Canadian Psychiatric Association
Association des psychiatres du Canada

In Review Series Article

The State of Opioid Agonist Therapy in Canada 20 Years after Federal Oversight

The Canadian Journal of Psychiatry / La Revue Canadienne de Psychiatrie
2017, Vol. 62(7) 444-450

DOI: 10.1177/0706743717711167
TheCJP.ca | LaRCP.ca
SAGE

Joseph K. Eibl, PhD[1], Kristen Morin, MPH[2], Esa Leinonen, BScN[1,3], and David C. Marsh, MD[1,3]

Abstract

Opioid agonist therapy was introduced in Canada in 1959 with the use of methadone for the treatment of opioid dependence. The regulation of methadone was the responsibility of Health Canada until 1995, when oversight was transferred to the provincial health systems. During the more than 20 years since the federal health authority transferred oversight of methadone to the provincial level, methadone programming has evolved differently in every province. The landscape of opioid dependence treatment is varied across the country, with generally increasing treatment capacity in all provinces and dramatic increases in some. Each province has an independent methadone program with differing policies, contingency management strategies, laboratory monitoring policies, and delivery methods. Treatment options have increased, with buprenorphine- and heroin-assisted treatment becoming available to limited degrees. Despite this, access remains a challenge in many parts of the country (particularly rural and remote areas) because the demand for treatment has increased even more rapidly than the capacity. Although treatment access remains a priority in many jurisdictions, there is also a need to attend to treatment quality as treatment access expands, including integration with addiction counselling, primary care, and mental health care. As well, coordinated monitoring and reporting of treatment need, quality, and delivery are required; implementing a national policy to promote planning would have tremendous value.

Abrégé

Le traitement par agonistes opioïdes a d'abord été instauré au Canada par l'utilisation de la méthadone pour le traitement de la dépendance aux opioïdes en 1959. La réglementation de la méthadone relevait de Santé Canada jusqu'en 1995, où la surveillance a été transférée aux systèmes de santé provinciaux. Il y a maintenant 20 ans que l'autorité fédérale en matière de santé a transféré la surveillance de la méthadone au niveau provincial; subséquemment, les programmes de méthadone ont évolué différemment dans chaque province. La scène des traitements de la dépendance aux opioïdes est variée dans tout le pays, toutes les provinces ont une capacité de traitement généralement croissante, et certaines connaissent des augmentations radicales. Chaque province a un programme de méthadone indépendant dont les politiques, les stratégies de gestion d'urgence, les politiques de contrôle en laboratoire et les méthodes de prestation sont toutes différentes. Plus d'options de traitement par buprénorphine et à l'aide d'héroïne ont également été offertes mais à un degré limité. Malgré cela, l'accès demeure un problème dans bien des secteurs du pays (surtout en régions rurales et éloignées) parce que la demande de traitement s'est accrue encore plus rapidement que la capacité. Comme l'accès au traitement demeure une priorité dans de nombreuses administrations, Il faut aussi surveiller la qualité du traitement à mesure que s'élargit l'accès, y compris l'intégration avec la consultation en toxicomanie, les soins de première ligne et les soins de santé mentale. Le besoin subsiste encore d'une surveillance et d'un suivi des besoins, de la qualité et de la prestation des traitements. La mise en œuvre d'une politique nationale de promotion de la planification aurait une valeur exceptionnelle pour le système.

Keywords

harm reduction, addiction, policy, rurality, telemedicine, rural

Methadone in Canada: 1959-1995

Opioid agonist therapy (OAT) was pioneered in British Columbia by Dr Robert Halliday at the Narcotics Addiction Foundation.[1] Around the same time in the United States,

[1] Northern Ontario School of Medicine, Sudbury, Ontario
[2] Laurentian University, Sudbury, Ontario
[3] Canadian Addiction Treatment Centers, Richmond Hill, Ontario

Corresponding Author:
David C. Marsh, MD, Northern Ontario School of Medicine, Sudbury, ON P3E 2C6 Canada.
Email: dmarsh@nosm.ca

Table 1. Summary of opioid agonist therapy by province[a].

