McMaster University | HEALTH FORUM

Evidence brief

Supporting the evidence-based use of cannabis for chronic pain in Canada

21 June 2023

Box 1: Approach and supporting materials

This document was prepared to inform a stakeholder dialogue, which provides individuals – specifically those who will be involved in or affected by decisions about the evidence-based use of cannabis for chronic pain in Canada – with an opportunity to deliberate about a problem and its causes, elements of an approach for addressing it, key implementation considerations, and next steps for different constituencies. A separate document contains 10 appendices:

1) background and methods for preparing this evidence brief
2) overview of policies and programs focused on the use of cannabis for medical purposes in Canada
3) summary of recommendations from the new evidence-based clinical practice guideline on cannabis for medical purposes and chronic pain
4) summary of patient values and preferences identified in the new evidence-based clinical practice guideline on cannabis for medical purposes and chronic pain
5) overview of professional regulatory bodies' policies and programs focused on cannabis for medical purposes in Canada
6) evidence syntheses relevant to element 1
7) evidence syntheses relevant to element 2
8) evidence syntheses relevant to element 3
9) evidence syntheses relevant to element 4
10) reference list.

Note that appendices 3 and 4 are subject to change and should not be copied, quoted or cited until the final version of the recommendations has been publicly released.

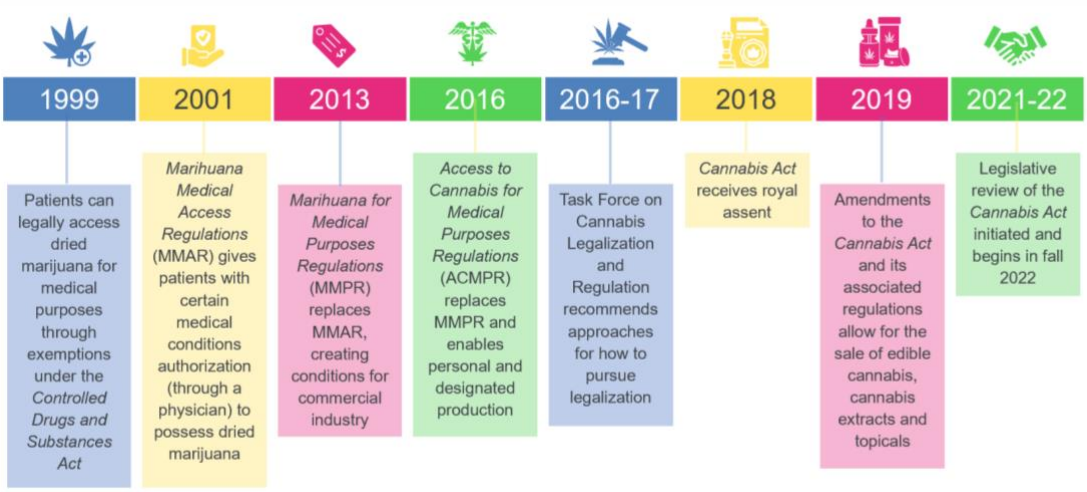
Context for the brief

Considerable attention is being paid in Canada and internationally to the role of cannabis in the management of several conditions, including chronic pain, which affects nearly one in five Canadians.(1-6) With Canadians consuming cannabis at some of the highest rates in the world and with trends suggesting these rates will continue to increase in the future, there are also calls to consider the known health risks associated with the use of cannabis, and to ensure government policymakers make decisions about its use from a public health perspective.(7; 8) The federal government began working through the balancing of benefits and harms during the process of establishing the framework for regulation – and eventually legalization – across the country, which started in 1999 and culminated in the passing of the *Cannabis Act* in 2018 (see timeline of key regulatory changes in the figure on the next page, adapted from (9)). Most provincial and territorial (PT) governments have since developed complementary legislation and programs that provide the framework within which cannabis is distributed and sold to Canadians (see Appendix 2), as well as complementary information about the responsible use of cannabis.

