

**ONTARIO COURT OF JUSTICE
(Northeast Region)**

B E T W E E N:

HER MAJESTY THE QUEEN

Respondent

- and -

DANE BEBAMASH

Applicant

AFFIDAVIT OF ZACHARY WALSH

I, Zachary Walsh, PhD., R. Psych, Professor, Department of Psychology at the University of British Columbia of 3333 University Way, Kelowna, British Columbia Campus, MAKE OATH AND SAY/AFFIRM:

Area of Expertise

1. My proposed area of expertise is cannabis, medical cannabis use and access, and medical cannabis in relation to holistic medicine.

Personal Qualifications

2. I am a Full Professor with the Department of Psychology at the University of British Columbia. Attached hereto and marked as exhibit "A" is a true copy of my Curriculum Vitae. I received my B.Ed. English 1997. I have been trained in Psychology: BA Honours 2001, MA Psychology 2004, and PhD Clinical Psychology 2008. I have conducted extensive research and have had research published in peer-reviewed journals on the subject of cannabis, medical cannabis access, and substance use generally. I have been consulted on cannabis-related issues by the Canadian House of Commons, Canadian Senate, Task Force on Legalization and several international organizations. I have also delivered cannabis education seminars and workshops for

diverse health professionals. Note that medical cannabis use and access in Canada has been among my key research topics. In the course of my research over the past decade I have had the opportunity to work with diverse participants in the medical cannabis industry including patients, physicians, operators and employees of licensed producers and dispensaries and countless other cannabis users. I was lead investigator for Canada's first clinical trial of cannabis to treat a mental health condition and have led several large surveys of medical and non-medical cannabis use in Canada. I was also a lead investigator for the Medical Cannabis Standards Engagement Evaluation and Dissemination (SEED) study, where I was the academic partner to assist in the development and implementation of a self-regulatory framework for medical cannabis dispensaries. I am currently funded by the Social Sciences and Humanities Research Council of Canada and the Canadian Institutes for Health Research to study cannabis use. I have authored highly cited reviews of the scientific literature on medical cannabis use and mental health and have been part of several panels to develop clinical guidelines and recommendations for medical cannabis use.

3. I acknowledge that it is my duty to give evidence in relation to this proceeding as follows:
 - (a) to provide opinion evidence that is fair, objective, impartial, and non-partisan;
 - (b) to provide opinion evidence that is related only to matters that are within my area of expertise; and
 - (c) to provide such additional assistance as the court may reasonably require, to determine a matter in issue.
4. I acknowledge that the duty referred to above prevails over any obligation which I may owe to any party by whom or on whose behalf I am engaged.

For what health issues can medical cannabis be therapeutic?

5. Now produced and marked as Exhibit "B" to this my affidavit is a copy of a 2013 article published in the *International Journal of Drug Policy* after a blind peer review process, entitled "Cannabis for Therapeutic Purposes: Patient Characteristics, Access and Reasons for Use" that is the culmination of research by myself and the other authors/participants in the *Cannabis Access for Medical Purposes* (CAMPS) study. The CAMPS study is among the largest detailed study to date

of medical cannabis consumers in Canada and has been referenced by over 300 subsequent articles. The CAMPS study was externally funded and reviewed by the UBC Institute for Healthy Living and Chronic Disease Prevention and was carried out between 2011 and 2012. I believe the CAMPS survey illustrates the methods used, the demographics with respect to the individuals, the medical conditions for which cannabis has been authorized and for which use continues, the medical condition systems indicated by the patients, and the patterns and modes of use by them. The findings of this study highlight the broad activity of cannabinoid medicines to impact multiple health concerns. Indeed, most respondents reporting using cannabis to address several co-occurring symptoms such that the average number of symptoms patients endorsed treating was more than 5. The most frequently endorsed symptoms were pain, anxiety, and sleep problems with more than half of respondents reporting cannabis use to address all three symptoms and more than 95% using cannabis to address at least one of those three symptoms. The high prevalence of these symptoms among those treated with medical cannabis is related to the high prevalence of these symptoms more broadly; although cannabinoid medicines may also be helpful for other disorders such as epilepsy, irritable bowel syndrome, and multiple sclerosis, the lower prevalence of these conditions in the general population is mirrored by lower prevalence among medical cannabis users.

6. Now produced and marked as Exhibit “C” to this my affidavit is another paper that I have authored with a group of clinical experts in cannabinoid medicine that makes specific recommendations for the use of medical cannabis based on a systematic review of the literature. The authors of this paper included health researchers from prominent Canadian universities including University of Toronto, McGill University and University of British Columbia. The paper is entitled “*Clinical practice guidelines for cannabis and cannabinoid-based medicines in the management of chronic pain and co-occurring conditions*” and has been blind peer reviewed and has now been published in the journal *Cannabis and Cannabinoid Research* published in advance online in March 2023. I believe the recommendations in these guidelines highlight some of the most prevalent health issues for which cannabis can be therapeutic. This review was published in 2023 but is generally consistent with the findings from the 2013 paper Exhibit “B”, in that it highlighted pain, sleep and anxiety as key conditions for which cannabis is used and demonstrates clinically meaningful effects. More specifically, based on a synthesis of 19 systematic reviews and 51 original

research studies, we concluded that cannabinoid medicines benefit chronic pain management, and may also benefit conditions that commonly co-occur with chronic pain such as sleep problems, anxiety, and suppressed appetite.

What is holistic medicine and does medical cannabis lend itself to a holistic medicine approach?

7. The term holistic medicine has broad meanings within healthcare that vary considerably in their degree of specificity, prescriptiveness, and authority. With that in mind, I interpret the term to generally refer to an orientation to medicine that emphasizes the comprehensive consideration of the entire person rather than prioritizing the physical and biological aspects of health as may be the case in more traditional, bio-medical models. Some conceptualizations of holistic medicine include alternative and complementary therapies. Other conceptualizations of holistic medicine emphasize an approach similar to the biopsychosocial–spiritual model of health which also endeavours to address the whole person.

8. Medical cannabis lends itself to both these conceptualization of holistic medicine in that it is often included among alternative and complementary approaches, and also because it is a medicine with the capacity to address factors that are not specific to a given physical symptom. As noted above in reference to Exhibit “B”, the majority of medical cannabis users report using cannabis to address several concurrent medical symptoms. In many cases these include both physical symptoms such as pain and inflammation and psychological symptoms such as anxiety and sleep disturbance. The capacity for cannabis to concurrently address psychological and physical symptoms is also noted in Exhibit “C” and is a distinct strength of cannabinoid medicines. As discussed below cannabis can also be used for spiritual purposes. Taken together, the capacity of cannabis to address biological, psychological and perhaps spiritual aspects of functioning makes it well suited to a holistic medicine approach.

Can medical cannabis create and enhance spiritual experiences?

9. Cannabis has an extensive and well-documented history of use as an entheogen. Entheogenic plants are plants used to enhance spiritual experience. There is evidence of entheogenic use of cannabis across diverse cultures and historical epochs. Currently the most

prominent entheogenic use of cannabis is among some practitioners of Hinduism where it has been used entheogenically for centuries if not millenia and is associated with the deity Shiva and the popular festival of Holi. Entheogenic use of cannabis is also prominent among adherents of Rastafarianism in Jamaica for whom use is a governmentally recognized sacrament and decriminalized accordingly.

10. The entheogenic use of cannabis appears to be increasing in Canada, in part through the adaptation of a tradition with historical roots in India that involves combining cannabis with yoga. Now produced and marked as Exhibit “D” to this my affidavit is a poster that I have authored with students under my supervision that presents the first systematic examination of the practice of combining cannabis and yoga in a Canadian context. This poster entitled “Combining Cannabis and Yoga: Practices and Motives.” has been peer reviewed and was accepted for presentation at the 2023 International Cannabinoid Research Society Symposium in Toronto and at the 2023 British Columbia Substance Use Conference in Vancouver. The research represented in that poster found that individuals who combined cannabis and yoga were more likely to experience a mystical experience. Specifically, scores on the Mystical subscale of the Mystical Experiences Questionnaire were significantly higher among yoga practitioners who added cannabis to their yoga practice, and 29% of those who combined cannabis and yoga experienced what is classified as a “complete mystical experience” compared to 0% of respondents who did not add cannabis to their yoga practice. Taken together with the extensive and longstanding entheogenic use of cannabis this evidence suggests that cannabis can be used to enhance and create spiritual experiences.

Is medical cannabis iterative in that there are many different strains of cannabis and it is often only through trial and error that helpful strains are found?

11. Cannabis is a green leafy plant with has many different strains. These cannabis “strains” are more properly described as chemovars. Clinical research trials that directly compare the therapeutic effects of different cannabis chemovars are generally lacking. However, a substantial number of patients and cannabis-focused health care providers report distinct therapeutic benefits of distinct strains of cannabis. In my experience it is not unusual for patients to work with the support of

clinicians to identify specific cannabis chemovars and products that are most helpful and others that are relatively less helpful.

12. Now produced and marked as Exhibit “E” to this my affidavit is another paper that I have authored with others with data drawn from the CAMPS study. This paper has also been blind peer reviewed and has now been published in the *International Journal of Drug Policy* at Volume 25 (2014) 691-699, entitled “Barriers to Access to Cannabis for Therapeutic Purposes in Canada” by myself and the other authors/participants mentioned accordingly. The results reported in Exhibit “E” indicate that medical cannabis users value access to specific strains of cannabis. The distinct therapeutic effects of distinct strains of cannabis is an area of ongoing scientific interest with a strong theoretical rationale based on the diverse of effects of the distinct cannabinoid profiles that characterize different strains. The importance of strains is reflected in empirical literature on patient preferences such as in “Exhibit E” and others, and by providers of medical cannabis, including licensed producers for both medical and nonmedical cannabis products, who highlight distinctions among the cannabis strains they provide. My personal experiences as a research scientist who has interacted extensively with medical cannabis patients also highlights the importance of access to specific strains of cannabis.

Are there different ways to consume cannabis?

13. There are several different ways to consume cannabis, including smoking and vaporizing dried cannabis flowers and concentrates derived from these flowers. There are also several varieties of edible products such as tinctures, foods and drinks as well as topical ointments and creams. Reports in Exhibit “B” identify smoking as the most prevalent modality of ingestion, followed by vaporization and oral ingestion. Pharmacokinetics differ according to modes of consumption with clinically relevant differences in time of onset, and nature and duration of effects. For these reasons many medical cannabis users will use more than one modality of consumption. The diversity of consumption options for cannabis products is clearly evidenced by the diverse offerings in Canada’s legal and medical cannabis markets.

If medical cannabis patients access medical cannabis through the recreational cannabis stream – as opposed to a source that is focused on the medicinal use of cannabis – might that result in reduced medical oversight and increase the chances of complications?

14. I believe that accessing cannabis through the medical rather than recreational stream has the potential to reduce complications and harms due to increased medical oversight. Now produced and marked as Exhibit “F” to this my affidavit is a paper that I have authored with a group of clinical experts in cannabinoid medicine that makes specific recommendations regarding the importance of maintaining a medical stream of cannabis access distinct from the recreational stream in order to optimize service delivery and protect patients. The paper is entitled “*Why a distinct medical stream is necessary to support patients using cannabis for medical purposes*”, and authors included health researchers from prominent Canadian universities including University of Toronto, McGill University and University of British Columbia. The paper has been blind peer reviewed and has now been published in the *Journal of Cannabis Research* published in advance online in May 2023. In the paper we conclude that the purposes and needs of medical cannabis users are sufficiently different as to necessitate distinct streams of access. A key reason for distinct streams is to facilitate support for both patients and for caregivers to minimize risks and optimize benefits. We specifically note that patients require guidance in determining the appropriateness of medical use and if appropriate may require further guidance related to dosage, product selection and potential interactions with other medications. For those reasons accessing cannabis through the medical stream is important for reducing the chances of complications and increasing medical oversight.

Are there risks to patient health in having medical cannabis patients obtain their medical cannabis from the manufacturer?

15. Obtaining cannabis from the manufacturer is not inherently dangerous providing that the manufacturer has the capacity to engage with other care providers and with clinically relevant aspects of the patient experience. Cannabinoid medicines are diverse in presentation and are used in a wide variety of contexts and as such it is important to provide multiple access points to reduce the barriers to access outlined in Exhibit “E”. It is my opinion that patients should have the opportunity to consult with experts in cannabinoid medicine in order to maximize benefits of use. The opportunities for such consultation are facilitated by in-person access such as provided by a

physical retail location. My personal experiences as a research scientist who has interacted with dispensary operators, employees, and customers highlight the important role of dispensaries in the health behaviors of patients. Dispensaries provide an opportunity for patients to discuss medical cannabis use with other patients and experts. In addition, many dispensary operators and workers are also medical cannabis patients and as such contribute to an informal information network. Such information networks may be particularly valued by medical cannabis users due to the chilling effect that fear of stigmatization might have on their ability and comfort in accessing more formal information related to medical cannabis use. In general, it is challenging for patients to access reliable information regarding the intricacies of medical cannabis use which adds to the perceived value of the low-barriers information exchange at dispensaries.

For medical cannabis patients, can medical cannabis derived from the plant be reliably replaced by synthetic cannabinoids?

16. Synthetic cannabinoids generally fall into two categories of 1) synthetic ‘designer molecules’ that produce psychoactive effects for recreational purposes and 2) prescription medications such as Nabilone and Marinol that are used for specific medical indications. It is my opinion that there is no medical situation in which the first category of recreational synthetic cannabinoids can reliably replace plant-based cannabinoids. These synthetic products have not undergone the safety analyses required to be considered medicines nor do they have a long history of use upon which to base estimations of safety. These products are generally unregulated or under-regulated and are designed primarily to circumvent legal restrictions on natural cannabinoids. They may be poorly characterized and untested for consistency. As such they are not acceptable replacements for natural cannabis medicines.

17. The second category of prescription synthetic cannabinoids may be suitable replacements for herbal cannabis in some contexts but their potential applications are more limited and, in my experience, they are generally less well-tolerated and accepted by patients relative to plant-based cannabis. The broad patient preference for herbal rather than synthetic cannabis may be related to perceptions of safety and general preferences for “natural” medicines. The preference may also reflect the differing effectiveness of a single synthetic molecule with more narrow band impacts

relative to the diverse constituents and potentially broader effects associated with herbal cannabis. As noted in Exhibit “E” and discussed above, many patients express distinct preferences among cannabis chemovars and these preferences can reasonably be assumed to extend to differences between synthetic and plant based products. Exhibit “E” also outlines that cost and physician communication are substantial barriers to accessing cannabinoid medicines. Synthetic cannabinoids are prescribed for specific conditions and as such require consistent access to a prescriber whereas herbal cannabis can in many cases be accessed more easily. Moreover, synthetic cannabinoids may be more expensive than herbal cannabis which can be self-produced or otherwise accessed at lower cost than synthetic cannabinoids which are available at a set price. In sum, limitations in access and patient preference mean that synthetic cannabinoids are in many cases not a reliable replacement for herbal cannabis products.

Documents relied on

I reviewed the following documents in forming my opinion:

- a. Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., & Holtzman, S. (2013). The Cannabis Access for Medical Purposes Study: Patient characteristics, reasons for use, and modes of access. *International Journal of Drug Policy*, 24, 511-516.
- b. Bell, A. D., MacCallum, C., Margolese, S., **Walsh, Z.**, Wright, P., Daeninck, P. J., Mandarino, E., Lacasse, G., Kaur Deol, J., de Freitas, L. and St. Pierre, M., & External Review Panel. (2023). Clinical practice guidelines for cannabis and cannabinoid-based medicines in the management of chronic pain and co-occurring conditions. *Cannabis and Cannabinoid Research*. Advance online publication.
- c. Belle-Isle, L.*, Walsh, Z.*, Lucas, P., Callaway, R., Capler, R., Kay, R., & Holtzman, S. (2014). Barrier to access for Canadians who use cannabis for therapeutic purposes. *International Journal of Drug Policy*, 25, 691-699. * co-

lead author

- d. Thomas, L., Daniels, S., & Walsh, Z. (2023). *Combining Cannabis and Yoga: Practices and Motives*. Poster presentation at the 33rd Annual International Cannabinoid Research Society Symposium on the Cannabinoids, Toronto, ON.
- e. Costiniuk C, MacCallum CA, Boivin M, Rueda S, Lacasse G, **Walsh Z**, Daeninck PJ, Margoiese S, Mandarino E, Deol JK, Sanchez T, Bell AD.(2023). Why a distinct medical stream is necessary to support patients using cannabis for medical purposes. *Journal of Cannabis Research* 5(1):25. doi: 10.1186/s42238-023-00195-8.

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC with commissioner Paul Lewin in the City of Toronto, ON.


Zachary Walsh

September 28, 2023

Date


Commissioner for taking affidavits
PAUL LEWIN

This is Exhibit A referred to in the
affidavit of Prof. Zachary Walsh
sworn before me, this 28th
day of September 20²³
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A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.

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EDUCATION

- 2008 Ph.D., Clinical Psychology
 Rosalind Franklin University/ Chicago Medical School, North Chicago, IL.
 Dissertation: *Psychopathy, ethnicity, socioeconomic status, and violence: A further examination.*
 Supervisor: David S. Kosson, Ph.D.
- 2004 M.S., Psychology
 Rosalind Franklin University/ Chicago Medical School, North Chicago, IL.
 Thesis: *The impact of socioeconomic status, ethnicity, and psychopathy on recidivism in a county jail population.*
 Supervisor: David S. Kosson, Ph.D.
- 2001 B.A. (Honours), Psychology
 University of Winnipeg, Winnipeg, MB.
 Thesis: *The expectations of reminders and action-state on prospective memory.*
 Supervisors: Evelyn Schaefer, Ph.D. & Ross Broughton, Ph.D.
- 1997 B.Ed., English (Secondary)
 University of Winnipeg, Winnipeg, MB.

INTERNSHIP & POSTGRADUATE TRAINING

- 2008 - 2009 Postdoctoral Research Fellowship, Brown University, Warren Alpert Medical School, Department of Psychiatry & Human Behavior, Providence, RI.
- 2007 - 2008 Clinical Psychology Internship, Brown University, Clinical Psychology Training Consortium, Providence, RI.

ACADEMIC APPOINTMENTS

- 2020 - Professor, University of British Columbia, Kelowna, BC.
- 2014 - 2020 Associate Professor, University of British Columbia, Kelowna, BC.
- 2009 - 2014 Assistant Professor, University of British Columbia, Kelowna, BC.

PROFESSIONAL LICENSURE

- 2012 - College of Psychologists of British Columbia - Registered Psychologist #2011

ORIGINAL PUBLICATIONS IN PEER-REVIEWED JOURNALS

(underline indicates supervised student authorship)

Costiniuk C, MacCallum CA, Boivin M, Rueda S, Lacasse G, **Walsh Z**, Daeninck PJ, Margolese S, Mandarino E, Deol JK, Sanchez T, Bell AD.(2023). Why a distinct medical stream is necessary to support patients using cannabis for medical purposes. *Journal of Cannabis Research* 5(1):25. doi: 10.1186/s42238-023-00195-8.

Reddon H, Lake S, Socias ME, Hayashi K, DeBeck K, **Walsh Z**, Milloy MJ. (2023). Cannabis use to manage opioid cravings among people who use unregulated opioids during a drug toxicity crisis. *International Journal of Drug Policy*. Advance online publication.

Lo LA, MacCallum CA, Nanson K, Koehn M, Mitchell I, Milloy MJ, **Walsh Z**, Fehr F. (2023) Cannabidiol as a harm reduction strategy for people who use drugs: A rapid review. *Canadian Journal of Psychiatry* 68(8):557-571. doi:10.1177/07067437231183525. Advance online publication.

Gagnon, M, Payne, A, **Walsh, Z**, Guta, A., & Strike, C. (2023). “The Box has become an indispensable part of my life”: A case study of Victoria Cannabis Buyers Club and its consumption space. *Contemporary Drug Problems* , doi:10.1177/00914509231183147

Tsang VWL, Tao B, Dames S, **Walsh Z**, Kryskow P. (2023). Safety and tolerability of intramuscular and sublingual ketamine for psychiatric treatment in the Roots To Thrive ketamine-assisted therapy program: a retrospective chart review. *Therapeutic Advances in Psychopharmacology*;13. doi:10.1177/20451253231171512

Tsang, V., Moyer, R., Kryskow, P., **Walsh, Z.**, & Dames, S. (2023). A pilot study comparing a community of practice group therapy program with and without concurrent Ketamine-assisted Therapy. *European Psychiatry*, 66(S1), S89-S89. doi:10.1192/j.eurpsy.2023.269

Bell, A. D., MacCallum, C., Margolese, S., **Walsh, Z.**, Wright, P., Daeninck, P. J., Mandarino, E., Lacasse, G., Kaur Deol, J., de Freitas, L. and St. Pierre, M., & External Review Panel. (2023). Clinical practice guidelines for cannabis and cannabinoid-based medicines in the management of chronic pain and co-occurring conditions. *Cannabis and Cannabinoid Research*. Advance online publication.

Grundmann, O., Veltri, C. A., Morcos, S., Smith, K. E., Singh, D., Corazza, O., Cinosi, E., Martinotti, G., **Walsh, Z.**, & Swogger, M. T. (2023). Correlations of kratom (*Mitragyna speciosa* Korth.) use behavior and psychiatric conditions from a cross-sectional survey. *Experimental and Clinical Psychopharmacology*. Advance online publication.

Lake, S., Buxton, J., **Walsh, Z.**, Cooper, Z. D., Socías, M. E., Fairbairn, N., Hayashi, K., & Milloy, M. J. (2023). Methadone dose, cannabis use, and treatment retention: Findings from a community-based sample of people who use unregulated drugs. *Journal of Addiction Medicine*, 17(1), e18-e26.

Lake, S., Kerr, T., Buxton, J., Walsh, Z., Cooper, Z., Socías, M. E., Fairbairn, N., Habyashi, K., & Milloy, M. J. (2023). The cannabis-dependent relationship between methadone treatment dose and illicit opioid use in a community-based cohort of people who use drugs. *Cannabis and Cannabinoid Research*, 8(1), 155-165.

St. Pierre, M., Daniels, S., Sanchez, T.A., Holtzman, S., Russo, E.B. & Walsh Z. (2022). The Naturalistic Cannabis Administration Protocol (NCAP): A Proof-of-Concept Study, *Journal of Psychoactive Drugs*, DOI: 10.1080/02791072.2022.2125466

Daniels S, St Pierre M, Sanchez T, Walsh Z. Physician Communication and Perceived Stigma in Prenatal Cannabis Use (2022). *Journal of Psychoactive Drugs*.55(3):290-298. doi: 10.1080/02791072.2022.2076179.

Grundmann, O., Veltri, C.A., Morcos, D., Knightes, D., Smith, K.E., Singh, D., Corazza, O., Cinosi, E., Martinotti, G., **Walsh, Z.** & Swogger, M.T. (2022) Exploring the self-reported motivations of kratom (*Mitragyna speciosa*) use: a cross-sectional investigation, *The American Journal of Drug and Alcohol Abuse*, 48:4, 433-444

Rootman, J.M., Kiraga, M., Kryskow, P., Harvey, H., Stamets, P., Santos-Brault, E., Kuypers, K & Walsh, Z. (2022). Psilocybin microdosers demonstrate greater observed improvements in mood and mental health at one month relative to non-microdosing controls. *Nature: Scientific Reports* 12, 11091.

Carranza, A. B., Wallis, C. R. D., Jonnson, M. R., Klonsky, E. D., & Walsh, Z. (2022). Nonsuicidal self-injury and intimate partner violence: Directionality of violence and motives for self-injury. *Journal of Interpersonal Violence*, 37(3-4), 1688-1707.

Millspaugh, S. B., Vaudreuil, E. T., **Walsh, Z.**, & Kosson, D. S. (2022). The relationship between psychopathy and conviction rates: Examining the conviction-to-charge ratio. *Psychology, Crime & Law*, 28(4), 315-341.

Walsh, Z., Mollaahmetoglu, M., Rootman, J., Golsof, S., Keeler, J., Marsh, B., Nutt, D. J., & Morgan, C. J. (2022). Ketamine for the treatment of mental health and substance use disorders: Comprehensive systematic review. *British Journal of Psychiatry- Open*, 8(1), e19.

Argento, E., Christie, D., Mackay, L., Callon, C., & Walsh, Z., (2021). Psychedelic-assisted psychotherapy after COVID-19: The therapeutic uses of psilocybin and MDMA for pandemic-related mental health problems. *Frontiers in Psychiatry*, 12, 716593.

Lafrance, A., Strahan, E., Bird, B.M., St. Pierre, M., & Walsh, Z. (2021). Classic psychedelic use and mechanisms of mental health: Exploring the mediating roles of spirituality and emotion processing on symptoms of anxiety, depressed mood, and disordered eating in a community sample. *Journal of Humanistic Psychology*, 00221678211048049.

Lucas, P., Boyd, S., Milloy, M. J., & **Walsh, Z.** (2021a) Cannabis significantly reduces the use of prescription opioids and improves quality of life in authorized patients: Results of a large prospective study. *Pain Medicine*, 22, 727-739.

Lucas, P., Boyd, S., Milloy, M. J., & Walsh, Z. (2021b). The impact of non-medical cannabis legalization and other exposures on retention in longitudinal cannabis research: A survival analysis of a prospective study of Canadian medical cannabis patients. *Journal of Cannabis Research*, 3(1), 1-14.

Lucas, P., Walsh, Z., Hendricks, P. S., Boyd, S., & Milloy, M. J. (2021). Self-reported reductions in tobacco and nicotine use following medical cannabis initiation: Results from a cross-sectional survey of authorized medical cannabis patients in Canada. *Journal of Substance Abuse Treatment*, 130, 108481.

Rootman, J. M., Kryskow, P., Harvey, H., Stamets, P., Santos-Brault, E., Kuypers, K., Polito, V., Bourzat, F., & Walsh, Z. (2021). Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers. *Nature: Scientific Reports*, 11(1), 22479.

Sihota, A., Smith, B. K., Ahmed, S. A., Bell, A., Blain, A., Clarke, H., Cooper, Z. D., Cyr, C., Daeninck, P., Deshpande, A., Ethans, K., Flusk, D., Le Foll, B., Milloy, M. J., Moulin, D. E., Naidoo, V., Ong, M., Perez, J., Rod, K., Sealey, R., Sulak, D., **Walsh, Z.**, & O'Connell, C. (2021). Consensus-based recommendations for titrating cannabinoids and tapering opioids for chronic pain control. *International Journal of Clinical Practice*, 75(8), e13871.

Capler, R., Lucas, P., & **Walsh, Z.** (2020). The Medical Cannabis Standards Engagement Evaluation and Dissemination (SEED) project: A community-based research approach to self-regulating medical cannabis dispensaries in Canada. *International Journal of Drug Policy*, 78, 102708.

Lucas, P., Boyd, S., Milloy, M. J., & **Walsh, Z.** (2020). Reductions in alcohol use following medical cannabis initiation: Results from a large cross-sectional survey of medical cannabis patients in Canada. *International Journal of Drug Policy*, 86, 102963.

Singh, D., Brown, P. N., Cinosi, E., Corazza, O., Henningfield, J. E., Garcia-Romeu, A., McCurdy, C. R., McMahon, L. R., Prozialeck, W. C., Smith, K. E., Swogger, M. T., Veltri, C., **Walsh Z.**, & Grundmann, O. (2020) Current and future potential impact of COVID-19 on kratom supply and use. *Frontiers in Psychiatry*, 11, 574483.

Lake S, Nosova E, Buxton J, **Walsh Z**, Socías ME, Hayashi K, et al. (2020) Characterizing motivations for cannabis use in a cohort of people who use illicit drugs: A latent class analysis. *PLoS ONE*, 15(5): e0233463.

St. Pierre, M., Russo E. & Walsh, Z. (2020) No evidence of altered reactivity to experimentally induced pain among regular cannabis users. *Clinical Journal of Pain*, 36, 589-593.

Wright, P., **Walsh, Z.**, Margolese, S., Sanchez, T., Arlt, S., Belle-Isle, L., St. Pierre, M., Bell, A., Daeninck, P., Gagnon, M., Lacasse, G., & Costiniuk, C. (2020). Canadian clinical practice guidelines for the use of plant-based cannabis and cannabinoid-based products in the management of chronic non-cancer pain and co-occurring conditions: protocol for a systematic literature review. *BMJ Open*, 10, 1-8.

Johnson, L. E., Balyan, L., Magdalany, A., Saeed, F., Salinas, R., Wallace, S., Veltri, C. A., Swogger, M. T., **Walsh, Z.**, & Grundmann, O. (2020). The potential for kratom as an antidepressant and antipsychotic. *The Yale Journal of Biology and Medicine*, 93(2), 283–289.

Walsh, Z. (2020). Cannabis epistemology and the case-series design: An invited commentary on a case series and dismissive response. *Journal of Alternative and Complementary Medicine*, 26, 259-260.

Beussink, C.N., Chi, T., **Walsh, Z.**, Riser, N.R. & Kosson, D.S. (2020) Employing matched tests to assess facial affect recognition anomalies in offenders high in psychopathy. *Personality and Individual Differences*, 160, 1-6.

St. Pierre, M., Matthews, L. & Walsh, Z. (2020). Cannabis education needs assessment among Canadian physicians-in-training. *Complementary Therapies in Medicine*, 49, doi: 10.1016/j.ctim.2020.102328.

Lake, S., Kerr, T., Buxton, J., **Walsh, Z.**, Marshall, B.D.M., Wood, E., and Milloy, M-J (2020). Does cannabis use modify the effect of post-traumatic stress disorder on severe depression and suicidal ideation? Evidence from a population-based cross-sectional study of Canadians, *Journal of Psychopharmacology*, 34, 181-188

Sapoznikow, A., Walsh, Z., Tupper, K.W., Erowid, E. & Erowid, F. (2019). The influence of context on ayahuasca experiences: An analysis of experience reports. *Journal of Psychedelic Studies*, 3, 288-294

Grundmann, O., Brown, P.N., Boyer, E.W., **Swogger, M.T.**, Walsh, Z., Prozialek, W., Kruegel, A.C., Veltri, C.A., Dudley, S. (2019). Critique of Kratom use and Toxicities in the United States. *Pharmacotherapy*, 39, 1119-1120.

Walsh, Z., (2019) A crude approach to evaluating cannabis legalization, *Canadian Medical Association Journal*, 191, 109

Mithoefer, M.C., Feduccia, A.A., Jerome, L., Wagner, M., **Walsh, Z.**, Hamilton, S., Yazar-Klosinsky, B., Emerson, A. & Doblin, R. (2019). MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. *Psychopharmacology*, 236, 2735-2745.

Lake, S., Kerr, T., Web, D., Haines-Saah, R., Fischer, B., Thomas, G., **Walsh, Z.**, Ware, M., Wood, E. & Milloy, M.J. (2019). Guidelines for public health and safety metrics to evaluate the potential harms and benefits of cannabis regulation in Canada. *Drug and Alcohol Review*, 38, 606-621.

Lake, S., **Walsh, Z.**, Kerr, T., Cooper, Z.D., Buxton, J., Wood, E., Ware, M.A. & Milloy, M.J. (2019). Frequency of cannabis use and illicit opioid use among people who use drugs and report chronic pain: A longitudinal analysis. *PLoS Medicine*, 16, 11.

Kosson, D.S., **Walsh, Z.**, Anderson, J.R. Brook, M. & Swogger, M.T. (2019) Evaluation of a cognitive-behavioral intervention for high- and medium-risk probationers, *Behavioral Sciences & the Law*, 37, 329-341.

Chou, F.N., Armstrong, H., Wang, L., Patterson, T., Lachowsky, N. **Walsh, Z.**, Hogg, R.S., Card, K., Roth, E., Bacani, N. Olarewaju, G., & Moore, D., (2019) A longitudinal analysis of cannabis use and mental health symptoms among gay, bisexual, and other men who have sex with men in Vancouver, Canada, *Journal of Affective Disorders*, 246, 125-133.

Kosson, D.S., Chi, T., Riser, N., **Walsh, Z.**, Beussink, C.N., Pera-Guardiola, V., & Briz, A.J. (2019). Facial affect recognition in college students with psychopathic traits: A comparison using tests matched in discriminating power. *Journal of Research in Personality*, 78, 52-60

Walsh, Z. & Thiessen, M.S. (2018). Psychedelics and the new behaviorism: Considering the integration of third-wave behavior therapies with psychedelic-assisted therapy. *International Review of Psychiatry*, 30, 343-349.

Grundmann, O., Brown, P.N., Henningfield, J., Swogger, M.T. & **Walsh, Z.**, (2018) The therapeutic potential of kratom, *Addiction*, 113, 1951-1953

Argento, E., Braschel, M., **Walsh, Z.**, Socias, E., & Shannon, K. (2018) The moderating effect of psychedelics on the prospective relationship between prescription opioid use and suicide risk among marginalized women, *Journal of Psychopharmacology*, 32, 1385-1391

Anderson, J.R., **Walsh, Z.**, Kosson, D.S. (2018) Psychopathy, self-identified race/ethnicity, and nonviolent recidivism: A longitudinal study *Law & Human Behavior*, 42, 531-544

Swogger, M. T., Montry, K. M., **Walsh, Z.**, & Kosson, D. S. (2018). Fantastic and uninviting behavior: Psychopathy, alcohol, and violence. *Journal of Aggression, Conflict, and Peace Research*, 10, 210-222

Thiessen, M.S., **Walsh, Z.**, Bird, B. & Lafrance, A. (2018). Psychedelic use and intimate partner violence: The role of emotion regulation. *Journal of Psychopharmacology*, 32, 749-755

Swogger, M.T & **Walsh, Z.** (2018). Kratom use and mental health: A systematic review. *Drug and Alcohol Dependence*, 183, 134-140

Hendricks, P., Crawford, M.S., Cropsey, K.L., Sweat, N.W., **Walsh, Z.** & Pavela, G., (2018). The relationship of classic psychedelic use with criminal behavior in the United States adult population. *Journal of Psychopharmacology*, 32, 37-48

Capler, R. **Walsh, Z.**, Crosby, K., Belle-Isle, L., Holtzman, S., Lucas, P., & Callaway, R., (2018). Are dispensaries indispensable? Patient experiences of access to cannabis from medical cannabis dispensaries in Canada. *International Journal of Drug Policy*, 47, 1-8

Jonsson, M., Langille, J. I., & **Walsh, Z.** (2018). The role of objectification in the victimization and perpetration of intimate partner violence. *Violence & Victims*, 33, 23-39

Fitzcharles, M.A., Brachaniec, M., Cooper, L., Dubin, R., Häuser, W.... **Walsh, Z.** & El-Gabalwy, H. (2017). A paradigm change to inform fibromyalgia research priorities by engaging patients and health care professionals. *Canadian Journal of Pain*, 1, 137-147

Timoney, L., **Walsh, Z.**, Shea, M.T., Yen, S., Edelen, M.O., Ansell, E.B., Morey, L.C., Grilo, C.M., Sanislow, C.A., Skodol, A.E., Gunderson, J.G., McGlashan, T.H. (2017). Personality and life events in a personality disorder sample. *Personality Disorders: Theory, Research & Treatment*, 8, 376-382

Thiessen, M.S., Matthews, L., & **Walsh, Z.** (2017). First, do no harm: The role of cannabis education in response to the opioid crisis. *University of British Columbia Medical Journal*, 7, 23-24.

Walsh, Z., Gonzalez, R., Crosby, K., Thiessen, M.S., Carroll, C., & Bonn-Miller, M.O., (2017). Medical cannabis and mental health: A systematic and guided review. *Clinical Psychology Review*, 51, 15-29.

Lucas, P. & **Walsh, Z.**, (2017). Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. *International Journal of Drug Policy*, 42, 30-35.

Erickson, K.A., Jonsson, M., Langille, J.I., & **Walsh, Z.** (2017). Victim gender, rater attitudes, and rater violence history influence perceptions of intimate partner violence. *Violence & Victims*, 32, 533-544.

Walsh, Z., Hendricks, P., Kosson, D.S., Thiessen, M.S., Lucas, P. & Swogger, M.T., (2016). Hallucinogen use and intimate partner violence: Prospective evidence consistent with protective effects among men with histories of problematic substance use. *Journal of Psychopharmacology*, 30, 601-607.

Lucas, P., **Walsh, Z.**, Crosby, K., Callaway, R., Belle-Isle, L., Kay, R., Capler, R. & Holtzman, S. (2016). Substituting cannabis for prescription drugs, alcohol, and other substances among medical cannabis patients: The impact of contextual factors. *Drug and Alcohol Review*, 35, 326-333.

Holtzman, S., Landis L., **Walsh, Z.**, Puterman, E., Roberts, D., & Saya-Moore, K., (2016). Predictors of HIV testing among men who have sex with men: A focus on men living outside major urban centres in Canada. *AIDS Care*, 28, 705-711.

Okano, M., Langille, J.I., & **Walsh, Z.**, (2016). Psychopathy, alcohol use and intimate partner violence: Evidence from two samples. *Law & Human Behavior*, 40, 517-523.

Fitzcharles, M.A., Ste-Marie, P., Häuser, W., Clauw, D., Jamal, S., Karsh, J., Landry, T., McDougall, J., Le Clercq, S., Shir, Y., Shojania, K., & **Walsh, Z.** (2016). Efficacy, tolerability and safety of cannabinoid treatments in the rheumatic diseases: A systematic review of randomized controlled trials. *Arthritis Care & Research*, 68, 681-688.

Edalati, H., **Walsh, Z.**, & Kosson, D.S. (2016). Attentional bias in psychopathy: An examination of the emotional dot-probe task in male jail inmates. *International Journal of Offender Therapy and Comparative Criminology*, 60, 1344-57.

Swogger, M.T., Hart, E., Priddy, B., Murray, T., Erowid, F., Erowid, E. & **Walsh, Z.** (2015). Experiences of kratom users: A qualitative analysis. *Journal of Psychoactive Drugs*, 47, 360-367.

Kosson, D.S., **Walsh, Z.**, Rosenthal, M.Z., & Lynch, T.R. (2015). Interpersonal assessment of Borderline Personality Disorder: Preliminary findings. *Journal of Personality Assessment*, 97, 278-290.

Trabold, N. Swogger, M.T., **Walsh, Z.**, Cerulli C. (2015). Childhood sexual abuse and the perpetration of intimate partner violence: The moderating role of gender. *Journal of Aggression, Maltreatment, & Trauma*, 24, 381-399

Swogger, M.T., **Walsh, Z.**, Christie, M., Priddy, B.M., & Conner, K.R. (2015). Instrumental versus premeditated aggression in the prediction of violent criminal recidivism. *Aggressive Behavior*, 41, 346-352.

Fitzcharles, M., Ste-marie, P.A., Clauw, D.J., Jamal, S., Karsh, J., Leclercq, S., McDougall, J.J., Shir, Y., Shojania, K., & **Walsh, Z.** (2014). Rheumatologists lack confidence in their knowledge of cannabinoids pertaining to the management of rheumatic complaints. *BMC Musculoskeletal Disorders*, 15, 258.

Belle-Isle, L.*, **Walsh, Z.***, Lucas, P., Callaway, R., Capler, R., Kay, R., & Holtzman, S. (2014). Barrier to access for Canadians who use cannabis for therapeutic purposes. *International Journal of Drug Policy*, 25, 691-699. * co-lead authors

Roemer, A., & **Walsh, Z.** (2014). Where you live matters: The roles of living arrangement and self-esteem on college students' hazardous drinking behaviors. *Addiction Research and Therapy*, 22, 474-480.

Swogger, M.T., **Walsh, Z.**, Maisto, S.A., & Conner, K.R. (2014). Reactive and proactive aggression and suicide attempts among criminal offenders. *Criminal Justice & Behavior*, 41, 337-344.

Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., & Holtzman, S. (2013). The Cannabis Access for Medical Purposes Study: Patient characteristics, reasons for use, and modes of access. *International Journal of Drug Policy*, 24, 511-516.

Walsh, Z. (2013). Psychopathy and criminal violence: The moderating effect of ethnicity. *Law & Human Behavior*, 37, 303-311.

Walsh, Z., Shea, M.T., Yen, S., Edelen, M.O., Hopwood, C.J., Markowitz, J.C., Ansell, E.B., Morey, L.C., Grilo, C.M., Sanislow, C.A., Skodol, A.E., Gunderson, J.G., Zanarini, M.C., & McGlashan, T.H. (2012). Socioeconomic-status and mental health in a personality disorder sample: The importance of neighbourhood factors. *Journal of Personality Disorders*, 26, 1-12.

Swogger, M.T., **Walsh, Z.**, Kosson, D.S., Cashman-Brown, S., & Caine, E.D. (2012). Self-reported childhood physical abuse and perpetration of intimate partner violence: The moderating role of psychopathic traits. *Criminal Justice & Behavior*, 39, 910-922.

Swogger, M.T., **Walsh, Z.**, Homaifar, B.Y., Caine, E.D., & Conner, K.R. (2012). Predicting self- and other-directed violence among discharged psychiatric patients: The roles of anger and psychopathic traits. *Psychological Medicine*, 42, 371-379.

Swogger, M.T., Conner, K.R., **Walsh, Z.**, & Maisto, S.A. (2011). Childhood abuse and harmful substance use among male and female criminal offenders. *Addictive Behaviors*, 36, 1205-1212.

Chatav-Schonbrun, Y., **Walsh, Z.**, Stuart, G.L., & Strong, D. (2011). Marital status and treatment seeking for alcohol use disorders. *Addictive Disorders and Their Treatment*, 10, 111-122.

Yen, S., Shea, M.T., **Walsh, Z.**, Edelen, M.O., Hopwood, C. J., Markowitz, J. C., Ansell, E. B., Morey, L.C., Grilo, C.M., Sanislow, C.A., Skodol, A.E., Gunderson, J.G., Zanarini, M.C., McGlashan, T.H. (2011). Self-harm subscale of the Schedule of Nonadaptive and Adaptive Personality (SNAP): Predicting suicide attempts over 8 years of follow-up. *Journal of Clinical Psychiatry*, 72, 1522-1528.

Walsh Z., Swogger, M.T., O' Connor, B.P., Stuart, G.L., Shea, M.T., & Chatav, Y. (2010). Psychopathy and subtypes of partner violent men and women. *Journal of Abnormal Psychology*, 119, 563-574.

Swogger, M.T., **Walsh, Z.**, Lejuez, C.J., & Kosson, D.S. (2010). Psychopathy and risk-taking among criminal offenders. *Criminal Justice and Behavior*, 37, 439-452.

