Pain Management of the Opioid Dependent Mother: An Updated Review of the Literature

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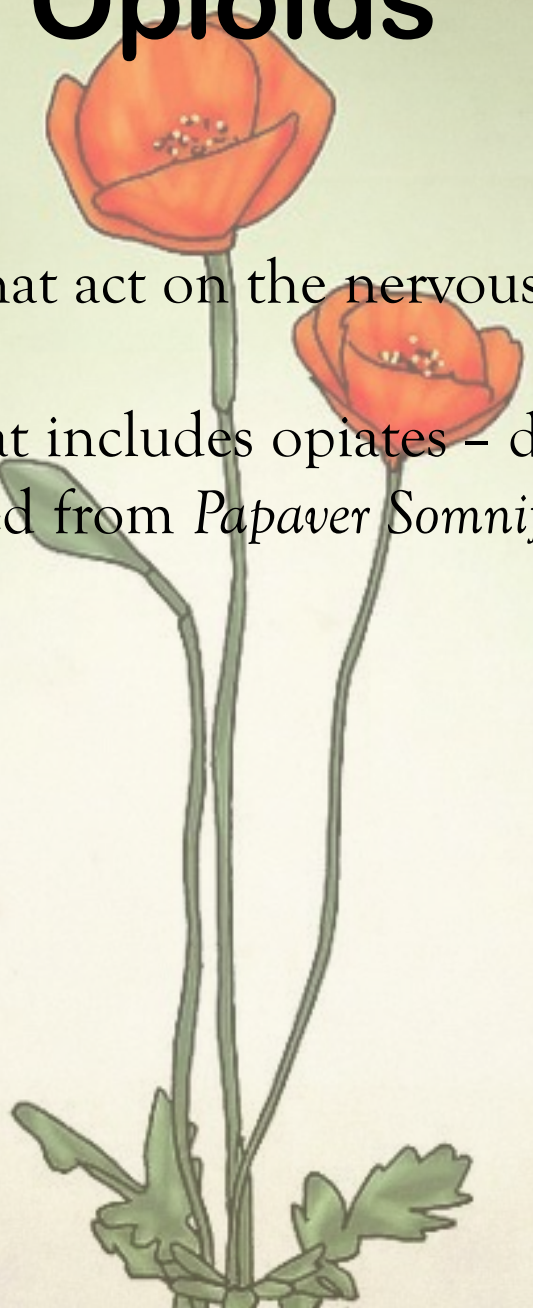
Learning Objectives

1. Understand the basic pharmacology of opioid addiction and opioid maintenance therapies.
2. To create at deeper understanding of the unique clinical challenges related to the topic.
3. To improve ability to safely and effectively provide pain management to pregnant women with opioid use disorders.

Definitions & Biology of Opioids

Opioids

- Opioids drugs that act on the nervous system to relieve pain
- Blanket term that includes opiates – drugs such as morphine derived from *Papaver Somniferum* the opium poppy



Opioid Types

Endogenous

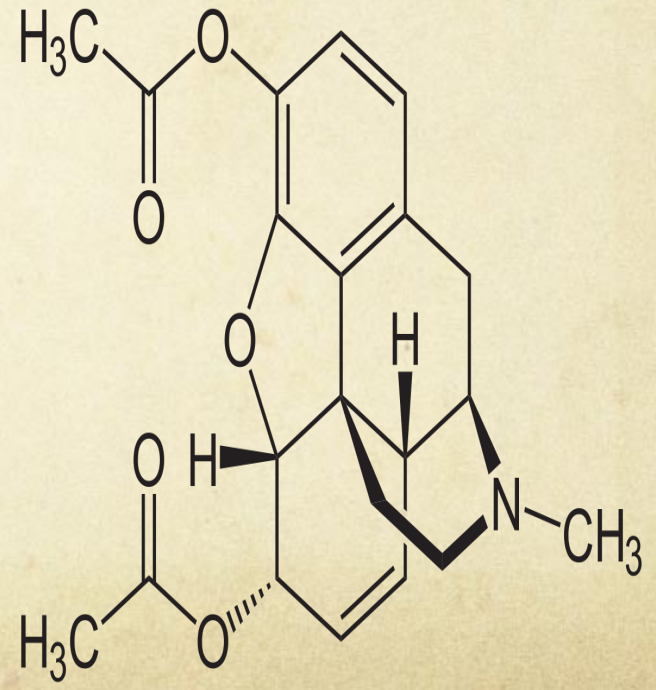
Endorphins

Exogenous

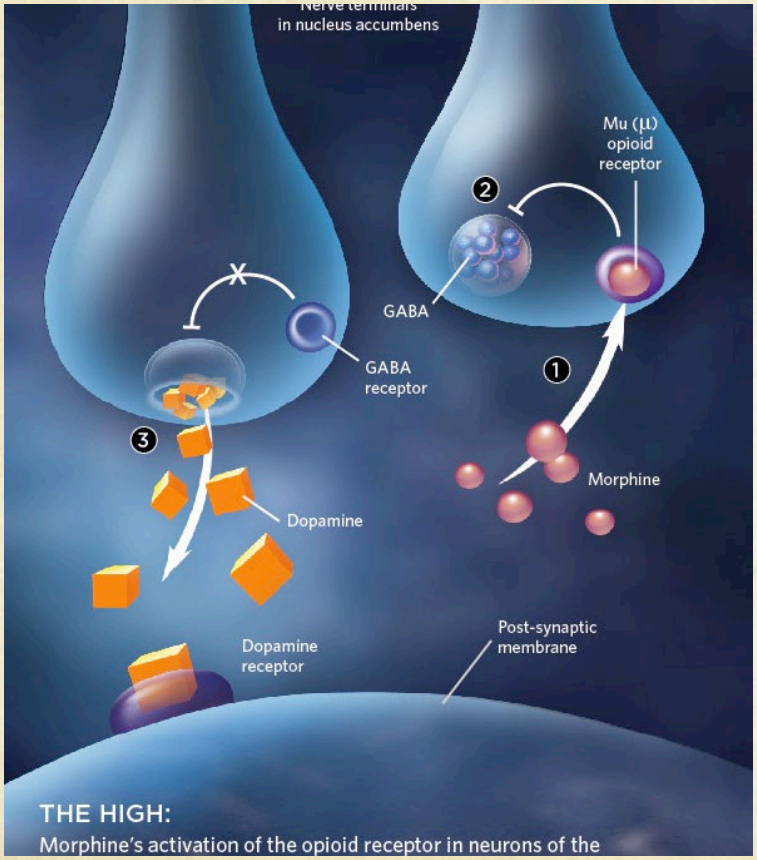
Natural

Semi-Synthetic

Synthetic



The Biology of Opioids



- Opioids attach to Mu (μ) receptors on nerve terminals in brain which
  - Inhibits transmission of pain signal.
  - Triggers release of gamma-aminobutyric acid (GABA)
    - GABA causes neighboring cell to release dopamine
    - Release of dopamine
    - Creates euphoria

