Heroin & Hydromorphone: Injectable Opioid Agonist Treatments

D. SCOTT MACDONALD MD
Physician Lead
PROVIDENCE CROSSTOWN CLINIC
HTTPS://TWITTER.COM/_DRSCOTT_
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DISCLOSURE OF COMMERCIAL SUPPORT

• None to report
FACULTY/PRESENTER DISCLOSURE

• Faculty: Scott MacDonald

• Will discuss off-label use of hydromorphone for treatment of severe opioid use disorder

• Relationships with commercial interests:
  - Nil
MITIGATING POTENTIAL BIAS

• Evidence from RCT supporting use of hydromorphone will be presented
Acknowledgements

• Study participants
• Frontline workers at the Crosstown clinic
• Research team
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  – Canadian Institutes of Health Research
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  – University of British Columbia
  – Center for Health Evaluation and Outcomes Science
  – Canada Research Chairs Program
  – BC Ministry of Health

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  – BCCSU
  – Dr. Nadia Fairburn
  – Health Canada and its many divisions
  – PHC/UBC Research Ethic Board
  – Data and Safety Monitoring Board
  – Community Advisory Board
Outline

• Treatments for OUD
• Injectable Diacetylmorphine and Hydromorphone - evidence from RCT’s
• SALOME rationale and results
• Politics and Policy
• BC iOAT guidance document
• Optimism and rising to meet a crisis
Background

- Opioid use disorder is a chronic relapsing disease.
- Oral agonist treatment with long-acting opioids (e.g. methadone, buprenorphine, SROM) works, however not for everyone, or all the time.
- Clinical evidence from Canada and European studies indicates that medically prescribed injectable DAM (diacetylmorphine, the active ingredient in heroin), is an effective, feasible and safe treatment approach.
- No single treatment is effective for all individuals, diverse treatment options are needed, including psychosocial approaches and pharmacological treatments (WHO guidelines on opioid dependency treatment).
A Limited Menu

- Avoid detoxification or withdrawal alone without immediate transition to opioid agonist treatment
- Suboxone (Buprenorphine/Naloxone)
- Methadone
- SROM (Kadian as sprinkles)
- Injectables (Diacetylmorphine and hydromorphone)

Summary of the evidence Diacetylmorphine: 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

• Retention, reduce street drug use, illicit activities, possibly mortality.

• Patient profile: those not benefiting (i.e., continue using street heroin whether retained or not) from oral MMT (or suboxone)
Who should pay?

1) Injectable costs covered by user (i.e. user pay)

2) Injectable costs integrated into health care system

3) Blended model
Cost-effectiveness of diacetylmorphine versus methadone for chronic opioid dependence refractory to treatment

- CMAJ study compared heroin to methadone in preventing relapses to illicit opioid use
- diacetylmorphine more effective and less costly than methadone among people with chronic opioid dependence refractory to treatment
- better outcomes at lower overall cost
- diacetylmorphine dominates methadone (in the population continuing illicit opioid use)

“An ineffective service is inefficient and cannot be cost-effective, no matter how cheaply it is provided”

COCHRANE, 1972
SALOME rationale

• Health Canada denied compassionate access for diacetylmorphine in May 2008:
  – “In the course of reviewing your request, we determined that there are other options (i.e., marketed drugs) that we would consider alternative to diamorphine at this time”.

• The injectable side of the clinic closed and patients were transferred to oral methadone. PHC kept the site open.

• NAOMI provided hydromorphone to 25 participants (to test for heroin metabolites in urine):
  – blinding was not broken;
  – almost identical treatment effect compared to diacetylmorphine (however, study not powered to test this hypothesis).
  – Similar profile that diacetylmorphine
  – Licensed opioid in Canada for analgesia
SALOME

• Tested the **non-inferiority** of hydromorphone compared to diacetylmorphine for long-term opioid dependence in a double-blind Randomized Clinical Trial.

• Non-inferiority trials are designed to test treatments that offer **ancillary advantages** over those that have shown to be effective in previous superiority studies.

