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ORIGINAL STUDY

A survey of medical cannabis use during perimenopause and postmenopause

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Abstract

Objective: Expanding access to legal cannabis has dovetailed with increased interest in medical cannabis (MC) use; however, there is a paucity of research examining MC use to alleviate menopause-related symptoms. This survey study assessed patterns of MC use in perimenopausal and postmenopausal individuals.

Methods: Participants (perimenopausal, $n = 131$; postmenopausal, $n = 127$) completed assessments of menopause-related symptomatology and cannabis use, including modes of use, type of use, and menopause-related symptoms addressed by MC use.

Results: Most participants reported current cannabis use (86.1%) and endorsed using MC for menopause-related symptoms (78.7%). The most common modes of use were smoking (84.3%) and edibles (78.3%), and the top menopause-related symptoms for MC use were sleep disturbance (67.4%) and mood/anxiety (46.1%). Relative to postmenopausal participants, perimenopausal participants reported significantly worse menopause-related symptomatology on the vasomotor and psychosocial subscales of the Menopause-Specific Quality of Life Questionnaire (Ps ≤ 0.04), including greater burden of anxiety ($P = 0.01$) and hot flash ($P = 0.04$) symptoms. In addition, perimenopausal participants reported higher incidence of depression ($P = 0.03$) and anxiety diagnoses ($P < 0.01$), as well as increased use of MC to treat menopause-related mood/anxiety symptoms relative to postmenopausal participants ($P = 0.01$).

Conclusions: Results suggest that many individuals are currently using MC as an adjunctive treatment for menopause-related symptoms, particularly sleep disturbance and mood/anxiety. Future research should examine the impact of different MC use characteristics (e.g., cannabinoid profiles) on the efficacy of MC use for menopause-related symptoms. Increased severity and prevalence of mood and anxiety symptoms in perimenopausal participants suggest promising targets for clinical trials of cannabinoid-based therapies.

Key Words: Cannabinoids – Cannabis – Marijuana – Menopause – Women's health – Survey.

Hormonal changes associated with menopause include significant fluctuations in estrogen and progesterone that can cause a variety of symptoms, including hot flashes, sleep disturbance, depression, and anxiety.[1] Vasomotor symptoms (e.g., hot flashes, night sweats) associated with dilation of blood vessels are most commonly reported (~60%-80%

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endorsement)[2] and may mediate other menopause-related symptoms, such as disturbances in sleep, mood, and cognitive function.[3,4] Overall, menopause-related symptoms represent a significant psychosocial and economic burden with more severe symptoms associated with increased shame, loss of productivity, and lower quality of life.[5,6] Although several treatment options (e.g., hormone therapy) are effective for treating menopause-related symptoms, most are associated with negative side effects (e.g., mood swings and fatigue) and increased risk of developing cancer.[7,8] Therefore, it is important to examine novel treatment strategies for menopausal symptoms that are both efficacious and have limited side effects.

The endocannabinoid system is involved in a variety of physiological and psychological processes (e.g., regulating body temperature, mood, anxiety, sleep), and evidence suggests that this system significantly impacts fertility and reproduction.[9] Specifically, the human ovary produces the endogenous cannabinoid anandamide with peak plasma levels occurring at ovulation and correlating with estrogen levels, suggesting that anandamide production may be controlled by this hormone.[10,11] Preclinical research using ovariectomy to simulate menopause demonstrated that estrogen administration significantly increased expression of cannabinoid receptors and plasma levels of anandamide; these responses were estrogen receptor dependent.[12] In addition, cannabinoid treatments, including administration of anandamide, as well as antagonists of cannabinoid degradative enzymes, improve postovariectomy complications and reduce anxiety.[13-15] Further, administration of cannabinoids typically results in vasorelaxation,[16] suggesting that cannabinoid-based therapies may be particularly salient for treating vasomotor symptoms of menopause. In particular, estrogen deficiency results in downregulation of systems involved in hemodynamic regulation and is associated with vasomotor symptoms; 2 weeks of treatment with anandamide has been shown to reverse this downregulation in ovariectomized rats.[15] Taken together, research indicates that medical cannabis (MC) may be a nonhormone treatment option with the potential to alleviate menopause-related symptoms with greater efficacy and possibly fewer side effects relative to existing treatments.

Given expanding legalization of MC, increasing numbers of individuals are exploring MC to alleviate symptoms for a variety of conditions; estimates indicate more than 5.5 million MC patients are registered in the United States.[17] Several observational studies have demonstrated that MC use is associated with various clinical benefits, including improvements on measures of anxiety, mood, sleep, and pain,[18-24] as well as cognitive improvement after treatment.[18,19,21] In addition, historical texts suggest that cannabinoid-based therapies have been utilized as safe and efficacious treatments for menopause-related symptoms throughout history.[25] However, although some recent work has focused on MC treatment for gynecological diseases, such as endometriosis,[26,27] few studies have examined the prevalence and efficacy of MC to alleviate menopause-related symptoms.[28]

The most comprehensive study to date used a survey to assess the impact of expectancy effects on cannabis use in perimenopausal and postmenopausal individuals, the majority of whom (87.8%) reported at least monthly cannabis use.[29] Results indicated that menopause symptoms correlated with frequency of cannabis use and that expectancies of cannabis use mediated this relationship. Interestingly, participants did not report equal expectancies of cannabis use for all menopause-related symptoms; the greatest expectancies were for cannabis to relieve symptoms of joint/muscle discomfort, irritability, sleep problems, depression, anxiety, and hot flashes. Although this study provides valuable insight regarding the impact of treatment expectancy effects, more research is critically needed.

