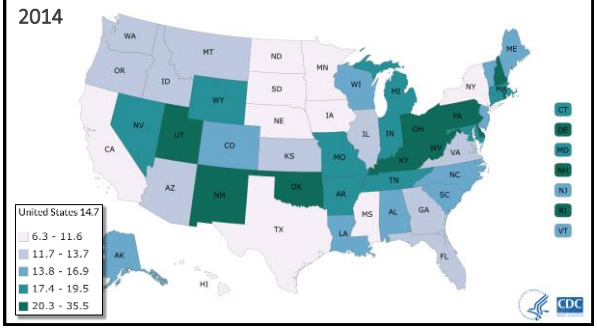
MAT: The Leader in Assists

Opioid Abuse Treatment Options

Layne Subera, DO, MA, FACOFP

2014



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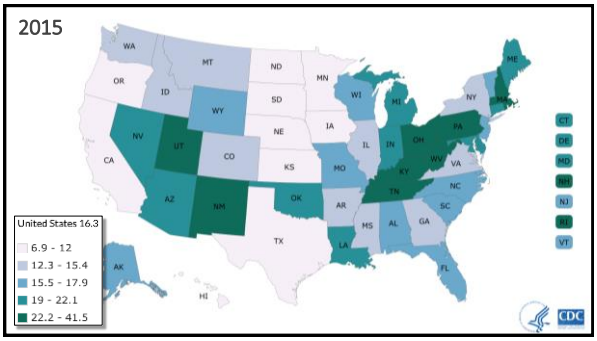

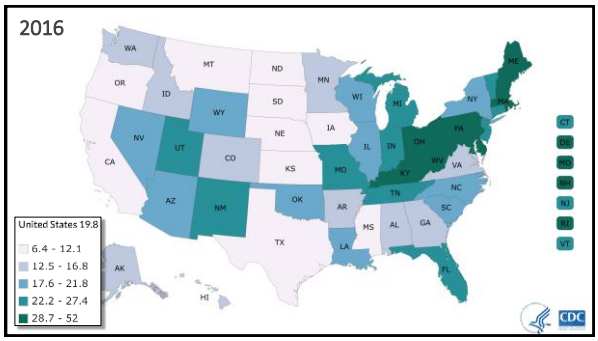
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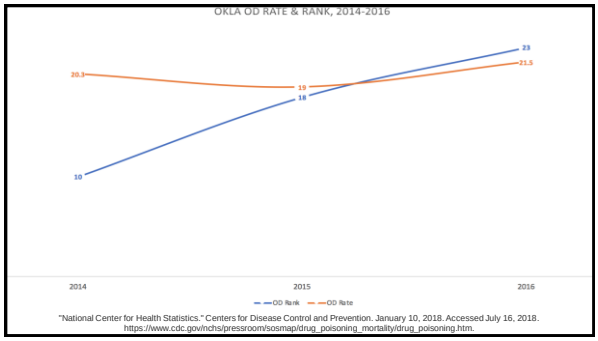
OKLA OD RATE & RANK, 2014-2016
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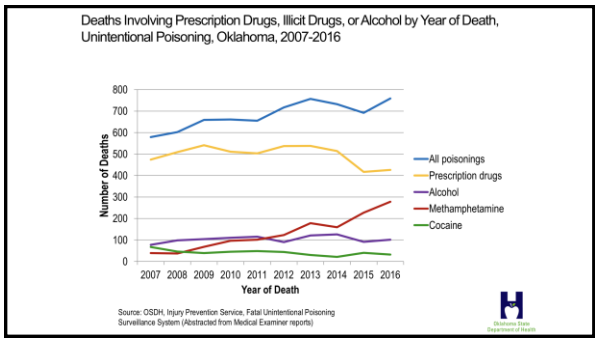
"National Center for Health Statistics." Centers for Disease Control and Prevention. January 10, 2018. Accessed July 16, 2018.
https://www.cdc.gov/nchs/pressroom/sosmap/drug_poisoning_mortality/drug_poisoning.htm.