Swogger, M.T., **Walsh, Z.**, Houston, R.J., Cashman-Brown, S., & Conner, K.R. (2010). Psychopathy and Axis I psychiatric disorders among criminal offenders: Relationships to impulsive and proactive aggression. *Aggressive Behavior*, 36, 45-53.

Stuart, G.L., O'Farrell, T.J., Leonard, K., Moore, T.M., Temple, J.R., Ramsey, S.E., Stout, R., Kahler, C., Bucossi, M., Andersen, S., Recupero, P., **Walsh, Z.**, Chatav, Y., Strong, D., Rothman, E., Rhatigan, D., & Monti, P. (2009). Examining the interface between substance misuse and intimate partner violence. *Substance Abuse: Research and Treatment*, 3, 25-29.

Walsh, Z., Swogger, M.T., & Kosson, D.S. (2009). Psychopathy and instrumental violence: Facet level relationships. *Journal of Personality Disorders*, 23, 416-424.

Swogger, M.T., **Walsh, Z.**, & Kosson, D.S. (2008). Psychopathy subtypes among African American county jail inmates. *Criminal Justice and Behavior*, 35, 1484-1499.

Walsh, Z., & Kosson, D.S. (2008). Psychopathy and violence: The importance of factor level interactions. *Psychological Assessment*, 20, 114-120.

Walsh, Z., Epstein, A.M., Munisamy, G., & King, A.C. (2008). The impact of depressive symptoms on the efficacy of naltrexone in smoking cessation. *Journal of Addictive Diseases*, 27, 65-72.

Swogger, M.T., **Walsh, Z.**, & Kosson, D.S. (2007). Domestic violence and psychopathic traits: Distinguishing the antisocial batterer from other antisocial offenders. *Aggressive Behavior*, 33, 253-260.

Walsh, Z., Allen, L.C., & Kosson, D.S. (2007). Beyond social deviance: Substance-specific relationships with PCL-R facets. *Journal of Personality Disorders*, 21, 273-288.

Walsh, Z., Swogger, M.T., Walsh, T., & Kosson, D.S. (2007). Psychopathy and violence: Increasing specificity. *Netherlands Journal of Psychology*, 63, 136-143.

Walsh, Z., & Kosson, D.S. (2007). Psychopathy and violence: A prospective study of the influence of socioeconomic status and ethnicity. *Law and Human Behavior*, 31, 209 -229.

Walsh, Z., & Walsh, T. (2006). The evidentiary introduction of PCL-R assessed psychopathy in U.S. courts: Extent and appropriateness. *Law and Human Behavior*, 30, 493-507.

Walsh, Z., Swogger, M.T., & Kosson, D.S. (2004). Psychopathy, IQ and violence in European American and African American county jail inmates. *Journal of Consulting and Clinical Psychology*, 72, 1165-1169.

BOOK CHAPTERS & REVIEWED PUBLICATIONS IN EDITED VOLUMES

St. Pierre, M., Daniels, S., & **Walsh, Z.** (2022). Cannabis substitution: A Canadian Perspective. Hathaway, A., (Ed.). *High North: Cannabis in Canada* (146-63). Vancouver, UBC Press.

Allan, J., Holder, M.D., & **Walsh, Z.** (2017). Cannabis and well-being. Preedy, V.R. (Ed.). *The Handbook of Cannabis and Related Pathologies: Biology, Diagnosis, Treatment and Pharmacology* (pp.308-317). Amsterdam, Netherlands: Elsevier.

Walsh, Z & Thiessen, M. (2017) *TheAnswerPage.com*. The Use of Cannabis as a Substitute Drug. Boston: The Answer Page, Inc.

Walsh, Z & Thiessen, M. (2017) *TheAnswerPage.com*. The Medical use of Cannabis and Cannabinoids in Post Traumatic Stress Disorder. Boston: The Answer Page, Inc.

Baker, A., Black, P.J., & **Walsh, Z** (2014). Deception. In Arrigo, B.A. & Golson, G. (Eds.). *Encyclopedia of Criminal Justice Ethics* (p.244). Thousand Oaks, CA: Sage Publications.

Black, P.J., & **Walsh, Z** (2014). Police profiling. In Arrigo, B.A. & Golson, G. (Eds.). *Encyclopedia of Criminal Justice Ethics* (p.670). Thousand Oaks, CA: Sage Publications.

Crosby, K., Hiles, M., & **Walsh, Z.** (2014). The war on drugs. In Arrigo, B.A. & Golson, G. (Eds.). *Encyclopedia of Criminal Justice Ethics* (p.1017). Thousand Oaks, CA: Sage Publications.

Langille, J.I., Peters, L. & **Walsh, Z.** (2014). Violence against women and girls. In Arrigo, B.A. & Golson, G. (Eds.). *Encyclopedia of Criminal Justice Ethics* (p.996). Thousand Oaks, CA: Sage Publications.

Peters, L. & Walsh, Z. (2014). Drug courts. In Arrigo, B.A. & Golson, G. (Eds.).
Encyclopedia of Criminal Justice Ethics (p.893). Thousand Oaks, CA: Sage Publications.

Hare, R.D., Black, P.J., & Walsh, Z. (2013). The PCL-R: Forensic applications and
limitations In R. P. Archer (Ed.). *Forensic use of clinical assessment instruments, Second*
Edition. (pp.230-265) Mahwah, NJ: Lawrence Erlbaum.

Stuart, G.L., Chatav Schonbrun, Y., & **Walsh, Z. (2009).** Treatment for substance abuse
reduces intimate partner violence. *DATA: The Brown University Digest of Addiction Theory*
and Application, 28, 8.

Walsh, Z., & Stuart, G.L. (2009). Antisocial Personality Disorder as a co-
occurring disorder with Substance Use Disorder. In G.L. Fisher & N. A.Roget (Eds.).
Encyclopedia of Substance Abuse Prevention, Treatment, and Recovery (pp.92-95). Thousand
Oaks, CA: Sage Publications.

Walsh, Z., & Stuart, G.L. (2009). Experimental substance use. In G.L. Fisher & N.A. Roget
(Eds.), *Encyclopedia of Substance Abuse Prevention, Treatment, and Recovery* (pp. 389-
391). Thousand Oaks, CA: Sage.

Walsh, Z., & Stuart, G.L. (2009). Moderation in use. In G.L. Fisher & N.A. Roget (Eds.),
Encyclopedia of Substance Abuse Prevention, Treatment, and Recovery (pp. 554-
555). Thousand Oaks, CA: Sage.

Walsh, T., **Walsh, Z., & Stuart, G.L. (2009).** Decriminalization. In G.L. Fisher & N.A. Roget
(Eds.), *Encyclopedia of Substance Abuse Prevention, Treatment, and Recovery* (pp. 263-
266). Thousand Oaks, CA: Sage.

Walsh, T., **Walsh, Z., & Stuart, G.L. (2009).** History of drug use laws. In G.L. Fisher & N.A.
Roget (Eds.), *Encyclopedia of Substance Abuse Prevention, Treatment, and Recovery* (pp.
327-330). Thousand Oaks, CA: Sage.

INVITED PRESENTATIONS

Walsh, Z. (2023). *Cannabis Research Ethics*. Invited presentation to the Research Ethics BC,
Vancouver, BC

Walsh, Z. (2023). *Cannabis & Ageing*. Invited panelist to the UBC IHLCDP Café
Scientifique Speaker Series, Kelowna, BC

Walsh, Z. (2023). *Cannabis Mental Health & Addiction*. Invited presentation to the UBC
Brain Wellness Speaker Series, Vancouver, BC

Walsh, Z. (2023). *Psilocybin Microdosing*. Invited presentation to the Rochester Psychedelic
Group, Rochester, NY, USA

Walsh, Z. (2022). *Psychedelics and mental health primer*. Invited 2-day clinical workshop for
Sarah Riel Society, Winnipeg, MB.

- Walsh, Z.** (2022). *Psychedelics in the treatment of PTSD*. Invited testimony to Senate of Canada – Subcommittee on Veterans Affairs, Ottawa, ON.
- Walsh, Z.** (2022). *Canadian Research in Psychedelic Psychotherapy*. Invited presentation at Matrix-N Translation in Action Conference, Vancouver BC
- Walsh, Z.** (2022). *Cannabis & Harm Reduction*. Invited consultant to the European Monitoring Centre for Drugs and Drug Addiction, Lisbon, Portugal.
- Walsh, Z.** (2022). *Cannabis, Substance Use and Public Health*. Invited panelist for the West Coast Brain Injury Conference 2022, Kelowna, BC.
- Walsh, Z.** (2022). *Future clinical applications of psychedelics*. Invited panelist for the Grow Up 2022 Conference, Victoria, BC.
- Walsh, Z.** (2022). *Psychedelics and addictions*. Invited panelist for the Catalyst 2022 Conference, Niagara Falls, ON.
- Walsh, Z.** (2022). *Cannabis and mental health primer*. Invited webinar of day-long clinical workshop for Hirose Seminars, Vancouver, BC.
- Walsh, Z.** (2022). *Understanding Addiction*. Invited presentation for Lake Country Health Planning Society, Lake Country, BC.
- Walsh, Z. & Farrell, L.** (2022). *Cannabis Use on Turtle Island*. Invited webinar presentation for Canadian Centre on Substance Use and Addiction, Ottawa, ON. (Delivered online).
- Walsh, Z.** (2022). *Cannabis and Mental Health*. Invited webinar presentation of day-long clinical workshop for Palliser Health Care Network, Medicine Hat AB. (Delivered online).
- Walsh, Z.** (2022). *Problematic Cannabis Use*. Invited webinar presentation for Execulinks Continuing Education, Calgary, AB. (Delivered online).
- Walsh, Z.** (2021). *Psychedelic Psychotherapy Primer*. Invited presentation of day-long clinical webinar for Hirose Seminars, Vancouver, BC. (Delivered online).
- Walsh, Z.** (2021). *New Methodologies in Cannabis Research*. Invited presentation to University of Colorado – Boulder, Bidwell Research Lab, Boulder CO.
- Walsh, Z.** (2021). *Recent Developments in Microdosing Research*. Invited address for the Catalyst Calgary 2021 Conference. Presented online due to COVID-19.
- Walsh, Z.** (2021). *Microdosing, Macrodosing and Ketamine Assisted Psychotherapy: Tracking New Developments in the Psychedelic Renaissance*. Invited colloquium at the Simon Fraser University, Department of Psychology, Vancouver, BC.
- Walsh, Z.** (2021). *Student mental health and substance use*. Invited Panelist – Bell Let's Talk Day, Kelowna, BC. (Delivered online).

Walsh, Z. (2020). *Potential of kratom as a therapy*. Invited Panelist – Kratom Leadership Summit, Tampa, FL. USA. (Delivered online).

Walsh, Z. (2020). *Cannabis Research and Legalization*. Invited Keynote – Healthy Campus Event Selkirk College, Castlegar, BC. (Delivered online).

Walsh, Z. (2020). *Psychedelics use, mindfulness and the new behaviorism*. Invited address for the Catalyst Calgary 2020 Conference. Presented online due to COVID-19.

Walsh, Z. (2020). *Efficacy of cannabis for the treatment of mental health – Investigations in process*. Invited presentation at the Faculty of Pharmacy, University of Costa Rica, San Jose, Costa Rica.

Walsh, Z. (2020). *Cannabis, pain, mental health & public health*. Invited presentation at the Vancouver and District Dental Society – Midwinter Meeting, Vancouver, BC.

Walsh, Z. (2019). *Cannabis, substance use disorders, and co-morbidities: Clinical considerations*. Invited panelist and moderator at BC Centre on Substance Use Cannabis for Harm Reduction Forum at the University of British Columbia, Vancouver, BC.

Walsh, Z. (2019). *Cannabis revised: Legalization, mental health & public health*. Invited colloquium at the University of British Columbia, Department of Psychology, Vancouver, BC.

Walsh, Z. (2019). *Mental health and cannabis in context*. Invited talk at International Perspectives on Cannabis and Mental Health Invited Meeting. University of Exeter, Exeter, UK.

Walsh, Z. (2019). *Psychedelics use, interpersonal violence and the new behaviorism*. Invited keynote address for the seminar on Psychedelic-assisted psychotherapy: on mindfulness and integration seminar. King's College, London, UK.

Walsh, Z. (2019). *Psychedelics as Medicine*. Invited talk at the annual BC Center on Substance Use Conference: Coming Together, Vancouver, BC.

Walsh, Z. (2019). *Ethics in cannabis research in Canada*. Invited plenary talk at the annual Island Health Research Ethics Board Education Event, Victoria, BC.

Walsh, Z. (2018). *Therapeutic cannabinoids in mental health*. Invited talk at Medical Cannabis in Naturopathic Practice Conference, New Westminster, BC.

Walsh, Z. (2018). *Cannabis, mental health and public health*. Invited talk at Vernon Signature Speaker Series, Vernon, BC.

Walsh, Z. (2018). *Cannabis and mental health primer*. Invited presentation of day-long clinical workshop (x 2) for Leading Edge Seminars, Vancouver, BC., & Toronto, ON.

Walsh, Z. (2018). *Cannabis use, mental health and addiction*. Invited talk at the Cannabinoid and Opioid Summit, Kamloops, BC.

Walsh, Z. (2018). *Cannabis research at UBC*. Invited keynote talk for the Annual UBC meeting of High School counsellors.

Walsh, Z. (2018). *Cannabis use, mental health and parenting*. Invited talk at the Federation of Law Societies of Canada National Family Law Conference, Vancouver, BC.

Walsh, Z. (2018). *Cannabis use, mental health and parenting*. Invited talk for Legal Aid Saskatchewan, Saskatoon, SK.

Walsh, Z. (2018). *Cannabis use and mental health*. Invited talk for the Saskatchewan Cannabinoid Symposium, Saskatoon, SK.

Walsh, Z. (2018). *Ethics in cannabis research in Canada*. Invited plenary talk at the annual meeting of the Canadian Association of Research Ethics Boards, Montreal, QC.

Walsh, Z. (2018). *Cannabis use and mental health*. Invited panelist at the Georgia Straight – Grassroots Cannabis Expo, Vancouver.

Walsh, Z. (2018). *Medicinal cannabis and mental health*. Invited panelist at Cannabis Hemp Conference and Expo, Vancouver, BC.

Walsh, Z. (2018). *Cannabis use, mental health and public health*. Invited talk at 1st Ciclo de Conferencias Sobre de Cannabis Medicinal Basado en Evidencias, University of Costa Rica, San Jose, Costa Rica.

Walsh, Z. (2018). *Cannabis research in Canada*. Invited talk at 1st Ciclo de Conferencias Sobre de Cannabis Medicinal Basado en Evidencias, Universidad Hispanoamericana, San Jose, Costa Rica.

Walsh, Z. (2018). *Beyond Harms: New Directions in Cannabis Research*. Invited talk at Envision Festival, Uvita, Costa Rica.

Walsh, Z. (2018). *Psychedelics and the New Behaviorism*. Invited talk at Envision Festival, Uvita, Costa Rica.

Walsh, Z. (2018). *Cannabis research after legalization*. Invited talk at Institute for Health Living and Chronic Disease Prevention Curious about Cannabis Forum, UBC, Kelowna, BC.

Walsh, Z. (2017). *Cannabis use, PTSD, and mental health*. Invited talk at 14th Annual Conference of the Natural Health Products Research Society of Canada, Vancouver, BC.

Walsh, Z. (2017). *Cannabis use and mental health*. Invited talk at Cannabis Expertise: Medical Cannabis Education Symposium, Columbus, Ohio.

Walsh, Z. (2017). *Medicinal use of cannabis*. Invited panelist at Cannabis Hemp Conference and Expo, Vancouver, BC.

Walsh, Z. (2017). *Beyond Harms: Public health and the end of cannabis prohibition*. Invited talk at Face to Face in Drug Plan Management Forum, Vancouver, BC.

Walsh, Z. (2017). *Psychedelic therapy and Third-Wave Behaviorism: New directions for the prevention of interpersonal violence*. Invited talk at Psychedelic Science, Oakland, CA.

Walsh, Z. (2017). *Marijuana for PTSD*. Invited panelist at Psychedelic Science, Oakland, CA.

Walsh, Z. (2017). *Cannabis and Post-Traumatic Stress Disorder – A case-based presentation*. Invited talk at the 2017 Canadian Centre for the Investigation of Cannabinoids' Cannabinoids in Clinical Practice Symposium, Toronto, ON.

Walsh, Z. (2017). *Cannabis and mental health*. Invited talk at the 2017 BC Centre on Substance Use's *Forum on Science of Cannabis: Defining a Research Agenda for Public Health*, St. Paul's Hospital, Vancouver, BC.

Walsh, Z. (2017). *Beyond Harms: Public health and the end of cannabis prohibition*. Invited talk at the University of Manitoba's Centre for Applied Ethics, Winnipeg, MB.

Walsh, Z. (2017). *Cannabis and mental health*. Invited talk for the Canadian Students for Sensible Drug Policy – UBC, Kelowna, BC.

Walsh, Z. (2017). *The opioid epidemic in the broader context of substance use*. Invited talk at UBC School of Social Works' Community Roundtable: "The epidemic of opioid overdose: Conceptualizing an effective community response", Kelowna, BC.

Walsh, Z. (2017). *Can Early Intervention Improve Mental Health Outcomes in Youth?* Invited panel participant at UBC Dialogues: Okanagan –Kelowna, BC.

Walsh, Z. (2016). *Psychedelics and the new behaviourism*. Invited presentation at the Basscoast Music Festival, Merritt, BC.

Walsh, Z. (2016). *Cannabis and public health*. Invited talk at the 2016 Interior Health Authority - Addiction Awareness Day, Kelowna, BC.

Walsh, Z. (2016). *Psychedelics and the new behaviourism*. Invited presentation at the Psychedelic Psychotherapy Forum, Victoria, BC.

Walsh, Z. (2016). *Cannabis and public health*. Invited talk at the Canada Marijuana Boom: Opportunities in Indigenous Territories, Native Nation Events, Vancouver, BC.

Walsh, Z. (2015). *Cannabis and pain in arthritis*. Invited talk at the Arthritis Society - Medical Cannabis Research Roundtable, Vancouver, BC.

Walsh, Z. (2015). *Medical cannabis research in Canada*. Invited talk at the Drug Policy Alliance - International Drug Policy Reform Conference, Washington, DC.

Walsh, Z. (2015). *Medical cannabis research and community impact*. Invited talk at the Central Okanagan Association for Cardiac Health -Healthcare Professional Development Day, Kelowna General Hospital, Kelowna, BC.

Walsh, Z. (2015). *Current research on medical marijuana*. Invited talk at the Medical Marijuana in the Workplace: What Employers Need to Know workshop, Worksafe BC & Work Reintegration and Accommodation Program, UBC, Kelowna, BC

Walsh, Z. (2015). *Cannabis for therapeutic purposes: Implications for public health and Mental Health*. Invited talk at the Merritt Public Library, Merritt, BC.

Walsh, Z. (2015). *Cannabis for the treatment of PTSD*. Invited speaker at the 2015 Psychedelic Psychotherapy Conference, Victoria, BC.

Walsh, Z. (2015). *Medicinal use of cannabis*. Invited panelist at the 2015 Vancouver Cannabis Conference, Vancouver, BC.

Walsh, Z. (2015). *Cannabis and public health*. Invited talk at the 2015 Medical Marijuana course by the Continuing Legal Education Society of British Columbia, Vancouver, BC.

Walsh, Z. (2015). *Cannabis for therapeutic purposes: Implications for public health and mental health*. Invited talk at the The Kootenay Boundary Medical Cannabis Conference, Grand Forks, BC.

Walsh, Z. (2015). *Cannabis and chronic pain*. Invited talk at the 2015 Café Scientifique, UBC, Kelowna, BC.

Walsh, Z. (2014). *Psychedelic psychotherapy and the new behaviourism*. Invited presentation at the 2014 Plant Teachers and Sacred Medicines Panel, UBC, Kelowna, BC.

Walsh, Z. (2014). *Cannabis as medicine: New directions in research*. Invited talk at the 2014, Cannabis Medicine Conference, Kyla's Quest, Kelowna, BC.

Walsh, Z. (2014). *New directions in psychedelic science: Rediscovering the behavioural health potential of ancient medicines* Invited talk at the 2014 Spirit Plant Medicine Conference, Vancouver, BC.

Walsh, Z. (2014). *Cannabis and public health: New perspectives*. Invited talk at UBC President's Research Lunch, Kelowna, BC.

Walsh, Z. (2014). *Making peace with cannabis*. Invited TED talk at TEDx -Penticton, Penticton, BC.

Walsh, Z. & Crosby, K. (2014). *Cannabis and arthritis*. Invited talk at UBC Institute for Healthy Living and Chronic Disease Prevention/ Interior Health Authority Partnership in Research Seminar, Kelowna, BC.

Crosby, K., Lozenski, K. & Walsh, Z. (2014). *Cannabis and arthritis*. Invited talk at Move It and Mingle Seniors Group, Army, Navy, and Air Force Club, Vernon, BC.

Walsh, Z. (2013). *Cannabis: Aspirin of the 21st century?* Invited talk at Annual Meeting of UBC Board of Governors - Learning and Research Subcommittee, Kelowna, BC.

Belle-Isle, L., **Walsh, Z.**, Callaway, R., Lucas, P., Capler, R., Kay, B., Stratton, T., & Holtzman, S. (2013). *Cannabis Access for Medical Purposes Survey: Preliminary findings on barriers to access.* Invited talk presented at BC Ministry of Health - Health Services and Health Policy Research Priorities Meeting, Victoria, BC.

Walsh, Z. (2012). *One size does not fit all: Psychopathy and subtypes of partner violence perpetrators.* Invited keynote lecture at the Intimate Partner Violence: Innovations in the Field Conference, Department of Psychiatry, University of Rochester, Rochester, NY.

Walsh, Z. & Callaway, R. (2012). *Barriers to accessing cannabis among individuals with chronic illness.* Invited talk at UBC Institute for Healthy Living and Chronic Disease Prevention/ Interior Health Authority Partnership in Research Seminar, Kelowna, BC.

Walsh, Z. & Capler, R. (2012). *Medical Cannabis: Standards Engagement, Evaluation and Dissemination (SEED).* Invited talk at the Peter Wall Solutions Initiative Grantee Celebration, Peter Wall Institute of Advanced Studies, University of British Columbia, Vancouver, BC.

ABSTRACTS & PRESENTATIONS

Thomas, L., Daniels, S., & Walsh, Z. (2023). *Combining Cannabis and Yoga: Practices and Motives.* Poster presentation at the 33rd Annual International Cannabinoid Research Society Symposium on the Cannabinoids, Toronto, ON.

Sharma, R.H., Hole, R., **Walsh, Z.**, Dow-Fleisner, S. (2022). *'Higher' Education: A Mixed Methods Exploration of ADHD Symptoms, Cannabis Use, and Academic Success Among Postsecondary Students* Poster presentation at CHADD 2022 Annual International Conference on ADHD, Dallas, TX, United States.

Lake, S., Kerr, T., Buxton, J., **Walsh, Z.**, & Milloy, M-J. *Cannabis use tempers the association between low treatment dose and illicit opioid use in a community cohort of patients on methadone maintenance treatment.* 30th Annual International Cannabinoid Research Society Symposium on the Cannabinoids, Galway, Conference cancelled.

Walsh, Z. (2019). *The Influence of Individual and Couple Use of Psychedelics on Conflict Negotiation in Intimate Relationships.* Poster presentation at the International Society for Research on Psychedelics, New Orleans, Louisiana, USA.

Sanchez, T. A., Daniels, S. E. A., St. Pierre, M., Walsh, Z., & Krank, M. (2019). *The Impact of Cannabis Legalization on the Social Norms of Cannabis Use in Youth.* Peer-reviewed paper presentation. International Society for the Study of Drug Policy. Paris, France.

Thiessen, M. S., Crosby, K., Sanchez, T. A., & Walsh, Z. (2019). *Substituting cannabis for alcohol: The impact of legalization.* Oral presentation given at 2019 Cannabis and Public Health Forum. Ottawa, Canada.

Thiessen, M. S., Walsh, Z., Russo, E., Daniels, S., Sanchez, T. A., & Crosby, K. (2018). *Cannabis and pain: Examining the relationship between frequent cannabis use and pain sensitivity*. Poster presented at the 28th Annual International Cannabinoid Research Society Symposium. Leiden, Netherlands.

Daniels, S., Thiessen, M., Sanchez, T. A., & Walsh, Z. (2018). *Therapeutic use of cannabis and substitution for pharmaceutical medications in a prenatal sample*. Poster presented at the 28th Annual Symposium of the International Cannabinoid Research Society. Leiden, Netherlands.

Thiessen, M. S., Matthews, L., Baba, K., Nemet, T., & Walsh, Z. (2018). *Cannabis education needs assessment among Canadian medical students*. Poster presented at the 29th International Congress of Applied Psychology. Montreal, Canada.

Daniels, S., Thiessen, M., & Walsh, Z. (2018). *Cannabis use during pregnancy perceived by mothers as acceptable for therapeutic purposes, and more acceptable than benzodiazepine use*. Poster presented at the 29th International Congress of Applied Psychology. Montreal, Canada.

Daniels, S., Thiessen, M., Sanchez, T., & Walsh, Z. (2018). *Prenatal Cannabis Use: Perceptions, Motives, and Patterns of Use*. Oral presentation at the 12th Annual Conference of the International Society for the Study of Drug Policy. Vancouver, Canada.

Walsh, Z. (2017). *Medical cannabis and mental health: A guided systematic review*. Talk at 38th Annual Conference of the Canadian Pain Society, Halifax, NS.

Walsh, Z., Thiessen, M. S., Crosby, K., Lucas, P., Fader, S., & Bonn-Miller, M.O. (2017) *The Composite Cannabis Assessment Tool (CCAT): Development and validation of a new measure of medical and nonmedical cannabis use*. Poster presented at the 27th Annual meeting of the International Cannabinoid Research Society, Montreal, QC.

Thiessen, M. S., Walsh, Z., Crosby, K., Russo, E., Chaudhuri, T., & Aggarwal, S. (2017) *Cannabis use in India: Characteristics, Access and Reasons for Use*. Poster presented at the 27th Annual meeting of the International Cannabinoid Research Society, Montreal, QC.

Crosby, K., Thiessen, M. S., & Walsh, Z., (2017) *Substituting cannabis for alcohol*. Poster presented at the 27th Annual meeting of the International Cannabinoid Research Society, Montreal, QC.

Walsh, Z. (2016). *Cannabis for the treatment of PTSD*. Talk presented at the 7th annual conference of the Canadian Institute for Military and Veteran Health Research, Vancouver, BC.

Thiessen, M. S., Walsh, Z., Crosby, K., & Carroll, C. (2016). *Preliminary Results for a Pilot Measure: Composite Cannabis Assessment Scale*. Poster presented at the 77th Annual Canadian Psychological Association Convention, Victoria, BC.

Crosby, K., Thiessen, M. S., Walsh, Z. (2016). *Problematic cannabis use and young adult attention deficit/hyperactivity disorder symptoms*. Poster presented at the 77th CPA Annual Convention. Victoria, BC.

Thiessen, M. S., Walsh, Z., Lafrance Robinson, A., & Bird, B. (2016). *Classic Hallucinogen Use, Emotional Regulation, and Disordered Eating: A Mediation Model*. Poster presented at the Interdisciplinary Conference on Psychedelics Research, Amsterdam, Holland.

Lucas, P., **Walsh, Z.** et al, (2016). *Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: The impact of contextual factors*. Poster presented at NIH Marijuana and Cannabinoids: A Neuroscience Summit. National Institute of Health, Bethesda, MD.

Walsh, Z., Shojania, K., Koehn, C., Crosby, K., Carroll, C. & Holtzman, S. (2015). *Cannabis for arthritis: Patient characteristics, reasons for use and perceived comparative efficacy*. Talk presented at the meeting of the International Cannabinoid Research Society, Wolfville, NS.

Capler, R., Crosby, K., Lucas, P. & **Walsh, Z.** (2015). *The SEED Project: Development of standards and certification program for medical cannabis dispensaries in Canada*. Talk presented at the meeting of the International Cannabinoid Research Society, Wolfville, NS.

Carroll, C., Crosby, K., **Walsh, Z.**, & Woodworth, M. (2015). *Cannabis and aggression: The importance of cannabis use motives and subtypes of aggression*. Talk presented at the meeting of the International Cannabinoid Research Society, Wolfville, NS.

Walsh, Z. (2015). *Cannabis for therapeutic purposes in a mental health framework: From the human endocannabinoid system to public health*. Talk presented at the meeting of the American Psychiatric Association, Toronto, ON.

Jonsson, M., Langille, J. I., & **Walsh, Z.** (2015). *Objectification, victim blaming, and intimate partner violence*. Poster presented at the meeting of the American Psychology-Law Society, San Diego, CA.

Erickson, K. A., Jonsson, M., Langille, J. I., & **Walsh, Z.** (2015). *Effects of gender and gender role attitudes on victim blaming in intimate partner violence*. Poster presented at the meeting of the American Psychology-Law Society, San Diego, CA.

Walsh, Z., Crosby, K., Lozanski, K. & Holtzman, S. (2014) *Cannabis, anxiety and pain: The importance of coping style*. Talk presented at the meeting of the International Cannabinoid Research Society, Baveno, Italy.

Lucas, P., **Walsh, Z.**, Crosby, K., Callaway, R., Belle-Isle, L., Capler, R., Holtzman, S., & Kay, B. (2014). *Substitution effects in medical cannabis patients: Results from the Cannabis Access for Medical Purposes Study*. Talk presented at the meeting of the International Cannabinoid Research Society, Baveno, Italy.

Crosby, K. & **Walsh, Z.** (2014) *Cannabis use and perpetration of intimate partner violence: The moderating role of problematic alcohol use*. Poster presented at the meeting of the International Cannabinoid Research Society, Baveno, Italy.

Walsh, Z. (2014). *The combined influence of alcohol dependence and psychopathy on perpetration of intimate partner violence: Prospective evidence from a jail sample*. Talk presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

Carroll, C., Crosby, K., **Walsh, Z.** & Woodworth, M. (2014). *A deeper look into cannabis use: Pinpointing schizotypal personality traits related to cannabis abuse and dependence*. Poster presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

Crosby, K., Carroll, C., Lozanski, K., & **Walsh, Z.** (2014). *An examination of broad and narrow band constructs of negative affect among cannabis users*. Poster presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

Lozenski, K., Crosby, K., Langille, J.I., & Walsh, Z. (2014). *Alcohol use accounts for the relationship between cannabis use and perpetration of intimate partner violence*. Poster presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

MacLean, S., Langille, J.I., Crosby, K., & Walsh, Z. (2014). *Depression and anxiety in victims of intimate partner violence: The role of self-esteem and belongingness social support*. Poster presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

Boulter, K., Langille, J.I., Crosby, K., & Walsh, Z. (2014). *Psychopathy, non-suicidal self-injury and intimate partner violence: Predicting self and other-directed violence*. Poster presented at the meeting of the Canadian Psychological Association, Vancouver, BC.

Walsh, Z., Crosby, K., Carroll, C., & Lozenski, K. (2014). *Coping motives partially mediate the relationship between delusional ideation and cannabis-related problems*. Poster presented at the meeting of American Psychological Society, San Francisco, CA.

Timoney, L.S. & Walsh, Z. (2014). *The five-factor model of personality and life events in a personality disorder sample*. Poster presented at the meeting of American Psychological Society, San Francisco, CA.

Walsh, Z., Swogger, M.T., & Crosby, K. (2013). *Cannabis use motives across contexts: Differences and similarities between college and correctional samples*. Poster presented at the annual Addiction Health Services Research meeting, Portland, OR.

Swogger, M.T., Hart, E., Priddy, B., Murray, T., Erowid, F., Erowid, E. & Walsh, Z. (2013). *Experiences of kratom users: A qualitative analysis*. Poster presented at the annual Addiction Health Services Research meeting, Portland, OR.

Capler, R., Balneaves, L., Walsh, Z., Bottorff, J., Belle-Isle, L., Callaway, R. (2013). *HEMMP team and CAMPS team. Cannabis for therapeutic purposes, physicians as gatekeepers, and the patient-physician relationship*. Talk presented at the Family Medicine Forum, Vancouver, BC.

Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, B., Lucas, P. & Holtzman, S. (2013). *Cannabis Access for Medical Purposes Survey: Patient characteristics, reasons for use and modes of access*. Talk presented at Symposium of the International Cannabinoid Research Society, Vancouver, BC.

Lucas, P., Crosby, K., Hiles, M., Swogger, M. T., & Walsh, Z. (2013). *Substance use among medical cannabis users: Substituting cannabis for alcohol and other substances*. Poster presented at the 75th Annual Scientific Meeting of the College on Problems of Drug Dependence. San Diego, CA.

Hiles, M., Crosby, K., Swogger, M. T., & Walsh, Z. (2013). *Cannabis use motives and frequency of use: Combined and distinct associations with cannabis use problems*. Poster presented at the 75th Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD). San Diego, CA.

Walsh, Z., Belle-Isle, L., Callaway, R., Capler, R., Kay, B., Lucas, P., Holtzman, S., Crosby, K. & Atkinson, B. (2013). *Use of cannabis to treat symptoms of anxiety and depression: Results from a survey of medical cannabis users*. Poster presented at meeting of Multidisciplinary Association for Psychedelic Studies, Oakland, CA.

Wafler, J. M., **Walsh, Z.**, Woodworth, M., & Porter, S. (2013). *The Okanagan General Remorse Exam (OGRE): Preliminary validation*. Poster presented at the meeting of the American Psychology-Law Society, Portland, OR.

Peters, L. R., Langille, J. I., Blanco Carranza, A., Okano, M., & **Walsh, Z.** (2013). *Bidirectional versus unidirectional violence: The roles of psychopathy and personality*. Poster presented at the meeting of American Psychology-Law Society, Portland, OR.

Walsh, Z., Callaway, R., Belle- Isle, L., Capler, R., Kay, R., Lucas, P., Stratton, T., Swogger, M.T. (2012). *Medical cannabis: Incentives and barriers among a Canadian sample*. Poster presented at Addiction Health Services Research Conference, New York, NY.

Erickson, K., Langille, J.I. & **Walsh, Z.** (2012). *Who's to blame? Gender roles and victim blaming in intimate partner violence*. Poster presented at the meeting of Canadian Psychological Association, Halifax, NS.

Roemer, A., Crosby, K. & **Walsh, Z.** (2012). *Psychopathic traits, alcohol use and female perpetration of intimate partner violence*. Poster presented at the meeting of American Psychological Society, Chicago, IL.

Krank, M.D., Goldstein, A., **Walsh, Z.** & Stewart, S. (2012). *Prevention targeting individualized misperceptions of peer use of alcohol and marijuana in a middle school*. Poster presented the meeting of the Research Society on Alcoholism, San Francisco, CA.

Roemer, A. & **Walsh, Z.** (2012). *Where you live matters: The role of living arrangement on self-esteem and hazardous drinking behaviors*. Poster presented the meeting of the Research Society on Alcoholism, San Francisco, CA.

Carranza, A.B., **Walsh, Z.** & Swogger, M.T. (2012). *Self-directed violence and IPV perpetration: The roles of psychopathy and emotion dysregulation*. Poster presented at the Intimate Partner Violence: Innovations in the Field Conference, Department of Psychiatry, University of Rochester, Rochester, NY.

Swogger, M.T., **Walsh, Z.**, Maisto, S.A. & Connor, K.R. (2011). *Harmful alcohol use moderates the link between proactive aggression and suicide attempts among criminal offenders*. Poster presented at Addiction Health Services Research Conference, Fairfax, VA.

Walsh, Z. (2011). *Psychopathy socio-economic status and criminal violence: Evidence consistent with social push*. Poster presented at the North American Correctional and Criminal Justice Psychology Conference, Toronto, ON.

Urch, G., **Walsh, Z.**, & Roemer, A., (2011). *Individual differences among perpetrators of violence against children: Negative affect and subcomponents of the psychopathic personality*. Poster presented at the conference of the Canadian Psychological Association, Toronto, ON.

Roemer, A., **Walsh, Z.**, Urch, G., & Wallace, G. (2011). *Pathways to college drinking: Gender differences in the association between parental bonds and hazardous alcohol use*. Poster presented at the conference of the Canadian Psychological Association, Toronto, ON.

Edalati, H., & **Walsh, Z.** (2011). *Psychopathy and emotional dot probe: Selective attention to happy faces*. Poster presented at the conference of the Society for the Scientific Study of Psychopathy, Montreal, QC.

Walsh, Z., & Swogger, M. T. (2011). *Predicting self-directed and other directed violence: The roles of psychopathic traits.* Poster presented at the conference of the Society for the Scientific Study of Psychopathy, Montreal, QC.

Langille, J. I., & Walsh, Z. (2011). *Psychopathy predicts intimate partner violence perpetration across gender.* Poster presented at the conference of the Society for the Scientific Study of Psychopathy, Montreal, QC.

Urch, G., & Walsh, Z. (2010). *Psychopathy and violence against children: Factor level relationships.* Poster presented at the International Society for Justice Research, Banff, AB.

Walsh, Z. (2010). *Psychopathy and criminal violence - The moderating effects of ethnicity.* Talk presented at the meeting of the American Psychology and Law Society, Vancouver, BC.

Swogger, M.T., & Walsh, Z. (2010). *Childhood abuse and substance use consequences among male and female criminal offenders.* Poster presented at the meeting of the American Psychology and Law Society, Vancouver, BC.

Manning, J., Walsh, Z., & Cioe, J. (2010). *Psychopathy, substance use and stress.* Poster presented at the meeting of the American Psychology and Law Society, Vancouver, BC.

Swogger, M. T., Conner, K. R., Walsh, Z., & Caine, E. D. (2010). *Testing traits of personality disorders as moderators of treatment efficacy among criminal offenders.* Abstract published in *Clinical and Translational Science*, 3, A-077.

Swogger, M. T., Walsh, Z., Cashman-Brown, S., Houston, R. J., & Conner, K. R. (2009). *Psychopathy, Axis I Disorders, and Subtypes of Aggression among Criminal Offenders.* Poster presented at the meeting of the American Psychological Association, Toronto, ON.

Walsh, Z. (2009). *The influence of ethnicity and neighborhood factors on the predictive power of psychopathy for violence: Social push or social potentiation?* Talk presented at the meeting of the Society for the Scientific Study of Psychopathy, New Orleans, LA.

Swogger, M. T., Walsh, Z., & Conner, K. R. (2009). *Predicting self-directed versus other-directed violence: The roles of anger and psychopathic traits.* Poster presented at the meeting of the Society for the Scientific Study of Psychopathy, New Orleans, LA.

Walsh, Z., Swogger, M. T., Chatav, Y., & Stuart, G. L. (2009). *Alcohol use and interpersonal violence: The importance of perpetrator subtypes.* Talk presented at the meeting of the Research Society on Alcoholism, San Diego, CA.

Walsh, Z., Swogger, M.T., Chatav, Y., & Stuart, G.L. (2008). *Psychopathy and subtypes of partner violent men and women.* Poster presented at the meeting of the Association for Behavioral and Cognitive Therapy, Orlando, FL.

King, A. C., Walsh, Z., Munisamy, G., & Epstein, A. M. (2007). *The impact of depressive symptoms on the efficacy of naltrexone in smoking cessation.* Talk presented at the meeting of the American Psychosomatic Society, Budapest, Hungary.

Kosson, D. S., Allen, L., McBride, C. K., Walsh, Z., Tercek, R., & Greco, J. (2007). *Preliminary evidence for negative affectivity and maladaptive emotion regulation strategies in youth with psychopathic traits.* Talk presented at the meeting of the Society for the Scientific Study of Psychopathy, St. Petersburg, FL.

Walsh, Z., & Kosson, D. S. (2007). *Psychopathy and terror management: Impact on perceptions of blue-collar and white-collar criminality.* Talk presented at the meeting of the Society for the Scientific Study of Psychopathy, St. Petersburg, FL.

Kosson, D. S., **Walsh, Z., & Swogger, M. T. (2007).** *Psychopathy, crime, & violence: What we know and what we don't know.* Invited talk presented to the Department of Criminal Sciences, Pontificia Universidade Catolica do Rio Grande do Sul, Brazil.

Walsh, Z., Stuart, G., & Shea, M. T. (2007). *Psychopathy and intimate partner violence: The moderating effect of substance use treatment.* Poster presented at the meeting of the Association for Behavioral and Cognitive Therapy, Philadelphia, PA.

Walsh, Z., & Kosson, D. S. (2006). *Psychopathy and violence: Two factors - better than one.* Talk presented at the meeting of American Psychology and Law Society, St. Petersburg, FL.

Swogger, M., **Walsh, Z., & Kosson, D. S. (2006).** *Domestic violence and psychopathic traits: Distinguishing the antisocial batterer from other antisocial offenders.* Talk presented at the meeting of American Psychology and Law Society, St. Petersburg, FL.

Walsh, Z., Allen, L. C., & Kosson, D.S. (2005). *Beyond social deviance: Substance-specific relationships with PCL-R facets.* Talk presented at the meeting of the American Psychology and the Law Society, San Diego, CA.

Walsh, Z., & Kosson, D. S. (2005). *Schematic processing in psychopathic and antisocial criminals: Mistrust, grandiosity and criminality.* Talk presented at the meeting of the Society for the Scientific Study of Psychopathy, Vancouver, BC.

Walsh, Z., Brook, M., & Kosson, D. S. (2005). *Psychopathy and violence: Two factors are still better than one.* Poster presented at the meeting of the Society for the Scientific Study of Psychopathy, Vancouver, BC.

Munisamy, G., Epstein, A. M., **Walsh, Z., & King, A. C. (2005).** *Higher sensation seeking predicts smoking relapse.* Poster presented at the meeting of the Society of Behavioral Medicine, Boston, MA.

Walsh, Z., Swogger, M. T., & Kosson, D. S. (2004). *Psychopathy, depression, and violence: The moderating role of rumination.* Poster presented at the meeting of the Society for Research in Psychopathology. St. Louis, MO.

Walsh, Z., Allen, L. C., Sullivan, E. A., & Kosson, D. S. (2004). *Beyond general social deviance: Substance-specific relationships with Psychopathy Checklist-Revised (PCL-R) facets.* Poster presented at the meeting of American Psychological Society, Chicago, IL.

Walsh, Z., & Kosson, D. S. (2004). *Psychopathy and recidivism in a county jail: The impact of ethnicity and socioeconomic status.* Poster presented at the meeting of the American Psychology and the Law Society, Scottsdale, AZ.

