



Research paper

Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients

Philippe Lucas^{a,b,c,*}, Zach Walsh^{d,e}^a Tilray, 1100 Maughan Rd., Nanaimo, BC V9X1J2, Canada^b Social Dimensions of Health, University of Victoria, 3800 Finnerty Rd., Victoria, BC V8P 5C2, Canada^c Centre for Addictions Research of British Columbia, 2300 McKenzie Ave, Victoria, BC V8N 5M8, Canada^d Department of Psychology, University of British Columbia, Okanagan, 3333 University Way, Kelowna, BC V1V 1V7, Canada^e Centre for the Advancement of Psychological Science and Law, University of British Columbia, Okanagan, 3333 University Way, Kelowna, BC V1V 1V7, Canada

ARTICLE INFO

Article history:

Received 27 September 2016

Received in revised form 15 December 2016

Accepted 10 January 2017

Available online xxx

Keywords:

Cannabis

Marijuana

Opioids

Substitution

Pain

Mental health

Addiction

ABSTRACT

Background: In 2014 Health Canada replaced the Marihuana for Medical Access Regulations (MMAR) with the Marihuana for Medical Purposes Regulations (MMPR). One of the primary changes in the new program has been to move from a single Licensed Producer (LP) of cannabis to multiple Licensed Producers. This is the first comprehensive survey of patients enrolled in the MMPR.

Methods: Patients registered to purchase cannabis from Tilray, a federally authorized Licenced Producer (LP) within the MMPR, were invited to complete an online survey consisting of 107 questions on demographics, patterns of use, and cannabis substitution effect. The survey was completed by 271 respondents.

Results: Cannabis is perceived to be an effective treatment for diverse conditions, with pain and mental health the most prominent. Findings include high self-reported use of cannabis as a substitute for prescription drugs (63%), particularly pharmaceutical opioids (30%), benzodiazepines (16%), and antidepressants (12%). Patients also reported substituting cannabis for alcohol (25%), cigarettes/tobacco (12%), and illicit drugs (3%). A significant percentage of patients (42%) reported accessing cannabis from illegal/unregulated sources in addition to access via LPs, and over half (55%) were charged to receive a medical recommendation to use cannabis, with nearly 25% paying \$300 or more.

Conclusion: The finding that patients report its use as a substitute for prescription drugs supports prior research on medical cannabis users; however, this study is the first to specify the classes of prescription drugs for which cannabis it is used as a substitute, and to match this substitution to specific diagnostic categories. The findings that some authorized patients purchase cannabis from unregulated sources and that a significant percentage of patients were charged for medical cannabis recommendations highlight ongoing policy challenges for this federal program.

© 2017 Elsevier B.V. All rights reserved.

Background

The past two decades have witnessed a resurgence of interest in the therapeutic potential of cannabis, with several nations and jurisdictions developing regulations to allow for access to cannabis for medical purposes (Fischer, Murphy, Kurdyak, Goldner, & Rehm, 2015). One potential salutary consequence of these developments

is the substitution of cannabis for other substances (Allsop et al., 2014; Lucas et al., 2013, 2016). Indeed, examinations of jurisdictions with legal access to medical cannabis have reported reductions in negative health outcomes associated with the use of other substances, such as opioid overdose (Bachhuber, Saloner, Cunningham, & Barry, 2014), and cannabis substitution has been forwarded as a mechanism to help explain these public health benefits. Consistent with this proposal, several large surveys confirm that medical cannabis users report substituting cannabis for other medications (Lucas, 2012a; Lucas et al., 2013, 2016; Reiman, 2009). Although extant surveys have provided broad evidence of cannabis substitution, the extent to which cannabis is

* Corresponding author at: Social Dimensions of Health, University of Victoria, 3800 Finnerty Rd., Victoria, BC, V8P 5C2, Canada.

E-mail addresses: plucas@uvic.ca, philippe@tilray.ca (P. Lucas).

used to substitute for distinct classes of substances by distinct patient groups has not been systematically examined from a patient-centred perspective. The present study addresses this knowledge gap by examining the extent to which physician-authorized medical cannabis users report using cannabis as a substitute for specific classes of substances, and by disaggregating this examination according to condition-based patient group. We also add to the nascent literature on medical cannabis use by describing patient characteristics, patterns of use and barriers to access.

