



## Research Paper

# Patients' and clinicians' perspectives of co-use of cannabis and opioids for chronic non-cancer pain management in primary care

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## ABSTRACT

**Background:** The prevalence of opioid-associated morbidity and mortality underscores the need for research on non-opioid treatments for chronic non-cancer pain (CNCP). Pain is the most common medical condition for which patients request medical cannabis. Limited research indicates that patients are interested in cannabis as a potential addition to or replacement for opioid medication. This analysis reports on CNCP patient and clinician perceptions about the co-use of cannabis and opioids for CNCP management.

**Methods:** We interviewed 23 clinicians and 46 CNCP patients, using semi-structured interview guides, from six safety-net clinics across the San Francisco Bay Area, and 5 key stakeholders involved in CNCP management. We used a modified grounded theory approach to code and analyze transcripts.

**Results:** CNCP patients described potential benefits of co-use of cannabis and opioids for pain management and concerns about dosing and addictive potential. Patients reported seeking cannabis when unable to obtain prescription opioids. Clinicians stated that their patients reported cannabis being helpful in managing pain symptoms. Clinicians expressed concerns about the potential exacerbation of mental health issues resulting from cannabis use.

**Conclusion:** Clinicians are hampered by a lack of clinically relevant information about cannabis use, efficacy and side-effects. Currently no guidelines exist for clinicians to address opioid and cannabis co-use, or to discuss the risk and benefits of cannabis for CNCP management, including side effects. Cannabis and opioid co-use was commonly reported by patients in our sample, yet rarely addressed during clinical CNCP care. Further research is needed on the risks and benefits of cannabis and opioid co-use.

## Introduction

Over 25 million adults in the United States experience chronic non-cancer pain (CNCP) (Nahin, 2015). Given the prevalence of opioid-associated morbidity and mortality, research on non-opioid treatments for CNCP, including cannabis, is needed. Pain is the most common medical condition for which patients request medical cannabis (Ilgen et al., 2013; Nussbaum, Thurstone, McGarry, Walker, & Sabel, 2015; Reiman, Welty, & Solomon, 2017). In two studies, medical cannabis users reported lower self-rated pain as well as reductions in pain following cannabis use (Ilgen et al., 2013; Webb & Webb, 2014). Findings regarding the efficacy of cannabis for CNCP are inconclusive. Results of a systemic review noted that cannabis is not universally effective for pain and may only be useful for the treatment of specific types of CNCP (e.g. neuropathic pain) (Nugent et al., 2017). Other reviews suggest that

inhaled cannabis improves some of the symptoms associated with CNCP. However, these benefits appear to be dependent on dose-response effects as well as the route of administration (Hill, Palastro, Johnson, & Ditre, 2017; Romero-Sandoval, Kolano, & Alvarado-Vázquez, 2017). While randomized control trials have evaluated the efficacy of cannabis, specifically for neuropathic pain, findings need to be interpreted with caution because the lack of appropriate placebo controls may result in an overestimation of benefits (Casarett, 2018). This lack of evidence regarding efficacy of cannabis for CNCP is coupled by a lack of knowledge about patients' frequency of and experience with cannabis use.

Recent evidence suggests that approximately 16% of CNCP patients co-use cannabis and prescription opioids (Degenhardt et al., 2015; Sohler et al., 2018). In addition, population health research has found associations between the legalization of medical cannabis and decreases

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in opioid-related deaths, hospitalizations, and overdoses, as well as reductions in expenditures related to prescription opioid overdose and misuse (Bachhuber, Saloner, Cunningham, & Barry, 2014; Bradford, Bradford, Abraham, & Adams, 2018; Hill & Saxon, 2018; Vyas, LeBaron, & Gilson, 2017). Adverse effects of both short and long-term cannabis use have been documented including, memory impairment, impaired motor coordination, paranoia, psychosis, cognitive impairment and increased risk for anxiety and depression (Volkow, Baler, Compton, & Weiss, 2014). As the legalization of cannabis continues to evolve in the United States, questions are emerging about the role of cannabis in clinical care.

