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Managing Acute Withdrawal in Pregnancy

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MACS for MOMs Consultant

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Learning objectives

- Review signs and symptoms of acute opioid withdrawal in pregnancy
- Explore pregnancy specific risks/concerns
- Discuss treatment options

Case

Mia is a 24yo G3P1101 at 37wga who presents to triage with the complaint of nausea, diarrhea, subjective fevers and malaise. She has limited prenatal care and just moved to the area from Virginia. She reports that she has preeclampsia in a previous pregnancy.

She is taken to a triage room and asked to undress, put on a gown and leave a urine sample. The nurse takes her vital signs and notes a BP of 155/98. Fetal heart rate monitoring is reassuring. The triage nurse then goes through a series of screening questions and the patient reports recent opioid use.

Case (cont)

Approximately one hour after her arrival to L&D, the triage physician, Dr. A, comes to evaluate Mia. The provider notes that Mia is “resting comfortably” and “not engaging in conversation”. Dr. A explains to Mia that she is concerned about preeclampsia. She orders continuous fetal monitoring, preeclampsia labs and blood pressures to be repeated every 15 minutes.

The triage nurse has difficulty drawing blood from the patient and calls phlebotomy. The labs are sent an hour later (2 hours after arrival).

Case (cont)

Two hours later (4 hours after arrival to L&D), the labs return and Dr. A notes that Mia has mildly elevated LFTs and proteinuria.

The triage nurse notifies Dr. A that Mia is “refusing” blood pressure monitoring and has removed her fetal heartrate monitor.

Dr. A enters the room to evaluate Mia, noting that Mia is restless and diaphoretic. Mia tells Dr. A that she has increasing abdominal pain. Dr. A performs an ultrasound and reassures Mia that the baby is healthy and that there are no signs of placental abruption. Dr. A performs a cervical exam, finding that she is 3cm dilated. Dr. A explains to Mia that she is likely in early labor.

Case (cont)

Dr. A leaves the room to put in admission orders and asks the nurse to repeat Mia's blood pressure and replace the FHR monitor. The nurse attempts to replace the monitor, but Mia takes it off saying that it is painful. The nurse again explains to Mia the importance of monitoring the baby.

When Dr. A returns to the room (5 hours after arrival to the unit) to consent Mia for delivery. Mia is increasingly agitated and asking to leave. Dr. A explains the risks of leaving against medical advice, including maternal stroke or seizure, placental abruption and neonatal death. Mia signs a paper accepting these risks and leaves.

Case analysis

- Presenting complaint – abdominal pain, subjective fevers, malaise
  - These concerns were not directly addressed
- Screen positive for substance use
  - Was not explored further
- Elevated BP
  - Availability and confirmation bias to assume preeclampsia
- Increasing agitation
  - Did not address this in any way or discuss it with Mia
  - Repeatedly explained risks of “refusing”

Types of bias

- Availability bias
  - Prioritize information that most easily comes to mind
- Confirmation bias
  - Seeking out information to confirm our hypothesis
- Anchoring bias
  - Prematurely favoring a specific diagnosis
- Framing bias
  - Information is weighed differently based on how it is presented
- Attentional bias

RECOGNIZING WITHDRAWAL

EXHIBIT 2.10. Physical Signs of Opioid Withdrawal and Time to Onset

STAGE	GRADE	PHYSICAL SIGNS/ SYMPTOMS
Early withdrawal Short-acting opioids: 8–24 hours after last use Long-acting opioids: Up to 36 hours after last use	Grade 1	Lacrimation, rhinorrhea, or both Diaphoresis Yawning Restlessness Insomnia
Early withdrawal Short-acting opioids: 8–24 hours after last use Long-acting opioids: Up to 36 hours after last use	Grade 2	Dilated pupils Piloerection Muscle twitching Myalgia Arthralgia Abdominal pain
Fully developed withdrawal Short-acting opioids: 1–3 days after last use Long-acting opioids: 72–96 hours after last use	Grade 3	Tachycardia Hypertension Tachypnea Fever Anorexia or nausea Extreme restlessness
Fully developed withdrawal Short-acting opioids: 1–3 days after last use Long-acting opioids: 72–96 hours after last use	Grade 4	Diarrhea, vomiting, or both Dehydration Hyperglycemia Hypotension Curled-up position

Total duration of withdrawal:

- Short-acting opioids: 7–10 days
- Long-acting opioids: 14 days or more

Withdrawal 101

Signs & Symptoms of Opioid Withdrawal

Symptoms	Signs
Anorexia & nausea	Restlessness
Abdominal pain	Yawning
Hot & cold flushes	Perspiration
Bone, joint & muscle pain	Rhinorrhoea
Insomnia & disturbed sleep	Dilated pupils
Cramps	Piloerection
Intense craving	Muscle twitching - restless legs when lying down
	Vomiting
	Diarrhoea

Average vital sign changes:

SBP increased 15-20mmHG
DBP increased 10mmHg
Pulse increases 10 BPM

Weisshaar, BJCP 2020

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Clinical Opiate Withdrawal Scale (COWS)