In 2001 Canada became one of the first nations to develop a program to allow access to cannabis for medical purposes. The program has undergone numerous convolutions, culminating in the 2014 establishment by Health Canada of the Marihuana for Medical Purposes Regulations (MMPR) (Walsh et al., 2013), and ultimately in the Access to Cannabis for Medical Purposes Regulations in August 2016. One of the primary changes of the MMAR was the authorization of multiple Licensed Producers of cannabis: as of August 2016 >30 federally authorized Licensed Producers provide hundreds of strains of cannabis, as well as cannabis extracts to approximately 67,075 patients (Office of Medical Cannabis, 2016). The ACMPR adds regulations by which patients can produce their own cannabis, an option that was removed in the transition from MMAR and MPMR, and subsequently re-established through a court decision (Allard et al. v. Canada).

In contravention of the MPMR/ACMPR, a large number of patients access cannabis through community-based outlets known as dispensaries or compassion clubs, as well as from friends and other sources. In addition, although many Provincial medical colleges expressly forbid physicians from charging patients for providing patients with medical cannabis prescriptions, 3rd party patient aggregator services have emerged that provide cannabis prescriptions, occasionally in exchange for a substantial fee. To date, the prevalence of this practice among clients of LPs has not been explicitly examined. In addition to providing a more granular examination of cannabis substitution, this study also adds to the growing literature chronicling patterns of medical cannabis use and user characteristics using a novel sampling methodology: whereas prior studies generally queried self-identified medical cannabis users who may not have obtained physician authorization (Lucas, 2012b; Lucas et al., 2013; Walsh et al., 2013), to our knowledge this is the first study since the establishment of the MPMR to include only those medical cannabis users with confirmed physician authorization to access cannabis for therapeutic purposes.

Design and methods

A password protected 107 question online cross-sectional survey was made available in French and English for a 2 week period in July 2015 to patients of Tilray—a licensed producer of cannabis. 1310 participants were notified of the opportunity to participate in this study via direct email to patients that had opted in to receive online communication from Tilray upon registration. Participants were compensated \$10 credit for Tilray cannabis. The study was approved by Institutional Review Board Services, and gathered data on demographics, patient experiences, patterns of use, and cannabis substitution effect. Respondents were not forced to answer a given question in order to proceed to the next and as such the number of recorded responses varies across items. All reported percentages are based on number of responses rather than on the entire sample; we accompany all reported percentages with number of responses.

Findings

The survey was started by 301 participants, and completed by over 90% of respondents (n=271). The 30 non-completers only filled out the demographic section of the study, and based on this information did not differ on age, gender, education, income or work status compared to those that completed the survey. The primary demographics of respondents corresponds with the greater Tilray patient population but was more male and Caucasian, single, disabled and of lower income than the general Canadian population, with over-representation in Western Canada and Ontario, and under-representation in Quebec (see Table 1 for demographic characteristics).

While an increasingly common medical treatment, cannabis is often used for symptom relief rather than as a curative agent, therefore it's important to distinguish between the primary conditions for which cannabis is officially prescribed by a physician, and the specific symptoms for which patients report relief. For example, while a patient might report having a prescription for MS, the list of symptoms impacted might include chronic pain, spasticity, and insomnia. In this survey, respondents could select a single primary condition from a drop-down list, but could then select multiple symptoms affected by the medical use of cannabis. In regards to conditions, pain-related conditions were the most common, reported by 53% of participants (n=144; chronic pain 36%; (n=98), arthritis 12% (n=32), headache 5% (n=14)). The second most prominent class was mental health (eating disorder, PTSD & psychiatric disorder), reported by 15% (n=41). Other prominent conditions included gastrointestinal I disorders (11%, n=29), insomnia (7%, n=18) and multiple sclerosis (4%, n=11).

In regards to symptoms; the most highly endorsed were chronic pain (73%, n=197), stress (60%, n=162), insomnia (57%, n=155), depression (46%, n=126) and headache (32%, n=87). Gastrointestinal (GI) issues also featured prominently, with 29% (n=79) citing appetite loss and another 29% (n=79) nausea. Cannabis was perceived to be very effective at symptom relief, with 95% (n=257) reporting that it “often” or “always” helped alleviate their symptoms.

