ORIGINAL RESEARCH

Perceptions and Preoccupations of Patients and Physicians Regarding Use of Medical Cannabis as an Intervention Against Chronic Musculoskeletal Pain: Results from a Qualitative Study

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Objective: Explore perceptions and preoccupations regarding use of medical cannabis against chronic musculoskeletal pain, among patients and physicians.

Design: Qualitative study using interviews with patients and physicians, based on the Theory of Planned Behavior (TPB).

Setting: The study was conducted in Quebec, Canada, in spring 2020.

Subjects: We included 27 adult patients and 11 physicians (GPs, anesthesiologists, psychiatrists, and a rheumatologist); the mean age of patients was 48.2 years; 59.3% of patients and 36.4% of physicians were women; 59.3% of patients used no medical cannabis at the time of study; 45.5% of physicians had never authorized it.

Methods: Semi-structured interviews were conducted, transcribed and for the qualitative analysis codes were developed in a hybrid, inductive and deductive approach. Guided by the TPB, facilitators and barriers, perceived benefits and harms, and perceived norms that may influence cannabis use or authorization were documented.

Results: Although medical cannabis is an interesting avenue for the relief of chronic musculoskeletal pain, doctors and patients agreed that it remained a last line option, due to the lack of scientific evidence regarding its safety and efficacy. The norms surrounding medical cannabis also play an important role in the social and professional acceptance of this therapeutic option.

Conclusion: Medical cannabis is seen as a last line option among interventions in the management of chronic pain, and attitudes and prior experiences play a role in the decision to use it. Study results may contribute to improved shared decision making between patients and physicians regarding this option.

Plain Language Summary: Little is known about the motivations, perceptions, and preoccupations of patients with chronic pain and their physicians regarding the use of medical cannabis against chronic pain. A qualitative study was done on the attitudes and perceptions of these patients and their physicians. We performed semi-structured interviews, guided by the Theory of Planned Behavior, with chronic pain patients and with physicians treating such patients. Results indicate that both patients and physicians consider medical cannabis as a last line therapeutic option against chronic pain. Also, both groups expressed a need for stronger evidence on the effectiveness and safety of medical cannabis, as well as for more and clearer guidance on when and how to use this additional option in the treatment of chronic pain.

Keywords: medical cannabis, theory of planned behavior, chronic musculoskeletal pain, qualitative study, lack of knowledge, stigma

Introduction

Chronic musculoskeletal (MSK) pain, defined as a condition persisting for at least three months, affects bones, muscles, ligaments and joints and results from underlying diseases or health problems such as gout, tendonitis, osteoarthritis, rheumatoid arthritis, and fibromyalgia, although in many cases the exact cause cannot be identified.¹ Chronic MSK pain is frequently associated with a range of problems such as sleep disorder, depression, anxiety, fatigue, reduced quality of life and inability to work or socialize.² Worldwide, 20% to 33% of the population is living with chronic MSK pain.³ Yelin and al. reported that one in two US Americans 18 and older lives with a musculoskeletal disease⁴ and in Canada approximately 17% of the adult population is affected, nearly half of whom (44%) is aged 65 years or older.¹ The number of people suffering from chronic MSK pain is on a rise specifically among the older population.⁴ Alongside non-pharmacological interventions such as physiotherapy, exercise, and the biopsychosocial approach⁵ pharmacological interventions, including injections of cortisone or botox, are widely used against chronic MSK pain.⁶ Pharmacological pain relief thus is frequently suboptimal, based on non-steroidal anti-inflammatories, gabapentinoids, antidepressants such as duloxetine or milnacipran, or opioids, and patients regularly encounter a wide range of adverse effect, including dependance problems with opioids.^{7–13} It is therefore urgent to explore new treatment options to relieve pain in persons affected by chronic MSK pain and thus improve their quality of life and well-being.^{14–17}

Many persons for whom chronic MSK pain is not satisfactorily relieved by existing treatment options are turning to alternative therapies, which they want to discuss with their physician. In recent years, cannabis has increasingly been perceived as an additional analgesic option.^{18,19} The scientific literature, however, remains somewhat inconclusive²⁰ regarding the effectiveness and safety of cannabis products and cannabinoids for the management of chronic MSK pain, with several systematic reviews and meta-analyses seeing little therapeutic potential,^{21–23} while more recent reviews and meta-analyses, using different methodologies and including wider pain definitions, come to more encouraging results,^{24,25} leading to careful recommendations for a therapeutic trial in some pain patients.^{26,27} Cannabis destined for medical use may represent a new option to manage chronic MSK pain and attracts increasing attention, which parallels growing possibilities for its prescribing and dispensing in several countries.²⁸

Historically, cannabis *Sativa* has been known for its analgesic and anti-inflammatory effects.²⁹ However, very few cannabis-based products are approved as medications. Sativex[®], Cesamet[®] and Marinol[®] are currently available in several countries,³⁰ but only Sativex[®], a plant derived spray containing equal parts of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), is indicated for pain treatment: Blake and al. (2006) reported a significant improvement with Sativex[®], compared to placebo, in pain with movement, pain at rest and in quality of sleep. Physicians and patients interested in cannabis to treat pain also turn towards herbal cannabis or an increasing number of other plant derived products, such as oral oils or inhalators. In the remainder of this article, the term medical cannabis will include such products and cannabinoids used for therapeutic purposes.

A prior scoping review³¹ has shown that little research was performed to understand why patients with chronic MSK pain and their physicians are trying a cannabis treatment or not,³² and has revealed severe knowledge gaps regarding patients' motivations. One conclusion was that it is difficult to access evidence-based information regarding efficiency, safety, routes of administration, delivery methods or dosage on the most appropriate treatment for a given case.^{33,34} Despite this lack of knowledge, both the use and, in Canada, the numbers of authorizations for medical cannabis or cannabinoids have increased.³⁵ However, little is known on motivations and perceptions of both patients with chronic MSK pain and their physicians regarding medical cannabis³¹ or cannabinoids. To fill this gap of knowledge and better understand the motivations, perceptions and needs of patients and physicians regarding therapeutic cannabis for chronic MSK pain, a study based on the Theory of Planned Behavior (TPB),^{36,37} was conducted.