Province oversight	Methadone training and exemption	Urine drug screening guidelines	Province-funded methadone (M) or buprenorphine (B)	Patient registry	Patients[b]	Physicians[b]
BC	✓	✓	M/B	✓	16,457 (351)	528 (11)
AB	✓	✓	M/B		>3500 (83)	50-100 (2)
SK	✓	✓	M/B		>2000 (176)	<50 (4)
MB	✓	✓	M		<1000 (77)	<50 (4)
ON	✓	✓	M/B		>42,000 (305)	475 (3)
QC	✓	✓	M/B		>3400 (41)	>230 (3)
NB	✓	✓	M/B		1916 (254)	>40 (5)
NS	✓	✓	M/B	✓	>1000 (106)	29 (3)
NF	✓	✓	M/B	✓	>1000 (189)	<10 (2)
PE	✓		M/B		>200 (137)	>10 (7)

[a]Data for Nunavut, Northwest Territories, and Yukon are not publically available.
[b]Expressed as number (with *n* per 100,000 in parentheses). These numbers represent the authors' best approximation based on available information at the time of publication.

Marie Nyswander and Vincent Dole were studying methadone as the first maintenance therapy for opioid dependence.[2] Methadone was officially introduced in Canada in 1964, and the "good medical practice" guidelines were established for the country.[3] From 1964 to 1995, Health Canada was responsible for oversight of methadone for use in treatment of opioid dependence. In 1995, the federal health authority decided to transfer oversight of physician practice aspects of methadone treatment from Health Canada to the provincial regulatory bodies that are responsible for physician practice.[4] While physicians continue to require an exemption from the federal controlled substances legislation issued by the federal Minister of Health in order to prescribe methadone, the oversight of methadone programming fundamentally became the responsibility of the College of Physicians and Surgeons of each province.[5] The year 2015 marked the twentieth year since the federal health authority transferred oversight of methadone to the provincial level; during that time, methadone programming has evolved differently in every province. Today, each province has an independent OAT program with differing policies, contingency management strategies, laboratory monitoring policies, and delivery methods. Moreover, Ontario[5,6] and British Columbia[7] have had rapid expansion of their OAT programs in the last 2 decades and are currently facing very different challenges than most other provinces, which are just starting to expand their OAT programming.[8]

In 2011, Luce and Strike[9] produced a report commissioned by the Canadian Executive Council on Addictions titled *A Cross-Canada Scan of Methadone Maintenance Treatment Policy Developments*. Since the Luce and Strike report, important and still emerging factors continue to influence the delivery of OAT across Canada, including the oxycodone epidemic, removal of OxyContin from the public formulary, the increased availability of buprenorphine-naloxone as an alternative to methadone, the adoption of telemedicine to deliver care, and the need to integrate mental health and psychosocial supports. Here we provide an update on the state of OAT across Canada.

Clinical Context of OAT in Canada

OAT is delivered in several clinical contexts across Canada. Patients enrolled in OAT will receive a daily scheduled dose of a less-reinforcing opioid (e.g., liquid methadone or sublingual buprenorphine-naloxone). Treatment is provided via observed dosing at a clinic, a physician's office, or a pharmacy. Following stabilization on OAT, patients are generally eligible to receive "carry" (or take-home) doses. OAT is delivered in 3 primary settings. (1) OAT is delivered in provincially funded addiction programming clinics with coordinated inclusion of comprehensive services across health professions, including doctors, counsellors, pharmacists, social workers, and case managers. (2) OAT is provided in a doctor's office completely subsidized by the provincially funded, physician fee-for-service compensation stream. This model has limited ability to provide comprehensive care unless there is collaboration with other agencies funded from entirely different funding programs. (3) OAT is provided to patients in federal and provincial correctional facilities. Patients enrolled in methadone treatment can continue observed dosing in the hospital setting. Some hospitals may provide comprehensive addiction and mental health services.

