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Research article

The effect of cannabis legislation on opioid and benzodiazepine use among aging Americans

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Abstract: Background: This study sought to evaluate whether medicinal cannabis (marijuana) laws (MMLs) influence opioid and benzodiazepine use through displacement from opioids and companion drugs toward cannabis for arguably better or comparable pain management among aging Americans (i.e., those aged 50 years and older) as opposed to concentrating on *older* people aged 65 years and above. This aging demographic is an understudied but vulnerable population to unknown or paradoxical policy effects amid the current medical and legal landscape. Should this displacement occur, the implementation of such legislation may ultimately aid in mitigating the adverse repercussions that ensue from an excessive dependence on these more traditional medications. However, it is also critical to assess whether these laws worsen outcomes among this population. **Methods:** To investigate these possibilities, 2022 data from the National Survey on Drug Use and Health (NSDUH) are used along with multiple logistic regression procedures to evaluate the use of opioids and benzodiazepines in MMLs for those aged 50 years and older compared to those younger. **Results:** Findings reveal that less opioid reliance is reported among the aging residing in MML states compared to non-MML states. However, no effect from the laws is observed for benzodiazepines or co-prescribed opioids and benzodiazepines among this population. **Conclusions:** MMLs may serve to attenuate the consequences of opioid reliance among the aging but not use of opiates in combination with benzodiazepines or the use of benzodiazepines alone.

Keywords: opioids; benzodiazepines; aging; medicinal cannabis; MMLs; chronic pain

1. Introduction

Medicinal cannabis has been promoted as providing an alternative to traditional drugs for the management of chronic or persistent pain, a condition impacting millions of Americans [1] and requiring long term management [2]. Along with the proliferation of states enacting more permissive medical marijuana laws (MMLs), little is known about substance use behaviors among aging Americans despite this demographic being more susceptible to pain related conditions [3,4]. This is a concern because along with aging populations being more disposed to persistent pain and related conditions compared to their younger counterparts, traditional medical management for pain has relied upon opioid analgesics (e.g., hydrocodone and codeine) and attendant drugs, such as benzodiazepines (e.g., Xanax and Valium), for treatment [5]. Problematically, this demographic group is also tied to impaired drug metabolism, which can exacerbate adverse effects and other negative outcomes linked with these medications [6]. Given this, the aging population faces a higher risk exposure, such as side effects, overdose, problematic substance use, or disordered behavior. This is troubling as those represented in the age category of 50 years and older account for over 70 million people, and answers related to the opioid epidemic and ancillary harms can be found by examining this population.

Amidst this backdrop, there is evidence that cannabis may attenuate reliance on other substances, such as opioids and benzodiazepines, while being associated with a safer risk profile [7,8]. However, there are critics who argue that this policy transition toward cannabis use is premature due to the limited knowledge regarding the potential adverse effects of utilizing cannabis as a pain management therapy, such as whether misuse of other substances is amplified amid more permissive legal environments [9,10]. Admittedly, the full consequences of cannabis related policy are yet unknown, and likewise, insufficient research has been conducted purposely examining the aging population in this legal context. With the proliferation of medical cannabis laws, it is critical to evaluate the nexus between medicinal cannabis laws, opioids, and other drugs, particularly for the most vulnerable to the potential negative direct and indirect consequences of these policies.

The intent of the current study, then, is to evaluate the nature of opioid and benzodiazepine use among the aging population, particularly in the context of medical cannabis legislation, by conducting analyses of data drawn from the 2022 National Survey on Drug Use and Health (NSDUH). The study specifically evaluates whether living in a medicinal cannabis state is associated with opioid and/or benzodiazepine reliance among those aged 50 years and older and should help to elucidate the impact of medicinal cannabis legislation on driving or alleviating opioid and/or benzodiazepine reliance for medical management. Toward this end, the effort relies upon multivariate logistic regression procedures finding that residing in a MML jurisdiction is associated with less reported reliance on opioids among this aging population but not benzodiazepines or their combined use.

1.1. Chronic pain management among the aging

Due to the higher likelihood of persistent pain among the aging, they are also more disposed to polypharmacy, which involves being prescribed many medications including opioids and benzodiazepines for management. Opioids as narcotic analgesics or pain medicines are prescribed to directly attend to pain by binding to the opioid receptors in the body that assist in communicating pain messages. Additionally, benzodiazepines, though not analgesics, lower sensitivity to stimuli and too

are often prescribed in clinical settings to treat ancillary issues of chronic pain (e.g., insomnia, anxiety, and muscle tension), often alongside opioids as a mainstay of chronic pain management [5].