Existing literature shows that the TPB can be used as a framework to explain cannabis use in different populations.^{38,39} In our study, this framework can, on the one hand, explain and predict patients' decisions to try

cannabis or not and, on the other hand, physicians' decisions to prescribe cannabis or not. For example, we expect that the intention to use cannabis is determined by three variables: 1) personal attitudes (patients' personal attitude towards cannabis use); 2) subjective norms (perceptions about what family, friends and colleagues think about cannabis use); and 3) perceived behavioral control (the extent to which patients believe they can control the use of cannabis). This implies that the intention to use cannabis is greater when patients have a positive attitude towards this behavior, when significant others approve the use of cannabis and when they believe they have the possibility of doing so. Specifically, as recommended by the authors of the TPB,³⁶ this study aims at identifying and documenting facilitators and barriers to the use or authorization of medical cannabis, perceived benefits and harms, and perceived norms that may influence cannabis use.

Methods

Setting

The study was performed in Canada, where recreational cannabis was legalized in 2018 in all provinces, giving legal access to cannabis for the adult population through a variety of dispensaries, according to provincial regulations.⁴⁰ Access to medical cannabis, regulated by the federal government for all provinces, is possible since 2001. The coexistence of different regulations for recreational and therapeutic cannabis contributes to confusion around access to medical cannabis among patients and physicians.⁴¹ In the province of Quebec, medical cannabis can only be obtained through a physician's authorization, which allows:

Buying directly from a federally licensed seller, registering with Health Canada to produce a limited amount of cannabis for their own medical purposes, [or] by designating someone to produce it for them.^{42,43}

In this context, specialized medical cannabis clinics, playing an intermediary role between physicians and the federal government, were created to facilitate access for patients and physicians, particularly by offering consultations with health professionals, including physicians with specialized knowledge on medical cannabis. Since 2018, the legalization of recreational cannabis enabled self-medication for patients with products bought from the provincial dispensaries for recreational cannabis.

Ethics

This project was approved by the Ethics Review Board of the Centre de recherche du Centre hospitalier universitaire de Québec-Université Laval (MP-20-2020-4962). Each interviewed participant agreed to participate in the study and the related interview on a voluntary basis. The participants gave verbal informed consent because, given the COVID pandemic, interviews were performed by telephone. A consent statement was read to the participant and consent was obtained before the interviewees participated in the interview, including agreement with the publication of anonymized responses. A file was kept with contact and consent information for the participants in a closed file cabinet in the study centre, accessible only to study team members. To preserve the anonymity of the participants, the personal data were replaced by pseudonyms or numbers depending on the case.

Study Population

Physicians

Physicians were recruited via the professional network of the research team, based on their medical specialties and clinical expertise. We first aimed to recruit 15 physicians with at least a third of them having authorized medical cannabis. We did not aim for representativeness, but for coverage of most relevant perceptions or saturation of information. We reached out to 12 physicians to participate in the project, but one of them declined to participate. After interviews with 11 physicians and following preliminary analyses of transcriptions, we realized that no new topics or different content had been added in the last two interviews (data saturation), and it was decided to stop recruitment of physicians. In qualitative research a sample size leading to saturation of data is deemed sufficient to examine a given subject thoroughly.³⁸ More specifically, the sample included 4 women and 7 men from 4 medical specialties. Five family

physicians (1 woman and 4 men), two psychiatrist (1 woman and 1 man), three anesthetists (2 women and 1 man) and one rheumatologist (man). Five of 11 never authorized medical cannabis, four had already authorized it but not as a common practice, including two who had only cannabinoids, and two who authorize medical cannabis frequently in their practice.

Patients

Patients were recruited through posters in the Saint-Sacrement Hospital in Ouébec City and through ads posted on social networks, ie the Facebook groups of the Quebec Network on Research in Pain, the Centre d'excellence sur le vieillissement de Québec, and on one of the co-author's LinkedIn webpage. For the first half of the recruitment period, we mentioned medical cannabis on the recruitment poster. For the second half, we specifically searched for patients living with chronic MSK pain but without allusion to cannabis, to include patients not having used medical cannabis in our study. Patients 18 years and older, speaking French, living with chronic MSK pain (>3 months) were eligible. We aimed to recruit 30 patients with at least a third of both women and men having used medical cannabis. We did not aim for representativeness, but for coverage of most or all relevant perceptions, or saturation of information. We recruited 29 patients, but two of them could not be reached (no return to our phone call despite completion of preliminary steps and study consent). After interviews with 27 patients and following preliminary analyses of transcriptions, it was decided to stop further patient recruitment since the point of data saturation had been reached, ie no new information was gained from additional interviews. The patient sample included 16 women and 11 men aged from 24 to 75 years (mean age 47.63 years; median age 48 years). All patients indicated to be suffering from chronic MSK pain; 15 of 27 suffered from one or multiple physical or psychological comorbidities. Sixteen of 27 patients were not using cannabis for their chronic MSK pain at the time of the interview and 11 were using cannabis. For 4 of 11 patients, medical cannabis had been authorized, while 7 out of 11 patients self medicated. Among the 11 patients using medical cannabis, the modes of use were: smoked (n=4); oral (n=4); vaporized (n=1), and 2 or more modes of use (n=2).

Data Collection

The study interviews were performed in Quebec City, Canada, in February and May 2020, and both patients and physicians came from different parts of the province. Semi-structured interviews, based on the TPB framework, were conducted with both patients and physicians until data saturation. The interview questions were validated by the research team, which included three clinicians and a patient partner, ie a chronic pain patient interested in medical cannabis and participating in this study. Interviews were conducted by the team's research professional and a postgraduate student, who were both trained and experienced in interviewing and qualitative research. All interviews were recorded using a voice recorder and transcribed integrally.