While OAT delivery is not exclusive to any medical specialty, family physicians, and to a lesser degree psychiatrists, are the most common types of physicians delivering OAT in Canada. Most provinces have implemented mandatory education, training, and preceptorship prior to being granted a federal methadone exemption; however, these requirements vary between provinces. Table 1 provides a summary of OAT by province based on publically available information at the time of publication.

Enhancing Access and Capacity of OAT Is a National Health Issue

Opioid dependence and opioid-related deaths have increased dramatically in the past 20 years.[10,11] While prescription and nonprescription opioids have been misused for more than a century, opioid dependence has increased dramatically in Canada following the advent of slow-release formulations in the Canadian market.[12-14] In 1999, the introduction of slow-release formulations of oxycodone coupled with increased prescribing of these medications resulted in an opioid dependence epidemic that persists in almost all geographic regions of the country. Opioid prescribing across Canada increased 24% from 2010 to 2014, with 21.7 million prescriptions dispensed in Canada in 2014.[15-17] The fallout from liberal opioid prescribing included a massive swell in the number of people who have become dependent on opioids.[18] Today, all jurisdictions across Canada are in need of expanded access to OAT, and northern, rural, and remote regions are disproportionately underserviced. Data for Ontario suggest that opioid-related deaths increased 242% between 1991 and 2010, and opioid use is now the leading cause of death for people aged 18 to 35 years.[10] In order to quantify, educate, and intervene, Ontario (Narcotic Monitoring System) and British Columbia (PharmaNet) have implemented sophisticated pharmacy monitoring programs[19,20]; however, these systems are not yet fully available in the other provinces and territories.

Prevention, while not a focus of this review, is also an important consideration, as current gaps in treatment infrastructure are largely related to the epidemic of dependence that has evolved in the last decade. In 2010, the National Opioid Use Guideline Group, which consisted of stakeholders from across the country, published the *Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain*[21] as a tool to help physicians more responsibly prescribe opioids for managing non-cancer-related pain. Resources directed at the patient and prescriber will continue to be important interventions to help reduce the number of patients who develop a dependence from prescription opioid use.

Considerations for OAT Expansion

The best-practice guidelines for OAT suggest that an ideal program should offer integrated components of counselling, social supports, and mental health services.[22,23] In large urban centers, integrating care with supportive services may be feasible; however, in northern, rural, and remote regions of the country, the feasibility of delivering care using this model is challenging due to the paucity of health professionals and services.[6,8] Our group recently demonstrated that patients in Northern Ontario are more likely to be retained in therapy compared with patients in Southern Ontario.[6] A potential explanation for this observation is that Northern patients have a considerably harder time accessing care than Southern patients, so when these Northern patients are able to enter care, they are perhaps more motivated to stay in OAT. Another consideration that may be relevant to the Canadian context is the phenomenon of decreasing OAT retention during OAT expansion. In 2006, Bell et al[24] reported that during the time of methadone expansion in New South Wales, Australia, treatment retention decreased and the number of patients cycling in and out of therapy increased. Appreciating that this phenomenon may arise where OAT programs are rapidly expanding could help those implementing programs to better strategize and allocate resources.

In Canada, Ontario's expansion of methadone programming has far outpaced that of other provinces with the exception of British Columbia.[5,7] Ontario has managed to engage a larger portion of the opioid-dependent population by delivering care via the Ontario Telemedicine Network.[25] The advantage of telemedicine-delivered care is that it allows for a single physician to service regions where no services or providers exist. While this strategy has been used to expand access to care, the services that fall outside of the Ontario Health Insurance Plan (OHIP) fee schedule are rarely delivered in these settings, the likely reasons being a gap in funding mechanism for nonphysician services and a lack of service coordination with other community service providers and funders.[9]

Integration with Mental Health Services

The concurrence of mental health conditions and substance use disorders is well established,[26] and integration of mental health services for those with opioid use disorders is the ideal of care.[22,23] Delivery of OAT with concurrent or referral psychiatry programming services is typically offered in provincially funded programs; however, expansion of these services to northern, rural, and remote regions is not common.[6,9] The delivery of psychiatric and counselling services by telemedicine at the OAT clinic is a strategy that could be deployed in almost all healthcare settings. Moreover, psychiatric care has been demonstrated to be effective when delivered via telemedicine.[27] A preliminary study from our group suggests that OAT delivered via telemedicine is as effective as in-person care (manuscript currently under review). Thus, it is conceivable that a coordinated effort by a given province or even Health Canada could establish a mechanism for OAT patients to access mental health services that are coordinated and delivered through telemedicine.

