

Commentary

Removing barriers to accessing medical cannabis for paediatric patients

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ABSTRACT

Medical cannabis (MC) may offer therapeutic benefits for children with complex neurological conditions and chronic diseases. In Canada, parents, and caregivers frequently report encountering barriers when accessing MC for their children. These include negative preconceived notions about risks and benefits, challenges connecting with a knowledgeable healthcare provider (HCP), the high cost of MC products, and navigating MC product shortages. In this manuscript, we explore several of these barriers and provide recommendations to decision-makers to enable a family-centered and evidence-based approach to MC medicine and research for children.

Keywords: Canada; Health Canada; Medical Cannabis; Paediatric.

PROBLEM STATEMENT

Canadian children can access medical cannabis (MC) by their parents or caregivers obtaining an authorization from a licensed health care provider (HCP)—either a physician or nurse practitioner. Specific requirements for HCPs to authorize MC are determined by their respective provincial or territorial regulatory bodies (1). Despite this, many parents face significant barriers to accessing MC for their children. We discuss these barriers and explore ways in which decision-makers, the medical community, and licensed cannabis producers (LCPs) can facilitate access. This commentary builds on our recent article in the Canadian Medical Association Journal with recommendations for addressing regulatory deficiencies that negatively impact paediatric patients (2).

Most children obtain MC as whole plant extracts containing a wide spectrum of cannabinoids including cannabidiol (CBD) and tetrahydrocannabinol (THC) and biologically active terpenes. MC in the form of purified CBD products makes up a very small minority of products available in Canada. Except for several studies assessing purified CBD to treat several forms of paediatric drug-resistant epilepsy (DRE) (3,4,5,6), evidence supporting the use of MC products for other paediatric indications is sparse and founded on non-randomized open-label studies and case series. These indications include spasticity, pain, and nausea associated with malignancy and chemotherapy, behavioral issues in autism spectrum disorder, and symptom management for children requiring palliative care (7,8,9,10,11). Despite limited evidence, many families of children with complex medical needs use or seek access to MC to treat symptoms not sufficiently addressed by conventional medical therapy (12).

In 2019, Elliott et al. identified barriers Canadian parents of children with DRE faced accessing MC for their children using semi-structured qualitative interviews of 19 parents of 19 children with DRE who had accessed MC. The parents expressed a desire to work with their child's healthcare team in pursuing MC. Just over half successfully obtained MC authorizations from their child's neurologist. The remainder sought authorizations outside of the child's normal circle of care (e.g., from a specialized MC clinic) (13). This coincides with the experience in a Canadian tertiary care paediatric hospital, where MC authorizations largely came from outside of the patient's regular care team (14). Social media and advocacy groups have become prominent information sources for parents regarding the use of MC but may promote misinformation about its benefits (15). When no support or guidance is provided by a child's HCPs, some parents may prepare homemade cannabis extracts or turn to other cannabis providers, including the illicit market (8). This has the potential to cause harm to the child from drug-drug interactions,

impurity, lack of standardization, unintentional overdosing, and intoxication (16,17,18,19).

A disconnect between a parent's wish to access MC for their child and the apprehension from HCPs regarding the use of MC in children may lead to tensions, distrust, and fragmented patient care if the parent seeks MC elsewhere. This apprehension in HCPs may be perceived by families as an unwillingness to help or as withholding a potentially beneficial treatment. The paucity of high-quality evidence assessing the safety, efficacy, appropriate dosing, and long-term neurodevelopmental impacts are all reasonable reasons why HCPs are reluctant to authorize MC, even if they believe it could be beneficial (20). This, combined with a lack of formal training about MC in Canadian medical schools, residency programs, and continuing professional education activities has contributed to discomfort with discussing and/or authorizing MC to paediatric patients (21). In fact, Canadian paediatric neurologists report reliance on self-education prior to authorizing MC (22). This shortage of educational opportunities has resulted in a small group of paediatricians and paediatric subspecialists with sufficient clinical expertise to be comfortable authorizing MC to their complex needs patients.