• Ancillary advantage of hydromorphone: is currently **licensed** for analgesia.
Participants’ profile

“Long-term injection opioid users who are not sufficiently benefiting from available therapies”

- Opioid Dependence as confirmed by DSM IV diagnostic criteria;
- 19 years of age or older;
- At least 5 years of opioid use;
- Injecting opioids regularly in the past year;
- At least two episodes of opioid addiction treatment (methadone maintenance, detoxification, residential care, etc.), including one or more episodes of substitution treatment;
- Poor physical, psychological, mental or psychosocial functioning
### SALOME patients and the chronic nature of opioid dependence

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Total n= 202 Mean ± SD/n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.3 ± 9.6</td>
</tr>
<tr>
<td>Age start using heroin</td>
<td>24.8 ± 8.7</td>
</tr>
<tr>
<td>Years injecting heroin in life</td>
<td>15.4 ± 9.4</td>
</tr>
<tr>
<td>Months abstinent of street opioids in lifetime</td>
<td>21.9 ± 40.2</td>
</tr>
<tr>
<td>Number of Methadone Maintenance Episodes in life</td>
<td>5.1 ± 3.4</td>
</tr>
<tr>
<td>Years receiving Methadone in life</td>
<td>4.8 ± 4.7</td>
</tr>
<tr>
<td>Times attempted outpatient withdrawal</td>
<td>5.6 ± 7.6</td>
</tr>
<tr>
<td>Times attempted residential treatment</td>
<td>2.2 ± 3.5</td>
</tr>
<tr>
<td>Ever accessed outpatient counselling</td>
<td>127 (62.9)</td>
</tr>
</tbody>
</table>
**Blinding**

- At baseline 83.2% of participants indicated that they wished to be randomized to injectable diacetylmorphine.
- When asked if only injectable hydromorphone was available, if participants would start this treatment, 82.2% responded yes.

- Participants did not correctly guess their treatment allocation beyond what would be expected by random guessing.
  - Specifically, 48% of participants in the hydromorphone group guessed they were receiving diacetylmorphine or were unsure. Likewise, 64% of participants in the diacetylmorphine group guessed they were receiving hydromorphone or were unsure.
Primary efficacy outcomes according to analysis population a six months

### Difference: DAM minus HDM (two-sided 90% CI)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ITT</th>
<th>PP</th>
<th>DAM</th>
<th>HDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of street heroin use in the prior month</td>
<td>5.50 (3.81 to 7.34)</td>
<td>4.08 (2.42 to 5.81)</td>
<td>3.15 (1.82 to 4.67)</td>
<td>2.64 (1.36 to 3.95)</td>
</tr>
<tr>
<td>Days of street opioid use in the prior month, including heroin</td>
<td>5.75 (4.07 to 7.62)</td>
<td>4.34 (2.66 to 6.18)</td>
<td>4.90 (3.34 to 6.79)</td>
<td>4.20 (2.62 to 5.88)</td>
</tr>
<tr>
<td>Proportion of urinalyses positive for street heroin metabolites in the 6th month visit urine sample</td>
<td>0.21 (0.13 to 0.30)</td>
<td>0.19 (0.11 to 0.28)</td>
<td>0.30 (0.20 to 0.40)</td>
<td>0.32 (0.22 to 0.42)</td>
</tr>
</tbody>
</table>
Retention

Time to First 30-Day SALOME Treatment Interruption

Events in Next Period / Subjects Currently at Risk:

<table>
<thead>
<tr>
<th></th>
<th>PP: HDM</th>
<th>PP: DAM</th>
<th>ITT: HDM</th>
<th>ITT: DAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0/64</td>
<td>1/64</td>
<td>0/63</td>
<td>0/83</td>
<td>0/83</td>
</tr>
<tr>
<td>0/63</td>
<td>0/63</td>
<td>0/83</td>
<td>0/83</td>
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<td>0/83</td>
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<td>0/83</td>
<td>0/83</td>
<td>0/83</td>
<td>0/83</td>
<td>0/83</td>
</tr>
</tbody>
</table>

