Opioid Treatment in Special Populations

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Objectives

- **Diagnose and discuss appropriate treatment of co-occurring substance use and other psychiatric disorders**
- Discuss strategies for treating acute, perioperative, and chronic pain for patients taking buprenorphine
- Describe appropriate treatment of opioid use disorder during pregnancy
- Discuss appropriate treatment of opioid use disorder in adolescents
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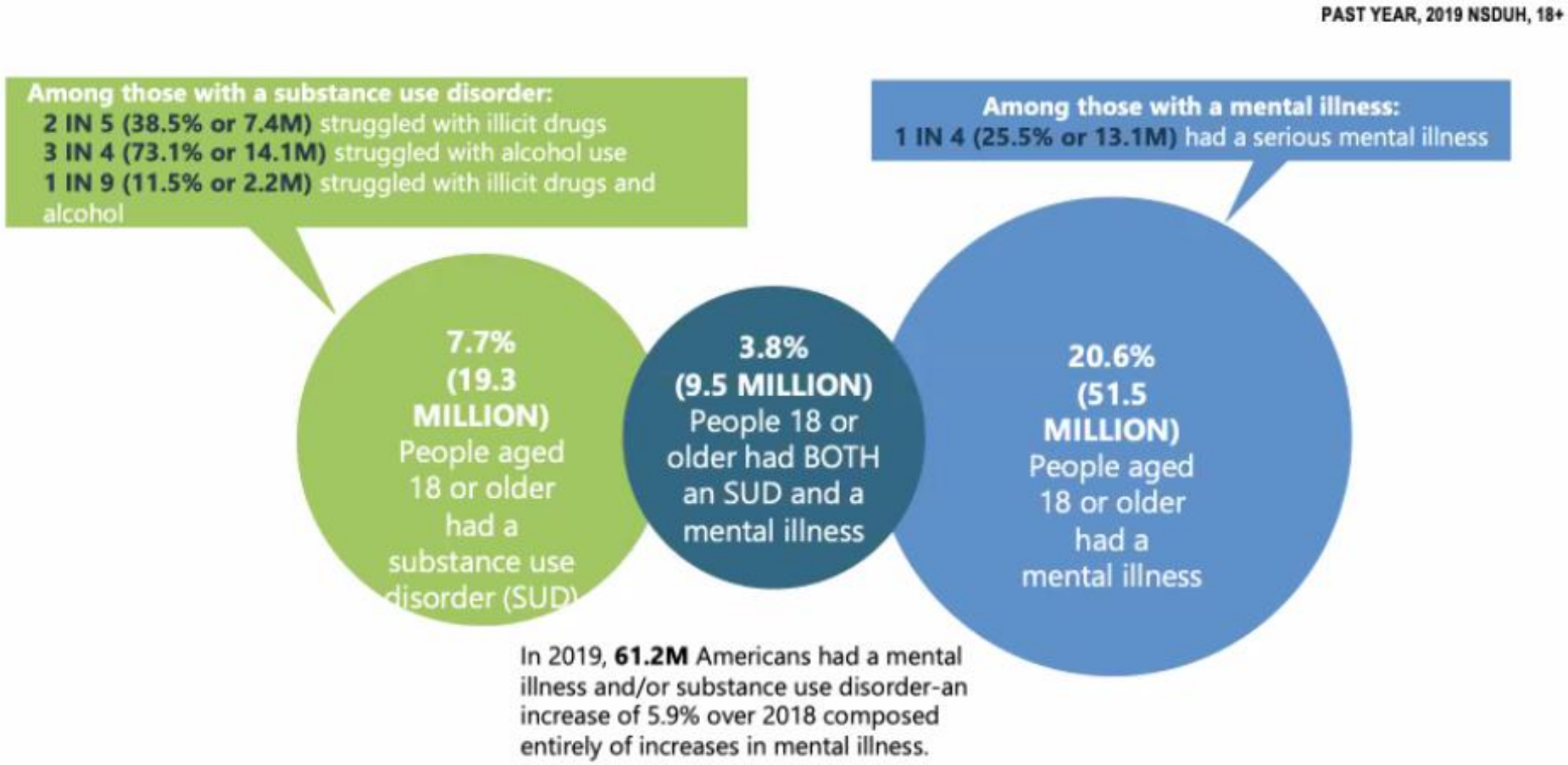
Mental Illness and Substance Use Disorders in the United States



Depressive and Anxiety Symptoms

- Mood instability and anxiety symptoms are common at treatment entry.
- Symptoms may resolve within few days of stable SUD treatment
- Symptoms that persist beyond acute intoxication and withdrawal can be worthwhile targets for treatment:
  - For example, with Selective Serotonin Reuptake Inhibitors
- Patients treated with MOUD respond to medications for depression and anxiety at rates similar to those without opioid use disorders

Trauma and Substance Use Disorder

- Trauma is highly associated with substance use disorders both before and after the onset.
  - Lifetime trauma is reported in up to 66% of treatment seeking patients.
- Post Traumatic Stress Disorder, PTSD, is known to precede the onset of SUDs
  - Prevalence of lifetime PTSD in patients with an SUD ranges from 26% to 52%
    - Women 27.9% - Men 51.9%
    - SUD seen 4.46 x more often in women **with** PTSD **than without**.
    - Men 3 times more often
- Comorbid illness is more difficult to treat than either individual disorder.
  - Treatment of the SUD often results in improvement of PTSD symptoms but not visa versa.
- Overtime the SUD will become a more difficult and persistent illness.
- Treatment should include both concurrently.
  - Combination of psychotherapeutic and pharmacologic management is most effective.