Patients indicate interest in medical cannabis as a potential addition to or replacement for opioid pain medication (Corroon, Mischley, & Sexton, 2017). However, patients often seek out medical cannabis recommendations from specialty medical cannabis clinics rather than from a primary care provider (Corroon et al., 2017; Satterlund, Lee, & Moore, 2015). Clinicians lack knowledge regarding the efficacy of cannabis and what role they should play in managing their patients' cannabis use (Maher et al., 2017). At the same time, research indicates that the prevalence of cannabis use has increased in recent years. Cannabis is the most commonly used "illicit" drug in the United States (Hasin et al., 2015; Volkow et al., 2014). Yet, cannabis use is not regularly discussed in patient-provider interactions (Satterlund et al., 2015). It is important to understand how and why patients use cannabis to manage CNCP. In this qualitative study, we present patients' and clinicians' perspectives on the co-use of cannabis and opioid among a sample of CNCP patients and clinicians in the safety net setting. While the focus of the overall study was CNCP management, the topic of cannabis emerged organically in interviews with patients and clinicians. Safety-net clinics are defined by the Institute of Medicine as those settings that "...offer care to patients regardless of their ability to pay for services, and [for which] a substantial share of their patients are uninsured, Medicaid, or other vulnerable patients" (Altman & Lewin, 2000; Andrusis & Siddiqui, 2011).

## Methods

### Recruitment and sample selection

The methods for this paper are described in detail elsewhere (Hurstak et al., 2017). In brief, between October 2013 and March 2014, we interviewed 23 primary care providers and 46 patients from six safety-net primary care clinics in the San Francisco Bay Area. To avoid identification, we did not collect demographic data on clinicians. Most of the clinicians were physicians (n = 18, 78%), four were nurse practitioners, and one was a physician assistant. Clinicians and patients were equally distributed across the clinics.

For each participating clinician, we recruited between one and four of their patients who had both CNCP and a history of past or current substance use (including illicit drugs and/or alcohol). Participants received a \$50 gift card for their participation. One clinic did not allow clinicians to accept compensation. All participants provided written informed consent. The Institutional Review Board at the University of California, San Francisco approved this study.

### Data collection

We developed a semi-structured interview guide organized by topic that included interviewer-directed open-ended questions. We sought contextual and conceptual depth in the interviews to identify interviewees' understandings and processes of pain management. We did not assume differences between clinicians and patients, nor did we seek to compare and contrast clinicians' and patients' responses a priori. In addition to recruiting clinicians, we identified and interviewed key informants who were selected based on their involvement in the development of pain management policies and the provision of services

**Table 1**

Relevant interview guide questions.

Patient interview Questions	
How do you manage your pain?	
How are you treating your pain?	
Tell me about your drug use (prescribed and not prescribed).	
What did you treat your pain with this morning?	
What seems to be the best way you've found to control your pain?	
If you could have any treatment / care in your toolkit, what would it be?	
Do you see a difference between street drugs and prescribed drugs?	
What would help you manage your pain better	
How do you talk about your pain with your doctor / provider?	
How do you feel about how that treatment is working?	
What were motivation to disclose (or not disclose) substance use with your doctor/provider	
Clinician interview questions	
Are there specific illicit substances (or alcohol) that affect CNCP management?	
How are patients with co-occurring CNCP and substance use who are on opioid analgesic therapy monitored at this clinic?	
How do you interpret and discuss substance use with the patient?	
Describe a positive experience involving a patient with co-occurring CNCP and substance use.	
Describe a challenging experience involving a patient with co-occurring CNCP and substance use.	
What are the clinic policies for co-occurring CNCP and substance use?	

related to CNCP management. We continued recruitment and interviews until we reached thematic saturation (i.e., a consensus that new themes and patterns were no longer emerging from the data) (Patton, 2002). Patients were asked questions pertaining to their living environment, experiences with pain, pain management, provider management of pain and socio-structural factors. Clinicians were asked questions pertaining to their professional training; how they understand, diagnose, and treat CNCP; and, socio-structural factors influencing CNCP treatment (Table 1).

### Data analysis

We used a modified grounded theory approach to code and analyze transcripts (Charmaz, 2014; Corbin, Strauss, & Strauss, 2014). After successive iterations of coding transcripts independently and discussing transcripts as a group, we developed distinct codebooks for patient and clinician interviews. We entered coded interviews into ATLAS.ti (ATLAS ti, 2011). For this analysis, one investigator (AC) reviewed interview transcripts and completed memos on the use of cannabis in pain management. Our analysis centered on benefits and concerns identified by clinicians and patients in regard to co-use of cannabis and opioids

## Results

Patients' demographic characteristics are presented in Table 2.