Accordingly, this survey study was designed to assess cannabis use in periperimenopausal and postmenopausal individuals. Given the wide variety of MC products currently commercially available, it is critical to identify which products are most commonly used. Therefore, this study assessed the modes of cannabis use endorsed by perimenopausal and postmenopausal individuals and the specific menopause-related symptoms indicated for MC use. Additional analyses examined variables associated with MC use for menopause-related symptoms. This information will help inform next steps for clinical trials designed to assess the efficacy of specific cannabinoid-based products.

METHODS

This study was approved by the Mass General Brigham (MGB) Institutional Review Board. Before beginning the survey, study procedures, risks, and benefits were presented to all participants; voluntary consent was required for participation. Average time to complete the study was ~16 minutes. Compensation was not provided.

Participants

Perimenopausal and postmenopausal participants were recruited through online postings on social media platforms (e.g., Facebook, Twitter, Reddit) and Rally, the MGB online recruitment platform. Targeted advertising was used to direct recruitment efforts toward individuals interested in women's health, as well as cannabis and cannabinoids. Study enrollment was conducted between March 3, 2020, and April 16, 2021, using voluntary response sampling to generate a nonprobability sample. Eligible participants included individuals who were 18 years or older, assigned female at birth, and reported perimenopausal or postmenopausal status.

Survey content

Participants completed self-report questionnaires via Research Electronic Data Capture,[30,31] which queried demographic information, self-reported medical conditions and medications, menopause-related symptoms, cannabis use in general, and MC use for menopause-related symptoms. Clinical scales completed by participants included the Menopause-Specific Quality of Life Questionnaire (MENQOL),[32] Day-to-Day Impact of Vaginal Aging Questionnaire (DIVA),[33] and the Arizona Sexual Experiences Scale (ASEX).[34] The MENQOL assesses the frequency and bothersomeness of 29 menopause-related symptoms over the past month. Given the significant overlap between the DIVA, ASEX, and MENQOL questions, only two of the four MENQOL domains (vasomotor and psychosocial) are reported.

Domain scores range from 1 to 8, with higher scores representative of more bothersome symptoms. The DIVA assesses the incidence of common vaginal symptoms and their effect on day-to-day life in five domains (daily living, emotional well-being, sexual functioning, self-concept, and body image). Each domain score ranges from 0 to 4, with higher scores indicating greater impact of symptoms. A total score was calculated by summing the five domain totals (range: 0-20). The ASEX assesses sexual health and sexual dysfunction; scores range from 5 to 30, with higher scores denoting greater dysfunction.

Participants also completed questions about their history of cannabis use and current cannabis use, including modes of use and type of use (i.e., medical use only, recreational use only, or mixed medical/recreational use). In addition, MC use for specific menopause-related symptoms was queried, as well as general interest in MC use for menopause-related symptoms and what would make participants more comfortable with MC use. Participants who did not endorse interest in MC use for menopause-related symptoms were queried about reasons for lack of interest.

Statistical analyses

For the primary analyses, χ^2 tests (for frequency data) and one-way analyses of variance (for scalar data) were conducted to assess differences between perimenopausal and postmenopausal participants. Exploratory binary logistic regression analyses examined variables associated with endorsing MC use for menopause-related symptoms via backward stepwise models calculated using removal testing based on the probability of the likelihood ratios (P(out) = 0.05). Initially, the predictor variables for regression analyses were demographic variables: age, race, ethnicity, income, education, marital status, and employment status, as well as menopause-related variables: menopause status, DIVA total score, MENQOL vasomotor and psychosocial subscale scores, and ASEX total score. However, race and ethnicity were removed from the models due to unequal

TABLE 1. *Demographic comparison of perimenopausal and postmenopausal survey participants (two-tailed)*