Current Role of Federal Methadone Regulation

To prescribe methadone for opioid dependence in Canada, physicians must obtain an exemption under Section 56 of the Controlled Drugs and Substances Act issued by the Federal Minister of Health.[28] The oversight of physician practice,

including that related to methadone, falls under the purview of each province's regulatory body (e.g., the College of Physicians and Surgeons). In several provinces, the College makes recommendations to Health Canada with respect to the issuance, term, and removal of these exemptions.

Health Canada is responsible for the provision of methadone for opioid dependence for First Nation, Metis, and Inuit patients. Funding for methadone treatment is provided by the First Nation Inuit Health Branch (FNIHB) of Health Canada. In the case of remote communities, FNIHB will provide transportation to and from the pharmacy for supervised administration for up to 4 months. Regarding distances these patients must travel, the average patient in northern rural Ontario is located 126 km from his or her care provider.[6] Thus, it is common for patients in this region to travel more than 100 km daily, each way, to and from the clinic. The term is intended to be time-limited under the expectation that the patient will be able to stabilize on methadone within 4 months and obtain "carry" doses to take home.[29] In Canada, OAT is tied to contingency management strategies that include increasing the number of doses that a patient is able to take home. These carry privileges are increased based on appointment attendance and consistently negative urine screens for opioids, stimulants, and other substances. Of note, the policies of most provinces require at least 8 months to achieve 6 take-home doses, which is equivalent to visiting the clinic once per week. Conversely, FNIHB travel funding will subsidize only the first 4 months of travel to the clinic.

Health Canada is also responsible for methadone in the federal corrections setting. In the correctional setting, patients who are in methadone therapy prior to entering a correctional facility are able to continue therapy, but patients who have left care prior to being arrested or have never been in therapy are often delayed in their ability to initiate either methadone or buprenorphine OAT due to limited resources.[9]

Current Status of OAT across Canada

Status of OAT in the Atlantic Provinces

The Atlantic Provinces are composed of Newfoundland and Labrador, Nova Scotia, New Brunswick, and Prince Edward Island. All four provinces have provincially funded methadone programs, and there are commonalities and differences across this geographic area. Limited access to OAT for new patients is a common issue across the region. Those who require access to methadone are typically placed on a waiting list until a person leaves the program or new capacity is developed. A recent study in New Brunswick showed the positive effects of a low-threshold/high-tolerance program for opioid-dependent patients who could not access comprehensive programming.[8] A low-threshold/high-tolerance program is a harm reduction strategy that has a low threshold for accessing care while maintaining a high tolerance for patients who continue to use nonmedication opioids during the initial phase of therapy; this strategy contrasts with a focus on early abstinence from all substances as a condition for continued care. In 2013, Christie et al[8] proposed an alternative model, whereby patients who are denied care because of limited resources in a community-based program are still able to access medical management using methadone. The authors demonstrated that in the absence of ancillary services, the provision of methadone was effective in reducing opioid-positive urine screens and retaining patients in the context of the New Brunswick setting.[8] Newfoundland and Labrador established methadone programming in 2005; however, the current program is described as severely underserviced, with reportedly only 7 physicians caring for more than 1000 patients.[9,18] Public statements from the former champions of methadone access and programming are now warning of the unsustainable structure of Newfoundland's current system.