Probability of Survival

Days from Treatment Initiation

- ITT: HDM
- ITT: DAM
- PP: HDM
- PP: DAM
# Secondary Outcomes

<table>
<thead>
<tr>
<th>Secondary outcomes in the prior 30 days</th>
<th>HDM (95%CI)</th>
<th>DAM (95%CI)</th>
<th>Difference: DAM minus HDM (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of participants receiving study medications ≥ 28 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>0.77 (0.69 to 0.85)</td>
<td>0.80 (0.72 to 0.88)</td>
<td>0.03 (-0.08 to 0.14)</td>
</tr>
<tr>
<td>PP</td>
<td>0.92 (0.86 to 0.98)</td>
<td>0.94 (0.89 to 0.99)</td>
<td>0.02 (-0.05 to 0.10)</td>
</tr>
<tr>
<td>MAP physical health &lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>11.70 (10.28 to 13.13)</td>
<td>11.71 (10.23 to 13.19)</td>
<td>0.00 (-2.02 to 2.03)</td>
</tr>
<tr>
<td>PP</td>
<td>12.12 (10.62 to 13.61)</td>
<td>11.98 (10.45 to 13.51)</td>
<td>-0.13 (-2.25 to 1.98)</td>
</tr>
<tr>
<td>MAP psychological health &lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>9.08 (7.58 to 10.58)</td>
<td>8.13 (6.55 to 9.71)</td>
<td>-0.95 (-3.09 to 1.19)</td>
</tr>
<tr>
<td>PP</td>
<td>9.51 (7.90 to 11.13)</td>
<td>8.11 (6.50 to 9.72)</td>
<td>-1.40 (-3.65 to 0.85)</td>
</tr>
<tr>
<td>Days of illegal activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>3.76 (2.14 to 5.66)</td>
<td>2.78 (1.65 to 4.21)</td>
<td>-0.98 (-3.11 to 1.04)</td>
</tr>
<tr>
<td>PP</td>
<td>3.73 (1.73 to 5.65)</td>
<td>2.78 (1.35 to 4.14)</td>
<td>-1.06 (-3.46 to 1.14)</td>
</tr>
<tr>
<td>Days of crack cocaine use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ITT</td>
<td>7.09 (5.04 to 9.72)</td>
<td>4.78 (3.17 to 7.02)</td>
<td>-2.31 (-4.73 to -0.21)&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>PP</td>
<td>6.43 (4.03 to 9.47)</td>
<td>4.87 (2.91 to 7.53)</td>
<td>-1.56 (-3.94 to 0.41)</td>
</tr>
</tbody>
</table>

<sup>a</sup> MAP data are presented as the group mean scores.
## Diacetylmorphine and methadone dose in RCTs (daily average)

<table>
<thead>
<tr>
<th>RCT</th>
<th>Participants</th>
<th>DAM</th>
<th>Oral MMT</th>
<th>HDM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genevea 1998</td>
<td>51</td>
<td>509 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands 2003</td>
<td>174</td>
<td>549 mg</td>
<td>71 mg</td>
<td></td>
</tr>
<tr>
<td>Spain 2006</td>
<td>62</td>
<td>274 mg</td>
<td>105 mg</td>
<td></td>
</tr>
<tr>
<td>Germany 2007</td>
<td>1032</td>
<td>442 mg</td>
<td>99 mg</td>
<td></td>
</tr>
<tr>
<td>NAOMI 2009</td>
<td>226</td>
<td>392 mg</td>
<td>96 mg</td>
<td>212 mg</td>
</tr>
<tr>
<td>UK 2010</td>
<td>127</td>
<td>399 mg</td>
<td>107 mg</td>
<td></td>
</tr>
<tr>
<td>Belgium 2015</td>
<td>74</td>
<td>573 mg</td>
<td>77 mg</td>
<td></td>
</tr>
<tr>
<td>SALOME 2016</td>
<td>202</td>
<td>506 mg</td>
<td>-</td>
<td>261 mg</td>
</tr>
<tr>
<td>SALOME 2016</td>
<td>202</td>
<td>506 mg</td>
<td>-</td>
<td>261 mg</td>
</tr>
</tbody>
</table>
True or False?
Most people want to take more than prescribed and vigilance is required to prevent dose escalation when prescribing injectable hydromorphone for the treatment of opioid use disorder.
Mean daily dose prescribed and received of DAM equivalent by arm
Adverse Events Summary

• All related AEs and SAEs were expected: mostly histamine reactions and over sedation.

• Hydromorphone had significantly less AEs and SAEs compared to diacetylmorphine.

• In the total 88,451 injections, there were 14 opioid overdoses that required naloxone, and 11 seizures (in 4 patients), all successfully treated on site without hospitalization.
True or False?

Most people want to take more than prescribed and vigilance is required to prevent dose escalation when prescribing injectable hydromorphone for the treatment of opioid use disorder.

