



*Opioid Agonist Therapy 101:  
An Introduction to Clinical Practice*

Treatment approaches:  
**The evidence and how it informs  
local practices**

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  - ▶ None identified

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# Faculty/Presenter Disclosure

- ▶ **Faculty:** Erin Knight

- ▶ **Relationships with commercial interests:**

- ▶ None



# Learning objectives



- ▶ Review the evidence-base underlying interventions for Opioid Use Disorder
  - ▶ Detoxification
  - ▶ Harm reduction
    - ▶ Needle/paraphernalia distribution & disposal
    - ▶ Supervised consumption
    - ▶ Naloxone distribution
  - ▶ Psychosocial treatment modalities
  - ▶ Opioid antagonists
  - ▶ Opioid Agonist Therapy (OAT)
    - ▶ Methadone vs. buprenorphine/naloxone
    - ▶ Alternative OAT



# Detoxification

- ▶ Inpatient detox alone, associated with:
  - ▶ HIV transmission
  - ▶ High rates of relapse
  - ▶ Morbidity and mortality
- ▶ Requests for detox can be an important 1<sup>st</sup> contact with health care
- ▶ Safety considerations for detox
  - ▶ Outpatient slow tapers
    - ▶ +/- antagonist treatment upon completion
    - ▶ +/- residential treatment
  - ▶ Intensive psychosocial follow-up
  - ▶ Take-home naloxone training



# Detoxification

- ▶ Psychosocial interventions during detox result in:
  - ▶ Increased completion of treatment
  - ▶ Decreased opiate use
  - ▶ Increased abstinence at follow-up
  - ▶ Increased clinical attendance
- ▶ Symptomatic relief with alpha-2 agonists
  - ▶ Use of clonidine or lofexidine was superior to placebo
  - ▶ Compared with methadone taper there were more adverse effects with alpha-2 agonists
- ▶ Taper with replacement opioid (methadone, buprenorphine/naloxone)
  - ▶ Slow tapering with methadone reduces withdrawal severity

**BUT, most patients relapse to opiate use  
Taper increases risk of overdose and death!**

# Detoxification

JAMA Clinical Guidelines Synopsis

## Clinical Management of Opioid Use Disorder

Beth Dunlap, MD; Adam S. Cifu, MD

**GUIDELINE TITLE** Guideline for the Clinical Management of Opioid Addiction

**DEVELOPER** Vancouver Coastal Health, Providence Health Care, and Ministry of Health, British Columbia, Canada

**RELEASE DATE** November 2015

**FUNDING SOURCE** Funded publicly through governmental grants

**TARGET POPULATION** Nonpregnant adult patients with opioid use disorder

### MAJOR RECOMMENDATIONS

- Opioid withdrawal alone is not recommended for treatment of opioid use disorder in most patients because of increased risks of overdose death and infectious disease, particularly HIV through intravenous drug use, following detoxification (moderate-quality evidence; strong recommendation).
- In the absence of contraindications, medically supervised opioid agonist treatment should be offered to patients. Buprenorphine/naloxone is the preferred first-line treatment. Methadone is an alternative in certain patient populations (high-quality evidence; strong recommendation).
- Psychosocial supports tailored to patient needs may be offered as an adjunct to medical treatment (moderate-quality evidence; conditional recommendation).

# Detoxification

## Management of opioid use disorders: a national clinical practice guideline

Julie Bruneau MD MSc, Keith Ahamad MD, Marie-Ève Goyer MD MSc, Ginette Poulin MD, Peter Selby MBBS MHSc, Benedikt Fischer PhD, T. Cameron Wild PhD, Evan Wood MD PhD; CIHR Canadian Research Initiative in Substance Misuse

■ Cite as: *CMAJ* 2018 March 5;190:E247-57. doi: 10.1503/cmaj.170958

### KEY POINTS

- Opioid use disorder is often a chronic, relapsing condition associated with increased morbidity and death; however, with appropriate treatment and follow-up, individuals can reach sustained long-term remission.
- This guideline strongly recommends opioid agonist treatment with buprenorphine–naloxone as the preferred first-line treatment when possible, because of buprenorphine’s multiple advantages, which include a superior safety profile in terms of overdose risk.
- Withdrawal management alone is not recommended, because this approach has been associated with elevated risks (e.g., syringe sharing) and death from overdose in comparison to providing no treatment, and high rates of relapse when implemented without immediate transition to long-term evidence-based treatment.
- This guideline supports using a stepped and integrated care approach, in which treatment intensity is continually adjusted to accommodate individual patient needs and circumstances over time, and recognizes that many individuals may benefit from the ability to move between treatments.