Patterns of use

The mean age of initiation was 18.50 (SD=7.42) for recreational use and 34.13 (SD=13.74) for medical use, as determined by responses to the question “How old were you when you first used cannabis” followed by “How old were you when you first used cannabis for medical purposes?”. It is notable that participants readily distinguished between their recreational and medical use of cannabis, with recreational cannabis use preceding medical use for 81% (n=220) of respondents, with 16% (n=44) reporting no history of recreational cannabis use, and 3% (n=7) reporting precedence of medical use prior to recreational use.

In regard to frequency, 88% (n=238) reported using cannabis at least daily, and the modal amount used per day was 1–2 g, with 29% (n=79) using a larger amount.

In regard to methods of use, 90% (n=243) had tried joints, 86% (n=234) vaporizers, 76% (n=207) oral/edibles (such as baked goods, butter, tincture, etc.) and 16% (n=44) had used cannabis-infused topical ointments. Regarding primary methods of use, vaporizers proved most popular (38%, n=102), followed by joints (25%, n=67), oral/edibles (14%, n=37), waterpipe/bongs (12%, n=33), pipes (11%, n=30), and topicals (1%, n=2). Regarding preferred method, vaporization was rated most highly by a plurality (44%, n=119), with oral/edibles second (23%, n=63). Respondents overwhelmingly reported that not all strains/types of cannabis were “equally effective” at relieving symptoms (77%, n=210): 82%

Table 1
Demographics.

	Tilray, survey respondents (n = 271) (%)	Tilray, all patients (n = 3077) ^a (%)	Canadian average, stats Canada, 2011 census ^b (%)
Gender			
Male	73	70	49
Female	27	30	51
Age	(Range: 20–77)		
Mean	40	44	41
Background			
Caucasian	94	N/A	77
Black	4	N/A	3
Aboriginal/Metis	3	N/A	4
South Asian	2	N/A	5
Asian	2	N/A	5
Marital status			
Married	43	N/A	46
Domestic partnership/civic union	9	N/A	11
Divorced/separated	10	N/A	8
Single	38	N/A	28
Education			(Age 25–64)
Less than high school	7	N/A	13
High school or equivalent	20	N/A	23
Some college/university	21	N/A	N/A
Technical and/or non-university degree	28	N/A	21
University degree	15	N/A	17
Graduate degree	8	N/A	10
Employment			15 years and over
Employed, full time	45	N/A	51
Employed, part time	12	N/A	12
Disabled	30	N/A	14
Not employed	8	N/A	7.8
Retired	5	N/A	N/A
Income			
Less than \$10,000	9	N/A	5
\$10,000–39,999	32	N/A	27
\$40,000–99,999	40	N/A	42
>\$100,000	19	N/A	26
Province of residence			
Prairies	24	19	18
British Columbia	17	22	13
Atlantic	8	7	7
Territories	1	1	1
Ontario	49	49	38
Quebec	2	2	24

^a As of July 31, 2015.^b Statistics Canada. Canadian census, 2011. <https://www12.statcan.gc.ca/census-recensement/2011/dp-pd/prof/index.cfm?Lang=E>.

(n = 222) reported a preferred cannabis type; 25% (n = 68) indicas, 21% hybrids (n = 56), 18% favoring strains high in cannabidiol (CBD) (n = 50), and 18% sativas (n = 48). While many Licensed Producers continue to identify cannabis by these phenotypes (*Cannabis sativa* and *Cannabis indica*) in keeping with classifications found in the black market, there is a growing academic debate about whether these classifications represent real and distinct genetic classifications, with evidence suggesting that the label of indica or sativa is not consistent with the actual genetics of many of these strains (Sawler et al., 2015). However, evidence that cannabinoids and terpenes are found at different ratios within each distinct cannabis phenotype supports the subjective differences between strains commonly reported by patients.