Physicians

Interviews with physicians began with a general question: "Could you briefly describe the characteristics of your practice?", before investigating topics related to their usual treatments of patients with chronic MSK pain and regarding authorization of medical cannabis. The interviews aimed to identify advantages and disadvantages, social and group norms, as well as facilitators and perceived barriers influencing the authorization of medical cannabis for their patients with chronic MSK pain. Interviews for physicians were conducted by telephone except for two: one was conducted in person and one by Zoom. The average duration was 29 minutes.

Patients

Interviews with patients began with a general question: "Can you describe yourself briefly?". Subsequently, three themes were investigated: 1) chronic MSK pain and their general health; 2) medication and non-medication treatment; and 3) use or not of medical cannabis. The interviews aimed to identify advantages and disadvantages, social and group norms, as well as facilitators and the perceived barriers influencing the use or not of therapeutic cannabis in the management of chronic MSK pain. Interviews for patients were conducted in the research teams' offices at the Saint-Sacrement Hospital or by telephone, depending on patients' preferences. The average duration was 42 minutes.

Data Analysis

All initial data analyses were performed using the French language interviews. The results section of this manuscript was then written in English. The coding of the interviews and their analyses were carried out by the research professional and the postgraduate student using NVivo 11 software (QSR International Pty Ltd version 11). A hybrid approach of inductive and deductive coding was used in our study. Based on the interviews, a code table was developed by two coders for one third of the interviews. The codes were then classified under five broad themes inspired by the TPB: 1) facilitators and barriers; 2) perceived benefits and harms; 3) and perceived norms for medical cannabis use or authorization. Another third of the interviews were coded according to the major themes (step 1) and sub-themes (step 2) to ensure that all content was captured. In this second step, sub-themes were added if they were missing. Finally, the last third was coded by two coders without adjustments to the code table All the interviews were coded by two people to reach a consensus on the codebook and increase the fidelity of the coding. At each step the coded interviews and the codebook were validated by the research team members and clinician collaborators. The entire process of codifying and analyzing data was developed in collaboration with a qualitative analyst (SP). Extracts from verbatim transcripts are used in this article to illustrate representative results of the general ideas put forward by the interviewees. The verbatim transcripts were collected and analyzed in French. For this article, they have been translated into English by a professional translator.

Results

The sample of interviewees consisted of 27 patients and 11 physicians, some of whom had used/authorized medical cannabis and some of whom had not. Although medical cannabis is seen as an interesting avenue for the relief of chronic musculoskeletal pain, doctors and patients agree that it remains a last line option due to the lack of scientific evidence regarding its safety and efficacy. Both women and men were interviewed; however, the content analyses of the interviews did not allow identifying gender related differences regarding factors related to cannabis use or authorization. An analysis specific to the role of gender was beyond the scope of this work.

Facilitators

Physician

Most interviewed physicians saw medical cannabis as *a last line option* for relief of chronic MSK pain, if any of the previous treatment options had failed to relieve patients of their chronic MSK pain: this was the only facilitator for the authorization of medical cannabis.

I don't want to get to that option, in my own sense, until I've tried what I have more experience with and more study on. (Anesthetist, has never authorized cannabis)

Patients

The main facilitator cited by patients was *having access to health professionals with specific knowledge about medical cannabis* to advise them about this option. Such an access is seen as a comforting function for patients choosing this therapeutic option.

[.] In general, I trust the specialists. If my doctor suggested it and gave me all the information, I would really listen. (31 years old, does not use medical cannabis)

The possibility of *having access to products that can be consumed orally* was the second facilitating factor in patients' perspective, since they cause fewer pulmonary and cardiac adverse effects than smoking.

I figure, if a cigarette isn't good for your health, I guess this is (not) too. Regarding oil, I figure it's not as bad. (48 years old, uses medical cannabis)

Finally, similarly to the stances of physicians, *medical cannabis was seen as a last line option* for relief of chronic MSK pain by most of the interviewed patients as well. The failure of any of the previous treatment options, therapeutic or non-therapeutic, to relieve their chronic MSK pain was a facilitator for exploring other options.

I couldn't find effective solutions in medication or physical therapy. Massage therapy feels good, but it feels good for an hour. [.] it was really because of the lack of effectiveness of other alternatives proposed by the medical teams. (27 years old, uses medical cannabis)

Barriers

Physicians

Each interviewed physician mentioned the *lack of evidence-based knowledge* as a barrier to authorizing medical cannabis for their patients with chronic MSK pain. More specifically, the lack of evidence about the efficacy, the safety and the innocuity of medical cannabis was identified by many participants. This lack of evidence-based data on medical cannabis for chronic MSK pain inspires caution for most physicians, decreasing the probability for them to authorize it.

I am someone [.] who really waits for studies to be conclusive before testing new medications. Medical cannabis has not been an obvious panacea for me until now. (Psychiatrist, has never authorized cannabis)

This precautionary attitude is partly caused by the *strong wish to not induce adverse effects or long-term negative consequences for their patients* ("primum non nocere"). The lack of evidence on long-term effects and consequences thus acts as a barrier to the authorization of medical cannabis.

We don't have any studies on people who take this for 10, 15, 20 years. I was one of those people in the 90s, during my residency, who prescribed opiates without limits or almost without limits because that's what we were told, that's what we knew at that time. [...] We caused a lot of problems for a lot of patients and now we're trying to manage it. I find that we are very poorly equipped in terms of cannabis to inform patients of the long-term consequences, because we don't know. For that reason, I tend to try most of the other options available before I go. So that means that, yes, I have theoretical information, but I have little clinical experience. At the clinic, the consultations that come in for medical cannabis are returned to the sender, it's not something you see. (Anesthetist, has never authorized cannabis)

More precisely, physicians seemed to be especially careful regarding smoking of cannabis, which may induce adverse respiratory and effects. This popular method of use of medical cannabis was seen as a barrier to its authorization since some physicians did not have much knowledge about other available methods of consumption.