The prohibitive cost of MC is another major barrier. Products without a Health Canada Drug Identification Number (DIN) such as MC are not covered through provincial or territorial drug formularies. Private insurance coverage for MC varies greatly, with many plans providing no coverage at all. Some parents have reported spending over \$1000 (in Canadian currency) per month for their child's MC (13). Despite compassionate pricing programs offered by several LCPs, the use of MC places a substantive financial burden on families already struggling to afford the cost of caring for a child with complex medical needs (23,24). With the introduction of the *Cannabis Act*, MC became subject to provincial and federal taxes making it even more cost prohibitive for families. Parents can claim MC as a tax-refundable medical expense; however, a family earning \$50,000 per year spending \$12,000 per year on MC can only claim an annual federal tax credit of \$1575 and a provincial/territorial tax credit ranging from \$420 to \$1134 (25). This tax benefit is not nearly enough to support these families. Cost concerns can result in parents administering doses to their children lower than those recommended by their HCPs (8,13).

MC products used by children are plant-based and subject to variations in the strain of cannabis and extraction techniques used resulting in considerable variation in concentrations of active ingredients. Many formulations are available reporting similar ratios of THC and CBD on their labels but having their own unique concentrations of minor cannabinoids and terpenes (2). This compounds product shortages that LCPs are not required to report to patients or HCPs as would be expected for other

Health Canada approved drugs (13). LCPs are currently not mandated to provide a certificate of analysis (CoA) to parents or healthcare providers confirming the full profile of each MC product batch, which causes undue stress for parents and HCPs searching for a comparable formulation when shortages occur.

RECOMMENDATIONS

To mitigate barriers to appropriate MC access for children, we provide the following facilitators (summarized in Figure 1):

Support high-quality paediatric MC research

High-quality basic and translational research as well as clinical studies including randomized clinical controlled trials evaluating appropriate indications, dosing, and safety of MC products in children are urgently needed to provide HCPs with the evidence they need to authorize MC to their paediatric patients. This is especially so for indications other than epilepsy including paediatric oncology and palliative care where evidence is particularly lacking. Several major barriers must be overcome to allow Canadian researchers to conduct this research.

The cost associated with conducting paediatric MC clinical trials is significant, as these studies often require multiple sites given the relative rarity of the conditions studied (26). Major funding agencies in Canada, such as the Canadian Institutes of Health Research (CIHR) have limited funds for clinical trials and have not yet made a special call for paediatric MC clinical trials. A potential model is provided by the Netherlands, where dedicated peer-reviewed funding for paediatric MC research is administered through a federal funding agency (ZonMW) (27). A percentage of revenue generated from the taxation of recreational cannabis sales should be earmarked for MC research, including dedicated paediatric funding. Federal or provincial funding agencies could administer these funds by providing the necessary independent scientific peer review. Additionally, LCPs could provide funds to charitable programs, including children's hospital foundations that would fund paediatric MC research through independent peer-review processes. Guidance on mechanisms to reduce conflict of interests for cannabis researchers is needed as clinical trial products, and matching

placebos, are cost-prohibitive necessitating collaboration with industry.

Several regulatory barriers also need to be addressed. Cannabis products sold in Canada must have Health Canada Good Production Practices (GPP) certification. However, to be used in clinical trials, products must obtain Good Manufacturing Practices (GMP) Certification. This inconsistency makes most MC products already on the market ineligible for study in clinical trials. Recognizing that obtaining GMP certification is costly and time-consuming for LCPs, with little financial incentive, we recommend that Health Canada align their production and research standards to allow GPP-certified MC products to be used in clinical trials or provide incentives for Canadian LCPs to obtain GMP certification. The requirement of product-specific pre-clinical data for products limits what products can be evaluated.

Until these challenges in conducting paediatric MC trials are resolved, greater weight should be placed on real-world evidence collected through patient registries such as being developed by the Canadian Collaborative for Childhood Cannabinoid Therapeutics (C4T).