Within the established legal framework, individuals with chronic pain seeking to use cannabis for medical purposes have three pathways to access:

1) through a medical authorization to obtain cannabis for medical purposes from a federal license holder, which:
   - may or may not provide them with access to a subsidy through a government program (such as the one available through Veterans Affairs Canada), workers' compensation programs in PT jurisdictions (such as those in Ontario, New Brunswick and Prince Edward Island), or through private-insurance programs (see Appendix 2)
   - provides them with access to products produced by companies who self-describe as producing 'medical cannabis' (e.g., Tilray Medical or Starseed Medicinal), as well as those that have a medical sales license
2) through a designated production license to grow cannabis for themselves

3) through PT-authorized recreational retailers where products developed by 'medical cannabis' producers are generally not available, subsidies are not available, and medical-expense claims can't be generated for use in tax returns.



With respect to the first pathway (medical authorization), physicians, nurse practitioners and practitioners in specialized pain clinics can either provide the authorizations themselves (although many do not because of the complexity of this 'gatekeeping' role, particularly in the absence of clear, evidence-based guidance on how to develop an appropriate plan for their patients' use of cannabis) or refer their patients to a 'cannabis clinic' (many of which have become high-volume providers of medical authorizations for cannabis). Individuals can access some of these cannabis clinics directly as well (i.e., without a referral). As of December 2021, nearly 300,000 Canadians were registered to access cannabis for medical purposes with either Health Canada or through one of the 135 federal license holders.(10) With respect to the second pathway, a small proportion (6%) of Canadians reported growing cannabis at home in 2022, with 20% reporting having obtained authorization to grow for medical purposes. With respect to the third pathway (recreational retailers) recent trends have shown that the number of Canadians with a medical authorization is on the decline, and that an increasing number of individuals accessing cannabis for medical purposes – which accounts for an estimated 36% of all cannabis users – are doing so through recreational retailers.(10; 11) The majority of Canadians who report using cannabis for medical purposes (73%) acquire products without any formal documentation from a health professional.(10; 12)

Box 2: Implications of the *Cannabis Act* legislative review

The legislative review could open up future options, such as:

- discontinuing the medical authorization process given that cannabis can be purchased without it
- making adjustments to the status quo
- treating cannabis products as a drug product (with a drug-identification number) so it can be prescribed without any additional paperwork.

The review also provides the opportunity to:

- revisit the monitoring and enforcement of health claims made by commercial vendors, particularly now that evidence-based guidelines are available
- explore ways to address potential conflicts of interest that may arise among high-volume prescribers (such conflicts can arise any time the 'diagnoser' of a need is also involved in the 'prescribing' of an approach to meet that need)
- facilitate or mandate the research needed to fill current gaps in the available evidence base.

Despite the perceived benefits reported by individuals using cannabis for medical purposes (including for chronic pain) and an increase in its use, there are significant gaps in knowledge about how it can be used most appropriately, and numerous calls for more high-quality clinical research into safety and efficacy.(9; 13) The Michael G. DeGroote Centre for Medicinal Cannabis Research has focused on building this knowledge base and recently completed an evidence-based clinical practice guideline on cannabis for medical purposes and chronic pain, mostly focused on non-inhaled medical cannabis and cannabinoids (see Appendices 3 and 4). The release of the guideline coincides with

a legislative review of the *Cannabis Act,* which potentially has implications for the future state of medical authorizations for cannabis in Canada (see Box 2).

The problem: Insufficient supports for appropriate cannabis use

Individuals with chronic pain are accessing cannabis for medical purposes through three pathways without the supports for its appropriate use

As noted above, individuals with chronic pain can access cannabis legally through three pathways – medical authorization, growing for themselves, and PT-authorized recreational retailers – and an increasing number are choosing the third pathway for medical purposes.(10; 11; 14). For example, the recently released Medical Cannabis Access and Experiences Survey found that:

- nearly half of all people who use cannabis for medical purposes don't hold a 'medical authorization' and as such access cannabis from PT-authorized recreational retailers (or the illicit market)
- of those with a medical authorization, more than half reported accessing cannabis for medical purposes from a PT-authorized recreational retailer
- previously authorized patients reported no longer seeing the need for authorization because they can now easily purchase cannabis from PT-authorized recreational stores, and perceive licensed sellers of cannabis for medical purposes to be too expensive
- individuals sourcing cannabis for medical purposes from multiple sources (e.g., federally licensed sellers plus in-person or online stores) reported experiencing difficulties finding the products they require.(11)