Swogger, M., **Walsh, Z., & Kosson, D. S. (2004).** *Psychopathy and domestic battery: Relationship to the four-facet model.* Poster presented at the meeting of the American Psychology and Law Society, St. Petersburg, FL.

Walsh, Z., Swogger, M. T., & Kosson, D. S. (2003). *Instrumental and reactive violence in psychopathic and nonpsychopathic violent offenders*. Poster presented at the meeting of the Society for Research in Psychopathology, Toronto, ON.

Walsh, Z., Swogger, M. T., & Kosson, D. S. (2003). *Psychopathy, head injury and child abuse: Predicting violent crime*. Poster presented at the meeting of Developmental and Neurosciences Perspectives on Psychopathy, Madison, WI.

Walsh, Z., Kosson, D. S., & Sullivan, E.A. (2002). *Psychopathy, I.Q. and violence*. Poster presented at the meeting of the Society for Research in Psychopathology, San Francisco, CA.

EXPERT OPINION & TESTIMONY

- 2023 *Doe, Jones & Kozmenski v. King* Expert witness response at the Federal Court of Canada, Ottawa ON.
- 2022 *Psychedelics in the treatment of PTSD*. Invited testimony to Senate of Canada – Subcommittee on Veterans Affairs, Ottawa, ON.
- 2021 *Doe, Jones & Kozmenski v. Queen* Expert witness testimony at the Federal Court of Canada, Ottawa ON.
- 2019 *Cannabis in the treatment of PTSD*. Invited testimony to House of Commons of Canada – Standing Committee on Veterans Affairs, Ottawa, ON.
- 2019 *Cannabinoids and Opioids Consensus Summit*. Invited consultant. Toronto, ON.
- 2018 *Workshop on National Standard for Cannabis Measurement*, Invited consultant to the CIHR Institute of Mental Health & Addiction, Ottawa, ON.
- 2018 *Cannabis in the treatment of PTSD*. Invited testimony to Senate of Canada – Subcommittee on Veterans Affairs, Ottawa, ON.
- 2017 *Needs Based Planning Expert Panel Focused on Cannabis Use Disorder*, Consultant to the BC Ministry of Mental Health and Addictions / Centre for Applied Research in Mental Health and Addiction, Vancouver, BC
- 2017 *Workshop on Health Research Needs and Priorities related to Cannabis Legalization and Regulation*, Consultant to the CIHR Institute of Population and Public Health, Montreal, QC
- 2017 *Phytos Apothecary & Wellness Centre v. Toronto* Expert witness testimony at the Ontario Superior Court of Justice, Toronto, ON.
- 2016 *Task Force on Marijuana Legalization and Regulation*. Consultant to the Attorney General of Canada and the Canadian Ministries of Justice, Public Safety and Health, Vancouver, BC.
- 2016 *National Research Agenda on Cannabis*. Consultant to the Canadian Centre on Substance Abuse, Ottawa, ON.
- 2016 *Mary Jane's Glass & Gifts v. Abbotsford* Expert witness testimony at the BC Provincial Supreme Court, Vancouver, BC.

- 2015 *Boehme v. Canada*. Expert witness testimony at the BC Provincial Supreme Court, Duncan, BC.
- 2015 *Allard v. Canada*. Expert witness testimony at the BC Provincial Supreme Court, Vancouver, BC.
- 2014 *Standing Committee on Health: Study on Marijuana's Health Risks and Harms*. Invited witness presentation to the House of Commons, Ottawa, ON.
- 2014 *International Forum: Update on the medical and therapeutic uses of cannabis*. Invited presentation and consultation to the Uruguayan National Office of Drugs and Ministry of Public Health, Montevideo, Uruguay.

GRANTS

Ongoing:

- 2023 - **Principal investigator** – *Etheridge Foundation*. “Standardized natural psilocybin-assisted psychotherapy for tapering of opioid medication in patients with chronic pain: an open-label feasibility study” \$110,000.
- 2023 - **Principal investigator** – *Mitacs Elevate Postdoc Program*. “Comparing acute effects of natural and synthetically derived psilocybin using a mixed-methods approach” \$160,000.
Industry partner: Mycomedica Life Sciences
- 2023 - **Principal investigator** – *Mitacs Accelerate Postdoc Program*. “Responsible stewardship of psychedelic-assisted therapy: An observational evaluation of a culturally safe and patient-centered program of care” \$160,000.
Industry partner: Roots to Thrive
- 2022 - **Co-Principal investigator** – *Canadian Institutes of Health Research*. Operating Grant “Longitudinally evaluating the health impacts of cannabis regulation among two sentinel populations with high rates of cannabis use and drug-related harms” \$490,345.
Co-principal investigator: M-J Milloy
- 2021 - **Co-Principal investigator** – *Interior University Research Coalition - Ministry of Health Research Grant*. Maverick Cannabis Project.” \$48,500.
Co-principal investigator: Florriann Fehr
- 2021 - **Co-investigator** – *University of British Columbia - Health Innovation Funding Investment Award*. “Harm Reduction Innovation: Exploring a Tri-Partnership Model for the delivery of Drug-checking Services on Campus and in the Community ” \$24,9750
Principal investigator: Lauren Airth
- 2021 - **Co-investigator** – *National Football League Players Association Joint Pain Management Committee* “Naturally produced cannabinoids for pain management & neuroprotection from concussion in contact sports. ” \$650,000.
Principal investigator: J Patrick Neary

- 2021 - **Supervisor** - *Social Sciences and Humanities Research Council*. Doctoral Fellowship Award "Cannabis Use and Cognitive Functioning" \$60,000.
Student awardee: Tashia Petker
- 2020 - **Principal investigator** – *Mitacs Accelerate Program*. "Observing Microdosing: Effects on Cognitive Performance and Mental Health" \$112,500.
Industry partner: Quantified Citizen
- 2020 - **Co-investigator** – *Canadian Institutes of Health Research*. Operating Grant "Evaluating tetrahydrocannabinol as an adjunct to opioid agonist therapy for individuals living with opioid use disorder: A Phase II, placebo-controlled, blinded, pilot study to assess safety and feasibility" \$279,000
Principal investigator: M-J Milloy
- 2020 - **Co-investigator** – *Canadian Institutes of Health Research*. Knowledge Synthesis Grant "A COVID-19 Patient Oriented Response and Recovery Effort: Working Across Sectors to Aid Healthcare Providers Suffering from Burnout, PTSD, or Treatment Resistant Depression (TRD)" \$50,000.
Principal investigator: Shannon Dames
- 2019 - **Co-investigator** – *Social Sciences and Humanities Research Council*. Partnership Grant "Univenture: A partnership to address heavy drinking and other substance misuse on Canadian university campuses" \$2,500,000
Principal investigator: Sherry Stewart
- 2018 - **Principal investigator** - *Social Sciences and Humanities Research Council*. Insight Grant "Beyond Reefer Madness: Capturing the normal cannabis user in a nomological net" \$250,950.
- 2018 - **Co-investigator** – *Canadian Institutes of Health Research*. Operating Grant "Smoking is better than taking pills": a longitudinal qualitative study of cannabis use and symptom management among people living with HIV" \$263,925
Principal investigator: Marilou Gagnon
- 2014 - **Consultant** - *Heffter Research Institute & University of Alabama at Birmingham*- "Psilocybin-facilitated treatment for cocaine use: A pilot study" \$20,000.
Principal investigator: Peter S. Hendricks

Completed:

- 2021 - 2023 **Supervisor** - *Social Sciences and Humanities Research Council*. Doctoral Fellowship Award "Cannabis and Alcohol Use" \$60,000.
Student awardee: Joseph Rootman
- 2020 - 2023 **Co-Principal investigator** – *Canadian Centre on Substance Use and Addiction*. Closing the Gaps in Cannabis Research Grant "Cannabis use among First Nations Peoples of Turtle Island: Motives for use, substitution and impacts of legalization." \$99,500.
Co-principal investigator: Lindsay Farrell

- 2020 - 2022 **Co-Principal investigator** – *Canadian Mental Health Commission*. Community Based Research Grant Grant “Cannabis si koom la Michinn (Cannabis as Medicine)” \$99,000.
Community Partner: Metis Nation of BC
- 2018 - 2022 **Principal investigator** – *Mitacs Accelerate Program*. “Cannabis and Mindfulness” \$90,000.
Industry partner: Doja - Health Canada licensed producer of medical cannabis
- 2018 - 2022 **Supervisor** - *Canadian Institutes of Health Research*. Vanier Doctoral Scholarship “Cannabis hyperalgesia” \$150,000.
Student awardee: Michelle Thiessen
- 2018 - 2022 **Co-investigator** - *Canadian Institutes of Health Research*. Planning Grant “Working Together to Develop Canadian Clinical Practice Guidelines for the Use of Cannabis in the Management of Chronic Pain and Co-Occurring Conditions (Sleep Disorders, Mood Disorders, Substance Use Disorders)” \$10,000.
Principal investigator: Gary Lacasse
- 2019 - 2021 **Supervisor** - *Social Sciences and Humanities Research Council*. Doctoral Fellowship Award “Cannabis use norms” \$60,000.
Student awardee: Tatiana Sanchez
- 2019 - 2021 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master’s Scholarship “Cannabis and Binge Drinking” \$17,500.
Student awardee: Joseph Rootman
- 2014 - 2021 **Principal investigator** – *Investigator Initiated Partnership* (Tilray – Health Canada licensed producer of medical cannabis). “Clinical trial of medical cannabis for PTSD” \$228,125.
- 2019 - 2020 **Co-principal investigator** – *Canadian Institutes of Health Research*. Catalyst Grant “Investigating cannabis as harm reduction during a community-wide overdose crisis” \$125,000
Co-principal investigator: M-J Milloy
- 2018 - 2020 **Principal investigator** – *Canadian Institutes of Health Research*. Catalyst Grant “The impact of cannabis legalization on campus health: A multi-method approach to establishing a baseline and monitoring change” \$97,170
- 2020 **Principal investigator** – *Mitacs Accelerate Program*. “Healthcare Utilization in Chronic Pain Patients: A Prospective Examination of Using Cannabis for Therapeutic Purposes” \$45,000. Industry partner: FLOWR - Health Canada licensed producer of medical cannabis – Declined due to Industry partner default
- 2018 - 2019 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master’s Scholarship “Legalization and cannabis norms” \$17,500.
Student awardee: Tatianna Sanchez.

- 2017 - 2018 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master's Scholarship "Prenatal cannabis use" \$17,500.
Student awardee: Sarah Daniels.
- 2017 - 2018 **Principal investigator** – *UBC Hampton Research Endowment Fund*. Bridge funding "Beyond Reefer Madness" \$5,000.
- 2014 - 2018 **Supervisor** - *Social Sciences and Humanities Research Council*. Doctoral Fellowship Award "Cannabis use and partner violence" - \$60,000.
Student awardee: Kimberley Crosby
- 2015 - 2016 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master's Scholarship "Development of the Composite Cannabis Assessment Tool" \$17,500.
Student awardee: Michelle Thiessen.
- 2014 - 2016 **Principal investigator** – *Mitacs Accelerate Program*. "Clinical trial of medical cannabis for PTSD" \$45,000. Industry partner: Tilray - Health Canada licensed producer of medical cannabis
- 2011 - 2016 **Principal investigator** - *Social Sciences and Humanities Research Council*. Standard Operating Grant "One size does not fit all: A prospective multimethod examination of subtypes of women and men involved in intimate partner violence" \$117,150.
- 2014 - 2016 **Primary partner** - *BC Alliance for Mental Health/ Illness and Addictions – Community Action Initiative* Service Innovation Grant "Caring for the Caregivers" \$200,000.
Principal awardees: Canadian Mental Health Association
- 2014 - 2015 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master's Scholarship "An examination of the associations between problematic substance use and experiences of intimate partner violence" \$17,500.
Student awardee: Kimberly Crosby.
- 2014 - 2015 **Mentor** - *Intersections of Mental Health Perspectives in Addictions Research Training*. Master's Fellowship "Substance use and intimate partner violence" \$18,000.
Student awardee: Kimberly Crosby.
- 2014 - 2015 **Mentor** - *Intersections of Mental Health Perspectives in Addictions Research Training*. Master's Fellowship "Cannabis use and subtypes of violence" \$18,000.
Student awardee: Chris Carroll.
- 2014 - 2015 **Consultant** - *University of Rochester Medical Center Office of Health Promotion*. Community Partnership Development Award "Assessing the effectiveness of a program for perpetrators of intimate partner violence" \$20,000.
Principal investigator: Marc T. Swogger, Ph.D.
- 2013 - 2015 **Principal investigator** - *Institute for Healthy Living and Chronic Disease Prevention* (BC Interior Health Authority / University of British Columbia). Research Interest Group Grant "Medical cannabis and arthritis: Barriers and pathways" \$10,000.

- 2012 - 2015 **Principal investigator** - *Peter Wall Endowment*
Peter Wall Solutions Initiative “Medical Cannabis – Standards, Engagement, Evaluation & Dissemination (SEED)” \$90,000.
- 2013 - 2014 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master’s Scholarship “Examining linguistic cues regarding intimate relationships in psychopathic versus non-psychopathic offenders” \$17,500.
Co-Supervisor Steven Porter, Student awardee: Lacy Peters.
- 2011 - 2014 **Supervisor** - *Social Sciences and Humanities Research Council*. Doctoral Fellowship Award “Social support needs of women involved in intimate partner violence \$60,000.
Student awardee: Jennifer I. Langille, MA
- 2010 - 2014 **Co-principal investigator** - *Canadian Foundation for Innovation*. Leaders Opportunity Fund “Centre for the Study of Psychology and Law” \$413,285
Co-Principal Investigators: Stephen Porter, Ph.D. & Michael Woodworth, Ph.D.
- 2011 - 2013 **Principal investigator** - *Institute for Healthy Living and Chronic Disease Prevention (BC Interior Health Authority / University of British Columbia)*. Research Interest Group Grant “Barriers to accessing medical cannabis among individuals with chronic illness” \$10,000.
- 2012 - 2013 **Co-investigator** - *Canadian Institutes of Health Research*. Planning grant “Cannabis for therapeutic purposes in provincial health systems: A priority setting workshop” \$24,471.
Principal investigator: Lynda G Balneaves, Ph.D.
- 2012 - 2012 **Principal investigator** - *Health Canada*. Drugs and Tobacco Initiatives “Targeted prevention for cannabis use among Canadian youth - Environmental scan and literature review” \$7,813
- 2010 - 2012 **Supervisor** - *Social Sciences and Humanities Research Council*. Joseph-Armand Bombardier Master’s Scholarship “Subtypes of male and female partner violence perpetrators”- \$17,500.
Student awardee: Alissa Fezatte
- 2010 - 2012 **Co-investigator** - *Canadian Institutes of Health Research*. Catalyst grant “Alternative intervention for marijuana use (AIM): Addressing individual risk factors for transitions to initiation and escalation of marijuana use in early adolescence.” \$87,001.
Principal investigator: Marvin Krank, Ph.D.
- 2010 - 2012 **Co-investigator** - *Institute for Healthy Living and Chronic Disease Prevention (BC Interior Health Authority / University of British Columbia)*. Research Interest Group Grant “Improving the health and well-being of men who have sex with men in the interior of British Columbia” \$10,000.
Principal investigator: Susan Holtzman, Ph.D.

2008 - 2009 **Principal investigator** - *Canadian Institutes of Health Research*. Fellowship Award in Clinical Research: "Personality disorder as a moderator of treatment outcome for male and female perpetrators of partner violence." \$60,000. Supervisors: Gregory L. Stuart, Ph.D. & M. Tracie Shea, Ph.D.

COURSES TAUGHT

Undergraduate

Drugs and Behaviour
Research Methods and Statistics
Introduction to Psychology-Basic Processes

Graduate

Psychological Interventions
Psychopathology

CLINICAL APPOINTMENTS

2023 - Consultant – Youth Substance Use Treatment – Interior Health Authority, Kelowna, BC.

2018 - Director – Problematic Substance Use Clinic - The UBC Interdisciplinary Clinic, Kelowna, BC.

2017 - 2018 Clinical supervisor – Psychological assessment and treatment program - The UBC Interdisciplinary Clinic, Kelowna, BC.

2014 - 2016 Clinical supervisor - Bridgeway residential addictions treatment - The Bridge, Kelowna, BC.

2013 - 2016 Independent rater - Phase 3 Clinical Trial - MDMA for PTSD - Multidisciplinary Association for Psychedelic Studies, Vancouver, BC.

2014 - 2015 Facilitator - Men's relationship group - Kelowna Family Centre, Kelowna, BC.

2008 - 2009 Research therapist - Brief Motivational Intervention for addictions and family violence, Butler Hospital, Providence, RI.

2008 - 2009 Research therapist - Cognitive Behavioral Therapy for anger and trauma, Providence Veterans Affairs Hospital, Providence, RI.

2007 - 2008 Graduate therapy intern - Cognitive Behavioral Therapy and Motivational Enhancement Therapy for addictions, Butler Hospital, Providence, RI.

2007 - 2008 Graduate therapy intern - Dialectical Behavior Therapy for women, Butler Hospital, Providence, RI.

2006 - 2007 Graduate therapy extern - Cognitive Behavioural Therapy for anxiety disorders, Clinics at Rosalind Franklin University, North Chicago, IL.

2005 - 2006 Graduate psychometrics extern - Forensic neuropsychological assessment, Isaac Ray Center, Chicago, IL.

- 2004 - 2005 Graduate therapy extern - Cognitive Behavioral Therapy and Motivational Enhancement for addictions, University of Chicago Hospital, Chicago, IL.
- 2004 - 2005 Graduate therapy extern - Dialectical Behavior Therapy for women, University of Chicago Hospital, / Emotion Management Program, Chicago, IL
- 2003 - 2004 Graduate psychometrics extern - Neuropsychology, University of Chicago Hospital, Chicago, IL.

OTHER APPOINTMENTS

- 2022 - Member - Editorial board, Nature-Scientific Reports
- 2021 - Member - Advisory board, Mycomedica Lifesciences
- 2020 - Member - Editorial board, Psychedelic Medicine
- 2020 - Member - Advisory board, Entheotech Biomed
- 2019 - Member - Advisory board, Numinus Wellness
- 2018 - Member – College of Reviewers, Canadian Institutes of Health Research
- 2018 - Affiliated Scientist – BC Centre on Substance Use (BCCSU)
- 2017 - Member - Cannabis Guidelines Task Force, Canadian AIDS Society
- 2014 - Member - Consultation Network of the Advisory Scientific Committee, Uruguayan National Drug Board, Montevideo, Uruguay
- 2012 - Member - Editorial board, Legal and Criminological Psychology
- 2012 - Member - Advisory board, Multidisciplinary Association for Psychedelic Studies (MAPS) Canada
- 2011 - Research affiliate – Canadian Institute of Substance Use Research (CISUR)
- 2017 Reviewer - Alberta Gaming Research Institute, Research Grant Program
- 2017 Reviewer – Mitacs Accelerate Program, Research Grant Program
- 2017 Reviewer - National Council of State Boards of Nursing, Report on Medical Marijuana and Nursing Practice
- 2016 - 2017 Member - Organizing committee, The BC Centre on Substance Use, Forum on Science of Cannabis: Defining a Research Agenda for Public Health
- 2011 - 2017 Co-Director - UBC Centre for Advancement of Psychological Science and Law
- 2013 - 2016 Research mentor - Intersections of Mental Health Perspective in Addictions Research Training (IMPART)
- 2010 - 2016 Member - Board of directors, John Howard Society of the Central and South Okanagan (Vice president 2014-15)

- 2015 Member – Planning committee, The Arthritis Society of Canada Medical Cannabis Research Roundtable & Priority Setting Workshop
- 2014 Member - Steering committee, The James Lind Alliance Priority-Setting Partnership, The Institute of Musculoskeletal Health and Arthritis, Canadian Institutes of Health Research
- 2014 Reviewer - UK Medical Research Council, Population Health Scientists Strategic Skill Fellowship Grant Program, Wiltshire, United Kingdom
- 2014 Topic expert - Online accredited continued medical education program on medical cannabis & Med School for You” Online patient education program on medical cannabis - mdBriefCase, Toronto, ON.
- 2013 Reviewer - German-Israeli Foundation for Scientific Research and Development, Young Scientist’s Program Grant
- 2012 Reviewer - Social Sciences and Humanities Research Council of Canada (SSHRC), Insight Grant Program
- 2008 - 2010 Psychiatry faculty - Personality and Impulse Disorders, Faculty of 1000 Medicine
- 2008 - 2009 Project manager - National Institute on Alcohol Abuse and Alcoholism - R01: *Brief intervention to reduce drinking among batterers*, PI: Gregory L. Stuart, Butler Hospital, Providence, RI.
- 2007 - 2008 Graduate research intern - National Institute of Mental Health - R01: *Collaborative longitudinal study of personality disorders*, site PI: M. Tracie Shea, Brown University, Providence, RI.
- 2004 - 2005 Group dynamics consultant- Tavistock Study Group, Northwestern University, Evanston, IL.
- 1997 - 2001 High school teacher - Manitoba School Divisions 1 & 6, Winnipeg, MB.
- 1990 - 1999 Organizer and fundraiser - Greenpeace, Winnipeg, MB.

MEMBERSHIPS IN SOCIETIES & ORGANIZATIONS

International Society for Research in Psychedelics

Canadian Consortium for the Investigation of Cannabinoids

International Cannabinoid Research Society

Canadian Psychological Association

Physicians for Human Rights

AD HOC REVIEWER (representative)

Addiction
BMC Psychiatry
Behavioral Sciences and Law
Criminal Justice and Behavior
Drug and Alcohol Dependence
Journal of Abnormal Child Psychology
Journal of Psychoactive Drugs
PLOS ONE
Psychological Assessment
Psychology of Addictive Behavior
Suicide and Life Threatening Behavior
Violence Against Women

Addictive Behaviors
BMC Public Health
Biological Psychology
Current Drug Abuse Reviews
International Journal of Drug Policy
Journal of Interpersonal Violence
Personality Disorders: Theory Research & Treatment
Social Science and Medicine
Substance Abuse Treatment, Prevention & Policy
Archives of Internal Medicine

HONOURS & AWARDS

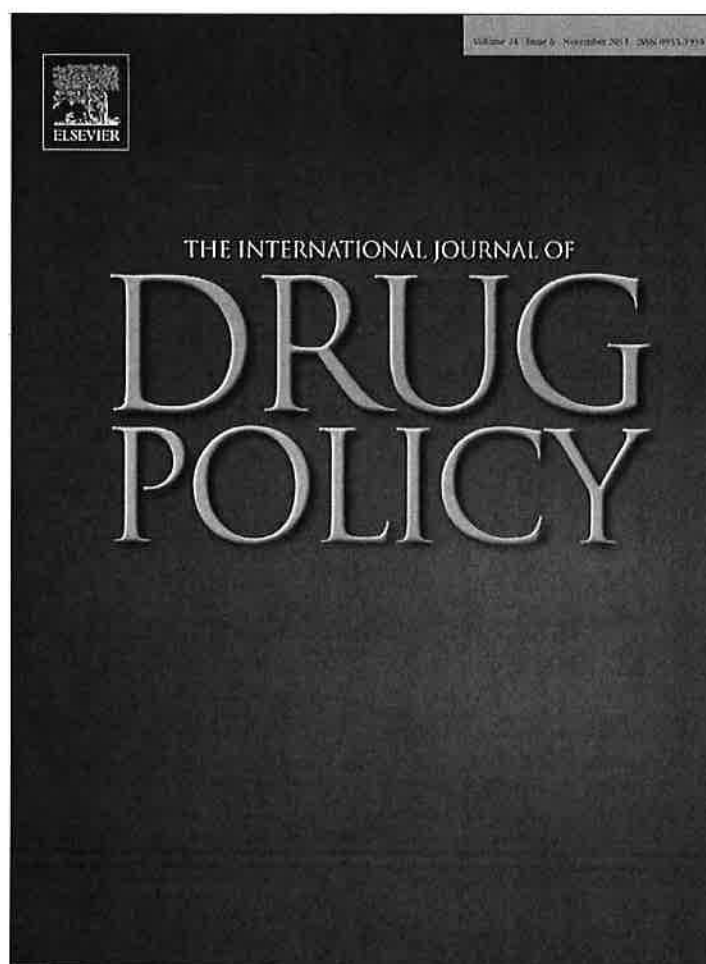
2023	Outstanding Faculty Member - UBC - Okanagan Clinical Graduate Student Body
2020	Award for Excellence in Research Activity – Health, UBC – Okanagan Campus
2018	Teaching Honour Roll Award, UBC
2016	Provosts Award for Excellence and Innovation in Teaching, UBC
2014	Teaching Honour Roll Award, UBC
2013	Teaching Honour Roll Award, UBC
2008	Internship Research Grant, Brown University
2006	Dissertation Award, American Academy of Forensic Psychiatry
2006	Dissertation Award, American Psychological Association
2004	Award for Research Excellence, Rosalind Franklin University

RESEARCH IMPACT (Google Scholar)

h-index - 38
i10index - 63
Citations - 4742

This is Exhibit B referred to in the
affidavit of Professor Zachary Walsh
sworn before me, this 28th
day of September 20²³
.....
A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.



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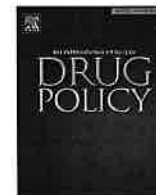
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Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Editors' choice

Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use

Zach Walsh^{a,*}, Robert Callaway^b, Lynne Belle-Isle^{c,d}, Rielle Capler^e, Robert Kay^f, Philippe Lucas^d, Susan Holtzman^a^a University of British Columbia, 3333 University Way, Kelowna, BC V1V1V7, Canada^b 1814B Edgehill Court, Kelowna, BC V1V 1R7, Canada^c Canadian AIDS Society, 190 O'Connor Street, Suite 100, Ottawa, ON K2P2R3, Canada^d Centre for Addictions Research of British Columbia, PO Box 1700 STN CSC, Victoria, BC V8W 2Y2, Canada^e Canadian Association of Medical Cannabis Dispensaries, Box 14, Lions Bay, BC V0N 2E0, Canada^f Green Cannapy Research and Development, 288 Highway 33W, Kelowna, BC V1X 1X7, Canada

ARTICLE INFO

Article history:

Received 18 April 2013

Received in revised form 10 August 2013

Accepted 30 August 2013

Keywords:

Cannabis

Medical marijuana

Access to cannabis

ABSTRACT

Background: The authorized and unauthorized use of cannabis for therapeutic purposes (CTP) has increased dramatically in recent years, and physicians have called for further research to better clarify the parameters of effective and appropriate use. We report findings from a large cross-sectional study of the use of CTP in Canada and compare use across medical conditions and across authorized and unauthorized users.

Methods: We examined cannabis use history, medical conditions and symptoms, patterns of current use of CTP, modes of access and perceived effectiveness among 628 self-selected Canadians consumers of CTP. Participants were recruited from medical cannabis dispensaries and from organizations that assist users of CTP.

Results: Patients reported using cannabis to treat multiple symptoms, with sleep, pain, and anxiety being the most common. Cannabis was perceived to provide effective symptoms relief across medical conditions. Patterns of use were also consistent across medical conditions. Notable differences were observed with regard to modes of access.

Conclusion: Across medical conditions respondents reported using cannabis to effectively address diverse symptoms. Results indicate a substantial disconnect between the therapeutic use of cannabis and research on the risks and benefits of such use; particularly with regard to the anxiolytic and sedative use of cannabis. Authorized and unauthorized users exhibited few meaningful differences with regard to medical conditions and patterns of use, but faced substantial differences regarding access.

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Cannabis has a long history of medical use (Abel, 1980; Earleywine, 2005; Iverson, 2008), and after decades of marginalization the therapeutic properties of cannabis and cannabis derivatives are receiving increased attention (Earleywine, 2005; Holland, 2010; Lucas, 2008). Indeed, robust and growing evidence indicates that cannabis has medical benefits for diverse conditions and an acceptable risk profile (Joy, Watson, & Benson, 2003). In response to legal recognition of the constitutional rights of Canadians to access cannabis for therapeutic purposes (CTP), the federal government enacted the *Marihuana Medical Access Regulations* and

initiated a centralized program in 2001, and in 2003 Health Canada began to provide CTP to patients. This program authorizes two categories of individuals to possess cannabis for medical purposes; Category 1 includes symptoms associated with HIV/AIDS, arthritis, spinal cord injury or disease, cancer, epilepsy, or MS, whereas Category 2 includes other symptoms and conditions assessed by a physician and a specialist. Those authorized can purchase dried cannabis from Health Canada, can purchase seeds to grow cannabis, or designate a person to grow cannabis on their behalf. In addition, medical cannabis dispensaries that operate under an ambiguous legal status provide CTP and related services to over 50,000 patients across Canada (Lucas, 2008).

Despite widespread concern with the efficiency of the Health Canada program (Holland, 2010), registration has grown exponentially from under 500 registrants in 2002 to over 26,000 in 2012 (Health Canada, 2012a). National surveys indicate substantial access outside of the Health Canada program; recent estimates

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suggest that 400,000 to 1,000,000 Canadians use CTP (Health Canada, 2011). Diverse reasons for use and multiple modes of access complicate the characterization of use of CTP, and health care professionals have expressed concern regarding the dearth of information on CTP; a recent Canadian Medical Association-sponsored survey reported that over 80% of physicians wanted more information on therapeutic indications, clinical guidelines, and risks and benefits of CTP (CMA, 2012).

Several studies have examined CTP use among Canadians. A regional survey reported that approximately 2% of adults used CTP in the past year, primarily to relieve nausea and pain (Braitstein et al., 2001), and a more recent national survey estimated that one million Canadians, or 4% of those aged 15 and older, used cannabis to treat self-defined medical conditions in the previous 12 months (Adlaf, Begin, & Sawka, 2005). Studies of persons living with HIV/AIDS report rates of 15–30% use of CTP, primarily for treatment of nausea, pain, and mood-related symptoms (Belle-Isle & Hathaway, 2007; Ware, Rueda, Singer, & Kilby, 2003). Studies of patients with MS and patients with chronic pain report similar results; approximately 15% of respondents report use of CTP with high levels of perceived effectiveness for diverse symptoms including nausea, pain, and mood (Belle-Isle & Hathaway, 2007; Ware et al., 2003; Clark, Ware, Yazer, Murray, & Lynch, 2004). Studies of CTP from the US, Europe, and Australia report findings that are consistent with those of Canadian studies; CTP is perceived to be an effective treatment for symptoms including pain, nausea, and negative mood (Grotenherman & Schnelle, 2003; Harris et al., 2000; Lucas, 2012; Reiman, 2007; Reinerman, Nunberg, Lanthier, & Heddleston, 2011; Swift, Gates, & Dillon, 2005; Ware, Adams, & Guy, 2005).

In sum, patient-centered research provides evidence for the acceptability and perceived effectiveness of CTP. However, substantial knowledge gaps remain and health care professionals have explicitly called for further research to better specify the parameters for appropriate use of CTP (CMA, 2012). Indeed, to date no studies have directly compared use of CTP across medical conditions or across modes of access (i.e., authorized vs. unauthorized). In the present study we report demographic characteristics, medical conditions and symptoms, reasons for use, perceived effects, and authorized and unauthorized modes of accessing CTP among Canadians. Comparing users of CTP across symptoms and across medical conditions with regard to patterns of use, and perceived effectiveness may help direct future controlled studies of the efficacy of CTP for specific conditions, and inform the development of tailored CTP regimens. In addition, comparing authorized and unauthorized CTP users may elucidate factors that underlie patient adoption of the Canadian CTP program, and help to guide the refinement of the complex process of CTP distribution and monitoring.

Method

Design

We obtained cross-sectional data in 2011–2012 from 628 self-selected current CTP users. Participants were recruited from two contexts; *national* participants completed the survey online from the location of their choice, and *local* participants completed the survey at a cannabis dispensary in the Interior region of British Columbia (BC). This recruitment strategy was designed to allow for comparison of the relatively less controlled online *national* condition with the confirmed CTP users queried in-person in the *local* condition. A total of 702 *national* participants completed the consent form, of whom 541 (77%) reported current CTP use. All 87 *local* participants who completed the consent form reported current CTP use. The *national* survey was promoted via organizations and media

Table 1
Demographics.

	CTP patients, % (n)	Census, %	Z
Male	71 (443)	49	11.03 ^a
Ethnicity			
White	92 (581)	80	7.52 ^a
Aboriginal	7 (47)	4	3.80 ^a
Age			
18–24yrs old	17 (99)	12	3.86 ^a
25–34	26 (158)	16	6.84 ^a
35–44	19 (115)	20	.63
45–54	24 (141)	20	2.51
55+	14 (85)	32	9.67 ^a
Education			
<high School	4 (27)	15	–7.86 ^a
HS Grad	37 (234)	24	7.63 ^a
% post secondary	58 (367)	61	–1.54
Income			
<\$20,000	33 (206)	44	–5.55 ^a
\$20,000–39,999	26 (165)	27	–.56
\$40,000–59,999	17 (103)	15	1.43
\$60,000 +	24 (146)	14	7.22 ^a
Residence			
Rural	22 (137)	20	1.25
Urban	78 (485)	80	–1.25

Note: Z = One sample Z-test for proportions, comparing medical cannabis users to values from the 2006 Canadian Census (Statistics Canada, 2006).

^a $p < .01$.

that serve users of CTP patients (e.g., Canadian AIDS Society, Canadian Aboriginal AIDS Network, Cannabis Culture), and by national advertisements at MC dispensaries. To preserve confidentiality, no identifying data (i.e. IP addresses) were collected for *national* participants. The *local* group was comprised of dispensary members who were either authorized to possess cannabis through Health Canada or had documented confirmation of a medical condition for which CTP is indicated. No confirmation of medical condition was provided for *national* participants; however such confirmation is required to obtain Health Canada authorization and to obtain dispensary membership. Participants in the *local* group were compensated \$10 and were aided by research assistants; participants in the *national* group were not assisted or financially compensated.

The survey was designed to be completed in less than one hour, and consisted of a total of 414 adaptive questions administered online without forced response. The survey was organized hierarchically such that many items were contingent on prior responses; as a result, respondents were presented with diverse item sets and response rates for specific items, and total response times varied accordingly. The survey was developed based on previous research, and on consultations with a community research board comprised of CTP patients and experts, and includes questions drawn from a prior study of CTP use (Belle-Isle & Hathaway, 2007). It queried access, perceived effectiveness, patterns and history of cannabis use, medical diagnoses and symptoms, mood, and demographics (a copy of the survey is available upon request from the first author). The study was approved by the Behavioural Research Ethics Board of the Okanagan campus of the University of British Columbia. All categorical data were compared using χ^2 . In light of varying response rates across items, total number of responses is reported for each analysis. Due to the large number of comparisons all significance testing was conducted at the $p < .01$ level to minimize the likelihood of interpreting chance results while maintaining power (Nakagawa, 2004).

Results

Preliminary analyses

We compared the responses of *local* participants who reported residency in the province of BC and accessing CTP via

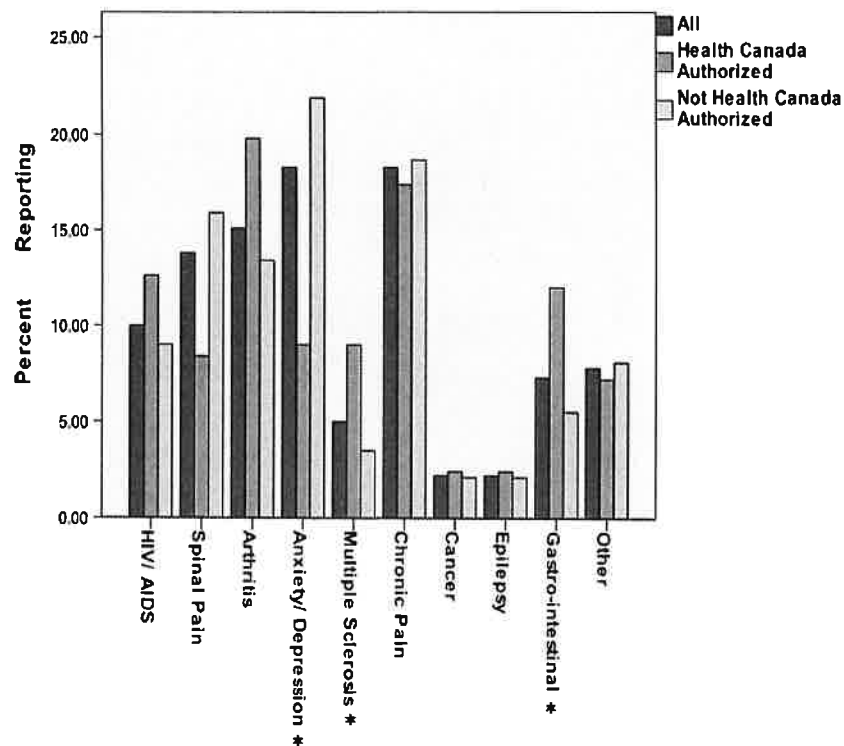


Fig. 1. Primary medical conditions treated with cannabis by authorization. *Note:* Sleep Disorders, Attention Deficit Disorder, Fibromyalgia, Hepatitis C, Parkinson's Disease, Wilson's Disease, Scleroderma, Tourette's Syndrome, and unspecified Psychotic Disorder Conditions each comprised less than 2% of the sample and were aggregated into the category 'Other'. The anxiety and mood disorders category included 35 participants who reported a primary illness/condition of anxiety, 34 who reported depression and 40 who reported both anxiety and depression. Comparisons of these groups indicated equivalent profiles with regard to demographic characteristics, health, and use of CTP, and were therefore aggregated for statistical analyses; $n = 502$ * = difference between proportion Health Canada Authorized and Unauthorized $p < .01$.

dispensary ($n = 63$) to national participants who reported BC residency and accessing CTP via dispensary ($n = 53$). Analysis indicated no differences with regard to quantity or frequency of cannabis use, and indicated substantial similarity with regard to primary medical condition; the only difference was a smaller proportion of local respondents reporting gastrointestinal (GI) condition as primary ($\chi^2 = 8.94$ (1), $p < .01$). This broad similarity between in-person confirmed users of CTP (i.e. local) and online respondents increased our confidence in the validity of online responses.

Demographics

Comparisons of the sample to values drawn from the Canadian 2006 Census of Population (Statistics Canada, 2006; Table 1) indicated that male, White, and Aboriginal participants were over-represented. The users of CTP were also younger, had a higher income, and were more likely to have completed high school. The regional distribution was consistent with participation in the Health Canada program (Health Canada, 2012b).

Medical conditions and symptoms

Participants were queried regarding a single primary condition treated with cannabis (Fig. 1). Participants also checked all applicable symptoms (Table 2) they treated with cannabis from a list. The mean number of symptoms patients endorsed treating was 6.74 ($n = 605$, $SD = 3.00$, Median = 6.00, Interquartile range = 4.00–8.00). Symptoms reportedly treated with CTP by fewer than 10% of the sample include high blood pressure (9%), tics (8%), regulating blood sugar (7%), seizures (6%), bladder dyscontrol (6%) and impotence (6%). Aggregate examination across condition indicated that pain, anxiety, and sleep problems were the most frequently endorsed

symptoms; 57% reported use to address all three symptoms, and 99% endorsed treating one or more of the three.

Symptoms treated with cannabis varied across condition (Table 2). Use to address pain symptoms was more prevalent among individuals whose primary conditions were pain-related (i.e., chronic spinal and non-spinal pain, arthritis). Chronic spinal pain participants were more likely to report treating muscle spasms. Participants with arthritis were more likely to report use for inflammation and ocular pressure, and less likely to report use to address anxiety and appetite. Participants who identified mood and anxiety disorders as their primary condition were more likely to use cannabis to address mental health-related symptoms (i.e., anxiety, depression, aggression, mania/psychosis), and were less likely to treat pain, inflammation, and muscle spasms. Participants who identified HIV/AIDS or GI as their primary conditions were more likely to treat symptoms of nausea and appetite, and HIV/AIDS was associated with less treatment of pain and aggression. Overall, cannabis was perceived to provide effective symptoms relief; 72% ($n = 439$) reported that CTP was *always* helpful and an additional 24% ($n = 147$) described it as *often* helpful. The proportion of participants who described CTP as *always* helpful was relatively consistent across conditions. The only difference across groups was relatively lower endorsement of *always* helpful (55%) by participants with HIV/AIDS ($\chi^2 = 10.04$ (1), $n = 593$, $p < .01$). Over half (57%, $n = 358$) of participants reported using other medications to address the symptoms they were treating with CTP. Of these, 79% ($n = 281$) described CTP as having fewer side effects than the concurrent treatment.

Use patterns

History of non-therapeutic cannabis use prior to therapeutic use was reported by 82% ($n = 441$) of participants.

Table 2
Symptoms addressed with medical cannabis by condition.

	All		Pain-spinal			Pain-nonspinal			Arthritis			Mood			HIV/AIDS			GI		
	n	%	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²
Sleep	502	85	68	83	0.35	93	85	<.01	80	90	1.91	99	93	5.7	47	78	2.4	33	77	2.54
Pain	486	82	80	98	15.13 ^a	102	94	11.56 ^a	86	97	14.67 ^a	56	52	81.21 ^a	41	68	9.07 ^a	40	93	3.62
Anxiety	463	79	65	79	0.04	85	78	0.02	57	64	12.92 ^a	106	99	32.81 ^a	44	73	1.05	29	67	3.34
Depression	394	67	55	67	<.01	68	62	1.16	51	57	4.24	98	92	36.26 ^a	34	57	3.08	27	63	0.33
Appetite/weight	331	56	43	52	0.52	56	51	1.21	35	39	11.98 ^a	61	57	0.04	46	77	11.47 ^a	33	77	8.02 ^a
Nausea	294	49	36	44	1.34	56	51	0.13	33	37	6.82 ^a	43	40	4.86	47	78	21.71 ^a	35	81	18.48 ^a
Inflammation	291	49	51	62	6.31	52	48	0.14	79	89	65.23 ^a	25	23	35.23 ^a	20	33	6.83 ^a	25	58	1.44
Spasms	280	48	58	71	20.69 ^a	53	49	0.07	50	56	3.2	23	22	35.33 ^a	20	33	5.34	22	51	0.255
Headache	237	40	44	54	7.21	56	51	6.99 ^a	36	40	<.01	38	36	1.18	15	25	6.4	12	28	2.9
Aggression	140	24	19	23	0.01	28	26	0.28	16	18	1.92	42	39	17.40 ^a	5	8	8.75 ^a	8	19	0.67
Drug Withdrawal	76	13	10	12	0.04	17	16	0.88	10	11	0.25	18	17	1.81	8	13	0.01	1	2	4.61
Ocular Pressure	68	12	11	13	0.33	11	10	0.27	19	21	9.92 ^a	8	8	2.1	7	12	<.01	1	2	3.85
Mania/Psychosis	67	11	9	11	0.01	11	10	0.21	7	8	1.27	25	23	18.72 ^a	4	7	1.46	5	12	<.01
Respiratory	67	11	5	6	2.62	20	18	6.5	14	16	1.99	12	11	<.01	3	5	2.68	6	14	0.31
Skin Conditions	63	11	8	10	0.08	7	6	2.54	13	15	1.7	16	15	2.51	3	5	2.26	5	12	0.04

Note: X² = Comparison of each groups versus aggregation of other groups.^a $p < .01$.