Status of OAT in Quebec and Ontario

Ontario and Quebec are the two most populous provinces in Canada, and the geographic contexts are similar in that the vast majority of the population live within the Great Lakes and St Lawrence corridor. Quebec has a population of approximately 8.5 million people, and Ontario's population is approximately 13.5 million according to the most recent Statistics Canada data.[30] In 2014, Centre de Recherche et d'Aide pour Narcomanes published a report outlining treatment for opioid dependence across the province of Quebec.[31] The document reported that of the 16 health regions in Quebec, 11 had active methadone programming. The number of clients reported to be receiving OAT in 2011 was 3462.[32] Of the clients receiving OAT, more than 60% access services in Montreal. Interestingly, Montreal is currently in line to establish several safe-injection sites.[33] These sites will be the second of their kind in Canada following the establishment of Insite in Vancouver's Downtown East Side more than a decade ago.[34] Insite has been demonstrated to increase referrals to addiction treatment, including OAT,[34-36] and a similar increase in treatment demand could be expected in Montreal.

Conversely, Ontario is reported to have more than 42,000 patients receiving OAT, with 475 physicians holding a methadone exemption.[37] OAT is primarily delivered in physician clinic settings in Ontario, and the presence of the Ontario Telemedicine Network (OTN) allows a relatively small number of physicians (located primarily in urban areas) to service the broad range of the province.[25] The most recent data from the OTN indicate that OAT is the largest user of OTN services in the province.[38] Even with the number of physicians currently delivering OAT, the need to continue to expand care is recognized. As a consequence of the need for OAT and the rapid nature by which OAT clinic expansion has occurred, publically funded supports including counselling, case managers, and social programming have been unable to keep pace. The current climate of OAT in Ontario is one where the provision of pharmacological

support (in the form of methadone or buprenorphine) is funded almost exclusively from physician fee-for-service billings and is separate from the mental health and specialized addiction treatment funding streams that support counselling and mental health programming. There is a recognized divide between the funding, planning, and delivery of these arms of the treatment system; further integration and coordination with primary care, addiction treatment, and mental health services could greatly benefit OAT clients in Ontario.

Status of OAT in Prairie Provinces

Guidelines for OAT in Manitoba differ from those in other provinces. In Manitoba, practitioners follow what are called "recommended practice" guidelines developed by the Addictions Foundation of Manitoba (AFM).[39] These guidelines make substantially less use of urine toxicology; the recommended practice document indicates that the patient needs one urine toxicology test at initiation of treatment and a test approximately every 6 months as clinically necessary. This contrasts with weekly testing in the Ontario guidelines. The main model of care in Manitoba is provincially funded programs run by the AFM, with limited provision of OAT in physician clinics or family practice settings funded by physician services fees.

In Saskatchewan, methadone maintenance treatment (MMT) is limited to physician clinics, community health centers, and prisons. A unique part of the Saskatchewan treatment guidelines[40] is that physicians are required to make referrals to addiction counselors.

In Alberta and Saskatchewan, the provincial Colleges of Physicians and Surgeons oversee MMT guidelines. Although provincial funding has increased somewhat, many access issues remain, especially in Northern Alberta, where there are many out-of-province workers who have difficulty accessing OAT.

In Alberta, like Ontario and British Columbia, opioid-related deaths are reported to be the primary cause of mortality of 18- to 35-year-olds.[41] An alarming increase in the yearly number of fentanyl-related overdoses has been reported in Alberta, and an estimated 300+ deaths were projected for 2015.[42] At the 2015 meeting of the Canadian Society of Addiction Medicine, Dr Hakique Virani recommended a provincial strategy that includes expanding OAT, providing safe injections sites, and distributing naloxone.[41,42]

Status of OAT in British Columbia

In British Columbia, the College of Physicians and Surgeons of British Columbia (CPSBC) oversees OAT guidelines. To track and monitor MMT patients and practitioners, CPSBC has a central patient registry. The CPSBC guidelines include defined admission criteria for people to be able to receive methadone. Through CPSBC, concurrent treatment of mental health and addictions is mandated.