False, in fact most people take less than prescribed and after the initiation phase doses stabilize within a few weeks.
Quote (Female Participant)
"uhm honestly, the other methods of treatment that I’ve done, they weren’t looking realistically at what I was needing, right, there was always trying to tell me what I needed. You know like uhm, abstinence programs for instance, have never worked for me, and I just haven’t, I’ve tried to explain that when I’ve gone into them, sort of been pushed into some of them, uhm, that I always just have felt that there is something wrong with me that I just couldn’t do that. Here I’m not told how I should be, it’s like, we understand what you’re asking for, here’s what we can provide you with..."
SALOME CONCLUSION

• In jurisdictions where diacetylmorphine is currently not available or for patients where it is contraindicated or unsuccessful, hydromorphone could be offered as an alternative within the supervised model of care.

• In a broader context, SALOME participants have provided key evidence to support the supervised model of care:
  – In a double-blind study, where participants did not guess the medication they were receiving beyond what is expected by chance, outcomes did not differ.
Politics and Policy

- siOAT = supervised injectable opioid agonist treatment
- Safe, effective, cost effective
- No controversy here folks
- Both diacetylmorphine and hydromorphone are needed
B.C. doctors given Health Canada approval to prescribe heroin

ANDREA WOO VANCOUVER — The Globe and Mail Published Friday, Sep. 20 2013

Health Canada on Friday authorized doctors to prescribe heroin to around 15 patients, The Globe and Mail has learned. The doctors had applied to Health Canada under its Special Access Programme (SAP), which grants doctors access to non-marketed or otherwise unapproved drugs for patients with “serious or life-threatening conditions when conventional therapies have failed, are unsuitable or unavailable,”
Ottawa vetoes prescription heroin treatment for addicts

ADRIAN MORROW and Andrea Woo

The Globe and Mail Published Thursday, Oct. 03 2013, 2:08 PM EDT

"Our policy is to take heroin out of the hands of addicts, not to put it into their arms."
Vancouver addicts soon to receive prescription heroin

ANDREA WOO  VANCOUVER — The Globe and Mail Published Saturday, Nov. 22 2014
Health Canada to allow imports of drugs needed to treat opioid addiction

- SHERYL UBEleckER, TORONTO, THE CANADIAN PRESS, JUNE 28, 2017
- "The new regulatory pathway will enable public health officials to access drugs that aren't approved in Canada that can be used in public health emergencies, like what we're seeing in the opioid crisis," Suzy McDonald, assistant deputy minister of the department's Opioid Response Team, told a media briefing from Ottawa.
Injectable Opioid Agonist Treatment (iOAT)

Nadia Fairbairn, MD FRCPC
Assistant Professor, Department of Medicine, UBC
Research Scientist, BC Centre on Substance Use
Objectives

- Incorporate iOAT as part of the continuum of care for opioid use disorder
- Evaluate patients for starting iOAT
- Safely initiate iOAT
- Provide ongoing clinical support to a patient on iOAT
- Consider patient safety and regulatory requirements for offering an iOAT program
Preferred treatments for severe OUD?

- 1) Abstinence only
- 2) Oral substitution treatment with methadone or suboxone
- 3) Injectable treatment with hydromorphone (Dilaudid) or diacetylmorphine (prescription heroin)
- 4) Residential treatment followed by Drug-Free Community living
- 5) Whatever works
iOAT in the Continuum of Care for OUD

1. Amato et al. 2013
2. Gowing et al. 2009
3. Gowing et al. 2014
4. Amato et al. 2011
5. Minozzi et al. 2011
8. Faggiano et al. 2003
9. Ferri et al. 2013
The Continuum of Care for Chronic Disease

**Individuals at risk:**
- Smokers
- Environmental exposure

**All patients:**
- Exercise-rehabilitation
- Smoking cessation
- Healthy lifestyle
- Patient education

<table>
<thead>
<tr>
<th>Increasing severity of COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza and pneumococcal immunizations</td>
</tr>
<tr>
<td>Therapy for mild symptoms: short-acting beta_2_ agonists and anticholinergics</td>
</tr>
<tr>
<td>Pulmonary rehabilitation</td>
</tr>
<tr>
<td>Additional therapy: inhaled long-acting beta_2_ agonists</td>
</tr>
<tr>
<td>Inhaled corticosteroids (in certain patients)</td>
</tr>
<tr>
<td>Oxygen</td>
</tr>
<tr>
<td>Theophylline (in certain patients)</td>
</tr>
<tr>
<td>Surgery (in certain patients)</td>
</tr>
<tr>
<td>End of life care</td>
</tr>
</tbody>
</table>

