# OUDPC 2019

## PREGNANCY AND OPIOID USE DISORDER

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# Faculty/Presenter Disclosure

- Faculty: Dr. Alice Ordean
- Relationships with commercial interests:
  - *Honorarium: Indivior*
  - *Other: None*

# Outline

- Review prevalence of opioid use and associated conditions during pregnancy
- Review standard approach to management of opioid use disorders during pregnancy
- Review protocols for high dose opioid use in pregnancy

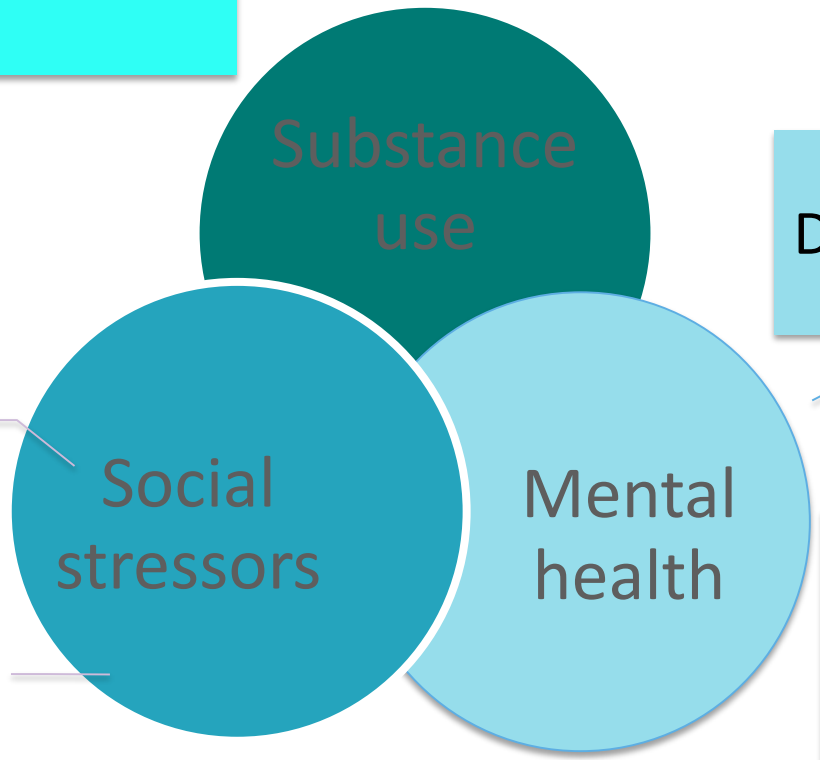
# Prevalence of opioid use and problematic use

| Period of exposure | Females | Males | Total |
|---|---|---|---|
| Past year use, 2017 | 12% | 11% | 12% (3.5 million) |
| Past year use, 2015 | 14% | 12% | 13% (3.8 million) |
| Problematic opioid use | 3% (875,000) | | |