MMT is provided in multidisciplinary clinics funded by the province,[41,42] in private clinics, in prisons, and in family medicine practices; most of the service outside of Vancouver is provided by family medicine physicians as part of their practice.[9] A number of innovative projects and models of care are available in Vancouver to meet the specific needs of this population. As an example, the Sheway Program is a specialized clinic for pregnant women receiving MMT. In addition, North America's first-ever clinical trials of prescribed injection heroin and hydromorphone took place from 2005 to 2008 (NAOMI) and 2011 to 2014 (SALOME) in Vancouver.[43] Over the past year, Supreme Court judgments have allowed study participants who benefited to continue receiving treatment with injection heroin.[44]

Status of OAT in the Territories

The territories are Canada's least populated region, containing approximately 100,000 people spread across a vast geography. Little if any OAT is available outside of Whitehorse, Yukon. The last available data were provided by Luce and Strike[9] in 2011.

Opportunity for a National Strategy on OAT

OAT is a critically important healthcare program for the opioid-dependent population. In 2005, the World Health Organization (WHO) added methadone and buprenorphine to the list of essential medicines because these medicines improve adherence to antiretroviral therapy and reduce the risk of HIV transmittance among injection drug users.[45] The WHO in collaboration with the United Nations Office on Drugs and Crime and the Joint United Nations Programme on HIV/AIDS produced the *Technical Guide for Countries to Set Targets for Universal Access to HIV Prevention, Treatment and Care for Injecting Drug Users.*[46] This document sets objective targets by which program effectiveness can be judged. Indicators include percentage of opioid-dependent people receiving OAT at census date (target >40%), percentage of OAT sites adhering to WHO guidelines (target >80%), percentage of OAT programs providing psychosocial support (target >80%), and percentage of individuals currently receiving OAT who have been on treatment continuously for the past 12 months (target 80%), among other metrics. As a nation, Canada is currently unable to report on the effectiveness or quality of OAT. We believe that the implementation of a national surveillance program would allow for reliable reporting on OAT indicators to inform provincial healthcare providers on both the effectiveness and quality of OAT across health jurisdictions.

Conclusions

The landscape of opioid dependence and treatment is varied across the country. Here, we noted important common themes. First, with the exception of a few regions, treatment capacity is generally increasing across all jurisdictions and is expanding dramatically in some regions (e.g., British Columbia and Ontario). Second, the use of evidence-based alternatives to methadone, such as buprenorphine-naloxone and injection heroin or hydromorphone, needs continued expansion where clinically appropriate and according to patient need. Buprenorphine-naloxone is becoming more available in some jurisdictions, and in some circumstances it has become first-line treatment for opioid dependence (e.g., remote First Nation communities where no methadone providers exist). Third, despite increasing access, challenges remain in many parts of the country, particularly rural and remote areas, because the demand for treatment has increased far beyond the capacity of the treatment system; telemedicine-delivered OAT is a way to increase access in these areas. Fourth, a monitoring system for assessing treatment need and accessing available treatment programs is currently missing in all jurisdictions, and a national planning and coordination strategy would have tremendous value. Fifth, improving treatment access remains a priority in many jurisdictions; however, there is also a need to attend to treatment quality, including integration with addiction counselling, primary care, and mental health care. As treatment capacity continues to grow, priority should be placed on delivering the highest quality of care possible. There is also a demonstrated need for broad distribution of naloxone kits to opioid users. Sixth, a major reason for the highlighted inadequacies in care is the rapid increase of opioid dependence over the previous decade. While not a specific focus of this review, prevention strategies that are aimed at opioid-use disorders should be made a priority provincially and nationally.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: David C. Marsh is the chief medical director of the Canadian Addiction Treatment Centers. All other authors report no conflicts of interest.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: J.K.E. is supported by a Canadian Observational Cohort Collaboration Postdoctoral Research Award and funding from the Northern Ontario Academic Medicine Clinical Innovation Award (DM). E.L. is supported by a Northern Ontario School of Medicine Dean's Research Award. The design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation and review of the manuscript were conducted by the authors independently from the funding sources.