### Patients' experiences with co-use of cannabis and opioids

Patients frequently discussed experiences with cannabis including cannabis use with and without prescription opioids. Major domains (Table 3) from the patient interviews were: potential benefits of cannabis and opioid co-use for pain management and concerns about the potential consequences of cannabis use.

### Benefits

Patients described the impact of CNCP (e.g., limited mobility, strain on interpersonal relationships, inability to sleep). They commented on the centrality of pain management in their everyday lives and on its high psychic toll. For one patients, cannabis was the only modality they felt provided a reprieve from a constant preoccupation with pain. As this patient described:

**Table 2**  
Patient Demographics.

Characteristic	Patients N = 46
Age (years)	
25–40	5
40–55	19
55 +	18
Gender	
Male	21
Female	25
Ethnicity/Race	
African American	28
White	14
Latino	3
Past 30 day drug use	
Cocaine	30
Marijuana	21
Methamphetamine	14
Heroin	11

**Table 3**  
Frequency of Domains.

Domain	n
<i>Patient interviews (N = 46)</i>	
Number of patients who discussed cannabis	32
Number of patients reporting benefits of cannabis	15
Number of patients reporting concerns related to cannabis	18
<i>Clinician interviews (N = 23)</i>	
Number of clinicians who discussed cannabis	8

[Cannabis is the] only thing what it manage, helps me with, it helps me to stop thinking about the pain because I'm so high up here. [laughter] You know, and I'm sitting here just smiling even when people are trying to insult me, you know, and it just, I'm just like, yeah. (Patient A)

Some patients interviewed expressed a preference for cannabis, over their opioid prescriptions to manage pain. Decisions on how treat their pain were made on a day-by-day basis. As one patient said:

They [opioids] help in so many hours to get through the day and then just go again. But some days is good days and some days bad. Some days is good to where I don't do the [opioid] pill, I just do the weed [cannabis]. Now some days when times is hard I just do the [opioid] pill and don't do the weed [cannabis]. Because I have to pay for the marijuana so, and some days I don't even have to take neither/or, it's just some good and some bad days. You know, sometimes [my leg] just lock up and then sometimes it don't. Sometimes I don't even limp, you wouldn't even know [that I had pain]. (Patient B)

Patients did not endorse claims that cannabis completely resolved their pain or was a cure to their CNCP. However, patients did discuss that cannabis provided moments of pain relief. As one patient described how cannabis helped manage pain:

Well, you know, actually I don't know what it is about that herb [cannabis], it does take away pain, it really does. But I don't know, it sends your mind to, I guess into a different, you know, galaxy or, you know, atmosphere to where you feel relaxed so much. Then you get hungry but you, you try to forget the pain for a moment of, of, you know, like serenity I guess, the way I want to feel, comfortable. But then all along the pain is going to do what it always does and it's going to surface. (Patient C)

When faced with a gap in their opioid prescription refills, patients reported using cannabis to help manage their pain. In interviews,

patients discussed running out of their prescription opioids, and being unable to obtain additional medication before their prescription refill date. Patients also expressed frustration, reporting feeling that their pain was undertreated when they took their opioids as prescribed. One patient explained how they used cannabis to manage pain in these instances:

At nighttime, I would just get some of that [cannabis] and then lay down and watch a movie and smoke one in the, with a blunt. And then it would just help me sleep, help me feel no pain and just sleep good. So I, I was just honest. So I just, just, you know, I just got tired of medicines [opioids] and stuff and I just said, "Okay, I'm going to try to take it [opioids] as prescribed, try follow all the rules and everything." And it just still seemed like at the end of the day I, just was still in pain and stuff. (Patient D)

Some patients who disclosed use of cannabis for pain management considered cannabis a medication. These patients stated that their use of cannabis was not for recreational purposes. They disliked the assumptions that others made about their cannabis use. As one patient described:

And I hate to say it but some of these kids today, I don't know what happened, they just don't understand and respect. [laughter] I don't know if [my daughter] think because I smoke weed that it's a game and it's fun activity because, you know, kids think you smoke weed, "Mama's cool, she smoking weed and we cool," and all that. Hell to the no. And none of my kids, I let them smoke no marijuana. They can do whatever they want when they turn that age, and so, you know, she was, couldn't wait to turn that age to smoke. But, see, she don't know she's abusing it. For myself, that's why she's like, "Mommy, can I hit your [cannabis]," I say, "Honey, this is my medication and it's not a game here, no." (Patient B)