Mean age was 17.30 years ($n=540$, $SD=7.08$, Median=16, Interquartile range=14.00–18.00) for first use and 28.35 years ($n=538$, $SD=11.25$, Median=25, Interquartile range=19.00–37.00) for first therapeutic use. Individuals with and without history of non-therapeutic use did not differ with regard to demographic characteristics, or conditions and symptoms. Most participants who reported prior use reported increased use with the initiation of therapeutic use; 33% reported a large increase and 32% a small increase, whereas 7% reported a large decrease and 10% a small decrease. Aggregate analyses indicated that 40% ($n=167$) of users fell into the modal quantity of use category of *more than 14 grams per week*, and that 42% ($n=226$) fell in the modal frequency of use group reporting *2–3 uses per day*. Among the group that used more than 14 grams per week, the median weekly amount used was 28 grams (Interquartile range=21–45). Comparisons of the six medical conditions that each account for 5% or more of the sample (Table 3) indicated no difference with regard to modes of use and few differences in patterns of use; a larger proportion of individuals identifying HIV/AIDS as primary condition were among the groups with lowest quantity and frequency of use, and those who identified anxiety and/or depression as primary conditions were less likely to fall in the most frequent use group. Overall health quality was also associated with frequency of use such that participants who described their overall health as *fair* or

poor (34%, $n=161$) were overrepresented in the most frequent use group ($X^2=8.31$ (1), $n=473$, $p<.01$).

Access

Aggregate examination indicated that 32% ($n=167$) of respondents had Health Canada authorization to possess CTP. An additional 12% ($n=64$) had applications in process, and 3% ($n=13$) had applied and been rejected. The proportion of authorized individuals varied across condition (Fig. 1); individuals who identified anxiety and/or depression as primary condition were less likely to be authorized ($X^2=13.13$ (1), $n=502$, $p<.01$), whereas a greater proportion of MS ($X^2=11.08$ (1), $n=502$, $p<.01$) and GI ($X^2=8.68$ (1), $n=502$, $p<.01$) participants were authorized. Most participants reported using more than one mode of accessing CTP; the mean number of access modalities was 1.89 ($n=500$, $SD=.88$, Median=2.00, Interquartile range=1.00–2.00). Authorization was a determinant of access (Fig. 2); the mean number of access modalities for authorized individuals was 2.11 ($n=162$, $SD=.98$, Median=2.00, Interquartile range=1.00–3.00) compared to 1.78 ($n=337$, $SD=.81$, Median=2.00, Interquartile range=1.00–2.00) for unauthorized users ($F(1, 497)=16.26$, $p<.01$). Authorized users were more likely to access CTP via Health Canada ($X^2=11.88$ (1), $n=443$, $p<.01$), to grow for themselves ($X^2=31.42$ (1), $n=493$,

Table 3
Characteristics of cannabis use by condition.

	All		Pain-spinal			Pain-nonspinal			Arthritis			Mood			HIV/AIDS			GI		
	n	%	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²	n	%	X ²
Amount per week (Grams)																				
≤2	42	9	5	8	0.1	9	10	0.13	3	4	2.59	9	10	0.3	11	27	18.01 ^a	1	3	1.68
2.1–5	60	13	8	13	<.01	11	12	0.05	10	13	0.04	11	13	<.01	5	12	<.01	0	0	5.46
5.1–9	85	18	7	11	2.44	22	24	2.81	11	15	0.63	24	28	6.81 ^a	6	15	0.33	6	17	0.02
9.1–14	76	16	15	24	3.04	15	16	<.01	15	20	1.06	11	13	0.89	4	10	1.3	6	17	0.04
>14	212	45	29	45	0.01	35	38	2	46	48	0.41	32	37	2.66	15	37	1.18	22	63	5.08
Frequency of use																				
< daily	58	11	6	9	0.4	13	13	0.31	3	4	4.72	13	14	1.06	13	25	10.85 ^a	2	5	1.4
1x day	71	14	7	10	0.71	16	16	0.43	12	16	0.32	17	19	2.31	8	15	0.12	1	3	4.17
2–3x	174	33	21	31	0.19	31	30	0.56	26	34	0.01	36	39	1.77	16	30	0.24	14	37	0.24
4x+	221	42	34	50	1.96	43	42	0.01	36	47	0.78	26	28	8.86 ^a	16	30	3.48	21	55	2.88
Preferred mode of use																				
Smoke ($n=513$)	293	57	35	54	0.33	62	61	0.94	41	53	0.55	48	53	0.86	35	67	2.45	24	65	0.98
Vaporize ($n=502$)	217	43	31	49	1.05	42	43	<.01	30	39	0.67	37	41	0.3	22	44	0.01	16	43	<.01
Oral ($n=501$)	139	28	16	26	0.13	29	30	0.21	29	39	5.25	25	26	0.1	15	31	0.22	8	22	0.75

Note: X² = Comparison of each groups versus aggregation of other groups.^a $p < .01$.

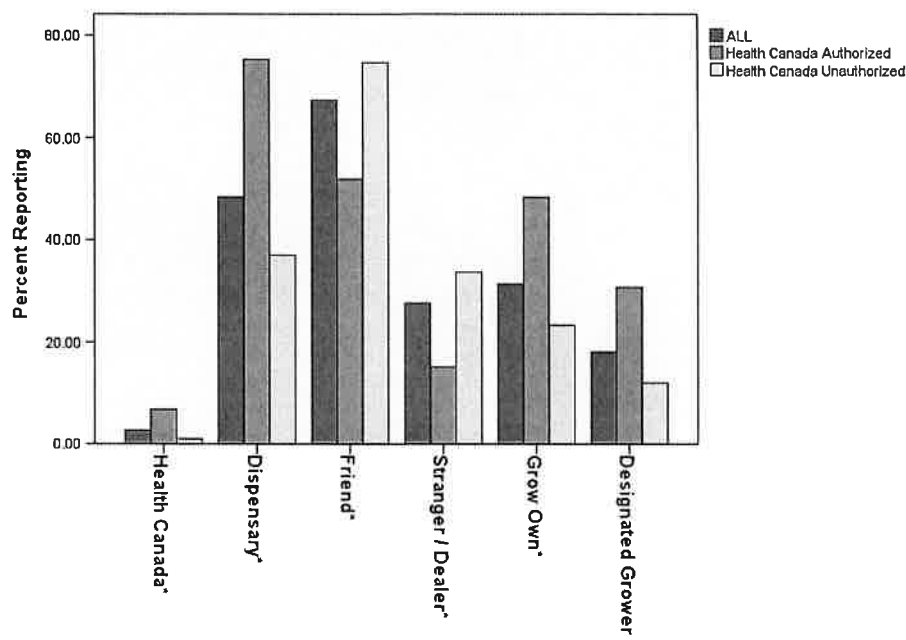


Fig. 2. Modes of Access. Note: * = difference between proportion Health Canada Authorized and Unauthorized $p < .01$; $n = 498$.

$p < .01$), have a designate grow for them ($X^2 = 25.85$ (1), $n = 493$, $p < .01$) or use a dispensary ($X^2 = 54.46$ (1), $n = 444$, $p < .01$). In contrast, unauthorized users were more likely to access CTP from a friend ($X^2 = 25.46$ (1), $n = 495$, $p < .01$) or from a stranger ($X^2 = 18.69$ (1), $n = 494$, $p < .01$).

Discussion

Canadians use cannabis to treat diverse conditions and symptoms in a manner that only partially overlaps with the federally authorized program. There is considerable consistency with regard to patterns of use and reported effectiveness; nearly all respondents used cannabis to treat pain, anxiety, or sleep disturbances, and over half used it to treat all three symptoms. We also observed consistency across participants with and without histories of non-therapeutic cannabis use, which suggests that, with regard to CTP, individuals who may enjoy non-therapeutic use of cannabis were not different with regard to therapeutic application of cannabis from those participants who may have been less likely to expect extra-therapeutic benefit. The substantial minority of respondents who were federally authorized to possess cannabis exhibited few differences from unauthorized users with regard to symptoms treated and patterns of use, but differed considerably with regard to mode of access.

Most respondents reported using CTP to treat conditions that are explicitly listed within the federal program; however, a large contingent also reported use for other conditions. Comparisons of symptoms treated across conditions indicated high levels of congruence (e.g., respondents with pain-related conditions were more likely to use cannabis to address pain symptoms), but also reflected substantial consistency across conditions. Specifically, use to treat sleep disturbances, and to a lesser extent anxiety and depression, was consistently high across conditions. However, despite widespread use for anxiolytic and sedative purposes, participants who reported anxiety or depression as primary reason for CTP use were less likely to have obtained federal authorization to access CTP. This may be due to the absence of these conditions among those explicitly listed by the federal program, but may also reflect accentuated stigma associated with the use of cannabis to address mental health issues. Indeed, stigma has been identified as a

substantial barrier to accessing care for mental health conditions such as depression and anxiety (Brown et al., 2010), and this may be compounded by the considerable stigma associated with use of CTP (Bottorf et al., 2013) to create a substantial barrier to accessing treatment. Research that further elucidates the appropriateness of using cannabis to treat anxiety and depression is required to guide effective treatment and help to reduce stigma.

Patterns of use were also consistent across medical conditions, with the only notable difference being slightly lower levels of use among respondents with HIV/AIDS, a difference which may be due to intermittent use to address nausea. Most participants reported initiating non-therapeutic use prior to use of CTP, and noted increased levels of use associated with the transition to therapeutic use. This reported increase is consistent with our observation that the median level of therapeutic use exceeds typical levels of non-therapeutic use (Reinarman, Cohen, & Kaal, 2004; Hazekamp et al., 2013; but see also Hazekamp & Heerdink, 2013), and suggests a potentially meaningful distinction between therapeutic and non-therapeutic use. In contrast, the relative consistency of use among CTP-users suggests that CTP regimens might transfer well across conditions, and enjoy good adherence. The most pronounced differences across respondents involved modes of access, such that unauthorized users were much less likely to access CTP from authorized, or semi-authorized (i.e. dispensaries) sources. This discrepancy contrasts with the pronounced similarity between authorized and unauthorized users on indicators of health and use of CTP, and suggests that the current system of authorization may not be discriminating among qualitatively different groups.

The primary limitations of this study are common to online medical surveys such as potential for multiple responses from a single respondent, a potentially unrepresentative sample, and lack of physician confirmation of medical conditions. In addition, response bias related to participant self-selection, and recruitment through organizations that support medical cannabis patients likely resulted in overrepresentation in our sample by individuals who respond favourably to CTP. In light of this potential bias, our characterization of the therapeutic use of cannabis should be interpreted with caution pending replication from research that employs a more systematic recruitment approach. However, these limitations are counterbalanced by several methodological

strengths including the inclusion of an in-person subsample, engagement of a community research board in the development and dissemination of the survey, and general adherence to established standards for reporting internet-based surveys (Eysenbach, 2004).

Conclusions

This was the largest and most comprehensive study to date of the therapeutic use of cannabis in Canada. We draw three primary conclusions from the data. First, reasons for use and perceived effectiveness were generally consistent across medical conditions; respondents overwhelmingly reported using cannabis to effectively address pain, sleep disturbance, and anxiety. Second, further research is required to address the substantial disconnect between the therapeutic use of cannabis and research on the risks and benefits of such use. This is particularly evident with regard to the anxiolytic and sedative use of cannabis; extrapolation from our sample to the national population of CTP users suggests levels of use for anxiolytic and sedative purposes that may be comparable to the number of Canadians who currently use benzodiazepine and other sedatives (Kassam & Patten, 2006). Such widespread use suggests a need for the systematic evaluation of the effectiveness and adverse effects of cannabis for the treatment of these conditions, as well as comparisons of cannabis with the widely-used pharmaceutical products that currently represent frontline treatments. Finally, our findings highlight the apparent discrepancy in access to cannabis across CTP users. Authorized and unauthorized users exhibit few meaningful differences with regard to medical conditions and patterns of use, but face substantial differences regarding access; many seriously ill Canadians risk increased stigma (Bottorf, Bissell, Balneaves, Oliffe, Capler & Buxton, 2013), legal sanction, and other negative outcomes associated with accessing cannabis from illegal markets. At the time of this writing the federal medical cannabis program is undergoing substantial structural changes. The present study provides a baseline for assessing the impact of these changes, the most important of which must surely involve providing a program that facilitates informed, safe, legal, and affordable access to a source of CTP for ill Canadians.

Acknowledgements

This research was supported by a grant from the UBC Institute for Healthy Living and Chronic Disease Prevention. The authors thank the people who took the time to respond to the survey. We would also like to thank Ben Atkinson, Kim Crosby and Megan Hiles for their contribution to data collection and management, and Brian Emerson for providing valuable feedback on the manuscript.

Conflict of interest statement

None of the authors have any conflicts of interest with regard to the contents of this manuscript. Access.

References

- Abel, E. L. (1980). *Marijuana: The first twelve thousand years*. New York: Plenum Press.
- Adlaf, E. M., Begin, P., & Sawka, E. (2005). *Canadian Addiction Survey (CAS): A national survey of Canadian's use of alcohol and other drugs: Prevalence of use and related harms: Detailed report*. Ottawa: Canadian Centre on Substance Use.
- Belle-Isle, L., & Hathaway, A. (2007). Barriers to access to medical cannabis for Canadians living with HIV/AIDS. *AIDS Care*, 19, 500–506. <http://dx.doi.org/10.1080/09540120701207833>
- Bottorf, J. L., Bissell, L. J., Balneaves, L. G., Oliffe, J. L., Capler, N. R., & Buxton, J. (2013). Perceptions of cannabis as a stigmatized medicine: a qualitative descriptive study. *Harm Reduction Journal*, 10, 1–10. <http://dx.doi.org/10.1186/1477-7517-10-2>
- Braitstein, P., Kendall, T., Chan, K., Wood, E., Montaner, J. S., O'Shaughnessy, M. V., & Hogg, R. S. (2001). Mary-Jane and her patients: Sociodemographic and clinical characteristics of HIV-positive individuals using medical marijuana and antiretroviral agents. *AIDS*, 15, 532–533.
- Brown, C., Conner, K., Copeland, V. C., Grote, N., Beach, S., Battista, D., & Reynolds, C. F. (2010). Depression stigma, race, and treatment seeking behavior and attitudes. *Journal of Community Psychology*, 38, 350–368.
- Canadian Medical Association. (2012). *Our members' views on medicinal marijuana*. Retrieved from <http://www.cma.ca/advocacy/epanel-medicinal-marijuana>.
- Clark, A. J., Ware, M. A., Yzer, E., Murray, T. J., & Lynch, M. E. (2004). Patterns of cannabis use among patients with multiple sclerosis. *Neurology*, 62, 2098–2100.
- Earleywine, M. (2005). *Understanding marijuana: A new look at the scientific evidence*. New York: Oxford University Press.
- Eysenbach, G. (2004). Improving the quality of web surveys: The checklist for reporting the results of internet e-surveys. *Journal of Medical Internet Research*, 3, e34. <http://dx.doi.org/10.2196/jmir.6.3.e34>
- Grotenherman, F., & Schnelle, M. (2003). Survey on the medical use of cannabis and THC in Germany. *Journal of Cannabis Therapeutics*, 3(2), 17–40. http://dx.doi.org/10.1300/J175v03n02_03
- Harris, D., Jones, R. T., Shank, R., Nath, R., Fernandez, E., Goldstein, K., & Mendelson, J. (2000). Self-reported marijuana effects and characteristics of 100 San Francisco medical marijuana club members. *Journal of Addictive Diseases*, 19(3), 89–103. http://dx.doi.org/10.1300/J069v19n03_07
- Hazekamp, A., & Heerdink, E. (2013). The prevalence and incidence of medicinal cannabis on prescription in The Netherlands. *European Journal of Clinical Pharmacology*, 69, 1575–1580. <http://dx.doi.org/10.1007/s00228-013-1503-y>
- Hazekamp, A., Mueller-Vahl, K., Ware, M., et al. (2013). The medicinal use of cannabis and cannabinoids; an international cross-sectional survey on methods of intake. *Journal of Psychoactive Drugs*, in press.
- Health Canada. (2011). *Canadian Alcohol and Drug Use Monitoring Survey (CADUMS)*. Retrieved from <http://www.hc-sc.gc.ca/hc-ps/drugs-drogués/stat/2011/summary-sommaire-eng.php>.
- Health Canada. (2012 (December 26)). *Harper government announces new marihuana for medical purposes regulatios: Changes improve public safety maintain patient access*. Retrieved from <http://www.hc-sc.gc.ca/ahc-asc/media/nr-cpf/2012/2012-193-eng.php>.
- Health Canada. (2012). *Marihuana medical access program statistics*. Retrieved from: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/stat/index-eng.php#a1>.
- Holland, J. (2010). *The pot book: A complete guide to cannabis: Its role in medicine, politics, science, and culture*. Toronto: Park Street Press.
- Iverson, L. L. (2008). *The science of marijuana* (2nd ed.). Oxford, UK: Oxford University Press.
- Joy, J., Watson, S., & Benson, J. (2003). *Marijuana and medicine*. Institute of Medicine: National Academy Press.
- Kassam, A., & Patten, S. B. (2006). Major depression, fibromyalgia and labour force participation: A population-based cross-sectional study. *BMC Musculoskeletal Disorders*, 7, 4. <http://dx.doi.org/10.1186/1471-2474-7-4>
- Lucas, P. (2008). Regulating compassion: An overview of Canada's federal medical cannabis policy and practice. *Harm Reduction Journal*, 5, 5. <http://dx.doi.org/10.1186/1477-7517-5-5>
- Lucas, P. (2012). It can't hurt to ask: A patient-centered quality of service assessment of Health Canada's medical cannabis policy and program. *Harm Reduction Journal*, 9(2) <http://dx.doi.org/10.1186/1477-7517-9-2>
- Nakagawa, S. (2004). A farewell to Bonferroni: The problems of low statistical power and publication bias. *Behavioral Ecology*, 15(6), 1044–1045.
- Reiman, A. (2007). Medical cannabis patients: Patient profiles and health care utilization patterns. *Complementary Health Practice Review*, 12, 31–50. <http://dx.doi.org/10.1177/1533210107301834>
- Reinarman, C., Cohen, P. D. A., & Kaal, H. L. (2004). The limited relevance of drug policy: Cannabis in Amsterdam and in San Francisco. *American Journal of Public Health*, 94, 836–842. <http://dx.doi.org/10.2105/AJPH.94.5.836>
- Reinarman, C., Nunberg, H., Lanthier, F., & Heddleston, T. (2011). Who are medical marijuana patients? Population characteristics from nine California assessment clinics. *Journal of Psychoactive Drugs*, 43, 128–135. <http://dx.doi.org/10.1080/02791072.2011.587700>
- Statistics Canada. (2006). *2006 census of population*. Retrieved from <http://www12.statcan.gc.ca/census-recensement/2006/index-eng.cfm>.
- Swift, W., Gates, P., & Dillon, P. (2005). Survey of Australians using cannabis for medical purposes. *Harm Reduction Journal*, 2, 18–27. <http://dx.doi.org/10.1186/1477-7517-2-18>
- Ware, M. A., Adams, H., & Guy, G. W. (2005). The medicinal use of cannabis in the UK: Results of a nationwide survey. *International Journal of Clinical Practice*, 59, 291–295. <http://dx.doi.org/10.1111/j.1368-5031.2005.00271.x>
- Ware, M. A., Rueda, S., Singer, J., & Kilby, D. (2003). Cannabis use by persons living with HIV/AIDS: Patterns and prevalence of use. *Journal of Cannabis Therapeutics*, 3(2), 3–15. http://dx.doi.org/10.1300/J175v03n02_02

This is Exhibit^C..... referred to in the
affidavit of Professor Zachary Walsh
sworn before me, this 28th
day of September 20²³
..... 
A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.



Clinical Practice Guidelines for Cannabis and Cannabinoid-Based Medicines in the Management of Chronic Pain and Co-Occurring Conditions

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Abstract

Background: One in five individuals live with chronic pain globally, which often co-occurs with sleep problems, anxiety, depression, and substance use disorders. Although these conditions are commonly managed with cannabinoid-based medicines (CBM), health care providers report lack of information on the risks, benefits, and appropriate use of CBM for therapeutic purposes.

Aims: We present these clinical practice guidelines to help clinicians and patients navigate appropriate CBM use in the management of chronic pain and co-occurring conditions.

Materials and Methods: We conducted a systematic review of studies investigating the use of CBM for the treatment of chronic pain. Articles were dually reviewed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Clinical recommendations were developed based on available evidence from the review. *Values and preferences* and *practical tips* have also been provided to support clinical application. The GRADE system was used to rate the strength of recommendations and quality of evidence.

Results: From our literature search, 70 articles met inclusion criteria and were utilized in guideline development, including 19 systematic reviews and 51 original research studies. Research typically demonstrates moderate benefit of CBM in chronic pain management. There is also evidence for efficacy of CBM in the management of comorbidities, including sleep problems, anxiety, appetite suppression, and for managing symptoms in some chronic conditions associated with pain including HIV, multiple sclerosis, fibromyalgia, and arthritis.

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Conclusions: All patients considering CBM should be educated on risks and adverse events. Patients and clinicians should work collaboratively to identify appropriate dosing, titration, and administration routes for each individual.

Systematic Review Registration: PROSPERO no. 135886.

Keywords: cannabinoids; cannabinoid-based medicines; cannabis; marijuana; chronic pain; sleep disorders

Introduction

Across the globe, one in five individuals live with chronic pain,¹ and estimates of chronic pain prevalence may be 20–25% in some countries and regions.² Two thirds of individuals report it as moderate to severe.^{3–5} Approximately 50% of these individuals have lived with chronic pain for more than 10 years.³ Chronic pain often co-occurs with insomnia, anxiety, depression, post-traumatic stress disorder (PTSD), and substance use disorders such as opioid and alcohol use disorder.^{6–12} Chronic pain and these co-occurring conditions are also among the most common conditions for which cannabinoid-based medicines (CBM), derived from the cannabis plant, are used therapeutically.^{13–16}

Recently, there has been a proliferation of systematic reviews on CBM and chronic pain and co-occurring conditions. Given new legal regimes globally regarding recreational cannabis and CBM derived from the cannabis plant, health care providers need to be aware of the potential efficacy and harms. Here, we present Clinical Practice Guidelines for the use of Cannabis and CBM in the Management of Chronic Pain and Co-occurring Conditions. These guidelines examine literature focused on cannabis and CBM derived from the cannabis plant rather than synthetic, pharmaceutical-grade cannabinoids in an effort to fill an important knowledge gap.

Materials and Methods

Our previously published protocol¹⁷ outlined the inclusion/exclusion criteria for studies (PICOS breakdown), process for data extraction (using Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] conventions) strategy for data synthesis, assessment of evidence and recommendations (GRADE system), risk of bias assessment, and procedures for data analysis/synthesis. Conclusions relate to availability of evidence, and the evidence available does not support doing this for every cannabinoid and cannabinoid combination.

When we report on adverse effects for specific cannabinoids (i.e., tetrahydrocannabinol [THC] vs. canna-

bidol [CBD] vs. THC/CBD products), the reason is that evidence exists for these specific cannabinoids or combinations. Note that we cannot extrapolate from one cannabinoid to another, nor from a combination product to one cannabinoid, since the evidence for doing so does not exist.

Practical tips were formulated qualitatively based on a discussion of panel members from their cumulative clinical experience, rather than a formal algorithm.

Search strategy and study eligibility

In May 2019, an electronic search was conducted for peer-reviewed articles (2001–2019), in English, in the following electronic databases: Academic Search Complete, Cochrane Database of Systematic Reviews, Evidence Based Medicine Reviews, OVID Medline, PsychINFO, PubMed, CINAHL, and Web of Science. The search strategy was as previously described.¹⁷ Studies focusing exclusively on efficacy of synthetic pharmaceutical cannabinoids (such as nabilone or dronabinol) were excluded.

In addition, studies reporting on results of a single patient ($n = 1$) were also excluded. As nabiximols contain plant-derived cannabinoids, they were included. Complete inclusion and exclusion criteria are listed in Supplementary Table S1 in the protocol.¹⁷ Study types including systematic reviews, meta-analyses, controlled trials, uncontrolled trials, observational studies, and cross-sectional designs were included, whereas systematic reviews and original research articles were summarized separately. Guideline development was primarily based on original research given the heterogeneity of previous systematic reviews.

Study screening and selection

Using the PRISMA conventions,¹⁸ a Data Synthesis Committee determined study eligibility by reading identified abstracts. Each abstract was independently dually reviewed. Full-text screening occurred in cases of uncertainty. Disagreements on inclusion were resolved through a discussion by two reviewers. Full-text screening was also independently dually reviewed.

Reference lists of included studies were searched for potential additions. A PRISMA flowchart outlines this process (Supplementary Appendix SA1).

Data extraction

Data were extracted independently using a standardized Data Extraction Form to create evidence tables. For each study, data were extracted related to study identification (author, year published, number and location of centres, funding, journal name), number of participants, form of CBM, dose and route, study design and setting, inclusion/exclusion criteria, aggregate demographic (age, sex, type of pain, co-occurring conditions) and clinical characteristics (co-morbidities), outcome measures, and results. We also identified types and frequencies of adverse events. Final evaluation of study quality (very low, low, moderate or high) included considerations of limitations, inconsistencies, indirectness, and imprecision.

Data synthesis

Data were extracted using standard data extraction tools. There is significant variability in cannabis research due to heterogeneity of sample populations, study types and lengths, and CBM interventions (e.g., CBM type, dosing, administration route, etc.). Patterns related to efficacy, safety, and tolerability were explored through narrative synthesis.^{19,20} Data were compiled based on availability of quality evidence. Consistent findings and discrepancies were discussed. Evidence for CBM in the management of chronic pain and co-occurring conditions related to efficacy, tolerability, safety, indications, dosing, drug interactions, adverse events, negative effects, and contraindications.

Assessment of evidence and recommendations

Clinical recommendations and indications were developed and presented in relation to CBM use for chronic pain and comorbidities. The Task Force used the GRADE system to rate quality of evidence and strength of recommendations.^{21–26} *Values and preferences* and *practical tips* have also been provided to support clinical application.

Strength of recommendations

Strength of recommendations was specified as strong or weak based on risk and benefit of CBM in the specific condition. Patient values and preferences, magnitude of effect, and confidence in the evidence were considered. A recommendation was deemed to be

strong if the committee considered the benefit to clearly outweigh the risk for most individuals. All other recommendations were specified as weak, indicating a need to consider individual clinical circumstances, values, and preferences.

Risk-of-bias assessment

Two reviewers (M.S.P. and P.W.) assessed potential bias and discrepancies were adjudicated by the Data Synthesis Committee (C.C., Z.W., S.M.). The National Institutes of Health risk-of-bias assessment tools²⁷ were used to assess study quality. These tools were developed specifically for different study design types, and therefore heterogeneity of the designs of included studies will not affect ability to assess quality appropriately. Study bias was graded as either “good quality” (score of 3), implying low risk of bias, “fair quality” (score of 2) implying some risk of bias, or “poor quality” (score of 1), implying high risk of bias. Assessments of bias were performed at the overall study level.

Results

We identified 4989 records following the removal of duplicates (Supplementary Appendix SA1). Following abstract review, 4824 records were excluded, resulting in full-text review of 165 articles. Reasons for exclusion are presented in Supplementary Appendix SA1. Seventy studies were included in the final review, including 19 systematic reviews (Supplementary Appendix SA2) and 51 original research studies (Supplementary Appendix SA3). To avoid redundancy, systematic reviews were considered independent of primary literature.

Characteristics of systematic reviews

Details of the 19 included systematic reviews are presented in Supplementary Appendix SA2, along with each review’s quality rating as an assessment of risk of bias. Most reviews were rated as either *good*, or *fair*, representing low or moderate risk of bias, respectively. Included reviews were published between 2007 and 2018, with 16 of 19 reviews published in 2015 or more recently. The majority of reviews (12) included only randomized controlled trials (RCTs).

Three reviews included only systematic reviews,^{28,29,30} three contained primary research,^{31–33} and one included other systematic reviews, in addition to primary research.³⁴ People with chronic pain were the most commonly studied population (14). One review focused on rheumatic disease-associated pain,³⁵ one included studies of multiple sclerosis (MS) or comparable

neuropathic pain,³⁶ one included systematic reviews that analyzed cannabinoids for pain, spasticity, or nausea and vomiting,²⁹ and two included people using medical cannabinoids regardless of indication.^{32,37}

Most reviews explored both pharmaceutical synthetic and plant-based cannabinoids (15/19). Three reviews focused exclusively on plant-based cannabis and plant-derived cannabinoid extracts.^{34,38,39} Park and Wu focused exclusively on non-synthetic cannabis, as their review solely included people using medical cannabis. Reviews that focused exclusively on pharmaceutical synthetic cannabinoids were excluded.

In terms of efficacy for chronic pain reduction, most reviews (14/19) reported that cannabinoids provided analgesia in at least some contexts. Nugent et al found non-synthetic cannabinoids beneficial for neuropathic pain, but they found insufficient evidence in other types of pain. In addition, Stockings et al reported nabiximols to be effective for MS-related pain; however, generally there was insufficient evidence for cannabinoids to be used as a pain treatment. Five reviews found inadequate evidence to support cannabinoids as an effective pain treatment.^{28,29–31,35}

Of the eight reviews that obtained a “good” quality rating, representing the lowest risk of bias, seven found cannabinoids to be beneficial for pain relief. However, in some instances, the analgesic effect of cannabinoids was described as “moderate”⁴⁰ or “small.”⁴¹

Most reviews analyzed prevalence of adverse events associated with cannabinoids. Although common, adverse events were typically mild to moderate in severity.^{34,39–42} Adverse events were similar between reviews and included drowsiness, dizziness, and dry mouth. Aviram and Samuelly-Leichtag suggested that adverse events could not entirely be attributed to cannabinoids as “the participating patients in the included trials had pre-existing diagnoses and in many of the trials, they used concomitant medications.”⁴³

A few reviews included analysis of pain comorbidities. Of the reviews that studied sleep and sleep problems within the context of chronic pain, analyses fairly consistently supported that cannabinoids provided at least partial benefit.^{32,33,35,37,40–42,44,45} Findings were more heterogeneous regarding the efficacy of cannabinoids for mood disorders and related issues. Four reviews reported that cannabinoids improved anxiety in pain populations.^{35,37,41,44}

Stockings et al did not find any significant difference between cannabinoid and comparator groups in overall emotional functioning or depressive or anxiety symp-

toms. Whiting et al reported significant improvement in anxiety with cannabinoids over placebo; however, in studies where anxiety was studied as a secondary outcome, they found no significant difference. Martin-Sanchez et al analyzed mood disturbances only within the context of adverse events but found euphoria to be a common occurrence with a number needed to harm (NNH) of 8, and dysphoria to be less common with an NNH of 29.

Finally, in a review focused on people living with chronic neuropathic pain, Mucke et al reported cannabinoids to be more efficacious than placebo for treating psychological distress.

Evidence summaries and clinical guideline recommendations

1. CBM use for people with chronic pain

Forty-seven studies relevant to pain management were reviewed, including 22 RCT,^{46–67} 11 pre-post studies or uncontrolled trials,^{68–78} 11 cross-sectional or observational cohort studies,^{79–89} and 3 case series.^{90–92} Most studies (38/47) reported at least moderate benefits of CBM for chronic pain,^{46–48,50,51,54,55,57,59–70,73–80,82–84,86–92} seven were inconclusive or found insufficient evidence,^{49,53,56,58,71,72,85} and two reported mixed results.^{52,81}

Associated improvements in secondary outcomes, including QoL, functionality, and mood, have also been observed with the use of medical cannabis in addition to reductions in pain severity, intensity, and interference. For details of the individual studies, see Appendix A in Supplementary Data.

Recommendations. 1. We recommend the use of CBM as monotherapy, replacement, or adjunct treatment, in people living with chronic pain, for the management of chronic pain including central and/or peripheral neuropathic pain to improve pain outcomes.

Strong Recommendation, Moderate-Quality Evidence

2. We recommend the use of CBM as monotherapy, replacement or adjunct treatment, in people living with chronic pain, for mobility in those not achieving adequate response to other modalities.

Weak Recommendation, Low-Quality Evidence

Values and preferences. The recommendations place high value on the improvement in chronic pain, functionality, and secondary outcomes, including time to sleep, quality of sleep, anxiety, and depression, in those living with chronic pain and using CBM

compared with placebo. The recommendations also outweigh the risks of non-serious adverse events with CBM (dizziness, disturbance in attention, somnolence, dry mouth, nausea, diarrhea) as compared with adverse events from standard analgesia (opioids and serotonin-norepinephrine reuptake inhibitors [SNRIs] or opioids monotherapy), including constipation, loss of appetite, unclear mentation, reduced affect, hemorrhoids, and substance use disorder.

Practical tip. A wide variety of formulations and routes including smoking, vaping, oral capsule, oral oil, and oromucosal sprays showed benefits in chronic pain, mood disorders, mobility, and sleep. Adverse events due to combustion, and exposure to second-hand smoke, make smoked CBM less favorable. The inhalation route of CBM is restricted to the vaporization of dried flower over combustion for the management of breakthrough pain due to rapid onset and shorter duration of action.

Oral products, as a route of administration may be preferred for the longer duration of action (6–8 h) compared with inhaled cannabis, particularly in the evening (due to somnolence). This will allow for greater symptom control in patients who experience chronic persistent daily symptoms and/or disease. Oral oil and capsule formulations can be easier to dose accurately (mg) and provide consistent and reproducible dosing.

Practical tip. The strongest evidence for reduction of chronic pain symptoms is for THC formulations, not CBD. The majority of adverse events are associated with THC. Adverse Events due to CBM are mild and may be better tolerated than other centrally acting prescription medications. Patients report that adverse effects generally subside within 48 h or when the titration phase is stopped. The best way to reduce the potential adverse effects with THC is with safe, low-dose initiation and titration (Fig. 2). In addition, a CBD dominant product can be used in combination with THC to attenuate side effects. The initiation of CBD during daytime with the addition of THC at bedtime can also further mitigate these effects.

2. CBM use for people with HIV and chronic pain

Three studies examined CBM to treat pain in people with HIV, including two RCTs^{46,51} and one cross-sectional study.⁸⁸ All three studies reported significant improvements in HIV-related pain management asso-

ciated with CBM use. For details of the individual studies, see Appendix B in Supplementary Data.

Recommendations. 1. We recommend the use of CBM for the management of muscular and neuropathic pain in people living with HIV who are not achieving adequate response, or those experiencing adverse effects to other treatment modalities.

Strong Recommendation, Moderate-Quality Evidence

2. We recommend CBM use for the management of HIV-related symptoms, including nausea, anxiety, depression, lack of appetite, and weight loss in people living with HIV. CBM use is for symptom management only and should not replace the use of antiretroviral therapies.

Strong Recommendation, Low-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of neuropathic and muscular pain relief in people with HIV over the risks of adverse events of a mainly non-serious nature such as dizziness, disturbance in attention, balance disorder, somnolence, dry mouth, nausea, diarrhea, fatigue, or confused state and those of a more serious nature such as pulmonary and cardiovascular effects of inhaled substances.

Practical tip. A wide variation is seen in the dose and administration routes of cannabinoids used to optimize the treatment effect and adverse event ratio. A slow dose titration, initiated with CBD-predominant cannabinoids, should be used to individualize treatment (Fig. 2).

Practical tip. Although benefit was observed in HIV nerve and muscle pain mostly with smoked formulations, oils and capsules have been shown to have the strongest evidence in MS. Oils and capsules provide the greatest consistency for dosage and titration and are not associated with potential adverse events associated with inhalation of CBM.

3. CBM use for people living with multiple sclerosis and chronic pain

Twelve studies examined CBM for pain in people with MS, including nine RCTs,^{50,52,53,55,58,65,66,67,77} two open-label studies,^{77,78} and one cross-sectional study.⁸² Seven studies involved nabiximols,^{49,52,53,55,58,77,78} three involved extracts delivered through capsule,^{65–67} and two involved whole plant cannabis.^{50,82} Study length ranged from 3 days to 2 years. Most studies (9/12) reported improvements in pain associated with CBM

use, including both studies involving whole plant cannabis and all three involving extracts delivered through capsules.

The majority of studies were limited by small numbers of participants, short duration of treatment, and some crossover and blinding deficiencies. For details of the individual studies, see Appendix C in Supplementary Data.

Recommendations. 1. We recommend the use of CBM, as adjunct treatment, for pain management in people with MS not achieving adequate response to other modalities.

Strong Recommendation, Moderate-Quality Evidence

2. We recommend the use of CBM, as adjunct treatment, for the management of muscle spasm in people living with MS in those not achieving adequate response to other modalities.

Strong Recommendation, Moderate-Quality Evidence

3. We recommend the use of CBM, as adjunct treatment, for the management of sleep disorder in people living with MS in those not achieving adequate response to other modalities.

Strong Recommendation, Low-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of pain, spasticity, and sleep disturbance relief seen in people with MS over the risks of adverse events, of a mainly non-serious nature, including dizziness, disturbance in attention, balance disorder, somnolence, dry mouth, nausea, diarrhea, fatigue, or confused state.

Practical tip. A wide dose variation of cannabinoids was used in studies involving MS patients. Total daily THC oral dose of 10–15 mg, as a divided dose twice daily, was most commonly used. A slow dose titration should be used to individualize treatment (Fig. 2).

Practical tip. Although benefit was observed in pain, spasticity, and sleep with oral oil, capsule, smoked and oromucosal formulations, the strongest evidence is for the use of oils and capsules. These formulations also provide the greatest consistency for dosage and titration and are not associated with potential adverse events associated with inhalation of CBM.

4. CBM use for people living with an arthritic condition experiencing chronic pain
One RCT,⁴⁸ one pre-post survey,⁷⁰ and one published abstract⁹³ have been identified in the literature search.

Both the RCT and published abstract demonstrated improvement in pain in patients with an arthritic condition. For details of the individual studies, see Appendix D in Supplementary Data.

Recommendation. 1. We recommend the use of CBM, as adjunct treatment, for the management of chronic pain in people living with arthritic conditions in those not achieving adequate response to other modalities.

Strong Recommendation, Low-Quality Evidence

Values and preferences. The recommendation places high value on the benefit of improvement in pain, sleep, and other co-morbid conditions over the risks of adverse events of a mainly non-serious nature such as dizziness, disturbance in attention, balance disorder, somnolence, dry mouth, nausea, diarrhea, fatigue, or confused state.

Practical tip. Best evidence of benefit is in participants with rheumatoid arthritis for improvement in pain, sleep, other co-morbid conditions, and markers of inflammation. A balanced THC/CBD oromucosal product titrated to ~15 mg of each component may be tried. If an oral formulation is used, a slow titration of THC as shown in Figure 2 should be employed.

Practical tip. As dizziness and falls have been identified as potential adverse events associated with CBM use, a clear understanding of risks should be achieved before CBM initiation, especially for populations with an increased risk of bone loss/osteoporosis. Consider a lower THC starting dose, slower titration period, and consistent monitoring.

Practical tip. A single abstract publication has suggested benefit from topical CBD 125 mg bid for localized pain management of knee osteoarthritis. This format can be applied to the affected joints as a cream, oil, or spray. This approach can be expected to be associated with a very low risk of any adverse events. More research is needed regarding the efficacy and safety of topical CBM.

5. CBM use for people living with fibromyalgia and chronic pain

There was a total of six studies that included participants with fibromyalgia and pain. Four of these studies included people with fibromyalgia as part of the study participants but the authors did not produce a separate analysis for pain management in fibromyalgia and

therefore these studies are not heavily considered in this section.^{72,76,91,92} Each of these studies found improvements in pain across their wider study sample. In an open-label study, two thirds of study participants living with fibromyalgia responded well to sublingual THC treatment.⁷² For details of the individual studies, see Appendix E in Supplementary Data.

Recommendation. 1. We recommend the use of CBM, as adjunct treatment, for management of back pain, fibromyalgia pain, or other chronic pain in people with fibromyalgia who are not achieving an adequate response to standard analgesics.

Strong Recommendation, Low-Quality Evidence

Values and preferences. This recommendation places high value on the improvement in back pain, chronic pain, fibromyalgia pain, and improvement in function, quality of life (QOL), and secondary outcomes, including anxiety, among patients living with fibromyalgia from CBM use, over the low risk of non-serious adverse events (reddening of the eyes, increased appetite, and sore throat) as compared with adverse events with standard analgesics (constipation, loss of appetite, lack of mental clarity, reduced affect, and hemorrhoids).

Practical tip. Fibromyalgia is a heterogeneous complex pain syndrome, which frequently occurs with other pain syndromes and symptom clusters. This needs to be considered when extrapolating this study information to other patients living with fibromyalgia.

Practical tip. In clinical practice, SNRI are used off-label as a multimodal treatment for symptoms such as insomnia, depression, and anxiety in patients suffering from fibromyalgia; likewise, CBM can treat these symptom clusters.

Practical tip. All patients using CBM should be educated on proper vaporization (to avoid harms of combustion/smoking) and/or cannabis oil/capsule dosing and titration regimens. To limit adverse effects while still achieving pain outcomes, THC dosing should be started low and titrated slowly to an individual response. For elderly and frail patients, consider a lower THC starting dose, slower titration period, and consistent monitoring.

6. CBM use for people experiencing chronic headache and migraine

Four included studies specifically measured associations between CBM and chronic headache or mi-

graine.^{70,88,94,95} One study was a conference abstract and included as gray literature.⁹⁴ Of these four studies, two utilized pre/post designs,^{70,94} and two were cross-sectional.^{88,95} Each study reported at least some improvement from cannabis in participants experiencing headaches. For details of the individual studies, see Appendix F in Supplementary Data.

