Opioid Agonist Therapy 101:
An Introduction to Clinical Practice Workshop

ASSESSING AND TREATING OPIOID USE DISORDER IN PREGNANCY

Marina Reinecke MBChB, CCFP(AM), ISAM

Faculty/Presenter Disclosure

- **Faculty:** Marina Reinecke
- **Relationships with commercial interests:** None

Declaration of off-label medication recommendations

- **During this presentation, I will make therapeutic recommendations for medications that have not received regulatory approval (i.e. off-label use of medication). I will verbally identify each off-label recommendations prior to discussing it.**

LEARNING OBJECTIVES

At the end of this educational activity, the participant will be able to:

- Discuss evidence based care for opioid use disorder in pregnancy.
- Discuss best practices related to managing pain and opioid withdrawal during labor and immediately postpartum in women with opioid use disorder.
- Discuss best practices for managing opioid withdrawal in the infant and how this relates to caring for mom

SCREENING FOR OPIOID USE DISORDER

- There is **no** simple screening tool for women with opioid use disorder
- A **detailed assessment** is required when opioid use disorder is suspected in pregnancy
- **All** pregnant women should be asked about current or past use of alcohol, tobacco, Rx, OTC and illicit drugs – **Universal screening!**

ASSESSMENT FOR OPIOID USE DISORDER IN WOMEN

- **Withdrawal symptoms**: diaphoresis (sweating), runny nose, runny eyes, nausea, vomiting ,diarrhea, myalgias (muscle pains), **remember if women is in withdrawal, the fetus is too!**

- **Chronic pain**: diagnosis, response to pain rating scale (dramatic or inconsistent), functional status, pain related to previous obstetrical events (epidurals, pelvic injuries)

- **Use of "hood doctors"** who will inject for a fee, resulting in self-injection, STBBI & assault risks.

ASSESSMENT FOR OPIOID USE DISORDER IN WOMEN

- Women are often introduced to opiates by a male partner….
- **Psychosocial assessment**: relationship status, living arrangements, parenting arrangements, safety of other children in home
- **Survival relationships and survival sex:** feeling unable to leave abusive partner who provides access to opioids; using sex to pay for drugs
- Unplanned pregnancy, multiple pregnancy terminations/associated trauma, substance using women are **POOR** users of fertility control
- **Physical/sexual abuse**: past history and **present risk**, ask repeatedly, safety plan, numbers for shelters and how to get there
- **When pregnant:** poor nutrition, escalation of domestic violence, increased stress levels, lack of prenatal care, poor support
- Time of heightened motivation to make changes

RISKS OF OPIOID USE DISORDER IN PREGNANCY

- Opioid use disorder during pregnancy has been associated with numerous adverse fetal outcomes secondary to the drug itself, as well as, secondary to poor nutrition and inadequate prenatal care

- Poor neonatal outcomes such as:
  1. Intrauterine growth restriction
  2. Lower birth weight
  3. Preterm rupture of membranes

RISKS OF OPIOID USE DISORDER

- Opioid withdrawal can trigger uterine contractions leading to an increased risk of **spontaneous abortion (miscarriage)** in the first trimester, **premature labor** in the third trimester

- Maternal complications include **pre-eclampsia** (pregnancy related high blood pressure) and **antenatal bleeding**

- Heroin can lead to intrauterine growth restriction

OPIOID WITHDRAWAL SYMPTOMS

Psychological

- Intense anxiety, agitation
- Intense craving for opiates
- Restlessness, insomnia, fatigue

Physical

In pregnancy: uterine irritability and a fetus at risk

- Muscle aches, flu-like symptoms “dope sick”
- Nausea, vomiting, cramps, diarrhea
- Sweating, goose bumps
- Dilated pupils
- Runny eyes

ABSTINENCE-BASED TREATMENT IN PREGNANCY

- Medical detoxification
  - Opioid tapering - **Not recommended!!** - due to **fetal risk** and **poor success rates** – however support women's choice & taper very slow!
  - Could consider if using low doses and done very slowly; mid trimester best
  - Note: Clonidine contraindicated in pregnancy
- NA, AA, self-help groups
- Residential or outpatient treatment
- Success requires major life changes/good supports