There is ubiquitous research documenting harms attributable to these drugs, whether used alone or in combination, demonstrating wide ranging personal and social burdens, for example see [5,7,8,11]. Apart from the risks for addiction, opioid drugs are tied to a myriad of negative outcomes, including premature death, overdose, drug interactions, hospitalizations, falls, personal and automobile accidents, and abnormal drug taking behaviors [7,8,12–16]. Collectively, these problems bear out in the aggregate having substantial social and economic burdens [1,2,11]. Similar to opiates, the use of benzodiazepines is accompanied by numerous complications along with being addictive and are similar to that seen with opioids, as noted above, such as ataxia, deficits in cognition and coordination, falls, traffic accidents, among other troublesome outcomes, including overdose [5,17].

Problematically and irrespective of experts discouraging the co-prescribing of opioids and benzodiazepines [18–20] and the 2016 black-box warning from the U.S. Food and Drug Administration against coadministration of these drugs, the practice continues. Thus, it is essential to recognize that the side effects and problems previously noted are exacerbated when the two substances are concurrently prescribed; however, aging individuals are commonly treated with both of these medications [21]. It is also noteworthy that combining these medications can lead to fatal respiratory depression [22]. Such lethal consequences are borne out in aggregate statistics. For example, according to the National Center on Drug Abuse, 14% of opioid deaths in 2021 were associated with the co-use of benzodiazepines with opioids [23]. Clearly, this exemplifies the need to find effective and less harmful treatments to manage the complexities associated with these patients.

1.2. The role of medicinal cannabis in chronic pain management among the aging

Research on the use of medical cannabis for pain management is expanding as more states provide for its use [24−31]. This research is varied in terms of the population studied, method and type of evaluation (e.g., clinical observation compared to studies surveying patients), and level of analysis. Observations from this body of research have resulted in "conclusive and substantial" evidence demonstrating the efficacy of cannabis in the treatment of chronic pain, as well as spasticity associated with multiple sclerosis among other conditions [29]. In recognition of this, the treatment of chronic pain is the most commonly approved condition under MMLs, with a majority of patients reporting treatment efficacy [32].

The question of whether the aging would alter their medication practices as a result of the proliferation of medicinal cannabis remains an important but elusive question. At this time, various studies speak to the issue indirectly, such as using age as a control variable. For example, research evaluating the influence of MMLs on opioid and benzodiazepine usage included age categories as a control showing that the reliance on these drugs, notwithstanding of MMLs, varies depending on age [8]. Other research simply isolates age groups variably, which may consist of comparing linearly those younger to those older. Additional work studying those defined as *older* patients (i.e., typically classified as 65 years and above) is telling but may be too restrictive by limiting study participants to retirement age, a somewhat arbitrary figure in this setting. Such an approach is seen in studies that inspect the influence of medicinal cannabis use on Medicare patients, isolating the study participants to those 65 years of age and above [33,34]. As a result of this disparity in approaches, much of this research is largely not comparable. For example, while some research suggests that younger populations make

modifications, specifically concerning opioids toward medicinal cannabis, the same was not found among the older subjects [35]. Yet, other research demonstrates a decline in opioid reliance among aging, habitual users, but there are limitations such as having a modest sample size, e.g., a treatment group of chronic pain, medicinal cannabis patients (n = 37, mean age of 54 years) compared to a control group (n = 29, mean age of 60 years) [36]. Consequently, findings cannot be considered conclusive given the current state of research in this area.

2. Materials and methods

To establish links between medicinal cannabis legislation and opioid and benzodiazepine usage among the aging, further empirical research is crucial. Given the above, a promising approach is to vet this issue by relying on subjects at or around the average age of medicinal cannabis users (i.e., about 50 years). Numerous research studies examining the use of medicinal cannabis find the average user to be in the age group of about 50 years and above, which corresponds to the common, aging, chronic pain patient. In observation of this, the cohort of those aged 50 years and above (compared to those younger) is used in the current study as it is more inclusive of the aging population than restricting investigation to those formally defined as *older* (≥65), as well as it being more specific and justifiable than other methods.