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

COWS Clinical Opiate Withdrawal Scale

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 Pulse rate 80 or below 1 Pulse rate 81-100 2 Pulse rate 101-120 4 Pulse rate greater than 120	GI Upset: *over last 1/2 hour* 0 No GI symptoms 1 Stomach cramps 2 Nausea or loose stool 3 Vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 No report of chills or flushing 1 Subjective report of chills or flushing 2 Flushed or observable moistness on face 3 Beads of sweat *on* brow or face 4 Sweat streaming off face	Tremor *observation of outstretched hands* 0 No tremor 1 Tremor can be felt, but not observed 2 Slight tremor observable 4 Gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 Able to sit still 1 Reports difficulty sifting still, but is able to do so 3 Frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	Yawning *Observation during assessment* 0 No yawning 1 Yawning once or twice during assessment 2 Yawning three or more times during assessment 4 Yawning several times/minute
Pupil size 0 Pupils pinned or normal size for room light 1 Pupils possibly larger than normal for room light 2 Pupils moderately dilated 5 Pupils so dilated that only the rim of the iris is visible	Anxiety or irritability 0 None 1 Patient reports increasing irritability or anxiousness 2 Patient obviously irritable anxious 4 Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 Not present 1 Mild diffuse discomfort 2 Patient reports severe diffuse aching of joints/ muscles 4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort	Gooseflesh skin 0 Skin is smooth 3 Piloerrection of skin can be felt or hairs standing up on arms 5 Prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 Not present 1 Nasal stuffiness or unusually moist eyes 2 Nose running or tearing 4 Nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing Assessment:_____

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

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Subjective Opiate Withdrawal Scale (SOWS)

Instructions: We want to know how you're feeling. In the column below today's date and time, use the scale to write in a number from 0-4 about how you feel about each symptom right now.

Scale: **0 = not at all** **1 = a little** **2 = moderately** **3 = quite a bit** **4 = extremely**

DATE						
TIME						
SYMPTOM		**SCORE**	**SCORE**	**SCORE**	**SCORE**	**SCORE**
1	I feel anxious					
2	I feel like yawning					
3	I am perspiring					
4	My eyes are tearing					
5	My nose is running					
6	I have goosebumps					
7	I am shaking					
8	I have hot flushes					
9	I have cold flushes					
10	My bones and muscles ache					
11	I feel restless					
12	I feel nauseous					
13	I feel like vomiting					
14	My muscles twitch					
15	I have stomach cramps					
16	I feel like using now					
TOTAL						

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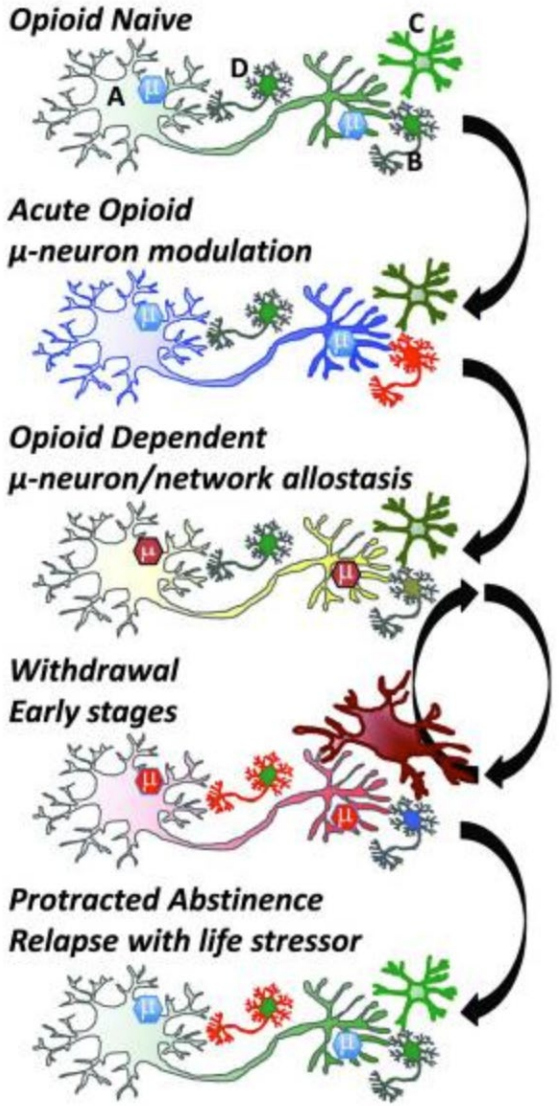
Things that Withdrawal can be mistaken for

- Mental health crisis
- GI distress
- Infection (tachycardia, diaphoresis, hot flashes, malaise)
- Hypertensive disorders of pregnancy
- Malingering



MANAGEMENT OF WITHDRAWAL

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The treatment of opioid withdrawal is opioids