References

1. Halliday R. Management of the narcotic addict. B C Med J. 1963;5:412-414.
2. Dole VP, Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction: a clinical trial with methadone hydrochloride. JAMA. 1965;193:646-650.
3. Fischer B. Prescriptions, power and politics: the turbulent history of methadone maintenance in Canada. J Public Health Policy. 2000;21(2):187-210.
4. Brands B, Marsh DC. Methadone maintenance treatment: a Canadian perspective. CMAJ. 1997;157(4):399-401.
5. Brands J, Brands B, Marsh DCT. The expansion of methadone prescribing in Ontario, 1996-1998. Addict Res. 2000;8(5): 485-496.
6. Eibl JK, Gomes T, Martins D, et al. Evaluating the effectiveness of first-time methadone maintenance therapy across northern, rural, and urban regions of Ontario, Canada. J Addict Med. 2015;9(6):440-446.
7. Nosyk B, Marsh DC, Sun H, et al. Trends in methadone maintenance treatment participation, retention, and compliance to dosing guidelines in British Columbia, Canada: 1996-2006. J Subst Abuse Treat. 2010;39(1):22-31.
8. Christie TK, Murugesan A, Manzer D, et al. Evaluation of a low-threshold/high-tolerance methadone maintenance treatment clinic in Saint John, New Brunswick, Canada: one year retention rate and illicit drug use. J Addict. 2013;2013:753409.
9. Luce J, Strike C. A cross-Canada scan of methadone maintenance treatment policy developments. Ottawa (ON): Canadian Executive Council on Addictions; 2011.
10. Gomes T, Mamdani MM, Dhalla IA, et al. The burden of premature opioid-related mortality. Addiction. 2014;109(9): 1482-1488.
11. Dhalla IA, Mamdani MM, Gomes T, et al. Clustering of opioid prescribing and opioid-related mortality among family physicians in Ontario. Can Fam Physician. 2011;57(3): e92-e96.
12. Gomes T, Mamdani MM, Paterson JM, et al. Trends in high-dose opioid prescribing in Canada. Can Fam Physician. 2014; 60(9):826-832.
13. Lynas K. Ontario pharmacists concerned about the risks arising from approval of generic OxyContin. Can Pharm J (Ott). 2013; 146(1):12-13.
14. Lynas K. Ontario police chiefs call on the federal government to keep generic OxyContin out of Canada. Can Pharm J (Ott). 2013;145(5):204.
15. Gladstone EJ, Smolina K, Morgan SG. Trends and sex differences in prescription opioid deaths in British Columbia, Canada. Inj Prev. 2016;22(4):288-290.
16. Gladstone EJ, Smolina K, Weymann D, et al. Geographic variations in prescription opioid dispensations and deaths among women and men in British Columbia, Canada. Med Care. 2015;53(11):954-959.
17. Woo A. Overprescribed opioids linked to higher rates of overdose, study says. The Globe and Mail (Vancouver). 25 October 2015.

