YALE PROGRAM IN ADDICTION MEDICINE

CORONAVIRUS (COVID-19) GUIDANCE

Hospital-Based Addiction Treatment

Disclaimer: This is meant to be a guide only and not to be used without clinical evaluation and decision making.

Background

- During the COVID-19 pandemic, patients with substance use disorders (SUD) may present to the hospital with high frequency and have poorer outcomes.
- SUD withdrawal and craving can complicate efforts to treat medical conditions that require hospitalization and if untreated result in patient-clinician conflicts and patients electing to leave the hospital rather than receiving those treatments.
- Patients with SUD have a high prevalence of substance inhalation, which may increase risk for pulmonary complications.
- Patients with SUD may have symptoms from substance withdrawal that mimic COVID-19 symptoms.
- Patients with SUD may have lost access to medication treatment and need interim medication management.
- Patients may have lost access to sterile supply of equipment for drug use and naloxone.
- Patients with untreated opioid use disorder (OUD) are at increased risk of unintentional overdose and infectious complications.
- Patients can be identified as having SUD with single question screening tools followed by a formal evaluation with the DSM-5 criteria. See Appendix for this information.
- Hospitalization is a reachable moment for SUD screening, engagement and treatment.
- Providing evidence-based medicine focused SUD treatment can improve outcomes, reduce hospital and ED visits, and improve chances of recovery.

PATIENTS WITH ALCOHOL USE DISORDER

Acute Alcohol Withdrawal

- Patients with a history of delirium tremens, seizure, age >65, multiple medical co-morbidities like advanced pulmonary, liver or renal disease, and unstable housing or homelessness generally require inpatient alcohol withdrawal management.
- The CIWA-AR is a freely available, validated assessment tool to determine the severity of alcohol withdrawal and guide treatment.
- Benzodiazepines combined with gabapentin are typically preferred for acute alcohol withdrawal over other agents.
- Offer medications for alcohol use disorder (MAUD) to reduce heavy alcohol drinking and increase chances of abstinence from alcohol - see section below.
- Refer to the new **ASAM Guideline on Alcohol Withdrawal Management** for further recommendations and treatment options.

Alcohol Use Disorder

There are three FDA-Approved Medications for Alcohol Use Disorder:

- Naltrexone 25-50mg oral once daily.
  - Ensure opioid abstinence for at least 7-10 days.
  - Monitor liver function every 6-12 months and avoid in patients with acute hepatitis or liver failure.

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- Naltrexone ER 380mg IM once every 28 days intramuscular (gluteal) injection.
  - Ensure opioid abstinence for at least 7-10 days.
  - Monitor liver function every 6-12 months and avoid in patients with acute hepatitis or liver failure.
- Acamprosate 333-666mg oral TID.
  - Monitor renal function 4 weeks after starting and then every 3-6 months after.
  - Reduced dose in patients with CrCl 30-50 mL/minute.
  - Avoid in patients with CrCl <30 mL/minute.
- Disulfiram 250-500mg oral once daily.
  - Monitor liver function every 6-12 months and avoid in patients with acute hepatitis, liver failure, and/or severe cardiac disease.