Ref: Canadian Tobacco, Alcohol and Drugs Survey (CTADS), 2017

# Clustering of risks

Polysubstance use: cocaine, cannabis, alcohol, nicotine, benzos




Domestic violence

Poor housing & nutrition

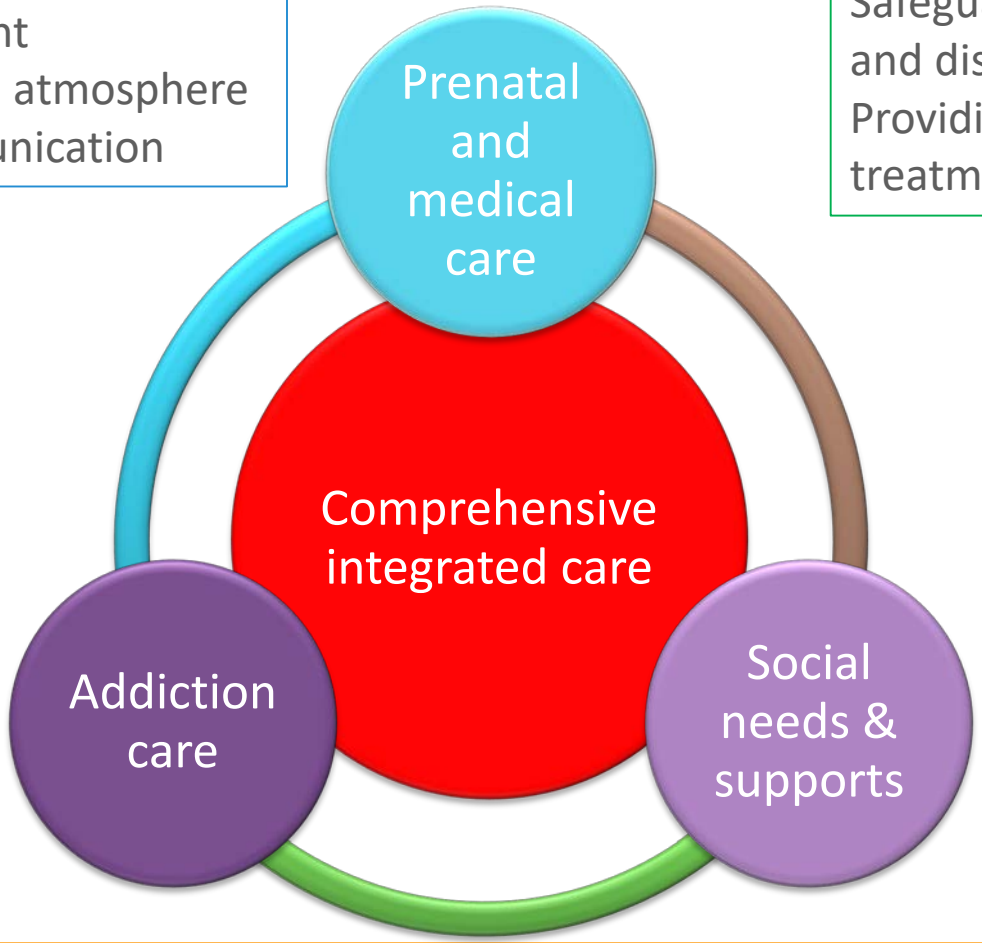
Lack of social support

Psychiatric comorbidities: depression, anxiety

# Integrated Care Programs

PRINCIPLES AND VALUES
Safe environment
Non-judgmental atmosphere
Effective communication

AIMS
Safeguarding against stigmatization and discrimination
Providing access to gender-sensitive treatment



# Case Study

**Anne is a 26-year-old, G5P2 history of heroin use x 3 years**

- Initially smoking then daily injection drug use for past 2 years
- Injects ½ gram twice per day to reduce withdrawal symptoms – chills, sweats, nausea, vomiting, leg pains
- Tried methadone for a few days only in the past
- She also used cocaine and alcohol in the past, abstinent x years
- She smokes cigarettes (½ ppd) daily
- She complaints about a two month history of progressive nausea, vomiting, abdominal pain
- Lives with partner, non-user, who is aware of drug use and concerned about her ongoing use

# Case Questions

What areas need to be addressed as part of her management plan?

What opioid agonist treatment would you offer her, if she were pregnant?

# Opioid Agonist Treatment (OAT) during Pregnancy

- Opioid Agonist Treatment
  - Methadone
  - Buprenorphine
  - Morphine

# Risks of Opioid misuse vs. Risks of OAT

## Risk of Opioid Misuse

Repeated cycles of intoxication and withdrawal

Increased risk of **miscarriage**, **prematurity** and **low birth weight** leading to increased neonatal morbidity & mortality