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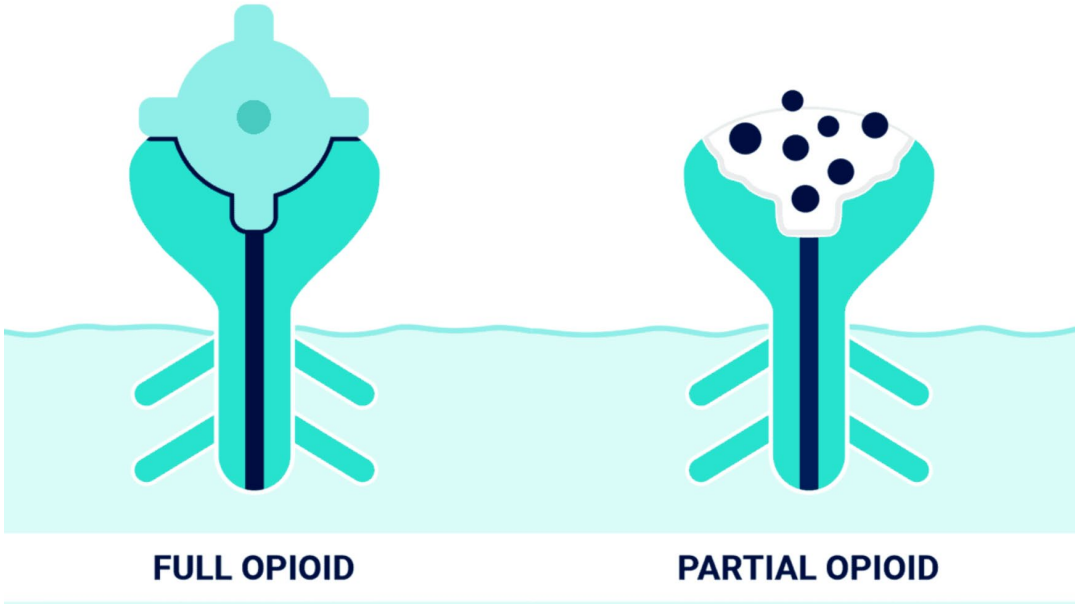
Acute treatment of opioid withdrawal

- Opioid agonists (oxycodone, methadone, buprenorphine)
- Often need to transition from fentanyl to full dose agonist then to buprenorphine once stabilized

Methadone versus buprenorphine



Methadone dosing

- Initial dose 20 – 50mg (SAMHSA updated guidelines)
- Often not sufficient for people using fentanyl
  - –Give additional doses of methadone in the same day (10mg q6 PRN)
  - –Or supplement with short acting opioids (5-10mg oxycodong q4-6 PRN)

Summary of Strategies

Day 1:

- Based on updated SAMHSA guidance, consider initial dose of 30-50mg
- Can give additional doses of methadone (ex. 10mg every 3-4 hours) for ongoing withdrawal
- Can also treat breakthrough withdrawal/pain with short-acting opioids (ex. oxycodone, hydromorphone)

Consider increase by 10-20mg per day to minimum therapeutic dose of 60-90mg daily for most patients

- Adjust/decrease for sedation

ORIGINAL RESEARCH

Standard Versus Rapid Inpatient Methadone Titration for Pregnant Patients With Opioid Use Disorder: A Retrospective Cohort Study

Neel S. Iyer, DO, MPH, Emily B. Ferguson, BA, Vivian Z. Yan, BS, Dennis J. Hand, PhD, Diane J. Abatemarco, PhD, MSW, and Rupsa C. Boelig, MD

- Standard titration - 30mg then 10mg q6 hours as needed
- "Rapid" titration – 30-40mg then 10mg q4 as needed
- Less frequent elopement in the rapid initiation group
- 196 patients (0.5%), one received Narcan in rapid initiation group

Feasibility of an Inpatient Split-Dose Rapid Methadone Induction Protocol for Pregnant Individuals

Nacev, Erin C. MD, MPH ; Prewitt, Kristin C. MD, MPH; Yang, Wei-Teng MD; Sokolski, Eleasa MD; Winer, James Michael MD; Rudolf, Vania MD; Englander, Honora MD; Liu, Patricia MD

TABLE 1 Inpatient Rapid, Split-dose Methadone Initiation Protocol Including Inclusion and Exclusion Criteria

Day	Methadone	Daily Maximum Dose (mg)	Daily Minimum Dose (mg)
1	30 mg x1 + 10 mg q4hr PRN x 4 doses	70	30
2	20 mg q12hr + 10 mg q4hr PRN x 4 doses	80	40
3	30 mg q12hr + 10 mg q4hr PRN x 4 doses	100	60
4	40 mg q12hr + 10 mg q4hr PRN x 4 doses	120	80
5	50 mg q12hr + 10 mg q4hr PRN x 4 doses	140	100
Inclusion criteria			

ED-Innovation Study

- 2,000 patients from 29 Emergency Rooms across the US
- Active opioid use, not in treatment
- Initiated 8mg sublingual buprenorphine or long-acting injectable buprenorphine when COWS > 4
- 0.8% incidence of precipitated withdrawal

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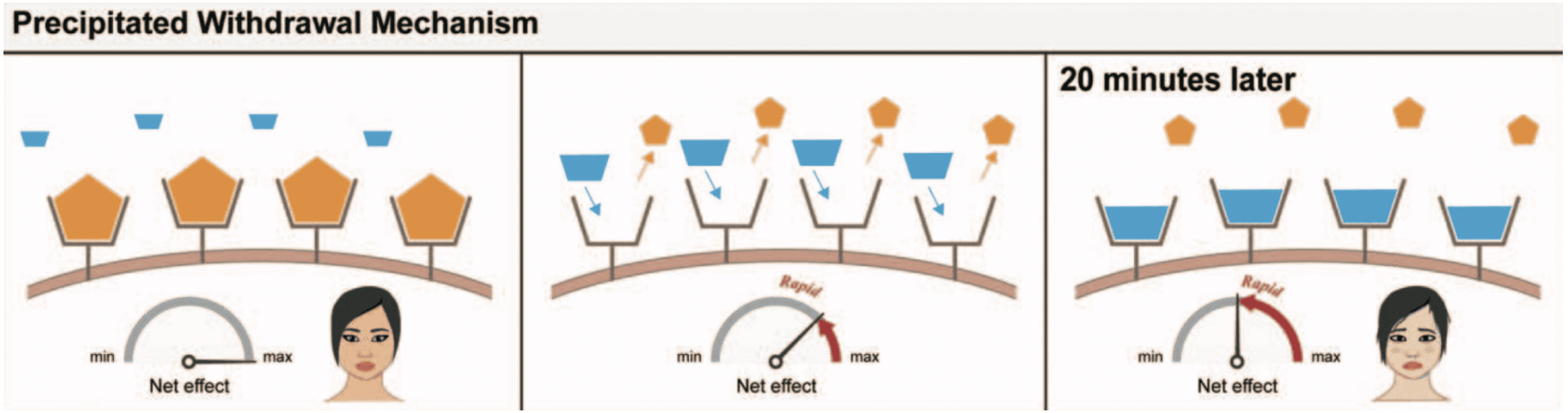
Precipitated withdrawal