Wave 2 of the National Epidemiologic Survey on Alcohol and Related Condition 2010
Sartor et al., 2011
McCauley, et al, Clin Psychol (New York). 2012 Sep 1; 19(3):

Treatment of Co-Occurring Psychiatric Disorders

- With consent obtain attempt to gain collateral information from other providers, and family or friends.
- Repeatedly review the Prescription Drug Monitoring Program.
- As previously outlined: **Avoid use of benzodiazepines**
  - Risk of misuse (taken other than prescribed), is an indicator of polysubstance use and associated with more erratic behavior
  - Increase risk of respiratory depression and overdose.
  - The first-Line treatments for anxiety and depression are:
    - Selective serotonin reuptake inhibitors alone or with norepinephrine reuptake inhibitors
    - Psychotherapy (e.g.: cognitive behavioral therapy)
- Stimulants
  - If there is concern for Attention Deficit Hyperactivity Disorder (ADHD), consider Adult ADHD Self-Report Scale (ASRS) or refer patient for a psychiatric assessment
  - Continue stimulants if the diagnosis has been definitively established.

Chang et al., 2005
Kampman et al., 2015

Treatment of Co-Occurring Psychiatric Disorders

- Attempt to facilitate treatment in an integrated care setting.
- Treat the co-occurring illnesses as equally important to manage.
- Reduction in use and for many abstinence, however, will be important in establishing improvement of symptoms (neurobiologic stabilization) and will often also improve adherence to psychotherapeutic and medication treatment recommendations

Chang et al., 2005
Kampman et al., 2015

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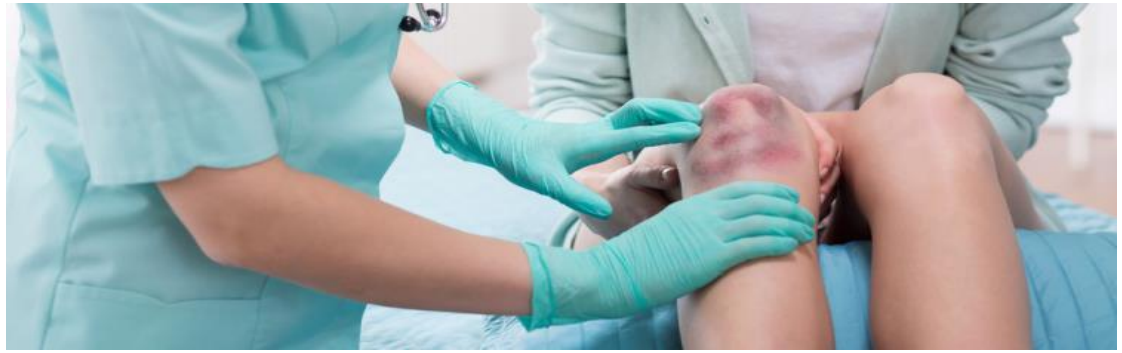
Acute Pain Management in Patients Receiving MOUD



- Different Approaches:
  - Initially non-opioid analgesics (ketorolac or NSAIDs)
  - Continue same buprenorphine dose but in a split regimen
    - Buprenorphine's analgesic duration is only a few hours
    - May add or continue non-opioid analgesics
  - Increase buprenorphine dose while continuing split dose
  - Add full opioid to buprenorphine regimen
    - Typically, only done in a controlled setting
  - Stop buprenorphine and initiate full agonist therapy dosed to effect. Then return to buprenorphine following stabilization.
    - (Note: this approach may destabilize the patient and lead to worsening outcomes)

Lembke A, et al, Pain Med. 2019
Buresh M, et al, J Gen Intern Med. 2020

Perioperative Management

- Problem to overcome:
  - Patients fear mistreatment
  - Providers fear deception
  - Lack of consensus in the field – often based on preference of surgical/anesthesia teams
- Pre-Op:
  - Confirm Multi-Party Consent
  - Coordination of care with providers
  - If patient is already on Partial Agonist:
    - There should be strong consideration for continuing buprenorphine on consultation with surgeon.
      - Continue and use full agonists as needed during and after procedure.
    - Alternatively discontinue buprenorphine 24 hrs prior to procedure.
    - Remember: Higher dosing of short-acting opioids may be required post surgical due to tolerance

Merrill et al., 2002
Wenzel et al., 2016
Ward et al 2018

Post Op Options for Patients Already on Buprenorphine

Options	***Considerations***
Continue partial agonist at optimized dosing, with full agonist as indicated for breakthrough pain as indicated. Return to maintenance partial agonist dose as tolerated post-op.	More frequent partial agonist dosing Consider an increase in total dose Review the plan with the patient and surgeon/anesthesiologist. Establish signs and symptoms indicating appropriate time to return to baseline dose.
Discontinue partial agonist, will have to provide additional full agonist opioid to treat both pain and to satisfy opioid debt in dependent patients. Reinduction onto partial agonist post-op as pain subsides.	Open communication with surgeon Short acting full agonists for breakthrough pain Discuss risk of relapse with the patient Review security and safety of agonist medication