Activation of the Mu Opioid Receptor

Mu RECEPTOR ACTIVIATION
Pain relief
Euphoria
Sedation

Opioid Agonists

Fully activate opioid receptors in the brain resulting in an opioid effect

Heroin
Oxycodone
Methadone
Hydrocodone
Morphine

Opioid Partial-Agonists

Partial activation of opioid receptors in the brain resulting in an opioid effect but lesser than that created by full agonist.

Butorphanol (Stadol)
Nalbuphine (Nubain)
Buprenorphine (Subutex)
Buprenorphine/naloxone (Suboxone)

Opioid Antagonist

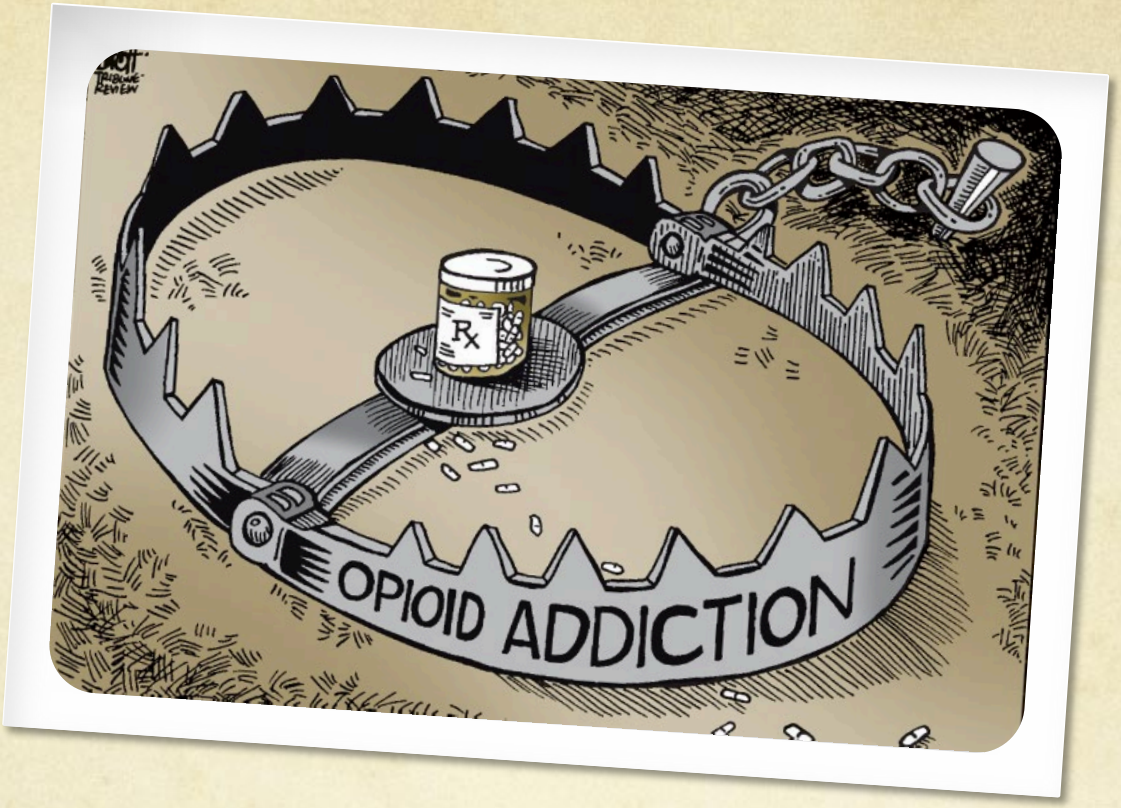
Block the action of opioids by binding to opioid receptors *without activating them*. Used to treat opioid overdose.

Naltrexone
Naloxone (Narcan)

Fundamentals of Opioid Use Disorders

Opioid Tolerance, Physical Dependence and Withdrawal

- With prolonged and/or heavy use of opioids, a person can develop **opioid tolerance**:
  - Higher amounts or higher potency opioids needed to generate the same effect on fewer receptors to achieve opioid effect and to prevent withdrawal symptoms.
- **Opioid withdrawal** occurs when the exogenous opioids are removed from the system and the remaining endogenous opioids are unable to sufficiently activate the remaining receptors.
- When the body relies on a external source of opioids to prevent withdrawal symptoms it is termed **physical dependence**.
- Physical dependence is ***not*** the same thing as addiction.