The strategy employed, which is further described below, will help determine if opioid and/or benzodiazepine use among the aging compared to those younger is associated with whether a respondent lives in a MML state (see Appendix for a table of MML states and other relevant information). From that, based on the findings, one can assume that if permissive medicinal cannabis legislation influences more traditional healthcare practices, the shift away from opioids and/or benzodiazepines should have an impact on their associated risks. While cannabis has been recognized as addictive, research suggests that medicinal cannabis laws reduce opioid-related negative outcomes, such as premature death from overdose [37]; however, this finding appears to be nuanced [38]. Given this, it may be one way to combat the negative consequences of opioids without increasing illicit drug use beyond recreational cannabis, see [39], as well as counter the augmented side effects from these medications among the aging. While these additional difficulties are not directly assessed in this study, their significance contributes to the motivation for the current analysis, which aims to determine the impact of MMLs on opioid and benzodiazepine use among the aging.

2.1. Data

Data for this study was drawn from the 2022 NSDUH, administered by the Substance Abuse and Mental Health Services Administration. The NSDUH provides a deidentified nationally representative sample of 59069 respondents, and its dataset is publicly accessible for research purposes without the need for Institutional Review Board approval. The survey includes comprehensive data on prescription drug usage and demographic information pertaining to the U.S. population that can be screened for age, thus making it a particularly suitable dataset for our purposes. Individuals under the age of 18 were excluded from this study. The NSDUH is available for download online at https://www.datafiles.samhsa.gov/.

2.2. Measures

2.2.1. Dependent variables

The dependent variables were operationalized as a series of binary dummy coded variables indicating whether respondents had used, misused (= 1) or not (= 0) opioids (dependent variable 1), benzodiazepines (dependent variable 2), or both (dependent variable 3) over the past year. From the NSDUH, the word *use* refers to consuming prescribed medications as directed by a healthcare provider as opposed to misuse, which would include any consumption not directly instructed by a healthcare provider, including using drugs without a prescription or in a manner differing from prescribed guidelines.

Prescription opioid analgesics are referred to as generic or brand name drugs to NSDUH respondents and include Hydrocodone, oxycodone, propoxyphene, tramadol, extended-release tramadol, codeine pills, morphine, extended-release morphine, fentanyl, buprenorphine, oxymorphone, extended-release oxymorphone, hydromorphone, extended-release hydromorphone, and methadone. Benzodiazepines are also referred to in the NSDUH as generic and brand name drugs when inquiring of respondents about their drug taking behavior, that is, alprazolam products (Xanax, Xanax XR, generic alprazolam, generic extended-release alprazolam), lorazepam products (Ativan, generic lorazepam), clonazepam products (Klonopin, generic clonazepam), and diazepam products (Valium, or generic diazepam). Further information can be found in the codebook, which is downloadable from the following website: https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health.

2.2.2. Independent variables

The independent variable of theoretical interest is "MML" state, a dummy variable identifying whether respondents resided in a state with an operational MML when they were interviewed. The survey does not include the respondents' state of residence to ascertain which MML state or not is being referred to. Controls for demographic factors such as age, sex, race/ethnicity, health status, health insurance, family income, metropolitan status, marital status, education level, employment status, and cannabis use are also utilized to isolate the effect of MMLs from other potential confounding factors. Table 1 houses further information concerning all variables used in this study.

2.3. Analytic procedures

The multivariate logistic regression procedure in SPSS 28 [40], an appropriate method for predicting the likelihood of a binary outcome (drug use vs. non-use) from a set of predictor variables, was used to analyze the data. The model's suitability was gauged by the Nagelkerke R^2, which adjusts the traditional R^2 for logistic regression, providing a relative measure of fit from 0 (indicating no explained variance) to 1 (indicating perfectly explained variance). Random samples of approximately 2500 cases were analyzed to ensure statistical robustness and comparability between models, given the extensive size of the NSDUH dataset. For clarity, B values describe the association between each predictor variable and the log odds of the binary outcome (slope), and the Exp(B) values are the odds ratios, which are reported in the analytical tables (Tables 2−4).

3. Results

3.1. Characteristics among respondents

Table 1. Description of variables included in the study.