Merrill et al., 2002
Wenzel et al., 2016
TIP 63 – SAMHSA 2019

Acute Pain Management for Patients Currently on Naltrexone

Clinical Scenario	Management Options
Mild Pain	Non-opioid options, e.g., Full dose of NSAIDS (e.g., ketorolac injection)
Elective Surgery	Schedule surgery in accordance with patient's treatment. · Oral naltrexone: Schedule surgery at least 72 hours after d/c naltrexone · Extended-release naltrexone: Schedule surgery at least 4 weeks after injection. May need to use oral product for a few days.
Major Pain or Emergency	· Reginal anesthesia · Conscious sedation · General anesthesia (Note: high potency fentanyl analogues may be needed to override blockade)

Alford et al., 2006
CSAT, 2004
Kampman et al., 2015
WHO, 2009

Acute Pain Management for Patients Currently on Methadone

- May split the dose to 3 or 4 times a day for greater analgesia.
- May require higher dosing of methadone and higher doses of additional full agonists, due to increased opioid tolerance.
- Consult a pain specialist or addiction medicine specialist

Individuals Treated with MOUD CoMorbid for a Chronic Pain Disorder

- Continue buprenorphine
  - Consider splitting the dose and/or increase as indicated.
- Try non-opioid and adjuvant analgesics
- Consider non-pharmacologic therapies
- Consider Multidisciplinary Team Approach
- Consider consulting a pain management specialist

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Opioid Use Disorder and Pregnancy

- Epidemiology:
  - 15% of pregnant women had used illicit substances in the past year
  - 7% of women report using prescription opioid pain relievers during pregnancy.
  - Of those, 1 in 5 report misuse of opioids
  - Amer. College of Obstetrics and Gynecology recommends screening all patients for alcohol and other drug use.
    - Important at first prenatal visit and then periodically.
- Approaches to screening:
  - Substance Use Risk Profile – Pregnancy (SURP-P) – High Sensitivity
  - 5P's (Parents, Peers, Partner, Past, Present) – High Sensitivity
  - NIDA Quick Screen – High specificity
  - CRAFFT (for women 26 years or younger) – High Sensitivity
  - W(Wayne)IDUS – Highest sensitivity for illicit drugs and opioids.

Vital Signs: Prescription Opioid Pain Reliever Use During Pregnancy — 34 U.S. Jurisdictions, 2019

ACOG/ASAM 2017 / Ondersma SJ et al., Addiction. 2019 Sep;114(9):1683-1693

Opioid Use Disorder and Pregnancy

- Pregnancy can increase motivation for a reduction in alcohol and other drug use and SUD treatment.
- Perinatal Opioid Agonist Treatment
  - MOUD has minimal long-term developmental impacts on children.
  - There is a risk of Neonatal Opioid Withdrawal Syndrome (NOWS).
    - However, there is a greater risks for NOWS with untreated OUD.
  - Pregnant women with OUD should be encouraged to start MOUD.
  - Women on MOUD who become pregnant should be encouraged to continue MOUD treatment throughout pregnancy.
- There is growing but as yet insufficient research on the safety and efficacy of naltrexone during pregnancy.
- All pregnant women who use nicotine products (particularly tobacco) should be encouraged to reduce or stop.
  - Along with other health benefits it can reduce the severity of NOWS.

Methadone Treatment in Pregnancy

- Commonly used for pregnant women with OUD
  - Though methadone and buprenorphine are both considered first line treatments
- Methadone adjustment during pregnancy:
  - Second and third trimester:
    - With advancing gestational age: Plasma levels of methadone progressively decrease, and clearance increases
      - The half-life of methadone falls from an average of 22–24 hours in non-pregnant women to 8.1 hours in pregnant women
    - Assess for increased craving or discomfort
      - Possible increased dose is often required for stabilization.
      - Split dosing is often required for adequate avoidance of opioid withdrawal symptoms and/or craving

ASAM Guidelines, 2015
J Addict Med. 2018

Use of Buprenorphine With or Without Naloxone in the Pregnant Patient

- Buprenorphine mono-product has been the most well studied.
  - Initial concerns:
    - naloxone fetal effect.
    - if injected it will not cause precipitated withdrawal.
- Buprenorphine/Naloxone – growing literature and recommendations
  - FDA designates **sublingual** naloxone:
    - No known teratogenic effects in animals
    - Controlled studies have not been conducted in humans
  - Evidence points to buprenorphine-naloxone safety in pregnancy, and it is frequently used.
    - Minimal naloxone absorption
    - Reducing injection drug use diversion.

Wiegand SL, et al., *Obstet Gynecol.* 2015, Debelak K, et al. *Am J Addict.* 2013
ASAM Updated OBOT Guidelines 2019, Lund et al., 2013

Buprenorphine Treatment in Pregnancy

- Initiation should begin when a woman shows objective, observable signs of withdrawal, but before severe withdrawal symptoms are evidenced.
  - >23 weeks gestation should have in-clinic observation during initiation of treatment with buprenorphine. Hospitalization may be advisable.
- Buprenorphine dosing is the same as in nonpregnant women.
  - Dosage is not linked to increased incidence of NOWS
- During pregnancy: No significant dose increases needed though may require split dosing in 3rd trimester
- Postpartum: Continue current dose of buprenorphine.
  - Return to the combination product if patient was converted to the mono product during pregnancy. No dosage changes.