OPIOID AGONIST THERAPY (methadone or buprenorphine)

- **Present standard of care for opioid use disorder in pregnancy is opioid agonist therapy**
- Can be initiated in hospital or in an outpatient setting
- Women on methadone/buprenorphine are less likely to experience withdrawal symptoms and drug cravings
- Pregnant women treated with OAT have **reduced obstetrical complications and improved outcomes**
- Ideally, prescribed in the context of comprehensive pregnancy care, including:

Counselling	**Housing**
Family therapy	**Food support**
Parenting planning	**Medical care**

LIMITATIONS OF OAT IN PREGNANCY

- Higher risk of overdose early in treatment (careful with methadone pharmacology!)
- Not all communities have OAT providers **(despite being the standard of care)**
- Major commitment of time for woman – very difficult for woman with children to attend daily
- Transport issues
- Woman's family/partner/other health care providers/CFS may NOT be supportive – "exchanging one drug for another"
- Some treatment agencies in MB has intake criteria not motivated by medical evidence

METHADONE TAPERING

- Some women want to decrease their OAT dose, so their baby won't experience withdrawal:
  - Explain benefits of stable dose; counsel regarding risks
  - Taper **slowly to avoid distress or labor** (mid trimester best)
  - Prolonged tapers typically poorly tolerated, can be destabilizing
- Some women require a dose increase in pregnancy: offer a pregnancy test if a patient stable on OAT requires an increased dose
- Likely to need increased methadone and suboxone dosing around 28wks due to plasma expansion; pts need to be counselled accordingly so they don't perceive this dose change as a sign of relapse/failure
- Methadone may require several dose increases (see her regularly in 3rd trimester)
- Tapers are associated with **increased overdose risk** in the first year postpartum (4x increase by pp month 7)

NON-STRESS TESTING & OAT

- Normal, reassuring, result depends on intact well oxygenated, non-sedated brain acting on a normal heart
- Fetus may have decreased movement in utero for two to four hours after a methadone dose; ?buprenorphine less so
- It is important to repeat testing after the peak level of opioid has been reached
- Standard practice is to perform more frequent fetal testing after 32 weeks **in any patient with maternal or fetal risk factors**
- Narcotics **alone** are **not** an indication for a NST; order NST for obstetrical reasons
- Monitoring using a combination of BPP (biophysical profile and NST) after 32 weeks may be helpful

- If NST is indicated, consider methadone, buprenorphine or other narcotic in interpretation

MICRO-DOSING INDUCTIONS IN PREGNANCY

- Admit women if considering micro-dosing induction of buprenorphine/naloxone in pregnancy
- NST can be considered first to ensure fetal well being in the unlikely event of precipitated WD
- Consult addiction specialist and obstetrician with experience as far as possible
- Document expert consultation and benefit risk discussion with patient

BUPRENORPHINE FOR OPIOID USE DISORDER

- Sublingual partial agonist; safer than methadone (ceiling effect)
- Buprenorphine is safe in pregnancy (speculation regarding effect on neurodevelopment of the fetus – minimal data from small studies)
- If a woman is on buprenorphine (Subutex® or Suboxone) prior to pregnancy she can stay on the same treatment
- Historically: Women on buprenorphine/naloxone (Suboxone®) were advised to transfer to buprenorphine alone product (Subutex®) due to unknown safety of naloxone in pregnancy
- Now ++ clinical experience, increased literature and Health Canada has removed its recommendation that patients need to be switched over!

The case for opioids other than methadone/buprenorphine…..