Cannabis substitution effect

Overall, 71% (n = 186) of participants report substituting cannabis for either prescription drugs, alcohol, tobacco/nicotine or illicit substances, with 63% reporting substitution for

prescription medication (n = 166), 25% for alcohol (n = 66), 12% for tobacco/nicotine (n = 31), and 3% for illicit substances (n = 9). To facilitate interpretation of substitution for prescription medications, pharmaceuticals were classed into the following 4 categories: *opioids*, *benzodiazepines*, *antidepressants* and a category of *other medication* that included diverse substances that were less frequently endorsed (e.g., NSAIDs, Methylphenidate). Respondents were allowed to report up to three medications for which they substituted cannabis; of those who explicitly listed prescription substitution 59% (n = 92) reported substituting for a single class of medications, 33% (n = 52) reported substituting for two classes, and 8% (n = 13) reported substituting cannabis for three classes. The most common form of substitution was for opioids (32%, n = 80), followed by benzodiazepines (16%, n = 40), and antidepressants (12%, n = 31) (Table 2). The reasons most frequently ranked as being most important for substituting cannabis for prescribed medications were “less adverse side effect” (39%, n = 68); “cannabis is safer” (27% n = 48), and “better symptom management” (16%, n = 28).

Table 2
Substitution for prescription medications.

Class	n	%
Opioids (Oxy/Oxyneo/Percocet/hydromorphone/morphine/codeine derivatives, etc.)	80	32
Benzodiazepines	40	16
Antidepressants	31	12
Other medication	100	40

Supplementary analyses examined variation across diagnostic groups, and indicated that respondents who used cannabis for pain-related conditions were more likely to substitute cannabis for opioids (42% (n = 57) vs. 20% (n = 23), $\chi^2 = 13.78(1)$, $p < 0.01$), whereas respondents who used cannabis to address mental health were more likely to substitute cannabis for benzodiazepines (31% (n = 12) vs. 13% (n = 28), $\chi^2 = 7.75(1)$, $p < 0.01$) and for antidepressants (26% (n = 10) vs. 10% (n = 21), $\chi^2 = 7.69(1)$, $p = 0.01$) (Fig. 1). Our data suggested no relationship between age, amount of cannabis used, mode of administration, access or affordability on substitution effect.

Access

Although all respondents accessed cannabis from Tilray, 21% (n = 56) also reported purchasing cannabis from another Licensed Producer, 25% (n = 67) purchased from dispensaries, 18% (n = 47) from a friend, and 8% (n = 20) buy from an illicit dealer. In total, 42% (n = 111) of respondents reported accessing from one or more unregulated sources. Regarding cost, 44% (n = 118) spend less than \$250 monthly and 78% (n = 212) spend less than \$500 per month on cannabis, whereas 4% spend \$1000 or more (n = 11). Capacity to “often” or “always” afford to buy enough cannabis to relieve symptoms was reported by 40% (n = 109), leaving 60% (n = 162) who report “sometimes” or “never” affording sufficient cannabis. Similarly, 53% (n = 146) reported choosing between medical cannabis and other necessities (food, rent, other medicines . . .) in the past year due to finances. Only 3% (n = 7) cited having 3rd party insurance coverage, and another 3% (n = 8) reported getting the cost of cannabis covered through Veterans Affairs Canada.

Finding a supportive physician was a reported challenge, with 31% (n = 78) having changed doctors in relation to medical cannabis use, and 55% reporting feeling discriminated against by their doctor because of medical cannabis use (n = 139). Paying a physician or clinic a fee for recommendations to use medical cannabis was reported by 55% (n = 140), with a modal price of between \$300–99 (n = 50) and

94% (n = 131) paying \$100 or more. It is therefore unsurprising that 29% (n = 75) reported that obtaining an authorization to use medical cannabis was “difficult” or “very difficult”.