Jones H, et.al, 2013; Jones et al., 2014; Lund et al., 2013).

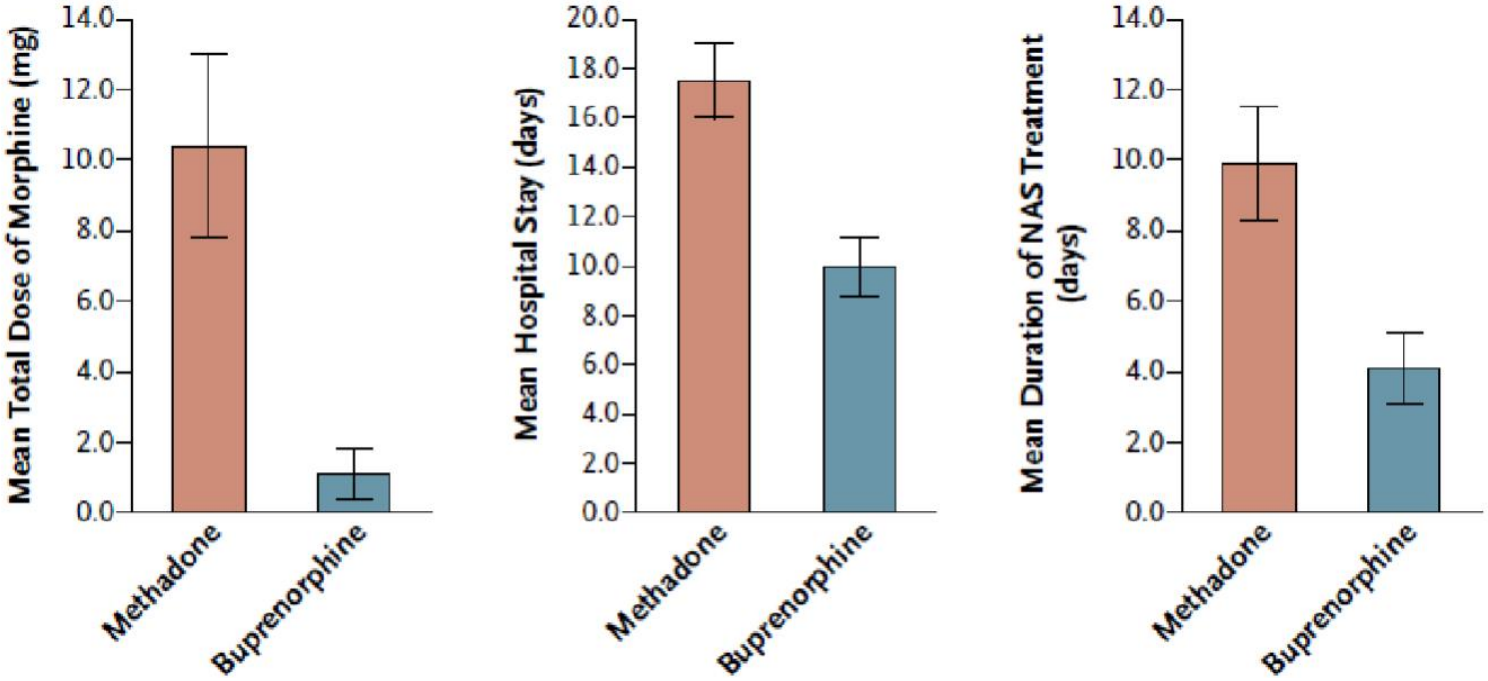
Neonatal Opioid Withdrawal Symptoms (NOWS)

- Epidemiology:
  - Increasing incidence of NOWS
  - Incidence of NOWS in newborns born to women with OUD is between 70 and 95% and ~50% of infants will need treatment
- Symptoms:
  - Irritability, fever, diarrhea, hyperreflexia, seizure
  - Begins 24-72 hours of birth, with peak symptoms at 3-4 days, and continues for up to one week
- Complications:
  - Associated with untreated maternal OUD
    - Increased risk of placental abruption, preterm labor, maternal obstetric complications, and fetal death