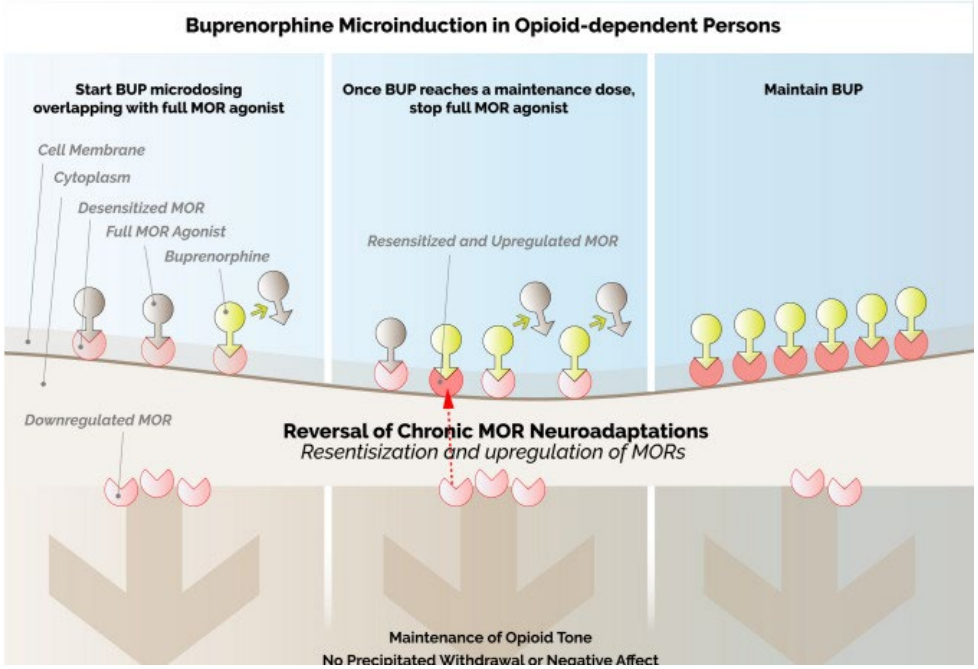
- Incidence 0.8 – 13.4%

Buprenorphine intitiation: Option #1

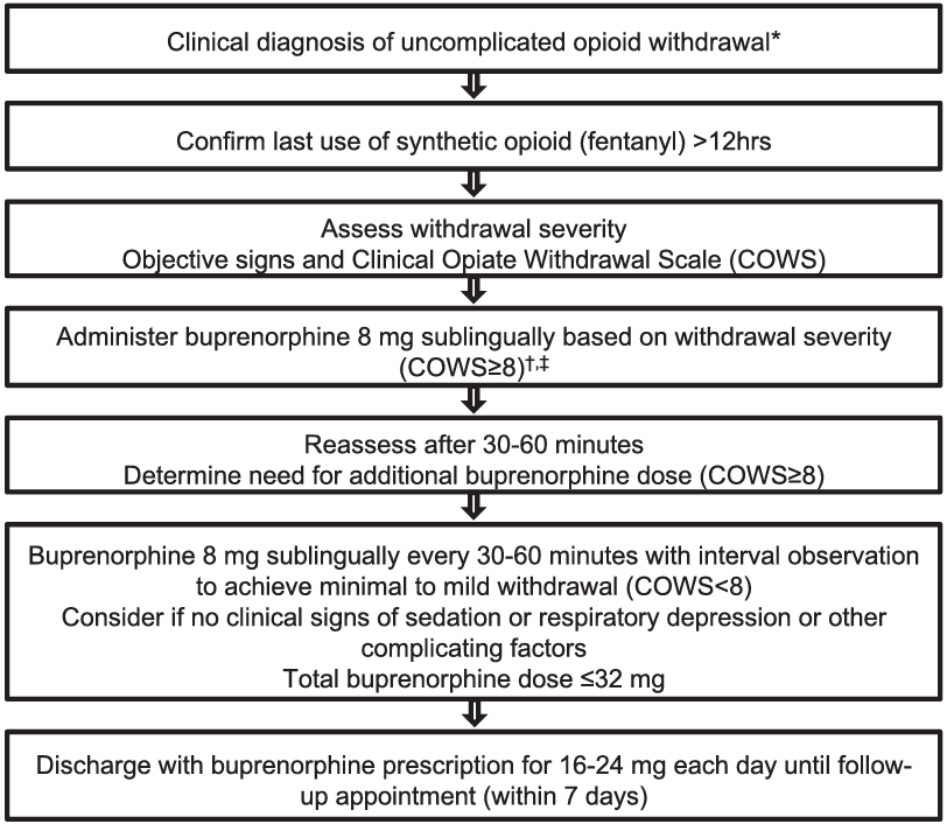
- Give test dose of 2mg buprenorphine
- If withdrawal dose not increase in 30 minutes, give additional 6mg
- If withdrawal worsens, give full opioid agonist (oxycodone, morphine)
- Repeat test dose in 4-6 hours