Interpretation

The finding that patients using cannabis to treat pain-related conditions have a higher rate of substitution for opioids, and that patients self-reporting mental health issues have a higher rate of substitution for benzodiazepines and antidepressants has significant public health implications. In light of the growing rate of morbidity and mortality associated with these prescription medications (Bachhuber et al., 2014; Fischer, Rehm, Goldman, & Popova, 2008), cannabis could play a significant role in reducing the health burden of problematic prescription drug use. Indeed, a recent study of US states that have legalized medical cannabis, found that the number of prescriptions significantly dropped for drugs that treat pain, depression, anxiety, nausea, psychoses, seizures and sleep disorders, with the annual number of doses prescribed for chronic pain falling by more than 11% per physician (Bradford & Bradford, 2016). Additionally, according to Veterans Affairs Canada, a recent significant increase in the use of medical cannabis by patients is paralleled by a nearly 30% decrease in the use of benzodiazepines and a 16% decrease in the use of opioids (Hager, 2016). Moreover, the finding that cannabis might be used to substitute for multiple medications is particularly promising in light of concerns patients may have regarding adherence to complex pharmaceutical regimens, and attendant side effects (Brown & Bussell, 2011; Ingersoll & Cohen, 2008; Sylvestre, Clements, & Malibu, 2006). Indeed, tolerability of side effects was identified as a prominent reason for cannabis substitution.

The finding that medical cannabis is used primarily to treat chronic pain is consistent with past research (Ware et al., 2010; Ware, Wang, Shapiro, & Collet, 2015). However, the extensive self-

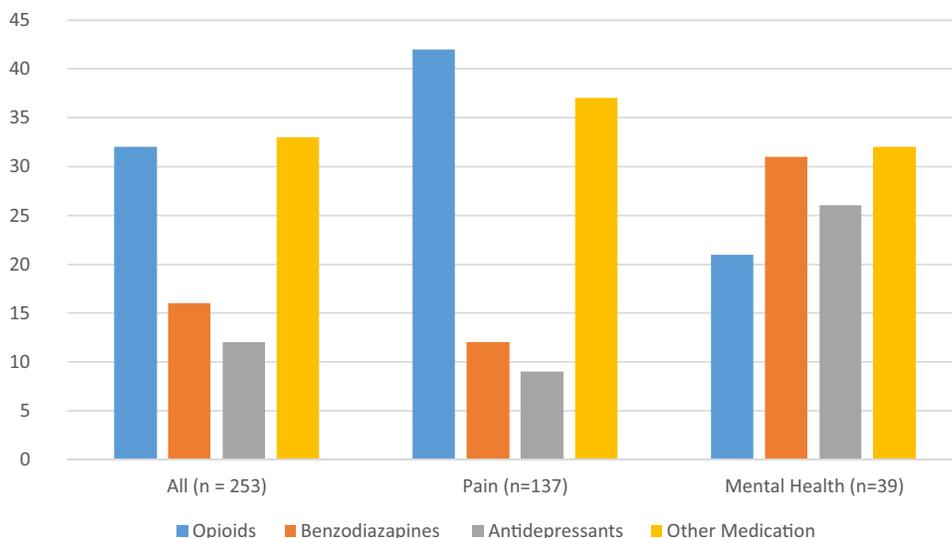


Fig. 1. Substitution by condition.

reported use to treat mental health conditions and associated symptoms represents a novel and interesting trend, and suggests that the conceptualization of cannabis as deleterious to mental health may not generalize across conditions or populations. Studies currently underway to investigate cannabis for the treatment of PTSD, anxiety, and other psychiatric conditions may soon provide more information on these potentially promising treatment options.

Our finding that most patients use 2 grams or less is consistent with past research (Carter, Weydt, Kyashna-Tocha, & Abrams, 2004; Clark, 2013; Hazekamp, Ware, Muller-Vahl, Abrams, & Grotenhermen, 2013). To our knowledge, this is the first patient survey to report vaporization as the primary method of ingestion, and non-smoked forms of ingestion as primary and preferred methods of ingestion. This marks a health conscious shift in medical cannabis use under the MMPR that may be attributed to a few factors: since patients in the MMPR require a physicians support to access medical cannabis, they may be more likely to be focused on safer methods of ingestion than non-MMPR patient populations; improvements in vaporizer technology and associated reductions in cost, patient outreach and education initiatives focused on safe and responsible use by cannabis vendors, and ongoing restrictions on smoking in the public realm.