Deaths Involving Prescription Drugs, Illicit Drugs, or Alcohol by Year of Death,
Unintentional Poisoning, Oklahoma, 2007-2016
Number of Deaths
800
700
600
500
400
300
200
100
0
2007 2008 2009 2010 2011 2012 2013 2014 2015 2016
Year of Death
All poisonings
Prescription drugs
Alcohol
Methamphetamine
Cocaine
Source: OSDH, Injury Prevention Service, Fatal Unintentional Poisoning
Surveillance System (Abstracted from Medical Examiner reports)

Background Statisitics

- ~2.5 million people in the United States have opioid addiction
- Less than 50% have access to Medication-Assisted Treatment (MAT)
- 2.2% of US physicians have obtained waivers (2014)
- The average state has 8 waivered physicians per 100,000 residents.
- 53.4% of US counties do not have a single prescriber of MAT
- Average number of patients for certified prescribers is 26.
- 25% of physicians with a waiver never prescribe.

Dunlap, Beth, and Adam S. Cifu. "Clinical Management of Opioid Use Disorder." *Jama* 316, no. 3 (2016): 338. doi:10.1001/jama.2016.9795.

Lecture Overview

- What is Medication Assisted Treatment?
- Recognizing Problems
  - Opioid Use Disorder
  - Dependence
- Starting Medication Assisted Treatment
- Counseling & Support Options
- Special Populations
- Emerging Treatment Options

What is Medication-assisted Treatment?

MAT Defined

- Medication-assisted treatment (MAT) is the use of medications with counseling and behavioral therapies to treat substance use disorders and prevent opioid overdose.

"Medication and Counseling Treatment." SAMHSA - Substance Abuse and Mental Health Services Administration. September 28, 2015. Accessed July 21, 2018. https://www.samhsa.gov/medication-assisted-treatment/treatment.

Drug Addiction Treatment Act of 2000

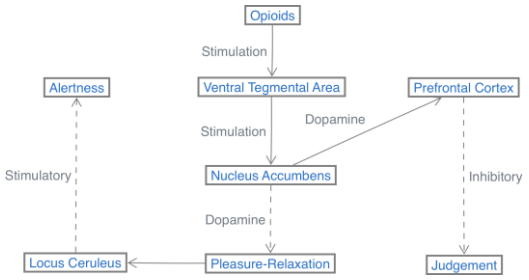
- Permits physicians who meet certain qualifications to treat opioid addiction with Schedule III, IV, and V narcotic medications that have been ***specifically approved by the Food and Drug Administration for that indication.***
- "Waiver"
  - 30, 100, 275 (CARA Act of 2016)

DEA. "Notices - 2006." - Dispensing Controlled Substances for the Treatment of Pain. September 6, 2006. Accessed June 09, 2016. http://www.deadiversion.usdoj.gov/fed_regs/notices/2006/fr09062.htm

MAT vs Tapering & Withdrawal

- Majority of patients relapse with withdrawal management alone
  - Including with tapering
  - Including residential detoxification
    - One 2010 prospective cohort study of 109 patients
    - 91% of patients relapsed
    - 59% relapsing in the first week

Smyth BP. Barry J, Keenan E. Ducray K. Lapse and relapse following inpatient treatment of opiate dependence. IrMedJ. 2010;103(6):176-179.



Attenuation and Addiction

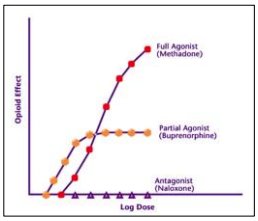
- With continued opioid use, the dopaminergic effect decreases and increased consumption is needed to maintain a "normal" state.
- Recreational users are motivated by positive reinforcement.
  - Excess dopamine activity.
- Addicted users are motivated by negative reinforcement.
  - Deficient dopamine activity.

How Buprenorphine Works

- Buprenorphine is an opioid partial mu-agonist.
  - Weaker than full agonists.
    - Morphine, methadone, heroin, etc.
  - Higher binding affinity than many opioids.
- Opioid effects level off.
  - Euphoria and respiratory depression.
  - "Ceiling effect"
    - Lowers the risk of misuse and side effects.