Buprenorphine initiation: Option #2

- Start with low doses of buprenorphine (< 1mg) q4-6 hours
- Give full acting opioids (oxycodone, morphine) simultaneously
- Increase buprenorphine
  - 1mg q6 hours x 4 doses
  - 2mg q6 hours x 4 doses
  - 8mg in a single dose
    - Discontinue full opioid agonist



Buprenorphine initiation: Option #3



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Initiation protocol comparisons

- Standard
  - –COWS > 8
  - –History of precipitated withdrawal or patient preference
- Low dose
  - –Fentanyl use
  - –COWS < 8 or no subjective symptoms of withdrawal
  - –History of precipitated withdrawal or patient preference
- High dose
  - –COWS > 8

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Adjunctive treatments for opioid withdrawal symptoms

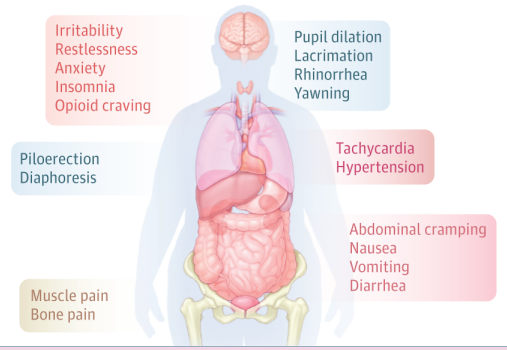
Symptoms	Medication	Usual effective dose range (adult)
Anxiety		
Anxiety, irritability, restlessness	Diphenhydramine*	50 to 100 mg orally every 4 to 6 hours as needed (maximum 300 mg daily)
	Hydroxyzine	25 to 100 mg orally every 6 to 8 hours as needed (maximum 400 mg daily)
	Clonazepam¶	0.5 to 1.5 mg orally every 6 to 8 hours as needed (maximum 6 mg daily)
	Lorazepam¶	1 mg orally every 4 to 6 hours as needed (maximum 6 mg daily)
	Oxazepam¶	15 to 30 mg orally every 6 to 8 hours as needed (maximum 120 mg daily)
Gastrointestinal		
Abdominal cramping	Dicyclomine*	10 to 20 mg orally every 6 to 8 hours as needed (maximum 160 mg daily)
Diarrhea	Bismuth*	~524 mg orally every 30 to 60 minutes as needed (up to 4200 mg daily)
	Loperamide	4 mg orally followed by 2 mg after each loose stool (maximum 16 mg daily)
Nausea/vomiting	Ondansetron*Δ	4 to 8 mg orally or IV every 12 hours as needed (maximum 16 mg/day)
	Prochlorperazine	5 to 10 mg orally three times daily before meals or every six hours as needed (maximum 40 mg/day)
	Promethazine	12.5 to 25 mg orally every 4 to 6 hours as needed (maximum 50 mg/day)
Insomnia, pain, muscle spasm, and restless legs		
Insomnia	Trazodone*	25 to 100 mg orally at bedtime
	Doxepin	6 to 50 mg orally at bedtime
	Mirtazapine	7.5 to 15 mg orally at bedtime
	Quetiapine	50 to 100 mg orally at bedtime
	Zolpidem¶	5 to 10 mg orally at bedtime
Muscle aches◇, joint pain, headache	Ibuprofen*§	400 mg orally every 4 to 6 hours as needed (maximum 2400 mg daily)
	Acetaminophen	650 to 1000 mg orally every 4 to 6 hours as needed (maximum 4000 mg daily)
	Ketorolac§	15 to 30 mg IV or IM every 6 hours as needed (maximum 120 mg daily)
	Naproxen§	500 mg orally twice daily with meals
Muscle spasm◇, restless legs	Cyclobenzaprine*	5 to 10 mg orally every 8 hours as needed (maximum 30 mg daily)
	Baclofen	5 to 10 mg orally every 8 hours as needed (maximum 60 mg daily)
	Diazepam¶	5 to 10 mg orally every 6 to 12 hours as needed (maximum 40 mg daily)
	Methocarbamol	750 to 1500 mg orally every 8 hours as needed (maximum 6 g daily)

JAMA Network™

From: **Caring for Hospitalized Adults With Opioid Use Disorder in the Era of Fentanyl: A Review**

JAMA Intern Med. 2024;184(6):691-701. doi:10.1001/jamainternmed.2023.7282

Opioid withdrawal characteristics



History:
- Encourage patients to report withdrawal, recognizing that many may fear disclosure given past negative experiences

Typical onset:
- 8-12 h After last use of most short-acting opioids (eg, heroin or oxycodone)
- 24-72 h After last use of long-acting opioids (eg, methadone)
- 8-24 h (Variable onset) after last use of fentanyl

Standardized assessments:
- Formal withdrawal assessments like the Clinical Opiate Withdrawal Scale (COWS) can guide clinicians when initiating or intensifying opioid withdrawal treatment, but are not required to treat opioid withdrawal. (COWS is an 11-point bedside assessment that incorporates objective and subjective signs).

Withdrawal severity: Objective signs such as sweating, pupil dilation, vomiting, diarrhea, irritability, shifting in bed, frequent yawning, and piloerection suggest severe withdrawal. Symptoms may be subjective or less severe in milder withdrawal.