Individuals with chronic pain choosing to access cannabis for medical purposes through PT-authorized recreational retailers may then not be benefiting from medical advice about its appropriate use, and these retailers are prohibited by law from providing this type of advice. The lack of supports for appropriate use also extend to those growing cannabis themselves, as well as those accessing the illicit market.(15; 16)

An evidence synthesis on patient perspectives that contributed to the development of the new guideline found that most patients would like to acquire both information and authorization for cannabis products from their regular physician, but feel this is not a viable option; sometimes they feel their physician is against cannabis for medical purposes, but more often they believe their physician does not have the required knowledge. In the absence of support from their own physician, they do their own online research and talk to salespeople at cannabis retailers, but often wonder how trustworthy the information they receive is (see Appendix 4).

There are also important equity dimensions of this issue that need to be considered, such as:

- income disparities: not all individuals can afford the cost of cannabis for medical purposes (which may be in addition to other medications purchased for pain management) and this may be particularly problematic for individuals requiring long-term authorizations, such as those with chronic pain (despite organizations like CanniMed that subsidize the cost for those experiencing financial challenges)

- geographical disparities: variability in access to legal cannabis suppliers has created 'postal-code injustice' with respect to accessing cannabis for medical purposes.(16)

Health professionals caring for individuals with chronic pain are having to make decisions about authorizations for and appropriate use of cannabis without training or guidance

Health professionals – in particular physicians and nurse practitioners – are expected to act as 'gatekeepers' to licensed sellers of cannabis products for medical purposes, a role that is enshrined in the legislative framework detailed in the timeline above. However, many healthcare professionals have raised concern with this role given they feel they don't have sufficient information to recommend or support shared decision-making on the use of cannabis for medical purposes.(17)

A recent survey from Health Canada showed that 40% of health professionals feel they are not informed enough about cannabis to support authorizations.(18) Initially, information developed using the type of robust process followed by the evidence-based guidelines described in this brief in Appendix 3 and 4 was not available to support those making decisions about dosing, indications and contraindications for specific conditions like chronic pain, which has in some instances resulted in patients taking unsafe doses.(19; 20)

Health Canada has created an online resource with information about cannabis for medical purposes,(21) and more recently, guidance has been prepared for family physicians by the College of Family Physicians of Canada (CFPC) about authorizing cannabis in primary care, including for chronic pain.(22) Many professional regulatory bodies and professional associations have also developed practice standards, guidance and educational resources that outline the expectations and responsibilities of physicians and nurse practitioners when authorizing cannabis to patients and supports (see Appendix 5), and position statements and institutional standards have been prepared to support those making decisions in specific areas such as mental health, pregnancy, the postnatal period and breastfeeding, and hospital-based care.(23-26)

The new evidence-based clinical practice guideline on cannabis for medical purposes has made four conditional recommendations, three of which focus on aspects of offering patients with chronic pain a trial of cannabis for medical purposes, and one on offering cannabis for medical purposes to patients interested in reducing their use of opioids (see Appendix 3, which should not be copied, quoted or cited). The guideline also flagged three particular clinical areas for which no recommendations could be made based on a lack of evidence, including how to:

- manage patients using cannabis for medical purposes that need to drive or operate heavy equipment for work
- taper patients off cannabis for medical purposes if they are not achieving important benefits, or if the associated harms exceed the benefits
- incorporate the potential for development of cannabis use disorder when considering offering a trial of cannabis for medical purposes to people living with chronic pain.

Administrators overseeing medical cannabis programs for individuals with chronic pain do not have the information needed to adjust programs in a way that supports the evidence-based use of cannabis

Administrators responsible for the design, execution and oversight of government programs (such as Veterans Affairs Canada's Cannabis for Medical Purposes reimbursement policy), workers' compensation programs and private insurance programs (see Appendix 2) have also faced a lack of informational support for the appropriate use of cannabis for medical purposes. This creates challenges in making decisions about what cannabis products should be covered (e.g., what specific cannabinoids and in what ratios, and through what method of administration to the patient), who should be covered (e.g., all individuals with chronic pain or only those for whom other treatments haven't worked), and how much is covered (e.g., the total cost of pre-specified amounts or a proportion of total costs).