Kakko et al., 2008
Patrick at al., 2015
Smith et al., 2017

Maternal Opioid Treatment: Human Experimental Research (MOTHER) Study

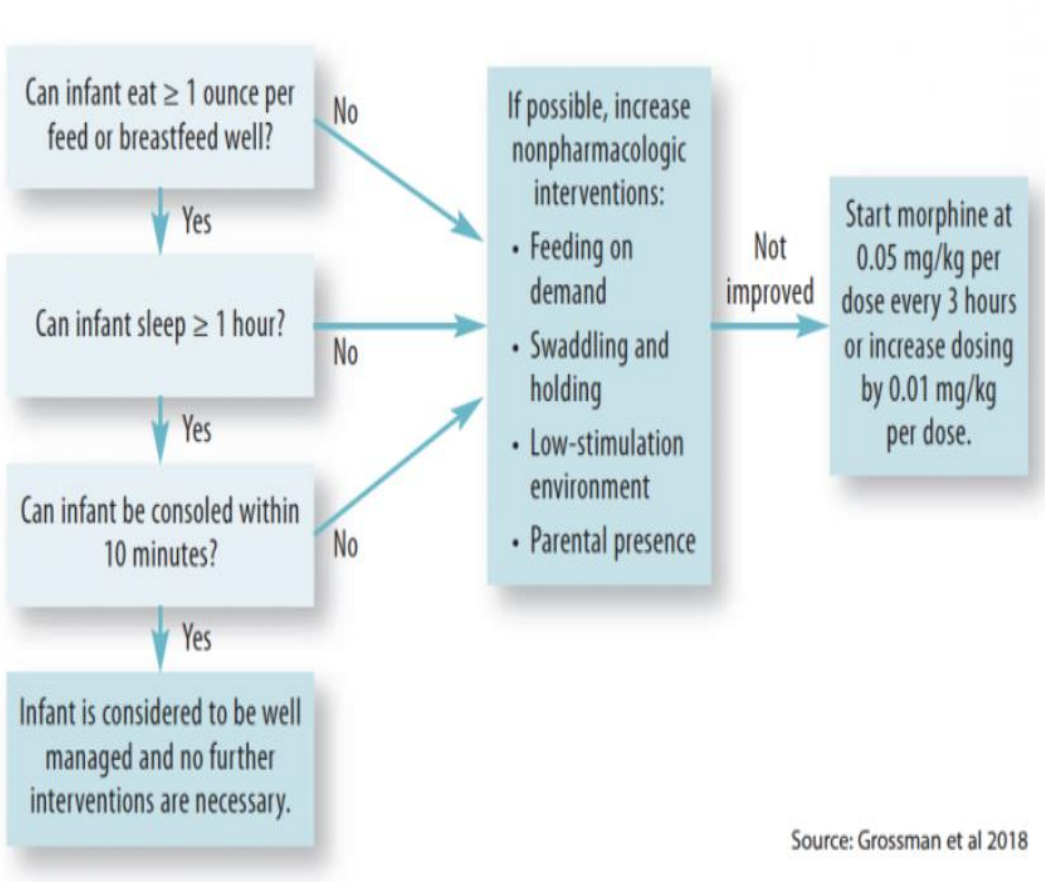
- Buprenorphine vs Methadone effect on NOWS
  - One tenth the amount of morphine needed to control symptoms
  - Nearly one half the time spent in the hospital
  - More than a third reduction in duration of treatment



Jones et al., 2010

Treatment of NOWS

- Non-Pharmacologic Novel Approaches:
  - "Eat, Sleep, Console"
  - Rooming in results in a reduction in NOWS length of stay and cost
- Medications:
  - Opioid therapy is preferred first-line intervention
    - PRN Morphine/Methadone
  - Clonidine



Holmes et al., 2016
Hudak et al., 2012
Slowiczek L, 2018

https://www.myamericannurse.com/caring-for-infants-and-families-affected-by-neonatal-abstinence-syndrome/

Buprenorphine vs. Methadone in Pregnant Patients with OUD

- Consider Availability, Patient Preference
- Advantages:

Buprenorphine (Mono or Combination Products)	Methadone
Office based treatment Similar efficacy as methadone Lower overdose potential Less medication interactions Less severe NOWS than methadone	More structure setting for care. OTP Less potential for diversion More long-term outcome data available

Fischer et al., 1998, 1999
Jones et al., 2010;
Kakko et al., 2008;
Kraft et al., 2017
ASAM Updated Guidelines 2020

Breast Feeding and MOUD

- Breast feeding is compatible with MOUD
  - Improved maternal and infant bonding
  - Favorable effects on NOWS
- Transferred amounts of methadone or buprenorphine (mono or combo) are insufficient to prevent symptoms of NOWS
- Levels in human milk are low with calculated infant exposures of the maternal weight-adjusted dose being:
  - <3% for methadone
  - 2.4% for buprenorphine