Withdrawal management

Opioid withdrawal

Oral methadone: Historical protocols start with 20-30 mg, followed by 10 mg 4-6 h later for ongoing symptoms. Fentanyl withdrawal may require 40-60 mg/d initially.

or

Sublingual buprenorphine: once COWS ≥8, 2-4 mg followed by 4 mg every 1-2 h for ongoing symptoms (typically up to 16-24 mg/d). Fentanyl withdrawal may require up to 32 mg/d.

Adjunctive medications targeted to symptoms: eg, clonidine, loperamide, NSAIDs, or ondansetron

Supplemental short-acting opioids: for ongoing opioid withdrawal after initial doses of methadone or as a bridge to buprenorphine; eg, start oxycodone 15-20 mg every 4 h as necessary for withdrawal or pain; titrate to response.

Periodically assess for ongoing withdrawal and oversedation

Consider early consultation with an addiction medicine specialist

Co-occurring withdrawal syndromes

Alcohol and benzodiazepine withdrawal

Characteristics: autonomic hyperactivity (eg, tremors, diaphoresis, nausea, anxiety, and tachycardia), seizures, delirium, and hallucinations

Onset: 2-3 h after last alcohol intake, or 24-72 h after last benzodiazepine use

Concurrent opioid withdrawal:
- Symptoms overlap
- Monitor closely for oversedation if coadministering opioids and benzodiazepines
- Early opioid management ensures that benzodiazepines are for alcohol or benzodiazepine withdrawal

Psychostimulant withdrawal

Characteristics: depressed mood, fatigue, increased appetite, psychomotor retardation, hypersomnia, and unpleasant dreams

Onset: 12-72 h after last psychostimulant use

Concurrent opioid withdrawal: psychostimulant withdrawal may be conflated for oversedation used to treat opioid withdrawal

Xylazine withdrawal

Characteristics: poorly characterized, but may involve anxiety, restlessness, and irritability, possibly with hypertenstion and/or tachycardia

Concurrent opioid withdrawal: until further evidence develops, maintain a broad differential and prioritize treatment of opioid withdrawal

Precipitated withdrawl: In perspective

- Initial reports of higher rate of preterm labor and IUFD in withdrawal based on low quality evidence
- Chronic withdrawal cycles increase stress and should be avoided
- Potential precipitated withdrawal is a time-limited process
- Both low dose and high dose buprenorphine initiation protocols in pregnancy have been reported to be successful
- Avoiding precipitated withdrawal should be viewed as a goal in order to increase likelihood of successful initiation

Sources: McCarthy & Terplan, AJOG 2016; Berry et al, Obstet Gynecol 2024, Campbell et al, Am J Obstet Gynecol 2016

Precipitated withdrawal: In perspective

- Rare occurrence
- Self-limited and treatable
- Should not be used as a reason to avoid or delay treatment
- UNTREATED OUD IS THE WORST OUTCOME

IMPERFECT ACTION IS BETTER THAN PERFECT INACTION

When in doubt….

- Short acting opioids are always a reasonable choice
- Titrate to patient comfort

Reframing treatment of OUD

You are NOT

… a "legal drug dealer"

… contributing to their addiction

You ARE

… a medical provider treating your patient

… treating a chronic medical condition

… engaging in harm reduction

… treating them with dignity and respect

Reframing treatment of OUD

Our patients are NOT	Our patient ARE
… drug seeking	… smart and resourceful
… looking for a legal high	… seeking help
… trying to trick you	… worthy of our respect