An audit of Veterans Affairs Canada's Cannabis for Medical Purposes (CMP) found that:

- 81% of individuals were being reimbursed for the maximum allowable amount (3g per day) or more than this amount as per 'exceptional criteria'

- 11 health professionals are responsible for a disproportionally large number of authorizations (more than 6,000 or 40% of Veterans being reimbursed)
- the number of individuals authorized under the program grew by 660% in five years, with more than 13,000 Veterans now being reimbursed
- spending on the program is set to expand by a factor of 3.5 in just six years, from $85.2 million in 2020 to more than $300 million in 2026 (with an additional $12 million for transactional costs).(27)

Coverage of the audit's findings often highlighted the lack of strong evidence and guidance available to both program administrators and health professionals.(28)

Research and innovation systems have left many questions unanswered about the use of cannabis for chronic pain

Past work completed by the Canadian Centre on Substance Use and Addiction has highlighted many unanswered questions about cannabis from a public health perspective,(8) and the work underpinning the new guideline has highlighted unanswered questions from a clinical perspective (in the specific context of chronic pain):

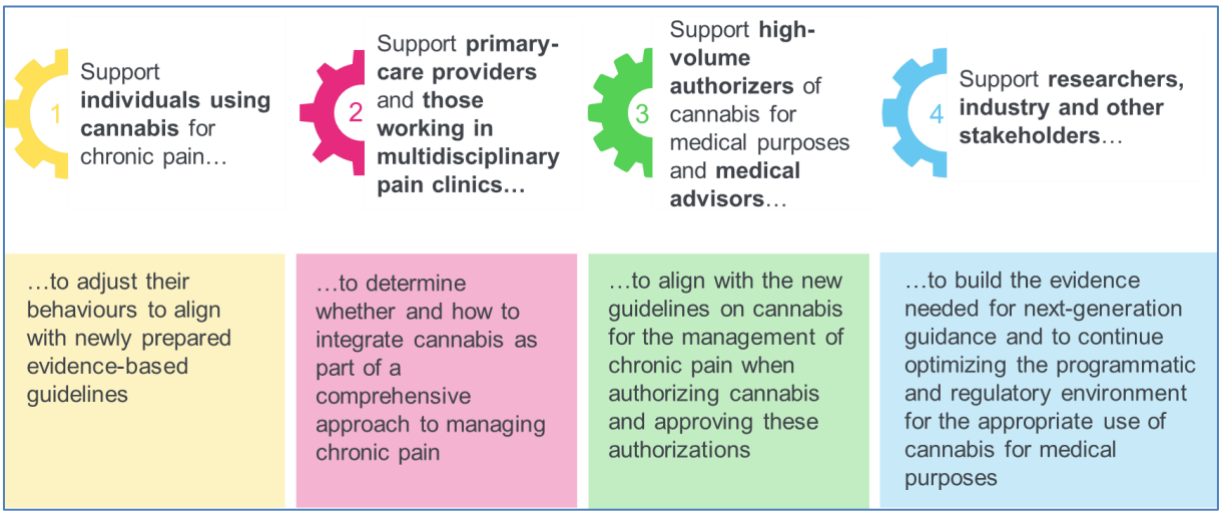
- those related to understanding **benefits**:
  - conducting head-to-head comparisons of cannabis for medical purposes versus other active comparators (including opioids) for chronic pain
  - determining whether or not cannabis for medical purposes reduces opioid use for chronic pain
  - determining if there are systematic differences in treatment effects of cannabis for medical purposes for: 1) chronic cancer pain versus chronic non-cancer pain; and 2) nociceptive versus neuropathic versus nociplastic pain
- those related to understanding **harms**:
  - understanding the long-term harms associated with cannabis use for medical purposes among people living with chronic pain
  - understanding the harms associated with cannabis for medical purposes in those who live with chronic pain and whose work involves driving/equipment operation
  - identifying the harms (and potential benefits) of inhaled forms of 'medical cannabis' (i.e., smoked or vaped)
- those related to optimizing **clinical decision-making**:
  - developing and validating tools to evaluate the risk of cannabis use disorder among individuals considering a trial of cannabis for medical purposes
  - identifying and assessing tapering strategies for people living with chronic pain who use cannabis for medical purposes and choose to taper
  - establishing the optimal dose, formulation and method of administration of cannabis for medical purposes
  - determining if there are systematic differences in treatment effects of different formulations and types of cannabis for medical purposes, including CBD, CBD:THC, THC and PEA.