- She doesn't want it despite intensive education
- No access
- An ethical crisis…

Pregnant women deserve special consideration…

- **Other opioids are effective:**
- Cochrane review; Little difference in newborn or maternal outcomes for pregnant opiate-dependent women who were maintained on methadone, buprenorphine, or oral slow release morphine

  (Minozzi et al, 2009)
- Proceed with caution! **OFF Label**
- Document, document, document….
- Treatment agreement
- Daily dispensing
- Slow release morphine (Kadian)
- Lowest functional dose with frequent follow - up

URINE DRUG SCREENS

- If urine drug screening is required as part of OAT treatment agreement, in hospital or by protection services, it must be with **maternal consent**

- If maternal drug use is suspected, and there are significant medical concerns for the neonate and the mother is unable or unwilling to give consent, then drug screens on neonate may be taken without consent

- **Note: An unexpected positive result merits confirmatory testing!** **(same sample if possible)**

ROLE OF UDS:
Child Protection Services

- Women involved with Child Protection Services often want to have regular UDS
- UDS provide objective evidence to CFS, to care providers and to the patient's families that they are not using illicit drugs
- In some cases, CFS insist on UDS as a condition for custody (arranged for and paid for by CFS)
- Such UDS's needs to be collected with chain of custody by certified lab

New Patients in Labor

- The mother should be asked about substance use and offered treatment and follow up
- Discuss UDS and benefit for medical assessment and treatment
- The infant should be monitored for neonatal withdrawal if:
  - The mother reports opioid use
  - The baby's UDS is positive for opioids
  - The baby shows signs of neonatal withdrawal
  - Caution: withdrawal presentation similar to other conditions e.g., sepsis, hypoglycemia, hypocalcemia

PAIN MANAGEMENT IN LABOUR

What can affect a woman's pain?

Personal factors

- Past negative experience
- Sexual abuse history
- Fear, anxiety
- Cultural perspective
- Tolerance

Labor: Occiput Posterior position

- Previous pelvic fracture

Hospital factors

- Lack of support
- Unwanted support
- Loss of control
- Hypervigilance
- Lack of privacy
- Harsh behavior by staff

LABOUR & DELIVERY

- Protect women from withdrawal in labor - this is miserable!
- Methadone and buprenorphine/naloxone users can bring carries and use own supply if dose is not promptly available; clarify time of typical dosing to avoid needless delay and ensure follow up on the postpartum ward
- If not on OAT, can use morphine for the management of withdrawal
- Labor hurts and pain experience is heightened in context of OUD
- Analgesia must be offered to all women in labor
- Methadone or buprenorphine alone is **NOT** adequate or appropriate analgesia for labor

LABOUR & DELIVERY ISSUES

- Epidural is good, particularly advantageous with OAT
- Adequate analgesia: women with OUD may require larger doses of analgesics - it will not worsen addiction
- Consult expert pain management team!
- Injection drug users may have poor IV access - planned IV access is recommended
- Methadone or buprenorphine/naloxone dose should be maintained during labor and post-partum.
- **Some women will need a reduction** in methadone dose postpartum, possibly for buprenorphine/naloxone as well – counsel re this being normal and plan with her to facilitate in hospital or from home!

RISKS OF METHADONE AND BUP FOR INFANT

- Only risk of methadone in pregnancy is the risk of neonatal opioid withdrawal
- Meta-analysis data indicate 60-80% of infants experience mild withdrawal
- A smaller percentage (~ 30%) require morphine treatment for significant withdrawal symptoms
- Most infants will respond to comfort measures
- No evidence of any long-term consequences associated with methadone use in pregnancy
- Literature describes an increased occurrence of strabismus in infants born to women receiving methadone
- **Buprenorphine/naloxone:** risk of neonatal opioid withdrawal appears reduced!

NEONATAL WITHDRAWAL

- There is mixed evidence regarding maternal OAT dose-relationship with severity of neonatal opioid withdrawal; **newer studies show no dose relationship with buprenorphine/naloxone.**

- Other **major** factors impacting severity of withdrawal and need for morphine treatment:

  Strong correlation with unstable use and recurrent withdrawal

  Breastfeeding (bottle if concerned)

  Rooming in (skin-to-skin)

  Mom on multiple medications associated with withdrawal

  Staff and Centre practices and attitudes

- "The best OAT dose is the one that stabilizes mom"

- NICU admissions very costly; so are apprehensions: managing women-infant-pair appropriately can reduce both!!!