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Pain management

- Multi-modal
- Non-opioid analgesia
- CONTINUE THEIR MOUD

DISCHARGE CONSIDERATIONS

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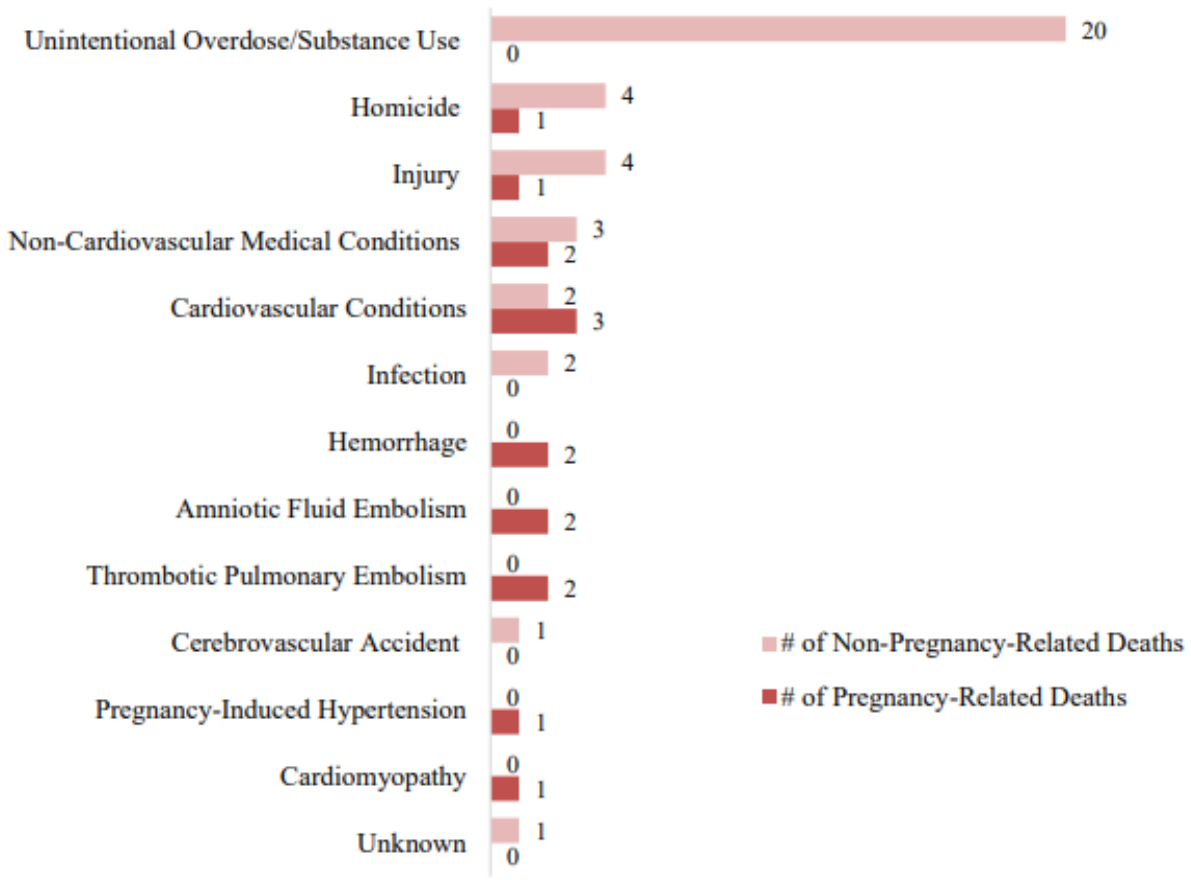
Figure 4. Number of Pregnancy-Related* and Non-Pregnancy-Related Deaths by Category of Cause of Death, Maryland, 2017 (Total Deaths = 52)**



* Deaths of women while pregnant or within 365 days of pregnancy from a cause related to or aggravated by pregnancy or its management.
** Deaths of women while pregnant or within 365 days of pregnancy from any cause not related to or aggravated by pregnancy or its management.
Data Source: MDH, VSA, and Maryland Maternal Mortality Review Program.