Increased risk of SIDS

## Risk of OAT

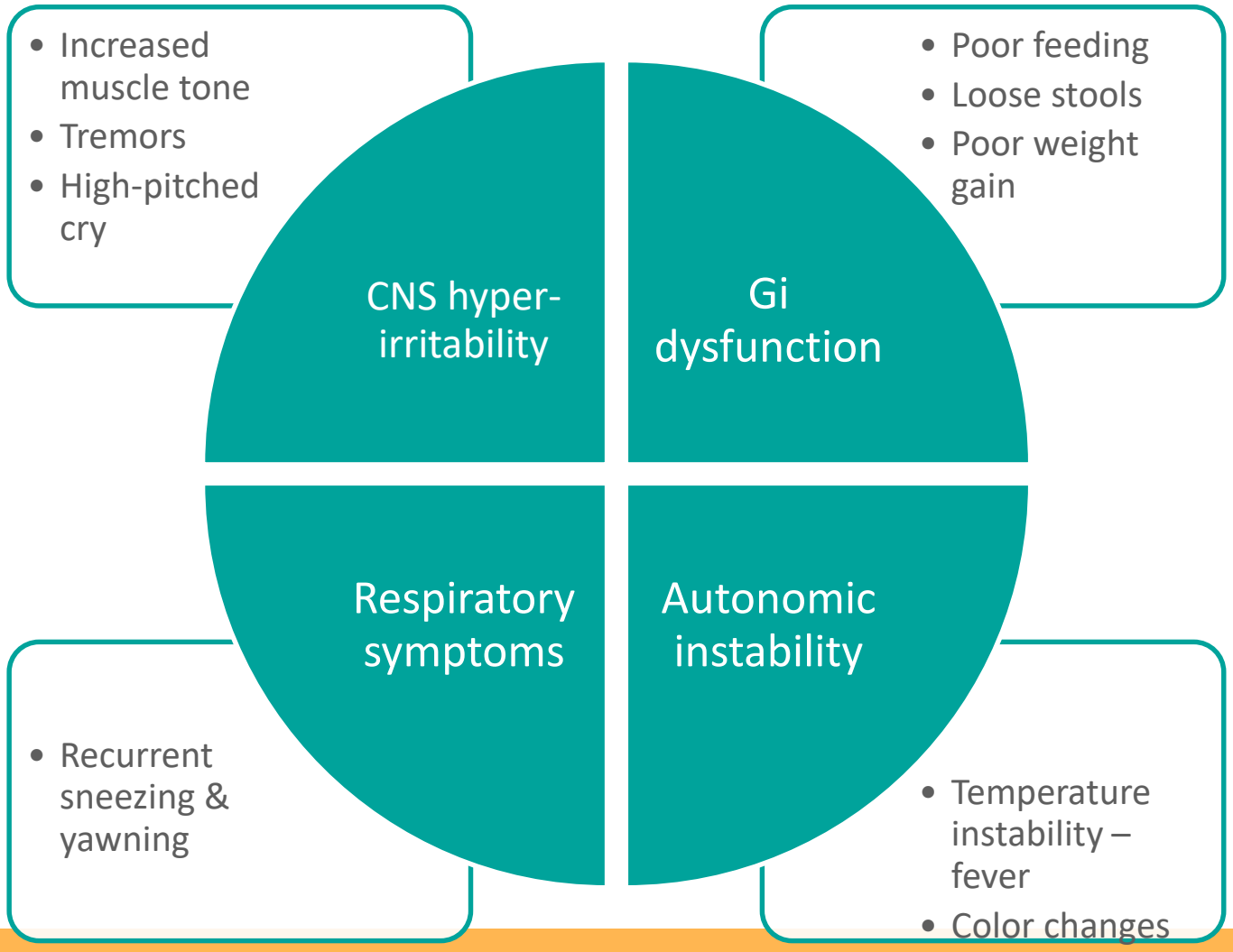
Methadone and buprenorphine cross placental barrier

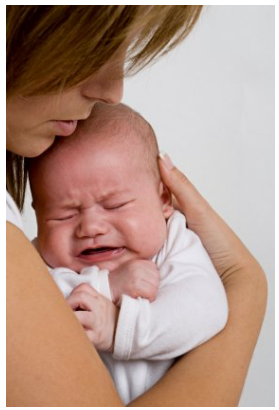
Mild intrauterine growth restriction (IUGR)