Cannabis is rather unique as a therapeutic treatment in that many patients report some permeability between recreational and medical use (Walsh et al., 2013). However, unlike opioids where medical use via prescription often precedes recreational use and dependence (Fischer et al., 2008), the pathways between the medical and recreational use of cannabis are reversed, with previous recreational use often a precursor to prescription medical use, while the reverse is rarely the case. Although most respondents in this study had experience with recreational cannabis use prior to initiation of medical use (81%, $n=220$), transition from medical use to recreational use was only reported by 7 participants (<3%), which is suggestive of a low risk of abuse associated with medical cannabis. Additionally, with so many patients reporting use for the relief of mental health conditions like stress, insomnia and depression, much of this medical use is ultimately focused on improving psychological well being and quality of life. This perhaps blurs the lines between traditional biomedical approaches to disease and more holistic approaches (such as yoga or naturopathic medicine) used as adjunct treatments to address the symptoms, side-effects and psychological impacts of long-term illness/disability and/or the modern pressures of every day life. This is supported by previous research that has found that patients who use medical cannabis often cite depression and anxiety as a primary symptoms for which they seek relief, regardless of their actual medical condition (Bonn-Miller, Boden, Bucossi, & Babson, 2014; Osborne, Smart, Weber, & Birchmore-Timney, 2000; Walsh et al., 2016), as well a growing amount of preclinical research supporting the use of CBD as a potential treatment for both anxiety (Blessing, Steenkamp, Manzanares, & Marmar, 2015) and depression (Linge et al., 2015).

Despite the legal protection and quality control offered through the MMPR, 42% of participants report accessing cannabis from unregulated sources which may be due to restrictions imposed on LPs by the MMPR during that period. At the time of this survey, LPs were only allowed to provide raw cannabis flowers, whereas other sources may have provided a diverse array of extracts and edibles. Since that time regulations have been altered to allow LPs to produce extracts, and to once again produce their own cannabis supply. Future research may determine whether this regulatory revision alters patient behaviour in regards to access through unregulated sources.

In light of consistent evidence that many lower income patients face affordability issues in regards to the cost of medical cannabis (Belle-Isle et al., 2014), the finding that so many patients had to pay high medical fees to gain access medical cannabis is concerning and suggests there may subsequently be an under-representation of low income patients in the MMPR/ACMPR.

Conclusions

The high rate of substitution for prescription drugs among patients with pain-related and mental health conditions suggests that medical cannabis may be an effective adjunct or substitute treatment to prescription drugs used to treat these conditions. Further research into the comparative efficacy of cannabis relative to front-line treatments for these conditions is warranted, and longitudinal research would help elucidate the context of cannabis substitution effect, and the potential impact of cannabis substitution on the quality of life of patients (in-progress, Lucas).

While the MMPR had only been in place for approximately 15 months when this survey took place, the findings that some authorized patients continue to purchase cannabis from unregulated sources and that a significant percentage of patients have had to pay high fees for medical cannabis recommendations highlight ongoing policy challenges for the federal medical cannabis program. As Canada's federal medical cannabis policy continues to evolve (both organically and in response to legal challenges) and as provinces and municipalities seek regulatory solutions to issues like dispensaries, personal production, and private medical cannabis clinics, it will be important to keep tracking the impact of these policy developments on patient access to and experiences with medical cannabis.

Limitations

The relatively low response rate to the survey (21%) leaves open the possibility this could potentially be an unrepresentative sample. It is not possible to confirm the impact of cannabis substitution on quantity of use of prescription drugs, alcohol or illicit drug use. Additionally, all data regarding the cannabis substitution effect in this study were self-reported by patients and did not benefit from biological drug detection to confirm use or non-use of a substance. In light of this potential bias, our characterisation of the therapeutic use of cannabis and/or cannabis substitution effect should be interpreted with caution pending replication by research that employs a more systematic recruitment approach, longitudinal monitoring, and biological drug testing.

However, these limitations are counterbalanced by several methodological strengths, including the large size of the sample, assurance that all participants were using medical cannabis with the support of a physician, and adherence to established standards for reporting Internet-based surveys (Eysenbach, 2004).

Declaration of interest

This study was funded by Tilray, a federally authorised medical cannabis production and research company. Philippe Lucas is currently employed as Vice-President, Patient Research and Advocacy for Tilray; however, his compensation is not tied in any way to the outcomes of this study.