Medical cannabis, for me, is cannabis that is smoked. Maybe I'm wrong, it could be consumed orally, but I must admit that (about) this part I am less knowledgeable. I don't want to give an opinion because I haven't informed myself. (Family physician, authorized cannabinoids but not cannabis)

Furthermore, for about half of the physicians interviewed, the *mistrust of the cannabis industry* was due to the lobbying and publicity around the product. Medical cannabis companies were perceived as financing biased studies presenting their product favorably but using unreliable data. This contributed to the perceived lack of knowledge and evidence around medical cannabis for chronic MSK pain.

There are studies being done, but they are studies done by the producing companies, so they are not worth much. (Anesthetist, has never authorized cannabis)

Their lack of trust towards medical cannabis was also related to the way it came to the market. Usually, new medications are rigorously tested before being approved by governmental authorization bodies and only then are they commercialized. Physicians point out that the opposite is true for medical cannabis. This fast commercialisation seems to have created a strong lobbying in the general population. Patients are interested in medical cannabis after being exposed to its publicity, but physicians feel that they cannot give them the information they need because of the lack of solid knowledge on it.

It's going to be extremely difficult to get rigorous studies, except for those funded by Health Canada or whatever. I feel like we're almost 30 years behind where we were with the pharmaceutical companies and the doctors. [...] But I still believe in this

product because, yes, I have [seen] patients who have improved [with medical cannabis], and I have not had to increase the doses [of other medication]. Nothing miraculous, but it has its place. It's a place that is not very big, but now the commercial side and the lack of rigour on that side, in my opinion, we are running away from the medical side. (Anesthetist, has authorized cannabis)

Patients

Like physicians, interviewed patients cited a lack of knowledge and information as a barrier to using medical cannabis against chronic MSK pain. Specifically, the lack of knowledge and information about the efficacy, safety, and security of medical cannabis made patients cautious about using it for therapeutic purposes.

First, there's a lack of information. Clearly, I would benefit from more education. [.] I have questions. I wonder, if I take it, let's say, am I fit to work when I'm on medical cannabis? [...] I don't know, in the long term, what it can do to the body. (24 years old, doesn't use medical cannabis)

This cautious attitude is reinforced by the lack of professional resources with specific knowledge prescribing medical cannabis.

There was a pharmacy [.] that had it, but it took a prescription from a doctor, but the doctor didn't know what to prescribe me [.]. It was: I don't know, ask your pharmacist; I don't know, ask your doctor. everyone was throwing the ball around. (46 years old, uses medical cannabis)

Furthermore, for many patients, difficulties in access to medical cannabis through health care channels represents a barrier to its use.

Yes, it was difficult. I researched on the Internet, I called doctors. Even in private clinics, they didn't really know, or they didn't want to. I finally found a site called Doctor Cannabis.it took time. (48 years old, uses medical cannabis)

Perceived Benefits of the Use of Medical Cannabis

For Patients using medical cannabis, it represents an aid to better pain management and improved quality of life. This therapeutic option is often seen as something that provides a moment of respite for people living with chronic MSK pain. Few adverse physical effects are perceived, representing an advantage to its use. Most adverse effects are perceived as minor in comparison to opiates. Participants reported that medical cannabis hardly interferes with domestic tasks and patients remain "functional". The mode of consumption appeared to have a major influence. Compared to oil, the inhaled mode of cannabis consumption may be an advantage for some patients using it. They report being able to control the product's effect rapidly and efficiently and to stop before they feel a "buzz", so that they mostly perceive a relaxing effect which helps them manage their pain. This "buzz", however, is of concern for non-users.

All the negative effects, which I had [with] traditional medication, are gone with medical cannabis. It makes me feel better. Physically, it eases some of the pain, it allows me to do my yoga, do little things. (48 years old, uses medical cannabis)

The only problem I have with Sativex is that I have a dry mouth. I must chew a lot of gum. Also, the throat. Those are the only drawbacks I have with these medications. (65 years old, uses medical cannabis)

The problem with other modes of consumption [others that vaping] [.] it's much harder to gauge the magnitude of the effect. When I'm vaping, I'm able to feel when I'm a little too high. [.]. (28 years old, uses medical cannabis)

Physicians

They reported establishing the treatment plan in collaboration with patients, focusing on their needs and preferences and aiming to empower them. Therefore, if patients want to try medical cannabis which can be integrated into the treatment plan, physicians may be more willing to authorize it, hoping it may contribute to an improved quality of life. In accordance with a patient centered care approach, such an improvement is one of the main advantages in authorizing

medical cannabis against chronic MSK pain. To reach this goal, physicians considered medical cannabis as a complementary approach to reduce their patients' chronic MSK pain. Existing treatments for these health conditions may lack in efficacy, and the addition of medical cannabis to these treatments, for an improved the quality of life, was seen as an advantage.

But I think that, in most cases, to see them as true partners in the management of problems that, after all, are their own, [.] that's what's going to make a more significant difference in the management of their pain. That would be a collateral benefit perhaps to the use of cannabis. (Rheumatologist, man, has authorized cannabis)

We talk about medical cannabis as a complementary approach and not as an alternative to the conventional medications used for this condition. [.] The main thing I tell my patients is to improve their quality of life, that's my main goal. [.] the elimination of conventional drugs is not our goal when we start out. (Anesthetist, has authorized cannabis)

Harms

Physicians

Interviewed physicians listed barriers, as shown above, but few harms effecting the authorization of medical cannabis for chronic MSK pain. Observed harms mostly relate to rare episodes of psychosis among young patients.

Patients

The mode of use "smoking", while mentioned as a barrier, is also cited as a disadvantage. This disadvantage does not prevent people from using cannabis, but they do mention that a mode of consumption with less pulmonary and cardiac impact and less odour nuisance would be preferable.

For example, you go somewhere, then you meet people you wouldn't want to see. They smell that you've been smoking, that's not so funny. There are people who are not in favor of that. (58 years old, uses medical cannabis)

The patients interviewed were aware that medical cannabis is not a curative solution to their condition. Although it provides temporary relief, they agree that a therapy to cure their chronic MSK pain, or a medication without adverse effects, would be preferable to medical cannabis.