**Neonatal opioid withdrawal (neonatal abstinence syndrome)**

Methadone: weak link with strabismus “cross-eyes” and nystagmus

# Neonatal Abstinence Syndrome



# Methadone vs. Buprenorphine

## Systematic Review and Meta-Analysis

| Type of studies | Outcomes | Results |
|---|---|---|
| 14 studies included (cohort studies or RCTs)<br>515 BMT-exposed vs. 855 MMT-exposed neonates who were born between 1996 to 2012 | Maternal and neonatal outcomes | No difference for maternal or neonatal outcomes<br>Methadone superior in terms of retention<br>Buprenorphine associated with less severe NAS |

**Buprenorphine is effective as methadone in treating opioid use disorder in pregnancy**

Ref: Brogly SB et al. Am J Epid 2014; 679-686

# Methadone initiation during pregnancy

- Access for pregnant women on **urgent basis**
- Improved pregnancy outcomes associated with longer duration on MMT
- **No demonstrated efficacy & safety of inpatient over outpatient stabilization**
- Inpatient admission allows for close monitoring of withdrawal (e.g. uterine irritability), prenatal care, referral to other team members (eg. social work) but may not feasible due to personal or systemic factors

# Methadone dose adjustments during pregnancy

Methadone maintenance dose should be optimized to relief withdrawal symptoms and to achieve abstinence

- Women on stable dose **should continue on pre-pregnancy dose**

Methadone metabolism, clearance rates, and volume of distribution increase from first to third trimester resulting in lower mean serum methadone level

- **Methadone dose increase will be required later in pregnancy in response to clinical symptoms** – typically in third trimester (~28-30 weeks gestational age)

# Buprenorphine initiation during pregnancy

- No studies about inpatient vs. outpatient induction
- Consider inpatient induction if concerned about risks of opioid withdrawal
- Pregnant woman needs to present in moderate opioid withdrawal to avoid precipitated withdrawal with buprenorphine initiation
- Pregnant women on methadone should not be transferred to buprenorphine risks associated with opioid withdrawal

# Buprenorphine dose adjustments during pregnancy

Buprenorphine maintenance dose should be titrated until withdrawal symptoms resolve and opioid use discontinued

- Maintain stable dose during early pregnancy once adequate dose achieved

Documented increase in buprenorphine renal clearance during pregnancy so dose adjustments may be required during pregnancy based on clinical symptoms and signs

- 3 RCTs showed dose increase in buprenorphine from first to last trimester was required (mean 2mg dose increase in third trimester)

# Maternal OAT dose and relationship to NAS

- Meta-analysis and MOTHER data shows **no relationship between maternal methadone or buprenorphine dose & severity of NAS**
- No effect on peak NAS score, total amount of morphine to treat NAS, duration of medical treatment of NAS or length of hospital stay
- Appropriate maintenance dose should be determined for each pregnant woman to control withdrawal symptoms and to maintain abstinence

Ref: Cleary et al. 2010, Klaman et al. 2017

# Buprenorphine/naloxone during Pregnancy

**Naloxone use during pregnancy is limited by lack of adequate human safety data**

Limited published evidence about effectiveness and safety of buprenorphine/naloxone combination product during pregnancy

**Question: Should women continue on buprenorphine combination product or be switched to monoproduct?**

# Buprenorphine/naloxone during Pregnancy: Evidence

| Type of studies | Participants | Results |
|---|---|---|
| N= 5 studies<br>2 in Canada<br>3 in USA | Total<br>N=190 women on buprenorphine/naloxone<br><br>Comparison groups:<br>non-users, methadone, other opioid use | Birth parameters and teratogenicity: no differences<br><br>Neonatal withdrawal:<br>Reduced NAS prevalence, lower peak NAS scores and shorter length of stay for bup/nlx newborns |

**No significant adverse neonatal outcomes in infants of mothers who were maintained on buprenorphine/naloxone during pregnancy**