NEONATAL WITHDRAWAL

- Occurs 2-4 days after birth, can last a couple of weeks
- Poor feeding, irritability, mottled skin, crying, jitteriness, inability to gain weight
- If rooming in and promoting breast feeding, comfort measures usually sufficient, morphine may be necessary
- Remember to look for other serious problems: sepsis, hypoglycemia, etc. in an unstable infant - do not assume signs due to neonatal withdrawal
- Should deliver in hospital with **Level II pediatric capabilities** for neonatology/pediatrics consult if infant is unstable

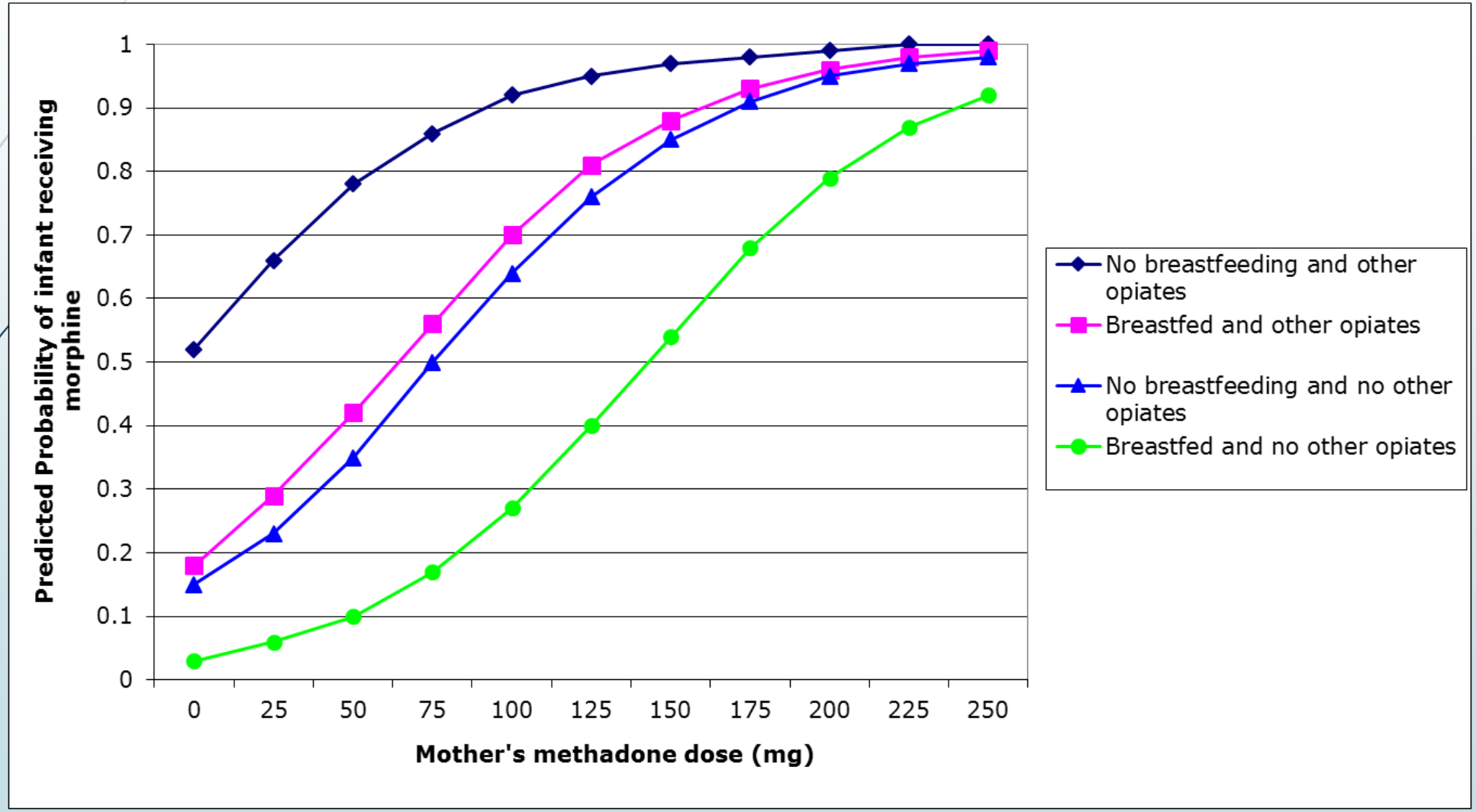
An Evaluation of Rooming-in Amongst Substance-Exposed Newborns in British Columbia
R. Abrahams et al SEPT JOGC, 2010