Demographic variables	All respondents, N = 258	Perimenopausal, n = 131	Postmenopausal, n = 127	Perimenopausal vs postmenopausal
Gender identity	n (%)	n (%)	n (%)	χ^2 = 2.00, P = 0.37
Female	256 (99.2%)	130 (99.2%)	126 (99.2%)	—
Male	1 (0.4%)	0 (0.0%)	1 (0.8%)	—
Nonbinary	1 (0.4%)	1 (0.8%)	0 (0.0%)	—
Current age	Mean ± SD	Mean ± SD	Mean ± SD	ANOVA
	51.37 ± 5.63	**49.07 ± 4.25**	**53.74 ± 5.90**	***F* = 53.57, *P* < 0.01**
Race[a,b]	n (%)	n (%)	n (%)	χ^2 (P)
American Indian	5 (2.0%)	3 (1.2%)	2 (0.8%)	0.16 (0.69)
Asian	4 (1.6%)	3 (2.3%)	1 (0.8%)	0.92 (0.34)
Black/African American	6 (2.4%)	1 (0.8%)	5 (4.0%)	2.93 (0.09)
White	246 (96.9%)	128 (98.5%)	118 (95.3%)	2.27 (0.13)
Ethnicity[c]	n (%)	n (%)	n (%)	χ^2 = 0.12, P = 0.73
Hispanic	13 (5.3%)	6 (4.8%)	7 (5.8%)	—
Non-Hispanic	231 (94.7%)	118 (95.2%)	113 (94.2%)	—
Income level[d]	n (%)	n (%)	n (%)	χ^2 = 1.95, P = 0.58
$0-$49,999	39 (20.3%)	17 (17.0%)	22 (23.9%)	—
$50,000-$99,999	72 (37.5%)	39 (39.0%)	33 (35.9%)	—
$100,000-$149,999	43 (22.4%)	25 (25.0%)	18 (19.6%)	—
$150,000 and up	38 (19.8%)	19 (19.0%)	19 (20.7%)	—
Education level[e]	n (%)	n (%)	n (%)	χ^2 = 6.07, P = 0.11
GED/high school diploma	16 (7.5%)	7 (6.3%)	9 (8.7%)	—
Some college/training/Associates	60 (28.0%)	25 (22.5%)	35 (34.0%)	—
Bachelor's	90 (42.1%)	55 (49.5%)	35 (34.0%)	—
Master's/Doctoral	48 (22.4%)	24 (21.6%)	24 (23.3%)	—
Marital status[e]	n (%)	n (%)	n (%)	χ^2= 5.89, P = 0.12
Single	31 (14.5%)	13 (11.7%)	18 (17.5%)	—
In a relationship	41 (19.2%)	18 (16.2%)	23 (22.3%)	—
Married	118 (55.1%)	70 (63.1%)	48 (46.6%)	—
Divorced/widowed	24 (11.2%)	10 (9.0%)	14 (13.6%)	—
Employment status[e]	n (%)	n (%)	n (%)	χ^2 = 0.27, P = 0.60
Employed (at least part-time)	145 (67.8%)	77 (69.4%)	68 (46.9%)	—
Unemployed/retired/disabled	69 (32.2%)	34 (30.6%)	35 (34.0%)	—
Self-reported medical conditions[f]	Median (IQR)	Median (IQR)	Median (IQR)	Mann-Whitney
No. medical conditions[g]	2 (2)	2 (2)	2 (2)	Z = −1.11, P = 0.27

Bold numbers are significant at $P \leq 0.05$.
ANOVA, analysis of variance; GED, general educational development; IQR, interquartile range; SD, standard deviation.
[a]Respondents were instructed to select all items that applied.
[b]n = 254 (perimenopausal = 130; postmenopausal = 124).
[c]n = 244 (perimenopausal = 124; postmenopausal = 120).
[d]n = 192 (perimenopausal = 100; postmenopausal = 92).
[e]n = 214 (perimenopausal = 111; postmenopausal = 103).
[f]n = 251 (perimenopausal = 127; postmenopausal = 124).
[g]Number of medical conditions was calculated using categories of medical conditions (e.g., psychiatric, pain, uterine/vaginal, sleep, cardiovascular/hematological, endocrine, oncological, gastrointestinal, dermatological, neurological/neurodegenerative, and other).

weighting for White (96.9%) or non-Hispanic (94.7%) participants; variance proportion calculations indicated our sample did not have enough data from non-White or Hispanic respondents to properly model race and ethnicity. In addition, collinearity analyses indicated that both marital status and employment status were significantly associated with income; as a result, marital status and employment were removed from the final analyses. All analyses were two-tailed ($\alpha = 0.05$) and were conducted using Statistical Package for Social Sciences version 24 (IBM Corp., Armonk, NY).

RESULTS

A total of 258 participants (perimenopausal, $n = 131$; postmenopausal, $n = 127$) were included in the analyses (recruitment flow chart in Supplemental Figure 1, http://links.lww.com/MENO/A996). Most participants completed the entire survey ($n = 214$, 82.9%). Missingness analyses were completed, and number of participants who completed the survey did not differ between menopause status (perimenopausal vs postmenopausal), suggesting that the primary independent variable was not biased by missingness. In addition, analyses were designed to use all available data for each item to further reduce the impact of missingness.