Part of the challenge lies with the research system, with federal government rules making it difficult to conduct clinical trials of many of the cannabis products available for sale to Canadians, given:

- they must be certified to meet Good Manufacturing Practices (GMP), which is the same as traditional pharmaceutical medicines, and can be difficult to achieve for plant-based products
- there must be sufficient and suitable pre-clinical data showing the product's toxicology and that it does not pose a cancer risk or damage to a developing fetus, which can be time-consuming and prohibitively expensive.(29; 30)

Paradoxically, products deemed safe for sale and consumption by Canadians are not considered safe enough to be studied in clinical trials.(30) Nine clinical trials funded by the Canadian Institutes for Health Research in 2019 had not begun enrolling patients more than two years later as investigators could not identify products available in Canada that met the federal government's requirements for use in a trial.(30) Another part of the challenge lies with industry and the innovation system more generally, with no incentives for cannabis producers to participate in research about whether a product that they can already sell actually 'works.' In contrast, the pharmaceutical industry faces strong incentives to participate in research about whether a drug product 'works' because this is required to gain approval from Health Canada for market access and to be assigned a Drug Identification Number.

Four elements of an approach to addressing the problem



1 Support individuals using cannabis for chronic pain to adjust their behaviours to align with newly prepared evidence-based guidelines

Drawing on a robust implementation-science approach that is underpinned by many syntheses and studies, this element would include:

- identifying, based on the new guidelines, what individuals using cannabis for chronic pain need to do differently to ensure they are using cannabis in ways that align with the guideline (e.g., using non-inhaled forms of cannabis when trialing its use as a treatment for their chronic pain)
- identifying the barriers and potential enablers to doing things differently (e.g., costs of and access to non-inhaled forms of cannabis)
- identifying the implementation strategies most likely to overcome the modifiable barriers and enhance enablers for the use of cannabis in ways that align with the guideline
- delivering, evaluating and adjusting as needed the implementation strategies.

Our searches for evidence syntheses about element 1 did not identify any that specifically addressed individual behaviours related to cannabis use for chronic pain (see Appendix 6), and those that we did find often focused on interventions that addressed problematic cannabis use in the context of substance use generally, rather than use for medical purposes. The three evidence syntheses we found suggest that computerized interventions and cognitive behavioural therapy sessions (individual and group) have demonstrated some promise in their ability to shape substance use behaviour, may be cost-effective, and are easy to disseminate, but the low quality of evidence available makes it difficult to draw definite conclusions.

2 Support primary-care providers and those working in multidisciplinary pain clinics to determine whether and how to integrate cannabis as part of a comprehensive approach to managing chronic pain

This element would use a similar approach:

- identifying, based on the new guidelines, what primary-care providers (e.g., family physicians, nurse practitioners and other healthcare professionals involved in the provision of primary care) and those working in multidisciplinary pain clinics need to do differently to ensure they are integrating cannabis into comprehensive approaches to address chronic pain in ways that align with the guideline (e.g., starting by offering a trial of cannabis when standard care has not worked)
- identifying the barriers and potential enablers to doing things differently
- identifying the implementation strategies most likely to overcome the modifiable barriers and enhance enablers for the integration of cannabis into comprehensive approaches for addressing chronic pain in ways that align with the guideline

- delivering, evaluating and adjusting as needed the implementation strategies.