Improve MC education for healthcare providers

Enhancing evidence-based education about MC would provide Canadian physicians, nurses, and pharmacists the knowledge necessary to safely advise on and authorize MC products. Improved curricula in nursing, pharmacy, and medical school and during residency training along with continuing medical education programs hosted by academic institutions or professional organizations including brief virtual case-based presentations would help bridge the knowledge gap faced by HCPs. This could be supported by organizations that stand independent from the cannabis industry such as C4T, the Cannabinoid Research Initiative of Saskatchewan (CRIS), the Canadian Paediatric Society (CPS), and the Canadian Consortium for the Investigation of Cannabinoids (CCIC). There are several Canadian experts in paediatric cannabinoid medicine who could serve as mentors and support MC education.

Decrease financial barriers to MC for children

The prohibitive costs faced by parents who desire to purchase MC for their children must be addressed. It would be ideal to

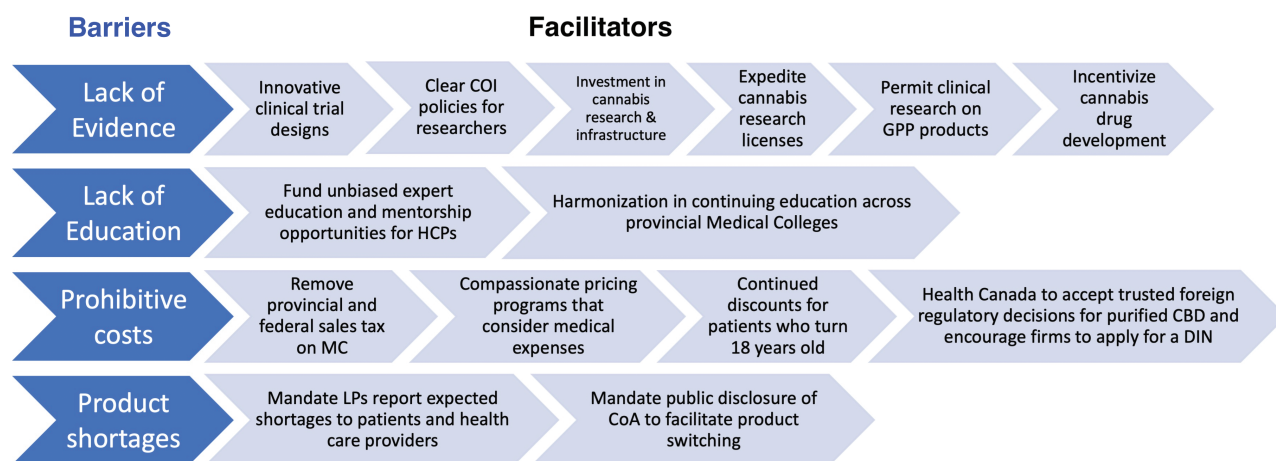


Figure 1. Summary of barriers to accessing medical cannabis for paediatric patients and their respective facilitators.

have medical cannabis products placed on provincial and territorial formularies, however, in the absence of a DIN, this is unlikely to occur. As such, we encourage LCPs to work in collaboration with Health Canada and the medical community to develop MC products that have a DIN available to paediatric patients. Health Canada is already considering using foreign regulatory decisions for other products, it should include using this mechanism for purified CBD products with a shorter period of post-market experience than the initially proposed 15 years.

Cannabis products used for medical purposes and authorized by an HCP should not be subject to the same taxation schedule as recreational cannabis products. MC products used by children, if authorized by a licensed HCP and purchased from a Health Canada-approved LCP, should be exempt from federal and provincial taxation. Requiring HCP oversight would prevent concerns about this tax-free status being taken advantage of when recreational products are purchased (28).

Until MC products are available on public formularies, Federal and Provincial/Territorial governments should increase the amount of tax credit that families are able to claim for their child's MC. Options for non-formulary public funding should also be considered, similar to those for necessary medical equipment and supplies for select conditions. We also encourage LCPs to offer differential costing for cannabis products used for medical and recreational purposes. Most compassionate cost programs are based solely on the patient's age (i.e., children under 18 years of age qualify) or on family income and do not take into consideration the medical complexity of the child and additional healthcare costs that families incur. Considerations for compassionate pricing that incorporates income and medical expenses without an age limit would be preferable.