Variable	Coding	Age<50 Proportion (Mean/S.D.)	Age 50+ Proportion (Mean/S.D.)
Opioid use	Coded 0/1. Refers to past year use	0.23	0.31
Benzodiazepine use		0.08	0.11
Opioid + benzodiazepine use		0.04	0.06
MML state	Coded 0/1	0.75	0.77
Female	Coded 0/1	0.56	0.56
Marijuana non-daily smoker	Coded 0/1. Ref. non-smoker past month or never used	0.15	0.06
Marijuana daily smoker		0.06	0.02
Non-Hispanic black	Coded 0/1. Ref. non-Hispanic white	0.12	0.10
Non-Hispanic Asian		0.08	0.05
Hispanic		0.19	0.09
Multi-racial		0.04	0.02
Self-reported health	Scale (1 = excellent, 5 = poor)	(2.32/0.95)	(2.61/1.00)
Health insurance	Coded 0/1	0.88	0.97
Living in poverty	Coded 0/1. Ref. more than 2x federal threshold	0.19	0.10
Living up to 2x federal threshold		0.21	0.17
Living in large metro	Coded 0/1. Ref. living in non-metro	0.45	0.46
Living in small metro		0.41	0.38
Widowed	Coded 0/1. Ref. married	0.00	0.11
Divorced/separated		0.07	0.19
Never married		0.56	0.09
Less than high school	Coded 0/1. Ref. college graduate	0.10	0.09
High school graduate		0.26	0.24
Some college		0.30	0.28
Part-time employed	Coded 0/1. Ref. full-time employed	0.16	0.11
Unemployed		0.06	0.02
Not in labor force		0.22	0.55
		N = 36540	N = 10560

*Note: A coding of 1 indicates the presence of the item the variable is measuring, whereas 0 indicates its absence. Ref. = reference category for a dummy set left out of the model for interpretation and comparison.

This study's results, depicted across multiple tables, highlight distinct demographic, health, and substance use patterns for the different age groups. Table 1 focuses on various demographic and health variables among the two age groups: individuals aged 50 and above (aging) and those below 50. A visual examination of Table 1 shows various age disparities among the respondents, with aging adults reporting higher use of opioids, benzodiazepines, and both opioids and benzodiazepines in the past

year compared to the younger group. In contrast, younger individuals are more apt than the aging respondents to use cannabis. Additionally, aging adults are more likely to live in a MML state, indicate poor health, exhibit elevated health insurance coverage, and report much less participation in the labor force. Marital status and ethnicity distributions also vary markedly between the two age groups, with younger individuals more represented as Hispanic and aging respondents more apt to be married.

3.2. Opioid use

Table 2. Logistic regression analysis predicting opioid use.

	Age<50			Age 50+		
	B	S.E.	Exp(B)	B	S.E.	Exp(B)
MML state	−0.133	0.116	0.876	−0.287**	0.113	0.751
Female	0.324**	0.106	1.382	0.501***	0.106	1.650
Marijuana non-daily smoker	0.498**	0.172	1.646	0.266	0.139	1.305
Marijuana daily smoker	0.365*	0.174	1.441	0.301	0.191	1.352
Non-Hispanic black	0.204	0.159	1.226	0.119	0.162	1.127
Non-Hispanic Asian	−0.382	0.215	0.683	−0.254	0.215	0.776
Hispanic	−0.293*	0.142	0.746	−0.407**	0.147	0.665
Multi-racial	0.387	0.237	1.473	0.289	0.236	1.335
Self-reported health	0.417***	0.054	1.518	0.409***	0.055	1.505
Health insurance	0.059	0.161	1.061	0.264	0.165	1.302
Living in poverty	−0.190	0.152	0.827	−0.061	0.152	0.941
Living up to 2x federal threshold	−0.002	0.134	0.998	0.114	0.129	1.121
Living in large metro	0.053	0.156	1.055	0.063	0.152	1.065
Living in small metro	−0.048	0.153	0.953	−0.042	0.150	0.959
Widowed	−0.674	0.832	0.510	−0.787	1.133	0.455
Divorced/separated	0.292	0.178	1.339	0.511**	0.188	1.668
Never married	−0.304**	0.116	0.738	−0.056	0.117	0.945
Less than high school	0.399*	0.201	1.491	0.454*	0.202	1.575
High school graduate	0.257	0.150	1.293	0.402**	0.152	1.495
Some college	0.435***	0.136	1.545	0.469***	0.135	1.599
Part-time employed	−0.052	0.150	0.950	−0.204	0.149	0.816
Unemployed	−0.032	0.215	0.968	−0.085	0.222	0.918
Not in labor force	−0.042	0.133	0.959	−0.110	0.136	0.896
Constant	−2.555	0.269	0.078	−2.811	0.271	0.060
Nagelkerke R^2	0.111			0.097		
Sample N	2483			2480		

*Note: *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$ (two-tailed tests). B indicates the slope, and the Exp(B) is the Odds Ratio.