Recommendation. 1. We recommend the use of CBM, as an adjunct treatment, for the management of chronic migraine or chronic headache, in those not achieving adequate response to other modalities.

Weak Recommendation, Low-Quality evidence

Values and preferences. The recommendations place high value on the benefit of migraine and headache relief over the risk of adverse events, which are mainly non-serious in nature and include somnolence and dizziness.

Practical tip. Some people also experience headache due to cannabis, therefore it will be important to assess the individual treatment response. Dosage form will be important to consider if CBM is used for prophylaxis versus treatment of migraine or headache, given different timing of onset.

Practical tip. To limit exposure to adverse events, individuals should *start low, go slow*, and follow a structured initiation and titration plan (Fig. 2). Patients and physicians should work collaboratively to identify appropriate administration route(s) that meet the needs of the individual.

7. CBM use for people living with chronic pain and nausea

Five studies analyzed participant perceptions of cannabis as a potential treatment for nausea as a comorbidity of pain.^{79,85,88,91,92} Each study involved whole plant cannabis in inhaled or oral formats, with patients reporting moderate relief. Although these five studies found improvements in nausea with cannabis use, other studies found nausea to be an adverse event associated with cannabis use among some participants.^{46–50,54,57–59,71,72,74,77,78}

These studies were limited by study design (case series or cross-sectional surveys), small numbers of patients, unknown duration or dosing of cannabis, and the possibility of selection and recall bias. It is also unclear which cannabis formulation or route of administration is optimal (smoked vs. oral, THC vs. CBD vs.

THC/CBD products) for nausea. For details of the individual studies, see Appendix G in Supplementary Data.

Recommendation. 1. We recommend considering the use of CBM to reduce nausea in people living with chronic pain as monotherapy or adjunct treatment for those not achieving adequate response to other treatment modalities.

Weak Recommendation, Low-Quality Evidence

Values and preferences. This recommendation does not refer to the use of CBM in cancer-related pain or emetogenic therapy, and places high value on the benefit of CBM for nausea relief, over the risk of adverse events, which are mainly non-serious in nature.

Practical tip. All published data on nausea benefit in chronic pain have come from survey or cross-sectional studies. As such, no practical tips on cannabis type, mode of administration, or concentration of THC or CBD can be made.

8. CBM use for people with sleep problems and symptoms of sleep deprivation experiencing chronic pain

Sleep issues are often a target symptom for cannabis use and 25 of the studies assessed impacts of CBMs on sleep, including 16 RCTs,^{47–49,52–55,57–60,65–67,74,75} four cross-sectional survey studies,^{79,80,82,87} three pre-post style studies,^{70,73,85} and two case series studies.^{91,92} Of these studies, 10 included consumption of whole plant cannabis by participants,^{60,70,73,79,80,82,85,87,91,92} 12 involved cannabis extracts (CEs) consumed by oromucosal spray,^{47–49,52–55,57–59,74,75} and 3 involved participants treated with cannabis extract capsules.^{65–67} Almost all studies found benefit for sleep in some or most participants. For details of the individual studies, see Appendix H in Supplementary Data.

Recommendation. 1. We recommend the use of CBM as monotherapy, replacement or adjunct treatment, to improve sleep and symptoms of sleep deprivation in people living with chronic pain not responsive to, or intolerant of, other modalities or pharmacologic treatment.

Strong Recommendation, Moderate-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of CBM for disturbances in sleep and poor sleep quality. Adverse events such as somnolence, drowsiness, and sleepiness rarely caused

withdrawal from studies and point to the potential benefits for patients with chronic pain states.

Practical tip. Many studies used CBM in the form of standardized-dose CE (nabiximols and others), which allowed for easier titration and effective dose-finding. The presence of products, including CBD, may reduce the incidence of psychiatric or euphoric effects. Oral formulations may also be considered and are not associated with potential adverse events associated with inhalation of CBM.

Practical tip. Sleep disturbances in patients with MS showed the most improvement with CBM used for pain and/or spasticity. This is a group who should be routinely assessed for the suitability of treatment with CBM.

Practical tip. To limit exposure to adverse events, individuals should *start low, go slow*, and follow a structured initiation and titration plan (Fig. 2).

9. CBM use for people living with chronic pain experiencing appetite loss

Seven studies assessed CBM use on appetite in participants experiencing chronic pain, including two RCTs,^{59,63} two cross-sectional studies,^{79,88} two case series,^{91,92} and one pre-post study.⁷⁰ The RCT assessed did not demonstrate a significant difference between CBM and placebo. The two case series and one cross-sectional study reported some improvement in appetite, whereas another case series did not find significant benefit. For details of the individual studies, see Appendix I in Supplementary Data.

Recommendation. 1. We recommend the use of THC-dominant cannabis for people with problematic loss of appetite in association with chronic pain, over no treatment.

Strong Recommendation, Low-Quality evidence

Values and preferences. The recommendation places high value on the benefit of improved appetite, and presumably nutrition, over the risks of adverse events of a mainly non-serious nature such as dizziness, disturbance in attention, balance disorder, somnolence, dry mouth, nausea, diarrhea, fatigue, or confused state.

Practical tip. All published data on appetite improvement in chronic pain have been associated with the use of THC dominant products. A single RCT failed to demonstrate benefit from CBD; however, this cannabinoid

may provide other benefits, including a reduction in pain and anxiety.

Practical tip. One cross-sectional study noted an increased risk of problematic cannabinoid use in patients using CBM for appetite improvement. All patients using CBM should be monitored for cannabis use disorder. The Cannabis Use Identification Test- Revised may be used for this purpose. To limit exposure to adverse events, individuals should follow a structured initiation and titration plan (Fig. 2). Patients and physicians should work collaboratively to identify appropriate administration route(s) that meet individual needs.

10. CBM use for people with chronic pain experiencing PTSD

Two studies included analysis of cannabis as a treatment for PTSD symptoms.^{70,79} One study evaluating cannabis in patients with PTSD as the primary condition rated the mean helpfulness of CBM in the moderately helpful range.⁷⁹ Among the larger sample ($n = 186$), higher levels of traumatic intrusions were associated with higher perceived helpfulness of cannabis.⁷⁹ The second study found that the numbers of participants with PTSD reporting severe pain at baseline dropped from 56% at baseline to 11% at 4 months of CBM use. Improvements were also reported in ability to cope with pain and overall QOL, mood, sleep, and concentration.⁷⁰ For details of the individual studies, see Appendix J in Supplementary Data.

Recommendation. 1. We recommend the use of CBM to improve PTSD symptoms in people living with chronic pain not responsive to, or intolerant of, non-pharmacologic treatment.

Weak Recommendation, Low-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of CBM for pain, intrusion symptoms, sleep disturbance, and improved mood and QOL seen in people living with PTSD over the risks of adverse events of a mainly non-serious nature such as dry mouth, disturbance in attention and memory, as well as the potential for the development of non-medical use.

Practical tip. The single study that reported dose suggested that 1–1.5 g/day of herbal cannabis was typical. However, other modes of administration were not discussed but might nonetheless be advantageous; oils

and capsules provide the greatest consistency for dosage and titration, are not associated with potential adverse events associated with inhalation of CBM, and may also offer advantages in the context of sleep disturbance and nightmares that are prominent among some individuals with PTSD.

11. CBM use for people living with chronic pain experiencing anxiety

Eight studies within this review examined the treatment of anxiety with CBM in people living with chronic pain.^{55,61,70,76,96–99} Although these studies utilized a variety of CBM approaches, most evidence—including the relatively higher quality studies—reported anxiolytic effects of cannabis. For details of the individual studies, see Appendix K in Supplementary Data.

Recommendation. 1. We recommend the use of CBM as adjunct therapy to improve symptoms of anxiety in people living with chronic pain not responsive to, or intolerant of, non-pharmacologic treatment.

Strong Recommendation, Moderate-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of CBM for anxiety symptoms over the risks of adverse events of a mainly non-serious nature such as dry mouth, disturbance in attention and memory, as well as the potential for acute transient increases in anxiety and panic.

Practical tip. The only RCT to compare doses of herbal cannabis suggested that chemovars (strains) with 9% THC—which would be generally considered a moderate to low strength herbal cannabis—are more effective than herbal cannabis with low to very low levels of THC, regardless of CBD content. To limit exposure to adverse events, individuals should follow a structured initiation and titration plan (Fig. 2).

Practical tip. Other modes of administration might also be advantageous; specifically, orally ingested CBMs provide the greatest consistency for dosage and titration, are not associated with potential adverse events associated with inhalation of CBM, and may also offer advantages in the context of sleep disturbance that may be prominent among some individuals with problematic anxiety.

Practical tip. It is well recognized that THC has the potential to trigger acute transient increases in anxiety and panic. Individuals should be warned of this adverse effect and closely followed for it.

12. CBM use for people living with chronic pain experiencing depression

Findings for depressive symptom outcomes appeared to be contingent on the types of CBMs used, with herbal cannabis appearing to be more effective than extracts. An RCT of smoked cannabis found that it improved depressive symptoms significantly with a medium-sized effect over placebo.⁶⁰ Three cross-sectional studies also report antidepressant effects of CBM.^{82,97,98} Studies involving the use of cannabis extracts are generally less positive regarding the benefits of CBM for treating depression in people with chronic pain. In contrast to these positive results, three RCTs found no significant difference between nabiximols and placebo in depression scores.^{53,55,58} For details of the individual studies, see Appendix L in Supplementary Data.

Recommendation. 1. We recommend the use of CBM as adjunct therapy to improve symptoms of depression in people living with chronic pain experiencing unsatisfactory results from standard treatment.

Weak Recommendation, Moderate-Quality Evidence

Values and preferences. The recommendations place high value on the benefit of CBM for depressive symptoms over the risks of adverse events of a mainly non-serious nature such as dry mouth, disorientation, and disturbance in attention and memory. The CBM should not take the place of other anti-depressant treatments, including pharmacological and non-pharmacological treatments, such as psychotherapeutic intervention.

Practical tip. The only RCT to compare doses of herbal cannabis suggested that chemovars with 9% THC—which would be generally considered a moderate to low strength herbal cannabis—are more effective than herbal cannabis with low to very low levels of THC. To limit exposure to adverse events, individuals should follow a structured initiation and titration plan (Fig. 2).

Practical tip. Other modes of administration might also be advantageous; specifically, orally ingested CBMs provide the greatest consistency for dosage and titration, are not associated with potential adverse events associated with inhalation of CBM, and may also offer advantages in the context of sleep disturbance that may be prominent among some individuals with depression.

13. Adjunctive CBM use for people living with chronic pain experiencing unsatisfactory analgesia from opioid treatment

Four studies specifically addressed the efficacy of combined opioid analgesics with cannabis therapy for chronic pain. One study evaluated the addition of vaporized cannabis to patients taking sustained-release opioids for a variety of chronic pain conditions.⁶⁸ These studies demonstrated a reduction in pain with the addition of CBM to their opioid regimen. Several additional studies found improvements in chronic pain associated with CBM use within samples that included participants concurrently using opioids to treat pain.^{52,54,60,100,101} For details of the individual studies, see Appendix M in Supplementary Data.

Recommendation. 1. We recommend the use of CBM, as adjunctive treatment to opioids, for the management of chronic pain in those experiencing unsatisfactory analgesia from opioid treatment.

Strong Recommendation, Moderate-Quality Evidence

Values and preferences. The recommendations place high value on the improvement in chronic pain, fibromyalgia pain, functionality, spasms, and secondary outcomes of depression and anxiety, in those with chronic pain using CBM adjunctly over the low risk of non-serious adverse events (fatigue, sedation, impairment in concentration, reduced salivation) as compared with adverse events with standard opioid analgesic therapy (constipation, loss of appetite, feeling of reduced mental acuity and flat affect, hemorrhoids, dependency, respiratory depression).

Practical tip. Evidence included in this review found efficacy of inhaled CBM as adjunct treatment for chronic pain. Inhalation as an administration route is advantageous for managing break-through pain due to rapid onset and shorter duration of action. Other routes of administration, including oils and capsules, may be preferred due to dosage consistency and lack of adverse events associated with inhalation, though further research with these routes is needed. Pain management can be individualized above baseline and can be managed on demand and titrated to desired effect.

Practical tip. Cannabis is rarely used as a first-line agent. It is important to assess and document the response to currently approved medications. This includes medication name, dose, duration, response, and tolerability. Some physicians will use cannabis in conditions

where other treatment options have failed or are not tolerated.

Practical tip. Concomitant analgesics can be tapered or discontinued once a stable CBM dose is established. This may lead to a reduction in polypharmacy, side effects, drug interactions, as well as an improvement in adherence and cost saving.

Practical tip. As there was no change in plasma opioid levels after exposure to cannabis, improved analgesic response in patients using cannabis and opioids is likely due to synergy or additive effect. More research is required especially regarding whether cannabis should be considered as a treatment option before opioid initiation based on the lower risk of adverse effects versus opioids.

Practical tip. Long-term pain control was observed through a reduction in pain scores. Tolerance to adverse effects occurs within 48 h of a THC dose increase; however, tolerance to benefits did not develop over time. Starting at a low dose and gradually titrating to the lowest effective dose without adverse effects is suggested (Fig. 2).

14. CBM use and opioid sparing for people using opioids as treatment for chronic pain

Opioid sparing, or the reduction of opioid use, resulting from the use of CBM for pain management was the primary outcome in one study⁸⁶ and a secondary outcome in six studies.^{69,73,81,84,87,91}

Three studies found positive associations between medical cannabis use and opioid sparing.^{69,73,102} Two other studies reported that the majority of participants reduced their routine pain medications by 60–70%; however, the extent to which opioid medications were specifically reduced was unclear.^{87,99} For details of the individual studies, see Appendix N in Supplementary Data.

Recommendations. 1. We recommend the use of CBM as adjunct treatment among people using moderate/high doses of opioids (> 50 morphine equivalent) for the management of chronic pain and/or to increase opioid sparing.

Strong Recommendation, Moderate-Quality Evidence

2. We recommend the use of CBM as adjunct treatment for chronic pain among people using any dose of opioids who are not reaching chronic pain goals, are

experiencing opioid-related adverse events, or display risk factors for opioid-related harm.

Strong Recommendation, Low-Quality Evidence

Values and preferences. The recommendations place high value on the reduction in the reliance on opioids with secondary outcomes improvements, including sleep, anxiety, and mood, in those living with chronic pain and using CBM as adjunct/concurrent to opioids over the low risk of non-serious adverse events (dry mouth, dizziness, increased appetite, sedation, concentration difficulties) as compared with adverse events with opioids/standard of care (constipation, loss of appetite, feeling of reduced mental acuity and flat affect, hemorrhoids, dependency, respiratory depression).

Practical tip. There is a physiologic rationale for co-administration of cannabis and opioids, which prevents opioid-tolerance and the need for dose escalation. In addition, cannabis can treat the symptoms of opioid withdrawal, reduce or replace opioids. Thus, cannabis is safer than opioids and makes opioid consumption safer. More research is required in this area.

Practical tip. Clinicians should re-evaluate any patient on > 50 mg morphine equivalent dose (MED) as their risk of fatal overdose is doubled compared to 20 mg MED; the risk increases 10-fold with > 90 mg MED. Both the United States and Canadian opioid guidelines advise clinicians to carefully reassess risk-benefit ratio when > 50 mg MED and to avoid > 90 mg MED as there is low evidence for improvements in pain, but a significant increase in the risk of harm.

Practical tip. Individuals should keep a daily log, including dosing and monitoring for efficacy, effects on mood and function, and possible side effects. This will encourage individuals to slowly titrate cannabis to symptom control, while minimizing adverse events. Once individuals using medical cannabis are stabilized, generally they do not require dose escalation over time.

Practical tip. Health care providers are encouraged to implement standardized self-administered questionnaires such as Patient Health Questionnaire-9, General Anxiety Disorder-7, or Brief Pain Inventory starting with the initial intake, and to continue in all subsequent follow ups to reassess risk benefit.

A Suggested Approach for Adjunct Cannabinoid Use for Opioid Sparing. Adapted from Sihota et al¹⁰³ is shown in Figure 1.

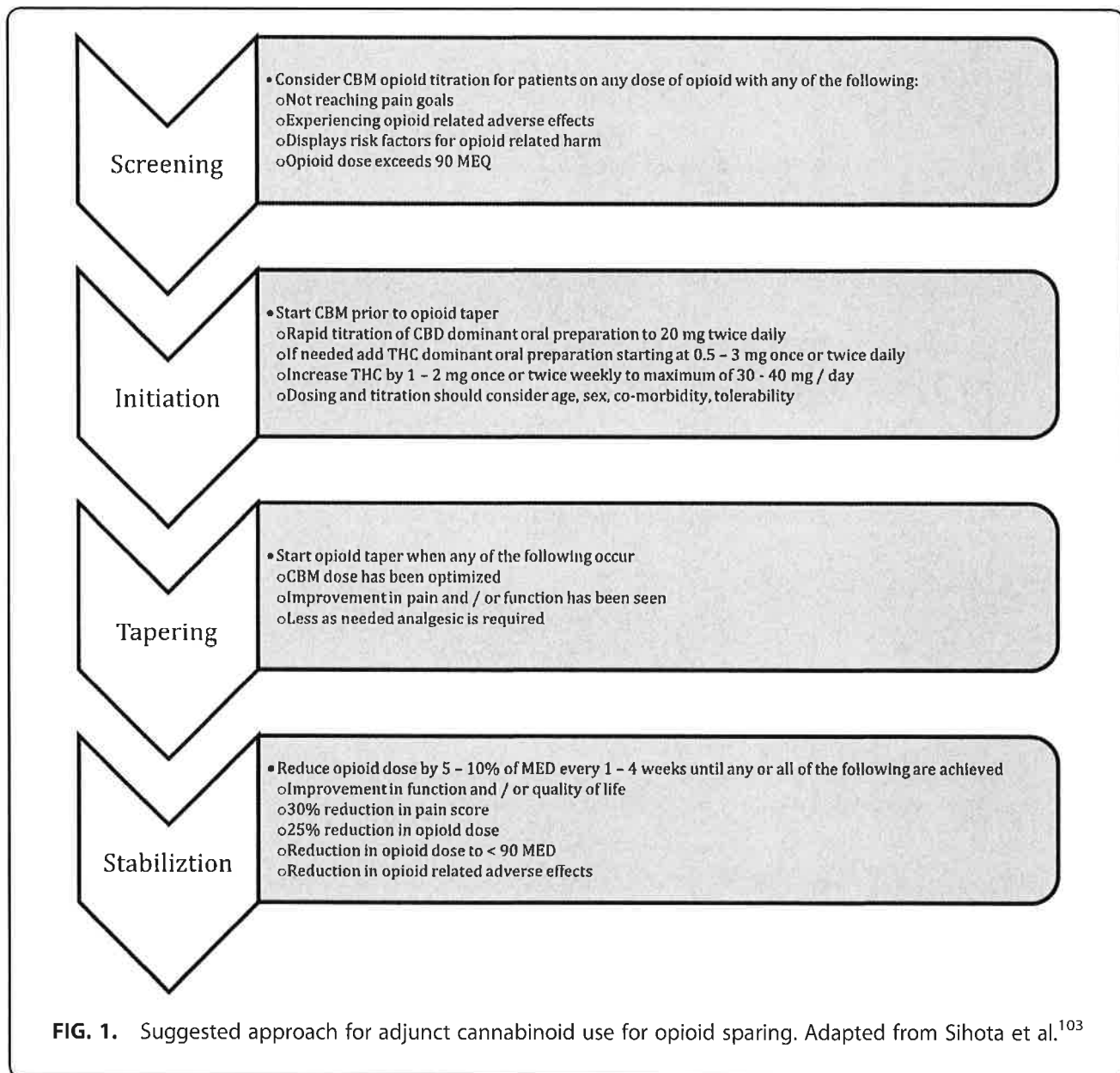


FIG. 1. Suggested approach for adjunct cannabinoid use for opioid sparing. Adapted from Sihota et al.¹⁰³

Additional Practical Considerations

Drug interactions

Both THC and CBD are predominantly metabolized, by the liver, through the action of the cytochrome P450 system.^{104,105} A paucity of clinical studies are available regarding the effect of cannabinoids on this enzyme system, but *in vitro* studies suggest that THC inhibits CYP3A4, CYP3A5, CYP2C9, and CYP2C19, whereas CBD inhibits CYP2C19, CYP3A4, and CYP3A5. Due to the weak inhibitory effect of these cannabinoids, higher concentrations than those seen

clinically are likely to be required for clinical inhibitory effect.¹⁰⁶

This, however, may be of concern when cannabinoids are co-administered with drugs having a narrow therapeutic window and also metabolized by these enzymes, such as direct acting oral anticoagulants metabolized through CYP3A4^{107,108} and clopidogrel requiring conversion to its active metabolite by CYP2C19.¹⁰⁹ Significantly elevated levels of the antiepileptic clobazam and its metabolite, n-desmethyloclobazam, have been observed when co-administered with very high doses

of CBD, likely due to co-metabolism through CYP2C19 and CYP3A4.¹¹⁰

Preclinical studies have reported that cannabinoids may also bind membrane transporters including breast cancer resistance protein¹¹¹ and P-gp,^{112,113} which can, theoretically, impact the effect of other medications. A comprehensive overview of the pharmacokinetic interactions of cannabinoids has been reported by Alsherbiny and Li.¹¹⁴ Pharmacodynamic interactions also need to be considered with CBM, particularly THC, administration. Additive effects can occur when cannabinoids are combined with sympathomimetics (e.g., tachycardia, hypertension), central nervous system depressants such as alcohol and opioids (e.g., drowsiness, ataxia), and anticholinergics (e.g., tachycardia, confusion).¹¹⁵

Adverse effects

- A concern from patients and clinicians are the adverse effects associated with cannabis use. The adverse effects that are the most commonly associated with cannabis are related to THC-dose and the route of administration.¹¹⁶ The THC-related adverse effects include dizziness, cognitive impairment, dry mouth, tachycardia, anxiety, drowsiness, and fatigue.¹¹⁶ There is evidence to suggest a positive association between cannabis use and development of psychosis, in people susceptible to psychotic disorders.^{117–119} Although no definitive causal effects have been established, there are case reports of stroke, acute coronary syndrome, and cardiac arrhythmias associated with use of cannabis.^{120,121} Maternal exposure to cannabis can adversely affect conception and/or maintenance of pregnancy.^{122–124} Significant decline in sperm count, concentration, and motility, as well as an increase in abnormal sperm morphology have been reported.

Smoking cannabis is associated with respiratory adverse effects such as cough, an increase in phlegm, and bronchitis.¹¹⁶ Long-term use is associated with risk of cannabis use disorder, hyperemesis syndrome, as well as withdrawal symptoms including insomnia, anxiety, depression, and tremulousness.^{125,126}

Adverse effects can be mitigated when initiating CBM through low-dose initiation, slow titration and avoiding smoked cannabis.¹¹⁶ In people experiencing adverse effects, clinicians can consider adjustment in the strain (chemovar) with higher CBD and lower THC, reduce the dose, or alter the route of administra-

tion to minimize these effects.¹¹⁶ The CBD can be associated with transaminitis, which is typically dose-related and more common at very high doses (800 mg/day). Transaminitis typically improves by lowering the dose of CBD. Patients using CBD regularly should undergo periodic monitoring of liver enzymes and should avoid excessive alcohol use.^{127,128}

Additional safety concerns

The CBM use is typically not recommended for children and youth.¹²⁹ In addition, parents and those living with children should use caution to avoid exposure to second-hand smoke. People living with chronic pain and prescribing clinicians should always have a clear understanding of risks and adverse events before CBM initiation, including legal ramifications such as the inability to drive after THC consumption. It is recommended that CBM use follow a structured initiation process and have clinical supervision throughout.

Dosing

Two publications and one poster addressing dosing of CBM have been identified.^{130–132} All are concordant with the concept of low starting dose to be titrated slowly to achieve optimal target symptom improvement with minimal off-target effects, including euphoria. The optimal therapeutic dose is the dose that allows the patient to reach treatment goals, including pain and symptom reduction and improvement in function, with minimal or no side effects. Patients do not need to feel “high” or impaired to have symptom improvement.

Bhaskar et al propose three dosing regimens based on the clinical situation (Fig. 2): a routine protocol appropriate for most patients, a rapid protocol for those with severe pain, terminal illness or those already taking higher dose CBM and a conservative protocol for those with frailty, severe comorbidities, and polypharmacy. PRN dosing and micro-dosing may also be acceptable for breakthrough symptom management.

Authorization

Wide variation in legal status of medical and recreational cannabis exists globally. Clinicians authorizing or prescribing CBM should understand and comply with local laws and other regulations regarding its use. Individuals with conditions where CBM may be useful are urged to consult and be guided by regulated health care professionals familiar with its use.

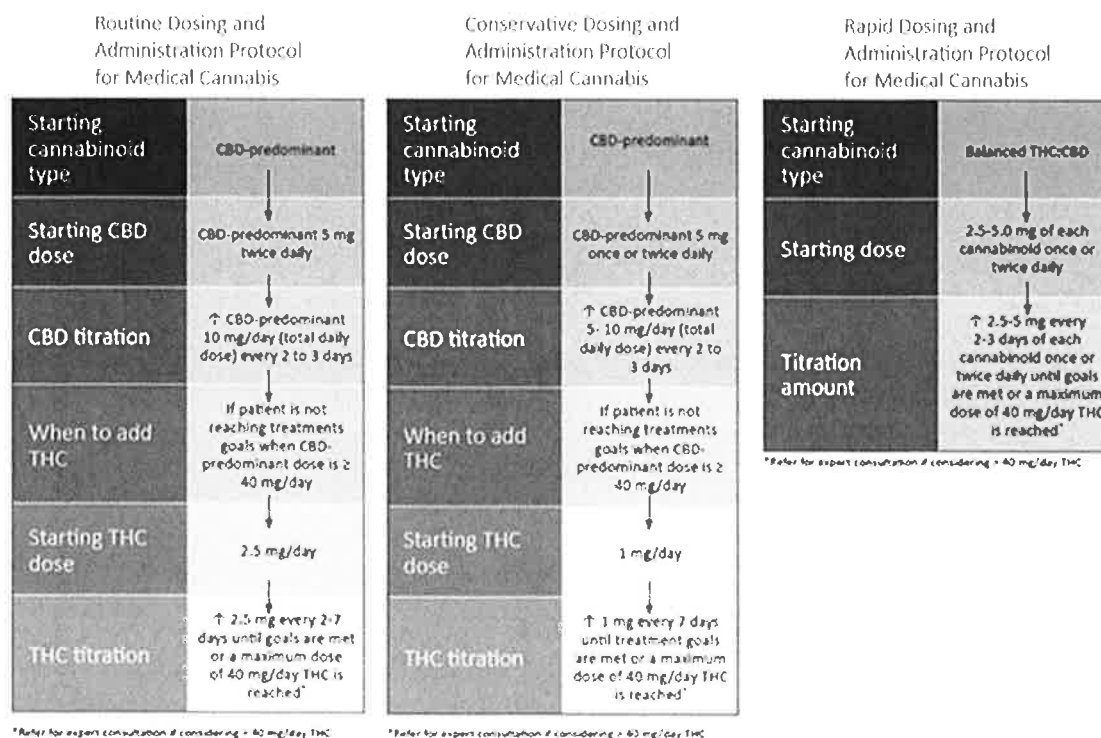


FIG. 2. Example of oral CBM Dosing and Titration Protocols. Reproduced with permission of Bhaskar et al.¹³³ CBM, cannabinoid-based medicines.

Strengths and limitations

These guidelines fill an important gap in the literature by providing guidance for clinicians and patients during a period of cannabis regulation changes. They include a thorough systematic review with rigorous study selection and methods for data extraction, quality assessment, and data synthesis. Although CBMs may be used for other purposes, these guidelines present recommendations for people living with chronic pain and for co-occurring conditions within the context of chronic pain and may not be transferable.

From the perspectives of people with lived experience, differences between sativa-predominant and indica-predominant chemovars of cannabis are important. For example, anecdotally, THC-dominant sativa tends to be stimulating and impede sleep, can augment anxiety and increase heart rate. However, the science behind the differences between sativa-predominant and indica-predominant chemovars is not well defined and the published research is undeveloped in this area. For these reasons, they were not included in the search results that are the foundation of the article.

There exist several challenges within CBM and chronic pain research. With respect to some co-occurring conditions, there still exist relatively few controlled trials. The data related to co-morbid conditions were typically not the primary focus of included studies and, subsequently, may be underpowered. The lack of comparative studies where the safety and efficacy of CBM is compared with typical pain treatments is also problematic. In addition, challenges commonly exist with unmasking in placebo-controlled trials, representing potential risk of bias, especially as pain and many comorbidities are measured with Visual Analog Scale or other subjective measures.

Acknowledgment

The authors thank Nancy Chow, Dr. Rob Sealey, and Dr. Lynda Balneaves for serving as external reviewers for these guidelines.

Patient and Public Involvement

Chronic pain and CBM patients were included on the guidelines task force and were involved at every stage

of development, including project inception, data synthesis, guideline development, and manuscript preparation.

Authors' Contributions

P.W. and L.B.-I. drafted the protocol. The Data Synthesis Committee (C.C., Z.W., S.M.) led and facilitated the systematic review and were consulted on guideline development. T.S. and S.A. conducted the literature search. M.S.P. and P.W. performed data extraction and data interpretation. A.D.B., C.M., C.C., E.M., Z.W., P.J.D., L.F., and P.J.D. drafted guideline sections and recommendations. All authors provided revisions to guidelines. P.W. and C.C. prepared the manuscript. All authors conceived and designed the review, and they read and approved the final manuscript. PW and CC are the guarantors of the review.

Author Disclosure Statement

T.S., S.A., L.B.-I., M.S.P., S.B., M.M.E., L.F., J.K.D., and J.O. do not have any conflicts of interest. P.W. and G.L.'s employer, the Canadian AIDS Society, has received a grant from Canopy Growth Corporation to support the development of the clinical practice guidelines. Z.W. is an advisory board member of Multidisciplinary Association for Psychedelic Studies—Canada. He has received research support from DOJA and Tilray licensed producers of cannabis and is a former Director of Clinical Research for Indigenous Bloom cannabis company. S.M. is the co-owner of a start-up company ("Cannabiscotti, Inc.") that will be applying for a cannabis processing license. She holds shares in Canopy Growth Corporation, Emblem Corp, and Aphria, Inc. She has received honorarium for research projects funded by Canopy Growth Corporation and Tilray. A.D.B. has received funding for consulting, speaking, and/or research from the following commercial organizations: Amgen, Bristol Myers Squibb, Janssen, AstraZeneca, Novartis, Pfizer, Bayer, Lilly, Boehringer Ingelheim, HLS Therapeutics, Spectrum Therapeutics, Sanofi, Bausch Health, Akcea, and Eisai. He holds shares in a wide variety of pharmaceutical companies and cannabis licensed producers. He has contributed, pro bono, to publications, position statements, and/or clinical practice guidelines from the following non-commercial organizations: Thrombosis Canada, Hypertension Canada, Heart and Stroke Foundation, Canadian Cardiovascular Society, and the Canadian Aids Society.

P.J.D. is a member of the Medical Advisory Board for Shoppers Drug Mart, a consultant for Reformulary Group, a member of the Speakers Bureau for Medical Cannabis Education for Shoppers Drug Mart and Spectrum Therapeutics, and participates in clinical trials for CancerCare Manitoba as per contract requirements. M.G. is the president and co-founder of the Harm Reduction Nurses Association. She was a board member of The Canadian HIV/AIDS Legal Network. She has received an honorarium payment from Merck for a presentation on HIV medication side-effects. C.M. is the Medical Director of Greenleaf Medical Clinic and Translational Life Sciences. She is on the Board of Directors for the Green Organic Dutchman. She is an advisor to Andira, and previously Emerald Health Therapeutics, Vitality Biopharma, Shoppers Drug Mart, True Leaf, Resolve Digital Health, Doja, and Compass Cannabis Clinics. She teaches medical cannabis to medical residents and pharmacy students at the University of British Columbia. She has provided medical consultation and/or received support for industry-sponsored continuing medical education from: Canopy/Spectrum, Tilray, Strainprint, Scientus Pharma, Aurora, MedReleaf & MD Briefcase.

E.M. is the co-owner of a start-up company ("Cannabiscotti, Inc.") that will be applying for a cannabis processing license, and is employed by MJardin Canada. C.C. has received cannabinoids from Tilray, Inc., for use in a clinical trial but has not received any grant support nor honoraria from the company. She has received research funding from Merck and Gilead, speaker honorarium from Gilead, and consultant fees from Viiv Healthcare. She has received funding to attend conferences from Gilead and Viiv Healthcare.

Funding Information

This work was supported by the Canadian Institutes for Health Research, grant no.: 402773; Arthritis Society of Canada, grant no.: NA; Canopy Growth Corporation, grant no.: NA. Neither the funders nor authors' affiliated institutions played any role in the development of the guidelines.

Supplementary Material

Supplementary Data
Supplementary Table S1
Supplementary Appendix SA1
Supplementary Appendix SA2
Supplementary Appendix SA3

References

- Goldberg DS, McGee SJ. Pain as a global public health priority. *BMC Public Health* 2011;11:770; doi: 10.1186/1471-2458-11-770
- Jackson TP, Stabile VS, McQueen KAK. The global burden of chronic pain. *ASA Newsl* 2014;78(6):24–27.
- Schopflocher D, Taenzer P, Jovey R. The prevalence of chronic pain in Canada. *Pain Res Manag* 2011;16(6):445–450.
- Reitsma ML, Tranmer JE, Buchanan DM, et al. The prevalence of chronic pain and pain-related interference in the Canadian population from 1994 to 2008. *Chronic Dis Inj Can* 2011;31(4):157–164.
- Steingrimsdóttir ÓA, Landmark T, Macfarlane GJ, et al. Defining chronic pain in epidemiological studies: A systematic review and meta-analysis. *Pain* 2017;158(11):2092–2107; doi: 10.1097/j.pain.0000000000001009
- Asmundson GJG, Katz J. Understanding the co-occurrence of anxiety disorders and chronic pain: state-of-the-art. *Depress Anxiety* 2009; 26(10):888–901; doi: 10.1002/da.20600
- Brennstuhl MJ, Tarquinio C, Montel S. Chronic pain and PTSD: Evolving views on their comorbidity. *Perspect Psychiatr Care* 2015;51(4):295–304; doi: 10.1111/ppc.12093
- Ilgen MA, Perron B, Czyz EK, et al. The timing of onset of pain and substance use disorders. *Am J Addict* 2010;19(5):409–415; doi: 10.1111/j.1521-0391.2010.00065.x
- Lerman SF, Rudich Z, Brill S, et al. Longitudinal associations between depression, anxiety, pain, and pain-related disability in chronic pain patients. *Psychosom Med* 2015;77(3):333–341; doi: 10.1097/PSY.0000000000000158
- Morasco BJ, Gritzner S, Lewis L, et al. Systematic review of prevalence, correlates, and treatment outcomes for chronic non-cancer pain in patients with comorbid substance use disorder. *Pain* 2011;152(3):488–497; doi: 10.1016/j.pain.2010.10.009
- Russo EB, Guy GW, Robson PJ. Cannabis, pain, and sleep: Lessons from therapeutic clinical trials of Sativex, a cannabis-based medicine. *Chem Biodivers* 2007;4(8):1729–1743; doi: 10.1002/cbdv.200790150
- Yalcin I, Barrot M. The anxiodepressive comorbidity in chronic pain. *Curr Opin Anaesthesiol* 2014;27(5):520–527; doi: 10.1097/ACO.0000000000000116
- Belle-Isle L, Hathaway A. Barriers to access to medical cannabis for Canadians living with HIV/AIDS. *AIDS Care* 2007;19(4):500–506; doi: 10.1080/09540120701207833
- Belle-Isle L, Walsh Z, Callaway R, et al. Barriers to access for Canadians who use cannabis for therapeutic purposes. *Int J Drug Policy* 2014;25(4): 691–699; doi: 10.1016/j.drugpo.2014.02.009
- Hill KP, Palastro MD, Johnson B, et al. Cannabis and pain: A clinical review. *Cannabis Cannabinoid Res* 2017;2(1):96–104; doi: 10.1089/can.2017.0017
- Walsh Z, Callaway R, Belle-Isle L, et al. Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use. *Int J Drug Policy* 2013;24(6):511–516; doi: 10.1016/j.drugpo.2013.08.010
- Wright P, Walsh Z, Margolese S, et al. Canadian clinical practice guidelines for the use of plant-based cannabis and cannabinoid-based products in the management of chronic non-cancer pain and co-occurring conditions: Protocol for a systematic literature review. *BMJ Open* 2020;10(5):e036114; doi: 10.1136/bmjopen-2019-036114
- Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1; doi: 10.1186/2046-4053-4-1
- Roen K, Arai L, Roberts H, et al. Extending systematic reviews to include evidence on implementation: Methodological work on a review of community-based initiatives to prevent injuries. *Soc Sci Med* 2006;63(4): 1060–1071; doi: 10.1016/j.socscimed.2006.02.013
- Armstrong R, Waters E, Roberts H, et al. The role and theoretical evolution of knowledge translation and exchange in public health. *J Public Health (Oxf)* 2006;28(4):384–389; doi: 10.1093/pubmed/fdl072
- Guyatt GH, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; 336(7650):924–926; doi: 10.1136/bmj.39489.470347.AD
- Guyatt GH, Oxman AD, Kunz R, et al. What is “quality of evidence” and why is it important to clinicians? *BMJ* 2008;336(7651):995–998; doi: 10.1136/bmj.39490.551019.BE
- Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* 2008;336(7652):1049–1051; doi: 10.1136/bmj.39493.646875.AE
- Jaeschke R, Guyatt GH, Dellinger P, et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. *BMJ* 2008;337:a744; doi: 10.1136/bmj.a744
- Schünemann HJ, Schünemann AHJ, Oxman AD, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *BMJ* 2008;336(7653):1106–1110; doi: 10.1136/bmj.39500.677199.AE
- Guyatt GH, Oxman AD, Kunz R, et al. Incorporating considerations of resources use into grading recommendations. *BMJ* 2008;336(7654): 1170–1173; doi: 10.1136/bmj.39504.506319.80
- National Heart Lung and Blood Institute. Study Quality Assessment Tools. NHLBI, NIH. 2020. Available from: <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools> [Last accessed: August 7, 2022].
- Häuser W, Petzke F, Fitzcharles MA. Efficacy, tolerability and safety of cannabis-based medicines for chronic pain management—An overview of systematic reviews. *Eur J Pain* 2018;22(3):455–470; doi: 10.1002/ejp.1118
- Allan GM, Finley CR, Ton J, et al. Systematic review of systematic reviews for medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms. *Can Fam Physician* 2018;64(2):e78–e94.
- Häuser W, Fitzcharles MA, Radbruch L, et al. Cannabinoids in pain management and palliative medicine. *Dtsch Arztebl Int* 2017;114(38): 627–634; doi: 10.3238/arztebl.2017.0627
- Madden K, van der Hoek N, Chona S, et al. Cannabinoids in the management of musculoskeletal pain: A critical review of the evidence. *JBJS Rev* 2018;6(5):e7; doi: 10.2106/JBJS.RVW.17.00153
- Park JY, Wu LT. Prevalence, reasons, perceived effects, and correlates of medical marijuana use: A review. *Drug Alcohol Depend* 2017;177:1–13; doi: 10.1016/j.drugalcdep.2017.03.009
- 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.0000000000001293
- Nugent SM, Morasco BJ, O’Neil ME, et al. The effects of cannabis among adults with chronic pain and an overview of general harms: A systematic review. *Ann Intern Med* 2017;167(5):319–331; doi: 10.7326/M17-0155
- Fitzcharles MA, Baerwald C, Ablin J, et al. 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
- Iskedjian M, Bereza B, Gordon A, et al. Meta-analysis of cannabis based treatments for neuropathic and multiple sclerosis-related pain. *Curr Med Res Opin* 2007;23(1):17–24; doi: 10.1185/030079906x158066
- 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
- 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
- Deshpande A, Mailis-Gagnon A, Zoheiry N, et al. Efficacy and adverse effects of medical marijuana for chronic noncancer pain: Systematic review of randomized controlled trials. *Can Fam Physician* 2015;61(8): e372–e381.
- Lynch ME, Campbell F. Cannabinoids for treatment of chronic non-cancer pain: a systematic review of randomized trials. *Br J Clin Pharmacol* 2011;72(5):735–744; doi: 10.1111/j.1365-2125.2011.03970.x
- Meng H, Johnston B, Englesakis M, et al. Selective cannabinoids for chronic neuropathic pain: A systematic review and meta-analysis. *Anesth Analg* 2017;125(5):1638–1652; doi: 10.1213/ANE.00000000000002110
- 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
- Aviram J, Samuely-Leichtag G. Efficacy of cannabis-based medicines for pain management: A systematic review and meta-analysis of randomized controlled trials. *Pain Physician* 2017;20(6):E755–E796.
- Boyчук DG, Goddard G, Mauro G, et al. The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: A