PATIENTS WITH OPIOID USE DISORDER

Background

- Opioid withdrawal is extremely uncomfortable and if untreated can impede the ability to provide care for acute medical issues, resulting in conflicts between patients and hospital staff and patients leaving against medical advice. It can occur in patients with DSM-5 diagnosed OUD and those who are prescribed long term opioids for pain who are not provided ongoing access to opioids.
- The Clinical Opiate Withdrawal Scale (COWS) is a freely available, validated assessment tool to determine the severity of opioid withdrawal and guide treatment.
- It is safe, legal, feasible and efficacious to administer medications for opioid use disorder (MOUD), including methadone and buprenorphine, in an emergency department and inpatient hospital setting.
  - Review **federal regulations** for administering or dispensing narcotic drugs.
- The most effective medications to alleviate opioid withdrawal symptoms are buprenorphine (partial opioid agonist) and methadone (full opioid agonist).
- The choice between buprenorphine and methadone is based on several factors including patient choice, concomitant pain, use of opioid agonist treatment, QTc prolongation, drug interactions, and patient history.
- While outpatient prescriptions for buprenorphine require that a prescriber has a Drug Addiction Treatment Act (DATA) waiver and DEA X number, patients who are hospitalized for medical conditions other than OUD can be started (or continued for an unlimited duration) on buprenorphine formulations by any practitioner with a DEA registration.
  - Review **SAMHSA guidance** on special circumstances for prescribing buprenorphine.
- A patient can legally receive methadone or buprenorphine for OUD if they are hospitalized for a medical or psychiatric reason other than opioid addiction or opioid withdrawal (this includes opioid overdose, abscess, endocarditis, osteomyelitis, etc).
- Outpatient medication treatment (buprenorphine or methadone) can be continued, adjusted, and/or changed as clinically indicated during the inpatient admission without restriction. If available, consultation with Addiction Medicine or Psychiatry is advised. If not available, consult with outpatient provider of buprenorphine or methadone.
- At discharge, buprenorphine formulations for treatment of OUD may only be prescribed by a clinician with a DEA X number.
- Providers may not prescribe methadone to treat OUD at discharge.

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Background *continued*

Buprenorphine Formulations (Combination Product Buprenorphine/Naloxone, Buprenorphine Monoproduct):

- Patients with OUD who are new to OUD treatment, have certain drug interactions, QTc prolongation, transportation limitations, or geographic limitations may be better candidates for buprenorphine.
- There is evidence supporting hospital and ED-initiated buprenorphine with follow up in community-based treatment.
- Review these **buprenorphine induction resources**.
- Consider alternative treatment in patients who are NPO.
- Clinicians with DEA X numbers can supply patients with up to a 30-day prescription in emergency situations consistent with the patient's clinical situation and stability.
- Telehealth is now available and legal for buprenorphine initiation and continuation in the outpatient setting, even without an initial face-to-face visit.

Methadone:

- Patients with OUD who have concomitant severe pain, use of opioid agonist treatment, or prior methadone treatment may be better treatment candidates for methadone.
- See pages 7-8 for sample hospital-based methadone induction protocol for patients not already treated at an opioid treatment program (OTP).
- For methadone treatment, confirm eligibility for outpatient treatment by documenting 12 months or more of opioid use.
- The QTc prolonging effects of methadone appears to be dose related. Doses of methadone >100mg are more likely to increase QT interval more than buprenorphine and naltrexone. QT should be monitored closely because medications used to treat COVID-19 may also increase QT interval.
- For patients who receive treatment at an OTP, always verify dose of methadone with the patient's OTP. If unable to verify methadone dose and patient is experiencing opioid withdrawal, it is appropriate to provide an initial daily oral dose of methadone of 20 mg. See pages 7-8 for a detailed induction schedule.
- Consult with a clinical pharmacist for methadone dosing in patients who are NPO.

Extended Release Naltrexone (intramuscular gluteal injection):

- Generally, not recommended as first-line treatment and should only be provided if a patient has not used or received short-acting opioids in the past 7-10 days and is not having acute hepatitis or liver failure.
- This may also cause problems with repeat injection due to limited in-person clinical availability in response to COVID-19.

Naloxone:

- All individuals with a history of opioid overdose, patients with OUD, and those receiving > 50 milligrams of morphine equivalents of prescription opioids should be discharged with intranasal naloxone and overdose prevention education. Visit **Prescribe to Prevent** to learn more about prescribing naloxone and overdose education.

PATIENTS WITH ACUTE BENZODIAZEPINE WITHDRAWAL

- Benzodiazepine withdrawal can lead to a life-threatening withdrawal syndrome, similar to alcohol withdrawal, and should be managed closely.
- Avoid abrupt cessation of benzodiazepines in the outpatient setting.

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PATIENTS WITH ACUTE BENZODIAZEPINE WITHDRAWAL *continued*

- Typically, advise use of longer acting benzodiazepines in a tapering fashion for benzodiazepine withdrawal, such as clonazepam or diazepam in a controlled setting.
- If possible, slow titration in the outpatient setting is recommended over acute titration in the acute hospital setting is advised. Review this **Benzodiazepine Tapering Flowsheet** for more guidance.