Table 2 presents a logistic regression analysis predicting opioid use among the two age groupings. Residing in a MML state is associated with a marked 25% decreased likelihood of opioid use among aging respondents. In contrast, no effect of living in a MML state on opioid use is observed for individuals under 50 years of age. Cannabis use is also associated with increased opioid usage among

younger but not aging respondents. Daily cannabis consumption is linked with younger respondents' higher usage of opioids by 44%, while non-daily cannabis use is associated with higher opioid use by 65%. Not surprisingly, poor reported health is associated with increased opioid use among both aging (51%) and younger (52%) respondents. Females have an enhanced proclivity for opioid use in both age groups. Ethnicity, marital status, and educational attainment also are positively related with opioid use, albeit with varying significance levels. Socioeconomic factors like poverty and employment status appear to have lesser impacts on opioid use. The explanatory power of the two models is modest, suggesting that the variables fail to capture all the variability in opioid use among the respondents.

3.3. Benzodiazepine use

Table 3. Logistic regression analysis predicting benzodiazepine use.

	Age <50			Age 50+		
	B	S.E.	Exp(B)	B	S.E.	Exp(B)
MML state	0.293	0.189	1.340	0.027	0.177	1.028
Female	0.636***	0.168	1.889	0.401*	0.164	1.493
Marijuana non-daily smoker	0.996***	0.224	2.707	0.722***	0.189	2.058
Marijuana daily smoker	0.577*	0.245	1.781	0.915***	0.262	2.496
Non-Hispanic black	−0.729**	0.281	0.482	−1.124**	0.360	0.325
Non-Hispanic Asian	−0.992**	0.405	0.371	−1.562**	0.521	0.210
Hispanic	−0.568**	0.232	0.567	−0.133	0.211	0.876
Multi-racial	−0.289	0.379	0.749	−0.010	0.365	0.990
Self-reported health	0.524***	0.083	1.688	0.450***	0.084	1.568
Health insurance	0.231	0.263	1.260	0.640*	0.306	1.897
Living in poverty	−0.129	0.242	0.879	0.145	0.228	1.156
Living up to 2x federal threshold	0.381*	0.195	1.464	−0.424	0.224	0.654
Living in large metro	0.457	0.260	1.579	0.036	0.244	1.036
Living in small metro	0.457	0.252	1.580	0.099	0.232	1.104
Widowed	1.087	0.626	2.966	0.251	0.848	1.285
Divorced/separated	0.505	0.268	1.658	0.413	0.259	1.512
Never married	0.042	0.178	1.043	−0.331	0.179	0.718
Less than high school	0.670*	0.319	0.512	−0.649*	0.336	0.523
High school graduate	−0.519*	0.230	0.595	−0.136	0.232	0.873
Some college	−0.282	0.198	0.754	−0.001	0.197	0.999
Part-time employed	0.127	0.232	1.135	−0.123	0.237	0.884
Unemployed	0.450	0.303	1.569	0.078	0.345	1.081
Not in labor force	0.323	0.199	1.382	0.024	0.204	1.024
Constant	−5.065	0.460	0.006	−4.195	0.447	0.015
Nagelkerke R^2	0.143			0.115		
Sample N	2477			2482		

*Note: *p < 0.05; **p < 0.01; ***p < 0.001 (two-tailed tests). B indicates the slope, and the Exp(B) is the Odds Ratio.

The logistic regression results for benzodiazepine use are reported in Table 3. No effect for MML state is found for either age group. An assessment of the table also reveals that gender, cannabis use, race, self-reported health, and less than a high school education each have a substantive effect on benzodiazepine usage across both age groups. Cannabis users, both non-daily and daily, in both age cohorts, are more apt to use benzodiazepines. The race of the respondent also is linked with benzodiazepine use, with non-Hispanic black and Asian respondents being less prone to rely on these medications. Both models show modest explanatory power, although slightly better for the younger cohort, indicating the partial capture of variance in benzodiazepine use by the included predictor variables.

3.4. Concurrent use of opioids and benzodiazepines

Table 4. Logistic regression analysis predicting opioid + benzodiazepine use.