Implement mechanisms to support patients during MC product shortages

In Canada, pharmaceutical companies are required to report expected shortages within 5 calendar days of becoming aware of an anticipated shortage/discontinuation. The same requirements should apply to MC products sold under medical authorization. While many LCPs do advise parents of impending shortages, this is not always the case. MC products not having a DIN is not a justifiable reason why LPs should be able to circumvent this rule. Patients, parents, and healthcare providers should have access to CoAs of the MC product to support a transition to an alternative product. Variations in the MC product profile may affect overall safety and efficacy in vulnerable patients such as children with complex care needs (29).

CONCLUSIONS

Obstacles faced by caregivers in accessing MC for their children with complex medical needs may seem insurmountable. Within this article, we discuss barriers and recommend facilitators to greatly improve the ability of all Canadian children with chronic diseases to access MC with the support of their HCPs. In reviewing these barriers, it becomes clear that many stem from the fact that while MC is used as a therapeutic intervention in many medically complex children it does not undergo the same processes and requirements of other pharmaceutical products.

Given the financial burden of paediatric chronic disease on health care systems, and the potential cost-effectiveness of MC, implementing the changes recommended in this manuscript could potentially have a significant positive impact on individual families as well as the health care system. We encourage industry, various levels of government, and funding agencies to work together to promote high-level, independent clinical research and education on cannabis to paediatric healthcare providers and their families, to ensure safe and equitable access to those who could potentially benefit from MC.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and design of the work, drafted the manuscript, revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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POTENTIAL CONFLICTS OF INTEREST

RJH and LEK served on Health Canada's Scientific Advisory Committee on Health Products Containing Cannabis whose views are not reflected in this manuscript. RJH received a grant from the Jim Pattison Children's Hospital Foundation for a study on medical cannabis in childhood refractory epilepsy and was Co-Chair, Health Canada Scientific Advisory Committee on Health Products Containing Cannabis (an unpaid position). EL received speaking fees from Spectrum Therapeutics and holds leadership positions in the following groups: Jamaican Medical Cannabis Corporation (unpaid position), Medical Cannabis Clinicians Society (UK), Canadian Collaborative for Childhood Cannabinoid Therapeutics, MedCan Support and Canadian Patient Advocacy & Support Services. CM-H is the controlling shareholder of a small publicly traded company that made an incremental \$1.7M investment in a biotechnology company involved in medical research related to minor cannabinoids. JA has participated in an advisory board for Zyus Life Science. REB is a member of the Advisory Council, Drug-Free Kids Canada, and was Co-Chair of the Cannabis Project Advisory Group, Canadian Paediatric Society (both unpaid positions). SC holds a leadership position on the Network of Networks (N2) Board of Directors. AG reports that this article was researched and written prior to her employment at Health Canada and any views, opinions, and recommendations expressed within are those of the authors and do not reflect the position of Health Canada and/or the Government of Canada. JJ received grants from NSERC, CIHR, AMA Pediatrics, and Alberta Children's Hospital Foundation, consulting fees from Eisai, UCB, and Pendopharm, payment/honoraria from Eisai, UCB, Pendopharm, and Sunovion, and travel reimbursement from Neurocrine. JJ also holds leadership positions in the American Epilepsy Society, the Canadian League Against Epilepsy, and Hope for Hypothalamic Hamartomas. MJR is a member of the Paediatrics & Child Health editorial board. Another editor was responsible for overseeing the peer review of this manuscript. AS is the founder of Shackelford Pharma., an emerging medical cannabis company. There is also a provisional patent application filed, but not yet issued, on behalf of Shackelford Pharma, Inc. RV was director of the Department of Pediatric Pharmacy, Children's Hospital of Eastern Ontario when this manuscript was written and submitted for publication but is now

Vice President of Pharmacy Affairs for BCE Pharma. He has received consulting fees from Harvest Medicine Clinic and recently concluded an 8-year term as a Director of the International Pharmaceutical Federation Foundation. LEK holds a Board of Directors position at the Canadian Consortium for the Investigation of Cannabinoids and holds funding from the Canadian Institutes of Health Research, the Canadian Cancer Society, and the SickKids Foundation for C4T. She holds a Mitacs Accelerate grant for a separate project in partnership with Canopy Growth. There are no other disclosures.

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