Fundamentals of Addiction

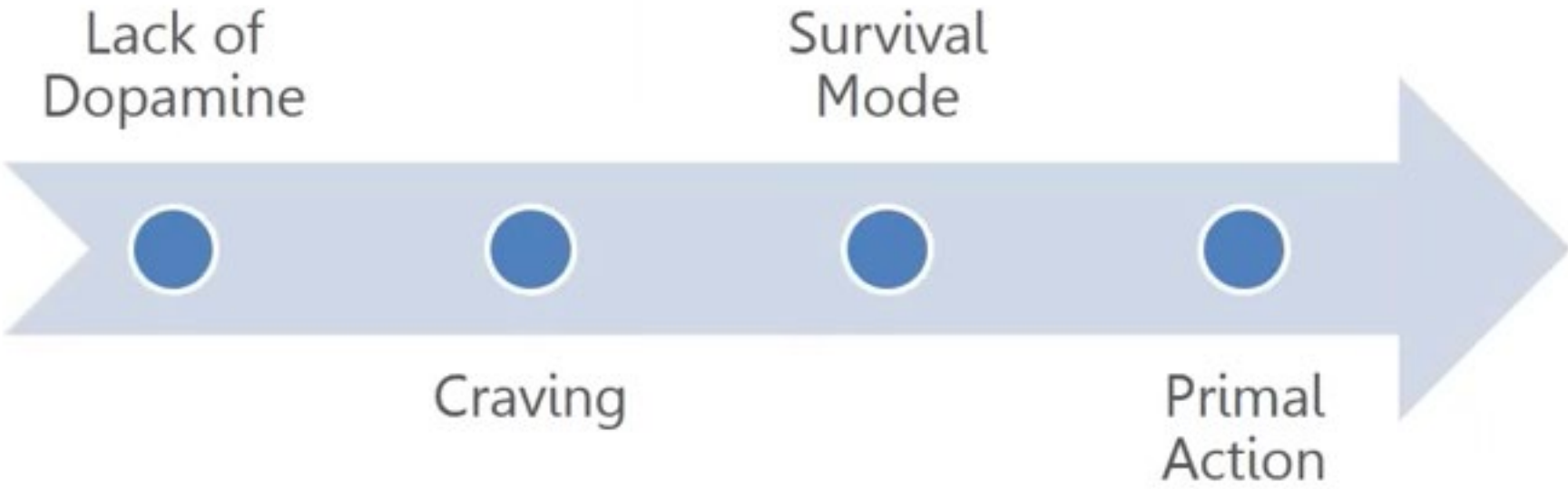
Tolerance

Dependence

ADDICATION

Addiction Behaviors

Craving for Dopamine



C. Waller, MD, Addiction 101: Impact of Long-term Opioid Use on the Brain. Opioid Collection Network, 2016.

Table. DSM-5 Diagnostic Criteria for Opioid Use Disorder[a]

1. Opioids are taken in larger amounts or duration than intended
2. Persistent desire/unsuccessful efforts to cut down or control opioid use
3. A great deal of time is spent obtaining, using, or recovering from the effects of opioids
4. Craving
5. Recurrent use of opioid results in failure to fulfill major role obligations at work, school, or home
6. Continued use despite social/interpersonal substance-related problems
7. Important social, occupational, or recreational activities are given up or reduced because of substance use
8. Recurrent use in hazardous situations
9. Continued use despite knowledge of having a persistent or recurrent opioid-related physical or psychological problem that is likely caused or exacerbated by opioid use
10. Tolerance[b]
11. Withdrawal[b]

Severity: Mild: 2-3 symptoms, Moderate: 4-5 symptoms, Severe: ≥ 6 symptoms

[a] The information above is only an overview of the criteria used. Consult the DSM-5 before making a diagnosis.

[b] Note: This criterion is not considered to be met for patients taking opioids solely under appropriate medical supervision

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: American Psychiatric

Opioid Maintenance Therapy

Non- pregnant patients success rate of 40-60 % after 1-2 years.

When patient come off OMT they relapse[47,48]

Recommended treatment for opioid use disorders in pregnancy [46]

Opioid Maintenance Therapy

Methadone-full opioid agonist

closer — Higher initiation rates for patients with severe conditions or those using long acting opioid formulations, monitoring with "a program", safer for patients also using benzos.

Buprenorphine – partial agonist

Improved safety profile/less risks of respiratory CNS depression, less NAS and less severe symptoms, not for use with pt with active Hep C/abnormal LFTs, using short acting opioids

Buprenorphine/Naloxone

safety — Naloxone as Abuse-deterrent, Emerging evidence confirming in pregnancy.

Medically Managed Withdrawal in Pregnancy with Opioid Use Disorder

SAFE does NOT EQUAL EFFECTIVE

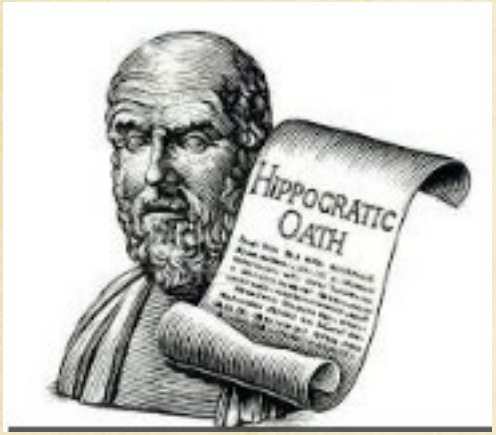
Bell et al , 2016 & Luty, 2003

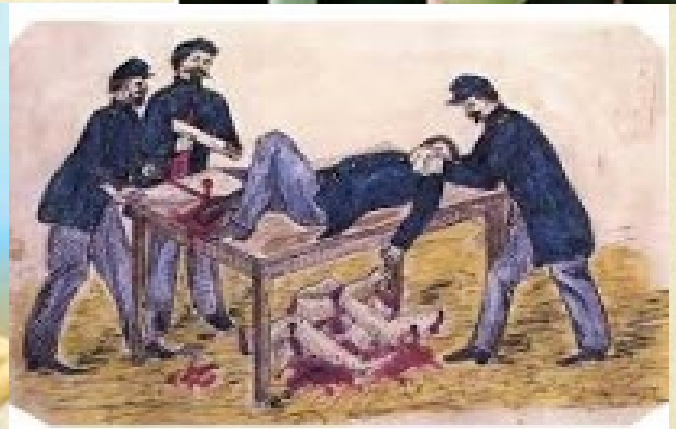
- ✓ **No fetal loss attributed to detox or adverse fetal affects**
- ✓ **Relapse rates for inpatient detox on release: 70-99 %**
- ✓ **In Bell et al NAS for inpatient detox and release 70%**

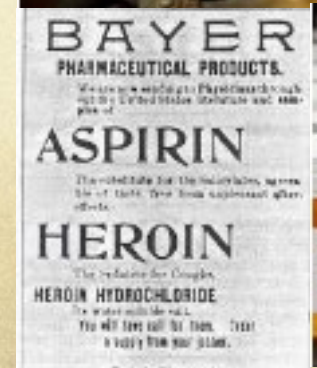
Improved maternal and fetal outcomes with OMT vs Detox[46]