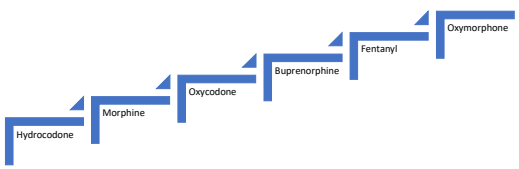
https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine

Affinity, Intrinsic Activity, and Dissociation



"The National Alliance of Advocates for Buprenorphine Treatment." Buprenorphine Treatment- Find Doctors. Accessed June 09, 2016. http://www.naabt.org/.

Opioid Receptor Affinity



Treatment Challenges

- It is not a “cure”.
- It is treating opioid addiction with an opioid.
- Withdrawal occurs upon discontinuation.
- Coverage for the counseling component can be a challenge.
- Abuse and diversion can happen.

Side Effects of Buprenorphine/naloxone

- Headaches
- Depression
- Nausea, vomiting, and constipation
- Muscle aches and cramps
- Cravings
- Inability to sleep
- Distress and irritability
- Fever

Buprenorphine Misuse and Abuse

- Buprenorphine mono can be misused.
  - Nasal route, smoking.
- Buprenorphine/naloxone decreases misuse potential.
  - Via the sublingual route, buprenorphine's opioid effects dominate.
  - Via the nasal or IV route: naloxone's antagonist effect dominates.
    - Can precipitate opioid withdrawals.

https://www.samhsa.gov/medication-assisted-treatment/treatment/buprenorphine

Buprenorphine vs. Methadone Abuse

- Nonmedical use of buprenorphine is associated with better outcomes versus methadone.
  - Hospitalization rates (32.2% vs. 67.4%),
  - Admission to intensive care units (15% vs. 50%)
  - Mortality (0% vs. 1.6%)
    - Changing substance abuse patterns may confound
      - Risk correlated with routes of use

Lee S, Klein-Schwartz W, Welsh C, et al. Medical outcomes associated with nonmedical use of methadone and buprenorphine. J Emerg Med. 2013;45:199–205.

Buprenorphine Diversion

- When diverted, buprenorphine/naloxone is likely used to manage withdrawal symptoms.
- The lack of access to MAT has been associated with use of diverted buprenorphine/naloxone and that expansion of access may limit diversion.

Lofwall MR. Havens JR. Inability to access buprenorphine treatment as a risk factor for using diverted buprenorphine. Drug Alcohol Depend. 2012;126(3):379-383.

Preventing Buprenorphine Diversion

- The 3 most common strategies used by buprenorphine prescribers[1]:
  - Limit 30-day prescriptions to compliant patients (72.4%)
  - Prescribe only the lowest effective daily dose (60.6%)
  - Require regular urine screening or other drug screening (59.3%)

[1]Yang A, Arfken CL, Johanson CE. Steps physicians report taking to reduce diversion of buprenorphine. Am J Addict. 2013;22:184–187.

Recognizing Problems

Confronting Biases and Logical Fallacies

- Continuation Bias
- Sunk Cost Fallacy
- Social Bias
- Uncertainty

Features of Opioid Withdrawal Syndrome

- Elevated pulse.
- Sweating.
- Restlessness.
- Tremors.
- Mydriasis.
- GI Upset.
- Anxiety or Irritability.
- Bone or Joint Aches.
- Yawning.
- Runny nose or Tearing.
- Goose Flesh.

Prescription Opioid Misuse

- Prescription misuse is usually the first sign of pathology.
- 40% incidence when non-cancer pain is treated with opioids.

Ives T.J., Chelminski P.R., Hammett-Stabler C.A., et al: **Predictors of opioid misuse in patients with chronic pain: a prospective cohort study.** BMC Health Serv Res 2006; 6: pp. 46

Risk Factors for Predicting Prescription Misuse

- Current misuse predicts future misuse.
- Past or current history of an addiction disorder to any substance.
- Negative affective disorders.
  - Major Depression, Anxiety, Personality Disorders.
- Previous or current history of sexual or physical abuse.
- Family history of substance use disorders.
- History of illegal activities.