Ref: 1. Debelak et al, 2013; 2. Wiegand et al, 2015; 3. Gawronski et al., 2014; 4. Dooley et al, 2016; 5. Jumah et al., 2016

# Case Revisited

- Pregnancy confirmed - 17 weeks GA
- Offered OAT and prenatal care
- Benefits and risks of buprenorphine and methadone were reviewed
- Woman opted to initiate methadone as outpatient
- Methadone initiated at 20mg od and dose increase offered q3-5 days
- Non-adherence to office visits, ongoing heroin use during T2 and T3
- Connected to social worker and community addiction treatment program
- Methadone dose escalated to 110mg by 35 weeks GA – discontinuation from heroin use at 33 weeks GA
- **Pregnancy outcome**: premature labour at 36 weeks resulting in live female child
- **Long-term outcome**: continued abstinence 3 years later, maintaining child custody and continued involvement in relapse prevention counselling

# OUDPC 2019

## Pregnancy and Opioid Use Disorder

High Dose Opioid Use in Pregnancy

# Faculty/Presenter Disclosure

- Faculty: Maya Nader
- Relationships with commercial interests:
  - *None*

# High Dose Opioid Use in Pregnancy

- G4P3L2 at 22wks
  - Late to prenatal care
  - Placenta previa on anatomy scan
  - Stillbirth at 32wks last pregnancy
  - Other children in CPS custody
  - Unstable housing, no partner
  - Admitted opioid use to OB provider
  - Fentanyl 5-6pts daily, IV
  - Previous methadone on/off
  - Co-injecting crystal meth

**What are current priorities?**

# Priorities

- Obstetrical priorities
  - Prenatal screening
  - Consider STI testing qTrimester
  - HIV VL in labour, consider AZT in labour if in window period
  - PLACENTAL PREVIA
  - Risk of stillbirth
- Social priorities
  - Consider self referral to CPS
  - Housing
  - Safety
  - Food

- Opioid use disorder treatment
  - **What would you offer? How would you counsel her?**

# Priorities

- Obstetrical priorities
  - Prenatal screening
  - Consider STI testing qTrimester
  - HIV VL in labour, consider AZT in labour if in window period
  - PLACENTAL PREVIA
  - Risk of stillbirth
- Social priorities
  - Consider self referral to CPS
  - Housing
  - Safety
  - Food
- Opioid use disorder treatment
  - AVOID WITHDRAWAL
    - Obstetrical emergency
    - Placenta previa
  - Consider patient priority
  - Inpatient = standard of care
    - Prevent w/d (= obstetrical emergency)
    - Titrate to therapeutic dose quickly
    - Monitoring re: w/d and sedation risk
    - Helps get prenatal screening done (BW, u/s, consults)
    - Engages women in care
  - Neonatal Abstinence Syndrome (NAS)

# Current Guidelines

- “The MMT physician should consider inpatient initiation during pregnancy in order to monitor for withdrawal severity and fetal distress.”
- Day 1: methadone 10-20mg then 5-10mg po q4h prn (max 35mg)
- Day 2: last day’s dose methadone + 5mg po q6h prn (max 45mg)
- Days 3-5: 45mg daily
- Follow outpatient titration schedule

# Inpatient Management of Opioid Use Disorder: Methadone

**Day 1: max daily dose 40 mg methadone**

| | |
|---|---|
| First dose | • Check COWS and Ramsay<br>• Administer 10-30mg methadone<br>• Recheck Ramsay in 1 hour |
| After 4 hours | • If endorsing withdrawal/cravings, check Ramsay<br>• If no sedation, order additional 5 - 10 mg dose<br>• Recheck Ramsay in 1 hour |
| After 4 hours | • If endorsing withdrawal/cravings, check Ramsay<br>• If no sedation and not at max daily dose, order additional 5-10 mg dose<br>• Recheck Ramsay in 1 hour |