Demographics

Participants were primarily White, non-Hispanic, middle-aged women (age = 51.37 ± 5.63 years) who reported an annual income reflecting middle-class status or above, completed an undergraduate degree or higher, were married or in a relationship, and were employed at least part-time (Table 1). Perimenopausal and postmenopausal participants were well matched on all demographic variables except for age; unsurprisingly, perimenopausal participants were significantly younger than postmenopausal participants ($P < 0.01$). With regard to general medical conditions and conventional medication use, perimenopausal participants reported significantly greater frequency of psychiatric conditions than postmenopausal participants ($P = 0.03$), which was driven by greater frequency of anxiety ($P < 0.01$) and depression ($P = 0.03$; Supplemental Table 1, http://links.lww.com/MENO/A997). Postmenopausal participants reported significantly greater frequency of neurological/neurodegenerative conditions than perimenopausal participants ($P < 0.01$), which was driven by significantly greater frequency of glaucoma ($P = 0.04$). No significant differences between perimenopausal and postmenopausal participants were observed for types of medication used (Supplemental Table 2, http://links.lww.com/MENO/A998).

Menopause-related symptoms

Relative to postmenopausal participants, perimenopausal participants reported significantly worse vasomotor ($P = 0.04$) and psychosocial ($P = 0.02$) menopause-related symptoms on the MENQOL (Table 2). Additionally, postmenopausal participants reported significantly worse sexual dysfunction measured by ASEX total score compared to perimenopausal participants ($P = 0.05$). Perimenopausal and postmenopausal participants reported similar scores on all subscales and total score of the DIVA. Ranking of symptom severity for individual items from the MENQOL indicated the top three most burdensome menopause-related symptoms among all participants were sleep, tiredness, and lack of energy. Interestingly, the severity of menopause-related symptoms did not differ between groups for most symptoms; however, anxiety ($P = 0.01$) and hot flashes ($P = 0.04$) were both rated as significantly more burdensome by perimenopausal participants.

TABLE 2. *Menopause-related clinical scales: comparison of perimenopausal and postmenopausal survey participants (two-tailed)*

Clinical scales	All respondents, $N = 251$ Mean ± SD	Perimenopausal, $n = 127$ Mean ± SD	Postmenopausal, $n = 124$ Mean ± SD	Perimenopausal vs postmenopausal F (P)
Menopause-related clinical scales				
MENQOL[a]				
Vasomotor	4.26 ± 2.31	**4.58 ± 2.15**	**3.93 ± 2.44**	**4.40(0.04)**
Psychosocial	4.10 ± 1.82	**4.39 ± 1.76**	**3.81 ± 1.83**	**5.85 (0.02)**
DIVA[b]				
Total	3.85 ± 3.38	3.68 ± 3.36	4.03 ± 3.39	0.61 (0.44)
Daily living	0.46 ± 0.69	0.42 ± 0.65	0.47 ± 0.73	0.23 (0.63)
Emotional	0.66 ± 0.94	0.67 ± 0.97	0.65 ± 0.92	0.04 (0.85)
Sexual function	1.29 ± 1.15	1.18 ± 1.14	1.40 ± 1.16	2.05 (0.15)
Self-concept	1.46 ± 1.37	1.40 ± 1.31	1.52 ± 1.43	0.37 (0.54)
ASEX[a]				
Total	17.73 ± 5.02	**17.08 ± 5.04**	**18.40 ± 4.93**	**3.82 (0.05)**
Menopause-related symptoms (based on individual items from the MENQOL)				
Top 3 most burdensome symptoms[b]				
(1) Sleep	5.26 ± 2.64	5.42 ± 2.57	5.10 ± 2.71	0.81 (0.37)
(2) Tiredness	5.01 ± 2.43	5.32 ± 2.35	4.69 ± 2.48	3.84 (0.05)
(3) Lack of energy	4.80 ± 2.52	5.12 ± 2.37	4.47 ± 2.64	3.62 (0.06)
Symptoms with significant between-groups differences[b]				
Anxiety	4.38 ± 2.53	**4.85 ± 2.46**	**3.90 ± 2.52**	**7.95 (0.01)**
Hot flashes	4.59 ± 2.55	**4.95 ± 2.36**	**4.22 ± 2.69**	**4.48 (0.04)**

Bold numbers are significant at $P \leq 0.05$.

ASEX, Arizona Sexual Experience Scale; DIVA, Day-to-Day Impact of Vaginal Aging Scale; MENQOL, Menopause-Specific Quality of Life Scale; SD, standard deviation.

[a] $n = 219$ (perimenopausal = 111; postmenopausal = 108).

[b] $n = 223$ (perimenopausal = 111; postmenopausal = 112).

Cannabis use

The majority of all participants reported at least one lifetime use of cannabis (92.0%), with average age of first use occurring in adolescence/emerging adulthood (19.57 ± 9.73; Table 3). Additionally, 83.5% of participants endorsed a history of regular cannabis use, defined as a period using cannabis at least once a month, and 86.1% reported current cannabis use. Approximately half of the current cannabis users (51.5%) reported mixed medical/recreational use; recreational only (30.8%) and medical only (17.7%) use were less frequently endorsed. The three most common current modes of using cannabis were smoking (e.g., joint, bowl, bong; 84.3%), edibles (78.3%), and vaping oil (52.6%). Perimenopausal and postmenopausal participants endorsed similar percentages for almost all modes of use, except for edibles; a significantly larger percentage of perimenopausal participants reported using edibles ($P = 0.03$). No differences were detected between perimenopausal and postmenopausal participants for current/past cannabis use, type of cannabis use, and age "first tried" cannabis.