Aberrant Drug Related Behaviors

- **Aberrant Behavior** is a patient behavior that breaches of mutually established medical boundaries.
- Categories:
  - Loss of control over use.
  - Compulsive use.
  - Continued use despite harm.

Portenoy, Russell K, **Opioid therapy for chronic nonmalignant pain: a review of the critical issues.** Journal of Pain and Symptom Management , Volume 11 , Issue 4 , 203 – 217 doi: 10.1016/0885-3924(95)00187-5

Behaviors Suggestive of Substance Abuse

- Frequent intoxication leading to failure to fulfill major role obligations.
- Recurrent use in hazardous situations (e.g., drunk driving).
- Recurrent substance-related legal problems.
- Continued use despite interpersonal problems related to use.
- Persistent desire to cut down.

- "Does it interfere with love, work or play?"

Harrington, Michelle. "Substance Use Disorders." Accessed August 17, 2016. http://www.samhsa.gov/disorders/substance-use.

ADRBs More Predictive of Addiction

- Prescription forgery.
- Stealing or "borrowing" drugs from others.
- Injecting oral formulations.
- Obtaining prescription drugs from nonmedical sources.
- **Concurrent abuse of alcohol or illicit drugs.**
- **Multiple dose escalations or other noncompliance despite warnings.**
- **Multiple episodes of prescription "loss".**
- Repeatedly seeking prescriptions from other clinicians or from emergency departments (EDs) without informing the prescriber or after a warning to desist.
- **Evidence of deterioration in the ability to function at work, in the family, or socially that appears to be related to use of the drug.**
- Repeated resistance to changes in therapy despite clear evidence of adverse physical or psychological effects from the drug.
- Selling prescription drugs.

Portenoy, Russell K, **Opioid therapy for chronic nonmalignant pain: a review of the critical issues.** Journal of Pain and Symptom Management , Volume 11 , Issue 4 , 203 – 217 doi: 10.1016/0885-3924(95)00187-5

Screening/Risk Tools for Substance Abuse

- Opioid Risk Tool (ORT): Categorizes patient risk for aberrancy.
  - Low (score of 3 or lower)
  - Moderate (score of 4 to 7)
  - High (score of 8 or higher)
- Current Opioid Misuse Measure (COMM): Can identify aberrant drug-related behavior in patients who are <u>currently</u> taking opioids.

Social History:	ORT	Note space: [illegible]47.8 PM
Do you have a Family History of Alcohol abuse?	Yes No	1 3
Do you have a Family History of Street drug abuse?	Yes No	2 3
Do you have a Family History of Prescription drug abuse?	Yes No	4 4
Do you have a Personal History of Alcohol abuse?	Yes No	3 3
Do you have a Personal History of Street drug abuse?	Yes No	4 4
Do you have a Personal History of Prescription drug abuse?	Yes No	5 5
Is your age between 16 and 45 years old?	Yes No	1 1
Do you have a Personal History of Preadolescent Sexual Abuse?	Yes No	3 0
Do you have a History of ADD, OCD, Bipolar or Schizophrenia?	Yes No	2 2
Do you have a Personal History of Depression?	Yes No	1 1