**Day 2: max daily dose 50 mg methadone**

| | |
|---|---|
| First dose | • Check Ramsay, proceed if no sedation<br>• Give total daily dose from day 1 as single dose<br>• Recheck Ramsay in 1 hour |
| After 4 hours | • If endorsing withdrawal/cravings, check Ramsay<br>• If no sedation, order additional 5 - 10 mg dose<br>• Recheck Ramsay in 1 hour |
| After 4 hours | • If endorsing withdrawal/cravings, check Ramsay<br>• If no sedation and not at max daily dose, order additional 5-10 mg dose<br>• Recheck Ramsay in 1 hour |

**Ramsay sedation score:**

1. Anxious/restless
2. Cooperative/oriented/tranquil
3. Response to commands
4. Brisk response to stimulus
5. Sluggish response to stimulus
6. No response to stimulus

**Day 3:** Follow instruction for day 2 above, but with first dose being total daily dose from day 2. Max dose on day 3 is 60 mg. Subsequent days: Do not increase dose for 5 days. Can increase by 10 mg every 5 days subsequently.

Coffa, D. et al.; Inpatient Management of Opioid Use Disorder: Methadone. (2018)

# Initiation and Rapid Titration of Methadone in an Acute Care Setting

| Admission Day | Methadone Scheduled, mg | Methadone PRN, mg | Total Daily Methadone,mg | Morphine Oral Liquid (MOS), mg | Total daily MOS, mg | Total Morphine Milligram Equivalent (MME), mg* |
|---|---|---|---|---|---|---|
| Day 1 | 30 | 3 × 10 | 60 | 5 × 10 | 50 | **530** |
| Day 2 | 30 | 4 × 10 | 70 | 5 × 10 | 50 | **610** |
| Day 3 | 50 | 2 × 10 | 70 | 2 × 10 | 20 | **580** |
| Day 4 | 50 | 10 | 60 | 2 × 10 | 20 | **500** |
| Day 5 | 50 | 2 × 10 | 70 | 2 × 10 | 20 | **580** |
| Day 6 | 50 | 10 | 60 | 10 | 10 | **490** |
| Day 7 | 50 | 10 | 60 | 10 | 10 | **490** |
| Day 8 | 50 | 0 | 50 | 3 × 10 | 30 | **430** |
| Day 9 | 50 | 2 × 10 | 70 | 0 | 0 | **560** |

*Methadone dose used to calculate morphine milligram equivalent (MME) based on morphine : methadone ratio of 8:1 (Wong and Walker, 2013).

# St Michael's Hospital Protocol

- Result of high opioid tolerance
- Inpatient protocol only
- Rapid methadone titration to 70-85 mg over 5-7 days
- Concurrent use of morphine IR consolidated to morphine SR
- Inpatient stay ~5-10 days
- Discharge script: methadone + morphine SR daily observed
- Goal: rapid and safe w/d management to prevent obstetrical consequences and keep patients engaged

# St Michael's Hospital Protocol

| Day 1 | Day 2 | Day 3 |
|---|---|---|
| • Methadone 40 mg<br>• Morphine IR 30-50 mg PO q2h standing while awake<br>• Morphine IR 30-50 mg PO q3h prn for mild w/d<br>• Morphine 20 mg IM for severe ongoing withdrawal or contractions | • Methadone 50 mg q1000 (↑ 10mg)<br>• Consolidate 50% of day 1 morphine dose to SROM at 1600<br>• Continue standing morphine and PRN orders | • Methadone 60 mg q1000 (↑ 10mg)<br>• SROM day 2 dose at 1000<br>• Switch standing morphine to PRN<br>  • Morphine IR 30-50 mg PO q2h prn<br>  • Morphine 20 mg IM for severe ongoing withdrawal or contractions |
| **Day 4** | **Day 5** | **Day 6** |
| • Methadone 70 mg q1000 (↑ 10mg)<br>• SROM day 2 dose + 50% of total morphine IR requirements of the last 24h<br>• Morphine IR unchanged PRN | • Methadone 70 mg q1000 (unchanged)<br>• SROM day 4 unchanged<br>• Morphine IR unchanged | • Methadone 70 mg q1000 (unchanged)<br>• SROM day 5 + 50% of additional IR requirements of last 24h<br>• Morphine IR unchanged |