Opioid Use Disorder
An American Epidemic

OPIOIDS: WE GO WAY BACK







THE AMERICAN OPIOID EPIDEMIC

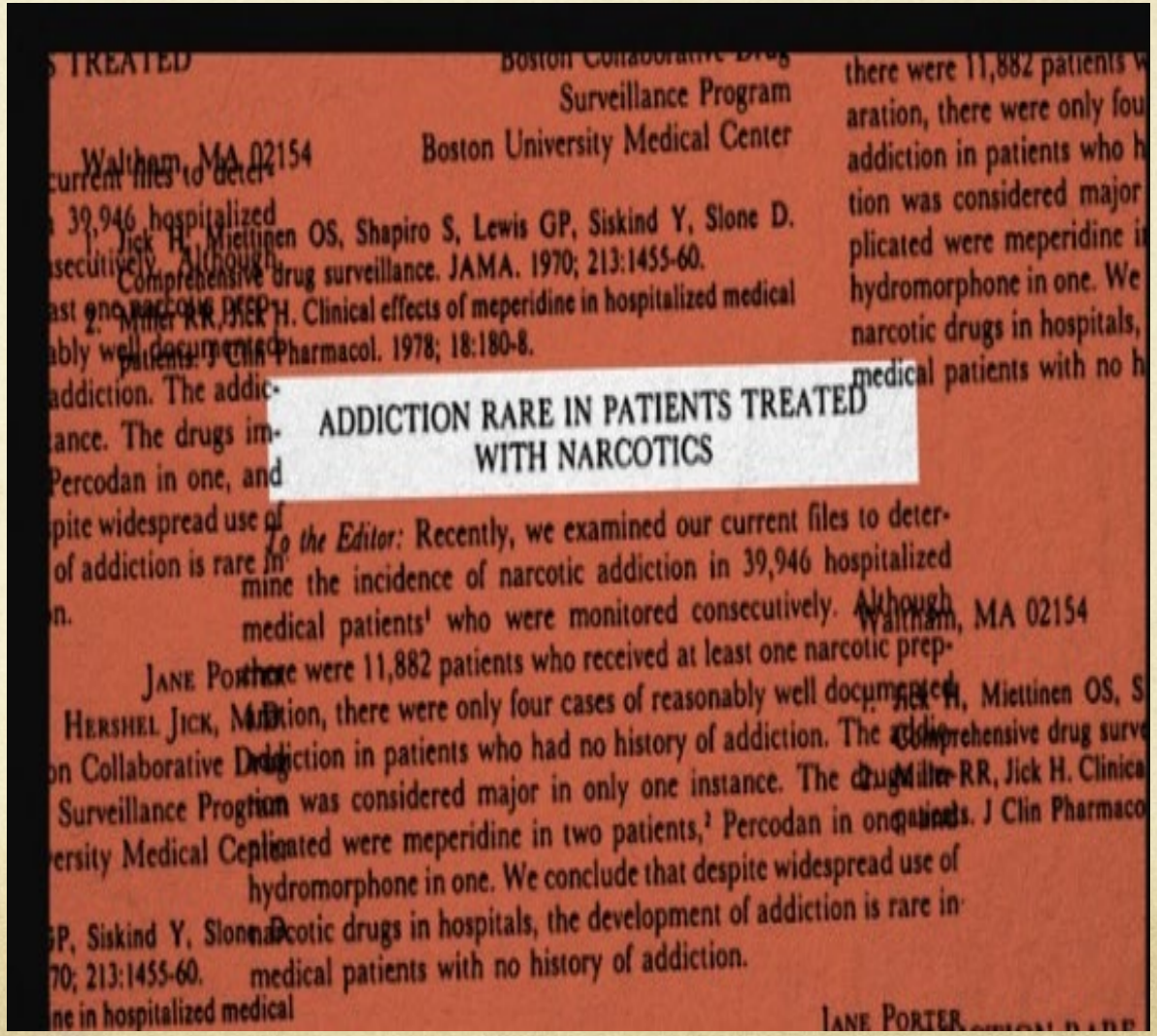
Major Contributing Factors

Big Pharma marketing non-addictive safety profile of opioids to providers

Development of Extended Release Opioids

Professional organization lobby to focus on patients undertreated pain. Pain as the "5th vital sign"

Excessive increase in supply of Rx opioids



ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER

Opioid Epidemic
1990s-Present

2000s: More deaths from opioid overdose then deaths from AIDS in the height of the AIDS epidemic

2011: Drug overdose deaths surpass MVAs as leading cause of accidental deaths in the US

2016 : 90 Americans die daily of opioid overdose

2017: Opioid use disorder declared a National Health Crisis

mailto:https://www.pbs.org/newshour/show/opioid-addiction-biggest-drug-epidemic-u-s-history-howd-get

Medical Opioid Use and Opioid Use Disorders

Many opioid use disorders (OUD) start with medical use of opioid.

- About 10-20% of patients who opioids for pain will develop OUD.

- Back pain is the most common indication for opioid prescriptions in the United States.

- Most people with opioid use disorders, however, did not begin using opioids in a prescribed manner.