18. CBC News. 19 September 2015. Methadone program pioneer now says it isn't working. CBC News [Internet]. Available from: http://www.cbc.ca/news/canada/newfoundland-labrador/methadone-program-pioneer-now-says-it-isn-t-working-1.3234892
19. Gomes T, Juurlink D, Yao Z, et al. Impact of legislation and a prescription monitoring program on the prevalence of potentially inappropriate prescriptions for monitored drugs in Ontario: a time series analysis. CMAJ Open. 2014;2(4):E256-E261.
20. Buxton JA, Kuo ME, Ramji S, et al. Methadone use in relation to hepatitis C virus testing in British Columbia. Can J Public Health. 2010;101(6):491-494.
21. National Opioid Use Guideline Group. Canadian guideline for safe and effective use of opioids for chronic non-cancer pain. Hamilton (ON): McMaster Press; 2010.
22. Health Canada. Best practices: methadone maintenance treatment. Ottawa (ON): Health Canada; 2002.
23. World Health Organization. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. Geneva (Switzerland): World Health Organization; 2009.
24. Bell J, Burrell T, Indig D, et al. Cycling in and out of treatment; participation in methadone treatment in NSW, 1990-2002. Drug Alcohol Depend. 2006;81(1):55-61.
25. Williams R. Telepsychiatry: virtual care for mental health and addictions [blog]. Ontario Telemedicine Network. 2013. Available from: https://support.otn.ca/en/blog/telepsychiatry%3A-virtual-care-for-mental-health-and-addictions
26. Brooner RK, Kidorf MS, King VL, et al. Managing psychiatric comorbidity within versus outside of methadone treatment settings: a randomized and controlled evaluation. Addiction. 2013;108(11):1942-1951.
27. Fortney JC, Pyne JM, Kimbrell TA, et al. Telemedicine-based collaborative care for posttraumatic stress disorder: a randomized clinical trial. JAMA Psychiatry. 2015;72(1):58-67.
28. Health Canada. Methadone exemption application. Ottawa (ON): Health Canada; 2015.
29. First Nations and Inuit Health (FNIH). Non-insured health benefits (NIHB) medical transportation policy framework. Ottawa (ON): FNIH; 2015.
30. Statistics Canada. Population by year, by province and territory. Ottawa (ON): Statistics Canada; 2013.
31. Centre de Recherche et d'Aide pour Narcomanes (CRAN). Enseignement & innovation, une relève pour demain. Montreal (QC): CRAN; 2014.
32. Centre de Recherche et d'Aide pour Narcomanes (CRAN). La dependance aux opioides: portrait des traitements de substitution au Québec. Montreal (QC): CRAN; 2011.
33. Valiante G. 15 November 2015. Supervised injection sites: Quebec expects federal approval. CBC News [Internet]. Available from: http://www.cbc.ca/news/canada/montreal/safe-injection-sites-supervised-trudeau-canada-government-quebec-1.3319725
34. Wood E, Kerr T, Lloyd-Smith E, et al. Methodology for evaluating Insite: Canada's first medically supervised safer injection facility for injection drug users. Harm Reduct J. 2004;1(1):9.
35. Callon C, Wood E, Marsh D, et al. Barriers and facilitators to methadone maintenance therapy use among illicit opiate injection drug users in Vancouver. J Opioid Manag. 2006;2(1):35-41.
36. Kerr T, Marsh D, Li K, et al. Factors associated with methadone maintenance therapy use among a cohort of polysubstance using injection drug users in Vancouver. Drug Alcohol Depend. 2005;80(3):329-335.
37. College of Physicians and Surgeons of Ontario. Paper presented at: CPSO Methadone Conference; 6 November 2015; Toronto, Canada.
38. Shapiro. Telemedicine and addiction: an indicator of things to come. Paper presented at: Northern Health Research Conference; 2015.
39. Fisher MHA, Lee L, Nepon J, et al. Manitoba methadone & buprenorphine maintenance. Manitoba, Canada: Addictions Foundation of Manitoba; 2014.
40. College of Physicians and Surgeons of Saskatchewan. Methadone guidelines and standards for the treatment of opioid addiction/dependence. March 2015. Available from: https://www.cps.sk.ca/imis/Documents/Programs%20and%20Services/Methadone/SK-Methadone-Guidelines-2015-Mar-FINAL.pdf
41. Virani H. What's up with down: treatment of opioid use disorder in Alberta. Paper presented at: the Canadian Society of Addiction Medicine annual conference. 12 November 2015; Banff, Alberta, Canada.
42. CBC News. 29 September 2015. Fentanyl deaths could reach 300 in Alberta by year's end police warn. CBC News [Internet]. Available from: http://www.cbc.ca/news/canada/calgary/fentanyl-deaths-could-reach-300-in-alberta-1.3249466
43. Oviedo-Joekes E, Brissette S, Marsh DC, et al. Diacetylmorphine versus methadone for the treatment of opioid addiction. N Engl J Med. 2009;361(8):777-786.
44. Keller J. Judge grants injunction allowing doctors to prescribe heroin to group of Vancouver addicts. National Post. 29 May 2014.
45. Herget G. Methadone and buprenorphine added to the WHO list of essential medicines. HIV AIDS Policy Law Rev. 2005;10(3):23-24.
46. World Health Organization. WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users. World Health Organization; United Nations Office on Drugs and Crime; United Nations Joint Programme on HIV/AIDS. World Health Organization: Geneva (Switzerland); 2009.