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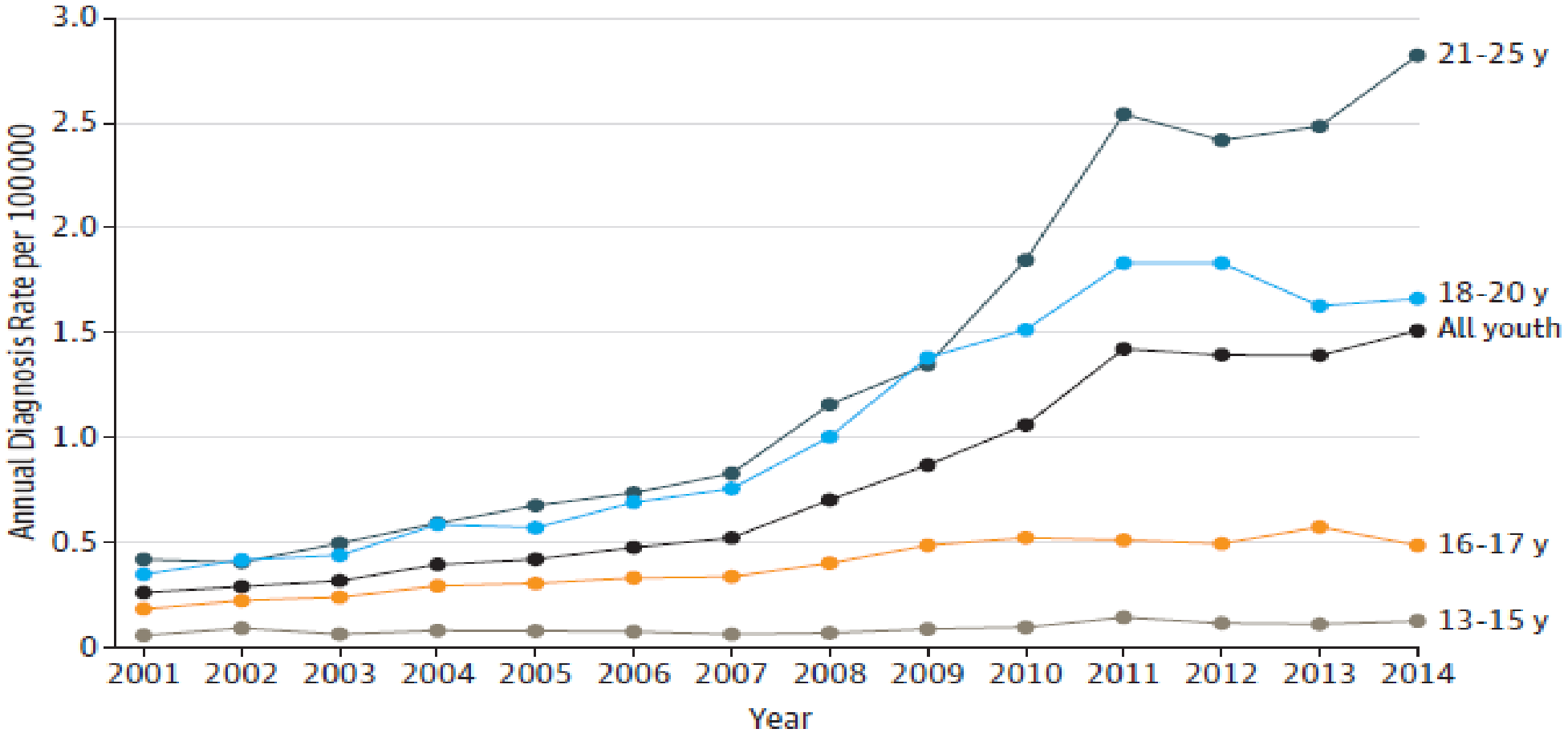
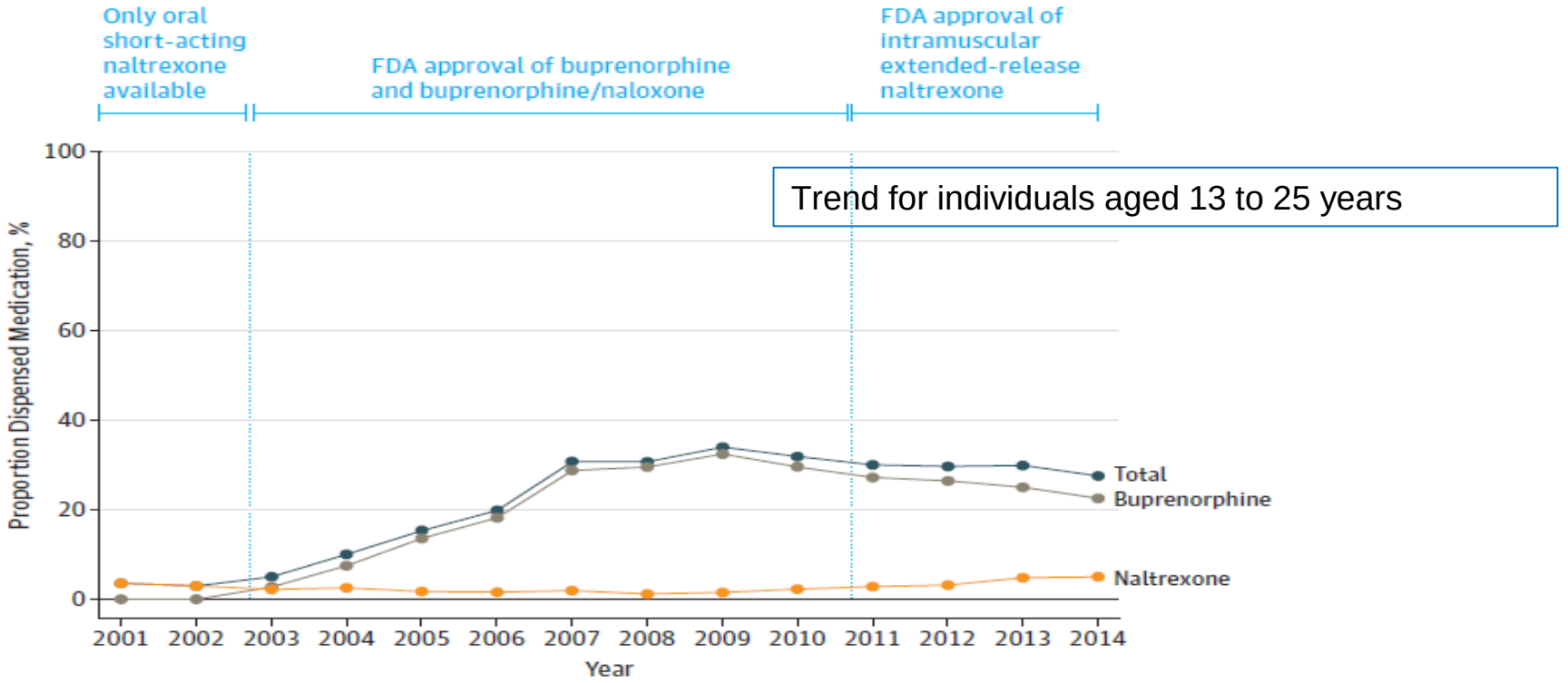
New Diagnoses of Opioid Use Disorder in Youth