Cannabis use for menopause-related symptoms

For participants who reported at least one lifetime use of cannabis, most reported using cannabis at some point to treat menopause-related symptoms (78.7%; Table 4). The top three menopause-related symptoms participants reported using cannabis to treat were sleep disturbance (67.4%), mood/anxiety (46.1%), and libido (30.4%). Frequency of endorsing MC use for specific menopause-related symptoms was similar between groups, except for mood/anxiety; more perimenopausal participants reported using cannabis to treat mood/anxiety relative to postmenopausal participants ($P = 0.01$).

Although the majority of participants reported using MC to treat menopause-related symptoms, most participants (78.5%) also indicated they were interested in additional exploration of cannabis-based products (e.g., vaginal suppositories) for these symptoms. For those not interested in exploring cannabis products for menopause-related symptoms, the top 2 reasons cited were lack of knowledge (39.1%) and no need/symptoms well-managed (32.6%). Additionally, all participants provided information on what would make them more comfortable using cannabis to treat menopause-related symptoms; the top two items endorsed were scientific data supporting efficacy (54.2%) and the ability to order online/mail order (54.5%). Backward stepwise binary logistic regression analyses (Table 5) indicated that use of MC to treat menopause-related symptoms was significantly associated with number of medical conditions ($P < 0.01$), menopause status ($P = 0.01$), and education level ($P = 0.05$). Specifically, greater number of medical conditions was associated with *increased* odds of MC use (OR = 1.67), whereas postmenopausal status and higher education level were associated with *reduced* odds of MC use (OR = 0.35 and 0.64, respectively).

DISCUSSION

The current study provides vital information about patterns of MC use among both peri- and postmenopausal individuals in a

TABLE 3. *Cannabis use information: comparison of perimenopausal and postmenopausal survey participants (two-tailed)*

Cannabis use variables	All respondents, $N = 250$ *n* (%) or Mean ± SD	Perimenopausal, $n = 126$ *n* (%) or Mean ± SD	Postmenopausal, $n = 124$ *n* (%) or Mean ± SD	Perimenopausal vs postmenopausal χ^2 or F (P)
Tried cannabis (lifetime)				0.94 (0.33)
No	20 (8.0%)	8 (6.3%)	12 (9.7%)	—
Yes	230 (92.0%)	118 (93.7%)	112 (90.3%)	—
Age first tried cannabis [a]	19.57 ± 9.73	20.73 ± 10.52	18.34 ± 8.70	3.50 (0.06)
History of regular cannabis use[a,b]				0.03 (0.86)
No	38 (16.5%)	19 (16.1%)	19 (17.0%)	—
Yes	192 (83.5%)	99 (83.9%)	93 (83.0%)	—
Cannabis use (current)[a]				1.70 (0.19)
No	32 (13.9%)	13 (11.0%)	19 (17.0%)	—
Yes	198 (86.1%)	105 (89.0%)	93 (83.0%)	—
Type of current cannabis use[c]				1.29 (0.53)
Mixed use (recreational and medical)	102 (51.5%)	51 (48.6%)	51 (54.8%)	—
Recreational only	61 (30.8%)	36 (34.3%)	25 (26.9%)	—
Medical only	35 (17.7%)	18 (17.1%)	17 (18.3%)	—
Current modes of use[a,d]				
Smoke (e.g., joint, bowl, bong)	194 (84.3%)	95 (80.5%)	99 (88.4%)	2.71 (0.10)
Edible	180 (78.3%)	**99 (83.9%)**	**81 (72.3%)**	**4.53 (0.03)**
Vape oil	121 (52.6%)	57 (48.3%)	64 (57.1%)	1.80 (0.18)
Tincture	93 (40.4%)	52 (44.1%)	41 (36.6%)	1.33 (0.25)
Vape flower	86 (37.4%)	42 (35.6%)	44 (39.3%)	0.34 (0.56)
Topical	59 (25.7%)	26 (22.0%)	33 (29.5%)	1.66 (0.20)
Capsule	27 (11.7%)	14 (11.9%)	13 (11.6%)	<0.01 (0.95)
Transdermal	9 (3.9%)	2 (1.7%)	7 (6.3%)	3.17 (0.08)
Suppository/lubricant	8 (3.5%)	4 (3.4%)	4 (3.6%)	0.01 (0.94)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	—

Bold numbers are significant at $P \leq 0.05$.
SD, standard deviation.
[a]Only answered if respondent reported trying cannabis ($n = 230$; perimenopausal = 118; postmenopausal = 112); one postmenopausal respondent did not provide age of last cannabis use ($n = 111$).
[b]Regular cannabis use was defined as the respondent reporting any period of time using cannabis at least once per month.
[c]Only answered if respondent reported current cannabis use ($n = 198$; perimenopausal = 105; postmenopausal = 93).
[d]Respondents were instructed to select all items that applied.