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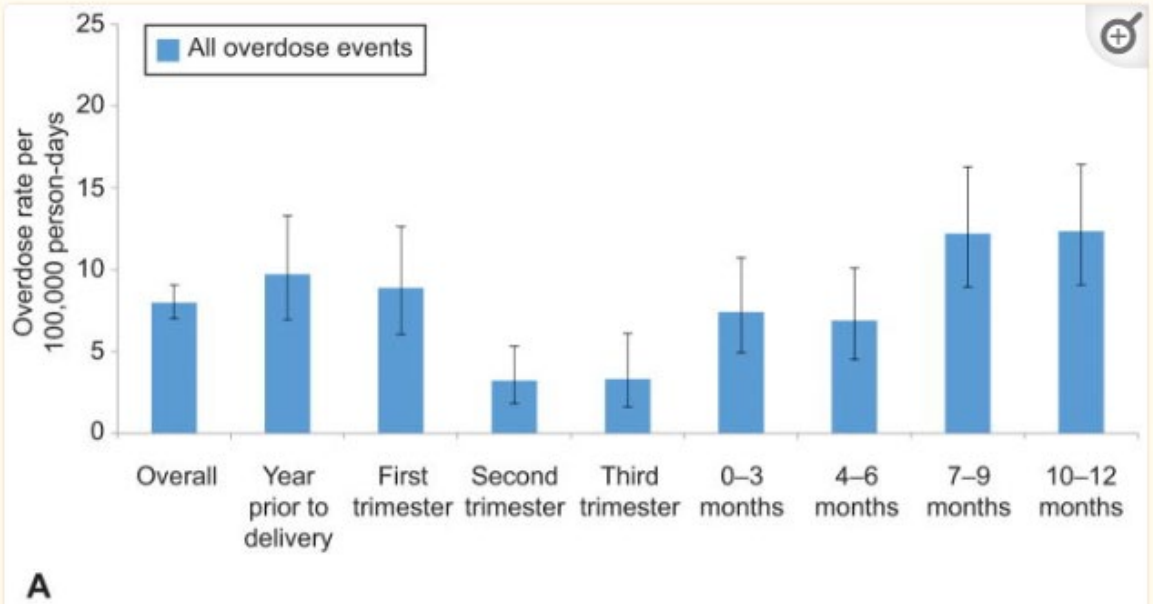
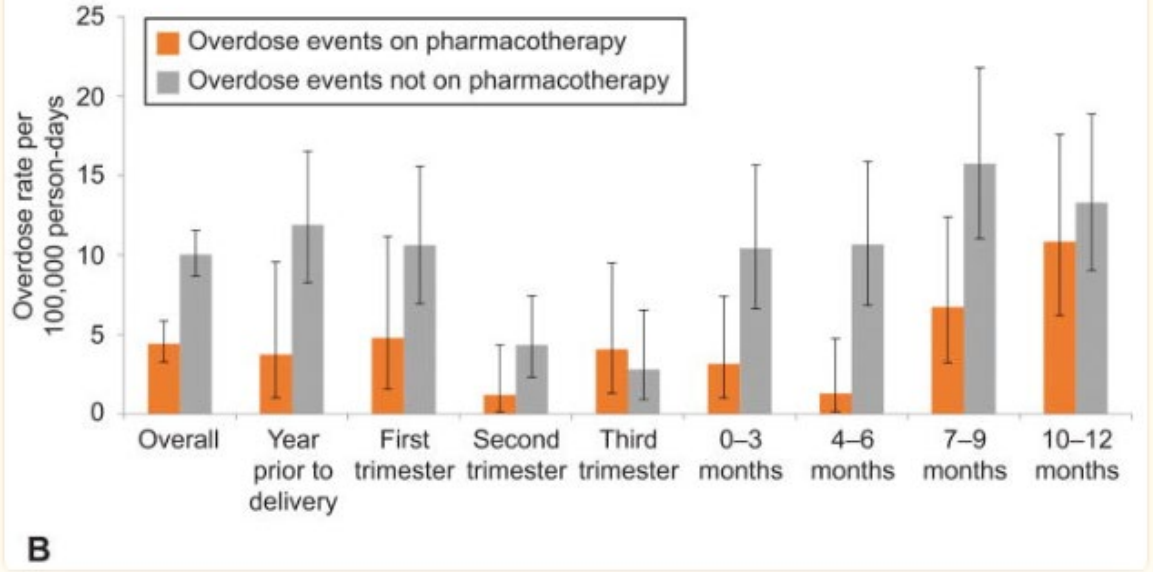
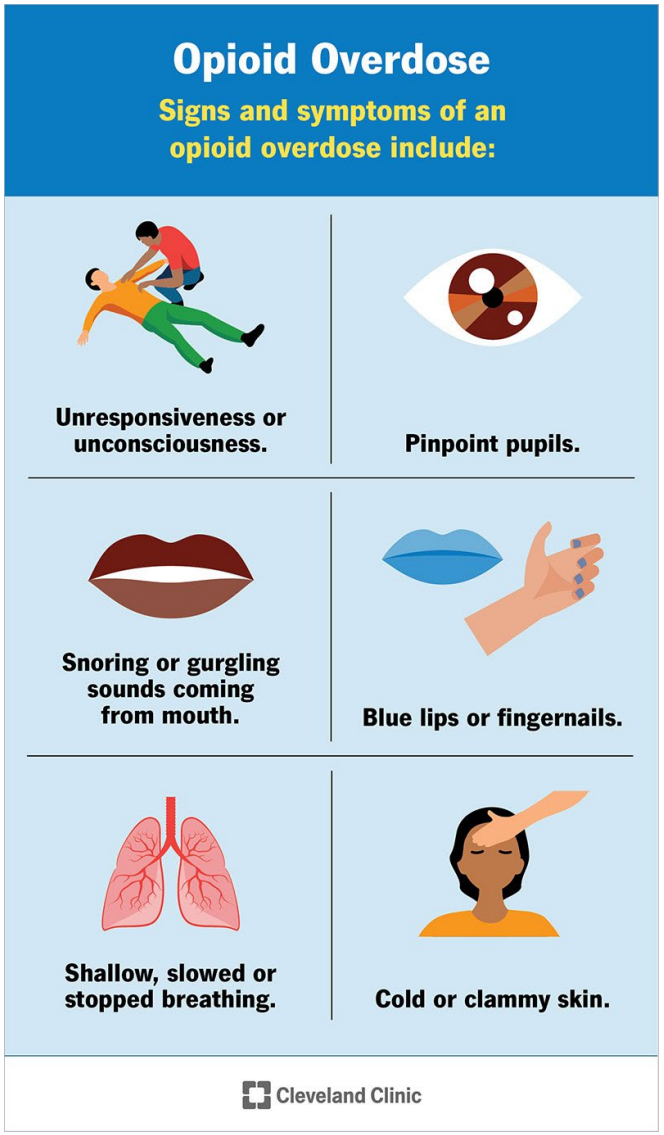




Schiff, Obstet Gynecol 2019

Opioid overdose

- Definition: Opioid use with
  - Pinpoint pupils
  - Unconsciousness
  - Difficulty breathing
- Not all overdoses are fatal



Naloxone

- Opioid overdose causes respiratory depression that can lead to death
- Naloxone is a full opioid antagonist/receptor blocker
- Naloxone education and distribution decreases overdose deaths in communities

Nida.gov

Naloxone distribution options

- Write a prescription - insurances cover it
- Naloxone standing order – all pharmacies should be able to dispense

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Substance Abuse and Mental Health Services Administration

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Search For Treatment

Confidential and anonymous resource for locating treatment facilities for mental and substance use disorders in the United States and its territories.

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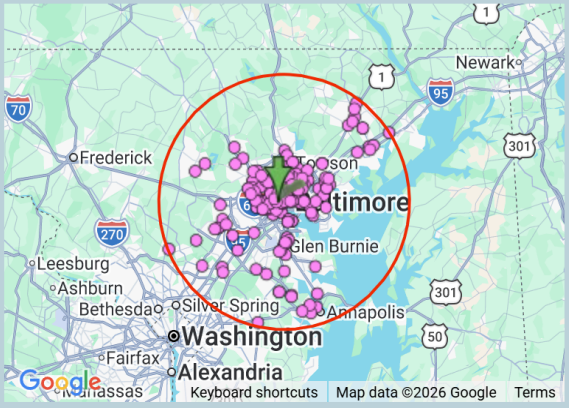

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Maryland Addiction Consultation Service *for MOMs*

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MACS for MOMs

Sign up for services

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Submit a request

Through our secure survey system, REDCap

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Reach out via email to
MACS@som.umaryland.edu