Pregnancy: A Window of Opportunity for OUD Treatment

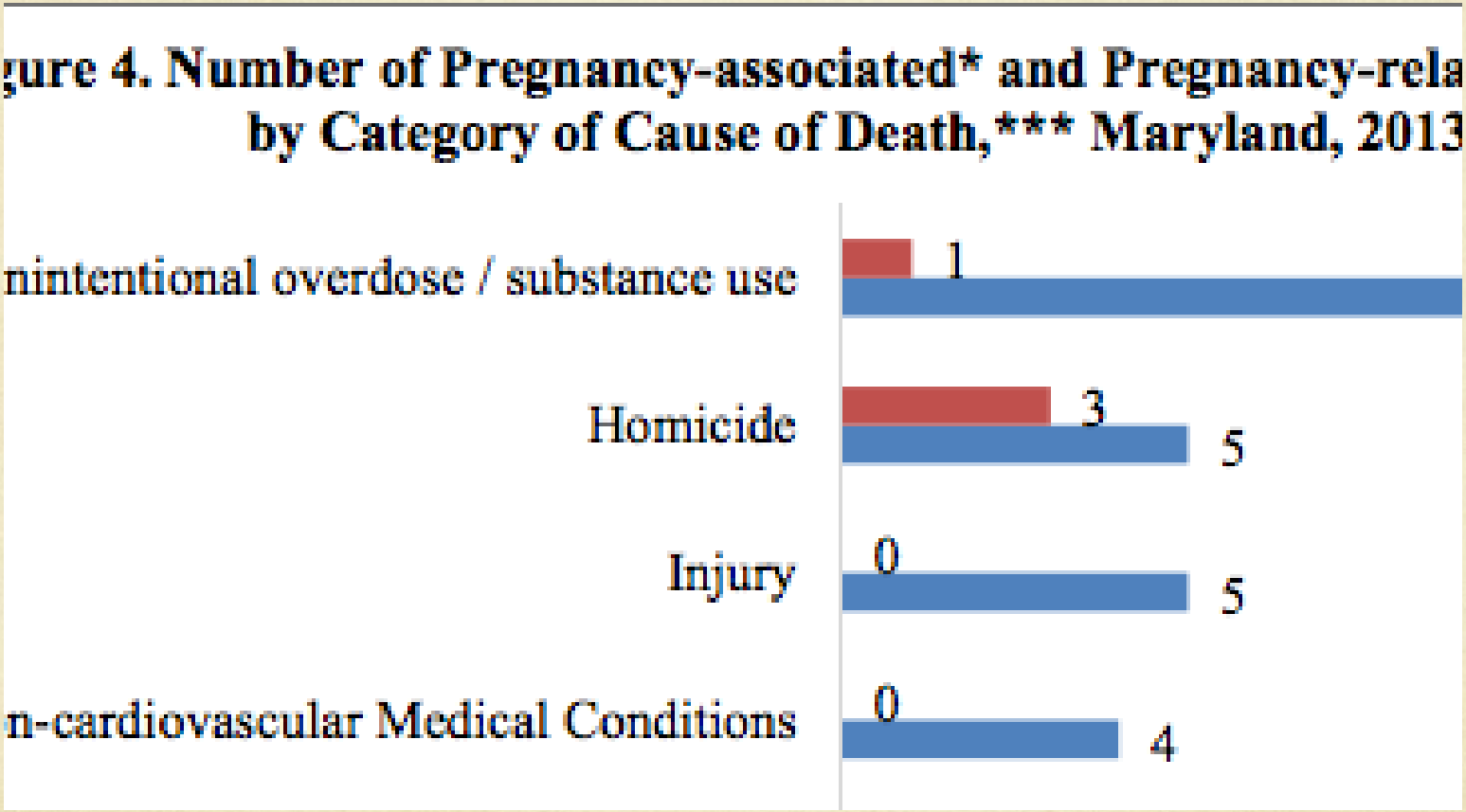
- The percentage of women with substance use disorders women who abstain from illicit drug use increases progressively as pregnancy progresses.

First trimester:	28%
Second:	76%
Third:	93%

Unfortunately, nearly 80% relapse postpartum period

Ebrahim, S. H., & Gfroerer, J. (2003). Pregnancy-related substance use in the United States during 1996–1998. Obstetrics & Gynecology, 101(2), 374-379.

Relevance to Clinical Practice



UNDERTREATMENT OF CHRONIC OR ACUTE PAIN SIGNFICANTLY INCREASES RISK OF RELAPSE IN PATIENTS WITH OPIOID USE DISORDERS.

Pain Management for Pregnant Women With Opioid Use Disorders

Clinical Challenges To Pain Management in Women with OUD

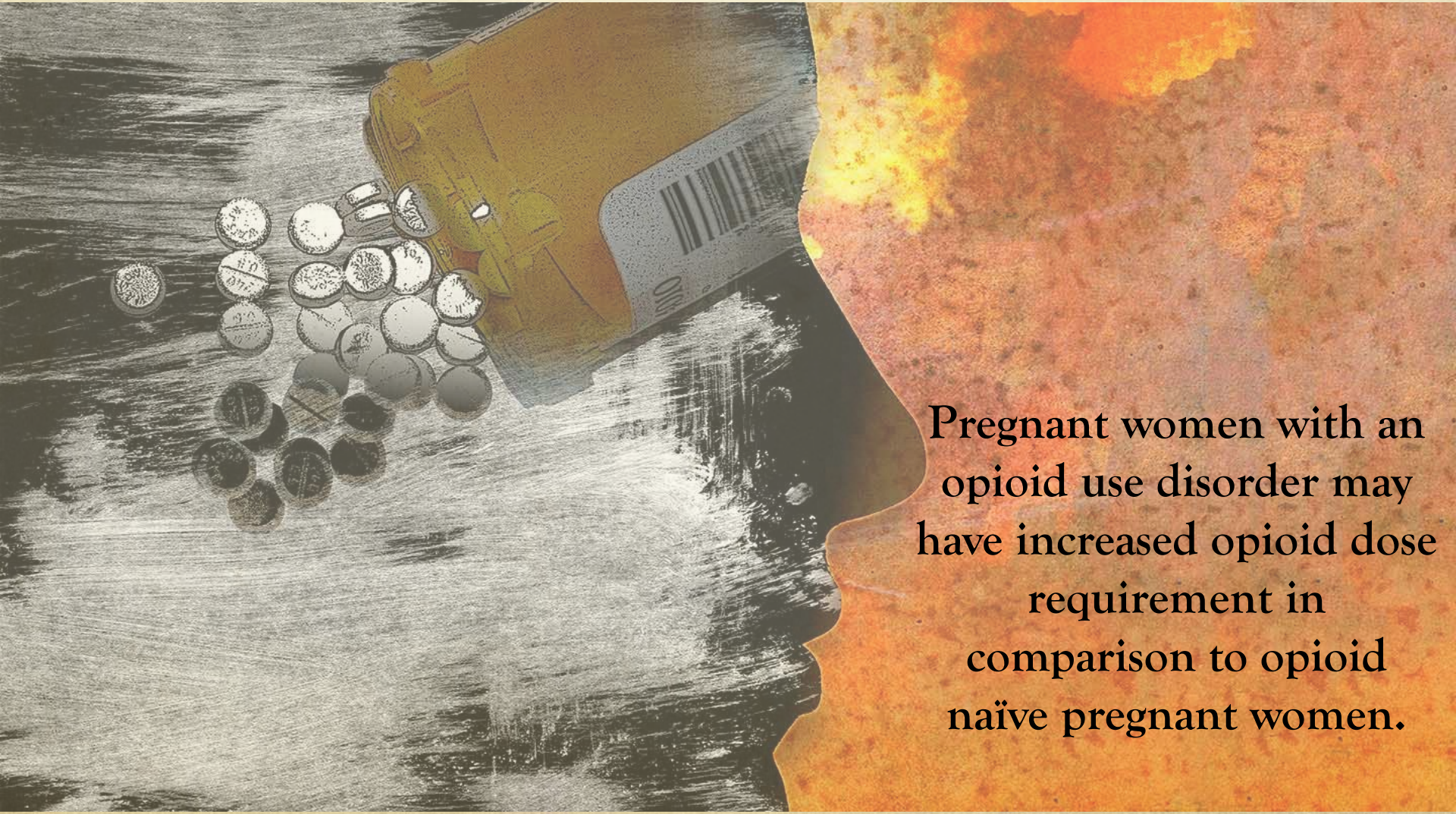
Opioid Tolerance

Opioid Cross-Tolerance

Hyperalgesia

Provider Bias/Misconceptions

Opioid Tolerance
Effect on Pain Management



Pregnant women with an opioid use disorder may have increased opioid dose requirement in comparison to opioid naïve pregnant women.