**OPIOID USE DISORDER IN PRIMARY CARE conference 2017**

#OUDPC
Preferred treatments from client perspective

- Opioid free living
- Illicit opioid free living
- Living free of injecting illicit opioids
- Injectable opioid agonist treatment
- A safe high
## Continuum of Care

<table>
<thead>
<tr>
<th>The Continuum of Care Should Include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully functioning referral pathways to addiction, recovery, and substance use treatment (e.g., psychosocial treatment, in/outpatient treatment, primary care)</td>
</tr>
<tr>
<td>Mechanisms to support appropriate movement along the continuum of care</td>
</tr>
<tr>
<td>Linkages to primary care</td>
</tr>
<tr>
<td>Increased access to psychosocial treatment interventions and supports</td>
</tr>
<tr>
<td>Decreased barriers to oral OAT</td>
</tr>
</tbody>
</table>
Models of Care in BC

1. A Comprehensive and Dedicated Supervised Injectable Opioid Agonist Treatment Program (e.g., Crosstown Clinic)

   - iOAT provided alongside life-skills counselling, housing referrals, and other psychosocial supports provided by on-site nurses, substance use counsellors, psychiatrists, addiction medicine physicians, nurse practitioners, Registered Social Workers, and Registered Clinical Social Workers
Models of Care in BC

2. Integrated or Embedded Supervised Injectable Opioid Agonist Treatment Program

– Similar to Comprehensive and Dedicated Supervised iOAT Program

– iOAT services integrated into existing community health clinics, harm reduction programs, acute care settings, supportive housing, and other existing health provider services
Models of Care in BC

3. Emerging Model: Pharmacy-Based Supervised Injectable Opioid Agonist Treatment Program

- Currently being piloted in Vancouver
- Titration performed at prescriber’s office or clinic
- Preparation, dispensation, and supervision of self-administered injection performed by trained pharmacists
Caring for a patient on iOAT

• iOAT is the highest intensity treatment option available for people with severe OUD who have been unsuccessful at reducing or ceasing illicit opioid use with the assistance of adequately dosed lower-intensity treatment options (i.e., oral OAT)

• Patients must be prepared to attend supervised injection at least daily

• Supervised injection includes limited options for injection sites (e.g., not injecting in jugular or femoral vein) in order to reduce the risks associated with any intravenous access
# Operations of an iOAT program

## Minimum Recommended Criteria

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dedicated space for supervised self-administration</td>
<td>MD, NP, RN, or RPN to provide intramuscular injection when clinically appropriate</td>
</tr>
<tr>
<td>At least one NP, RN, RPN, or pharmacist who has the authority and experience to manage opioids under the Controlled Drugs and Substances Act to oversee the program</td>
<td>A plan for patient safety in case of overdose and appropriate equipment to manage an overdose prior to transfer to a higher level of care</td>
</tr>
<tr>
<td>A plan to prevent diversion and manage attempts at diversion (may include suspension from the program to a less intensive method of treatment)</td>
<td>Provision for access to medication up to 12 hours per day (minimum 3 hours required between doses, most patients require 2 or 3 doses per day), seven days per week</td>
</tr>
<tr>
<td>Secure, locked storage for medication</td>
<td>Staff-to-patient ratio appropriate to space and number of patients</td>
</tr>
<tr>
<td>Ability to provide individually titrated, patient-specific doses</td>
<td>Ongoing and consistent access to prescriber to allow medication adjustment</td>
</tr>
<tr>
<td>Capacity to observe patients before, during, and after administration</td>
<td>Ability to link patients to ancillary services</td>
</tr>
</tbody>
</table>
Patient Selection

• Clinicians should use their discretion in determining which pharmacological and/or non-pharmacological treatments for opioid use disorder have the highest likelihood of ensuring the goals of care

• Goals of care include survival, reduction in the use of illicit opioids, and the least intensive level of care possible
Eligibility