# Harm Reduction

## Needle/paraphernalia distribution

- ▶ Needle/Syringe programs associated with:
  - ▶ Reduction in injecting risk behavior
  - ▶ Reduction in HIV infection and other blood-borne infections
- ▶ “one of the most cost-effective public health interventions ever funded”
  - ▶ Cost-effective from societal and health sector perspectives
  - ▶ Net financial benefit identified in all high- and low-income settings
- ▶ In Winnipeg...safer injection supplies (& safer crack kits) available through:
  - ▶ Street Connections
  - ▶ Several community health centres and community services
  - ▶ Check [http://www.streetconnections.ca/service\\_map.php](http://www.streetconnections.ca/service_map.php)

# Harm Reduction

## Supervised consumption

- ▶ Insite
  - ▶ Canada's first supervised injection site
  - ▶ Located in Vancouver's Downtown East Side
- ▶ Evidence of benefit
  - ▶ Decreased syringe sharing, positive changes in injection practice
  - ▶ Increased referral to detox and community services
  - ▶ No increase in drug dealing, drug-related crime, new IDU or relapse to IDU
  - ▶ Conservative estimates show prevention of:
    - ▶ 35 cases of HIV per year
    - ▶ 3 deaths per year
  - ▶ Overall cost-savings over 6 million\$ per year after program costs



# Harm Reduction

## Naloxone distribution/ Take Home Naloxone

- ▶ WHO guidelines on Community Management of Opioid Overdose, 2014
  - ▶ “people likely to witness an opioid overdose should have access to naloxone and be instructed in its administration”
- ▶ Conclusion from a narrative systematic review
  - ▶ THN programs reduce overdose mortality rates in community, AND
  - ▶ Have a low rate of associated adverse events, THUS
  - ▶ **“THN distribution to at-risk users should be introduced as standard of care”**
- ▶ In Winnipeg...THN kits and training available at:
  - ▶ Street Connections
  - ▶ Brothers Pharmacy, Tache Pharmacy, Grand Medicine...
    - ▶ <https://www.cphm.ca/uploaded/web/For%20the%20Public/Naloxone/Naloxone%20Kits%20Pharmacy%20List.pdf>
    - ▶ Covered by NIHB with Rx
    - ▶ Available over the counter (at a cost) – 30-50\$



# Psychosocial Treatment

- ▶ No large scale reviews or meta-analyses available
- ▶ Residential treatment (abstinence-based)
  - ▶ Relapse common after discharge
    - ▶ Factors associated with earlier relapse
      - ▶ Younger age
      - ▶ Higher heroin use prior to treatment
      - ▶ History of injecting
      - ▶ Failure to complete full inpatient treatment program
      - ▶ Failure to attend aftercare
    - ▶ NA/AA attendance associated with increased abstinence
      - ▶ Higher frequency of attendance (>1/week) associated with increased likelihood of abstinence



# Psychosocial Treatment

- ▶ Non 12-step based peer-support:
  - ▶ SMART Recovery
    - ▶ Manualized, (peer) counselor led group
    - ▶ Based on Rational Emotive Behavioural Therapy
    - ▶ Focuses on development of practical skills for relapse prevention
  - ▶ Recovery Dharma
  - ▶ Secular Organizations for Sobriety
  - ▶ Jib Stop
  - ▶ Etc...
- ▶ Emerging evidence for Contingency Management and Abstinence-contingent recovery housing (with or without intensive day treatment)
- ▶ Motivational Interviewing

# Psychosocial Treatment



**Cochrane  
Library**

Cochrane Database of Systematic Reviews

## **Psychosocial treatment for opiate abuse and dependence (Review)**

Mayet S, Farrell MF, Ferri M, Amato L, Davoli M

### **Authors' conclusions**

The available evidence has low numbers and is heterogeneous. At present psychosocial treatments alone are not adequately proved treatment modalities or superior to any other type of treatment.