I'll roll my joint and then I'll smoke it outside. Then I go back inside and I'm fine. After 2–3 hours the pain comes back. It doesn't last, it's not a medication [.] (58 years old, uses medical cannabis)

If a traditional medication took away my pain and I didn't have adverse effects, [.], if it was equivalent, probably I'd go for that (48 years old, uses medical cannabis)

Finally, the adverse effect of anxiety was mentioned by some patients during the interviews.

With THC, I get very anxious. [.]. It makes me think a lot, a lot, a lot. (48 years old, uses medical cannabis)

Norms

Physicians

For the interviewed physicians, norms around medical cannabis had an important influence regarding its authorization. This influence was positive when peers also authorized it and physicians could get advice from a colleague who already had experience with authorizing medical cannabis for chronic MSK pain.

... it's reassuring to talk to someone whom you can ask questions of and who can reassure you about different types of patients they have seen. (Family physician, has prescribed cannabis)

In contrast, social norms had a negative influence on the authorization of medical cannabis against chronic MSK pain when physicians thought they were the only ones in their setting to do so. Going against the norms of their setting by authorizing medical cannabis could have a stigmatizing effect on them and the authorization would be harder to justify. For sure, having guidelines and knowing that others are doing it would make you more comfortable, because when you're alone doing something, doctors hesitate, whereas when it's recommended or it's proven, it's easier to justify it at that point. (Family physician, has prescribed cannabis)

Patients

For the interviewed patients, norms around medical cannabis had an important influence regarding its use, like for physicians. First, the use of medical cannabis is perceived more favorably by patients, whether they use it or not, than the use of recreational cannabis. Specifically, due to the social norms surrounding cannabis use, patients tend to feel that they need to have an authorization from their doctor for a valid medical condition.

I felt illegal [when recreational cannabis was not legalized], I didn't like it. [.] I thought I needed a prescription to make me feel good about my situation and to make it easier for people around me to accept (48 years old, uses medical cannabis)

Furthermore, some patients mention that social norms have a negative influence on their use of medical cannabis against chronic MSK pain. The stigma of cannabis as such thus limits their propensity to use this therapeutic option.

To them, people who smoked cannabis, were people who were on drugs. That was really what it was. That's why I was reluctant. (48 years old, uses medical cannabis)

Finally, many patients would like to be able to discuss this option with their medical team. However, due to stigmatisation, they do not know how to approach the subject with their health care team.

I would feel more comfortable asking him: what do you think about cannabis? Maybe he'd be embarrassed, [.] there's [.] a kind of collective perception that comes to influence how you approach it with the doctor. [.]. I think I'm able to get past some of the prejudices [.], but is the doctor able to do the same thing? [.]. (42 years old, doesn't use medical cannabis)

Discussion

This study, based on the TPB, identified perceived facilitators and barriers, norms, benefits and harms, among patients with chronic pain and their physicians, influencing the use or authorisation of medical cannabis for chronic MSK pain.

The main facilitator for use or authorization of medical cannabis was using it as a last-line therapeutic option, which is in accordance with most national guidelines,^{42,44} endorsing it as a second or third-line treatment, in specific pain conditions. This guidance is explained by the lack of robust evidence on the effectiveness and safety of medical cannabis, preventing it from being part of regular treatment plans.^{6,16,17,21}

Patients and physicians identified different barriers for the use or authorization of medical cannabis. The most important barrier for physicians was the lack of evidence-based knowledge, consistent with the results of a systematic review by Gardiner et al⁴⁵ highlighting a universal lack of self-perceived knowledge about medical cannabis in different healthcare professionals. The low quality of available primary evidence was also stated in multiple systematic reviews about the efficacy, safety and innocuity of medical cannabis.^{6,16,17,21} Four other identified barriers were related to the lack of high-quality evidence. First, the cautious attitude to authorization reported by many physicians was linked to the absence of certainty regarding the effectiveness of cannabis against chronic MSK pain. Second, physicians were concerned about the negative effects of cannabis, particularly in the long-term, which agrees with the Agency for Healthcare Research and Quality's living systematic review.¹⁷ stating that the medium to long-term consequences of medical cannabis are unknown. Third, the "smoked" method of use was a barrier to cannabis authorization considering its respiratory effects; some physicians felt they did not know about other available methods for use. Lastly, the publicity and lobbying around medical cannabis created a climate of mistrust towards its producers.⁴⁶ Physicians were wary of the industry's efforts to affiliate physicians to their websites, given the possibility of strong conflicts of interest. The fast commercialization of medical cannabis products also put physicians in an uncomfortable position. Patients ask for authorization for medical cannabis, while physicians felt that not enough reliable evidence was available to answer their questions and justify authorization.⁴⁷

All advantages identified by physicians concerned patient centered care.⁴⁸ Medical cannabis was seen as an option to improve patients' quality of life, and as a possible complementary treatment to reduce chronic MSK pain. This view is reflected in an overview of empirical evidence about common treatments for the management of chronic pain, by Turk,⁴⁹ concluding that there was no cure for chronic pain and that one single intervention was often not enough to manage patients' pain, placing the treatment focus on improving quality of life and symptom relief, including alternate treatments or combining them with conventional ones.

Interestingly, the physicians interviewed for this study named barriers to the authorization of medical cannabis for chronic MSK pain, but they identified no harms. According to the TPB,³⁷ barriers influence perceived behavioral control. If the barriers faced by physicians, such as the lack of knowledge about medical cannabis, were diminished, they might then perceive more ease in authorizing it. Similarly, a scoping review⁵⁰ identified that health care trainees do not receive any structured education on this topic and that it is up to them to find knowledge resources. By adding medical cannabis to their curriculum, this barrier might be lessened, making professionals more comfortable counselling their patients with chronic MSK pain about medical cannabis.

Finally, physicians indicated social norms around medical cannabis authorization as an important factor of influence, which is consistent with the TPB.³⁷ If physicians collaborate with colleagues authorizing medical cannabis for chronic MSK pain, they feel more positive towards it, and the contrary holds too. In the past years, interest in medical cannabis has increased following different forms of legalization in many countries, and while recommendations from different instances have been made, there still is need for more regulation and clinical practice guidelines.⁴⁴ This need has been identified by the interviewed physicians, who sometimes feared stigmatization if they went against the norms of their place of practice and authorized medical cannabis without clear guidelines backing them.