Zach Walsh is currently the Primary Investigator in a Tilray-sponsored randomized clinical trial of medical cannabis and PTSD, but he receives no financial compensation for that study nor for assisting with the analysis and writing of this paper.

Acknowledgements

Funding for this study was provided by Tilray. We would like to thank all of the Tilray patients that have shared their thoughts and experiences with us, as well as Kim Crosby for assisting with some of the data analysis of this survey.

References

- Allsop, D. J., Dunlop, A. J., Saddler, C., Rivas, G. R., McGregor, I. S., & Copeland, J. (2014). Changes in cigarette and alcohol use during cannabis abstinence. *Drug and Alcohol Dependence*, 138(1), 54–60. <http://dx.doi.org/10.1016/j.drugalcdep.2014.01.022>.
- Bachhuber, M. A., Saloner, B., Cunningham, C. O., & Barry, C. L. (2014). Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010. *JAMA Internal Medicine*, 4, 1–6. <http://dx.doi.org/10.1001/jamainternmed.2014.4005>.
- Belle-Isle, L., Walsh, Z., Callaway, R., Lucas, P., Capler, R., Kay, R., & Holtzman, S. (2014). Barriers to access for Canadians who use cannabis for therapeutic purposes. *International Journal of Drug Policy*, 25(4), 691–699. <http://dx.doi.org/10.1016/j.drugpo.2014.02.009>.
- Blessing, E. M., Steenkamp, M. M., Manzanera, J., & Marmar, C. R. (2015). Cannabidiol as a potential treatment for anxiety disorders. *Neurotherapeutics*, 12(4), 825–836. <http://dx.doi.org/10.1007/s13311-015-0387-1>.
- Bonn-Miller, M. O., Boden, M. T., Bucossi, M. M., & Babson, K. A. (2014). Self-reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. *The American Journal of Drug and Alcohol Abuse*, 40(1), 23–30. <http://dx.doi.org/10.3109/00952990.2013.821477>.
- Bradford, A. C., & Bradford, W. D. (2016). Medical marijuana laws reduce prescription medication use in medicare part D. *Health Affairs*, 35(7), 1230–1236. <http://dx.doi.org/10.1377/hlthaff.2015.1661>.
- Brown, M. T., & Bussell, J. K. (2011). Medication adherence: WHO cares? *Mayo Clinic Proceedings*, 86(4), 304–314. <http://dx.doi.org/10.4065/mcp.2010.0575>.
- Carter, G. T., Weydt, P., Kyashna-Tocha, M., & Abrams, D. I. (2004). Medicinal cannabis: Rational guidelines for dosing. *IDrugs: The Investigational Drugs Journal*, 7(5), 464–470 Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15154108>.
- Clark, C. (2013). The state of play. *International Journal of Play* 1–14. <http://dx.doi.org/10.1080/21594937.2013.853462>.
- Eysenbach, G. (2004). Improving the quality of web surveys: The checklist for reporting results of internet e-surveys (CHERRIES). *Journal of Medical Internet Research*, 6(3), e34+. <http://dx.doi.org/10.2196/jmir.6.3.e34>.
- Fischer, B., Murphy, Y., Kurdyak, P., Goldner, E., & Rehm, J. (2015). Medical marijuana programs—Why might they matter for public health and why should we better understand their impacts? *PMEDR*, 2, 53–56. <http://dx.doi.org/10.1016/j.pmedr.2014.12.006>.
- Fischer, B., Rehm, J., Goldman, B., & Popova, S. (2008). Non-medical use of prescription opioids and public health in Canada: An urgent call for research and interventions development. *Canadian Journal of Public Health*, 99(3), 182–184 Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18615937>.
- Hager, M. (2016). *Among veterans, opioid prescription requests down in step with rise in medical pot*. Globe and Mail Retrieved from <http://www.theglobeandmail.com/news/national/among-veterans-opioid-prescription-requests-down-in-step-with-rise-in-medical-pot/article30285591/>.