It is important to develop a better evidence base for psychosocial interventions to assist in future rationale planning of opioid use drug treatment services.

# Psychosocial Treatment

## Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence (Review)

Amato L, Minozzi S, Davoli M, Vecchi S

### Authors' conclusions

For the considered outcomes, it seems that adding any psychosocial support to standard maintenance treatments do not add additional benefits. Data do not show differences also for contingency approaches, contrary to all expectations. Duration of the studies was too short to analyse relevant outcomes such as mortality. It should be noted that the control intervention used in the studies included in the review on maintenance treatments, is a program that routinely offers counselling sessions in addition to methadone; thus the review, actually, did not evaluate the question of whether any ancillary psychosocial intervention is needed when methadone maintenance is provided, but the narrower question of whether a specific more structured intervention provides any additional benefit to a standard psychosocial support. These interventions probably can be measured and evaluated by employing diverse criteria for evaluating treatment outcomes, aimed to rigorously assess changes in emotional, interpersonal, vocational and physical health areas of life functioning.

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# Opioid antagonists

- ▶ Sustained release naltrexone
  - ▶ Insufficient evidence to evaluate effectiveness (Cochrane 2009)
  - ▶ Non-inferiority trial vs. buprenorphine/naloxone published in JAMA Psychiatry December 2017
  - ▶ Comparative effectiveness vs. buprenorphine/naloxone published The Lancet January 2018
- ▶ Oral naltrexone
  - ▶ Insufficient evidence to evaluate effectiveness (Cochrane 2011)
    - ▶ Low treatment retention (28%)
- ▶ Naltrexone
  - ▶ Only oral naltrexone (daily administration) is available in Canada





# Opioid Agonist Therapy

## Methadone vs. buprenorphine/naloxone

- ▶ Suboxone (buprenorphine + naloxone)
  - ▶ Doses > 2mg retain people in treatment
  - ▶ Doses  $\geq 16$  mg decrease illicit opiate use
- ▶ Methadone
  - ▶ Increased retention in treatment
  - ▶ Decreased use of heroin
- ▶ Efficacy comparing buprenorphine/naloxone vs. methadone
  - ▶ Early studies showed decreased retention in treatment compared to methadone
    - ▶ These were using low doses and slow induction rates
  - ▶ At flexible doses, and with appropriate induction rates, there is no significant difference in:
    - ▶ abstinence from illicit opioids
    - ▶ retention in treatment
    - ▶ decrease in cocaine use

# Opioid Agonist Therapy

<b>Buprenorphine/naloxone</b>	<b>Methadone</b>
Sublingual tablet -Takes up to 10 minutes to dissolve -May take upwards of 30 minutes for full witnessed dose in pharmacy	Cherry-flavoured Methadose
Daily witnessed ingestion during stabilization -earlier/more flexible carries possible	Daily witnessed ingestion x minimum 2 m -early carries not easily negotiable
Must be in moderate withdrawal to start -client must be able to tolerate withdrawal -consider initiation while in detox/hospital	May start at any time -starting in detox/hospital may allow quicker titration
Achieve target dose in 1-3 days	Achieve target dose in 3+ weeks
Requires baseline bloodwork (and likely treatment agreement)	Requires baseline bloodwork and treatment agreement
Planned long-term maintenance program	Planned long-term maintenance program

# Opioid Agonist Therapy

- reduces high risk drug-related behaviours

## Substitution treatment of injecting opioid users for prevention of HIV infection (Review)

Gowing L, Farrell M, Bornemann R, Sullivan LE, Ali R

### Authors' conclusions

Oral substitution treatment for injecting opioid users reduces drug-related behaviours with a high risk of HIV transmission, but has less effect on sex-related risk behaviours. The lack of data from randomised controlled studies limits the strength of the evidence presented in this review.