- systematic review. *J Oral Facial Pain Headache* 2015;29(1):7–14; doi: 10.11607/ofph.1274
45. Mücke M, Phillips T, Radbruch L, et al. Cannabis-based medicines for chronic neuropathic pain in adults. *Cochrane Database Syst Rev* 2018;3: CD012182; doi: 10.1002/14651858.CD012182.pub2
 46. Abrams DI, Jay CA, Shade SB, et al. Cannabis in painful HIV-associated sensory neuropathy: A randomized placebo-controlled trial. *Neurology* 2007;68(7):515–521; doi: 10.1212/01.wnl.0000253187.66183.9c
 47. Berman JS, Symonds C, Birch R. Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: Results of a randomised controlled trial. *Pain* 2004;112(3):299–306; doi: 10.1016/j.pain.2004.09.013
 48. Blake DR, Robson P, Ho M, et al. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology (Oxford)* 2006;45(1):50–52; doi: 10.1093/rheumatology/kei183
 49. Collin C, Ehler E, Waberszinek G, et al. A double-blind, randomized, placebo-controlled, parallel-group study of Sativex, in subjects with symptoms of spasticity due to multiple sclerosis. *Neurol Res* 2010;32(5): 451–459; doi: 10.1179/016164109X12590518685660
 50. Corey-Bloom J, Wolfson T, Gamst A, et al. Smoked cannabis for spasticity in multiple sclerosis: A randomized, placebo-controlled trial. *CMAJ* 2012; 184(10):1143–1150; doi: 10.1503/cmaj.110837
 51. Ellis RJ, Toperoff W, Vaida F, et al. Smoked medicinal cannabis for neuropathic pain in HIV: A randomized, crossover clinical trial. *Neuropsychopharmacology* 2009;34(3):672–680; doi: 10.1038/npp.2008.120
 52. Langford RM, Mares J, Novotna A, et al. A double-blind, randomized, placebo-controlled, parallel-group study of THC/CBD oromucosal spray in combination with the existing treatment regimen, in the relief of central neuropathic pain in patients with multiple sclerosis. *J Neurol* 2013;260(4):984–997; doi: 10.1007/s00415-012-6739-4
 53. Novotna A, Mares J, Ratcliffe S, et al. A randomized, double-blind, placebo-controlled, parallel-group, enriched-design study of nabiximols* (Sativex®), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. *Eur J Neurol* 2011;18(9):1122–1131; doi: 10.1111/j.1468-1331.2010.03328.x
 54. Nurmikko TJ, Serpell MG, Hoggart B, et al. Sativex successfully treats neuropathic pain characterised by allodynia: A randomised, double-blind, placebo-controlled clinical trial. *Pain* 2007;133(1–3):210–220; doi: 10.1016/j.pain.2007.08.028
 55. Rog DJ, Nurmikko TJ, Friede T, et al. Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis. *Neurology* 2005;65(6):812–819; doi: 10.1212/01.wnl.0000176753.45410.8b
 56. Selvarajah D, Gandhi R, Emery CJ, et al. Randomized placebo-controlled double-blind clinical trial of cannabis-based medicinal product (Sativex) in painful diabetic neuropathy: Depression is a major confounding factor. *Diabetes Care* 2010;33(1):128–130; doi: 10.2337/dc09-1029
 57. Serpell M, Ratcliffe S, Hovorka J, et al. A double-blind, randomized, placebo-controlled, parallel group study of THC/CBD spray in peripheral neuropathic pain treatment. *Eur J Pain* 2014;18(7):999–1012; doi: 10.1002/j.1532-2149.2013.00445.x
 58. Wade DT, Makela P, Robson P, et al. Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomized, placebo-controlled study on 160 patients. *Mult Scler* 2004;10(4):434–441; doi: 10.1191/1352458504ms1082oa
 59. Wade DT, Robson P, House H, et al. A preliminary controlled study to determine whether whole-plant cannabis extracts can improve intractable neurogenic symptoms. *Clin Rehabil* 2003;17(1):21–29; doi: 10.1191/0269215503cr581oa
 60. Ware MA, Wang T, Shapiro S, et al. Smoked cannabis for chronic neuropathic pain: A randomized controlled trial. *CMAJ* 2010;182(14):E694–E701; doi: 10.1503/cmaj.091414
 61. Weizman L, Dayan L, Brill S, et al. Cannabis analgesia in chronic neuropathic pain is associated with altered brain connectivity. *Neurology* 2018;91(14):e1285–e1294; doi: 10.1212/WNL.0000000000006293
 62. Wilsey B, Marcotte T, Deutsch R, et al. Low-dose vaporized cannabis significantly improves neuropathic pain. *J Pain* 2013;14(2):136–148; doi: 10.1016/j.jpain.2012.10.009
 63. Wilsey B, Marcotte T, Tsodikov A, et al. A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. *J Pain* 2008;9(6):506–521; doi: 10.1016/j.jpain.2007.12.010
 64. Wilsey B, Marcotte TD, Deutsch R, et al. An exploratory human laboratory experiment evaluating vaporized cannabis in the treatment of neuropathic pain from spinal cord injury and disease. *J Pain* 2016;17(9):982–1000; doi: 10.1016/j.jpain.2016.05.010
 65. Zajicek J, Fox P, Sanders H, et al. Cannabinoids for treatment of spasticity and other symptoms related to multiple sclerosis (CAMS study): Multi-centre randomised placebo-controlled trial. *Lancet* 2003;362(9395): 1517–1526; doi: 10.1016/S0140-6736(03)14738-1
 66. Zajicek JP, Hobart JC, Slade A, et al. MUSEC Research Group. Multiple sclerosis and extract of cannabis: Results of the MUSEC trial. *J Neurol Neurosurg Psychiatry* 2012;83(11):1125–1132; doi: 10.1136/jnnp-2012-302468
 67. Zajicek JP, Sanders HP, Wright DE, et al. Cannabinoids in multiple sclerosis (CAMS) study: Safety and efficacy data for 12 months follow up. *J Neurol Neurosurg Psychiatry* 2005;76(12):1664–1669; doi: 10.1136/jnnp.2005.070136
 68. Abrams DI, Couey P, Shade SB, et al. Cannabinoid-opioid interaction in chronic pain. *Clin Pharmacol Ther* 2011;90(6):844–851; doi: 10.1038/clpt.2011.188
 69. Bellnier T, Brown GW, Ortega TR. Preliminary evaluation of the efficacy, safety, and costs associated with the treatment of chronic pain with medical cannabis. *Ment Health Clin* 2018;8(3):110–115; doi: 10.9740/mhc.2018.05.110
 70. Chan S, Blake A, Wolt A, et al. Medical cannabis use for patients with post-traumatic stress disorder (PTSD). *J Pain Manage* 2017;10(4):385–396.
 71. Cufetti L, Manzo L, Peyraube R, et al. Chronic pain treatment with cannabidiol in kidney transplant patients in Uruguay. *Transplant Proc* 2018;50(2):461–464; doi: 10.1016/j.transproceed.2017.12.042
 72. Haroutianian S, Rosen G, Shouval R, et al. Open-label, add-on study of tetrahydrocannabinol for chronic nonmalignant pain. *J Pain Palliat Care Pharmacother* 2008;22(3):213–217; doi: 10.1080/15360280802251215
 73. Haroutianian S, Ratz Y, Ginosar Y, et al. The effect of medicinal cannabis on pain and quality-of-life outcomes in chronic pain: A prospective open-label study. *Clin J Pain* 2016;32(12):1036–1043; doi: 10.1097/AJP.0000000000000364
 74. Hoggart B, Ratcliffe S, Ehler E, et al. A multicentre, open-label, follow-on study to assess the long-term maintenance of effect, tolerance and safety of THC/CBD oromucosal spray in the management of neuropathic pain. *J Neurol* 2015;262(1):27–40; doi: 10.1007/s00415-014-7502-9
 75. Notcutt W, Price M, Miller R, et al. Initial experiences with medicinal extracts of cannabis for chronic pain: Results from 34 “N of 1” studies. *Anaesthesia* 2004;59(5):440–452; doi: 10.1111/j.1365-2044.2004.03674.x
 76. Poli P, Crestani F, Salvadori C, et al. Medical cannabis in patients with chronic pain: Effect on pain relief, pain disability, and psychological aspects. A prospective non randomized single arm clinical trial. *Clin Ter* 2018;169(3):e102–e107; doi: 10.7417/7.2018.2062
 77. Rog DJ, Nurmikko TJ, Young CA. Oromucosal delta9-tetrahydrocannabinol/cannabidiol for neuropathic pain associated with multiple sclerosis: An uncontrolled, open-label, 2-year extension trial. *Clin Ther* 2007;29(9):2068–2079; doi: 10.1016/j.clinthera.2007.09.013
 78. Russo M, Naro A, Leo A, et al. Evaluating Sativex® in neuropathic pain management: A clinical and neurophysiological assessment in multiple sclerosis. *Pain Med* 2016;17(6):1145–1154; doi: 10.1093/pm/pnv080
 79. Bonn-Miller MO, Boden MT, Bucossi MM, et al. Self-reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. *Am J Drug Alcohol Abuse* 2014;40(1):23–30; doi: 10.3109/00952990.2013.821477
 80. Brunt TM, van Genugten M, Höner-Snoeken K, et al. Therapeutic satisfaction and subjective effects of different strains of pharmaceutical-grade cannabis. *J Clin Psychopharmacol* 2014;34(3):344–349; doi: 10.1097/JCP.0000000000000129
 81. Campbell G, Hall WD, Peacock A, et al. Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: Findings from a 4-year prospective cohort study. *Lancet Public Health* 2018;3(7):e341–e350; doi: 10.1016/S2468-S2667(18)30110-5
 82. Clark AJ, Ware MA, Yazer E, et al. Patterns of cannabis use among patients with multiple sclerosis. *Neurology* 2004;62(11):2098–2100; doi: 10.1212/01.wnl.0000127707.07621.72
 83. Degenhardt L, Lintzeris N, Campbell G, et al. Experience of adjunctive cannabis use for chronic non-cancer pain: Findings from the Pain and

- Opioids IN Treatment (POINT) study. *Drug Alcohol Depend* 2015;147:144–150; doi: 10.1016/j.drugalcdep.2014.11.031
84. Nugent SM, Yarborough BJ, Smith NX, et al. Patterns and correlates of medical cannabis use for pain among patients prescribed long-term opioid therapy. *Gen Hosp Psychiatry* 2018;50:104–110; doi: 10.1016/j.genhosppsych.2017.11.001
 85. Tripp DA, Nickel JC, Katz L, et al. A survey of cannabis (marijuana) use and self-reported benefit in men with chronic prostatitis/chronic pelvic pain syndrome. *Can Urol Assoc J* 2014;8(11–12):E901–E905; doi: 10.5489/cuaj.2268
 86. Vigil JM, Stith SS, Adams IM, et al. Associations between medical cannabis and prescription opioid use in chronic pain patients: A preliminary cohort study. *PLoS One* 2017;12(11):e0187795; doi: 10.1371/journal.pone.0187795
 87. Ware MA, Doyle CR, Woods R, et al. 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
 88. Woolridge E, Barton S, Samuel J, et al. Cannabis use in HIV for pain and other medical symptoms. *J Pain Symptom Manage* 2005;29(4):358–367; doi: 10.1016/j.jpainsymman.2004.07.011
 89. Yassin M, Oron A, Robinson D. Effect of adding medical cannabis to analgesic treatment in patients with low back pain related to fibromyalgia: An observational cross-over single centre study. *Clin Exp Rheumatol* 2019;37 Suppl 116(1):13–20.
 90. Fanelli G, De Carolis G, Leonardi C, et al. Cannabis and intractable chronic pain: An explorative retrospective analysis of Italian cohort of 614 patients. *J Pain Res* 2017;10:1217–1224; doi: 10.2147/JPR.S132814
 91. Lynch ME, Young J, Clark AJ. A case series of patients using medicinal marijuana for management of chronic pain under the Canadian Marijuana Medical Access Regulations. *J Pain Symptom Manage* 2006;32(5):497–501; doi: 10.1016/j.jpainsymman.2006.05.016
 92. Ware MA, Gamsa A, Persson J, et al. Cannabis for chronic pain: Case series and implications for clinicians. *Pain Res Manag* 2002;7(2):95–99; doi: 10.1155/2002/380509
 93. Hunter D, Oldfield G, Tich N, et al. Synthetic transdermal cannabidiol for the treatment of knee pain due to osteoarthritis. *Osteoarthritis Cartilage* 2018;26:S26; doi: 10.1016/j.joca.2018.02.067
 94. Nicolodi M, Sandoval V, Terrine A. Therapeutic use of cannabinoids—Dose finding, effects, and pilot data of effects in chronic migraine and cluster headache. Abstract presented at 3rd congress of the European Academy of Neurology, June 24–27, 2017, Amsterdam, the Netherlands.
 95. Rhyne DN, Anderson SL, Gedde M, et al. Effects of medical marijuana on migraine headache frequency in an adult population. *Pharmacotherapy* 2016;36(5):505–510; doi: 10.1002/phar.1673
 96. Wilsey B, Marcotte TD, Deutsch R, et al. Low dose vaporized cannabis significantly improves neuropathic pain. *J Pain* 2013;14(2):136–148; doi: 10.1016/j.jpain.2012.10.009
 97. Woolridge E, Barton S, Samuel J, et al. Cannabis use in HIV for pain and other medical symptoms. *J Pain Symptom Manage* 2005;29(4):358–367; doi: 10.1016/j.jpainsymman.2004.07.011
 98. Bonn-Miller MO, Boden MT, Bucossi MM, et al. Self-reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. *Am J Drug Alcohol Abuse* 2014;40(1):23–30; doi: 10.3109/00952990.2013.821477
 99. Lynch ME, Young J, Clark AJ. A case series of patients using medicinal marijuana for management of chronic pain under the Canadian marijuana medical access regulations. *J Pain Symptom Manage* 2006;32(5):497–501; doi: 10.1016/j.jpainsymman.2006.05.016
 100. Nugent SM, Yarborough BJ, Smith NX, et al. Patterns and correlates of medical cannabis use for pain among patients prescribed long-term opioid therapy. *Gen Hosp Psychiatry* 2018;50:104–110; doi: 10.1016/j.genhosppsych.2017.11.001
 101. Campbell G, Hall WD, Peacock A, et al. Cannabis use, pain and prescription opioid use in people living with chronic non-cancer pain: Findings from a four-year prospective cohort. *Lancet Public Health* 2018;3(7):e341–e350; doi: 10.1016/S2468–S2667(18)30110-5
 102. Vigil JM, Stith SS, Adams IM, et al. Associations between medical cannabis and prescription opioid use in chronic pain patients: A preliminary cohort study. *PLoS One* 2017;12(11):e0187795; doi: 10.1371/journal.pone.0187795
 103. Sihota A, Smith BK, Ahmed SA, et al. Consensus-based recommendations for titrating cannabinoids and tapering opioids for chronic pain control. *Int J Clin Pract* 2021;75(8):e13871; doi: 10.1111/ijcp.13871
 104. Huestis MA. Human cannabinoid pharmacokinetics. *Chem Biodivers* 2007;4(8):1770–1804; doi: 10.1002/cbdv.200790152
 105. Agurell S, Halldin M, Lindgren JE, et al. Pharmacokinetics and metabolism of delta 1-tetrahydrocannabinol and other cannabinoids with emphasis on man. *Pharmacol Rev* 1986;38(1):21–43.
 106. Yamaori S, Kushihara M, Yamamoto I, et al. Characterization of major phytocannabinoids, cannabidiol and cannabinol, as isoform-selective and potent inhibitors of human CYP1 enzymes. *Biochem Pharmacol* 2010;79(11):1691–1698; doi: 10.1016/j.bcp.2010.01.028
 107. Bayer, Inc. Xarelto Product Monograph. Bayer Inc. 2018. Available from: https://pdf.hres.ca/dpd_pm/00043960.PDF [Last accessed: April 13, 2018].
 108. Pfizer Canada. Eliquis Product Monograph. Pfizer Canada: Quebec, Canada; 2018.
 109. Sanofi-Aventis. Plavix Product Monograph. Sanofi Aventis: Quebec, Canada; 2022.
 110. Geoffrey AL, Pollack SF, Bruno PL, et al. Drug-drug interaction between clobazam and cannabidiol in children with refractory epilepsy. *Epilepsia* 2015;56(8):1246–1251; doi: 10.1111/epi.13060
 111. Holland ML, Lau DTT, Allen JD, et al. The multidrug transporter ABCG2 (BCRP) is inhibited by plant-derived cannabinoids. *Br J Pharmacol* 2007;152(5):815–824; doi: 10.1038/sj.bjp.0707467
 112. Holland ML, Panetta JA, Hoskins JM, et al. The effects of cannabinoids on P-glycoprotein transport and expression in multidrug resistant cells. *Biochem Pharmacol* 2006;71(8):1146–1154; doi: 10.1016/j.bcp.2005.12.033
 113. Zhu HJ, Wang JS, Markowitz JS, et al. Characterization of P-glycoprotein inhibition by major cannabinoids from marijuana. *J Pharmacol Exp Ther* 2006;317(2):850–857; doi: 10.1124/jpet.105.098541
 114. Alsherbiny MA, Li CG. Medicinal cannabis-potential drug interactions. *Medicines (Basel)* 2018;6(1):E3; doi: 10.3390/medicines6010003
 115. Lucas CJ, Galettis P, Schneider J. The pharmacokinetics and the pharmacodynamics of cannabinoids. *Br J Clin Pharmacol* 2018;84(11):2477–2482; doi: 10.1111/bcp.13710
 116. MacCallum CA, Lo LA, Boivin M. “Is medical cannabis safe for my patients?” A practical review of cannabis safety considerations. *Eur J Intern Med* 2021;89:10–18; doi: 10.1016/j.ejim.2021.05.002
 117. van Os J, Bak M, Hanssen M, et al. Cannabis use and psychosis: A longitudinal population-based study. *Am J Epidemiol* 2002;156(4):319–327; doi: 10.1093/aje/kwf043
 118. D’Souza DC, Abi-Saab WM, Madonick S, et al. Delta-9-tetrahydrocannabinol effects in schizophrenia: Implications for cognition, psychosis, and addiction. *Biol Psychiatry* 2005;57(6):594–608; doi: 10.1016/j.biopsych.2004.12.006
 119. D’Souza DC, Perry E, MacDougall L, et al. The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: Implications for psychosis. *Neuropsychopharmacology* 2004;29(8):1558–1572; doi: 10.1038/sj.npp.1300496
 120. Health Canada. Information for Health Care Professionals: Cannabis (Marijuana, Marijuana) and the Cannabinoids. aem. 2018. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html> [Last accessed: June 20, 2020].
 121. Ravi D, Ghasemiesfe M, Korenstein D, et al. Associations between marijuana use and cardiovascular risk factors and outcomes: A systematic review. *Ann Intern Med* 2018;168(3):187–194; doi: 10.7326/M17-1548
 122. Battista N, Pasquariello N, Di Tommaso M, et al. Interplay between endocannabinoids, steroids and cytokines in the control of human reproduction. *J Neuroendocrinol* 2008;20 Suppl 1:82–89; doi: 10.1111/j.1365-2826.2008.01684.x
 123. Fried PA. Conceptual issues in behavioral teratology and their application in determining long-term sequelae of prenatal marijuana exposure. *J Child Psychol Psychiatry* 2002;43(1):81–102; doi: 10.1111/1469-7610.00005
 124. Hembree WC, Nahas GG, Zeidenberg P, et al. Changes in human spermatozoa associated with high dose marijuana smoking. *Adv Biosci* 1978;22–23:429–439; doi: 10.1016/b978-0-08-023759-6.50038-x
 125. Bonnet U, Preuss UW. The cannabis withdrawal syndrome: Current insights. *Subst Abuse Rehabil* 2017;8:9–37; doi: 10.2147/SAR.S109576

126. Russo EB, Spooner C, May L, et al. Cannabinoid hyperemesis syndrome survey and genomic investigation. *Cannabis Cannabinoid Res* 2022;7(3): 336–344; doi: 10.1089/can.2021.0046
127. Goyal H, Rahman MR, Perisetti A, et al. Cannabis in liver disorders: A friend or a foe? *Eur J Gastroenterol Hepatol* 2018;30(11):1283–1290; doi: 10.1097/MEG.0000000000001256
128. Andrews CN, Devlin SM, Le Foll B, et al. Canadian association of gastroenterology position statement: Use of cannabis in gastroenterological and hepatic disorders. *J Can Assoc Gastroenterol* 2019;2(1):37–43; doi: 10.1093/jcag/gwy064
129. Rieder MJ, Canadian Paediatric Society, Drug Therapy and Hazardous Substances Committee. Is the medical use of cannabis a therapeutic option for children? *Paediatr Child Health* 2016;21(1):31–34; doi: 10.1093/pch/21.1.31
130. MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *Eur J Intern Med* 2018;49:12–19; doi: 10.1016/j.ejim.2018.01.004
131. MacCallum CA, de Freitas L, Lo LA, et al. Cannabinoid-based medicines: dosing, titration & monitoring. In: *Cannabinoids and Pain* (Narouze SN, ed.) Springer International Publishing: Cham, Switzerland; 2021; pp. 167–178.
132. Boehnke KF, Clauw DJ. Brief commentary: Cannabinoid dosing for chronic pain management. *Ann Intern Med* 2019;170(2):118; doi: 10.7326/M18-2972
133. 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.

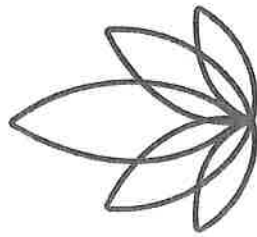
Cite this article as: Bell AD, MacCallum C, Margoese S, Walsh Z, Wright P, Daeninck PJ, Mandarino E, Lacasse G, Deol JK, Freitas L, St. Pierre M, Belle-Isle L, Gagnon M, Bevan S, Sanchez T, Arlt S, Monahan-Ellison M, O'Hara J, Boivin M, Costiniuk C; and External Review Panel (2023) Clinical practice guidelines for cannabis and cannabinoid-based medicines in the management of chronic pain and co-occurring conditions, *Cannabis and Cannabinoid Research* X:X, 1–19, DOI: 10.1089/can.2021.0156.

Abbreviations Used

CBD = cannabidiol
 CBM = cannabinoid-based medicines
 CEs = cannabis extracts
 MED = morphine equivalent dose
 MS = multiple sclerosis
 NNH = number needed to harm
 PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
 PTSD = post-traumatic stress disorder
 QOL = quality of life
 RCTs = randomized controlled trials
 THC = tetrahydrocannabinol

This is Exhibit D referred to in the
affidavit of Professor Zachary Walsh
sworn before me, this 28th
day of September 20²³
..... 
A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.



Combining Cannabis and Yoga

Practices and Motives

Lakoda Thomas BSc (hons), Sarah Daniels MA, Zach Walsh PhD



Study Aims

To characterize practices and motives of individuals who combine cannabis and yoga (CY)

Introduction

- First study to systematically describe combined cannabis and yoga practices
- Yoga and cannabis both have an ancient history of use in ceremony and religious traditions
 - CY combined in India since at least 7th century (Godlaski, 2012)
- Health professionals feel unprepared to guide patients on best practices for medical cannabis (St. Pierre et al., 2020; Zolotorov et al., 2021)
- Combining cannabis and yoga has the potential to inform the development of best practices for cannabis self administration for health related motives
- A complete mystical experience requires affirmative responses to 60% on each of the 4 subscales: Ineffability, mystical experiences, transcendence of time and space, positive mood

- Therapeutic impacts of mystical experiences: Promotes:
 - Personally meaningful insight
 - Openness in personality
 - Substantial change in perception

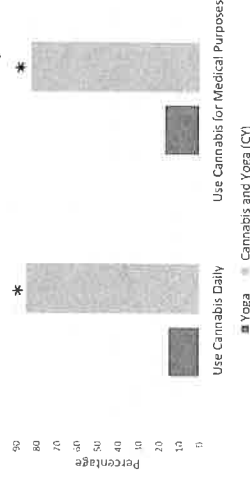


Methodology

- The study was an online self report survey
- For recruitment:
 - Advertised on online cannabis and yoga forums
 - Advertised at local yoga studios



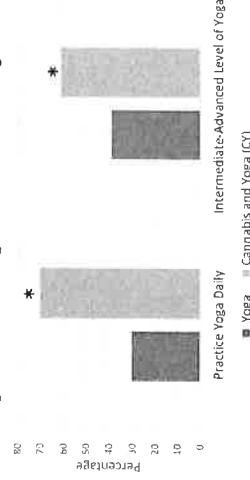
Cannabis Use for Yoga vs Cannabis and Yoga



CY use cannabis more often ($\chi^2(1, n = 350) = 17.86, p = .001$)

CY more likely to use cannabis for medical purposes ($\chi^2(1, n = 343) = 17.50, p = .001$)

Yoga Practice for Yoga vs Cannabis and Yoga



CY more likely to practice yoga daily ($\chi^2(1, n = 339) = 17.98, p = .001$)

CY at a more advanced level of yoga ($\chi^2(1, n = 388) = 32.08, p = .001$)

Motivations for CY that were rated as **Very/Extremely Important:**

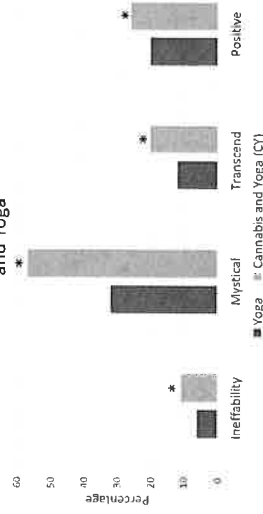
- Enhance connection to their body ($n = 229$; 81%)
- Enhance physical relaxation ($n = 208$; 73%)
- Enhance mental relaxation ($n = 204$; 71%)

Cannabis and yoga was rated as

Very/Completely Effective at treating the following:

- Anxiety ($n = 156$; 77%)
- Pain ($n = 140$; 69%)
- Depression ($n = 138$; 68%)
- Physical other than pain ($n = 113$; 56%)
- Other mental health ($n = 112$; 55%)

Mystical Experience Subscales for Yoga vs Cannabis and Yoga



Demographics

- 401 participants
- Ages 18 to 77 ($M = 32$)
- From Canada or the United States
- 82% White ($n = 330$)
- 84% Female ($n = 335$)
- 72% practiced cannabis and yoga ($n = 288$)

Conclusions

- CY practitioners were notably experienced with yoga and cannabis
- Motivations for CY reflected wellness-related intentions
- CY practitioners were more likely to have a complete mystical experience
- CY practitioners used the combined practice to alleviate health conditions

Implications

- Reports of positive experiences suggest potential application for patients who use cannabis for medical purposes.
- The dearth of evidence on how health care providers might best support patient who use cannabis suggest that further research on this promising approach is warranted

Discussion

Limitations:

- Based on a self report survey and self selection for participation
- The sample included an overrepresentation of female gender and White ethnicity
- Future Directions
 - Compare outcomes of unstructured cannabis use to CY
 - Study the therapeutic impacts of mystical experiences induced by CY

References

Godlaski, C. (2012). Cannabis Use and Yoga: A Review of the Literature. *Journal of Cannabis Research*, 1(1), 1-10. <https://doi.org/10.1080/21502195.2012.688888>

St. Pierre, R., & Zolotorov, A. (2020). Cannabis Use and Yoga: A Review of the Literature. *Journal of Cannabis Research*, 1(1), 1-10. <https://doi.org/10.1080/21502195.2020.1811111>

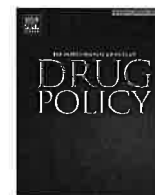
Zolotorov, A., & St. Pierre, R. (2021). Cannabis Use and Yoga: A Review of the Literature. *Journal of Cannabis Research*, 1(1), 1-10. <https://doi.org/10.1080/21502195.2021.1911111>



THE UNIVERSITY
OF BRITISH COLUMBIA

This is Exhibit E referred to in the
affidavit of Professor Zachary Walsh
sworn before me, this 28th
day of September 20²³
.....
A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.



Research paper

Barriers to access for Canadians who use cannabis for therapeutic purposes



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ARTICLE INFO

Article history:

Received 29 November 2013

Received in revised form 5 February 2014

Accepted 16 February 2014

Keywords:

Cannabis

Medical cannabis

Cannabis for therapeutic purposes

Regulations

Barriers to access

Health services analytical framework

Canada

ABSTRACT

Background: There is increased interest in the therapeutic potential of cannabis in recent decades. Canada, the Netherlands, Israel and some states in the United States have developed programs to allow access to cannabis for therapeutic purposes (CTP). In Canada, enrollment in the federal CTP program represents fewer than 5% of the estimated users of CTP. The discrepancy between the number of Canadians who report using CTP and the rate of utilization of the federal CTP program suggests the existence of barriers to access to this program.

Methods: In the present study we employ a health services analytical framework to examine barriers to access to CTP among 628 current CTP users. We define barriers to access as areas of poor fit between clients and services. We use five dimensions of *accommodation, accessibility, availability, affordability, and acceptability* to examine access to CTP.

Results: Our findings reveal that it is difficult for Canadians to find a physician to support their application to access CTP. Accessing CTP from unauthorized sources was common; only 7% of respondents accessed CTP exclusively from authorized sources. Access to CTP was positively associated with the presence of medical cannabis dispensaries, which were not included in the regulatory regime. Access to CTP varied by medical condition and general quality of health. Affordability of CTP was a substantial barrier to access. **Conclusions:** Strategies need to be developed to encourage scientific inquiry into CTP and address the barriers to access to CTP and the stigma and controversy that surround CTP and strain patient–physician relationships.

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Background

After a period of marginalization, recent decades have witnessed increased interest in the therapeutic potential of cannabis (Holland, 2010). Canada, the Netherlands, Israel and some states in the United States have developed programs to allow access to cannabis for therapeutic purposes (CTP) (Shelef, Mashiah, Schumacher, Shine, & Baruch, 2011). An estimated one million Canadians, or 4% of

those aged 15 and older, reported using cannabis in the previous 12 months to treat self-defined medical conditions (Adlaf, Begin, & Sawka, 2005; Belle-Isle & Hathaway, 2007). Court cases in Canada have confirmed the constitutional right of Canadians to choose cannabis as medicine without fear of criminal sanction (e.g. *R. v. Parker*, *Wakeford v. Canada*, *Hitzig et al. v. Canada*, *R. v. Mernagh*, *R. v. Smith*), and in 2001, the *Marihuana Medical Access Regulations* (MMAR) established guidelines for Canadians to obtain legal authorization to possess CTP. As of December 2012, 28,115 Canadians had obtained an authorization under these regulations to possess CTP and obtain CTP from a legal source (Health Canada, 2013). Although uptake of the federal program has increased in recent years, this enrollment represents fewer than 5% of the estimated users of CTP in Canada. The discrepancy between the number of Canadians who report using CTP and the rate of utilization of the

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federal CTP program suggests the existence of barriers to access to this program.

To obtain authorization to legally possess CTP under the MMAR, Canadians are required to obtain the written support of a physician on an application form and then apply to a federal authority. Those authorized can purchase dried cannabis from Health Canada, produce their own cannabis, or designate a person to grow cannabis on their behalf. In 2014, the MMAR are scheduled to be replaced by the *Marihuana for Medical Purposes Regulations* (MMPR). Under the MMPR, Canadians who wish to use CTP will need to obtain a medical document directly from a physician or nurse practitioner, similar to a prescription, which they will then submit to a commercial licensed producer. No onsite dispensing is allowed. Orders are shipped to patients. Both personal and designated licences to produce cannabis obtained under the MMAR will be phased out. These imminent changes, coupled with growing international interest, make it timely to analyse barriers to access to CTP under the current regulatory regime and to examine how new programs might address or exacerbate existing barriers.

In addition to authorized sources of CTP, medical cannabis dispensaries, also known as compassion clubs, represent a parallel source of CTP, providing CTP and related services to over 40,000 patients in Canada (Canadian Association of Medical Cannabis Dispensaries, 2013). Medical cannabis dispensaries arose in Canada in 1997 in response to demand for a community-based, safe, and quality controlled source of CTP (Capler, 2010). These dispensaries predate, and are not officially recognized by, the MMAR and operate under a legally ambiguous status (Belle-Isle, 2006). Additionally, many Canadians access CTP through friends, illicit self-production, and the street market.

The present study draws on data from the largest survey of Canadians who use CTP to date, the Cannabis Access for Medical Purposes Survey (CAMPS). We employ a health services analytical framework, developed to define the concept of 'access' and its relationship to patient satisfaction (Penchansky & Thomas, 1981), to examine barriers to access to CTP under the current program.

A health services analytical framework to examine barriers to access

Penchansky and Thomas (1981) offered a framework to define 'access' and its relationship to patient satisfaction in the context of health services research. Others have adapted this framework to examine barriers to health care and health services (Jacobs, Ir, Bigdeli, Annear, & Van Damme, 2012; Peters et al., 2008). For the purposes of our study, and in keeping with Penchansky and Thomas (1981), we define barriers to access as areas of poor fit between clients and services and use five dimensions to examine access to CTP: *accommodation*, *accessibility*, *availability*, *affordability*, and *acceptability*. Our study uses these dimensions as a lens through which to consider both access to authorization to possess CTP, as well as access to a source of CTP.

Accommodation refers to the "relationship between the manner in which the supply resources are organized to accept clients... and clients' ability to accommodate to these factors and the clients' perception of their appropriateness" (Penchansky & Thomas, 1981, p. 128). We conceptualize accommodation as an overarching dimension that broadly taps the appropriateness of the current model of CTP access in Canada with regard to meeting patients' needs. *Accessibility* refers primarily to the geographic location of services in relation to the location of the people in need of those services (Penchansky & Thomas, 1981; Peters et al., 2008). With regard to CTP, we examine the influence of provincial region of residence and community type (i.e. rural, suburban, and urban) on access both to physicians to obtain support to possess CTP, and to a source of

cannabis. *Availability* refers to the adequacy of available services according to the nature of patient needs (Penchansky & Thomas, 1981; Peters et al., 2008). In the CTP context, we examine how medical conditions and general quality of health impact availability of physicians to support applications, the responsiveness of the administrative process required to obtaining authorization to possess CTP, and the availability of sources of CTP. *Affordability* reflects the relationship between the costs of services and products and the patients' willingness and ability to pay for them (Penchansky & Thomas, 1981; Peters et al., 2008). We address this dimension by examining associations among income, costs associated with CTP, and ability to access CTP. *Acceptability* covers patients' attitudes regarding service providers and how they perceive their service providers' attitudes toward them (Penchansky & Thomas, 1981; Peters et al., 2008). To examine this dimension we review indices of patient–physician communication, stigma with regard to communication with physicians, and patients' attitudes to the federal program.

A few studies have touched on issues related to barriers to access to CTP in Canada. In 2005, the Canadian AIDS Society conducted a survey of people living with HIV/AIDS which revealed that the majority of those who used or wanted to use CTP had spoken to their physician about CTP, and that only a small minority reported lack of physician support to be a substantial barrier to access (Belle-Isle & Hathaway, 2007). That study also found that just over one third of respondents had applied to the federal medical cannabis program, with many respondents describing barriers including the onerous, complicated or intimidating requirements of the program, mistrust of government, concerns about the repercussions, negative impression of the program, and lack of awareness of the program. Further, 86% of respondents reported obtaining CTP from unauthorized sources, including friends, dispensaries, unauthorized self-cultivation, and street dealers, whereas 8% had a license to produce their own CTP, 4% had a licensed designated grower and fewer than 2% reporting purchasing CTP from Health Canada. A more recent survey that was limited to federally authorized users of CTP reported similarly low levels of obtaining CTP from Health Canada, and high levels via dispensaries and licenced self-cultivation; however, these respondents reported generally high levels of satisfaction with the federal program (Lucas, 2012a).

Studies of physicians' attitudes and practices have identified their substantial concerns with the current state of CTP use and regulation in Canada. Jones and Hathaway (2008) found that the majority among a sample of family physicians, medical residents and medical students felt that, with regard to CTP, they "did not have access to the quality of evidence to which they are accustomed and with which they felt comfortable" (p. 170). The investigators also found that physicians tended not to ask their patients about their cannabis use and patients tended not to tell. A recent survey conducted by the Canadian Medical Association (Canadian Medical Association, 2012) revealed similar results; the majority of physicians believe they lack sufficient information on risks, benefits, and appropriate use of CTP. The same survey reported that one third of physicians never support their patients' request for CTP, whereas more than half do so only occasionally or seldom.

In sum, findings regarding CTP use in Canada indicate relatively low uptake of the authorized program on the part of patients and substantial discomfort on the part of physicians, suggesting a generally poor degree of "fit" between client and service. The present study presents a theoretically informed examination of the extent and nature of barriers to accessing CTP as experienced by Canadians. In light of the internationally expanding role of cannabis within the medical pharmacopeia, the elucidation of these barriers has the potential to inform and refine the development of CTP

programs, and might more broadly contribute to the understanding of barriers to access for emerging and potentially stigmatized therapies.

Methods

The study was approved by the Behavioural Research Ethics Board of the University of British Columbia. The research team consisted of academic researchers, representatives from community-based organizations and non-governmental organizations, and people who use CTP. The research thus borrowed from a participatory approach. The survey collected cross-sectional data from 628 self-identified current users of CTP in 2011–2012, both online at the *national* level and at a *local* British Columbia medical cannabis dispensary. Organizations and media that serve people who use CTP as well as dispensaries assisted with promoting the *national* survey (e.g., Canadian AIDS Society, Canadian Aboriginal AIDS Network, social media). No identifying data (i.e. IP addresses) were collected, to ensure confidentiality. Participants in the *local* group received \$10 compensation and participants in the *national* group were not financially compensated. Of the 702 *national* participants, 541 (77%) reported current CTP use. Participants in the *local* group were recruited via advertising posters and word of mouth at the medical cannabis dispensary where data were collected. All 87 *local* participants who completed the consent form reported current CTP use. The *local* group consisted of members of the dispensary who were either authorized to possess cannabis through Health Canada or had documented confirmation of a medical condition for which CTP is indicated. This recruitment design allowed a comparison of the online *national* condition with the confirmed CTP users' queried in-person in the *local* condition, and preliminary analyses indicated broad similarity between local and national respondents (see Walsh et al., 2013 for a detailed comparison of local and national groups). Participants in the *local* group completed the survey online on a tablet provided by an onsite researcher assistant and received help as needed from research assistants.

The questionnaire consisted of 414 questions designed to be completed in less than one hour. It queried demographics, detailed CTP use, communications with health care providers, access to and experiences with the federal medical cannabis program and a supply of CTP and general indicators of health and well-being. The questionnaire also included questions drawn from the Barriers Questionnaire (Ward et al., 1993) and from prior studies of CTP use (Belle-Isle & Hathaway, 2007; Lucas, 2012a). It was administered online, and organized in a hierarchical manner such that exposure to many items was contingent on prior responses. As a result, the number of recorded responses varies across items and no participants completed all items. All reported percentages are based on number of responses to given items rather than on the entire sample. In order to enhance clarity we accompany all reported percentages with number of responses.

Analyses were conducted in a manner that reflected the health services framework that guided this investigation. Specifically, to address *accommodation* we use descriptive statistics to broadly represent the extent to which patient needs for access were met by the program with a focus on general obstacles, physician access, the application process and source of CTP. To analyse *accessibility* we compare patients across regions and types of community. To analyse differences in *availability* we examine variability in access across medical conditions and global health status. To analyse the *affordability* of CTP, we compare access across income groups and examine the extent to which the impact of cost-related barriers varied according to global health status. Finally, to examine *acceptability* we describe patient perceptions of caregiver attitudes and communication. All comparisons involved discrete groups for both

Table 1

Demographic information about study participants.

	<i>n</i>	%
Gender		
Male	443	70.8
Female	180	28.7
Transgender/other	3	0.5
Ethnic origin		
Caucasian	581	92.5
First Nation	31	4.9
Metis	16	2.5
Age distribution		
18–24	98	16.4
25–34	158	26.5
35–44	115	19.3
45–54	141	23.6
55 and over	85	14.2
Completed level of education		
Elementary school	27	4.3
Secondary school	234	37.3
Technical college	225	35.8
University – undergraduate	108	17.2
University – graduate	34	5.4
Yearly household income		
Under \$20,000	206	33.2
\$20,000–\$39,999	165	26.6
\$40,000–\$59,999	103	16.6
\$60,000 and over	146	23.6
Area of residence		
Urban	289	46.5
Suburban	196	31.5
Rural or remote	137	22.0
Provincial region		
British Columbia	221	35.4
Prairies ^a	88	14.1
Ontario	242	38.7
Quebec	30	4.8
Maritimes ^b	44	7.0
Health status		
Excellent	22	4.6
Very good	114	24.0
Good	177	37.3
Fair	107	22.5
Poor	55	11.6

^a Prairies include Alberta, Saskatchewan, Manitoba and Northwest Territories.

^b Maritimes include New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador.

selection and outcome variables and were therefore conducted using χ^2 tests.

Results

Demographics

The 628 respondents were 71% male, 29% female and 0.5% transgender and other genders, 92% Caucasians and 7% First Nations and Metis. Mean age was 39.10 years ($SD = 13.12$), median household income was \$30,000–\$39,999, 96% had completed secondary school and 58% had completed some post-secondary education. Responses were obtained from all ten Canadian provinces and one of the three territories, and respondents reported living in urban (47%), suburban (32%), and rural or remote areas (22%) (Table 1). Respondents reported using CTP for anxiety and depression, pain, arthritis, spinal pain, HIV/AIDS, multiple sclerosis, cancer, epilepsy and a variety of other illnesses. Medical use of cannabis was mainly reported for the treatment of pain, followed by nausea, mood, spasticity and other symptoms. A detailed description of the demographic and medical characteristics of this sample is available elsewhere (Walsh et al., 2013).

Table 2

Accommodation: Appropriateness of the current model to meeting patients' needs.

Obstacles
• 86% (n = 420) experienced obstacles in accessing CTP
Physicians
• 32% (n = 156) sought another physician in relation to use of CTP
◦ 57% (n = 89) of whom changed physicians more than once
• 29% reported that physician recommended CTP but refused to endorse application for authorized access (n = 143)
Application for authorization
• 48% (n = 245) had applied for authorized access
◦ 59% (n = 145) of whom found the process difficult or very difficult
◦ 47% (n = 114) of whom reported being somewhat or completely unsatisfied with the program
Access to an authorized source of CTP^a
• 31% (n = 139) accessed CTP from an authorized source
◦ 76% (n = 106) of them also accessed CTP from unauthorized sources ^b
• 7% (n = 33) accessed CTP exclusively through authorized sources
• 31% (n = 155) reported self-producing CTP for personal use, of whom 50% (n = 77) were licensed
• 34% (n = 42) of self-producers reported that it was difficult or very difficult to learn to cultivate cannabis; 16% (n = 24) reported arrests; 12% (n = 19) reported break ins
• Reported reasons for not self-producing CTP (n = 339) included: lack of space (43%, n = 146), expense of set up (37% n = 124), and legal concerns (32%, n = 108).
• The most important reason for self-producing was quality (39%, n = 52), followed by price (36%, n = 47), avoiding the black market (29%, n = 40), selection of a specific strain of cannabis (24%, n = 33), and safety (12%, n = 15).
• Of those who reported that someone else produced CTP for them (18%, n = 90), 67% (n = 60) had designated producers who were licensed. 39% (n = 35) of respondents with designated producers reported difficulties in finding one.

^a Under the MMAR, authorized sources were limited to licensed self-production, licensed designated producer or direct purchase from the federal program.

^b Unauthorized sources include medical cannabis dispensaries, friends, street market, unlicensed self-production, and unlicensed designated producers.

