IOAT: Injectable Opioid Agonist Treatment

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Metaphi webinar

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Disclosures

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OAT prescriber

Objectives

- Understand the problem of insufficient retention in oral Opioid Agonist Treatment
- Describe the strong evidence for IOAT
- Describe IOAT: what is it?
- Describe the process of IOAT and opioid dosing
- Understand the barriers to widely scaled implementation

Background

- Opioid Use Disorder (OUD) is a pressing public health issue
- 38, 514 Canadians died from an apparent opioid-related toxicity between January 2016 and March 2023 https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/#

Select an item from each list below:

Substance

Opioids

Data source

Deaths

Data breakdown

Overall numbers

Type of event

Total apparent opioid toxicity dea

Region

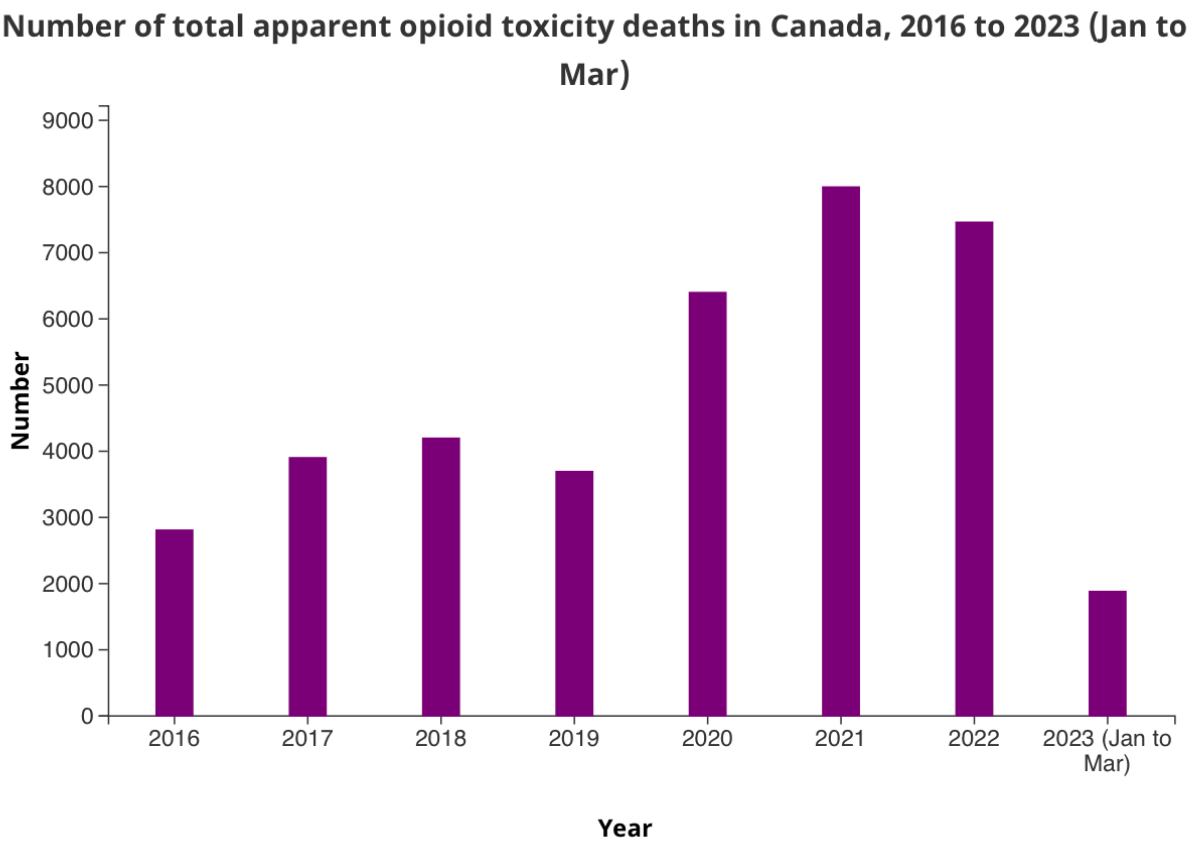
Canada

Time period

By year

Unit

Number



Download Data

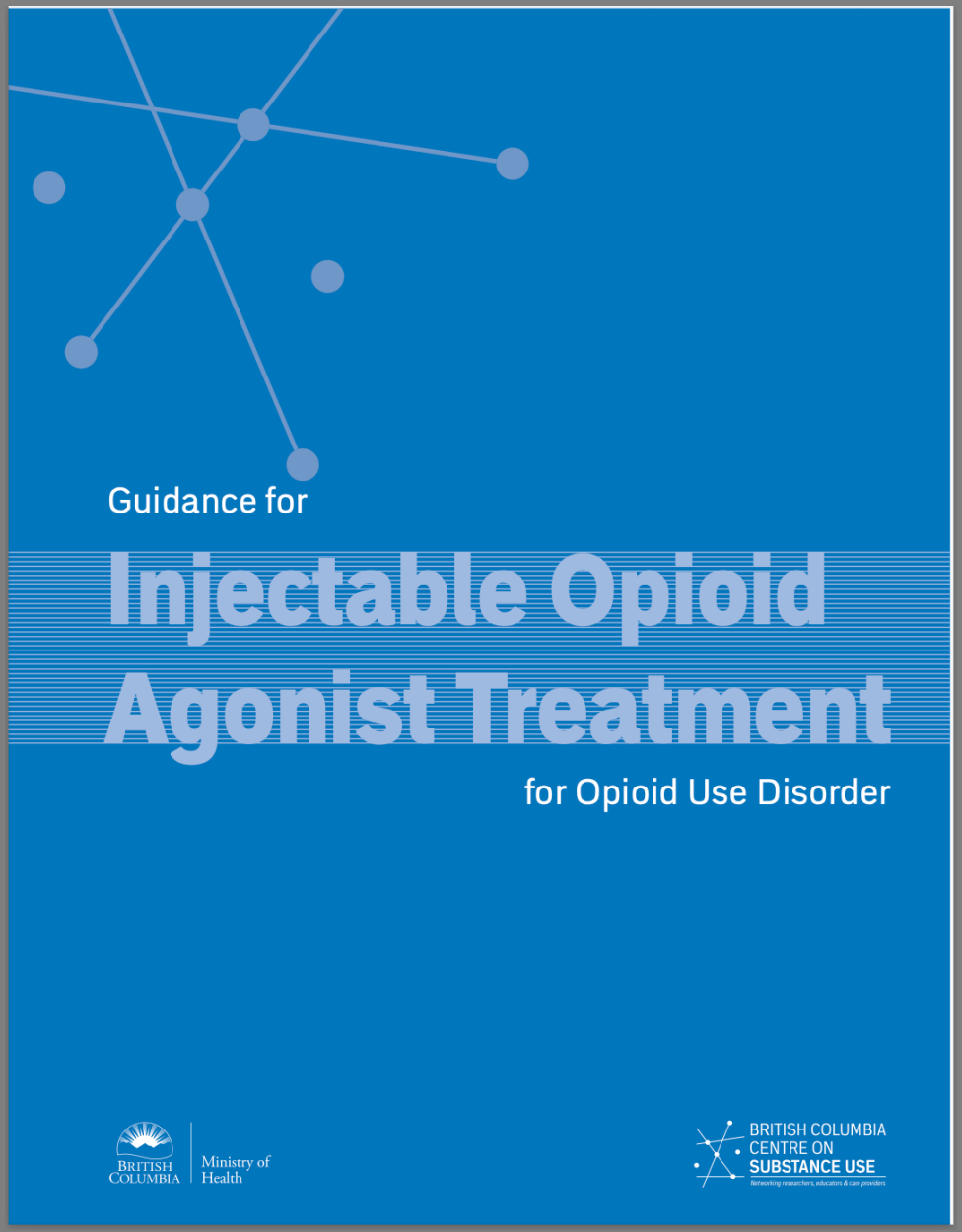
Background

- Opioid Agonist Treatment (OAT) with long-acting oral opioids (methadone, buprenorphine, Slow-Release Oral Morphine, SROM) is the gold standard for OUD treatment, with benefits to health, social functioning, and mortality
- However, long-term (> 6 months) retention in OAT is poor. Median 57% at 12 months https://doi.org/10.1371/journal.pone.0232086

Summary

- 46-65% of patients discontinue methadone treatment in the first year[10,16,17]
- 40-70% of patients discontinue buprenorphine/naloxone treatment in the first six months[19,20]
- Diacetylmorphine treatment is beneficial in terms of reducing illegal or non-medical opioid use, treatment drop-out, criminal activity, incarceration, and mortality[3,4,21]