	Age <50			Age 50+		
	B	S.E.	Exp(B)	B	S.E.	Exp(B)
MML state	−0.256	0.236	0.774	−0.224	0.270	0.799
Female	0.478*	0.225	1.613	0.250	0.247	1.284
Marijuana non-daily smoker	1.053***	0.249	2.866	0.801**	0.281	2.227
Marijuana daily smoker	1.043***	0.306	2.838	0.951**	0.376	2.589
Non-Hispanic black	−0.681	0.381	0.506	−1.884**	0.738	0.152
Non-Hispanic Asian	−0.563	0.534	0.569	−0.763	0.612	0.466
Hispanic	−0.873**	0.352	0.418	−0.228	0.316	0.796
Multi-racial	0.039	0.431	1.040	0.120	0.473	1.127
Self-reported health	0.562***	0.113	1.755	0.703***	0.127	2.019
Health insurance	0.559	0.412	1.749	0.479	0.454	1.615
Living in poverty	0.235	0.296	1.265	0.403	0.357	1.497
Living up to 2x federal threshold	0.186	0.280	1.204	0.487	0.300	1.627
Living in large metro	0.532	0.340	1.702	0.368	0.378	1.445
Living in small metro	0.298	0.327	1.347	0.378	0.362	1.459
Widowed	--	--	--	0.409	1.198	1.505
Divorced/separated	0.285	0.347	1.329	0.133	0.399	1.143
Never married	-0.236	0.245	0.790	−0.316	0.274	0.729
Less than high school	0.333	0.411	1.395	−1.074*	0.549	0.342
High school graduate	0.268	0.335	1.307	−0.308	0.365	0.735
Some college	0.473	0.295	1.604	0.209	0.303	1.232
Part-time employed	−0.185	0.336	0.831	−0.724	0.405	0.485
Unemployed	0.340	0.398	1.405	−0.253	0.562	0.777
Not in labor force	0.140	0.266	1.150	0.119	0.294	1.126
Constant	−6.008	0.655	0.002	−5.901	0.687	0.003
Nagelkerke R^2	0.127			0.137		
Sample N	2477			2480		

*Note: *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$ (two-tailed tests). B indicates the slope, and the Exp(B) is the Odds Ratio.

Table 4 presents the logistic regression results relating to the concurrent use of opioids and benzodiazepines. Results show little effect of the MML variable on either age group for combined drug use. Cannabis use is found with amplified odds of combining opioids and benzodiazepines in both age groups, with noticeable differences between the age groups in the magnitude of the effect. Self-reported health is related to combined drug use for both age groups. While the racial/ethnic variables and the less than a high school education variable show mixed effects, the remaining variables included in models are observed to have little impact in predicting the combined drug use outcome.

4. Discussion

4.1. Discussion

The principal objective of this work was to investigate the impact of MMLs on the joint and separate use of opioids and benzodiazepines, with a particular emphasis on differences across age demographics (above and below 50 years of age). In addressing that aim, this research endeavor informed the ongoing debate regarding the potential of MMLs to attenuate the iatrogenic and societal costs associated with these substances. The idea that MMLs might inadvertently raise consumption levels, potentially heightening the risk of substance use disorders, was also examined and therefore addressed the supposition that cannabis-friendly environments might be associated with heightened drug taking behaviors.

The results from the present work indicate that the aging are to some extent displacing their use of opioids toward medicinal cannabis. However, such displacement was not observed with the use of benzodiazepines alone or the concurrent use of opioids with benzodiazepines. This information is crucial and has ramifications for the opioid epidemic, but the findings fail to evince any impact on the use of benzodiazepines and by extension their negative consequences associated with use of the drug. While no impact from MMLs was observed for the use of benzodiazepines alone or their combined use with opioids, less patients relying solely on opioids for pain management in MMLs states alleviates the associated negative consequences of that reliance. Furthermore, substituting opioids to any extent can help reduce the potential hazards of concurrently giving benzodiazepines and opioids to individuals who need further pain management as their conditions deteriorate. Thus, while a change in the coadministration of these drugs was not observed in this research, it is possible that patients were able to entirely avoid coadministration or a shift occurred prior to the study period. In other words, it may be that patients previously substituted cannabis for one or both of these drugs. Patients and physicians in such circumstances may have found it more manageable to rely on cannabis or combined medicinal cannabis with benzodiazepines or opioids rather than combining benzodiazepines with opioids, which carries additional risks. Such dynamics may have been operating but went unobserved here due to the data and methodology employed. Though it does not seem from these findings that direct displacement of benzodiazepines with or without opioids toward cannabis is occurring, more investigation is warranted to further elucidate the decision-making processes of physicians and patients concerning treatment with these drugs.

Notwithstanding the above, it would be a mistake to see medicinal cannabis as a panacea for the treatment of aging, chronic pain patients. Attendant issues also exist with medicinal cannabis despite its safer profile than opioids and other drugs for medical management of persistent pain and attendant

complaints in the aging. Clearly, the well-known side effects of medicinal cannabis in this context and population are not without concern.