Review of Body Systems: Circle your symptoms. Write in any others. Circle "OK" if no symptoms present.	
Constitution	OK Fever Chills Fatigue Weight loss Weight gain of : pounds in: weeks.
Ears/Throat	OK Sore throat Ear pain Congestion Drainage Sinus pain Hearing Loss
Heart	OK Chest pain Chest pressure Forceful beats Irregular beat High blood pressure
Lungs	OK Cough Cough up blood Cough up mucus Short of Breath Wheezing Asthma
Digestive	OK Heartburn Nausea Vomiting Diarrhea Constipation Blood in stool Dark stools
Genital-Urinary	OK Burning Frequency Blood in urine Nocturnal urination Pregnancy Erectile problem
Blood & Glands	OK Anemia Easy bruising Easy bleeding Lymph node enlargement
Eyes	OK Double vision Mattering Itchiness Blurring Loss of vision
Hormones	OK Excess thirst Excess urination Cold or heat intolerance Menstrual problems
Bones & Muscle	OK Joint pain Joint stiffness Joint swelling Muscle aches Gout Back pain Ankle swelling
Nerves	OK Headache Dizziness Numbness Weakness Fainting Seizures Tremors
Allergies	OK Medicine allergy Dye allergy Seasonal allergy Food allergy Latex allergy
Skin	OK Rashes Lumps Dryness Change in moles Change in pigment or color
Emotions	OK Depression Poor sleep Anxiety Stress Memory disturbance Suicidal thinking

Opioid Use Disorder (DSM-V) Slide 1

A maladaptive pattern of use leading to significant impairment or distress, as manifested by at least two of the following occurring within a 12-month period:

- The opioid is often taken in larger amounts or over a longer period than intended.
- There is a persistent desire or unsuccessful efforts to cut down or control use.
- A great deal of time is spent on activities necessary to obtain, use, or recover from the effects of the opioid.
- Recurrent use results in failure to fulfill major role obligations.
- Use is continued despite persistent or recurrent social or interpersonal problems caused or exacerbated by the substance.

Opioid Use Disorder (DSM-V) Slide 2

- Important social, occupational, or recreational activities are reduced because of use.
- Use occurs in situations in which it is physically hazardous.
- Use is continued despite knowledge of a persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by the opioid.
- Tolerance is present (not counted for those taking medications under medical supervision).
- Withdrawal occurs (not counted for those taking medications under medical supervision).
- There is craving or a strong desire or urge to use the opioid.

ICD-10d: 3 Pathologic Syndromes

- Opioid intoxication
  - Evidence of psychoactive substance at sufficient dose levels, signs and symptoms of intoxication, and cannot be accounted for by a medical disorder unrelated to substance use disorder.
  - There must be dysfunctional behavior and one 1 sign of intoxication.
- Opioid dependence syndrome
  - Three or more of the following manifestations should have occurred together for at least 1 month, or if persists <1 month, should have occurred together repeatedly within a 12-month period:
  - A strong desire or sense of compulsion to take opioids
  - Impaired capacity to control substance-taking behavior in terms of its onset, termination, or levels of use
  - A physiologic withdrawal state when use is reduced or ceased, or use of same substance with intention of relieving or avoiding withdrawal symptoms
  - Tolerance: marked increase in amount with marked decrease in effect
  - Preoccupation with opioid use: more time spent to obtain, take, or recover from effects of substance
  - Persistent opioid use despite clear evidence of harmful consequences.
- Opioid withdrawal state
  - There must be clear evidence of recent cessation or reduction of opioid use after repeated, and usually prolonged and/or high-dose, use of that substance.
  - Symptoms and signs compatible with known features of withdrawal state. Any 3 of the following signs must be present for opioid withdrawal state: craving for opioid drug, rhinorrhea or sneezing, lacrimation, muscle aches or cramps, abdominal cramps, nausea or vomiting, diarrhea, pupillary dilatation, piloerection, recurrent chills, tachycardia, hypertension, yawning, or restless sleep.
- Symptoms and signs cannot be accounted for by a medical disorder unrelated to opioid use disorder.

World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. 1992. http://www.who.int/ (last accessed 13 September 2017).

Opioid Use Disorder (DSM-V) Severity

- Mild: Presence of 2–3 symptoms. F11.10
- Moderate: Presence of 4–5 symptoms. F11.20
- Severe: Presence of 6 or more symptoms. F11.20

Patterns Suggestive of Addiction (4 C's)

- Preoccupation with use because of **C**raving
- Impaired **C**ontrol
- **C**ompulsive use
- Continued use in spite of adverse **C**onsequences

Key Points for Detecting Opioid Use Disorder

- Physical dependence occurs when opioid use is prolonged.
- Opioid misuse is usually the first sign of pathology.
- Failing social obligations suggest addiction.
- Craving is the hallmark of addiction.
- Use motivated by negative reinforcement indicates addiction.
- People with substance use problems need good care, too.