PATIENTS WITH TOBACCO USE DISORDER

- Offer tobacco cessation treatment to patients.
- The CT Quit Line is a helpful resource: **www.quitnow.net/connecticut**
  - The national tobacco quitline, 1-800-QUIT-NOW, will connect the caller to their state's quitline.
- We do not recommend transition to e-cigarettes or vaping.
- FDA-approved medications for the treatment of tobacco use disorder include:
  - Varenicline 0.5mg PO daily x 3 days, then 0.5mg PO BID x 4 days, then 1mg PO BID.
  - Bupropion 150mg PO daily x 3 days, then 150mg PO BID.
  - Nicotine replacement therapies including patches, gum, lozenges, nasal spray and inhalers
    - Dual nicotine treatment (e.g. patch plus gum or lozenge) is considered the most effective
    - 21mg patch for >10 cigarettes/day
    - 14mg patch for <10 cigarettes/day
    - 7mg patch use for tapering

OTHER INPATIENT CONSIDERATIONS

Facilitating Addiction Treatment in the Hospital Setting

- Consider the option of telehealth in combination with the primary team's evaluation for inpatient addiction medicine consults as most treatment can now be initiated over the phone.
- Continue to obtain objective measures of substance use disorder such as initial urine drug toxicology.

Patients Needing Prolonged IV Antibiotics for Infectious Complications of IV Drugs

- Studies show benefit of starting MOUD and consideration of outpatient parenteral antibiotic therapy (OPAT) with IV home infusions vs staying in the hospital for the entire parenteral antibiotic course.
- Consider use of the 9-point criteria to determine patients who can be safely discharged home for ongoing antibiotic treatment (table provided on page 5).
- There is no direct contraindication to placement of a indwelling catheter (e.g. PICC line) in a hospitalized patient or a patient planning to be discharged with a history of IV drug use, though you would want to ensure the following:
  - Use of MOUD
  - Safe home environment with clean water and heat
  - Significant supports in the home like a spouse or parent who can help monitor the patient
  - Ability to set up visiting nursing and infusion services

See following page for the Intraveneous Antibiotics and Addiction Team (IVAT) 9-Point Risk Assessment.

Supplemental Table 1. Intraveneous Antibiotics and Addiction Team (IVAT) 9-Point Risk Assessment

Risk Factor	Score (0-1)
1. Cravings	
2. Unstable Home Environment	
3. Dual Psychiatric Diagnosis	
4. History of Drug Overdose	
5. History of Multiple Relapses	
6. Polysubstance Abuse	
7. Family History of Addiction	
8. History of Trauma	
9. Limited Willingness to Change	
Total Score =	

One point is given for each of the above risk factors
Mild risk is defined as a total score of 1-3
Moderate risk is defined as a total score of 4-6
High risk is defined as a total score of ≥7

Source: *Eaton, Mathews, Lane, et al. A 9-point Risk assessment for patients who inject drugs and require antibiotics. Clinical Infectious Diseases, Volume 68, Issue 6, 2019: 1041-1043.*
https://academic.oup.com/cid/article/68/6/1041/5079079#supplementary-data

MOUD Discharge Options & Virtual Counseling Resources

- Review the **Yale Program in Addiction Medicine Guidance for Clinicians**.
- For information about and locate local syringe exchange options, visit **211 CT.org**.

Other Important Discharge Information

Harm Reduction Guidance for People Who Use Substances:
https://yale.app.box.com/v/COVID19HarmReductionGuidance

https://harmreduction.org/wp-content/uploads/2020/03/COVID19-safer-drug-use-1.pdf

NEXT Distro Mail Order Harm Reduction Supplies:
https://nextdistro.org/

Other Resources

Tools to Support Hospital-Based Addiction Care: Core Components, Values, and Activities of the Improving Addiction Care Team:
https://journals.lww.com/journaladdictionmedicine/Fulltext/2019/04000/Tools_to_Support_Hospital_Based_Addiction_Care_.2.aspx

My Top Care (Urine Testing Interpretation Assistance and Other Opioid Management Information):
http://mytopcare.org/