In large part, medicinal cannabis is well-tolerated and knowledge of its side effects is common. Transient cognitive impairment and memory problems, feelings of euphoria, reduced anxiety, and increased sensory perceptions are notable side effects of cannabis intoxication, with increased anxiety, panic, and disorientation linked with higher doses [41]. In addition, cannabis linked psychosis is a rare risk of cannabis exposure (with THC) predominantly for predisposed patients; however, further investigation finds that schizophrenia among the predisposed is more implicated, which is also exceptionally rare [41]. While such associations may be spurious, caution is warranted and individuals having such a history should avoid the substance.

Also noteworthy are cardiovascular effects of cannabis, including increased heart rate (i.e., tachycardia), associated effects on blood pressure, and for some, heart attack, with the influence on heart rate and blood pressure varying based on dosing and sensitivity that potentially diminishes over time with tolerance [41,42]. Effects linked with the heart and blood pressure likely bear more prominence for the aging population as the prevalence of these conditions increases with advancing age. Caution should consequently be employed when dealing with patients having a history of angina and heart attack, as well as schizophrenia or a family history of such psychotic disorders [41].

In addition to known side effects of cannabis generally, scholars have attempted to clarify any potential dangers associated with depending specifically on medicinal cannabis. Toward that end, there is some limited information available with respect to the aging. Research had evaluated a group of older patients (aged 65 years and above, n = 184, mean age of 81.2 years) who utilized medicinal cannabis to alleviate chronic pain and other ailments finding that nearly 60% of the participants continued using cannabis after 6 months, approximately 85% of the participants reported experienced improvements, while around one-third encountered adverse events [43]. The most often reported negative effects were dizziness (12.1%) and fatigue/sleepiness (11.2%) [43]. Though the reported adverse events seemed tolerable for most patients, there remains concern noted in that research and otherwise that interactions with other pharmaceuticals may yet exist and that fatigue, sleepiness, impairment of coordination or dizziness may lead to accidents and injuries as well as associated hospitalizations for these patients. Furthermore, due to its impact on the heart, including causing tachycardia, and affecting blood pressure, aging individuals may be more susceptible to negative repercussions resulting from these effects compared to younger individuals as discussed above. Thus, even with its safer profile, caution is still warranted for patients seeking to move away from opioids and benzodiazepines toward medical cannabis. It is noteworthy nevertheless that since medicinal cannabis does not depress the respiratory system, the risks from overdose deaths seen with opioids and benzodiazepines appear absent [41].

4.2. Limitations and future research

While the present work offered a step forward in this area, limitations exist. Namely, detailed information about the jurisdictions that the study subjects resided in was not available due to data formatting and design of the NSDUH. Specifically, this deidentified, public use data did not include the actual state that the respondents lived in. Rather, subjects were asked whether or not they lived in a MML state, which resulted in an inability to flesh out further details, such as determining the number of dispensaries, duration of the MML, and other pertinent information regarding a MML state.

However, it is noteworthy that any potential impacts resulting from these more detailed characteristics of MMLs would be arguably and randomly incorporated under being in the category of MML compared to non-MML because of the level of aggregation used in the current study. This mitigates concerns to a degree, but further evaluation is recommended nonetheless.

Specifically, while beyond the methodology employed here, there are those who contend that the MML passage date is an insufficient measure in this context as there are numerous factors that influence the implementation of legislation and the use of cannabis by patients [44]. Therefore, it is argued that the implementation date is the better measure. While this was beyond the scope of the present work and there was an inability to identify this aspect with this data, we offer a perspective and believe that our approach is sound. The MML states (see Appendix) that would have been identified in the NSDUH sample show that the vast majority of statutes have been longstanding. Kentucky (2023 - post study survey year, not applicable), Mississippi (2022 - during survey year and might have been coded as 0 – non-MML by the NSDUH given their reported methodology), Alabama (2021 - during survey and might have been coded as 0 – non-MML by the NSDUH given their reported methodology), Virginia (2021 - during survey and might have been coded as 0 – non-MML by the NSDUH given their reported methodology), and South Dakota (2020), however, are the exception and would have had limited time for implementation compared to the rest of the states. However, given four of these states were not relevant for this analysis because they were either post survey timeframe or reasonably coded 0 as non-MML because the statute went into effect during survey administration, there is less concern here. Since most statutes have been in effect for a significant number of years, some for multiple decades, and in particular for such an extended time prior to the survey years used in this study, we contend that the concern over enactment versus implementation of the statute does not reasonably preclude the present approach or findings, see Appendix for the years various MMLs were passed. In almost all cases, the several years it may have taken for implementation is also many years prior to a respondent being identified as living in a MML state. It is not likely hindering their access. However, for patients from South Dakota noted above, there may be access issues thus limiting observation of the impact of MMLs for these patients. Nevertheless, if there was an access issue from a state, it would bias the results toward showing no impact from the law -not an impact because the law would not be in operation. Given this, we have confidence in the findings to the extent that they mirror others' research that find displacement from opioids to cannabis. In that way, it is a replication of these findings but specified to a population of aging Americans. This suggests that our findings are robust. Further scrutiny of these details with another data set, however, is thus left for future work.