<table>
<thead>
<tr>
<th>Eligibility considerations for injectable opioid agonist treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capacity to consent to and fully understand the goals of treatment, including:</td>
</tr>
<tr>
<td>• Level of intensity of treatment (i.e., multiple clinical visits per day)</td>
</tr>
<tr>
<td>• Risks of iOAT</td>
</tr>
<tr>
<td>• Requirements of inclusion in the program</td>
</tr>
<tr>
<td>• Requirements of supervised self-administration</td>
</tr>
<tr>
<td>Well-established history of injection drug use with opioids and severe opioid use disorder (DSM-V)</td>
</tr>
<tr>
<td>Able to self-administer (i.e., inject via intravenous or intramuscular route) medication under supervision</td>
</tr>
<tr>
<td>Significant risk of medical consequences of injection drug use that would likely benefit from increased health system involvement and engagement in care, or existing significant medical and/or psychiatric comorbidities (e.g., HIV positive and antiretroviral non-adherence, acute hepatitis, cardiopulmonary disease, severe mental health challenges, history of multiple overdoses)</td>
</tr>
<tr>
<td>At least 18 years old</td>
</tr>
</tbody>
</table>
Eligibility

Eligibility considerations for injectable opioid agonist treatment:

Current opioid injection drug use confirmed by:
- Patient report
- Signs of injection drug use (e.g., fresh puncture wounds or “track” marks)
- Documented opioid-positive urine drug tests (at least two recommended)

Able to attend clinic or pharmacy up to three times daily (physically able and reside in proximity)

No co-prescribed benzodiazepines and/or z-drugs

Past experience with appropriately dosed oral agonist therapies and evidence of regular and ongoing IV opioid use while trialed on oral OAT OR multiple attempts at oral agonist therapies without reaching therapeutic dose or successfully reducing/discontinuing illicit opioid use with continued health and social consequences

Does not fit the criteria for active moderate or severe alcohol use disorder or sedative use disorder
## Precautions

<table>
<thead>
<tr>
<th>Caution</th>
<th>Extreme Caution (oral OAT preferable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic medical conditions (e.g., respiratory, hepatic or renal disease), acute conditions, or recent head injury</td>
<td>Existing injection-related infections (e.g., septicemia, endocarditis, pneumonia, infective osteomyelitis)</td>
</tr>
<tr>
<td>Youth and older adults</td>
<td>*Clinicians should carefully consider drug-drug interactions</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
</tr>
<tr>
<td>Inability to self-administer medication due to either inadequate venous access in ‘low-risk’ sites (with consequent injecting in neck or groin veins), or persistently poor injecting technique not remedied by education about intramuscular injection</td>
<td>Coagulation disorders (e.g., patients prescribed anticoagulants, severe hepatic disease, deep vein thrombosis).</td>
</tr>
</tbody>
</table>
Patient Selection

Additional steps when considering eligibility:

• Consult patient’s extended care network for individual situation and risks
• Determine appropriateness of iOAT in concert with primary care provider and OAT prescriber
• Prescriber-patient relationship, clinical judgment, and information from extended care network inform decision to start iOAT
• Formulate biopsychosocial treatment goals with extended care network
• Informed consent required
• Peer orientation recommended
iOAT Titration Process

• Initial adjustment of iOAT dose over a three to five-day titration period
• Prescribers can lower dose or suggest more gradual titration based on patient’s response and safety concerns at any time during titration period
• Doses must be titrated specifically for each patient in order to achieve a safe and effective dose
• A lower starting dose or slower titration process can be followed, per patient’s medical history or clinical experience, under direction of the prescriber
iOAT Titration Process

• Dose increases need to be tolerated in order to continue at that dose. Doses not tolerated, per pre- or post- injection assessment, should be reduced

• Doses should be titrated to clinical effect (i.e., cessation of illicit opioid use and opioid cravings) and avoidance of side effects (e.g., sedation, narcotic bowel, opioid-induced hyperalgesia)

• Dose and frequency of daily injection sessions (≤3) can be adjusted by patient and prescriber (review dose received history and consult, as necessary, with health care professional who has performed pre/post assessments)
## Accelerated HDM Titration Schedule

<table>
<thead>
<tr>
<th>Session 1</th>
<th>Session 2</th>
<th>Session 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td><strong>Day 2</strong></td>
<td><strong>Day 3</strong></td>
</tr>
<tr>
<td>1. Give 20 mg Wait 20 min 1. If tolerated dose, give 20 mg Wait 20 min (Max dose 40 mg)</td>
<td>1. Give 40 mg Wait 20 min 1. If tolerated dose, give 20 mg Wait 20 min (Max dose 60 mg)</td>
<td>1. Give 60 mg Wait 20 min 1. If tolerated, Give 20 mg Wait 20 min (Max dose 80 mg)</td>
</tr>
<tr>
<td><strong>Day 2</strong></td>
<td>1. Administer 40% of total daily dose at Day 1 (to max of 70 mg) Wait 20 min 1. If tolerated, Give 20 mg Wait 20 min (Max dose 90 mg)</td>
<td>1. Give 90 mg Wait 20 min 1. If tolerated dose, give 20 mg Wait 20 min (Max dose 110 mg)</td>
</tr>
<tr>
<td><strong>Day 3</strong></td>
<td>Administer the maximum tolerated amount at Day 2 (Max 130 mg) Wait 20 min</td>
<td>Administer the maximum tolerated amount at Day 2 (Max 130 mg) Wait 20 min</td>
</tr>
</tbody>
</table>
Dose Stabilization