Patients

Patients reported additional facilitators for the use of medical cannabis against chronic MSK pain which were somewhat associated with the barriers mentioned by physicians, such as lack of knowledge. Better knowledge by physicians may facilitate the use of medical cannabis for the patients. Furthermore, access to oral cannabis products is considered as a facilitator.

Another barrier patients identified is the lack of professional resources with precise knowledge on how to use medical cannabis, as well as difficulties with access to it through the usual channels of the health system. This agrees with the review of Zeng⁵¹ which mentioned that cost, legal status and accessibility of medical cannabis all played a role in the preference of patients. Patients also mentioned adverse effects as a barrier to using medical cannabis, such as cognitive impairment, drowsiness, dizziness, nausea and impaired attention.⁵¹

Both patients and physicians recognized the advantage of medical cannabis as a therapeutic option giving patients a better quality of life. Most patients mentioned that it gives them a moment of respite from their pain. This observation agrees with a systematic review finding moderate to high certainty evidence that medical cannabis gives patients symptoms relief.²⁴ Importantly, the mode of consumption of medical cannabis may be part of patients' perceived advantage of this strategy. Indeed, inhalation of cannabis allows better control of the psychoactive effect that comes with many cannabis products. Similarly, losing control was found to be a disincentive for use of medical cannabis in a review by Zeng.⁵¹ It is thus not surprising that patients named this mode of consumption as an advantage. However, inhalation may also be seen as a disadvantage. Some patients said that they would prefer a mode of consumption with less pulmonary and cardiac adverse effects and less odour nuisance. Anxiety was another adverse effect named as disadvantage, which agrees with a critical review by Andreae.⁵² Furthermore, the mentioned advantage of a short respite is only temporary, and patients suggested they would rather have a cure or a long-lasting pain treatment, rather than only short periods of respite in their day.

Finally, social norms affect the behavior of patients in a similar way as the behavior of physicians, as also reported by Zeng.⁵¹ Social norms mostly had a negative effect on both groups' propensity to use or authorize medical cannabis. Even if medical cannabis could help reduce patients' pain, the stigmatization surrounding it can play a major role in the decision to try it or not. Consequently, for patients, a medical authorization increases the acceptability of medical cannabis in their social environments, making this type of document important for several patients, and even more so in a place where recreational cannabis is not legalized. Ultimately, negative social norms regarding the use of medical cannabis may sufficiently worry patients about the health team's reaction to refrain them from discussing this option. Certainly, decreasing the stigma, with a better understanding of the medical purpose of cannabis, may contribute to better acceptance and to encouraging patients to initiate meaningful discussions about cannabis with their health care providers.

Limitations

This qualitative study, relying on the theoretical framework of the TPB, highlighted the factors that prompted physicians to try medical cannabis as a therapeutic option in the management of chronic MSK pain, as well as patients' motivations for use. The study is limited to patients and physicians in the province of Quebec, Canada, and there may be other or additional factors at play in different countries. In Canada, however, legal norms hold country-wide and regulations, which are similar across the country although enacted by the provinces. Specialized cannabis clinics exist in most provinces and the training curricula of health care professionals are comparable (Committee on Accreditation of Canadian Medical Schools.⁵³ Although information obtained through the interviews had reached the point of saturation, we cannot exclude that for individual patients or physicians, additional factors may be important regarding medical cannabis for chronic MSK pain. Also, interviewed physicians may have views differing from other Canadian physicians or from physicians elsewhere. According to the laws and regulations in different countries and jurisdictions, medical cannabis might be authorized, prescribed or distributed by health professionals other than physicians, and we believe that the perceptions, needs and attitudes expressed by physicians in this study may, at least partly, also apply to these other health professionals.

Despite these limitations, it is apparent that many physicians are open to the therapeutic option of medical cannabis if it may improve their patients' quality of life. However, they express the need for more high-quality knowledge and for specific guidance to be comfortable authorizing. Some patients not having found sufficient pain relief with conventional treatments were inclined to try medical cannabis but did not know how to talk about this with their physicians, feeling a lack of knowledge and information from health professionals to guide them.

Conclusions

The voices of patients highlighted the need for health professionals' improved knowledge about medical cannabis, a need for oral cannabis products, ambiguity regarding smoked cannabis and preoccupations with social norms surrounding these products. Physicians mentioned the lack of large, rigorous, randomized, controlled trials on the effectiveness and safety of medical cannabis to manage specific types of chronic musculoskeletal pain. Their wish for more robust and specific research underlined the urgent need for high quality primary research on which constituents in the cannabis plant may show effectiveness against specific forms of chronic pain, in which forms and dosage, and with which adverse effects. This view of physicians, echoed in recent publications,^{54,55} has been voiced together with the medical paradigm of "primum non nocere",⁵⁶ the strong wish to not use treatments possibly inflicting more harm than benefit.

The need for improved management of chronic pain also calls for careful and cautious guidance on the use of medical cannabis to manage chronic pain, for both patients and their care providers. Some progress has recently been made in this regard, eg by the Arthritis Foundation of Canada (<u>https://arthrite.ca/search?q=cannabis</u>), the Mayo Clinic's website (<u>https://www.mayoclinic.org/search/search-results?q=cannabis</u>) and by our team in French (bd-cannabis-12-2022.pdf (gerermadouleur.ca) and English (<u>https://www.ciusss-capitalenationale.gouv.qc.ca/sites/d8/files/docs/ProfSante/CEVQ/BD-Medical-cannabis-chronic-pain.pdf</u>).

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Disclosure

All authors declare that they have no conflicts of interest to report in this work.