Accommodation

Accommodation refers to the appropriateness of the MMAR model of CTP access (in effect at the time of this study) to meeting patients' needs. Table 2 summarizes the key findings related to accommodation. The majority of respondents experienced obstacles to accessing CTP. Respondents described obstacles as affecting their mood, enjoyment of life, sleep, general activity, normal work outside or inside the home, and relationships (Fig. 1). Most respondents (81.1%; n = 489) reported discussing the use of CTP with a physician, and almost one third of respondents (Table 2) reported that they had sought a new physician in relation to their use of CTP, with the majority of those changing physicians more than once. Respondents reported equivocation on the part of physicians with regard to recommending and authorizing use of CTP. Among respondents who discussed CTP with their physicians, more than a

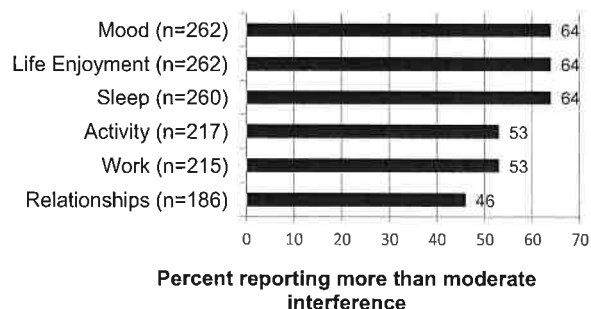


Fig. 1. Effects of barriers to access to cannabis for therapeutic purposes on life domains.

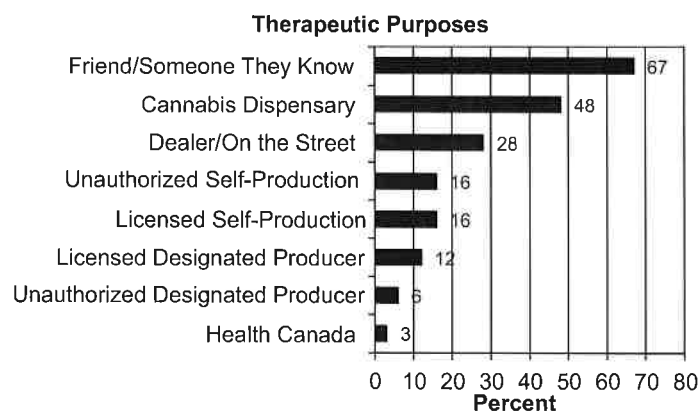


Fig. 2. Reported sources of cannabis for therapeutic purposes.

quarter of them reported that physicians recommended they access CTP but refused to endorse their application for authorized access.

Nearly half of respondents had applied for a federal authorization to possess CTP, of whom 68% (n = 167) received authorization, 5% (n = 13) reported they did not, and 26% (n = 63) had applications that were under review at the time of the survey. Among applicants to the federal CTP program, more than half found the process difficult or very difficult, and almost half reported being somewhat or completely unsatisfied with the program.

Incongruent accommodation between patients and services is further evidenced in access to a source of CTP; the federal program makes available a single strain of dried cannabis, whereas 93% (n = 415) of respondents identified access to a specific preferred strain, a variety of strains, and/or alternative CTP products (e.g. baked goods, tinctures) as important options. Indeed, less than one third of respondents (Table 2) accessed CTP from authorized sources (i.e. licensed self-production, licensed designated producer, direct purchase from the federal program), and more than three quarters of respondents who had access to authorized sources also accessed CTP from unauthorized sources (i.e. dispensary, friend, street, unlicensed self-production, unlicensed designated producer). Overall, only 7% of respondents accessed CTP exclusively through authorized sources. Fig. 2 provides a detailed breakdown of sources of CTP.

Almost one third of respondents reported self-producing CTP, of whom half were licensed to produce CTP for personal use (Table 2). Approximately one third of self-producers reported that it was difficult or very difficult to learn to cultivate cannabis. Other reported difficulties associated with self-production included arrest and break-ins. Among respondents who provided reasons for not self-producing CTP, the most prominent reasons were lack of space, expense of set up, and legal concerns. The most important reason for self-producing was quality, followed by price, avoiding the black market, selection of a specific strain of cannabis, and safety. Of those who reported that someone else produced CTP for them, two thirds had designated producers who were licensed. More than a third of them reported having difficulties finding a designated producer.

Accessibility

Accessibility refers to the influence of provincial region of residence and community type (i.e. rural, suburban, and urban) on access both to physicians to obtain support for an authorization to possess CTP and to a source of CTP. Table 3 summarizes the key findings for accessibility. The rate of experiencing obstacles to access to CTP did not differ according to provincial region or community type. The proportion of those who had spoken to a physician regarding CTP use varied according to region, with the highest level

Table 3

Accessibility: Influence of provincial region and community type on access.

Obstacles

- No difference in rate of experiencing obstacles to access to CTP by provincial region^a ($\chi^2 = 5.32$ (4), $p = .27$) or community type^b ($\chi^2 = 1.39$ (2), $p = .50$).

Physicians

- Regional differences in proportion of respondents who had spoken to a physician regarding CTP use ($\chi^2 = 16.58$ (4); $p < .01$); highest in British Columbia (88%, $n = 191$) and lowest in the Maritimes (71%, $n = 29$).
- Rural respondents more likely than urban and suburban respondents to discuss CTP with physicians ($\chi^2 = 7.59$ (2); $p = .02$); 89% ($n = 116$) rural, 80% ($n = 224$) urban, 77% ($n = 144$) suburban
- No difference in the proportion of respondents who reported changing physicians for reasons related to CTP across provincial regions ($\chi^2 = 3.11$ (4); $p = .54$) or community types ($\chi^2 = .19$ (2); $p = .67$).

Application for authorization

- Rural residents more likely to report having received federal authorization to possess CTP compared to suburban and urban dwellers ($\chi^2 = 8.69$ (2), $p = .01$): 41% ($n = 45$) rural, 36% ($n = 58$) suburban, 26% ($n = 63$) urban.

Access to a source of CTP

- Regional differences in the proportion of respondents who accessed CTP from a medical cannabis dispensary ($\chi^2 = 62.61$ (4); $p < .01$), with higher levels in British Columbia (70%, $n = 118$) and Ontario (41%, $n = 68$) and lower levels in the Prairies (18%, $n = 11$) and Maritime (25%, $n = 7$).
- Complementary regional differences in the proportion of respondents who accessed CTP from a friend or acquaintance ($\chi^2 = 18.23$ (4), $p < .01$), with higher levels in the Prairies (80%, $n = 52$) and Maritimes (88%, $n = 28$) and lower levels in British Columbia (58%, $n = 106$).
- Self-production of cannabis differed by community type ($\chi^2 = 18.25$ (2); $p < .01$), with the highest level among respondents from rural areas (48%, $n = 51$), followed by suburban (31%, $n = 46$) and urban residents (25%, $n = 58$).

^a Provincial regions include British Columbia, the Prairies (Alberta, Saskatchewan, Manitoba and the Northwest Territories), Ontario, Quebec, and the Maritimes (New Brunswick, Nova Scotia, Newfoundland and Labrador and Prince Edward Island).

^b Community type refers to self-reported urban, suburban or rural area of residence.

in British Columbia and lowest in the Maritimes. Across regions, respondents from rural areas were more likely than urban or suburban respondents to discuss CTP with physicians. The proportion of respondents who reported changing physicians for reasons related to CTP use was stable across provincial regions and community types. Rural residents were more likely to report having received

federal authorization to possess CTP relative to suburban and urban dwellers.

With regard to accessibility to sources of CTP, regional differences were identified in the proportion of respondents who accessed CTP from a medical cannabis dispensary, with higher levels among respondents from British Columbia and Ontario and lower use among residents of the Prairies and Maritimes. A complementary pattern of results emerges from examining access to cannabis from a friend or acquaintance, with higher levels among residents of the Prairies and Maritimes and lower levels from British Columbia. Fig. 3 provides a detailed breakdown of sources of CTP by provincial region. Self-production of cannabis differed by community type, with the highest level of self-production among respondents from rural areas, followed by suburban and urban residents.

Availability

Availability in this context refers to how medical conditions and general quality of health impact availability of physicians to support applications to access CTP, the responsiveness of the federal government's administrative process required to obtaining authorization to possess CTP, and the availability of sources of CTP. Table 4 summarizes key findings related to availability. The rate of experiencing obstacles to access to CTP differed across medical conditions, such that individuals who identified HIV/AIDS as their primary condition were less likely to report obstacles. Physician communication also varied according to medical conditions, such that a greater proportion of individuals with HIV/AIDS and arthritis discussed CTP with physicians, whereas respondents with anxiety/depression as primary condition were less likely to discuss CTP with physicians. Respondents with HIV/AIDS were also relatively less likely than other patients to change physicians for reasons related to CTP. Having physicians recommend CTP but refuse to endorse applications for authorized access was less prevalent among respondents with HIV/AIDS, and more common among respondents with chronic pain that was not due to spinal injury or arthritis.

To maximize power and facilitate interpretation we dichotomized health status into *fair to poor* (34%, $n = 162$) and

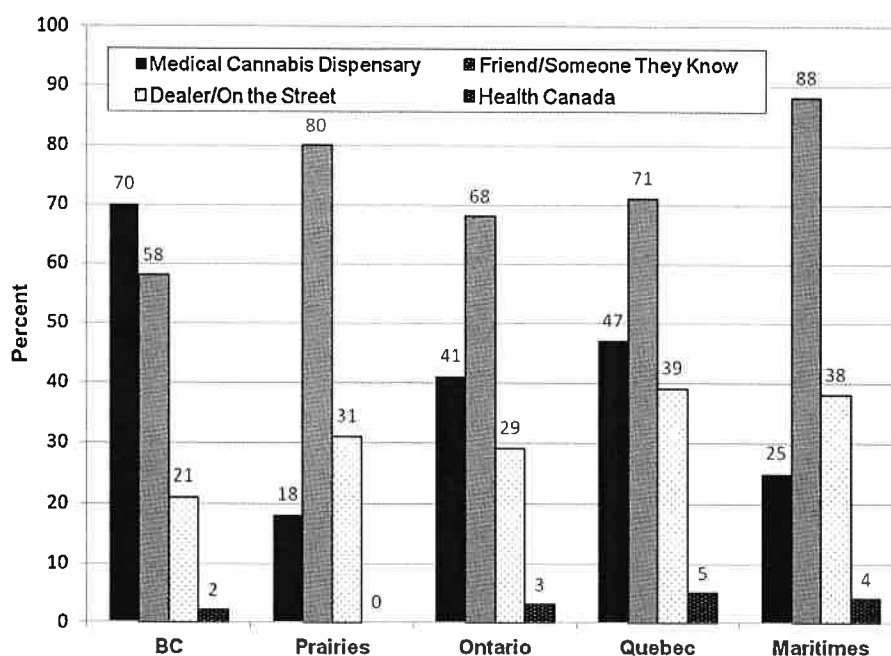


Fig. 3. Sources of purchased cannabis for therapeutic purposes by provincial region.

Table 4

Availability: Impact of medical conditions and general quality of health on access.

Obstacles

- Individuals who identified HIV/AIDS as their primary condition were less likely to report experiencing obstacles to access to CTP than other respondents (70%, $n = 33$) ($\chi^2 = 10.29$ (1); $p < .01$).
- No differences in experiencing obstacles to access to CTP according to reported general health status ($\chi^2 = .16$ (1); $p = .68$).

Physicians

- Compared to respondents with other medical conditions, respondents living with HIV/AIDS were:
 - more likely to discuss CTP with physicians (93%, $n = 55$) ($\chi^2 = 5.51$ (1); $p = .02$).
 - less likely than other patients to change physicians for reasons related to CTP (11%, $n = 6$) ($\chi^2 = 13.14$ (1); $p < .01$).
 - less likely to have physicians recommend CTP but refuse to endorse applications for authorized access (13%, $n = 7$) ($\chi^2 = 10.90$ (1); $p < .01$).
- Respondents with arthritis were also more likely than other respondents to discuss CTP with their physician (91%, $n = 80$) ($\chi^2 = 4.54$ (1); $p = .02$).
- Respondents with anxiety/depression were less likely to discuss CTP with a physician (64%, $n = 69$) ($\chi^2 = 27.68$ (1); $p < .01$).
- Respondents who reported *fair to poor* general health were more likely than respondents who reported *good to excellent* general health to discuss CTP with a physician (91%, $n = 147$) (77%, $n = 240$) ($\chi^2 = 13.59$ (1); $p < .01$).
- No differences according to general health status in changing physicians related to CTP ($\chi^2 = .39$ (1); $p = .57$), or having physicians recommend CTP but refuse to endorse an application for authorization ($\chi^2 = .08$ (1); $p = .81$).
- Respondents with chronic pain that was not due to spinal injury or arthritis were more likely to have physicians recommend CTP but refuse to endorse applications for authorized access (51%, $n = 40$) ($\chi^2 = 12.43$ (1); $p < .01$).

Application for authorization

- Respondents who reported *fair to poor* general health were more likely than respondents who reported *good to excellent* general health to have obtained federal authorization (42%, $n = 68$) (27%, $n = 85$) ($\chi^2 = 10.59$ (1); $p < .01$).

Access to an authorized source of CTP

- Respondents who reported *fair to poor* general health were more likely than respondents who reported *good to excellent* general health to access CTP through authorized means (36%, $n = 57$) (25%, $n = 76$) ($\chi^2 = 6.00$ (1); $p = .02$).
- The proportion of licensed versus unlicensed self-producers was consistent across medical conditions ($\chi^2 = 2.01$ (8); $p = .98$).
- Self-producers of CTP who reported *fair to poor* general health were more likely to be licensed (64%, $n = 30$) than were those who reported *good to excellent* general health (42%, $n = 43$) ($\chi^2 = 6.05$ (1); $p = .01$).
- The proportion of self-producers who reported difficulty in learning to cultivate was consistent across medical conditions ($\chi^2 = 9.04$ (8); $p = .34$) and general health quality ($\chi^2 = .39$ (2); $p = .58$).
- The proportion of respondents reporting difficulties finding a designated producer was stable across medical conditions ($\chi^2 = 7.14$ (8); $p = .52$) and health quality ($\chi^2 = .27$ (1); $p = .66$).

good to excellent (66%, $n = 313$), based on a median split and parsimony. Respondents who reported *fair to poor* general health were more likely than respondents who reported *good to excellent* general health to discuss CTP with a physician, to have obtained federal authorization, and to access CTP through authorized means. However, comparisons according to general health of respondents identified no differences with regard to experiencing obstacles, changing physicians related to CTP, or having physicians recommend CTP but refuse to endorse an application for authorization.

With regard to sources of CTP, the proportion of licensed versus unlicensed self-producers was consistent across medical conditions. However, self-producers who reported *fair to poor* general health were more likely to be licensed than were those who reported *good to excellent* general health. The proportion of self-producers who reported difficulty in learning to cultivate was consistent across medical conditions and general health quality. The proportion of respondents reporting difficulties finding a

Table 5

Affordability: Ability to pay for access to CTP according to income.

Physicians

- Income was not associated with discussing CTP with a physician ($\chi^2 = 1.48$ (3); $p = .69$) or with changing physicians for reasons associated with CTP ($\chi^2 = 1.14$ (3); $p = .79$).
- 40% ($n = 98$) of applicants were charged by physicians for the service of having their application completed, with charges ranging from \$10 to \$800.
- a relatively smaller proportion of the lowest income group ($\leq \$20,000/\text{yr}$) were charged (30%, $n = 26$, $\chi^2 = 7.18$ (1); $p < .01$), and a larger proportion of the \$40,000–60,000/yr group were charged (62%, $n = 21$, $\chi^2 = 6.76$ (1); $p = .01$).

Application for authorization

- 40% ($n = 68$) of respondents in the lowest income group obtained authorization compared to 28% ($n = 95$) of respondents from higher income groups ($\chi^2 = 6.86$ (1); $p = .01$).

Access to a source of CTP

- Among participants who reported buying CTP ($n = 433$), the median amount reportedly spent was \$200 (Inter-quartile Range = \$100–\$400) per month.
- 54% ($n = 278$) of respondents reported that they were *sometimes or never* able to afford to buy sufficient quantity of CTP to relieve their symptoms
- Respondents in the lower income group were most likely to report that they were *sometimes or never* able to afford to buy sufficient quantity of CTP (72%, $n = 123$) and those in the highest income group ($\geq \$60,000/\text{yr}$) were least likely (30%, $n = 36$) ($\chi^2 = 51.26$ (3); $p < .01$).
- 33% ($n = 173$) reported that they often or always choose between cannabis and other necessities (e.g. food, rent, other medicines) because of lack of money, with the highest levels of reporting among lowest income (51%, $n = 88$) and lower levels at highest income (11%, $n = 13$) ($\chi^2 = 56.93$ (3); $p < .01$).
- 67% ($n = 107$) of respondents who reported *fair to poor* general health were *sometimes or never* able to afford sufficient CTP compared to 48% ($n = 147$) of respondents who reported *good to excellent* health ($\chi^2 = 15.56$ (1); $p < .01$).
- Respondents reporting poorer health were nearly twice as likely to report choosing between CTP and other necessities (48% ($n = 78$) versus 25% ($n = 79$), $\chi^2 = 25.85$ (1); $p < .01$).
- Income was not associated with accessing CTP from an authorized source ($\chi^2 = 2.61$ (3); $p = .46$).

designated producer was stable across medical conditions and health quality.

Affordability

Affordability refers to costs associated with CTP and ability to pay according to income. Costs to access CTP occur both in the process of obtaining physician support for authorization to possess CTP and in obtaining a supply of cannabis. Table 5 summarizes the key findings related to affordability. Many applicants were charged by their physician for the service of having their application completed, with charges ranging from \$10 to \$800. A relatively smaller proportion of the lowest income group and a larger proportion of the \$40,000–60,000/year group were charged.

Among participants who reported buying CTP, the median amount spent was \$200 (Inter-quartile Range = \$100–\$400) per month. More than half of respondents reported that they were *sometimes or never* able to afford to buy sufficient quantity of CTP to relieve their symptoms, and approximately one third reported that they often or always choose between cannabis and other necessities (e.g. food, rent, other medicines) because of lack of money. The proportion of respondents who reported that they were *sometimes or never* able to afford to buy sufficient quantity of CTP differed according to income such that it was most frequently reported by the lower income group and least frequently reported by the highest income group. The frequency of reports of choosing between CTP and other necessities followed a similar pattern, with highest levels of reporting among lowest income and lower levels at highest income.

Table 6

Acceptability: Patients' perceptions of physicians' attitudes with regard to CTP.

Physicians

- 48% (n = 277) reported that they had at some time wanted to discuss CTP with a physician but had not done so.
- 38% (n = 105) had not discussed CTP with any physician.
- The most frequent reason for not discussing CTP despite a desire to do so was "don't feel comfortable" (62%, n = 172), followed by "illegal" (46%, n = 127), and "can't afford cannabis" (9%, n = 25).
- Reported reasons for respondents avoiding CTP in the past included: "I could be discriminated against" (60%, n = 326), "Doctors might find it annoying to be asked about cannabis" (51%, n = 275), "Discussing cannabis could distract a doctor" (17%, n = 90) and "It could make me drowsy" (17%, n = 90).
- Reported perceived negative responses from physicians to CTP included: "After multiple negative responses from doc, I've stopped broaching the subject."; "He shut me down every time I brought it up."
- Respondents feared a negative impact on their patient/physician relationship: "fear of getting no treatment at all"; "fear of losing my doctor"; "I am afraid they will black list me as a patient and I would not have access to health care!"
- Compared to their communication with their physician regarding other medical issues, 50% (n = 235) of respondents were less satisfied with their communication about the use of CTP, and 31% (n = 146) reported that they often or always felt discriminated against by their physician because of their use of CTP.

The proportion of respondents who reported financial strain associated with CTP varied according to health status such that approximately two thirds of respondents who reported *fair to poor* general health were *sometimes or never* able to afford sufficient CTP compared to almost half of respondents who reported *good to excellent* health. Respondents reporting poorer health were also nearly twice as likely to report choosing between CTP and other necessities.

The proportion of respondents who obtained authorization varied according to income, such that a greater proportion of respondents in the lowest annual income group obtained authorization compared to respondents from higher income groups. Income was not associated with discussing CTP with a physician or with changing physicians for reasons associated with CTP. Income was also not associated with accessing CTP from an authorized source.

Acceptability

Acceptability refers to patients' perceptions of physicians' attitudes regarding CTP and of the federal program, as well as indices of patient–physician communications. Table 6 summarizes the key findings related to acceptability. Respondents reported some reluctance regarding communication with physicians related to CTP. Approximately half of the respondents reported that they had at some time wanted to discuss CTP with a physician but had not done so. Among respondents who wanted to discuss CTP but refrained, more than one third had not discussed CTP with any physician. The most frequent reason for not discussing CTP despite a desire to do so was "don't feel comfortable", followed by "illegal", and "can't afford cannabis".

Although our sample was comprised of *current* users of CTP, queries regarding *past* avoidance of CTP also evinced patient concerns regarding potential reactions from physicians and others. The most frequently cited reason for avoiding CTP was "I could be discriminated against", followed by "Doctors might find it annoying to be asked about cannabis", "Discussing cannabis could distract a doctor" and "It could make me drowsy".

Answers to an open ended question related to physicians' perceived negative response to CTP included: "After multiple negative responses from doc, I've stopped broaching the subject."; "He shut me down every time I brought it up." Several responses also

indicated concern that discussing CTP with a physician might have a negative impact on their patient/physician relationship: "fear of getting no treatment at all"; "fear of losing my doctor"; "I am afraid they will black list me as a patient and I would not have access to health care!" Compared to their communication with their physician regarding other medical issues, half of the respondents were less satisfied with their communication about the use of CTP, and almost one third reported that they often or always felt discriminated against by their physician because of their use of CTP.

Discussion

Utilizing a health services analytical framework, we examine barriers to access to CTP in terms of dimensions of *accommodation, accessibility, availability, affordability, and acceptability*. This in-depth analysis of barriers to access to CTP provides insights into access to CTP under the MMAR and may more broadly inform the safe, efficient and equitable provision of CTP under future programs. Our results suggest that, under the MMAR, Canadians faced substantial barriers to both legal authorization to possess CTP and access to a source of CTP. In addition, based on our findings, we conclude that many of these barriers do not appear to be addressed by the new MMPR and that the MMPR may exacerbate some barriers to access, particularly with regard to affordability.

Finding a physician to support an application to access CTP is a challenge for many Canadians who use CTP. Obtaining authorization to possess CTP requires the support of a physician, and the majority of respondents had discussed the use of CTP with a physician. However, a large proportion of respondents spoke to several physicians and many changed physicians in order to access CTP. Ultimately, less than one third of respondents had obtained authorization that allowed them to legally possess CTP, suggesting that despite the existence of a legal framework, a substantial number of chronically and seriously ill Canadians continue to access CTP without legal authorization and from illegal sources. This discrepancy may point to poor *accommodation* of the federal CTP program to client needs. Indeed more than 85% of respondents reported experiencing obstacles to accessing CTP. Among the minority of respondents who engaged with the federal program, over half found the process difficult, and nearly half were dissatisfied with the program.

Under the new MMPR, Canadians will need to obtain a medical document similar to a prescription from a physician or a nurse practitioner in order to have legal access to CTP. Given the reservations physicians had with signing a medical declaration on the application form under the MMAR, it is possible that physicians will be even more reluctant to prescribe CTP within the new regulatory framework, as noted in a recent statement by the Canadian Medical Association citing insufficient clinical evidence regarding CTP (Canadian Medical Association, 2013). Our findings support the need to build a stronger body of evidence regarding the appropriate therapeutic uses of cannabis for specific conditions as well as the need to better inform physicians of the evidence that *does* exist. Nurse practitioners will be allowed to prescribe CTP under the new MMPR in jurisdictions where they can prescribe, though it remains to be seen whether this will result in better access to CTP.

The current system also fails to accommodate access to a legal source of CTP. Among those who managed to obtain access to authorized sources of CTP (direct purchase from Health Canada, licensed self-production or licensed designated production), three quarters also accessed unauthorized sources. Only 7% of our sample accessed CTP exclusively from authorized sources, which suggests substantial barriers to efficient and acceptable authorized access.

The MMAR did not include medical cannabis dispensaries within the regulatory system, now do the new MMPR. The omission of

dispensaries from the revised regulatory framework may serve to maintain barriers to access; our findings suggest that *accessibility* to CTP was associated with the presence of medical cannabis dispensaries. British Columbia and Ontario have numerous medical cannabis dispensaries, whereas other regions have few, if any, dispensaries. Our finding of regional differences in the *accessibility* to CTP, with residents in BC and Ontario more likely to access CTP from a dispensary, was expected. Other regional differences may also be attributable to the presence of dispensaries. Specifically, BC has the greatest density and longest history of dispensary activity (Lucas, 2012b), and BC residents were more likely to have discussed CTP with a physician and less likely to purchase CTP from a friend or acquaintance. Although the cross-sectional nature of our study prevents assertions regarding causality, these findings suggest that services offered by medical cannabis dispensaries may reduce barriers in terms of *accommodation* by increasing options for sources of CTP, available strains and products, *accessibility* in terms of geographic location and store front services, and *acceptability* in terms of increasing physician consultation around CTP and reducing prevalence of illegal access through friends and acquaintances.

Access to CTP varied by medical condition and general quality of health. In particular, our findings indicate that respondents living with HIV/AIDS experienced fewer obstacles, were more likely to discuss CTP with physicians, less likely to change physicians related to CTP, and less likely to have physicians recommend CTP but refuse to endorse authorization. The relatively lower levels of obstacles faced by people living with HIV/AIDS may be attributed to several factors, including the relatively more established efficacy of the therapeutic uses of cannabis for the management of symptoms related to HIV/AIDS, the long history of grassroots advocacy for the use of CTP by the HIV/AIDS movement, and the potentially greater alliance between health care providers and patients among this community. These findings suggest that further research into factors that have facilitated access to CTP among people living with HIV/AIDS might help develop strategies to improve access for other groups. These findings also raise the possibility that prior research that focused exclusively on HIV/AIDS patients who use CTP (e.g. Belle-Isle & Hathaway, 2007) may present an underestimate of the obstacles experienced by the broader community of people who use CTP.

Also related to the dimension of *availability*, individuals who identified anxiety and/or depression as primary reasons for using CTP were less likely to discuss CTP use with physicians. This difference may reflect characteristics of these conditions, as behavioral inhibition and reduced communication may be associated with depression and anxiety (Angélico, Crippa, & Loureiro, 2013; Tse & Bond, 2004). This finding may also reflect concerns regarding stigmatization as the stigmas associated with mental illness and with cannabis use may combine to create a formidable barrier to open patient–caregiver communication. Alternately, this finding may reflect perceived reluctance on the part of physicians to recommend CTP for psychiatric symptoms. Given the prevalence of anxiety and depression in the general population, and the substantial problems with extant pharmacological treatments such as benzodiazepines and SSRIs (Gartlehner et al., 2011; Uzun, Kozumplik, Jakovljević, & Sedić, 2010), our findings of high levels of unauthorized CTP use to address these conditions suggest that further effort is required to better determine the antidepressant and anxiolytic efficacy of CTP.

General health status was also associated with difference in the availability of CTP, such that poorer health was associated with higher rates of physician communication and authorized access. Perhaps this finding indicates that Canadians wait until they are in desperate need of therapeutic options where other options have failed before they gather enough courage to speak to their physician

about CTP. Perhaps physicians are more comfortable supporting the use of CTP for Canadians who are in poorer health. Further inquiry could shed light on this finding. However, no differences according to general health status were observed with regard to experiencing obstacles to access, changing physicians related to CTP and physicians recommending CTP but refusing to endorse applications for authorized access. Nevertheless, our findings indicate that over a quarter of patients in poor health had the experience of physicians recommending CTP and refusing to assist with authorization. This finding points to the need for further education to address equivocation and reluctance on the part of physicians to assist patients in obtaining legal access to CTP.

Affordability of CTP is a significant barrier to access for many. Under the MMAR, Health Canada offered its cannabis at \$5 CDN per gram, plus applicable taxes. Cannabis on the street market ranges between as low as \$7 per gram to as high as \$28 per gram in Canada's northernmost region (priceofweed.com). Medical cannabis dispensaries tend to follow street market prices or offer cannabis at slightly lower cost, sometimes with sliding scale prices or limited donations for lower income clients (Lucas, P., pers. commun.). Commercial licensed producers offer cannabis between \$6 and \$12 per gram, confirming that the price of CTP increased as indicated in the government's Regulatory Impact Analysis Statement regarding the new MMPR (Government of Canada, 2012).

Our findings reveal that over half of respondents indicated that financial considerations interfered with their ability to treat symptoms with cannabis. Lower income individuals were most vulnerable to this obstacle, with approximately half of participants in the lowest income group reporting having to choose between CTP and other necessities. However, even a third of the highest income group reported difficulty affording CTP. Affordability appeared to disproportionately impact the most seriously ill patients, such that the group who reported fair to poor health were twice as likely as healthier patients to report having to choose between CTP and other necessities. Surprisingly, the lowest income group were more likely to have obtained authorization to possess, which suggests that it is the cost of cannabis per se, rather than the cost of obtaining authorization, that presents the primary barrier to affordability. The ubiquity of CTP-related financial strain highlights the need for developing approaches to mitigate financial barriers and integrate CTP within a subsidized medicine framework. This is increasingly important under the new MMPR, since Canadians who use CTP no longer have the cost-effective options of producing their own cannabis or obtaining a designated producer.

Finally, barriers to acceptability due to stigma and controversy that surrounds the use of CTP need to be addressed. In light of this stigma and controversy (Bottoroff et al., 2013), and evidence from surveys of physicians that indicate discomfort with CTP (Canadian Medical Association, 2012; Jones & Hathaway, 2008), we were not surprised that patients' perception of service providers' attitudes toward CTP users constituted substantial barriers to *acceptability* of services. Our findings allude to impeded frank and open discussions about CTP and a negative impact on continuity of care.

Indeed, almost half of the respondents had at some point wanted to discuss cannabis for medical purposes with a physician but avoided doing so, most commonly citing fear of discrimination and feelings of discomfort. Reports of patient–physician interaction suggest that such fears may not be unfounded; half of respondents were relatively less satisfied with CTP-related physician interactions than with interactions that were unrelated to CTP, and nearly one third reported experiencing CTP-related discrimination on the part of physicians. The large proportion of patients who changed doctors to access CTP, and who reported that physicians recommended CTP but would not sign official authorizations, provides further evidence of lingering discomfort related to CTP on the part of some physicians. This discomfort may stem from their stated

lack of knowledge about the medical use of cannabis (Canadian Medical Association, 2012; Jones & Hathaway, 2008) and their disapproval of smoking as a route of administration for any treatment (Canadian Medical Association, 2012). It may also stem from their personal views on cannabis use, which may be an interesting topic for further inquiry. Organizations such as the Canadian Consortium for the Investigation of Cannabinoids have developed programs to help educate physicians on the relative harms and benefits of CTP, and the past decade has witnessed a notable increase in the international acceptance of the therapeutic potential of cannabis. This increased prominence, together with the concerted efforts of CTP advocates and educators, may play a valuable role in helping to reduce barriers related to acceptability of services.

The ongoing prohibition of cannabis and associated anti-cannabis messages have tarnished its reputation as a potentially beneficial and safe therapeutic option, thwarted scientific inquiry and stigmatized both the plant and its users. Perhaps the current international climate of cannabis policy reform will bring about alternative policies to regulate cannabis and will slowly open doors for more rational and sensible investigation and education regarding its therapeutic uses.

Our study has several limitations. The cross-sectional nature does not permit causal inferences and it is possible that unmeasured factors may play an important role in determining access to CTP. Our sample consisted of mostly male, Caucasian and well educated respondents and our findings may not reflect the situation of other Canadians who use CTP. An additional limitation involves response biases related to participant self-selection, and recruitment through organizations that support people who use CTP. These factors likely resulted in overrepresentation in our sample by individuals who are strongly invested in increasing access to CTP. Conversely, barriers to access to CTP may be greater for those who may not have access to online resources or organizations that support people who use CTP. We also focused on barriers to access for those who are using CTP and did not delve into the barriers for people who may want to use CTP but are not able to overcome barriers to access. In light of these factors replication using a more systematic approach to recruitment is required to conclusively determine the extent to which the CTP users in our sample are representative of the broader community of Canadian CTP users. Also, our use of broad diagnostic categories and a single item measure of global health provide somewhat crude indices of health status. Although the use of discrete categories and single item measures of health are widely used (Bowling, 2005), future studies that employ more fine-grained assessments might provide additional valuable information.

These limitations are balanced by several strengths, including a relatively large national sample that tapped into both authorized and unauthorized CTP users across diverse medical conditions and health statuses. The engagement of both community and academic experts in the construction and dissemination of the survey is a further strength of our study, as it increased the breadth, relevance and validity of our queries. More broadly, our examination of issues related to access to CTP was guided by a theoretically informed analytical framework which added to our confidence regarding the dimensions that are central to access to health services.

Acknowledgements

This work is supported by a grant from the UBC Okanagan Institute for Healthy Living and Chronic Disease Prevention. The authors thank the people who took the time to respond to the survey. We also appreciate Audra Roemer and Kim Crosby's contribution to the data analysis.

Conflict of interest statement

None declared.

References

- Adlaf, E. M., Begin, P., & Sawka, E. (Eds.). (2005). *Canadian Addiction Survey (CAS): A national survey of Canadians' use of alcohol and other drugs: Prevalence of use and related harms: Detailed report*. Ottawa: Canadian Centre on Substance Abuse.
- Angélico, A. P., Crippa, J. A. S., & Loureiro, S. R. (2013). Social anxiety disorder and social skills: A critical review of the literature. *International Journal of Behavioural Consultation and Therapy*, 7(4), 16–23.
- Belle-Isle, L. (2006). *Cannabis as therapy for people living with HIV/AIDS: Our right, our choice*. Ottawa: Canadian AIDS Society.
- Belle-Isle, L., & Hathaway, A. (2007). Barriers to access to medical cannabis for Canadians living with HIV/AIDS. *AIDS Care*, 19(4), 500–506.
- Bottorff, J. L., Bissell, L. J. L., Balneaves, L. G., Olliffe, J. L., Capler, N. R., & Buxton, J. (2013). Perceptions of cannabis as a stigmatized medicine: A qualitative descriptive study. *Harm Reduction Journal*, 10(2). Retrieved from <http://www.harmreductionjournal.com/content/10/1/2>
- Bowling, A. (2005). Just one question: If one question works, why as several? *Journal of Epidemiology and Community Health*, 59, 342–345.
- Canadian Association of Medical Cannabis Dispensaries. (2013). *Dispensaries are indispensable: Compassion clubs launch first certification program*. Retrieved from <http://www.newswire.ca/en/story/1187053/dispensaries-are-indispensable-compassion-clubs-launch-first-certification-program>
- Canadian Medical Association. (2012). *MD role in use of medical marijuana baffles many doctors: Survey*. Retrieved from <http://www.cma.ca/md-role-medical-marijuana-baffles>
- Canadian Medical Association. (2013). *Statement from the Canadian Medical Association on new regulations on medical marijuana*. Retrieved from <http://www.cma.ca/multimedia/CMA/Content/Images/Inside.cma/Media.Release/2013/Statement.Medical.Marijuana.regulations.en.pdf>
- Capler, N. R. (2010). Canadian Compassion Clubs. In J. Holland (Ed.), *The pot book: A complete guide to cannabis* (pp. 432–440). Rochester, Vermont: Park Street Press.
- Gartlehner, G., Hansen, R. A., Morgan, L. C., Thaler, K., Lux, L., Van Noord, M., et al. (2011). Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: An updated meta-analysis. *Annals of Internal Medicine*, 155(11), 772–785. <http://dx.doi.org/10.1059/0003-4819-155-11-201112060-00009>
- Government of Canada. (2012). *Marihuana for medical purposes regulations*. *Canada Gazette*, 146(50). Retrieved from <http://gazette.gc.ca/rp-pr/p1/2012/2012-12-15/html/reg4eng.html>
- Health Canada. (2013). *Marihuana medical access program statistics*. Retrieved from <http://www.hc-sc.gc.ca/dhp-mps/marihuana/stat/index-eng.php>
- Holland, J. (Ed.). (2010). *The pot book: A complete guide to cannabis: Its role in medicine, politics, science, and culture*. Rochester, Vermont: Park Street Press.
- Jacobs, B., Ir, P., Bigdeli, M., Annear, P. L., & Van Damme, W. (2012). Addressing access barriers to health services: An analytical framework for selecting appropriate interventions in low-income Asian countries. *Health Policy and Planning*, 27, 288–300.
- Jones, C., & Hathaway, A. D. (2008). Marijuana medicine and Canadian physicians: Challenges to meaningful drug policy reform. *Contemporary Justice Review: Issues in Criminal, Social, and Restorative Justice*, 11(2), 165–175.
- Lucas, P. (2012a). It can't hurt to ask: A patient-centered quality of service assessment of Health Canada's medical cannabis policy and program. *Harm Reduction Journal*, 9(2). Retrieved from <http://www.harmreductionjournal.com.ezproxy.library.uvic.ca/content/pdf/1477-7517-9-2.pdf>
- Lucas, P. (2012b). Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. *Journal of Psychoactive Drugs*, 44(2), 125–133.
- Penchansky, R., & Thomas, J. W. (1981). The concept of access: Definition and relationship to consumer satisfaction. *Medical Care*, XIX(2), 127–140.
- Peters, D. H., Garg, A., Bloom, G., Walker, D. G., Brieger, W. R., & Rahman, M. H. (2008). Poverty and access to health care in developing countries. *Annals of the New York Academy of Sciences*, 1136, 161–171.
- Shelef, A., Mashiah, M., Schumacher, I., Shine, O., & Baruch, Y. (2011). Medical grade cannabis (MGC): Regulation mechanisms, the present situation around the world and in Israel. *Harefuah*, 150(12), 913–917.
- Tse, W. S., & Bond, A. J. (2004). The impact of depression on social skills: A review. *Journal of Nervous and Mental Disease*, 192, 260–268. <http://dx.doi.org/10.1097/01.nmd.0000120884.60002.2b>
- Uzun, S., Kozumplik, O., Jakovljević, M., & Sedić, B. (2010). Side effects of treatment with benzodiazepines. *Psychiatria Danubina*, 22(1), 90–93.
- Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., et al. (2013). Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use. *International Journal of Drug Policy*, 25(6), 511–516.
- Ward, S. E., Goldberg, N., Miller-McCauley, V., Mueller, C., Nolan, A., Pawlik-Plank, D., et al. (1993). Patient-related barriers to management of cancer pain. *Pain*, 52(3), 319–324.

This is Exhibit F referred to in the
affidavit of Professor Zachary Walsh
sworn before me, this 28th
day of September 20²³
.....
A COMMISSIONER, ETC

Sworn remotely by Prof. Zachary Walsh in the City of West Kelowna, BC
with commissioner Paul Lewin in the City of Toronto, ON.

COMMENTARY

Open Access



Why a distinct medical stream is necessary to support patients using cannabis for medical purposes

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Abstract

Background Since 2001, Canadians have been able to obtain cannabis for medical purposes, initially through the Access to Cannabis for Medical Purposes Regulations (ACMPR). The Cannabis Act (Bill C-45) came into force on October 17, 2018, replacing the ACMPR. The Cannabis Act enables Canadians to possess cannabis purchased from a licensed retailer without authorization for either medical or nonmedical purposes. The Cannabis Act is currently the guiding legislation which governs both medical and nonmedical access. The Cannabis Act contains some improvements for patients but is essentially the same as its previous legislation. Beginning in October 2022, the federal government is conducting a review of the Cannabis Act and is questioning whether a distinct medical cannabis stream is still required, given the ease of access to cannabis and cannabis products. Although there is overlap in the reasons for medical and recreational cannabis use, the distinct legislation of medical versus recreational use of cannabis in Canada may be under threat.

Main body A large segment of the medical, academic, research, and lay communities agree that there is a need for distinct medical and recreational cannabis streams. Perhaps most importantly, separation of these streams is necessary to ensure that both medical cannabis patients and healthcare providers receive the required support needed to optimize benefits while minimizing risks associated with medical cannabis use. Preservation of distinct medical and recreational streams can help to ensure that needs of different stakeholders are met. For example, patients require guidance in the form of assessing the appropriateness of cannabis use, selection of appropriate products and dosage forms, dosing titration, screening for drug interactions, and safety monitoring. Healthcare providers require access to undergraduate and continuing health education as well as support from their professional organizations to ensure medical cannabis is appropriately prescribed. Although there are challenges in conducting research, as motives for cannabis use frequently straddle boundaries between medical versus recreational cannabis use, maintenance of a distinct medical stream is also necessary to ensure adequate supply of cannabis products appropriate for medical use, to reduce stigma associated with cannabis in both patients and providers, to help enable reimbursement for patients, to facilitate removal of taxation on cannabis used for medical purposes, and to promote research on all aspects of medical cannabis.

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Conclusion Cannabis products for medical and recreational purposes have different objectives and needs, requiring different methods of distribution, access, and monitoring. HCPs, patients, and the commercial cannabis industry would serve Canadians well to continue to advocate to policy makers to ensure the continued existence of two distinct streams and must strive to make ongoing improvements to the current programs.

Keywords Cannabis, Cannabinoid-based medicine, Medical cannabis, Access

Background

In 2001, the Marijuana for Medical Purposes Regulations (MMPR), which has since evolved into the Access to Cannabis for Medical Purposes Regulations (ACMPR), was introduced, allowing individuals to obtain cannabis and cannabis products for the management of medical symptoms and diseases (Health Canada 2005). The ACMPR ensured that individuals can legally possess cannabis providing they have clinician authorization (Health Canada 2005). On October 17, 2018, the Cannabis Act (Bill C-45) came into force, replacing ACMPR regulations. These new regulations enable Canadians to possess medical or non-medical cannabis purchased from a licensed retailer without authorization (House of Commons of Canada 2022). The overarching goals of this legislation were to eliminate the illicit cannabis market, to provide a safe regulated supply, and to prevent youth from accessing cannabis (House of Commons of Canada 2022). Beginning October 2022, the federal government is conducting a review of the Cannabis Act and is questioning whether a distinct medical stream is still required, given the ease of access to cannabis and cannabis products. As seen in Uruguay and certain US states, where cannabis has also been legalized, there is debate surrounding the best policy approach to cannabis use (Kilmer 2019). In a systematic review on international perspectives regarding implications of cannabis legalization, Bahji et al. identified 36 studies which explored various aspects of cannabis legalization including health, epidemiology, health service utilization, public policy, crime, and economic implications (Bahji and Stephenson 2019). The majority of studies reported that cannabis use increased over time, and there were increases in the number and rates of emergency room visits for cannabis-related presentations, such as cannabis intoxication and cannabis-related hyperemesis; however, reductions in the rates of opioid prescribing were also noted. Rates of major crime have also fallen by 15–30% in US states with legalized cannabis (Bahji and Stephenson 2019). There remains significant controversy regarding the overall impact of legalization, especially on mental health and public policy (Bahji and Stephenson 2019). Bahji et al. concluded that there is a paucity of findings related to cannabis legalization, and

available studies are relatively heterogeneous, making conclusions difficult to draw at this time (Bahji and Stephenson 2019).