- Hazekamp, A., Ware, M. A., Muller-Vahl, K., Abrams, D., & Grotenhermen, F. (2013). The medicinal use of cannabis and cannabinoids—An international cross-sectional survey on administration forms. *Journal of Psychoactive Drugs*, 45(3), 199–210. <http://dx.doi.org/10.1080/02791072.2013.805976>.
- Ingersoll, K. S., & Cohen, J. (2008). The impact of medication regimen factors on adherence to chronic treatment: A review of literature. *Journal of Behavioral Medicine*, 31(3), 213–224. <http://dx.doi.org/10.1007/s10865-007-9147-y>.
- Linge, R., Jiménez-Sánchez, L., Campa, L., Pilar-Cuellar, F., Vidal, R., Pazos, A., . . . Díaz, Á. (2015). Cannabidiol induces rapid-acting antidepressant-like effects and enhances cortical 5-HT/glutamate neurotransmission: Role of 5-HT1A receptors. *Neuropharmacology*, 103, 16–26. <http://dx.doi.org/10.1016/j.neuropharm.2015.12.017>.
- Lucas, P. (2012a). Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. *Journal of Psychoactive Drugs*, 44(2), 125–133. <http://dx.doi.org/10.1080/02791072.2012.684624>.
- Lucas, P. (2012b). 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(1), 2. <http://dx.doi.org/10.1186/1477-7517-9-2>.
- Lucas, P., Reiman, A., Earleywine, M., McGowan, S. K., Oleson, M., Coward, M. P., & Thomas, B. (2013). Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients. *Addiction Research & Theory*, 21(5), 435–442. <http://dx.doi.org/10.3109/16066359.2012.733465>.
- Lucas, P., Walsh, Z., Crosby, K., Callaway, R., Belle-Isle, L., Kay, 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(3), 326–333. <http://dx.doi.org/10.1111/dar.12323>.
- Office of Medical Cannabis (2016). *MMPR market statistics, January–May*. Ottawa: Office of Medical Cannabis 2016.
- Ogborne, A. C., Smart, R. G., Weber, T., & Birchmore-Timney, C. (2000). Who is using cannabis as a medicine and why: An exploratory study. *Journal of Psychoactive Drugs*, 32(4), 435–443. <http://dx.doi.org/10.1080/02791072.2000.10400245>.
- Reiman, A. (2009). Cannabis as a substitute for alcohol and other drugs. *Harm Reduction Journal*, 6, 35. <http://dx.doi.org/10.1186/1477-7517-6-35>.
- Sawler, J., Stout, J. M., Gardner, K. M., Hudson, D., Vidmar, J., Butler, L., . . . Cockerham, C. (2015). The genetic structure of marijuana and hemp. *PLoS One*, 10(8), e0133292. <http://dx.doi.org/10.1371/journal.pone.0133292>.
- Sylvestre, D. L., Clements, B. J., & Malibu, Y. (2006). Cannabis use improves retention and virological outcomes in patients treated for hepatitis C. *European Journal of Gastroenterology & Hepatology*, 18(10), 1057–1063. <http://dx.doi.org/10.1097/01.meg.0000216934.22114.51>.
- Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., & Holtzman, S. (2013). Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use. *International Journal of Drug Policy*, 24(6), 511–516. <http://dx.doi.org/10.1016/j.drugpo.2013.08.010>.
- Walsh, Z., Gonzalez, R., Crosby, K., Thiessen, M., Carroll, C., & Bonn-Miller, M. O. (2016). Medical cannabis and mental health: A guided systematic review. *Clinical Psychology Review* 15–29. <http://dx.doi.org/10.1016/j.cpr.2016.10.002>.
- Ware, M. A., Wang, T., Shapiro, S., Robinson, A., Ducruet, T., Huynh, T., . . . Collet, J. P. (2010). Smoked cannabis for chronic neuropathic pain: A randomized controlled trial. *Cmaj*, 182(14), 1–8. <http://dx.doi.org/10.1503/cmaj.091414>.
- Ware, M. A., Wang, T., Shapiro, S., & Collet, J.-P. (2015). Cannabis for the management of pain: Assessment of safety study (COMPASS). *The Journal of Pain* 1233–1242. <http://dx.doi.org/10.1016/j.jpain.2015.07.014>.