- 67-88% of patients retained on diacetylmorphine in the first year[22,24,25]
- 77% of patients retained on hydromorphone in the first six months[3]
- Average length of diacetylmorphine treatment is approximately three years[23]

Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder, BCCSU



https://www.bccsu.ca/wp-content/uploads/2021/07/BC_iOAT_Guideline.pdf

What is IOAT?

Among OUD patients who are treatment refractory to methadone, prescription diacetylmorphine (DAM)—administered under the supervision of trained health professionals in a clinic setting—is beneficial in terms of reducing illicit opioid use, treatment drop-out, criminal activity, incarceration, and mortality.

What is IOAT?

- DAM is supplemented with flexible doses of oral OAT at the patient's and prescriber's discretion.
- In almost all countries where it is available, prescription DAM is provided within supervised clinic settings (which ensures compliance and allows monitoring for safety and to prevent diversion), and to specific patients with severe, treatment-refractory OUD.

Evidence for IOAT

- “Several randomized trials and cohort studies have shown that iOAT provided in dedicated clinics is feasible, safe, and effective when treating long-term, chronic injecting opioid users for whom the available treatments have not been effective.
- In these studies, patients treated with diacetylmorphine and hydromorphone showed improvements in a number of dimensions, including reductions in illicit heroin (and, in the SALOME trial, other illicit opioids) and cocaine use, decreased criminal activity, and improvements in physical and mental health.”

