal of the International Neuropsychological Society*, 27, 515–519. https://doi.org/ 10.1017/S1355617721000874
- Lucas, C. J., Galettis, P., & Schneider, J. (2018). The pharmacokinetics and the pharmacodynamics of cannabinoids. *British Journal of Clinical Pharmacology*, 84, 2477–2482. https://doi.org/10.1111/bcp.13710
- Maxwell, C. J., Jesdale, B. M., & Lapane, K. L. (2021). Recent trends in cannabis use in older Americans. Annals of Internal Medicine, 174, 133–135. https:// doi.org/10.7326/M20-0863
- McCleery, A., & Nuechterlein, K. H. (2019). Cognitive impairment in psychotic illness: Prevalence, profile of impairment, developmental course, and treatment considerations. *Dialogues in Clinical Neuroscience*, 21, 239–248. https://doi.org/10.31887/DCNS.2019.21.3/amccleery
- 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
- Meier, M. H., Caspi, A., Danese, A., Fisher, H. L., Houts, R., Arseneault, L., & Moffitt, T. E. (2018). Associations between adolescent cannabis use and neuropsychological decline: A longitudinal co-twin control study:

Adolescent cannabis use and IQ decline. Addiction, 113, 257–265. https://doi.org/10.1111/add.13946

- Mitchell, A. J., Beaumont, H., Ferguson, D., Yadegarfar, M., & Stubbs, B. (2014). Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: Meta-analysis. Acta Psychiatrica Scandinavica, 130, 439–451. https://doi.org/10.1111/acps.12336
- Mukamal, K. J., Kuller, L. H., Fitzpatrick, A. L., Longstreth, J.W.T., Mittleman, M. A., & Siscovick, D. S. (2003). Prospective study of alcohol consumption and risk of dementia in older adults. *JAMA*, 289, 1405–1413. https://doi.org/ 10.1001/jama.289.11.1405
- Ranganathan, M., & D'Souza, D. C. (2006). The acute effects of cannabinoids on memory in humans: A review. *Psychopharmacology*, 188, 425–444. https:// doi.org/10.1007/s00213-006-0508-y
- Richardson-Vejlgaard, R., Dawes, S., Heaton, R. K., & Bell, M. D. (2009). Validity of cognitive complaints in substance-abusing patients and nonclinical controls: The Patient's Assessment of Own Functioning Inventory (PAOFI). *Psychiatry Research*, 169, 70–74. https://doi.org/10.1016/j. psychres.2008.06.018
- Rock, P. L., Roiser, J. P., Riedel, W. J., & Blackwell, A. D. (2014). Cognitive impairment in depression: A systematic review and meta-analysis. *Psychological Medicine*, 44, 2029–2040. https://doi.org/10.1017/ S0033291713002535
- Rosenberg, A., Mangialasche, F., Ngandu, T., Solomon, A., & Kivipelto, M. (2019). Multidomain interventions to prevent cognitive impairment, Alzheimer's disease, and dementia: From FINGER to World-Wide FINGERS. *The Journal of Prevention of Alzheimer's Disease*, 7(1), 1–8. https://doi.org/10.14283/jpad.2019.41
- Ross, J. M., Ellingson, J. M., Rhee, S. H., Hewitt, J. K., Corley, R. P., Lessem, J. M., & Friedman, N. P. (2020). Investigating the causal effect of cannabis use on cognitive function with a quasi-experimental co-twin design. *Drug and Alcohol Dependence*, 206, 107712. https://doi.org/10.1016/j.drugalcdep. 2019.107712
- Ruitenberg, A., van Swieten, J. C., Witteman, J. C., Mehta, K. M., van Duijn, C. M., Hofman, A., & Breteler, M. M. (2002). Alcohol consumption and risk of dementia: The Rotterdam Study. *The Lancet*, 359, 281–286. https://doi. org/10.1016/S0140-6736(02)07493-7
- Sagar, K. A., Dahlgren, M. K., Lambros, A. M., Smith, R. T., El-Abboud, C., & Gruber, S. A. (2021). An observational, longitudinal study of cognition in medical cannabis patients over the course of 12 months of treatment: Preliminary results. *Journal of the International Neuropsychological Society*, 27, 648–660. https://doi.org/10.1017/ S1355617721000114
- SAS Institute. (n.d.). SAS (13.1).
- Scott, E. P., Brennan, E., & Benitez, A. (2019). A systematic review of the neurocognitive effects of cannabis use in older adults. *Current Addiction Reports*, 6, 443–455. https://doi.org/10.1007/s40429-019-00285-9
- Sommerlad, A., Ruegger, J., Singh-Manoux, A., Lewis, G., & Livingston, G. (2018). Marriage and risk of dementia: Systematic review and meta-analysis of observational studies. *Journal of Neurology, Neurosurgery & Psychiatry*, 89, 231–238. https://doi.org/10.1136/jnnp-2017-316274
- Stern, Y. (2009). Cognitive reserve. Neuropsychologia, 47, 2015–2028. https:// doi.org/10.1016/j.neuropsychologia.2009.03.004
- Substance Abuse and Mental Health Services Administration. (2014). Results from the 2013 national survey on drug use and health: Summary of national findings (NSDUH Series H-48, HHS Publication No. (SMA) 14-4863; p. 184). Substance Abuse and Mental Health Services Administration.
- Topiwala, A., & Ebmeier, K. P. (2018). Effects of drinking on late-life brain and cognition. *Evidence-Based Mental Health*, 21, 12–15. https://doi.org/10.1136/ eb-2017-102820
- Tucker, A. M. (2012). Cognitive reserve in aging. 13.
- US Census Bureau. (2001, October 3). Population by age, sex, race, and Hispanic or Latino origin for the United States: 2000. Census.Gov. https://www.census. gov/data/tables/2000/dec/phc-t-09.html

- 2019-age-sex-composition.html Vacaflor, B. E., Beauchet, O., Jarvis, G. E., Schiavetto, A., & Rej, S. (2020). Mental health and cognition in older cannabis users: A review. *Canadian Geriatrics Journal*, 23, 237–244. https://doi.org/10.5770/cgj.23.399
- Volkow, N. D., Swanson, J. M., Evins, A. E., DeLisi, L. E., Meier, M. H., Gonzalez, R., Bloomfield, M. A. P., Curran, H. V., & Baler, R. (2016). Effects of cannabis use on human behavior, including cognition, motivation,

and psychosis: A review. JAMA Psychiatry, 73, 292. https://doi.org/10.1001/jamapsychiatry.2015.3278

- Weinstein, G., & Sznitman, S. R. (2020). The implications of late-life cannabis use on brain health: A mapping review and implications for future research. *Ageing Research Reviews*, 59, 101041. https://doi.org/10.1016/j.arr.2020. 101041
- Wu, L.-T., & Blazer, D. G. (2011). Illicit and nonmedical drug use among older adults: A review. *Journal of Aging and Health*, 23, 481–504. https://doi.org/ 10.1177/0898264310386224