• Adjust the dosage once a week, or as needed, until:
  – Patient feels comfortable (i.e., reduced cravings and withdrawal symptoms)
  – No excessive intoxication or respiratory depression, or
  – Maximum dose is reached

• Dose increases are discouraged on weekends and holiday

• Some patients may miss titration sessions due to unstable housing and other issues, requiring a modified protocol over multiple days
Co-Prescription of Oral Opioid Agonist Treatments

- Oral OAT (methadone or SROM) can be added at any time to avoid withdrawal symptoms between injections or reduce number of daily visits
- SROM is preferred due to its improved safety profile
- Oral OAT dosing should be patient-lead to optimize comfort and decrease cravings
# Pre-Injection Assessment

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Assessment Date and Time:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

- ☐ ☐ ☐ Severe anxiety or agitation
- ☐ ☐ ☐ Dyskinetic
- ☐ ☐ ☐ Overly sedated
- ☐ ☐ ☐ Slurred speech
- ☐ ☐ ☐ Smells of alcohol

Baseline respiration rate: ________ breaths / minute
Pasero Opioid-induced Sedation Scale\(^5\) (POSS) level:

Breathalyzer required: Yes ☐ No ☐
If yes, breathalyzer reading:

Notes:

Assessment completed by:
## Safety Considerations

<table>
<thead>
<tr>
<th>Consideration</th>
<th>Frequency</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory depression</td>
<td>1 in 6000 injections</td>
<td>Significantly lower than street heroin; each safely managed</td>
</tr>
<tr>
<td>Infection complications (e.g., sepsis, osteomyelitis, cellulitis, abscesses)</td>
<td>2 SAEs involving sepsis/other infections, 3 SAEs involving abscesses or cellulitis across 89,924 injections in 12-month NAOMI trial</td>
<td>Risk of infection and infectious sequelae in a sterile and supervised setting is only a fraction of the risk for those injecting street heroin</td>
</tr>
<tr>
<td></td>
<td>18 adverse events involving infectious complications across 85,451 injections in 6-month SALOME trial</td>
<td></td>
</tr>
<tr>
<td>Blood-borne illness (e.g., HIV, hepatitis C) through equipment sharing</td>
<td>-</td>
<td>Risk is eliminated with use of sterile equipment in supervised setting</td>
</tr>
</tbody>
</table>
Safety Considerations

Benefits of supervised injection

Ensure safety before (e.g., no signs of intoxication) and after injection (e.g., over-sedation, respiratory depression)

Immediate onsite treatment in case of overdose

Prevents diversion

No negative effects on public safety
Resources

- Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder
Optimism
U.S. Senate’s Most Powerful committee hears about Vancouver Clinics – June 2016
Former Ottawa police chief and current senator Vern White is applauding an opioid replacement program being set up by Ottawa Inner City Health. He has been calling for similar programs across the country.
Alberta approves pilot programs for injectable opioid therapy

BY KEITH GEREIN
ORIGINALLY PUBLISHED: NOV 1, 2017

Albertans who have struggled with traditional forms of opioid treatment such as suboxone and methadone could soon have access to an injectable form of therapy.
Example Case: Baseline

• Ms. MJ is a 38 year old female with severe opioid use disorder. She is originally from Ontario and identifies as aboriginal
• She suffered serial abuse and trauma in childhood
• She has used injectable opioids since age 17, over 20 years.
• She tried methadone at least 5 times and up to a dose of 150mg but continued to use heroin.
• She tried detox and residential treatment but relapsed to illicit opioids after discharge
Case: Consequences

• She has had overdoses requiring resuscitation with Narcan
• She was involved in the sex trade to support her opioid needs.
• She has had criminal charges due to illicit activities to obtain opioids and prevent withdrawal.
• She acquired Hepatitis C through needle use.
Case: siOAT