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# Opioid Agonist Therapy

## - improves adherence to HIV treatment

Addiction

RESEARCH REPORT

SSA SOCIETY FOR THE STUDY OF ADDICTION

doi:10.1111/add.12970

### Dose–response relationship between methadone dose and adherence to antiretroviral therapy among HIV-positive people who use illicit opioids

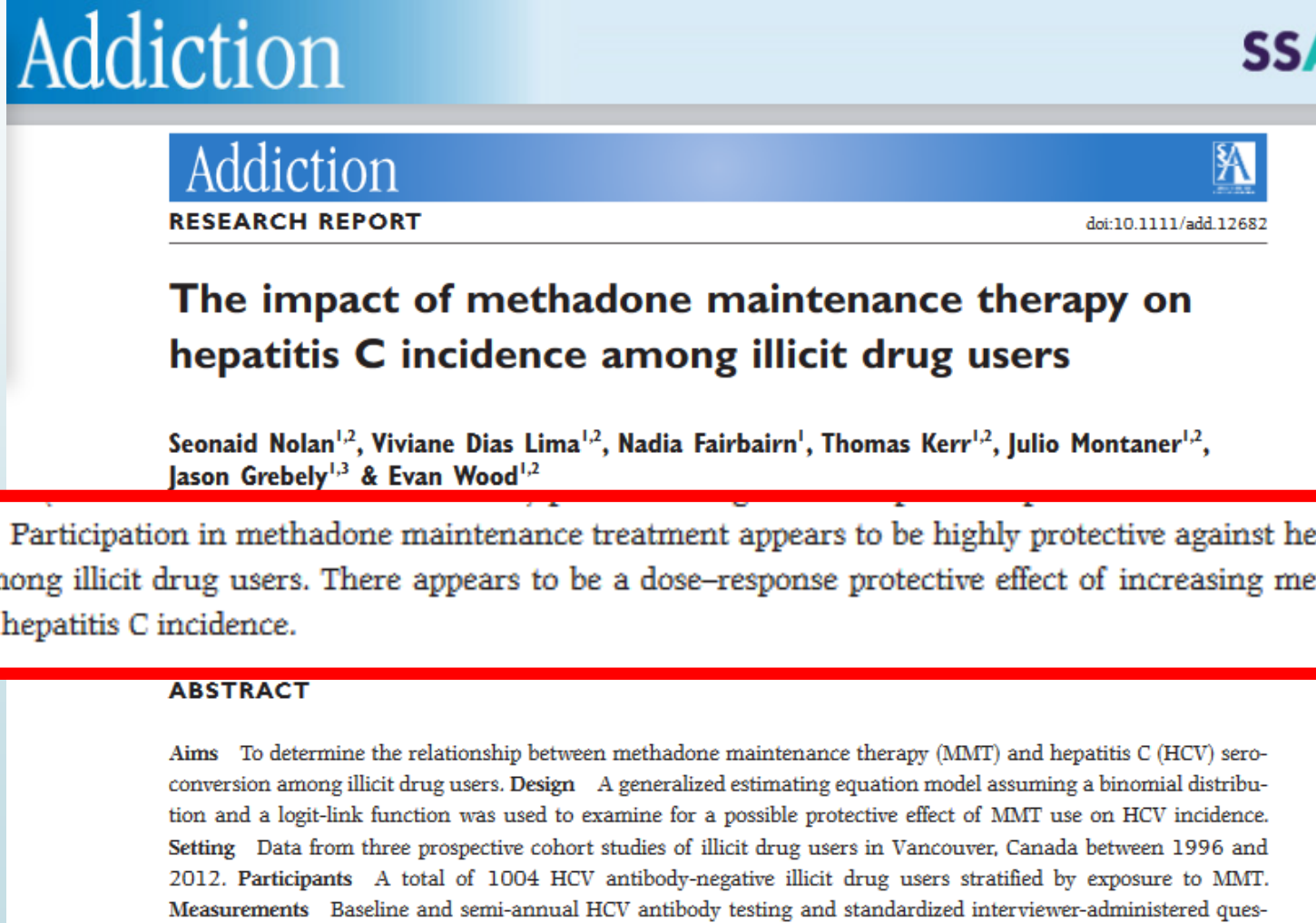
Leslie Lappalainen<sup>1,2</sup>, Seonaid Nolan<sup>1,3</sup>, Sabina Dobrer<sup>1</sup>, Cathy Puszczas<sup>1,4</sup>, Julio Montaner<sup>1,3</sup>, Keith Ahamad<sup>1,2</sup>, Huiru Dong<sup>1</sup>, Thomas Kerr<sup>1,3</sup>, Evan Wood<sup>1,3</sup> & M.-J. Milloy<sup>1,3</sup>

(AOR = 1.06 per 20 mg/day increase, 95% CI = 1.00–1.12). **Conclusion** Among HIV-positive individuals in methadone maintenance therapy, those receiving higher doses of methadone ( $\geq 100$  mg/day) are more likely to achieve  $\geq 95\%$  adherence to antiretroviral therapy than those receiving lower doses.