What are the pros and cons of the current medical system?

The current medical access program for cannabis has both strengths and limitations. Advantages of legalization of nonmedical cannabis include reducing harms from criminalization of cannabis possession, regulating the distribution and content of product, and increasing government revenue through taxation. However, one of the most important limitations is that the Cannabis Act does not ensure medical cannabis patients will obtain any healthcare provider support as the act does not require this interaction. The Cannabis Act should provide mechanisms to support both patients and healthcare providers. Patients using cannabis for medical purposes require reliable sources of information and guidance from well-trained healthcare providers. Similarly, healthcare providers require ongoing support such as continuing education programs and appropriate documents for authorizing cannabis. Although some resources currently exist for healthcare providers and the public including information provided on websites by the government of Canada and programs created by universities, they are sparse and inadequate (Health Canada 2018; UBC CPD 2020).

Beyond direct patient benefits, medical involvement has contributed to the discovery of new therapeutic applications for cannabinoids including chronic pain management, multiple sclerosis, chemotherapy-induced nausea and vomiting, epilepsy, and palliative care, in patients who are insufficiently managed via other modalities. As such, cannabinoids are generally a highly acceptable option for many patients and may play a useful role as an adjunct therapy (Busse et al. 2021; Wang et al. 2021; Health Canada n.d.). In some reports, over half of cannabis consumers were able to reduce or adjust their use of other medications, including opioids, through addition of medical cannabis to their regimens (Minhas and Lunn 2022). In a systematic review, Nielsen et al. identified 19 preclinical and 9 clinical studies which provided evidence of an opioid-sparing effect of cannabinoids (Nielsen et al. 2017). Of the 19 preclinical studies, 17 provided evidence

of synergistic effects from cannabinoids and opioid co-administration (Nielsen et al. 2017).

In general, randomized clinical trials provide stronger evidence than do observational studies, while rigorous observational studies provide stronger evidence than uncontrolled case series. Indications approved by national regulatory authorities, and for which they document conclusive or substantive evidence in a 2017 publication, includes chemotherapy-induced nausea and vomiting, patient-reported multiple sclerosis spasticity symptoms, and chronic neuropathic pain (National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda 2017). Authors report moderate evidence for improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis and limited evidence for cannabis and HIV-associated cachexia, symptoms of Tourette syndrome, anxiety symptoms (as assessed by a public speaking test, in individuals with social anxiety disorders), and posttraumatic stress disorder (National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda 2017). A more recent systematic review and meta-analysis also reported on potential therapeutic benefit of cannabinoids (McKee et al. 2021). The authors concluded there is limited evidence of the effectiveness of CBD to treat psychiatric symptoms (McKee et al. 2021). Similarly, a systematic review on the effectiveness of medical cannabis for psychiatric, movement and neurodegenerative disorders reported that a definitive conclusion on cannabinoid efficacy could not be drawn (Lim et al. 2017). It reported that upon evaluation of trials, there were significant methodological issues including inadequate description of allocation concealment, blinding, and underpowered sample size (Lim et al. 2017). Another publication included an evidence map of 44 systematic reviews which included evidence from 158 individual studies (Montero-Oleas et al. 2020). Conditions included in the analysis were multiple sclerosis, movement disorders (Tourette's syndrome, Parkinson disease), psychiatry conditions, Alzheimer's disease, epilepsy, acute and chronic pain, cancer pain, neuropathic pain, symptoms related to cancer (vomiting, anorexia related to chemotherapy), rheumatic disorders, HIV-related symptoms, glaucoma, and COPD. Evidence was heterogeneous regarding the conclusions and quality of primary studies (Montero-Oleas et al. 2020). Medical cannabis has also been examined for conditions such as

gynecologic pain conditions, with most data from surveys of women in prospective cohort studies (Liang et al. 2022). Although most women reported pain reduction, the authors caution that interpretation of data is limited due to varying cannabis formulations, delivery methods, and dosages precluding definitive conclusions (Liang et al. 2022). Taken together, although cannabinoids' effectiveness has been examined in a wide spectrum of conditions, conclusions are often weak due to important methodological limitations.

Through the Cannabis Act, these changes can be documented and supported under medical supervision. Moreover, to better understand potential harms associated with cannabis use, Health Canada maintains a system for reporting adverse events associated with cannabis products through its Canada Vigilance website (Health Canada 2020a). The government of Canada outlines adverse event responsibilities for both retailer and healthcare providers. Consumers or patients who are using cannabis products for medical or nonmedical purposes and who have experienced a side effect are encouraged to consult with their healthcare practitioner for both management and for completion of side effect reports. This can be done online or via a toll-free telephone number. Guidance on how to complete the report is provided on the website, and additional information can be found at MedEffect Canada (Health Canada 2020b).

The premise of fairness and equity is the backbone of Canada's healthcare system, which provides universal and publicly funded healthcare. It was created from the Canada Health Act and strives to comply with the five pillars of that act, which states that the system must be universal, publicly administered, have comprehensive coverage, portable across provinces, and accessible to the population. An important limitation of the current Cannabis Act is that decisions about retail cannabis distribution are delegated to individual provinces and territories, resulting in regional heterogeneity in retail approaches. For example, in Quebec, there are government retailers which sell cannabis, whereas in British Columbia, there are mixed public and private retail businesses (Fischer et al. 2021; Wilkins and Rychert 2021). In terms of access, there are inequities across provinces. The Cannabis Act permits direct mail order and home delivery anywhere in Canada for individuals medically authorized to use cannabis. However, this is only available in certain provinces under the Cannabis Act, thereby limiting access to eligible patients. Regulatory variations across provinces contribute to uncertainty of healthcare providers about appropriateness of authorizing medical cannabis, namely cannabidiol (CBD), to pediatric populations for the treatment of epilepsy (Minhas and Lunn 2022). As prescription CBD products are not available in Canada, the

Cannabis Act is the only legal mechanism to obtain CBD for disorders such as pediatric epilepsy (Huntsman et al. 2021). Provincial discrepancies have also raised concerns about disparities in cannabis use and harms. Following legalization of recreational cannabis, there has been increased concentrations of cannabis retailers in neighbourhoods of lower socioeconomic status (Myran et al. 2022). The variation has been fuelled by rapid expansion of retail outlets in certain jurisdictions, especially those with a private retail market (Myran et al. 2022).

There are also limitations with the existing medical document which requires the clinician to provide the quantity authorized in grams of dried flower per day. Cannabinoids extracted from dry flower varies, which renders daily dosage conversion from milligrams of the desired cannabinoid to grams of dried cannabis highly variable and complicating the authorization process. Furthermore, different processes for cannabinoid extraction from dried cannabis plant may result in extracts with distinct cannabinoid, terpenoid, and residual solvent profile (Hazekamp 2018). The most appropriate form of medical cannabis depends on the indications for use. Accurate and appropriate prescription of oral oils and capsules requires specifying milligrams of extracted delta-9 tetrahydrocannabinol (THC) and CBD. Furthermore, the medical document does not require specific dosing instructions. Documents should also be revised to allow for the inclusion of more than one product and those administered by different routes (i.e., oil taken orally vs vaporized) on the same form. The most appropriate, accurate, and pragmatic solution is the use of a standard medical prescription document for all clinicians who authorize cannabis.

From a fiscal perspective, there are also important considerations for accessibility to cannabis. The Cannabis Act allows costs for Canadian veterans and other patients, such as those suffering from workplace injury, to be covered by some public or private insurers. This process recognizes cannabis as a medical necessity for these patients. The process of medical authorization of cannabis enables coverage to be determined and maintained as deemed medically appropriate. Additionally, in contrast to other prescription medication, sales and excise tax add further inappropriate financial burden to patients. Most patients pay out of pocket due to lack of insurance coverage. A survey by Health Canada reported that 91% of persons using cannabis for medical reasons reported no insurance coverage (Health Canada 2021). As with all prescription medications, opioids are not taxed and are covered by government and insurance plans; there is concern that patients may choose opioids over cannabis even though they are less safe, on a patient and societal level, for long-term use (Minhas and Lunn 2022).

There are also noteworthy limitations with the Cannabis Act. Despite a regulatory system in place which allows access to cannabis for medical purposes since 2001, regulatory requirements restrict researchers to using exclusively products manufactured under Good Manufacturing Practices (GMP) in human clinical trials. The purpose for this restriction is to ensure products adhere to quality standards of consistency and control (Rueda et al. 2022a). This restriction is problematic since commercial cannabis, purchased and used by patients and consumers in the “real-world” setting, is manufactured under Good Production Practices (GPP). GMP cannabis not being commercially manufactured, renders the product, for the most part unavailable severely impeding research. Since the cannabis industry is not required to partake in the standard drug approval process when seeking approval for medical use, there is little incentive to support research to have their products approved for the medical market (Rueda et al. 2022a). Furthermore, researchers must wait in the same cue as licensed producers when seeking approvals from Health Canada, making for potentially lengthy waiting times and delaying study initiation.

Is a distinct medical access program necessary to provide individuals with reasonable access to cannabis for medical purposes?

The goals of medical and nonmedical cannabis are very distinct. In our view, access to medical cannabis cannot be ensured through the current nonmedical framework, and these two streams require distinct access streams. Reasons for the separation of the two streams are outlined in Table 1.

Patient perspective

Several studies have been conducted on the use of cannabis for the management of diverse types of chronic pain. Research typically demonstrates moderate benefit of cannabis in chronic pain management. There is also evidence

Table 1 Reasons requiring maintenance of a separate stream for cannabinoid-based medicine (CBM)

• Ensure adequate guidance from healthcare providers (HCPs) to medical cannabis user
• Provide monitoring for adverse events and completion of adverse drug event forms by HCP
• Eliminate stigma experienced by CBM users and providers
• Enable reimbursement of CBM
• Facilitate removal of taxation on CBM
• Promote research on all aspects of CBM
• Ensure adequate supply of medical CBM products

for efficacy of cannabis in the management of comorbidities, including sleep disorders, anxiety, and appetite suppression, and for managing symptoms in some chronic conditions associated with pain including HIV, multiple sclerosis, fibromyalgia, and arthritis. However, there exist several challenges within cannabis-based medicines and chronic pain research. With respect to some co-occurring conditions, there still exist relatively few controlled trials. As we reviewed, data related to comorbid conditions, it was not typically the primary focus of included studies and, subsequently, may be underpowered. The lack of comparative studies where the safety and efficacy of cannabis and cannabis-based medicine are compared with typical pain treatments is also problematic. In addition, challenges commonly exist with unmasking in placebo-controlled trials, representing potential risk of bias, especially as pain and many comorbidities are measured with VAS or other subjective measures (Bell et al. 2023).

Importantly, cannabis use may also be associated with both short-term and long-term harms, and these effects have significant inter-patient variability (Health Canada 2023). Short-term risks include drowsiness, slowing of reaction time, reducing ability to pay attention, and impaired coordination, all of which can impact driving or operating equipment. Learning and memory can be adversely impacted. Cannabis can also affect mental health and induce panic and anxiety or trigger a psychotic episode (Health Canada 2023; Siklos-Whillans et al. 2021). In the long-term, inhalation of smoked cannabis is associated with exposure to the same toxic chemicals as found in cigarette smoke. Over time, cannabis use can result in cannabis dependence in the form of addiction, cannabis use disorder, and problematic cannabis use. Addiction can lead to serious harm to health, social life, occupation, and financial future (Health Canada 2023; Siklos-Whillans et al. 2021). Each method of cannabis consumption carries different health and safety risks, and each person's response is different and depends on sex, age, THC and CBD content, preexisting medical conditions, previous experience with cannabis, frequency of use, and consumption of food, alcohol, or other drugs or health products. Everyone's response to cannabis may also vary from one time to the next (Health Canada 2023; Siklos-Whillans et al. 2021).

As with all medications, optimal therapy requires clinical guidance to provide appropriate patient selection, safe dosing, method of administration, monitoring of efficacy and tolerability, avoidance of side effects, drug and disease interactions, and patient education (Huntsman et al. 2021; Wright et al. 2020). Pediatric use, usually for management of refractory epilepsy, is an extreme example of the need for a medical stream to ensure not only safety and efficacy but also for access to specific CBD products

(Huntsman et al. 2021). Under the law, cannabis treatment for children must be authorized by a physician or nurse practitioners, which provides an opportunity for patient counselling and education (Huntsman et al. 2021). This can only be provided through a medical framework. Patients must not rely on the advice of cannabis salespersons, commonly referred to as "budtenders," who lack the knowledge, experience, training, and motivation for the task. Additionally, if the medical cannabis stream is removed, then pediatric patients will be required to obtain cannabis from a dispensary. However, currently to purchase recreational cannabis, you must be 19 years of age. Thus, for a pediatric patient to obtain medical cannabis, their parent would need to purchase it under their name and then "divert" the cannabis to the child, which is clearly inappropriate. Another major consideration pertains to the stigma associated with cannabis, which remains a major barrier to use (Troup et al. 2022; Ng et al. 2021). Patients require the support of a healthcare provider not only to manage their own trepidation but also to legitimize use to their family, employer, and broader social network. Moreover, the fact that licensed naturopathic doctors (NDs) are not included in the list of HCPs who can authorize cannabis should be re-examined. NDs are the very HCPs who are specifically trained in botanical medicine and pharmacognosy (the science of natural drugs obtained from organisms such as most plants, microbes, and animals), but they were entirely overlooked in the Cannabis Act. NDs have prescriptive authority in Ontario and British Columbia, and naturopathic medicine is a regulated health profession with government oversight. Therefore, the Cannabis Act may benefit from an amendment to include a regulated health profession that is most familiar with plant-based medicines. Finally, government photo identification is required to purchase cannabis via dispensaries, but not in medical stream. This creates a further barrier for individuals without photo identification, as may be the case for homeless individuals who could benefit from using cannabis as a harm reduction tool.

The healthcare system

Cost is a major barrier to utilization of medical cannabis. For example, 40 mg of CBD + 10 mg THC daily is approximately US \$170 CAD/month. While some insurers and Veteran's Affairs provide coverage for cannabis accessed through the medical program, it is unlikely to continue in the absence of such a program. Important issues also exist related to taxation. Currently, medical cannabis users in Canada must pay full sales tax. Additionally, federal excise ("sin") tax is applied to all products containing THC in the amount of US \$1 CAD/g or 10% of the final price. Additionally, 4 provinces add provincial/territorial

excise (“sin”) tax, including Alberta, Ontario, Saskatchewan, and Nunavut. While this is appropriate for non-medical use, cannabis is the only prescribed medication to which any taxation applies. We believe this is inappropriate. An Environics poll indicated that 62% of Canadians opposed taxation on medical cannabis, and there is strong patient advocacy to eliminate this tax (Canadians for Fair Access to Medical Marijuana (CFAMM) n.d.). Currently, patients can claim costs of medical cannabis as a deductible medical expense, if approved by a physician, when filing their annual income tax. The absence of a cannabis medical stream will exclude any possibility of elimination of unfair taxation and remove the medical expense deduction. In Canada, prices of legal cannabis are significantly higher than those from illicit sources, largely due to taxation (Health Canada 2022). This disincentivizes use of the safe legal source (Rosic et al. 2021). Therefore, while the Cannabis Act was designed to remove the illicit market, it may actually be strengthening the illicit market when retail prices are too high.

Despite the wide spectrum of opinions regarding the need for distinct medical versus recreational streams, there is broad agreement that there is an urgent need for medical cannabis research. There are many areas of cannabis medicine which require better understanding. In addition to regulatory challenges with conducting research, there are also challenges related to the fact that motives for cannabis use frequently straddle boundaries between medical versus recreational use. For example, in the context of stress management and anxiety, individuals frequently report cannabis use for these indications as both medicinal and recreational (Mannes et al. 2018; Bruce et al. 2020). In a self-report assessment of 709 cannabis users in Canada prior to federal cannabis legalization, Turna et al., characterized patterns of cannabis use (recreational and medical), other substance use, and psychiatric symptoms (Turna et al. 2020). Sixty-one percent of participants endorsed exclusively recreational use, and 39% reported some level of medical use. Compared to recreational users, medical users reported more problematic cannabis use and greater burden of psychiatric symptoms, such as anxiety, depression, and trauma. A large majority of medical users also reported using recreationally, while exclusive medical use was less frequent (81% vs. 19%, respectively) (Turna et al. 2020). Participants in the dual-motives group reported more daily cannabis use and more alcohol and tobacco use. Moreover, participants using cannabis for both medical and recreational purposes more often used cannabis to treat psychiatric conditions compared to participants endorsing medical-only use. Interestingly, several participants reported decreasing their other medications, such as analgesics, anti-inflammatories, and antidepressants in

lieu of cannabis (Turna et al. 2020). As the authors highlight, reduction of antidepressant doses may be the cause for concern given that antidepressants are first-line efficacious for anxiety and depression. Thus, differences in cannabis use patterns and preferences exist between recreational and medical cannabis users and within medical users. As suggested by the authors, dual motive individuals who use cannabis may warrant special attention as a subpopulation (Turna et al. 2020).

Research funding opportunities are made available, both at the federal level, for example, by the Canadian Institutes for Health Research and various provincial initiatives. The absence of a cannabis medical stream will work strongly against ongoing research support (Rueda et al. 2022b; C. B. C. Radio 2021; Webster 2021). In terms of strain and format availability, under the current 2-stream model, licensed cannabis producers offer a wide variety of medical cannabis products (e.g., flower, oil, capsules) and ranges of CBD, THC, and combined forms. However, nonmedical cannabis users tend to focus on smoked cannabis, with high THC and low CBD levels. The absence of a dedicated medical cannabis stream will likely reduce demand for high CBD and low THC chemotypes in oral formulations. As many licensed producers tend to be fiscally motivated, the absence of a cannabis medical stream may reduce availability of appropriate chemotypes and accurate dosing formats.

The healthcare provider

Although most trainees had little exposure to cannabis and cannabinoid-based medicine (CBM) in their curricula in the past (Elkrief et al. 2020; St Pierre et al. 2020), most Canadian medical schools have now incorporated CBM into their programs. Accredited continuing health education programs on CBM are widely available. However, the absence of a cannabis medical stream will likely reduce or eliminate the availability of ongoing medical education. Furthermore, stigma directed at CBM prescribers will likely persist, or even worsen, in the absence of a medical cannabis stream (Troup et al. 2022; Ng et al. 2021).

There is controversy within the medical community about the need for separate medical and recreational streams for cannabis (Owens 2018). The Canadian Medical Association does not support the maintenance of separate streams “primarily related to the limited evidence to support many of the therapeutic claims made regarding cannabis for medical purposes, and the need to support health practitioners in their practice” (Canadian Medical Association 2019). In contrast, the Canadian Nurses Association (CNA) statement on medical cannabis is as follows: “The CNA supports and advocates for two streams (medical and non-medical). Supporting

these two streams aligns with CNA's work on access to care and equity" (Canadian Nurses Association n.d.). The Canadian Pharmacists Association statement on medical cannabis indicates that "two distinct streams will allow for the unique needs of medical patients to be met, will contribute to harm reduction, that patients should not be expected to self medicate without support from HCP, it will protect the supply chain to meet patient needs, could lead to more systemic benefits" (Canadian Pharmacists Association 2016). A distinct medical stream for cannabis is also supported by the Arthritis Society of Canada, the Canadian Spondylitis Association, the Canadian Arthritis Patient Alliance, and the Canadian Society of Intestinal Research (GI Society n.d.; Canadian Arthritis Patient Alliance n.d.; Canadian Spondylitis Association n.d.; Arthritis Society of Canada n.d.). Our views are consistent with these latter healthcare associations which are in favor of separate medical and recreational streams.

What specific reforms are recommended?

We recommend the continuation of a distinct medical cannabis stream, in addition to several adjustments to improve the current systems in place, as outlined in Table 2. New therapeutic potential for cannabinoids is discovered when observations are documented by HCPs and reporting under medical supervision, as provided through the Cannabis Act. Adverse event reporting could take place through the Canada Vigilance Program (Huntsman et al. 2021). Community pharmacies are ideally placed to dispense medical cannabis products, as most already have the necessary infrastructure and experience in place for ordering and storing controlled substances and providing education and ongoing support (Huntsman et al. 2021). Additionally, although it is

not standard across the country, some colleges, such as the Ontario College of Pharmacists (Ontario College of Pharmacist n.d.), mandate cannabis education for all pharmacist who are licensed to provide direct patient care by their college. As pharmacists are trained to assess drug-drug interactions and adverse effects, we support the CPHA position statement on medical cannabis which states that pharmacists are best suited to advise patients and oversee the safe storage and dispensing of medical cannabis (Huntsman et al. 2021; Canadian Pharmacists Association 2016). Health Canada should also mandate reporting of serious adverse effects associated with medical cannabis by pharmacists and other healthcare providers.

From an HCP perspective, we suggest creation of a simplified authorization process to help clinicians (i.e., use specific dosing in mg, not grams of flower/day), and that the medical document emulates a standard medical "prescription" specifying a total quantity of each cannabinoid and clear instruction on dosing, for example, *THC 5 mg capsules taken by mouth twice daily, CBD 20 mg capsules taken by mouth twice daily, dispense 1 month supply*. The tax placed on medical cannabis should be removed.

We urge reform to the act permitting the use of GPP cannabis in clinical research as people who use cannabis for medical purposes currently access commercial products manufactured under GPP standards. We also urge for review the quality control regulations of products under the Cannabis Act, since patients who require close dose monitoring and particular formulations require assurance that their products are manufactured to an acceptable standard of quality. It is necessary to incorporate the consumer health

Table 2 Recommended reforms for the current medical cannabis stream

- Encourage documentation and reporting by healthcare providers (HCPs), such as when new observations are made regarding the use of medical cannabis
- Mandate adverse event reporting by HCPs through the Canada Vigilance Program
- Increase the involvement of pharmacists in the dispensation of cannabis, screening for drug interactions, and on provision of counseling for medical cannabis
- Encourage colleges of pharmacists to strongly encourage cannabis education for pharmacists
- Mandate reporting of serious adverse effects associated with medical cannabis by pharmacists and other healthcare providers
- Create a simplified authorization process to help clinicians and create a medical document emulating a standard medical "prescription" which specifies a total quantity of each cannabinoid and clear dosing instructions
- Remove the tax on medical cannabis
- Reform the Cannabis Act to permit the use of Good Production Practices (GPP) cannabis clinical research
- Review the quality control regulations of products under the Access to Cannabis for Medical Purposes Regulations (ACMPR) or the Cannabis Act
- Incorporate the consumer health products framework, which will have impact on medical access to cannabidiol (CBD) products and allow the ACMPR to focus on access to delta-9 tetrahydrocannabinol (THC)
- Expand all forms of research, including that on harm reduction and cost-effectiveness of cannabis
- Take into consideration the perspectives of diverse patient representatives prior to implementing changes to the Cannabis Act

products framework, since this will have impact on medical access to CBD products (enabling pharmacy support) and allow the Cannabis Act to focus on access to THC. Expanding all forms of research, including that on harm reduction and cost-effectiveness of cannabis, since real-world evidence suggests that access to medical cannabis is associated with reduced prescribed medication and healthcare utilization. Individuals using medical cannabis have less opioid use (Boehnke et al. 2016; Reiman et al. 2017). In prospective cohorts in Vancouver of persons at high risk of opioid overdose, consistent cannabis use was associated with increased engagement in opioid agonist treatment for opioid use disorder (Hurd et al. 2019), reduced frequency of illicit opioid use for chronic pain, and lower rates of fentanyl exposure (Lake et al. 2019, 2020). Lastly, we suggest ensuring the perspectives of diverse patient representatives are taken into account prior to implementing any changes to the Cannabis Act. These reforms could substantially improve health-related outcomes as well as effectiveness and cost-effectiveness of many healthcare interventions. Patient engagement with HCP has been associated with positive treatment outcomes including improved control of diabetes, better physical functioning in rheumatic diseases, enhanced patients' compliance with secondary prevention measures, and improved health in individuals who have suffered myocardial infarction (Arnetz et al. 2004, 2008; Rachmani et al. 2002; Loh et al. 2007). In fact, patient participation is not only regarded as a legal right of patients but is also considered an international gold standard for healthcare systems (Vahdat et al. 2014).

Abbreviations

CBD	Cannabidiol
ACMPR	Access to Cannabis for Medical Purposes Regulations
CNA	Canadian Nurses Association
GMP	Good manufacturing practices
GPP	Good Production Practices
HCP	Healthcare provider
MMPR	Marijuana for Medical Purposes Regulations
NDs	Naturopathic doctors
THC	Delta-9 tetrahydrocannabinol

Acknowledgements

Not applicable.

Contributors

We are a diverse group of stakeholders consisting of clinicians, clinician researchers, nurses, pharmacists, and patient advocates active in the field of medical cannabis. Based on the need to fill a clinical knowledge gap related to cannabis-based medicines for the management of chronic non-cancer pain and co-occurring conditions, we performed an extensive systematic review to guide healthcare providers and patients. The resulting guidelines, "Clinical Practice Guidelines for Cannabis and Cannabinoid-Based Medicines in the Management of Chronic Pain and Co-Occurring Conditions," have been published online ahead of print in the *Journal of Cannabis and Cannabinoid Research* (2023 Mar 27. doi: 10.1089/can.2021.0156) at the time of publishing this commentary.

Authors' contributions

CTC and AB drafted the commentary. CM edited the commentary. All co-authors provided input into the contents of the commentary and critically revised and approved the final version.

Authors' information

Not applicable.

Funding

None to declare.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

SR, TS, and JD declare that they have no competing interests. CC has received cannabinoid capsules in-kind from Tilray Inc, for use in a pilot clinical trial and small grant support from Tilray Inc, to conduct a survey on healthcare practitioner perceptions on barriers impacting cannabis prescribing practices. G. L.'s former employer, the Canadian AIDS Society, has received a grant from Canopy Growth Corporation to support the development of clinical practice guidelines on the use of cannabis and cannabinoid-based medicine for chronic non-cancer pain. Z. W. is an advisory board member of Multidisciplinary Association for Psychedelic Studies — Canada, and for the Canadian Association of Medical Cannabis Dispensaries. He is in the planning phases of becoming an investigator on a survey study sponsored by Doja, from which he does not receive any direct financial compensation; however, graduate students in his lab receive paid research assistantships. He is the coordinating principal investigator on a clinical trial of cannabis for PTSD that is sponsored by Tilray, from which he does not receive any direct financial compensation. Graduate students in his lab receive paid research assistantships from Tilray. SM is the co-owner of a start-up company ("Cannabiscotti Inc.") that will be applying for a cannabis processing license. She holds shares in Canopy Growth Corporation, Emblem Corp., and Aphria Inc. She has received honorarium for research projects funded by Canopy Growth Corporation and Tilray. A. B. has received funding for consulting, speaking, and/or research from the following commercial organizations: Amgen, Bristol Myers Squibb, Janssen, AstraZeneca, Novartis, Pfizer, Bayer, Lilly, Boehringer Ingelheim, HLS Therapeutics, Spectrum Therapeutics, Sanofi, Bausch Health, Akcea, and Eisai. He has contributed, pro bono, to publications, position statements, and/or clinical practice guidelines from the following noncommercial organizations: Thrombosis Canada, Hypertension Canada, Heart and Stroke Foundation, Canadian Cardiovascular Society, and the Canadian Aids Society. P. J. D. is a consultant for Reformulary Group, a member of the Speakers Bureau for Medical Cannabis Education for Spectrum Therapeutics, and participates in clinical trials for CancerCare Manitoba as per contract requirements. C. M. is the Medical Director of Greenleaf Medical Clinic and Chief Medical Officer for Translational Life Sciences. She is an advisor to PreveCeutical, Pinnacle Care, Africana, EO Care, Andira Medicine, Active Patch Technologies, Syqe Medical, and Dosist. She was previously on the Board of Directors for The Green Organic Dutchman. Additionally, she has provided medical consultation and/or received support for industry-sponsored continuing medical education from Aleafia, Aurora, Canopy, Tilray, and Emerald Health. E. M. is the co-owner of a start-up company ("Cannabiscotti Inc.") that will be applying for a cannabis processing license and is employed by MJardin Canada.

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Received: 18 January 2023 Accepted: 21 June 2023
Published online: 04 July 2023

References

- Arnetz JE, Almin I, Bergström K, Franzén Y, Nilsson H. Active patient involvement in the establishment of physical therapy goals: effects on treatment outcome and quality of care. *Adv Physiother.* 2004;6(2):50–69.
- Arnetz JE, Winblad U, Arnetz BB, Höglund AT. Physicians' and nurses' perceptions of patient involvement in myocardial infarction care. *Eur J Cardiovasc Nurs.* 2008;7(2):113–20.
- Arthritis Society of Canada. Medical cannabis - CBD & THC, n.d. Available from: <https://arthritis.ca/treatment/medication/medical-cannabis>. Cited 2022 Dec 31.
- Bahji A, Stephenson C. International perspectives on the implications of cannabis legalization: a systematic review & thematic analysis. *Int J Environ Res Public Health.* 2019;16(17):3095.
- Bell AD, MacCallum C, Margoese S, Walsh Z, Wright P, Daenincx PJ, et al. Clinical practice guidelines for cannabis and cannabinoid-based medicines in the management of chronic pain and co-occurring conditions. *Cannabis Cannabinoid Res.* 2023. Available from: <https://www.liebertpub.com/doi/10.1089/can.2021.0156>. Cited 2023 May 17.
- Boehne 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):739–44.
- Bruce D, Bouris AM, Bowers S, Blocker O, Lee SY, Glidden MF, et al. Medical, therapeutic, and recreational use of cannabis among young men who have sex with men living with HIV. *Addict Res Theory.* 2020;28(3):250–9.
- Busse JW, Vankrunkelsven P, Zeng L, Heen AF, Merglen A, Campbell F, et al. Medical cannabis or cannabinoids for chronic pain: a clinical practice guideline. *BMJ.* 2021;374:n2040.
- C. B. C. Radio. After 20 years of medical cannabis, gaps in product testing leave some Canadians feeling like guinea pigs | CBC Radio. CBC; 2021. Available from: <https://www.cbc.ca/radio/the-current/the-current-for-may-11-2021-1.6021707/after-20-years-of-medical-cannabis-gaps-in-product-testing-leave-some-canadians-feeling-like-guinea-pigs-1.6026923>. Cited 2023 Mar 13.
- Canadian Arthritis Patient Alliance. Medical cannabis. n.d. Available from: <https://arthritispatient.ca/medical-cannabis/>. Cited 2022 Dec 31.
- Canadian Medical Association. Cannabis for medical purposes. 2019. Available from: <https://policybase.cma.ca/media/PolicyPDF/PD11-02.pdf>. Cited 2023 Mar 13.
- Canadian Nurses Association. Cannabis. n.d. Available from: <https://www.cna-aic.ca/en/policy-advocacy/advocacy-priorities/cannabis>. Cited 2022 Dec 31.
- Canadian Pharmacists Association. Submission to the task force on marijuana legalization and regulation. 2016. Available from: https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/TaskForce_MarijuanaLegalizationRegulation_CPhA_Final.pdf. Cited 2022 Dec 31.
- Canadian Spondylitis Association. Cannabis. n.d. Available from: <https://spondylitis.ca/support-community/advocacy/position-papers/cannabis/>. Cited 2022 Dec 31.
- Canadians for Fair Access to Medical Marijuana (CFAMM). #DontTaxMedicine campaign goes on the offensive against unjust taxes on medical cannabis. n.d. Available from: <https://www.newswire.ca/news-releases/-dont-tax-medicine-campaign-goes-on-the-offensive-against-unjust-taxes-on-medical-cannabis-820875943.html>. Cited 2022 Dec 31.
- Elkrief L, Belliveau J, D'Ignazio T, Simard P, Jutras-Aswad D. Assessing the current state of medical education on cannabis in Canada: preliminary findings from Quebec. *Paediatr Child Health.* 2020;25(Suppl 1):S29–33.
- Fischer B, Russell C, Boyd N. A century of cannabis control in Canada: a brief overview of history, context and policy frameworks from prohibition to legalization. In: Decorte T, Lenton S, Wilkins C, editors. *Legalizing cannabis: experiences, lessons and scenarios*. First issued in paperback. London, New York: Routledge, Taylor & Francis Group; 2021. (Routledge studies in crime and society).
- GI Society. Medical Cannabis. Gastrointestinal Society; n.d. Available from: <https://badgut.org/information-centre/a-z-digestive-topics/cannabis/>. Cited 2022 Dec 31.
- Hazekamp A. The trouble with CBD oil. *Med Cannabis Cannabinoids.* 2018;1(1):65–72.
- Health Canada. Cannabis for medical purposes under the Cannabis Act: information and improvements. 2005. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/medical-use-cannabis.html>. Cited 2022 Dec 31.
- Health Canada. Talk about cannabis: cannabis in Canada - get the facts. 2018. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/resources.html>. Cited 2023 Mar 13.
- Health Canada. Report side effects from cannabis products. 2020a. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/recalls-adverse-reactions-reporting/report-side-effects-cannabis-products.html>. Cited 2022 Dec 31.
- Health Canada. Report side effects from cannabis products. 2020b. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/recalls-adverse-reactions-reporting/report-side-effects-cannabis-products.html>. Cited 2023 Mar 15.
- Health Canada. Canadian cannabis survey 2021: summary. 2021. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/canadian-cannabis-survey-2021-summary.html>. Cited 2023 Jan 8.
- Health Canada. Canadian cannabis survey 2022: summary. 2022. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/canadian-cannabis-survey-2022-summary.html>. Cited 2023 Mar 15.
- Health Canada. Cannabis use, effects and risks. 2023. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/health-effects.html>. Cited 2023 Mar 13.
- Health Canada. Information for health care professionals: cannabis (marijuana, marijuana) and the cannabinoids. n.d. Available from: <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html>. Cited 2023 Feb 12.
- House of Commons of Canada. Bill C-45 - an act respecting cannabis and to amend the Controlled Drugs and Substances Act, the criminal code and other acts. Available from: <https://www.parl.ca/legisinfo/en/bill/42-1/C-45>. Cited 2022 Dec 31.
- Huntsman RJ, Kelly LE, Alcorn J, Appendino JP, Bélanger RE, Crooks B, et al. Improving the regulation of medical cannabis in Canada to better serve pediatric patients. *CMAJ.* 2021;193(41):E1596–9.
- Hurd YL, Spriggs S, Alshayev J, Winkel G, Gurgov K, Kudrich C, et al. Cannabidiol for the reduction of cue-induced craving and anxiety in drug-abstinent individuals with heroin use disorder: a double-blind randomized placebo-controlled trial. *Am J Psychiatry.* 2019;176(11):911–22.
- Kilmer B. How will cannabis legalization affect health, safety, and social equity outcomes? It largely depends on the 14 Ps. *Am J Drug Alcohol Abuse.* 2019;45(6):664–72.
- Lake S, Walsh Z, Kerr T, Cooper ZD, Buxton J, Wood E, et al. Frequency of cannabis and illicit opioid use among people who use drugs and report chronic pain: a longitudinal analysis. *PLoS Med.* 2019;16(11):e1002967.
- Lake S, Socias ME, Milloy MJ. Evidence shows that cannabis has fewer relative harms than opioids. *CMAJ.* 2020;192(7):E166–7.
- Liang AL, Ginger EL, Coleman JS. Medical cannabis for gynecologic pain conditions: a systematic review. *Obstet Gynecol.* 2022;139(2):287–96.
- Lim K, See YM, Lee J. A systematic review of the effectiveness of medical cannabis for psychiatric, movement and neurodegenerative disorders. *Clin*

- Psychopharmacol Neurosci Off Sci J Korean Coll Neuropsychopharmacol. 2017;15(4):301–12.
- Loh A, Leonhart R, Wills CE, Simon D, Härter M. The impact of patient participation on adherence and clinical outcome in primary care of depression. *Patient Educ Couns*. 2007;65(1):69–78.
- Mannes ZL, Burrell LE, Ferguson EG, Zhou Z, Lu H, Somboonwit C, et al. The association of therapeutic versus recreational marijuana use and antiretroviral adherence among adults living with HIV in Florida. *Patient Prefer Adherence*. 2018;12:1363–72.
- McKee KA, Hmidan A, Crocker CE, Lam RW, Meyer JH, Crockford D, et al. Potential therapeutic benefits of cannabinoid products in adult psychiatric disorders: a systematic review and meta-analysis of randomised controlled trials. *J Psychiatr Res*. 2021;140:267–81.
- Minhas M, Lunn SE. Letter to the editor: the need for equitable health care among medical cannabis patients in Canada. *Cannabis Cannabinoid Res*. 2022;7(5):719–21.
- Montero-Oleas N, Arevalo-Rodriguez I, Nuñez-González S, Viteri-García A, Simancas-Racines D. Therapeutic use of cannabis and cannabinoids: an evidence mapping and appraisal of systematic reviews. *BMC Complement Med Ther*. 2020;20(1):12.
- Myran DT, Staykov E, Cantor N, Taljaard M, Quach BI, Hawken S, et al. How has access to legal cannabis changed over time? An analysis of the cannabis retail market in Canada 2 years following the legalisation of recreational cannabis. *Drug Alcohol Rev*. 2022;41(2):377–85.
- National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Board on Population Health and Public Health Practice, Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington (DC): National Academies Press (US); 2017. (The National Academies Collection: Reports funded by National Institutes of Health). Available from: <http://www.ncbi.nlm.nih.gov/books/NBK423845/>. Cited 2023 Feb 12.
- Ng JY, Gilotra K, Usman S, Chang Y, Busse JW. Attitudes toward medical cannabis among family physicians practising in Ontario, Canada: a qualitative research study. *Can Med Assoc Open Access J*. 2021;9(2):E342–8.
- Nielsen S, Sabioni P, Trigo JM, Ware MA, Betz-Stablein BD, Murnion B, et al. Opioid-sparing effect of cannabinoids: a systematic review and meta-analysis. *Neuropsychopharmacol Off Publ Am Coll Neuropsychopharmacol*. 2017;42(9):1752–65.
- Ontario College of Pharmacists. Cannabis training requirements and courses. OCPInfo.com; n.d. Available from: <https://www.ocpinfo.com/practice-education/practice-tools/support-materials/cannabis-training-requirements-courses/>. Cited 2023 Jan 8.
- Owens B. CMA position against separate regulations for medical cannabis draws ire and insults. *CMAJ Can Med Assoc J J Assoc Medicale Can*. 2018;190(18):E574–5.
- Rachmani R, Levi Z, Slavachevski I, Avin M, Ravid M. Teaching patients to monitor their risk factors retards the progression of vascular complications in high-risk patients with type 2 diabetes mellitus—a randomized prospective study. *Diabet Med J Br Diabet Assoc*. 2002;19(5):385–92.
- Reiman A, Welty M, Solomon P. Cannabis as a substitute for opioid-based pain medication: patient self-report. *Cannabis Cannabinoid Res*. 2017;2(1):160–6.
- Rosic T, Sanger N, Panesar B, Foster G, Marsh DC, Rieb L, et al. Cannabis use in patients treated for opioid use disorder pre- and post-recreational cannabis legalization in Canada. *Subst Abuse Treat Prev Policy*. 2021;16(1):34.
- Rueda S, Limanto E, Chaiton M. Cannabis clinical research in purgatory: Canadian researchers caught between an inflexible regulatory environment and a conflicted industry. *Lancet Reg Health - Am*. 2022b;7:100171.
- Rueda S, Limanto E, Chaiton M. Cannabis clinical research in purgatory: Canadian researchers caught between an inflexible regulatory environment and a conflicted industry. *Lancet Reg Health - Am*. 2022a;7. Available from: [https://www.thelancet.com/journals/lanam/article/PIIS2667-193X\(21\)00167-8/fulltext](https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00167-8/fulltext). Cited 2022a Dec 31.
- Siklos-Whillans J, Bacchus A, Manwell LA. A scoping review of the use of cannabis and its extracts as potential harm reduction strategies: insights from preclinical and clinical research. *Int J Ment Health Addict*. 2021;19(5):1527–50.
- St Pierre M, Matthews L, Walsh Z. Cannabis education needs assessment among Canadian physicians-in-training. *Complement Ther Med*. 2020;49:102328.
- Troup LJ, Erridge S, Ciesluk B, Sodergren MH. Perceived stigma of patients undergoing treatment with cannabis-based medicinal products. *Int J Environ Res Public Health*. 2022;19(12):7499.
- Turna J, Balodis I, Munn C, Van Ameringen M, Busse J, MacKillop J. Overlapping patterns of recreational and medical cannabis use in a large community sample of cannabis users. *Compr Psychiatry*. 2020;102:152188.
- UBC CPD. Cannabis Education for Health Care Providers Toolkit. UBC CPD; 2020. Available from: <https://ubccpd.ca/learn/resources-recordings/toolkits/cannabis-education-toolkit>. Cited 2023 Mar 13.
- Vahdat S, Hamzehgardeshi L, Hessam S, Hamzehgardeshi Z. Patient involvement in health care decision making: a review. *Iran Red Crescent Med J*. 2014;16(1):e12454.
- Wang L, Hong PJ, May C, Rehman Y, Oparin Y, Hong CJ, et al. Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. *BMJ*. 2021;374:n1034.
- Webster P. Hundreds of scientists sign letter arguing that regulation is stifling cannabis research. *Nat Med*. 2021. Available from: <https://www.nature.com/articles/d41591-021-00023-7>. Cited 2023 Mar 13.
- Wilkins C, Rychert M. Assessing New Zealand's cannabis legalization and control bill: prospects and challenges. *Addict Abingdon Engl*. 2021;116(2):222–30.
- Wright P, Walsh Z, Margolese S, Sanchez T, Arlt S, Belle-Isle L, et al. Canadian clinical practice guidelines for the use of plant-based cannabis and cannabinoid-based products in the management of chronic non-cancer pain and co-occurring conditions: protocol for a systematic literature review. *BMJ Open*. 2020;10(5):e036114.

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