Opioid Cross-Tolerance Effect on Pain Management

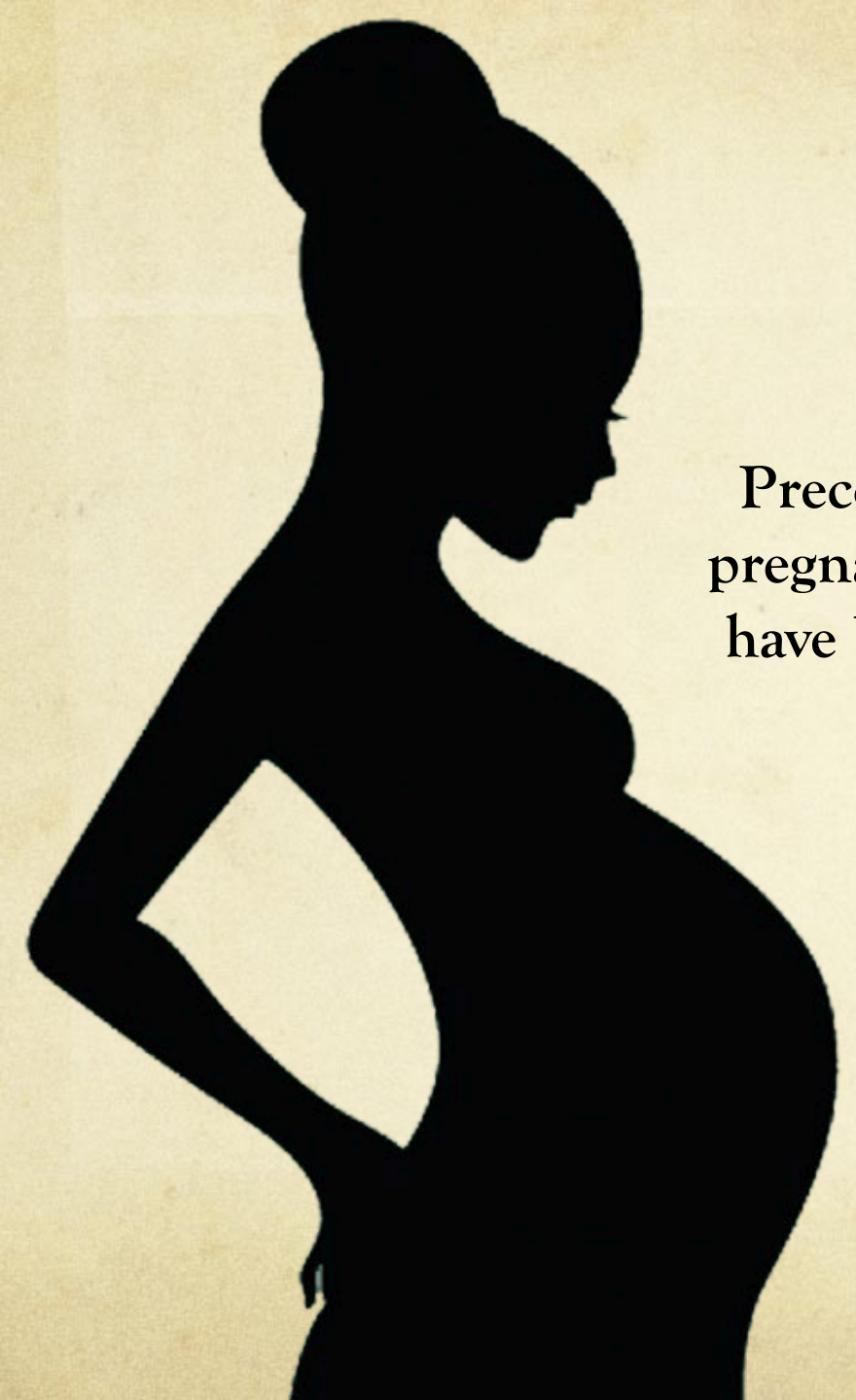
Cross-tolerance: tolerance for one drug leads to tolerance for another.

For example, studies have shown morphine and methadone have a significant cross-tolerance effect [11]

Hyperalgesia
Effect on Pain Management

Hyperalgesia: pathologically heightened sensitivity to pain

- Patients on opioid maintenance therapy (OMT) have:
  - Decreased tolerance to pain
  - Increased sensitivity to pain
- No difference in tolerance or sensitivity to pain based on agent (buprenorphine versus methadone) (Compton, ***, Wacholtz ***)
- Patients with a history of OMT had increased tolerance and sensitivity to pain (Wacholtz, ***)



Preconceived beliefs and ideas regarding pregnant women with opioid use disorders have been shown to negatively impact the clinical care of pain. [18]

Management of Pain in Women with Opioid Use Disorders: Common Provider Misconceptions

- Administration or prescribing of opioids for acute pain will result in relapse
- Opioid maintenance therapy provides analgesia so no additional pain medications are necessary.
- Opioid dependent patients reporting acute pain are usually drug-seeking [12,20]

Clinical Management of Pain in Pregnant Women on Opioid Maintenance Therapy

ANTEPARTUM

Antepartum Overview

- Pain Prevention
- Discomforts of pregnancy
- Acute pain
- Chronic pain

Antepartum Pain Prevention

- Focus on care components of routine antenatal care that can affect a woman's experience of pain:
  - Psychosocial well-being
  - Sleep hygiene
  - Smoking cessation

Mental Health Care

- Mental health disorders can negatively impact the pain experience.
- 56-73% of opioid dependent pregnant women have mental health conditions.
- Most common:
  - Depression
  - Anxiety
  - PTSD
- Improved mental health may improve the pain experience for pregnant women with opioid use disorders.[20,22,23]