#### ABSTRACT

**Background and Aims** For HIV-positive individuals who use illicit opioids, engagement in methadone maintenance therapy (MMT) can contribute to improved HIV treatment outcomes. However, to our knowledge, the role of methadone dosing in adherence to antiretroviral therapy (ART) has not yet been investigated. We sought to examine the relationship between methadone dose and ART adherence among a cohort of people who use illicit opioids. **Design and Setting** We used data from the AIDS Care Cohort to Evaluate Access to Survival Services (ACCESS) study, an ongoing prospective ob-

# Opioid Agonist Therapy - reduces incidence of HCV infection



Addiction

SSA

Addiction

RESEARCH REPORT

doi:10.1111/add.12682

## The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users

Seonaid Nolan<sup>1,2</sup>, Viviane Dias Lima<sup>1,2</sup>, Nadia Fairbairn<sup>1</sup>, Thomas Kerr<sup>1,2</sup>, Julio Montaner<sup>1,2</sup>, Jason Grebely<sup>1,3</sup> & Evan Wood<sup>1,2</sup>

**Conclusion** Participation in methadone maintenance treatment appears to be highly protective against hepatitis C incidence among illicit drug users. There appears to be a dose-response protective effect of increasing methadone exposure on hepatitis C incidence.

### ABSTRACT

**Aims** To determine the relationship between methadone maintenance therapy (MMT) and hepatitis C (HCV) seroconversion among illicit drug users. **Design** A generalized estimating equation model assuming a binomial distribution and a logit-link function was used to examine for a possible protective effect of MMT use on HCV incidence. **Setting** Data from three prospective cohort studies of illicit drug users in Vancouver, Canada between 1996 and 2012. **Participants** A total of 1004 HCV antibody-negative illicit drug users stratified by exposure to MMT. **Measurements** Baseline and semi-annual HCV antibody testing and standardized interviewer-administered ques-

# Opioid Agonist Therapy

- tapers should be slow and gradual

Addiction

RESEARCH REPORT



doi:10.1111/j.1360-0443.2012.03870.x

## Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study

Bohdan Nosyk<sup>1,2</sup>, Huiying Sun<sup>3</sup>, Elizabeth Evans<sup>2</sup>, David C. Marsh<sup>4</sup>, M. Douglas Anglin<sup>2</sup>, Yih-Ing Hser<sup>2</sup> & Aslam H. Anis<sup>3,5</sup>

**Conclusions** The majority of patients attempting to taper from methadone maintenance treatment will not succeed. Success is enhanced by gradual dose reductions interspersed with periods of stabilization. These results can inform the development of a more refined guideline for future clinical practice.

Out of **4917** taper attempts,  
**646** sustained success (**13%**)

### FACTORS

For every 1% increase  
in adherence

**+2%**  
increased odds  
of success

Taper over a *long period*  
(3 months–1 year)  
*Taper over 12–52 weeks vs < 12 weeks*

**+258%**  
increased odds  
of success

Plan dose reductions to occur  
bi-weekly or monthly  
*As opposed to more or less frequently*