### Concerns

Patients reported needing assistance in navigating changes in policies related to accessing cannabis. None of the patients interviewed described their cannabis use as being part of their pain management plan, meaning that they did not discuss quantity, frequency of use, or route of administration with a clinician. In addition, none of the patients disclosed that their cannabis use was being monitored by a clinician. As one patient said:

He [the physician] asks me, "Are you doing any drugs?" "Yeah, I still smoke a little marijuana every now and then. I don't snort no [cocaine] and I don't smoke no more crack but, yeah, I still smoke marijuana." I forgot to ask him when I was in there Wednesday, too, I need a [cannabis] card. I got to ask him that when I go back to see him, I got to be legal. I don't like walking around if I got weed in my pocket. (Patient E)

Many patients in our study experienced multiple co-morbid health conditions. Cannabis use sometimes complicated the challenges of managing multiple medications. One patient said:

You know, I have a regimen of medicines that I already take, so many different medications, and it's hard, it's hard for me to stay on top of all of that because, you know, like I said, I smoke the marijuana and sometimes I just, I'll smoke and then I'll fall asleep, and so sometimes I'll miss taking my medicine. But overall I try to be as efficient as I can when it comes to my medications because that has a bearing on my health. I'm a diabetic, I have arthritis in both my knees and in my hips so that's more of a consistent pain. (Patient F)

Patients had concerns about how they could determine which species of cannabis (e.g. cannabis sativa, cannabis indica) might work best to manage their pain. This concern led patients to guess or turn to non-clinician help with cannabis selection and dosing recommendations. One patient said:

I don't know if I smoked the wrong kind [of cannabis] or something, it just felt like my, it felt like my body, I could still feel the pain one time and then, and it felt like this was just like heavy, my head was really heavy [laughter] and I think at that time I was smoking some [cannabis] sativa. So then they said, "Why don't you just try a little bit of everything, the body high and the [other types of cannabis]" "Just try a little bit of everything [all types of cannabis]," and I did, it works. (Patient A)

Not all patients endorsed cannabis. Some patients expressed concern that while cannabis helped with pain management, it might lead to dependency or addiction. As one patient said:

I've tried it [cannabis] for a little bit but it helped, and it, it wasn't for, to get high or anything like that, it did help the pain a little bit, but my thing is that I really don't want to take it because I don't want to get addicted to it. (Patient G)

Patients with a history of substance use disorder expressed concerns about medical cannabis use, as a potential threat to their sobriety. In this sense, cannabis was viewed as equivocal to other illicit substances. One patient remarked:

In November of last year I went off all of my pain meds and I was still in [Alcoholics Anonymous], and then in March I relapsed, I smoked a couple hits off of pot because one of the girls was smoking it in the house, and the trigger was just too great. And I hadn't smoked marijuana, and it's almost been twenty years, you know, but just smelling it. And so my sobriety date changed to March 19. So I have more than six, a little more than six months now. (Patient H)

#### *Clinicians' experiences with co-use of cannabis and opioids*

Compared to patients, clinicians discussed cannabis use less frequently during interviews. In the clinics where data were collected, cannabis use was not treated like other substances such as alcohol or cocaine. Unlike these substances, cannabis use was not viewed as a violation of patients' pain agreements, nor was it routinely tested for in urine toxicology tests. Major domains from clinician interviews (Table 3) included: perceptions of cannabis, disclosure and patient trust, and concerns about patients' cannabis use.

#### *Perceptions of cannabis use*

Clinicians did not ask about or engage in conversations with patients about their use of cannabis. In contrast, clinicians discussed their concerns about patients' misuse of substances, including their opioid medications, as well as alcohol and crack/cocaine. The lack of questions about cannabis use may be a reflection of clinicians' perceptions about its potential efficacy and widespread use. While clinicians did not cite specific evidence, those who discussed cannabis, express beliefs that cannabis helped to manage patients' pain and improve their quality of life. One clinician remarked:

I used to get, when it [the urine toxicology screening test] included marijuana, almost everybody was on marijuana and I didn't feel like that [cannabis use] was enough reason to stop the opioids. That was my belief. I think other doctors might feel differently. But I'm, I was, you know, I mean, [patients] take [cannabis] at night to relax and it helps the pain so, you know, that's, so I kind of, you know, I mean, you're dealing with a, with an impoverished population who are struggling to get through their life and they're, and many of them are using these drugs, I think, as a way of getting through their day.