TABLE 4. *Medical cannabis use for menopause-related symptoms: comparison of perimenopausal and postmenopausal survey participants (two-tailed)*

Medical cannabis use variables	All respondents, $N = 214$ *n* (%)	Perimenopausal, $n = 111$ *n* (%)	Postmenopausal, $n = 103$ *n* (%)	Perimenopausal vs postmenopausal χ^2 (*p*)
Medical cannabis use for menopause-related symptoms[a,b]				
Sleep disturbance	155 (67.4%)	85 (72.0%)	70 (62.5%)	2.38 (0.12)
Mood/anxiety	106 (46.1%)	**64 (54.2%)**	**42 (37.5%)**	**6.48 (0.01)**
Libido	70 (30.4%)	41 (34.7%)	29 (25.9%)	2.13 (0.15)
Sexual pleasure	43 (18.7%)	24 (20.3%)	19 (17.0%)	0.43 (0.51)
Hot flashes	30 (13.0%)	15 (12.7%)	15 (13.4%)	0.02 (0.88)
Night sweats	29 (12.6%)	14 (11.9%)	15 (13.4%)	0.12 (0.73)
Other body pain	13 (5.7%)	9 (7.6%)	4 (3.6%)	1.77 (0.18)
Vaginal dryness	9 (3.9%)	5 (4.2%)	4 (3.6%)	0.07 (0.80)
Vaginal pain	8 (3.5%)	6 (5.1%)	2 (1.8%)	1.86 (0.17)
Other	4 (1.7%)	2 (1.7%)	2 (1.8%)	<0.01 (0.96)
Not used for menopause	49 (21.3%)	22 (18.6%)	27 (24.1%)	1.02 (0.31)
Interested in exploring medical cannabis or hemp-based products for menopause-related symptoms?				0.38 (0.54)
No	46 (21.5%)	22 (19.8%)	24 (23.3%)	—
Yes	168 (78.5%)	89 (80.2%)	79 (76.7%)	—
If not interested, why?[b,c]				
Lack of knowledge	18 (39.1%)	9 (40.9%)	9 (37.5%)	0.06 (0.81)
No need/symptoms well-managed	15 (32.6%)	5 (22.7%)	10 (41.7%)	1.87 (0.17)
Access to products	7 (15.2%)	5 (22.7%)	2 (8.3%)	1.84 (0.18)
Fear of intoxication	7 (15.2%)	5 (22.7%)	2 (8.3%)	1.84 (0.18)
Cost	7 (15.2%)	4 (18.2%)	3 (12.5%)	0.29 (0.59)
Fear of the unknown	5 (10.9%)	1 (4.5%)	4 (16.7%)	1.74 (0.19)
Previous negative side effects	4 (8.7%)	3 (13.6%)	1 (4.2%)	1.30 (0.26)
Tried before and did not work	3 (6.5%)	1 (4.5%)	2 (8.3%)	0.27 (0.60)
Do not want to use suppositories	3 (6.5%)	1 (4.5%)	2 (8.3%)	0.27 (0.60)
Partner acceptance	2 (4.3%)	1 (4.5%)	1 (4.2%)	<0.01 (0.95)
Physical limitations	1 (2.2%)	1 (4.5%)	0 (0.0%)	1.12 (0.29)
Shame	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
What would make you more comfortable using a medical cannabis or hemp-based product for menopause-related symptoms? [b]				
Data to support its use	117 (54.7%)	61 (55.0%)	56 (54.4%)	0.01 (0.93)
Able to order online/mail order	116 (54.2%)	58 (52.3%)	58 (56.3%)	0.35 (0.55)
Education about the risks/benefits	76 (35.5%)	43 (38.7%)	33 (32.0%)	1.05 (0.31)
Buying over-the-counter	60 (28.0%)	31 (27.9%)	29 (28.2%)	<0.01 (0.97)
Already use/not uncomfortable	8 (3.7%)	6 (5.4%)	2 (1.9%)	1.78 (0.18)
No need for use	5 (2.3%)	2 (1.8%)	3 (2.9%)	0.29 (0.59)
Legalization	3 (1.4%)	3 (2.7%)	0 (0.0%)	2.82 (0.09)
Other	6 (2.8%)	3 (2.7%)	3 (2.9%)	0.01 (0.97)

Bold numbers are significant at $P \leq 0.05$.
[a]Only answered if respondent reported trying cannabis ($n = 230$; perimenopausal = 118; postmenopausal = 112).
[b]Respondents were instructed to select all items that applied.
[c]Only answered if respondent reported not interested in exploring medical cannabis/hemp for menopause-related symptoms ($n = 46$; perimenopausal = 22; postmenopausal = 24).

sample primarily comprised of current cannabis consumers. The majority of participants endorsed MC use to treat menopause-related symptoms, and regression analyses indicated increased number of medical conditions, perimenopausal status, and lower education level were significantly associated with increased odds of MC use for menopause-related symptoms. Interestingly, although