Mental Health Care

- Non-pharmacologic interventions are 1st line treatment [24]
  - Cognitive behavior therapy (CBT)
  - Mindfulness-based stress reduction (MBSR) [25]

Sleep Hygiene

- Poor sleep quality increases sensitivity to pain and increases risk of relapse
- Pregnant women with OUD increased risk of impaired sleep
    - Sleep quality impaired at every level of opioid use
    - Sleep quality may be impaired by pregnancy[26]

Sleep Hygiene

Do's

Regular sleep routine

Exercise regularly before 2 pm

Dark room, comfortable temp

Don'ts

Read or watch TV in bed

Light and sensory stimuli
Smoke tobacco prior to going to bed

Lay aware for more then 10 min in bed

Nicotine Dependence

- Nicotine dependence is associated with increased pain sensitivity. [10,20]
- There is cross-tolerance between nicotine and morphine[27]
- Abrupt cessation due to hospital admission is associated with higher inpatient analgesia requirements to treat pain[20,27]
- No published research examining relationship between nicotine dependence and pain in pregnancy

Nicotine Dependence Interventions

- Brief Intervention/ Patient education (SBIRT)
- Referral to smoking cessation program (1-800-quit-now)
- Offer smoking cessation aids during antepartum period
- Offer nicotine replacement during inpatient admission.

Discomforts of Pregnancy Special Considerations

- Nausea
  - Promethazine potentiates opioid effects of OMT.
  - Alternative anti-emetic as first line[29]
- Musculoskeletal pain
  - May be more pronounced secondary to hyperalgesia common in this population [30]
  - No available research on management for opioid dependent pregnant patients

Acute Pain Management General Principles

- Providers should evaluate patient complaints of pain and not dismiss these complaints as drug-seeking behavior.
- Higher doses of pain medication may be necessary to treat pain
- Opioid maintenance therapy (OMT) should not be part of pain management plan
- Do NOT discontinue OMT while providing pain treatment [8,9,12]

Acute Pain Management American Society of Pain

- Maximizing non-pharmacologic interventions and non-opioid analgesia
- Acute pain that is unresponsive to above treatment can be treated with a limited course of a short-acting full opioid agonist
  - Morphine
  - Fentanyl
  - Oxycodone
  - Hydrocodone
  - Acetaminophen/Codeine
  - Meperidine
- Higher doses may be required due to tolerance/cross-tolerance [17]
- Do NOT use opioid agonist-antagonist to treat pain [5]
  - Butorphanol (Stadol)
  - Nalbupine (Nubain)

Acute Pain in the Outpatient Setting

1st Line Treatment

Non- pharmacologic interventions

2nd Line Treatment

Non-opioid pharmacologic interventions

3rd Line Treatment

May add short course of short-acting full agonist opioid

1) review patient in Maryland PDMP

2) Typically treat for 3 d and no more then 5-7 d (CDC Opioid Prescribing Recommendations, 2017)

3) consider plan for urine drug testing following treatment with patient consent.

Chronic Pain

Pregnancy may aggravate chronic pain conditions.

- Chronic pain is frequently undertreated in pregnancy.[16,17,21,31]
- Multimodal multidisciplinary approach is recommended for treatment of chronic pain in pregnancy [21,33]
- **Refer to :**

CDC Guidelines on Treatment of Chronic Pain (2017)

ACOG POSITION PAPER ON OPIOID USE AND OPIOID USE DISODERS IN PREGNANCY (2017)

Antepartum Pain Plan

OMT in PREGNANCY: PAIN MANAGEMENT CHECKLIST

Patient Name: Estimated Due Date:

Addiction Provider/Clinic name: Phone number:

Opioid Maintenance Therapy(OMT): __ Methadone ___ Buprenorphine

OMT Dose: _____ Verification date_____

Best contact/after hours contact information to confirm OMT dose_____

Antepartum Co-Morbidities:

Chronic non-pregnant pain: __Y __ N Referral_____

Mental Health Plan Referral to CBT____ Referral to MBSR____ Last seen _____

Tobacco Smoking Cessation Plan: # of cigarettes daily___ Last reviewed_____

Counseled on nicotine dependence and pain ___

Contact information for quit line ___

Offered cessation aids : ___patch ____nicotine gum __

Sleep Quality:

___ Counsel on relationship b/w sleep and pain _ review of patient sleep hygiene

___ Counsel on appropriate sleep hygiene . ___Guideline handout given to patient.

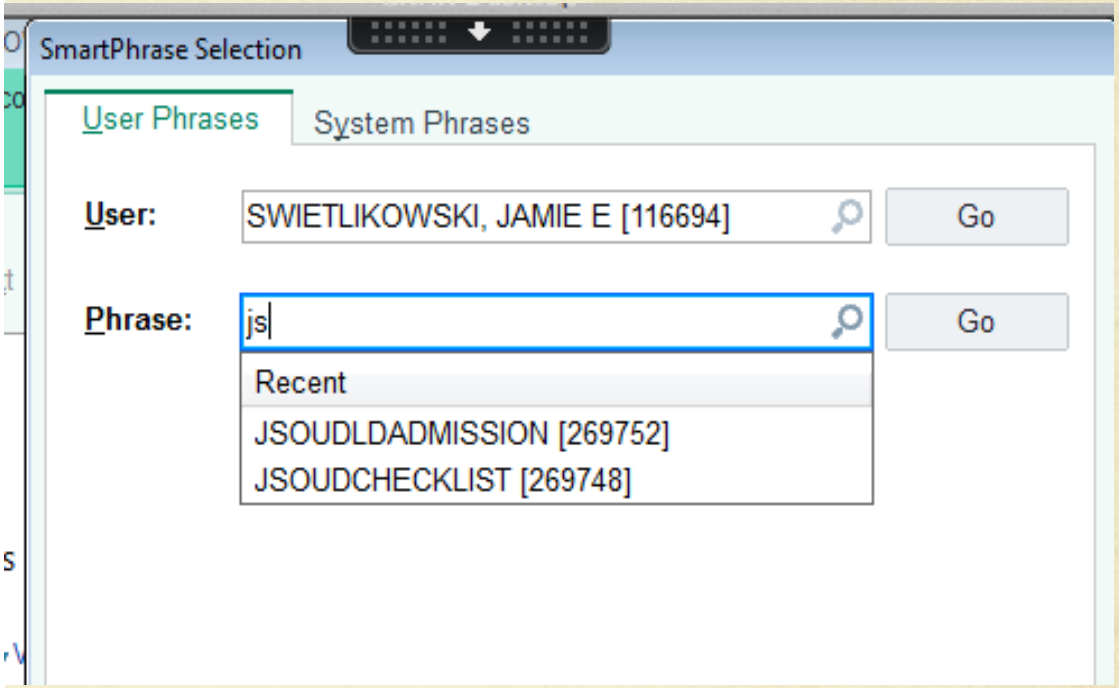
Labor plan:

Labor pain management plan: ____NCB ____ Epidural

CBE_____Early labor plan (non-pharm methods) _____ Doula _Y__ N_

___ Anesthesiology consult _____ Pain Management/Substance Abuse Consult

Nicotine replacement on admission: __Y __N



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Clinical Management of Pain in Pregnant Women on Opioid Maintenance Therapy

INTRAPARTUM

Intrapartum Overview

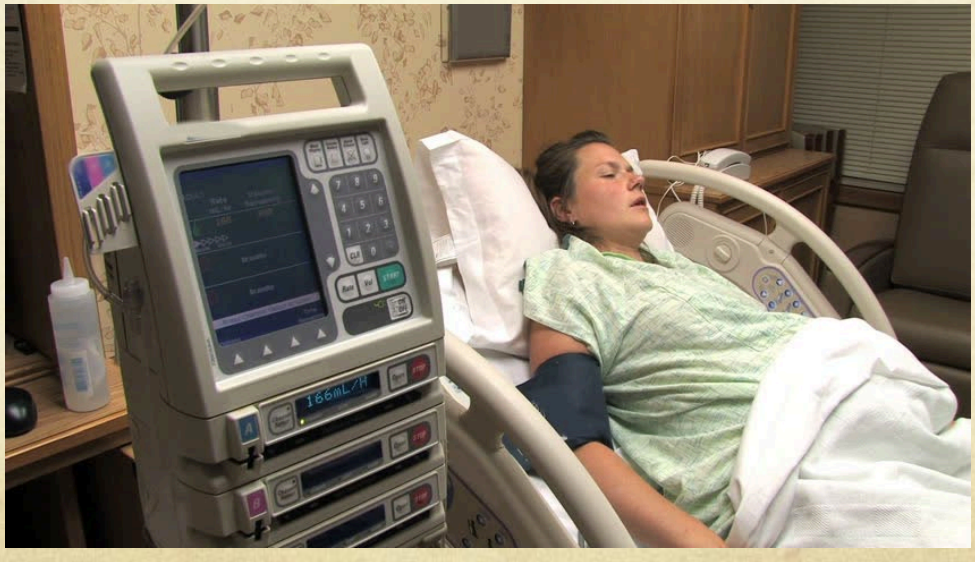
- ACOG has issued a position statement with consensus findings based mainly on expert opinion.
- There are four independent research studies that address the pain management of opioid dependent women in labor.

Findings from the Literature

- Adequate pain control with epidural anesthesia [35, 36]
- Comparison of women on OMT and those who were opioid naïve:
  - No difference in reported pain intrapartum
  - No difference in IV narcotic use
  - No difference in epidural use in two studies [35,36]
  - One study found increased epidural use in OMT population[27]
- Women on methadone for OMT required more supplemental anesthesia after epidural placement than opioid naïve patients[34,36]
- Intrapartum pain for women on buprenorphine for OMT was adequately treated with short-acting full opioids and epidural anesthesia. [35,37]

Intrapartum Pain Management Principles

1) Continue opioid maintenance therapy during labor
2) Provide adequate analgesia
3) Do not use opioid agonist-antagonist [5]



Intrapartum Special Considerations for BMT

- Theoretical concern regarding effective labor pain management given BMT "ceiling effect"
- Intrapartum pain for women on BMT was adequately treated with short-acting opioids and epidural anesthesia[35,26]
- Split BMT dosing during IP stay: some authors suggest this strategy but no conclusive evidence exists at this time[7,11]
- BMT and pain management therapy should be given concurrently[5]
- If unable to adequately control BMT intrapartum pain an anesthesia and addiction services should be considered.

Clinical Management of Pain in Pregnant Women on Opioid Maintenance Therapy

POSTPARTUM

Findings from the Literature

- Postpartum, pain management deteriorates[34, 36-38]
- Continued reports of pain may indicate worse management, not drug-seeking[35]
- Hesitance to give opioids to women on OMT[27]

Postpartum Pain Management

- May need more frequent and higher doses of pain medication[9, 15]
- IV: Short-acting opioids, acetaminophen and NSAIDs; titrate to oral versions[6,7,9,11,35,37,38]
- Consider scheduled dosing instead of PRN[6]
- Adjuvant methods and nicotine replacement[40]
- Continue OMT during entirety of hospital stay

Discharge

- Ensure continuity of OMT
- Discharge pain medications
  - Generally the same as non-opioid-dependent women[34]
- Follow-up appointments
  - Cesarean: oral opioids tapering by end of week 1, early follow-up[7]
- HIGH RISK of RELAPSE
  - Related to under-treatment of postpartum pain and other social risk factors NOT to short-term opioid analgesia[9,40]

Clinical Management of Pain in Pregnant Women on Opioid Maintenance Therapy

SUMMARY

Consensus Evidence & Recommendations

1. Opioid-dependence alters pain experience*
2. Pain must be treated adequately*
3. Pain, and desire for pain management, is individual [*7,11,17,21,27,31,35,36,41-43]
4. Optimal pain management is a team effort[21,30,33]
5. Opioid agonist-antagonists are contraindicated[5,7,17,31]
6. Research on pain management in pregnant women dependent on opioids is minimal[25,35-38]
7. Continue OMT[5,6,27,31,33,35,41]
8. OMT does not address acute pain[ibid]
9. Acute pain must be assessed and treated appropriately[ibid]
10. Many barriers exist to appropriate pain management

"...every patient with pain, including those with substance abuse, ha[s] the right to be treated with dignity, respect, and high quality pain assessment and management."

- The American Society of Pain Management

Resource List

Mindfulness-Based Stress Reduction

Sleep Hygiene Check List

Pain Plan Check List

CDC Chronic Pain Guidelines

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