-BCCSU IOAT Guidance

Other Jurisdictions

- Prescription diacetylmorphine treatment has been available in Switzerland starting with a national clinical study in 1994, and as a standard drug treatment since 1999
- Germany, Denmark and the Netherlands also adopted supervised prescription diacetylmorphine treatment for those with severe, treatment-refractory OUD
- In these countries, diacetylmorphine is used for <1% to 8% of all patients engaged in treatment for OUD
- Comprehensive European model: patients receive comprehensive addictions care, with the aim of meeting as many of the patient's health and psychosocial needs as possible on-site

Summary of the evidence: Cochrane Review 2012

- Eight randomized clinical trials involving 2007 patients.
- If all the studies comparing heroin provision in any conditions vs any other treatment are pooled, the direction of effect remain in favour of heroin.
- Adverse events were consistently more frequent in the heroin groups
- Benefits to retention, reduced street drug use, illicit activities, possibly mortality.
- Patient profile: those not benefiting (i.e., continue using street heroin whether retained or not) from oral MM

Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin-dependent individuals. Cochrane Database of Systematic Reviews 2011, Issue 12. Art. No.: CD003410. DOI: 10.1002/14651858.CD003410.pub4. Accessed 03 December 2023.

Controlled Dispensing

Supervised Injection Treatment

2 Canadian studies: NAOMI & SALOME

- NAOMI: Compared IOAT with DAM to MMT in people with 2 previous failed methadone attempts. Randomized to DAM or optimized MTD. Retention in IOAT was 87.8%, MTD 54.1%
- SALOME: non-inferiority trial of DAM vs hydromorphone (HM). HM non-inferior to DAM. (rationale: DAM is hard to obtain in N. America while injectable HM is widely available)

How does it work?

- Meds must be prepared in NAPRA-compliant pharmacies (same standards as chemotherapy, TPN).
- Clients attend the IOAT site up to 3 times per day for self-administration of injectable meds
- Pre- and post-visit assessments by HCP: no excessive sedation before or after injection
- Clients typically are co-prescribed an oral long-acting OAT med such as methadone or SROM

Dosing

- High inter-individual variability. Just as with oral OAT, doses must be individually titrated
- In SALOME, max 3 doses per day, max 200 mg HM in any single dose, max 500 mg per day total
- Median daily total dose in SALOME was …?

- 270 mg HM

Dosing

- 50 mg/ mL preparation of injectable HM is necessary to achieve the needed doses
- Ontario ODB Formulary: only 10 mg/mL is covered

Risks & adverse effects

- Optimizing patient safety has been an important factor in the designation of iOAT as a second-line intervention, and requiring doses to be administered in structured, supervised clinical settings.
- Any frequently administered injectable treatment is associated with higher risks of cutaneous and infectious complications compared to its equivalent oral formulation.
- When the skin is punctured (even with a sterile needle in a clinical setting), it provides a potential port of entry for bacteria or other microorganisms, particularly when the injections are being given multiple times per day
- Any frequently administered injectable treatment is associated with higher risks of cutaneous and infectious complications compared to its equivalent oral formulation.

Risks & adverse effects

- iOAT should only be administered in designated clinical settings, with sterile supplies and in clean and safe conditions, and under supervision of qualified staff trained to intervene in the event of an adverse event or emergency
- Studies in Europe and Canada have reported instances of significant respiratory depression events in people receiving injectable opioids, at an overall rate of about 1 in every 6000 injections, which is significantly
  lower than the risk present when injecting street heroin.
- The majority of serious adverse events (SAEs) occur within a few minutes of receiving an injection; therefore, the recommended post-injection supervision period of 15-20 minutes, which would be required regardless of program type or treatment setting

Risks & adverse effects

- In the 12-month NAOMI trial, two SAEs involving sepsis or other infections were reported, while three SAEs involving abscesses or cellulitis were reported, across a total of 89,924 injections.
- In the SALOME trial, over the 180-day treatment period, 18 adverse events involving infectious complications were reported (14 cellulitis, 4 subcutaneous abscesses) over a total of 85,451 injections
- Provision of injectable opioids under supervision also ensures the safety of the community by, for example, *preventing diversion of a prescribed injectable opioid into the street for illicit use*. (Emphasis mine)

Potential scalable models

- Dedicated clinic (e.g. Crosstown clinic in Vancouver)
- Embedded with other services (e.g. CHCs)
- Pharmacy-based (clients inject on site at pharmacy)

Why isn't IOAT more widely available??

- Costs: Bricks and mortar site, staff, and meds
- Pharmacy College regulations for NAPRA-compliant meds compounding
- Provincial governments have not supported it
- Federal government has not supported this model
- Studies on IOAT were done in the heroin era. Is HM even strong enough now, in the fentanyl era?
- Other --?

Take-home messages

- Retention in oral OAT is not good enough
- Optimized methadone arm in NAOMI did very well, for people who had previously failed methadone
- Supervised IOAT with high dose injectable opioids improves retention and health outcomes in people who have not sufficiently benefitted from oral OAT
- There remain significant barriers to implementation

Thank you!

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