References

- 1. Arthritis Society. Arthritis in Canada. Facts & Figures. The Arthritis Society of Canada; 2015.
- Moore RA, Derry S, Taylor RS, Straube S, Phillips CJ. The costs and consequences of adequately managed chronic non-cancer pain and chronic neuropathic pain. *Pain Pract.* 2014;14(1):79–94. doi:10.1111/papr.12050
- 3. World Health Organisation, Bank TW. World report on disability; 2011.
- 4. Yelin E, Weinstein S, King T. The burden of musculoskeletal diseases in the United States. *Semin Arthritis Rheum.* 2016;46(3):259–260. doi:10.1016/j.semarthrit.2016.07.013
- 5. van Erp RMA, Huijnen IPJ, Jakobs MLG, Kleijnen J, Smeets R. Effectiveness of primary care interventions using a biopsychosocial approach in chronic low back pain: a systematic review. *Pain Pract.* 2019;19(2):224–241. doi:10.1111/papr.12735
- Fitzcharles MA, Baerwald C, Ablin J, Hauser W. Efficacy, tolerability and safety of cannabinoids in chronic pain associated with rheumatic diseases (fibromyalgia syndrome, back pain, osteoarthritis, rheumatoid arthritis): a systematic review of randomized controlled trials. *Schmerz*. 2016;30(1):47–61. doi:10.1007/s00482-015-0084-3
- 7. Goldenberg DL, Clauw DJ, Fitzcharles MA. New concepts in pain research and pain management of the rheumatic diseases. *Semin Arthritis Rheum*. 2011;41(3):319–334. doi:10.1016/j.semarthrit.2011.04.005
- Petzke F, Enax-Krumova EK, Hauser W. Wirksamkeit, Verträglichkeit und Sicherheit von Cannabinoiden bei neuropathischen Schmerzsyndromen [Efficacy, tolerability and safety of cannabinoids for chronic neuropathic pain: a systematic review of randomized controlled studies]. *Der Schmerz.* 2016;30(1):62–88. German. doi:10.1007/s00482-015-0089-y
- 9. Schaefert R, Welsch P, Klose P, Sommer C, Petzke F, Hauser W. Opioide bei chronischem Arthroseschmerz Systematische Übersicht und Metaanalyse der Wirksamkeit, Verträglichkeit und Sicherheit in randomisierten, placebokontrollierten Studien über mindestens 4 Wochen [Opioids in chronic osteoarthritis pain. A systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks duration]. Schmerz. 2015;29(1):47–59. German. doi:10.1007/s00482-014-1451-1
- 10. Atluri S, Sudarshan G, Manchikanti L. Assessment of the trends in medical use and misuse of opioid analgesics from 2004 to 2011. *Pain Phys.* 2014;17(2):E119–28. doi:10.36076/ppj.2014/17/E119
- 11. Ballantyne JC. Opioid therapy in chronic pain. Phys Med Rehabil Clin N Am. 2015;26(2):201-218. doi:10.1016/j.pmr.2014.12.001
- 12. Hauser W, Petzke F, Radbruch L, Tolle TR. The opioid epidemic and the long-term opioid therapy for chronic noncancer pain revisited: a transatlantic perspective. *Pain Manag.* 2016;6(3):249–263. doi:10.2217/pmt.16.5
- 13. Tobin DG, Andrews R, Becker WC. Prescribing opioids in primary care: safely starting, monitoring, and stopping. *Cleve Clin J Med.* 2016;83 (3):207–215. doi:10.3949/ccjm.83a.15034
- 14. Rowe J, Caprio AJ. Chronic pain: challenges and opportunities for relieving suffering. N C Med J. 2013;74(3):201-204. doi:10.18043/ ncm.74.3.201
- 15. Gereau RW, Sluka KA, Maixner W, et al. A pain research agenda for the 21st century. J Pain. 2014;15(12):1203-1214. doi:10.1016/j. jpain.2014.09.004
- 16. Lynch ME, Ware MA. Cannabinoids for the treatment of chronic non-cancer pain: an updated systematic review of randomized controlled trials. *J Neuroimmune Pharmacol.* 2015;10(2):293–301. doi:10.1007/s11481-015-9600-6
- 17. McDonagh MS, Wagner J, Ahmed AY, et al. *Living Systematic Review on Cannabis and Other Plant-Based Treatments for Chronic Pain.* Rockville, MD: Agency for Healthcare Research and Quality; 2022.
- 18. Elikottil J, Gupta P, Gupta K. The analgesic potential of cannabinoids. J Opioid Manag. 2009;5(6):341-357. doi:10.5055/jom.2009.0034
- 19. Boehnke KF, Litinas E, Clauw DJ. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. J Pain. 2016;17(6):739–744. doi:10.1016/j.jpain.2016.03.002
- 20. Kröger E, Dionne CE. Medical cannabis for chronic pain. BMJ. 2021;374:n1942. doi:10.1136/bmj.n1942
- 21. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA*. 2015;313(24):2456–2473. doi:10.1001/jama.2015.6358
- 22. Fitzcharles MA, Ste-Marie PA, Hauser W, et al. Efficacy, tolerability, and safety of cannabinoid treatments in the rheumatic diseases: a systematic review of randomized controlled trials. *Arthritis Care Res.* 2016;68(5):681–688. doi:10.1002/acr.22727
- 23. Stockings E, Campbell G, Hall WD, et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. *Pain*. 2018;159(10):1932–1954. doi:10.1097/j. pain.000000000001293
- 24. Wang L, Hong PJMC, Oparin Y, et al. Medical cannabis for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. *Br Med J.* 2021;n1034. doi:10.1136/bmj.n1034
- 25. National Academies of Sciences, Engineering aMWD. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. In: *Agenda*. Wasahington: National Academies Press (US); 2017.
- 26. Busse JW, Vankrunkelsven PZL, Heen A, et al. Medical cannabis and cannabinoids for chronic pain: a clinical practice guideline. *Br Med J*. 2021;2021:1.
- 27. Bhaskar A, Bell A, Boivin M, et al. Consensus recommendations on dosing and administration of medical cannabis to treat chronic pain: results of a modified Delphi process. *J Cannabis Res.* 2021;3(1):22. doi:10.1186/s42238-021-00073-1
- 28. Canada Gd. Cannabis for medical purposes under the Cannabis act: information and improvements; 2021.
- 29. Ashton JC. Cannabinoids for the treatment of inflammation. Curr Opin Investig Drugs. 2007;8(5):373-384.