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Other Resources *continued*

Opioid and Benzodiazepine Tapering Guidance:
https://www.oregonpainguidance.org/app/content/uploads/2016/05/Opioid-and-Benzodiazepine-Tapering-flow-sheets.pdf

Appendix

PCSS Screening, Assessment and Treatment Initiation for SUD:
https://learning.pcssnow.org/p/ScreenAssessTreat

Single-Item Screening Questions for Unhealthy Alcohol and Drug Use:
McNeely J, Cleland CM, Strauss SM, Palamar JJ, Rotrosen J, Saitz R. Validation of Self-Administered Single-Item Screening Questions (SISQs) for Unhealth Alcohol and Drug Use in Primary Care Patients. J Gen Intern Med. 2015 May 19.

Alcohol Screening Tool:
Men: "How many times in the past year have you had 5 or more drinks in a day?"
Women: How many times in the past year have you had 4 or more drinks in a day?"
Positive: >Never

Drug Screening Tool:
"How many times in the past year have you used a recreational drug or used a prescription medication for nonmedical reasons?"
Positive: >Never

If positive screen, obtain information from the patient about their alcohol or drug use such as quantity of use, route of use, length of use, prior treatment attempts, and current treatment goals.

Confirm diagnosis with the DSM-5 Criteria for substance use disorder:
Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA: American Psychiatric Association, 2013.

In the past year, have you had

- Inability to fulfill role obligations
- Social or interpersonal problems due to substance use
- Use in hazardous situations
- Tolerance
- Withdrawal/physician dependence
- Use the substance in larger amounts or over longer period of time
- Had unsuccessful efforts to cut down or control substance use
- Spent a great deal of time obtaining the substance
- Given up or reduced important activities due to use of the substance
- Continued to use the substance despite physical or psychological harms
- Craving

Meeting 2-3 criteria = Mild SUD | Meeting 4-5 criteria = Moderate SUD | Meeting >6 criteria = Severe SUD

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Sample Buprenorphine Induction Protocols

ED Buprenorphine Initiation Clinical Decision Support:
https://medicine.yale.edu/edbup/

See pages 3-60 in the **SAMHSA Medications for Opioid Use Disorder Treatment Improvement Protocol (TIP) 63** for more information.

- Obtain urine drug test, check for fentanyl, if possible.
- Stop full opioid agonist medications and wait 6-12 hours.
- Wait for Clinical Opioid Withdrawal Scale of >10.
- For high likelihood of fentanyl, wait minimum of 24 hours and COWS >12.
- For patients who have recently taken methadone, wait 48-72 hours from last dose of methadone before starting buprenorphine.
- Push fluids.

	Buprenorphine/naloxone dose
Day 1	Start 4mg SL After 1 hour, give another 4mg for COWS > 5 After 1 hour, given another 4mg for COWS >5 Total dose of 8-16mg per clinical need Only use adjuvant medications if needed (see table below)
Day 2	Give dose from Day 1 After 1 hour, give another 4mg for COWS > 5 Total dose up to 16-24mg *(Most patients stabilize on 16mg of buprenorphine)*
Day 3	Give dose from Day 2 Continue to dose as needed for ongoing withdrawal symptoms Do not exceed 24mg

Protocols to Consider in Rare Situations:

Low Dose Buprenorphine Induction Protocol for the Outpatient Setting:
- Consider for patients with high likelihood of fentanyl use.
- Consider for patients who have failed "traditional" buprenorphine induction strategies

(Ghosh et al, Canadian Journal of Addiction, 2019)

Day	SL Buprenorphine/naloxone dose	Full agonist dose
1	0.5mg once daily	Continue at current dose
2	0.5mg BID	Continue at current dose
3	1mg BID	Continue at current dose
4	2mg BID	Continue at current dose
5	4mg BID	Continue at current dose
6	4mg TID	Continue at current dose
7	4mg TID (can increase to 8mg BID needed)	STOP full agonist (no taper)

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Patients Transitioning From Long-term Opioids for Pain:

Becker WC, Frank JW, Edens EL. Switching From High-Dose, Long-Term Opioids to Buprenorphine: A Case Series. Ann Intern Med. 2020; [Epub ahead of print 7 April 2020]