- Retrospective comparison of Rooming-in (n=371) vs. Standard care (n=834) using BC Perinatal Heath Program Data.

- Rooming-in associated with:
  - Significant decrease in admissions to NICU
  - Increased likelihood of breastfeeding during hospital stay
  - Increased odds of baby being discharged home with his/her mother

- **Review supports the finding that rooming-in is both safe and beneficial for substance-exposed babies.**

Probability Methadone/Morphine Tx JOGC, May, 2011



BREASTFEEDING

- Methadone enters breast milk in very small quantities
- Safe to breastfeed on methadone and buprenorphine regardless of dose (buprenorphine/naloxone included)
- **Rooming-in** is the best option to encourage attachment and development of parenting skills
- If baby needs to go to the NICU or nursery, parents should accompany and be encouraged to hold and cuddle infant 24/7 if possible
- What about other substances and breastfeeding??

Health Canada Santé Canada

Aug 2nd, 2018

Summary Safety Review – METHADOSE and METADOL-D - Assessing the potential risk of serious harm in children exposed to methadone through breast milk

Product: Methadose, Metadol-D (methadone hydrochloride)

Potential Safety Issue: Risk of serious harm (including death) in children breastfed by mothers in methadone treatment

Key Messages

- Methadose and Metadol-D are methadone-containing drugs used to treat addiction to opioids (such as heroin) in adults. They work to prevent withdrawal symptoms, which are side effects caused by stopping the use of other opioids.
- Health Canada became aware of a published article[1] that reported 2 Canadian cases of death in children who had increased levels of methadone in their blood because they were being breastfed by mothers in treatment programs for opioid addiction (methadone maintenance programs).
- Health Canada's review of the available information found that there may be a link between methadone and the risk of serious harm (including death) in children exposed through breast milk. Health Canada will be working with the manufacturers of Methadose and Metadol-D to strengthen the existing product information to specifically include the risk of serious harm, including death, in children exposed to methadone through breast milk.

Breastfeeding and Methadone

Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants

Factsheet#11- BREASTFEEDING CONSIDERATIONS FOR INFANTS AT RISK FOR NEONATAL ABSTINENCE SYNDROME
https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054:
Substance Abuse and Mental Health Services Administration; January 2018.

Handout (Factsheet # 11)

POSTPARTUM CARE

- Promote wrap-around care for the full postpartum year
- OAT tapers and discontinuance has a very high rate of relapse and increases the risk of overdose death
- Suicide rates are high in this population: primary care and OAT providers should be notified of delivery and prompted to follow up emergency dept visits with a wellness check as these often herald waning mental health
- Regular ongoing support by stable team of caregivers is best predictor of good outcome
- Ensure safety, food, shelter, baby supplies
- Link parents to community supports and parenting resources

CHILD PROTECTION CONCERNS

- In Canada, the fetus is not a person; caregiver must only speak to child protection services IF a child, not a fetus, is unsafe.
- “Anyone who has reasonable grounds to suspect that a child may be in need of protection must make a report directly to Child Protection Services.”
- Speak to the mother first; ideally, she would call the CPS herself, requesting support be put in place prior to delivery
- **Self-report** prenatally increases self-efficacy, dignity, & stability while promoting optimal relations with child protection authorities.

Questions??

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