- Abuhasira R, Shbiro L, Landschaft Y. Medical use of cannabis and cannabinoids containing products Regulations in Europe and North America. Eur J Intern Med. 2018;49:2–6. doi:10.1016/j.ejim.2018.01.001
- 31. Furrer D, Kröger E, Marcotte M, et al. Cannabis against chronic musculoskeletal pain: a scoping review on users and their perceptions. *J Cannabis Res.* 2021;3(1):41. doi:10.1186/s42238-021-00096-8
- 32. Ware MA, Doyle CR, Woods R, Lynch ME, Clark AJ. Cannabis use for chronic non-cancer pain: results of a prospective survey. *Pain*. 2003;102(1–2):211–216. doi:10.1016/s0304-3959(02)00400-1
- Beaulieu P, Boulanger A, Desroches J, Clark AJ. Medical cannabis: considerations for the anesthesiologist and pain physician. Can Anesth. 2016;63 (5):608–624. doi:10.1007/s12630-016-0598-x
- 34. Ko GD, Bober SL, Mindra S, Moreau JM, Ko G. Medical cannabis the Canadian perspective. J Pain Res. 2016;9:735-744. doi:10.2147/JPR.S98182
- 35. Rotermann M. Looking back from 2020, how cannabis use and related behaviours changed in Canada. *Health Rep.* 2021;32:3–14. doi:10.25318/82-003-x202100400001-eng
- 36. Fishbein M, Ajzen I. Predicting and Changing Behavior: The Reasoned Action Approach. New York: Taylor & Francis; 2011.
- 37. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process. 1991;50:179-211. doi:10.1016/0749-5978(91)90020-T
- Saunders B, Sim JA-O, Kingstone T, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant*. 2018;52:1893–1907. doi:10.1007/s11135-017-0574-8
- Korn L, Haynie DL, Luk JW, Sita K, Simons-Morton BG. Attitudes, subjective norms, and perceived behavioral control associated with age of first use of Cannabis among adolescents. J Sch Health. 2021;91(1):50–58. doi:10.1111/josh.12977
- 40. Government of Canada. Cannabis act, SC 2018, c 16; 2018. Available from: https://laws-lois.justice.gc.ca/eng/acts/C-24.5/FullText.html. Accessed 11 October 2023.
- 41. Collège des médecins du Québec. Cannabis à des fins médicales: la SQDC n'est pas une option! [Cannabis for medical purposes: the SQDC is not an option!]; 2019.
- 42. Collège des médecins du Québec. Ordonnance de cannabis à des fins médicales [Authorization of cannabis for medical purposes]; 2018.
- 43. Government of Canada. Cannabis for medical purposes under the Cannabis Act: information and improvements. Ottawa: Health Canada; 2020. Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/medical-use-cannabis.html. Accessed 11 October 2023.
- 44. Chang Y, Zhu M, Vannabouathong C, Mundi R, Chou RS, Bhandari M. Medical Cannabis for chronic noncancer pain: a systematic review of health care recommendations. *Pain Res Manag.* 2021;2021:8857948. doi:10.1155/2021/8857948
- 45. Gardiner KM, Singleton JA, Sheridan J, Kyle GJ, Nissen LM. Health professional beliefs, knowledge, and concerns surrounding medicinal cannabis – a systematic review. PLoS One. 2019;14(5):e0216556. doi:10.1371/journal.pone.0216556
- 46. Bell RF, Kalso EA. Cannabinoids for pain or profit? Pain. 2021;162(Suppl 1):S125-s6. doi:10.1097/j.pain.00000000001930
- 47. Alexander SPH. Barriers to the wider adoption of medicinal Cannabis. Br J Pain. 2020;14(2):122–132. doi:10.1177/2049463720922884
- 48. Epstein RM, Street RL. The values and value of patient-centered care. Ann Fam Med. 2011;9(2):100–103. doi:10.1370/afm.1239
- 49. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. Lancet. 2011;377(9784):2226-2235. doi:10.1016/S0140-6736(11)60402-9
- 50. Zolotov Y, Metri S, Calabria E, Kogan M. Medical cannabis education among healthcare trainees: a scoping review. *Complement Ther Med.* 2021;58:102675. doi:10.1016/j.ctim.2021.102675
- Zeng L, Lytvyn L, Wang X, et al. Values and preferences towards medical cannabis among people living with chronic pain: a mixed-methods systematic review. BMJ open. 2021;11(9):e050831. doi:10.1136/bmjopen-2021-050831
- Andreae MH, Carter GM, Shaparin N, et al. Inhaled cannabis for chronic neuropathic pain: a meta-analysis of individual patient data. J Pain. 2015;16(12):1221–1232. doi:10.1016/j.jpain.2015.07.009
- 53. (CACMS) CotAoCMS. CACMS 101: a primer on accreditation of Canadian MD programs by the committee on the accreditation of Canadian medical schools (CACMS) Licensed under CC BY-NC-SA 4.0; 2023. Available from: https://cacms-cafmc.ca/wp-content/uploads/2023/03/CACMS-101-A-Primer-on-CACMS-Accreditation.pdf. Accessed September 29, 2023.
- 54. Cannabis IP, Analgesia C. International association for the study of pain presidential task force on cannabis and cannabinoid analgesia position statement. *Pain*. 2021;162:S1–S2.
- 55. Barakji J, Korang SK, Feinberg J, et al. Cannabinoids versus placebo for pain: a systematic review with meta-analysis and trial sequential analysis. *PLoS One.* 2023;18(1):e0267420. doi:10.1371/journal.pone.0267420
- Pennypacker SD, Cunnane K, Cash MC, Romero-Sandoval EA. Potency and therapeutic THC and CBD ratios: US cannabis markets overshoot. Front Pharmacol. 2022;13:921493.

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