Table 1. Daily Schedule of Buprenorphine Uptitration and Discontinuation of Full Agonist Opioid Therapy for Patient Receiving Controlled-Release Oxycodone, 80 mg 3 Times Daily

Day	Buprenorphine-Naloxone (Only Buprenorphine Dosage Listed)	Controlled-Release Oxycodone Dosage
1	0.5 mg twice daily*	80 mg 3 times daily
2	1 mg twice daily†	80 mg 3 times daily
3	1 mg 3 times daily†	80 mg 3 times daily
4	2 mg 3 times daily	80 mg twice daily
5	4 mg 3 times daily	None
≥6	Adjust dose to symptoms	None

* One-quarter 2-mg tablet.
† One-half 2-mg tablet.

Resource: **PCSS Managing Pain in the Patient with Opioid Use Disorder: Inpatient Management**

- Dose buprenorphine BID or TID and/or increase overall dose.
  - Usually do not exceed buprenorphine 24mg/day.
- Option: Add additional opioid ON TOP of buprenorphine.
  - Choose opioid with a high affinity for the mu opioid receptor (hydromorphone or fentanyl).
  - Dose hydromorphone at higher dose to compete at the mu opioid receptor.
    - Example: Buprenorphine 24mg per day, add hydromorphone 4-6mg every 4-6 hours PRN.
- Use scheduled adjuvant therapies (ketamine, nerve block, NSAID, acetaminophen, gabapentin, SNRI, etc).
- Taper additional opioids after tissue healing.

Methadone Dosing

- Obtain urine drug test and EKG, hold for QTc > 500ms.
- Day 1 – Give between 10-30mg dose of methadone based on patient opioid tolerance.
- After 2-4 hours, if patient still symptomatic, can give another 10mg of methadone.
- Do not exceed 40mg in the first 24 hours.
- Day 2 – Give between 30-40mg of methadone depending on how patient did on Day 1.
- Assess peak effect of methadone at 4 hours after the dose.
- If you do not have outpatient methadone treatment available, do not increase dose.
- If you have outpatient methadone treatment available, consider dose increase by no more than 5-10mg.
- Day 3- continue once daily dosing of methadone and do not increase any faster than 5mg every 3-5 days, consult addiction medicine or addiction psychiatry if available.

References

Page 3-27 of TIP 63: **https://medicine.yale.edu/edbup/resources/TIP_63_338482_284_42920_v1.pdf**
Safe Methadone Induction and Stabilization: Report of an Expert Panel, J Addict Med _ Volume 7, Number 6, November/December 2013 **https://journals.lww.com/journaladdictionmedicine/Pages/toc.aspx?year=2013&issue=11000**

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Adjunct Medications for Withdrawal Symptom Management

Drug	Dose	Targeted Opioid Withdrawal Symptoms
Clonidine* *Obtain BP before each dose and hold for SBP < 90 mmHg & DBP < 60 mmHg	Taper Option: 0.2 mg P.O. Q6H x 4 days 0.1 mg P.O. Q6H x 2 days 0.05 mg Q12H x 1 day PRN Option: Clonidine 0.1 mg P.O. Q4H PRN COWS > 10; Clonidine Not to Exceed 1.2 mg/24 hour period	Agitation, sympathetic overdrive
Loperamide	4 mg P.O. x1, then 2 mg Q6H PRN	Diarrhea
Dicyclomine	20 mg P.O. Q6H PRN	Abdominal Cramps
Ondansetron	8 mg P.O. Q6H PRN	Nausea
Prochlorperazine	10 mg PO Q6H PRN	Nausea
Ibuprofen	400 mg P.O. Q6H PRN	Myalgia
Trazodone	50 mg P.O. QHS PRN	Insomnia
Acetaminophen	650 mg P.O Q6H PRN	Myalgia
Hydroxyzine	25 mg P.O. Q6H PRN	Anxiety
Thiamine	100 mg P.O. Daily	N/A
Multivitamin	1 tablet P.O. Daily	N/A
Folic Acid	1 mg P.O. Daily	N/A