The present study also did not include indices of difficulty in patient access to medicinal cannabis, such as registries, qualifying criteria, doctor licensing, sources and quantities of cannabis supplied to patients, and legal change, because such variables were unavailable as noted above. However, this is not entirely problematic. To further elaborate, the aggregate MML variable assumes the contextual variables established by Pacula and associates [44]. For example, chronic pain is the most prevalent qualifying condition across MML legislation, making it a constant in the analysis and assumed in the aggregate by the simple presence of a MML statute. Furthermore, if differences in MMLs hinder physicians and patients from acquiring medicinal cannabis, the legislation will have little impact. Nonetheless, significant findings support the validity of our models' conclusions, which are consistent with diverse research indicating displacement to varying degrees is occurring, particularly for opioids. This also demonstrates that method effects, such as those that occur from model misspecification through omitting crucial variables or other factors, are insufficient to supplant displacement in that

context. Given this, researchers and others can have some confidence that medical cannabis is replacing some pharmaceuticals through MMLs, despite the aforementioned issues, as the consistency of findings across samples, methodologies, and levels of analysis supports this assumption. Nevertheless, in accordance with scholars [44], future research would benefit from including contextual and statutory factors that may influence the availability of medicinal cannabis in order to inform policymakers [38].

Future work should also seek to specifically vet the adverse effects of cannabis on the aging population. Such information was not available for the current work. Presently, research assessing cannabis side effects tends to focus on the general population of patients. However, the aging are different and research should be extended to examine these higher risk populations. For example, although the occurrence of cannabis related psychosis with persistence is rare and the research in this area is muddled, newer evidence fails to evince a connection between the legalization of cannabis and a rise in insurance claims connected to the mental condition [45]. While this finding runs counter to other evidence examining this area [46] and is certainly not conclusive, the results are encouraging and counter alarms concerning this risk with the proliferation of medicinal cannabis generally. It is important to note too that while the aging were not the target in the study, different populations presented with different levels of adverse event risk. In a supplemental analysis to that study, nuanced findings were present. Results demonstrated a significantly increased rate of psychosis for people aged 55 to 64 years old in recreational cannabis states [45]. Such work highlights the need to expressly investigate the presence and impact of side effects on the aging in MMLs in order to gain a thorough grasp of the nuance and hazards involved in the promotion of cannabis as a treatment alternative. Clearly, all areas of adverse event risk for the aging demand added scrutiny within the appropriate and varying contexts.

Finally, it is noteworthy that while we did observe a significant effect from MMLs on the use of opioids among the aging, what was conspicuously absent was an impact of the laws on the use of opioids and/or benzodiazepines among the younger populations. This observation is not unexpected, considering the prevalence of pain disorders among the aging. Nevertheless, this underscores the necessity of conducting a more thorough assessment of the effects of these laws on groups from a variety of demographics in order to gain a more comprehensive understanding of the potential effect of these statutes on alleviating the opioid burden for specific populations. While beyond the scope of the present work, our results indicate that further investigation in this area is warranted, particularly given the extent of harm attributable to these drugs to individuals and society.

5. Conclusions

The current work provided evidence that the aging are substituting opioids for medicinal cannabis. This carries implications for attenuating the consequences of the opioid epidemic. However, effects were not observed in the same manner for benzodiazepines. Irrespective, there is hope that the negative consequences of coadministration of opioids and benzodiazepines will diminish with time as replacing either of these drugs with medicinal cannabis will lessen the risk of death for these patients. Even so, there is much left to understand concerning the circumstances and contexts with which the aging are most apt to utilize medicinal cannabis. While medicinal cannabis does not pose the same risks as opioids and benzodiazepines with respect to adverse events, drug interactions, and overdose related fatalities, further vetting concerning the adverse event risk of medicinal cannabis to the aging population is crucial.

Author contributions

All authors participated to varied degrees in the conceptualization, methodology, validation, data curation, and composition of this work and have reviewed and consented to the published version of the manuscript.

Use of AI tools declaration

The authors declare that they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

All authors declare no conflict of interest in this paper.

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