Our searches for evidence syntheses about element 2 again did not identify any that specifically addressed the behaviours of providers working in primary care or in multidisciplinary pain clinics, or about ways to support providers to integrate cannabis as part of a comprehensive approach to address chronic pain (see Appendix 7). The six evidence syntheses we did identify mostly focused on providers' views about and experiences with cannabis for medical purposes. Overall, these syntheses found:

- while most health professionals feel that cannabis can be useful for treating pain, low prescribing or authorization rates are likely due to a lack of formal training and evidence-based guidelines, and beliefs of some providers about its lack of efficacy
- pharmacists are often not consulted about cannabis for medical purposes and feel they require additional education and training to adequately discuss and/or dispense cannabis.

Support high-volume authorizers of cannabis for medical purposes and medical advisors to align with the new guidelines on cannabis for the management of chronic pain when authorizing cannabis and approving these authorizations

This element would take a similar approach to elements 1 and 2, but focus on ensuring that those authorizing cannabis for medical use at high volumes, as well as medical advisors overseeing government programs, are aligning their approach with the new guideline (e.g., deciding to cover non-inhaled cannabis for medical purposes). We identified 10 evidence syntheses that focused on prescribing behaviours and prescription monitoring in general (although those focused on chronic pain most often focused on opioid prescribing rather than cannabis authorization) and one synthesis that focused on providing preliminary guidance on authorizing smoked cannabis for chronic pain (see Appendix 8). In general, the syntheses we identified about prescription monitoring programs found them to be mostly effective for changing clinical decision-making and prescription behaviour, but their effects on medication appropriateness and patient outcomes remain unknown, and they were associated with unintended consequences (e.g., patient dissatisfaction, increases in illicit drug use). The one synthesis on smoked cannabis for chronic pain called for the development of robust guidelines to inform decision-making among those authorizing cannabis.

Again, an experienced implementation-science team could rapidly design and deploy an initiative contextualized to each of the above approach elements and to Canada.

Support researchers, industry and other stakeholders to build the evidence needed for next-generation guidance and to continue optimizing the programmatic and regulatory environment for the appropriate use of cannabis for medical purposes

This element focuses on putting in place approaches that can confirm the priorities for research (drawing on those already listed above) and revisiting the incentive structure for researchers and industry to address the priorities. One approach that could be used is the James Lind Alliance Priority Setting Partnerships (PSP) methodology, which brings together patients, carers and health professionals to work through a number of steps to iteratively and collectively identify a 'top 10' list of research priorities in a particular area.(31) This element would also include efforts to adjust the research environment to enable research focused on cannabis for medical purposes (including clinical trials) in Canada. Seventeen evidence syntheses were identified in searches related to element 4 (see Appendix 9). Six of these syntheses focused on research and innovation systems more generally and found that:

- responsible research and innovation approaches should include efforts to promote public engagement and social inclusion, and should report representation aims, eligibility criteria and justification for these criteria, as well as representation achievement
- more research on training methods and supports for involving the public and stakeholders in health research decision-making is needed to address barriers to input in research agendas, and responsibilities for public-involvement activities supporting research should be institutionalized
- the development of reporting standards and best practices for public inclusion activities (PIA) objectives and methods, as well as the assessment of decision-makers' perspectives of PIA, can facilitate implementation of PIA findings in decision-making processes.

The additional 11 syntheses identified were more specifically focused on priority setting processes – including the James Lind Alliance approach – in particular clinical areas (e.g., obesity, plastic surgery, women's health), and noted the importance of systematic and transparent approaches that engage all relevant stakeholders, as well as the need for rigorous monitoring and evaluation. Any such work should be informed by the recently completed summaries of research projects funded by the Canadian Centre on Substance Use and Addiction and should strive to ensure coverage of all needed forms of evidence (e.g., data analytics, evaluations, behavioural/implementation research, qualitative insights) across all relevant domains (e.g., clinical practice, public-health measures, health-system arrangements, and industry behaviours). None of the evidence syntheses addressed incentives directly.

Implementation considerations

Some examples of the key barriers and facilitators to pursuing the approach elements are listed below.

References – see Appendix 10

Moat KA, Bain T, Bhuiya A, Demaio P, Alam S, Lavis JN. Evidence brief: Supporting the evidence-based e use of cannabis for chronic pain in Canada. Hamilton: McMaster Health Forum, 21 June 2023.

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