TABLE 5. *Stepwise regression models assessing predictors of medical cannabis use for menopause-related symptoms (two-tailed)*

Cannabis use for menopause-related symptoms	*P*	OR	OR 95% CI LB	OR 95% CI UB
Backward stepwise[a]				
Number of medical conditions[b]	**<0.01**	**1.67**	**1.21**	**2.30**
Menopause status[c]	**0.01**	**0.35**	**0.16**	**0.76**
Education level[d]	**0.05**	**0.64**	**0.41**	**0.99**

Bold numbers are significant at $P \leq 0.05$.
LB, lower bound; OR, odds ratio; UB, upper bound.
[a]Model summary: $\chi^2(3, N = 178) = 21.028$, $p < 0.001$.
[b]Number of medical conditions is a count variable calculated using categories of medical conditions (e.g., psychiatric, pain, uterine/vaginal, sleep, cardiovascular/hematological, endocrine, oncological, gastrointestinal, dermatological, neurological/neurodegenerative, and other).
[c]Menopause status: perimenopausal (ref.) versus postmenopausal.
[d]Education level is a ranked variable (1-4): 1, general educational development (GED)/high school diploma; 2, some college/training/Associate's degree; 3, Bachelor's degree; 4, Master's/Doctoral degree.

smoking and edibles were the most commonly endorsed modes of use, six different current modes of use were endorsed by at least a quarter of participants; this finding dovetails with previous research indicating that MC patients frequently seek a broad variety of products with diverse cannabinoid profiles.[35,36]

The top menopause-related symptoms indicated for MC use were sleep disturbance and mood/anxiety. Interestingly, studies have shown some evidence for differential prevalence of anxiety and depressive symptoms during peri- and postmenopause.[37,38] In the current study, perimenopausal participants reported higher incidence of depression and anxiety as well as greater severity of anxiety as a menopause-related symptom relative to postmenopausal participants. Additionally, more perimenopausal participants endorsed MC use to treat menopause-related mood and anxiety symptoms relative to postmenopausal participants. Preclinical research suggests that estrogen may modulate anxiety through the endocannabinoid system and administration of cannabinoid-based therapies reduces anxiety in ovariectomized animals.[13,14] Further, use of MC to address symptoms of anxiety and mood have been reported in several human observational studies of MC examining a broad variety of medical conditions (but not specifically menopause-related symptoms).[18-23] Taken together, these findings suggest that mood and anxiety symptoms may be especially problematic during menopause, particularly perimenopause, and may be a salient target for future clinical trials of cannabinoid-based therapies.

Vasomotor symptoms, such as hot flashes and night sweats, are commonly reported during menopause,[2] and preclinical research indicates that cannabinoid-based therapies can induce vasorelaxation[16] and may help alleviate disruption of hemodynamic regulation systems due to estrogen deficiency.[15] Although the use of MC to address these symptoms was *not* commonly reported in the current study (e.g., hot flashes = 13.0%; night sweats = 12.6%), the most prevalent and burdensome symptoms reported in this study (i.e., sleep disturbance, anxiety, and mood) may be mediated by vasomotor symptoms.[3,4] Given that relatively few participants endorsed MC use to directly alleviate vasomotor symptoms of menopause, clinical trials may be better options for examining the efficacy of MC to treat vasomotor symptoms beyond preclinical research.

Overall, future research is clearly needed to comprehensively assess the risks and benefits of MC treatment. Current research on the efficacy and long-term impact of specific MC products is limited, and no research thus far has specifically examined the efficacy of MC to treat menopause-related symptoms.[39] Although federal regulations currently prohibit the direct administration of commercially-available MC products in clinical research studies, the impact of commercially-available products can be assessed using nonrandomized, observational study designs, and certain novel products can be assessed using clinical trials.

MC use during menopause: potential areas of concern

Although an enormous variety of MC products are commercially available, very little guidance is available to consumers, which is concerning given that different characteristics of products (e.g., mode of use, cannabinoid profile) can yield different results and side effects.[40] For example, inhalation routes of administration such as smoking and vaping are associated with faster onset and shorter duration of effects relative to other routes of administration such as ingestion of edibles.[41] In the current study, smoking cannabis was the most popular mode of use reported by all participants, which may represent a potential public health concern. Research suggests that hormonal and metabolic changes during menopause may result in poorer respiratory function, and that smoking tobacco cigarettes can increase the magnitude of this respiratory impairment.[42] Although there is evidence that smoking cannabis may have differential effects on respiratory function than smoking tobacco,[43,44] the additive impact of smoking cannabis and menopause-related changes on respiratory functioning has not been assessed. Although current and former tobacco cigarette smoking is associated with increased risk of early natural menopause,[45] it is unknown whether smoking cannabis (or cannabis use in general) is also associated with increased risk. Future research should continue to investigate the impact of smoked and vaped cannabis on respiratory health and assess the association between cannabis use and age of natural menopause.