# Day 7

- Increase methadone 85 mg q1000 if needed
- SROM unchanged
- Morphine IR:
  - Morphine IR 30-50 mg PO q4-6h prn
  - Morphine 10-20 mg IM for severe ongoing withdrawal or contractions

# Key Points

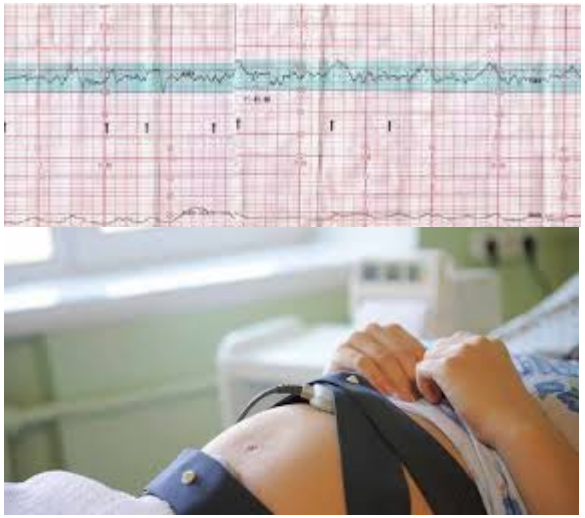
- Start methadone 40 mg, increase by 10 mg daily until 70 mg
- Hold methadone at 70mg x 3days
- Concurrent standing morphine IR q2h + PRN for w/d
- Consolidate to SROM q2d, based on 50% IR requirements
- Most stays 5-10 days
- Split dosing avoided if possible
  - Unstable population = twice daily observed doses
  - Leads to missed doses post-discharge
  - Mostly unavoidable in T3

# Key Points

- ~ 50 pregnant patients stabilized using this protocol
- No case of over sedation/overdose
- For highly tolerant opioid population
  - 3-10 points of fentanyl daily +/- co-injecting with stimulants

# Other Considerations

- Referrals
  - High risk OB/OB referral
  - Consider pediatrics referral (NAS treatment)
- Screening
  - Ensure prenatal and infectious screen up to date
- Monitoring
  - Usual vitals
  - NST on admission + whenever cramping
  - IA daily and upon return to floor if has left >30min



# Other Considerations

- Diet
  - Double portions + Ensure
- Other
  - Avoid nicotine withdrawal (i.e. prevent leaving the floor) – offer NRT
  - Consider nabilone for cannabis withdrawal
  - Early epidural when in labour
- Post-partum
  - Patient guided medication change
  - Consolidate to methadone

# Case 2


- Patient consent
- Grandmultip, NFA, in/out jail
- Fentanyl 1g+ at presentation, subsequent carfentanil use
- Crack, EtOH, Benzodiazepines, Nicotine
- Presented to our program in T1
- 10yr hx on methadone on/off (max 120mg, current 60mg)
- 5 admissions during pregnancy for opioid titration
- Methadone 145mg + SROM 400mg

# Case 2

- Release from jail: 5 OD requiring naloxone over 14 days
  - Methadone 50mg + SROM 15mg
- Re-admitted to hospital (T3)
  - Methadone 135mg + SROM 400mg
  - 2 more OD (carfentanil, benzodiazepine-laced)
- **What to do?**

# iOAT in Pregnancy

## Pregnancy and Birth under Maintenance Treatment with Diamorphine (Heroin): A Case Report

Christina Hartwig[a] Christian Haasen[a] Jens Reimer[a] Werner Garbe[b] Dirk Lichtermann[c]
Linde Wuellenweber[d] Christoph Dilg[c]

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## Case report: Pregnancy and birth under heroin-assisted treatment (HAT)

Adrian Groh[1], Florian Urlichs[1,2], Thomas Hillemacher[1], Stefan Bleich[1], and Annemarie Heberlein[1]