**+61%**  
increased odds  
of success



# Opioid Agonist Therapy

## Alternative OAT

- ▶ Sustained release oral morphine
  - ▶ Cochrane review 2013
    - ▶ Insufficient evidence to evaluate its effectiveness
  - ▶ Newer evidence supports its role as an alternative to methadone or buprenorphine
    - ▶ Beck et al. *Addiction*, 2014. – randomized cross-over non-inferiority study – UNBLINDED!!
      - ▶ Non-inferior to methadone for retention in treatment, illicit heroin
      - ▶ Superior to methadone for mental symptoms, treatment satisfaction, heroin craving
    - ▶ Hammig et al. *Journal of Substance Abuse Treatment*, 2014.
      - ▶ Mean Qtc with methadone > morphine
      - ▶ Morphine associated with higher satisfaction, fewer cravings, lower mental stress
    - ▶ Verthein et al. *European Addiction Research*, 2014.
      - ▶ Improved mental symptoms and treatment satisfaction for morphine vs. methadone
      - ▶ No difference in drug use
    - ▶ Falcato et al. *Journal of Clinical Psychopharmacology*, 2015.
      - ▶ Reduced craving for heroin in morphine vs. methadone
  - ▶ New Canadian guidelines outline its use as a 3<sup>rd</sup> line option for OAT



# Opioid Agonist Therapy

## Alternative OAT

- ▶ Injectable options (heroin/diacetylmorphine, hydromorphone) – Crosstown Clinic, Vancouver
  - ▶ SALOME and NAOMI trials
    - ▶ Decreased use of illicit substances
    - ▶ Decreased criminal activity and incarceration
    - ▶ Possible decrease in mortality
    - ▶ Increased retention in treatment
    - ▶ BUT, increased rate of serious adverse events
- ▶ Only to be used for people with chronic injection opioid use who have failed other first-line treatments

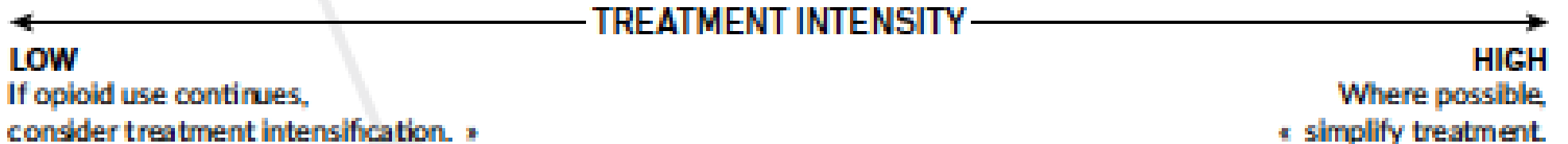


# Summary – treatment options for OUD

**WITHDRAWAL MANAGEMENT** <sup>1-3</sup>  
Tapered methadone, buprenorphine, or alpha<sub>2</sub>-adrenergic agonists  
+/- psychosocial treatment <sup>4</sup>  
+/- residential treatment  
+/- oral naltrexone <sup>5</sup>

**AGONIST THERAPIES**  
Buprenorphine/  
naloxone <sup>6</sup>      Methadone <sup>7,8</sup>  
(preferred)  
+/- psychosocial treatment  
+/- residential treatment

**SPECIALIST-LED ALTERNATIVE APPROACHES**  
Slow-release oral morphine <sup>9,10</sup>  
+/- psychosocial treatment  
+/- residential treatment



## **HARM REDUCTION** <sup>11-13</sup>

Across the treatment intensity spectrum, evidence-based harm reduction should be offered to all, including

- Education re: safer user of sterile syringes/needles and other applicable substance use equipment
- Access to sterile syringes, needles, and other supplies
- Access to Supervised Injection Sites (SIS)
- Take-Home-Naloxone (THN) kits

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# Case study 1

- ▶ 22 year old woman presents to the emergency department at your local hospital where you have admitting privileges. She asks for a hospital admission to help her detox from the oxycodone she's been using. She says she has done well after detox from previous crack cocaine use, so that's all she needs to quit using oxy.
  - ▶ What else do you want to know?
  - ▶ What do you do about the detox form?
  - ▶ What else can you offer?



## Case study 2

- ▶ 44 year old man comes in requesting refill of Percocet for vague descriptions of chronic pain secondary to multiple MSK injuries. On DPIN review, he has seen multiple other physicians, all for short Rx of different opioids. He is on no other regular medications and does not seem to have a regular provider. He's mildly agitated, having difficulty sitting still, and appears diaphoretic. Although he's wearing long sleeves, you notice what looks like track marks on his hands.
  - ▶ What else do you want to know?
  - ▶ What do you do about the Percocet?
  - ▶ What else can you offer?