Hadland et al., 2017

Proportion of Youth Receiving Treatment Within 6 Months of Diagnosis

- Individuals with OUD younger than 18 receiving MOUD:
  - **13 to 15 years = 1.4%**
  - **16 to 17 years = 9.7%**



Hadland et al., 2017
Feder KA, et al.,2017

Adolescents

- ***American Academy of Pediatrics***:
  - Recommends that pediatricians consider offering MOUD to their adolescent.
- ***FDA Approved Medication Options:***
  - Buprenorphine (approved for patients>16yo)
    - Often considered to be the first choice
    - Much better treatment retention in comparison to no MOUD
    - Decreased injection drug use
  - Methadone
    - A person under 18 years of age is required to have had two documented unsuccessful attempts at short-term detoxification or non-medication treatment.
    - Parental of guardian consent.
  - Naltrexone ER (approved for patients>18yo)
- ***Psychosocial Treatment Options:***
  - Motivational Interviewing
  - Family intervention approaches
  - Educational and/or Vocational support
  - Behavioral interventions; CBT and Contingency Management

AAP, 2016; Fishman et al., 2010; ASAM Guidelines 2015; Woody et al., 2008

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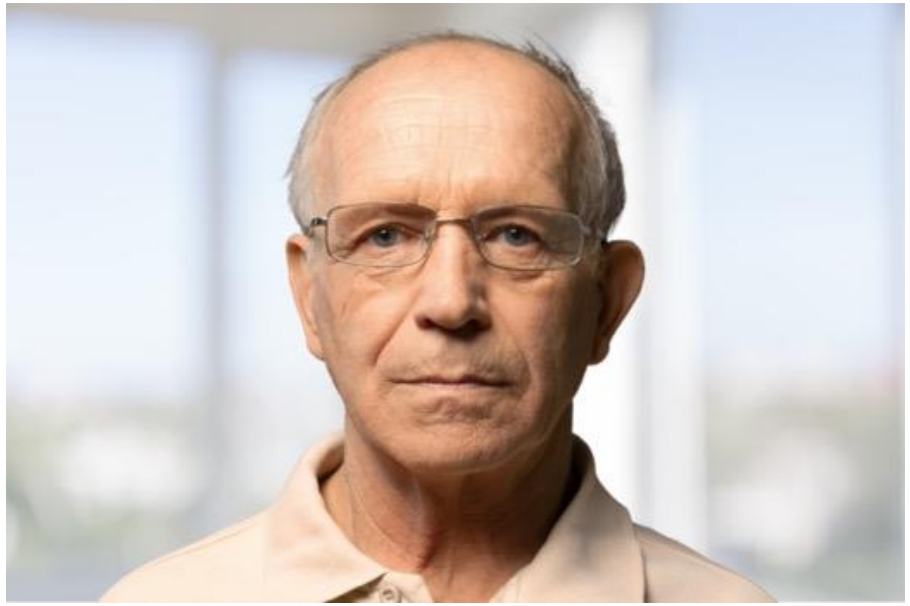
Older Adults and Substance Use

- General population of older adults:
  - United States: 1 in 5 U.S. Residents will be age 65+ (by 2030)
- SUDs in older adults (2014):
  - 1 million individuals
    - 978,000 with alcohol use disorder and,
    - 161,000 with illicit drug use disorder
- Limited high-quality research on prescription drug misuse in older adults.
  - Past year prevalence of non-medical use of opioids is ~1.4%



Maree et al., 2016; Mattson et al., 2017; West et al., 2015; Wu et al., 2014

Older Adults and Opioid Use

- Unique features:
  - Physiologic changes:
    - Decreased metabolism of medications
    - Increased elimination time
  - Polypharmacy
  - Multiple co-morbidities (including cognitive decline)
  - High prevalence of pain in older adults:
    - 25-50% of those living in community dwellings
    - 70% of those living in nursing homes
    - 80% of those living in long-term care
- Risks:
  - Self-poisoning has been reported as frequent mechanism of suicide

Chau et al., 2008;
West et al., 2015;
Wu et al., 2014

Older Adults – Treatment Considerations

- Evaluation:
  - Conduct thorough screening
  - Assist patients with cognitive impairments
  - Assess for suicidality
    - Self-poisoning a frequent mechanism of suicide in older adults.
- Medication Recommendations:
  - Buprenorphine:
    - Considered a good choice; d/t increased susceptibility to respiratory compromise in this population..
    - Start low and go slow with dosing
    - Hepatic metabolism is slowed in older adults,
      - Buprenorphine doses may be lower than in younger patients.
  - Methadone:
    - Potential for medication interactions
    - QT Prolongation
    - Higher risk of overdose

Chau et al., 2008; West et al., 2015; Wu et al., 2014

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HIV-Infected Patients

- CYP 3A4 is the primary hepatic enzyme involved in metabolism of both methadone and buprenorphine
  - There are no clinically relevant buprenorphine-ART interactions.
  - This was most frequently an issue with older ART and methadone
  - There is little or no interactions with naltrexone
- Providers should consider:
  - referral to specialized HIV treatment programs and services – if available
  - coinfection with HIV and HCV is common (62%–80%) among injection-drug users who have HIV.
    - People with HIV/AIDS should be vaccinated against hepatitis A and B and tested for hepatitis B and hepatitis C.
    - Consider screening for STIs and TB