#### **Disclosure and patient trust**

Clinicians reported difficulty determining which patients were using non-prescription substances. Thus, voluntary disclosure of cannabis use

might be interpreted by clinicians as an indication of a patient's trust in their relationship and as a way to have an open conversation about substance use. One clinician said:

Do I feel like this patient is telling me the truth [about their substance use]?" If I feel like they're telling me the truth, then a) I don't need to get the UTOX, and b) if they tell me they're using marijuana then I feel super, super comfortable that they're probably not using a bunch of other stuff because they've told me they're using marijuana and they've, I feel, you know, you can tell when people are being upfront with you and when they're not.

#### *Cannabis concerns*

An area of concern for clinicians was patients' co-use of cannabis with other illicit substances. For one clinician in particular, lack of screening for cannabis was problematic. This clinician felt that cannabis use would likely lead to the use of other substances. This clinician said:

Because it's [cannabis use] so prevalent here. When, initially, not to toot my own horn but I was initially the only provider who raised my hand and said, "Are we not, why are we not testing for marijuana anymore?" Because we know from studies that [cannabis] is the gateway drug to even harder illicit drugs.

Concerns about cannabis use were discussed by one clinician in terms of mental health. In the clinics where data collection was done, urine toxicology screens are a routine part of clinical practice. However, cannabis is not included in the screen. We interviewed a behavioral health specialist, who, after a referral, requested a urine toxicology screening test for a patient. This specialist remarked on the relationship between cannabis use and paranoia and discussed the difficulties of distinguishing between an underlying psychiatric disorder and a substance-induced psychosis. This clinician explained:

There's this one guy that I just saw recently and he was saying that he wanted help for depression and paranoia, and described the paranoia. Sounded very real but he's also applying for disability so I'm kind of, you don't know if somebody's just trying to get disability. So I think I surprised him by asking him to give a sample of urine that day, but he gave it. It's so surprising to me when people, I mean, sometimes they'll try to get off and they'll say, "Oh, I don't have time right now," but I'm more often than not surprised when, see, people agree to give a urine sample when they know they're going to get caught. He gave his urine and then I went ahead and started him on an antipsychotic because I didn't have the results right away. And then in the meantime before his next appointment, which he forgot, it came back positive for marijuana. I'm like, you know, probably explains his, his paranoia and he, he told me he doesn't use any drugs including marijuana, you know. So now when he comes back for his follow-up I'm going to address [the cannabis use] with him and say, you know, "That's probably the cause of your paranoia so I think let's have you stop the marijuana for a while, see if it persists."

#### **Discussion**

Patients with CNCP in this study discussed their use of cannabis with and in place of opioids for pain management. These results are consistent with previous findings on patients' use of cannabis for pain management (Degenhardt et al., 2015; Maher et al., 2017). Medical cannabis use often co-occurs with recreational use and boundaries between therapeutic and non-therapeutic uses of cannabis are not always clear (Kondrad & Reid, 2013; O'Connell & Bou-Matar, 2007).

Cannabis use exists in both a legal and clinical "grey area" (Angela, Jonathan, Beau, & Mark, 2013; Pacula, Boustead, & Hunt, 2014). The level of engagement about cannabis has been left to provider discretion,

concurrent with increased monitoring of opioid prescriptions. Our results align with literature that suggests that clinicians are not comfortable discussing and/or providing cannabis in clinical settings (Brooks, Gundersen, Flynn, Brooks-Russell, & Bull, 2017; Harle et al., 2015; Herzig et al., 2006; Holland et al., 2016). Clinicians in our study did not routinely discuss cannabis with patients and patients described making decisions to use cannabis for pain management without clinician input. Patients noted concerns about the use of cannabis with other medications, the type of cannabis to use, and concerns regarding their own substance use histories.