In addition, over 500 constituents have been identified in cannabis thus far.[46] Constituent profiles as well as dosage of individual cannabinoids can significantly impact the efficacy and safety of MC products. For example, Δ-9-tetrahydrocannabinol (THC), the primary intoxicating constituent of cannabis, has demonstrated a biphasic, dose-dependent response with regard to symptoms of anxiety; lower dosages are associated with anxiolytic effects whereas higher doses are associated with anxiogenic effects.[47] Further, research suggests that full- or broad-spectrum products, which have diverse profiles of cannabinoids and other compounds including terpenoids and flavonoids, may produce synergistic effects resulting in therapeutic response at lower doses with reduced risk of side effects relative to single compound, isolate products.[48–50] Minimizing the dosage of MC products to the lowest level necessary to achieve therapeutic benefit is particularly important given that a number of cannabinoids interact with cytochrome P450 enzymes,[51,52] and significant drug-drug interactions have been reported between cannabis use and other medications such as antidepressants.[53] Consumers should be aware of this potential issue and the impact MC use may have on other medications.

Concerns regarding abuse liability also differ for various cannabinoids. In the US, THC remains a Schedule I substance, associated with high potential for abuse, but the World Health Organization notes that other cannabinoids, such as cannabidiol (CBD), which are nonintoxicating, lack rewarding effects, and do not cause tolerance or withdrawal may have lower potential for abuse.[54] Interestingly, recent evidence from an observational study found that MC patients exhibit few signs of problematic use even after a year after initiating MC treatment.[55] Future research should further examine MC use characteristics in peri- and postmenopausal individuals and assess the association between specific cannabinoids and abuse liability in this population.

Limitations

In the current study, participants were predominantly White, middle-class women who endorsed current regular cannabis use

(≥1/month). However, evidence suggests that race and ethnicity significantly impact menopause symptom presentation with Black individuals at higher risk for vasomotor symptoms and Hispanic individuals at greater risk for mood changes relative to White individuals[56]; therefore, results from the current study may not be generalizable to more diverse samples of peri- and postmenopausal individuals. Additionally, given that most participants in the current study endorsed current cannabis use, results may not generalize to past consumers or cannabis naïve individuals. A recent survey assessing willingness to use MC to address pain related to gynecological conditions found that the majority of participants who currently or previously used cannabis were more willing to use MC compared to cannabis-naïve individuals.[57] In the current study, among participants who were not interested in using MC, the most common reason for not using was lack of knowledge, suggesting that increased education about MC treatment may be beneficial for those whose symptoms are not well managed. Overall, to ensure generalizability of results, replication of assessments should be considered in a more diverse sample with greater representation of racial and ethnic groups as well more diverse cannabis use history.

The current study was a cross-sectional, observational survey designed to collect information at a single time point focused on identifying specific menopause-related symptoms most commonly reported for MC use rather than efficacy of MC use. Although interesting, efficacy data would be based entirely on self-report measures from individuals already using MC, and therefore inherently limited. Instead, future studies should rigorously evaluate the efficacy of MC treatment for menopause-related symptoms using longitudinal, observational studies and clinical trials, which include baseline assessments completed *before the initiation of MC treatment* compared to follow-up assessments over time. In addition, findings from this survey study rely exclusively on self-report and may have been impacted by self-report bias and inaccurate recall. It is of note, however, that well-validated clinical scales were utilized to reduce bias and inaccuracies. Additional research using varied study designs, including clinical trials, are warranted to address this limitation.

As discussed above, cannabinoid profiles and dosage can significantly impact the efficacy and safety of MC products. Although the current study assessed modes of use, future research should query additional cannabis use characteristics, including cannabinoid profiles of individual products used as well as frequency and magnitude of use. Future research should also examine the impact of MC use on menopause-related cognitive impairment as observational studies in humans[18,19,21] and preclinical research on ovariectomized mice[58] indicate that cannabinoid-based therapies may be associated with improved cognitive outcomes after treatment. Lastly, expectancy of MC treatment effects was not assessed in the current study. A previous survey of peri- and postmenopausal participants demonstrated that expectancy of MC treatment effects mediated the effects of cannabis on menopause-related symptoms with more symptoms and increased expectancy associated with increased frequency of cannabis use.[29] Future research should include assessments of MC treatment expectancy and its impact on efficacy and side effects.

CONCLUSIONS

The current study indicates that many individuals are currently using commercially available MC products as an adjunct treatment for menopause-related symptoms via a variety of different modes of use. The most commonly reported indications for MC use were menopause-related disturbance of sleep and mood/anxiety, indicating these symptoms may be salient targets for future clinical trials of cannabinoid-based therapies. In particular, perimenopausal participants reported significantly greater severity and prevalence of mood/anxiety symptoms as well as greater endorsement of MC use to alleviate these symptoms, indicating a significant need for symptom relief in this group. Overall, future research should continue to examine MC use for menopause-related symptoms, including assessing how unique cannabinoid profiles, modes of use, and other MC use characteristics impact safety and efficacy.

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