Medication-assisted Treatment

Treatment Phases

- Selection Phase
- Induction Phase
- Stabilization Phase
- Maintenance Phase
- Discontinuation Phase

The Selection Phase

- The ideal candidate…
  - Objectively diagnosed with an opioid dependency.
  - Do not have contraindications for using buprenorphine.
  - Are willing to follow safety precautions.
  - Valid informed consent process.
    - Capacity.
    - Reviewed other treatment options.
    - Participation.
- Develop expectations:
  - Ex: Stabilize x 4-6 months then wean x 4-6 months.

Buprenorphine Precautions

- Avoid Polypharmacy.
- Avoid co-sedation.
  - Alcohol, sedatives, tranquilizers.
  - Respiratory depression.
- Consider liver-related disease and hepatotoxicity.

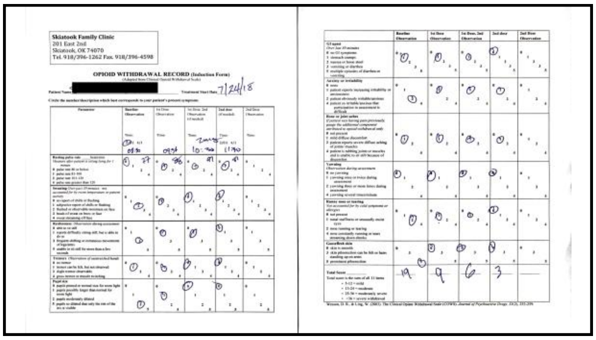
The Induction Phase

- Monitored initiation of buprenorphine treatment.
- Approved buprenorphine products only.
- Moderate withdrawal.
  - Short acting opioids: 12 to 24 hours.
  - Long-acting opioids: 48 to 72 hours.
- Look for physical signs to avoid precipitating an acute withdrawal episode.

Induction Verifies Medical Necessity

- 50% of doctors routinely induct patients while in opioid withdrawal.
- 50% start while displaying no symptoms of active opioid withdrawal.

Lofwall MR, Wunsch MJ, Nuzzo PA, et al. Efficacy of continuing medical education to reduce the risk of buprenorphine diversion. J Subst Abuse Treat. 2011;41: 321–329.


Skiatook Family Clinic
201 East 2nd
Skiatook, OK 74070
Tel. 918/396-1262 Fax. 918/396-4598

OPIOID WITHDRAWAL RECORD (Induction Form)

Patient Name [redacted] Treatment Start Date 7/24/18

The Stabilization Phase

- Duration: First 3 months.
- After successful induction.
- Dose titration to suppress craving.
- Monitor for adverse events and side effects.
- Start develop social support and skills.
- "Have you been offered drugs since our last visit? What happened?"

Counseling & Support Options

- Family buy-in
- Self-efficiency is the goal.
  - "Low levels of self-efficacy (confidence that one can self-manage symptoms) are linked to higher symptom burdens and increased substance use."[1]
- Referrals to agencies and programs
- Psychologists
- LADCs
- NA/AA

[1]Addict Behav. 2018 Feb;77:225-231. doi: 10.1016/j.addbeh.2017.10.012. Epub 2017 Oct 18.

Narcotics Anonymous

- Free
- Common
- 12-step
- Builds social connections
- Drug-free approach
  - Does not endorse medication-assisted treatment

The Maintenance Phase

- Duration: Different to each patient and could be indefinite.
- Patient is stable on a steady dose of buprenorphine.
- Continue building skills and repairing relationships.
- "Tell me something good that's happened since the last visit?"
- "What should our plan be for the next six months?"

The Discontinuation Phase

- The FDA approved treatment duration is open ended.
- When to wean:
  - When patient is ready.
    - When social circumstances have stabilized.
    - When bad actors are no longer present.
- Slow, supportive titration.
- Plateaus can happen.