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*2 Department of Pediatric Pneumology, Allergology and Neonatology, Hannover Medical School, Germany, EU*

# iOAT in Pregnancy

- Off label use
- Criteria for iOAT (general)

1. Severe and refractory OUD
2. Failed OAT (either MMT/BUP/SROM)
   - Either multiple unsuccessful attempts OR significant risk of OD

https://www.bccsu.ca/wp-content/uploads/2019/03/BC_iOAT_Guideline.pdf

Table 8: Hydromorphone Induction Dosage Chart—3 Doses Per Day

| Dose # | Dose Administered | Additional Dose* (if appropriate) |
|---|---|---|
| Day 1 | | |
| 1 | 10mg | 10mg |
| 2 | 20mg | 10mg |
| 3 | 30mg | 10mg |
| Total | 60-90mg | |
| Day 2 | | |
| 1 | 40mg | 10mg |
| 2 | 50mg | 10mg |
| 3 | 60mg | 10mg |
| Total | 150-180mg | |
| Day 3 | | |
| 1 | 70mg | 10mg |
| 2 | 80mg | 10mg |
| 3 | 90mg | -- |
| Total | 240-260mg | |

** Wait 15-20 minutes after initial dose. If no intoxication, give additional dose based on clinical judgment and discussion with patient.*

https://www.bccsu.ca/wp-content/uploads/2019/03/BC_iOAT_Guideline.pdf

Table 4: Pre-Injection Assessment

| Patient Name: | Assessment Date and Time: |
|---|---|
| Yes No Unknown<br>☐ ☐ ☐ Severely anxious or agitated<br>☐ ☐ ☐ Dyskinectic<br>☐ ☐ ☐ Overly sedated<br>☐ ☐ ☐ Slurred speech<br>☐ ☐ ☐ Smells of alcohol | |
| Baseline respiration rate: _____ breaths / minute<br>Pasero Opioid-induced Sedation Scale[56] (POSS) level:<br><br>Breathalyzer required: Yes ☐ No ☐<br>If yes, breathalyzer reading: | |
| Notes: | |
| Assessment completed by: | |

Table 5: Post-Injection Assessment

| Patient Name: | Assessment Date and Time: |
|---|---|
| Yes No Unknown<br>☐ ☐ ☐ Severely anxious or agitated<br>☐ ☐ ☐ Dyskinectic<br>☐ ☐ ☐ Overly sedated<br>☐ ☐ ☐ Slurred speech<br>☐ ☐ ☐ Smells of alcohol<br>☐ ☐ ☐ Decreased respiration rate | |
| Respiration rate: _____<br>Pasero Opioid-induced Sedation Scale[56] (POSS) level: | |
| Notes: | |
| Assessment completed by: | |

Table 6: Modified Pasero Opioid-induced Sedation Scale (POSS)

| Level of Sedation | Appropriate Action |
|---|---|
| 1. Awake and alert | Acceptable; no action necessary; may continue with opioid dose |
| 2. Slightly drowsy, easily aroused | Acceptable; no action necessary; may continue with opioid dose |
| 3. Frequently drowsy, arousable, drifts off to sleep during conversation | Unacceptable; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory; notify prescriber for orders. |
| 4. Somnolent, minimal or no response to verbal or physical stimulation | Unacceptable; hold opioid; consider administering naloxone; notify prescriber; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory. |

https://www.bccsu.ca/wp-content/uploads/2019/03/BC_iOAT_Guideline.pdf

# Case 2

- Re-admission (#5)
- Methadone 135mg + SROM 600mg + morphine IR 40mg q2h
- High dose HM initiated following BC protocol
  - iOAT: HM 90mg IV/IM bid, tapered down to 75mg IV/IM bid
- Initially self injected and MD supervised; then MD provided (IV/IM)

- SVD at term
- NAS at day 4 (morphine + clonidine), NICU stay 47d
- Post-partum: methadone 145mg + SROM 600mg

# Questions?

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