- Attends Crosstown twice daily and has extinguished her illicit opioid use
- She has stopped all illegal activities
- She has obtained better housing
- She has reconnected with family
- Working part time at her housing
Client Centered Goals: Short Term

- Reduce illicit opioid use
- See a dentist
- Work on getting ID
- Wants a haircut before ID
- See psychiatry regarding stimulant use, interested in long acting treatment - dexamphetamine spansules (1.)
- Consider NRT, would try puffer, not today
- Apply for status card

Longer term client centered goals

- Get ID & status card
- Get dental work done, and maybe dentures or implants
- Work more, not ready for full time
- Treat Hepatitis C
Participant Perceptions of Treatment Effectiveness and Trial Findings in the SALOME Clinical Trial

Heather Palis
PHD candidate
School of Population and Public Health, University of British Columbia
## Emergent Themes

<table>
<thead>
<tr>
<th>Why is treatment effective?</th>
<th>Total (N=191)</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved Health</td>
<td>79</td>
<td>41%</td>
</tr>
<tr>
<td>Improved Quality of Life</td>
<td>64</td>
<td>34%</td>
</tr>
<tr>
<td>Stopped or reduced street use</td>
<td>57</td>
<td>30%</td>
</tr>
<tr>
<td>Stopped or reduced illegal activity</td>
<td>41</td>
<td>21%</td>
</tr>
<tr>
<td>Reduced craving or withdrawal</td>
<td>39</td>
<td>20%</td>
</tr>
<tr>
<td>Spending money on things other than drugs</td>
<td>24</td>
<td>13%</td>
</tr>
<tr>
<td>Model of Care</td>
<td>24</td>
<td>13%</td>
</tr>
</tbody>
</table>

Total column refers to the total number of participants that made a reference at a given theme. Total % column refers to the percent of participants referencing a given theme out of all participants that provided a response (n=191). (E.g. for Improved Health: 79/191= 41%).
Improved Health

• “Everything in my life has changed, I have housing now, I eat every day, I'm sleeping better, I am way healthier, less stressed. I have a cat now that I spayed and vaccinated and take care of - I haven't had a pet in 10 years because I was too all over the place mentally. I also have regained my relationship with my mom, my siblings, my kids, my partner. I was so wrapped up in addiction that I became a non-person. Now I'm woken up. I'm back.”

(Participant 6089)
Improved Quality of Life

• “I am very content with what I'm getting and the whole program. It's given me time to reflect on things I was too busy to reflect on before. Being wired is a full time job. Getting the coin, scoring, enjoying the high: it consumes a big part of your day. Now, I have more time, and I'm finding more things to do that I like, like cycling. I'm helping one of the other participants become a better reader. Hanging out with friends, playing pool.”

(Participant 6125)
Stopped or Reduced Illegal Activity

• “I'm taking care of business now, getting my life on track, of course my money situation has improved, healthier now, I was doing crime before, and now there's no need for money, for doing whatever to get money, I have a choice now, and I choose to do hardly any crime”.

(Participant 6201)
Model of Care: Quotes

“See the thing about the program too is its not just the whole group of support it’s the dietician it’s the doctors, it’s the social workers that help you get housing, help you get ID, help you hook up with your families again... There is such a big program of support around you and they help people build their lives again in a very strong way and it is really effective. The staff go above and beyond its just amazing, they help people with their medications every day help them with appointments... Its a very big picture its not just about the initial drug.”

“Like when we have problems, there’s always a sympathetic ear there. [It] makes us feel more valuable, when you’re out here on the street, you don’t feel much value a lot of the time, the way people treat you.”
Model of Care

- Honour the individual and respect choice
- Engage, Engage, Engage
- Patient centered, patient centered, patient centered
siOAT (DAM & HDM) Conclusions

• It is an intensified treatment option for those who continue to use street drugs, with all the risks that entails – injecting-related infections and overdose.

• It substantially reduces people’s need for street drugs, reduces crime and leads to more engagement with healthcare and allied services.

• In jurisdictions where diacetylmorphine (prescription heroin) is unavailable, hydromorphone may be an alternative.
Questions?
References

- Cochrane Database Syst Rev, 2011 Dec 7;(12):CD003410
Additional References


BC reference documents

• Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder

• Guideline for the Clinical Management of Opioid Use Disorder