In our study, patients did not discuss issues with cannabis dosing, but did question which type of cannabis might be most beneficial for pain. From the patient interviews, it is unclear how patients determined the dose of cannabis they needed to manage pain or why they chose a certain route of administration. Research indicates that smoking cannabis is the most common route of administration (Cranford, Bohnert, Perron, Bourque, & Ilgen, 2016). Given the high prevalence of tobacco and cannabis co-use, clinicians need information regarding the short and long term risks of chronic obstructive pulmonary disease and other respiratory problems associated with smoking (Joshi, Joshi, & Bartter, 2014; Lee & Hancox, 2011; Macleod et al., 2015). While a smaller percentage of patients used edible cannabis, the cannabinoid and tetrahydrocannabinol contents of edible products may not be accurate (Vandrey et al., 2015). More research is needed to determine if the route of administration influences the efficacy of cannabis, and it is therefore difficult for clinicians to educate themselves or patients regarding its use. The many forms of cannabis (e.g. tinctures, edibles, oils) add to challenges and preclude clinician guidance.

Clinicians might consider including discussions about cannabis in a manner similar to discussions of complementary and alternative medicines (CAM). Guidelines to support effective communication about CAM exist (Schofield, Diggins, Charleson, Marigliani, & Jefford, 2010), and may provide guidance for clinicians to have conversations about cannabis use that promote open dialogue, while being clear about the limited available evidence on risks and benefits. Clinicians may want to discuss their patient's cannabis use to communicate concerns about intoxication, abuse, withdrawal symptoms, drug interactions, and side effects. (Strouse, 2015). Clinicians in this study reported that they did not screen for cannabis use or include it in their CNCP management plans. These results warrant consideration as recent research suggests that clinicians should counsel patients on the use of medical cannabis (Parmar, Forrest, & Freeman, 2016). Such recommendations could help clinicians assess the risks and benefits of cannabis use in the context of patients' medical and substance use histories.

Real difficulties exist in discussing the medicinal benefits of cannabis in clinical settings. Despite laws permitting cannabis use in 29 states and the District of Columbia, cannabis is classified federally by the Controlled Substances Act of 1970 as a schedule 1 substance. This contributes to the lack of scientific evidence on cannabis that could inform clinicians about dosing, clinical efficacy, routes of administration, and contraindications (Maher et al., 2017). There is insufficient data to provide evidence-based clinical guidance for cannabis-based medicine (e.g. sativex/nabiximol) (Maher et al., 2017).

Research indicates that the prevalence of cannabis use has significantly increased in recent years, as has the prevalence of DSM-IV diagnosis of cannabis use disorder (Hasin et al., 2015). Questions about the appropriateness of cannabis for specific patients did come up in clinician interviews when they discussed concerns about co-use of cannabis and opioids and mental health. It may be possible to confer the benefits of cannabis, described by patients (e.g. escaping pain) through other CAM modalities such as mindfulness practices. Patients indicated potential cognitive problems stemming from cannabis use. It is unclear how these side-effects might impact CNCP patients specifically, particularly in relation to their mental health and long term use.

This study has several limitations. It was not explicitly designed to assess cannabis use or cannabis and opioids co-use. Rather, cannabis

use was a topic that emerged organically and data explored after patients or clinicians introduced the topic. The fact that the topic emerged organically in 70% of patient interviews underscores the potential relevance of the topic to this patient population. However, because not all patients were directly queried about cannabis, the data may not represent the breadth of perceptions in our sample. We conducted our study in safety-net settings serving patients with substance use histories, therefore our results may not be generalizable to other patients with CNCP. Clinicians in our study may have more experience treating pain and addiction and may perceive risks differently than clinicians without such expertise. Clinicians who agreed to participate may be different from other clinicians who treat CNCP in safety-net clinical settings. The patients who clinicians identified for participation in our study may be different from other individuals with substance use and CNCP. Finally, both clinician and patient interviewees may have answered questions in ways that fostered a positive portrayal.

As legalization of cannabis continues to spread across the United States, cannabis will become more widely available and used more frequently. Clinician lack of communication about patients' cannabis use can place the burden of negotiating issues of dosing and medication management on the patient and hinders patient-clinician communication. At the same time, clinicians are unable to move forward without clinically relevant guidelines. Clinicians need tools to communicate effectively with patients about the perceived benefits and risks of cannabis use, especially among CNCP patient populations in which cannabis use may be common.

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## Conflict of interest

No conflicts, the authors have no conflicts of interest to disclose.

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