CSAT, 2004
McCance-Katz et al., 2010
Moatti et al., 2000
Montoya et al., 1995
Centers for Disease Control and Prevention; 2017

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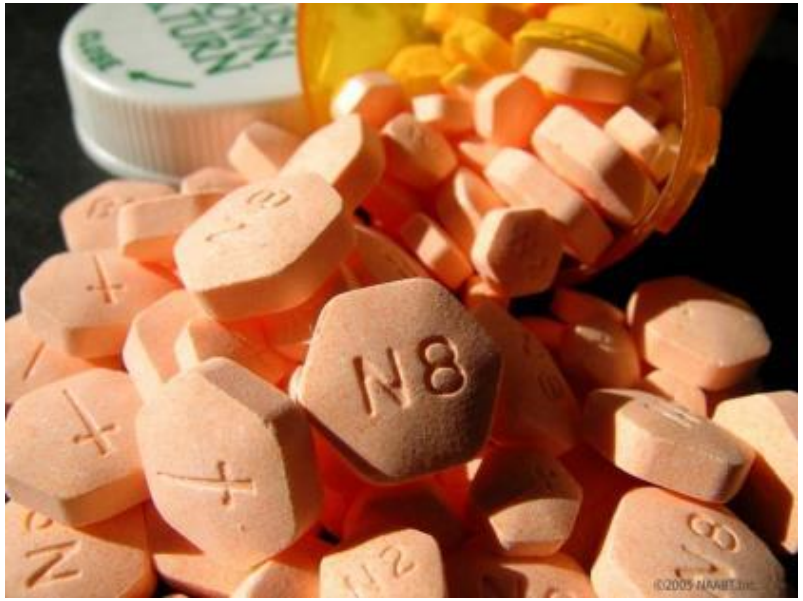
Patients with Renal Failure

- Suitable to use MOUD medications in patients with renal failure
- No significant difference in kinetics of buprenorphine in patients with renal failure versus healthy controls
- No significant side effects in patients with renal failure
- Buprenorphine and methadone can be prescribed to patients undergoing hemodialysis
- Naltrexone is safe in dialysis, but blood should be continually monitored.



Patients with Compromised Hepatic Function

- Buprenorphine and Methadone undergo hepatic metabolism, primarily by the CYP450 3A4 system
- Patients with compromised hepatic function,
  - LFTs 3-5 times normal, could have reduced metabolism of buprenorphine, with resultant higher blood levels of the medication.
  - Patients LFTs and total bilirubin should be monitored periodically in patients with underlying liver disease.
- No specific hepatotoxicity has been demonstrated for either methadone or buprenorphine

Hepatitis and MOUD

- Buprenorphine or Methadone are:
  - Not contraindicated in patients with mildly elevated liver enzymes.
  - Moderately elevated levels (>3times the upper limit of normal) should be monitored.
  - Acute fulminant hepatitis should be appropriately evaluated and treated.
    - Consider the risks of delaying treatment.
  - Etiology of moderate or markedly elevated liver function tests should be determined and treated.

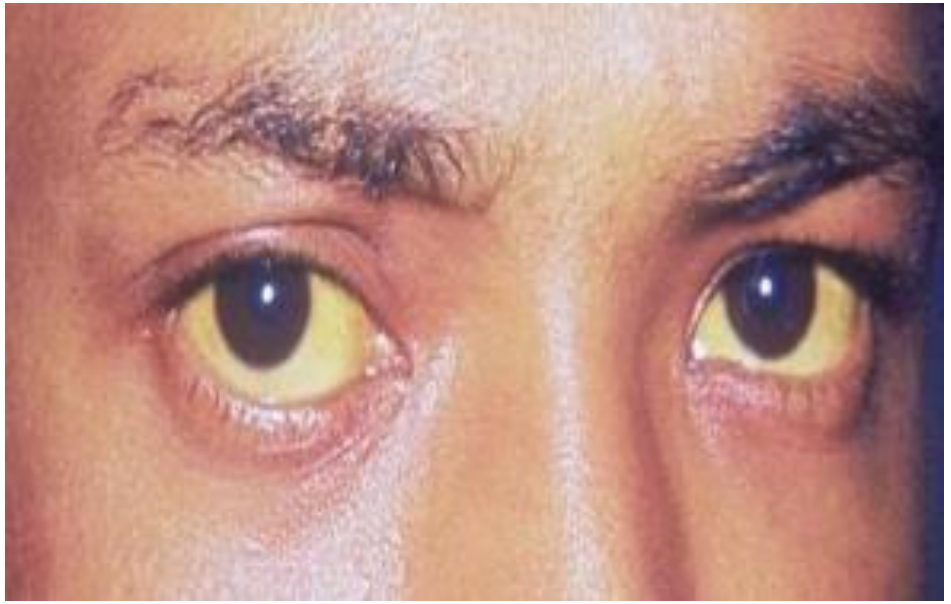


Photo by: CDC/Dr. Thomas F. Sellers/Emory University
Bruce RD, Am J Drug Alcohol Abuse, 2007

Conclusion

Medications for Opioid Use Disorder can be used in different special populations

The clinician should be aware of differences in the available options when using in special populations

Questions