Special Populations

Special Populations

- Dual-diagnosis patients.
- Cardiac patients.
- Pregnant women.
- Methadone patients.
- Prisoners

U.S. Food and Drug Administration
Protecting and Promoting Your Health

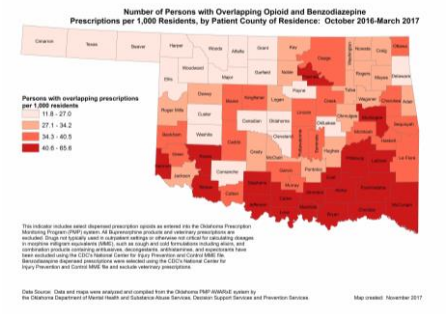
Drug Safety Communications

FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks

This provides updated information to the FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning issued on August 31, 2016.

Safety Announcement

[9-20-2017] Based on our additional review, the U.S. Food and Drug Administration (FDA) is advising that the opioid addiction medications buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of



Cardiovascular Patients

- Opioid withdrawal is associated with relative surge in sympathomimetic tone.
- Can precipitate heart failure in susceptible persons.

Kosten, Thomas, and Tony George. "The Neurobiology of Opioid Dependence: Implications for Treatment." *Science & Practice Perspectives SPP* 1, no. 1 (2002): 13-20. doi:10.1151/spp021113.

Pregnant or Breastfeeding Women

- Methadone preferred for pregnant women opioid dependency.
- Buprenorphine mono when buprenorphine is necessary.
- Pregnancy Category C.

Methadone Transfers

- Taper to ≤30 mg/day if possible (normal transfer).
  - Through their methadone provider.
  - Attempt 72 hours abstinence before induction.
- Transfers are possible between a >30-60 mg/day.
  - "High-dose transfer".
- Transfers from >60 mg/day are not recommended.

Dosing Guide For Optimal Management of Opioid Dependence. Accessed August 2, 2016. http://www.naabt.org/documents/Suboxone_Dosing_guide.pdf.

Prisoners and Detainees

- Jails are not required to continue medication-assisted treatment.
- Unsupervised, drug-free detoxification is dangerous.
- "Prisoners are 40 times more likely to overdose in the first two weeks after release than the average citizen."
- 11 times more likely to overdose within the first year.

Ranapurwala, Shabbar I., Meghan E. Shanahan, Apostolos A. Alexandridis, Scott K. Proescholdbell, Rebecca B. Naumann, Daniel Edwards, and Stephen W. Marshall. "Opioid Overdose Mortality Among Former North Carolina Inmates: 2000–2015." *American Journal of Public Health*, July 19, 2018, E1-E7. Accessed August 4, 2018. doi:10.2105/ajph.2018.304514.

Emerging Options

Depot Buprenorphine/Naloxone

- The first once-monthly injectable buprenorphine.
- Moderate-to-severe opioid use disorder (OUD) in adult patients who have initiated treatment with a transmucosal buprenorphine.
- Must be stable on SL dosing for a minimum of seven days.

Commissioner, Office Of the. "Press Announcements - FDA Approves First Once-monthly Buprenorphine Injection, a Medication-assisted Treatment Option for Opioid Use Disorder." U S Food and Drug Administration Home Page. November 30, 2017. Accessed July 21, 2018.

Lofexidine

- Mitigation of withdrawal symptoms to facilitate abrupt discontinuation of opioids in adults.
- May not completely prevent withdrawal symptoms
- Approved for treatment for up to 14 days.
- Lofexidine is not a treatment for opioid use disorder (OUD)
- Can be part of the treatment plan for managing OUD.

Commissioner, Office Of the. "Press Announcements - FDA Approves the First Non-opioid Treatment for Management of Opioid Withdrawal Symptoms in Adults." U S Food and Drug Administration Home Page. May 16, 2018. Accessed July 21, 2018.

"Make it a practice to judge persons and things in the most favorable light at all times and under all circumstances."

-St. Vincent de Paul