ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

Agenda

Zoom link to join from PC, Mac, iOS or Android**:** https://echo.zoom.us/j/156261634

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Zoom Meeting ID: 156 261 634

For attendance, purposes please text the following code: COSSUV to 608-260-7097

Session Date: Friday February 21, 2020

Didactic Topic and Presenter:
Opioid Withdrawal Management
Alyssa Tilhou, MD – UW Madison Addiction Medicine Fellow

Content Experts:
Ritu Bhatnagar, MD and Susan Mindock, CSAC; and Sheila Weix, MSN, RN, CARN

- 12:30 PM: Attendance text-in – Introductions
- 12:45 PM: Case Presentation
    - Presenter: Geoffrey Watters, RN, BSN, DNP
- 1:10 PM: Didactic Presentation
    - Presenter: Alyssa Tilhou, MD UW Madison Addiction Medicine Fellow
- 1:30 PM End of Session

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ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2018-2020

Opioid Intoxication and Withdrawal

Friday February 21, 2020

Alyssa Tilhou, MD – UW Madison Addiction Medicine Fellow
Geoffrey Watters, RN, BSN, DNP

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Physicians, Physician Assistants, Nurses, Social Workers, Pharmacists and Counselors.

Objectives:

As a result of this educational regularly scheduled series, learners will be able to:

1. Review appropriate opioid prescribing and monitoring practices.
2. Participate in office-based management of substance use disorders.
3. Seek, with greater frequency, overdose prevention education.
4. Identify the role of medication-assisted therapies, such as methadone, naltrexone, and buprenorphine in the management of substance use disorders.

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Name/Role	Financial Relationship Disclosures	Discussion of Unlabeled/Unapproved uses of drugs/devices in presentation?
Geoffrey Watters, RN, BSN, DNP, Presenter	No relevant financial relationships to disclose	No
Alyssa Tilhou, MD, Planner, Presenter	No relevant financial relationships to disclose	No
Kathleen Maher, RSS Coordinator	No relevant financial relationships to disclose	N/A
Briana Kleinfeldt, RSS Coordinator	No relevant financial relationships to disclose	N/A
Randy Brown, RSS Chair	No relevant financial relationships to disclose	Yes
Paul Hutson, Planner, Pharmacy	Consultant for Projections Research Inc.	Yes
Ritu Bhatnagar, Planner, Psychiatrist	No relevant financial relationships to disclose	Yes
Melissa Ngo, Planner, Pharmacist	No relevant financial relationships to disclose	N/A
Susan Mindock, Planner, AODA Counselor	No relevant financial relationships to disclose	No
Sheila Weix, Planner, Nurse	No relevant financial relationships to disclose	No
Lindsey Peterson, MS, CRC, Planner	No relevant financial relationships to disclose	No
Kim Sprecker, OCPD Staff	No relevant financial relationships to disclose	No

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Opioid Intoxication and Withdrawal

Alyssa Tilhou, MD, PhD

ECHO Presentation 2/21/20

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Overview

- What are opioids
- Intoxication
  - Symptoms, diagnosis and complications
  - Physiology and pharmacokinetics of intoxication
  - Intoxication management
- Withdrawal
  - Symptoms and diagnosis
  - Post-acute withdrawal
  - Withdrawal assessment and management
- Conclusions

Opiates vs Opioids

- Opiates: direct products from opium, the naturally occurring juice of the opium poppy, *Papaver somniferum*

Opiates v Opioids

- Opiates: morphine, codeine and thebaine
- Semi-synthetics: heroin, hydrocodone, hydromorphone, oxycodone, buprenorphine
  - break down to morphine, hydromorphone, other
  - sometimes show up on drug screens, sometimes not
- Opioids: drugs that function like opiates
  - Mu, kappa, delta, ORL1 receptors
  - Fully synthetics: methadone, fentanyl, tramadol
  - Usually missed on standard urine drug screens

Intoxication symptoms

- Heroin Overdose Syndrome
  - Altered mental status (stupor, coma)
  - Respiratory depression
  - Miosis

- Opioid Overdose Diagnosis
  - Altered mental status +1:
    - Respiratory depression < 12/min
    - Miosis
    - Signs of use (track marks, soft tissue infection)

Intoxication symptoms

- Other intoxication signs and symptoms
  - Autonomic: hypotension, hypothermia and bradycardia
  - Neuro: Sedation, miosis, analgesia
  - GI: decreased bowel sounds, nausea, vomiting
  - Respiratory: decreased tidal volume (1st), rate

- Alternative presentations:
  - Co-ingestion (amphetamine, ephedrine, cocaine, ecstasy)
  - Meperidine (normal pupils)
  - Serotonin syndrome (tramadol, meperidine, other)

→ *Respiratory rate is best predictor of toxicity*

Intoxication complications

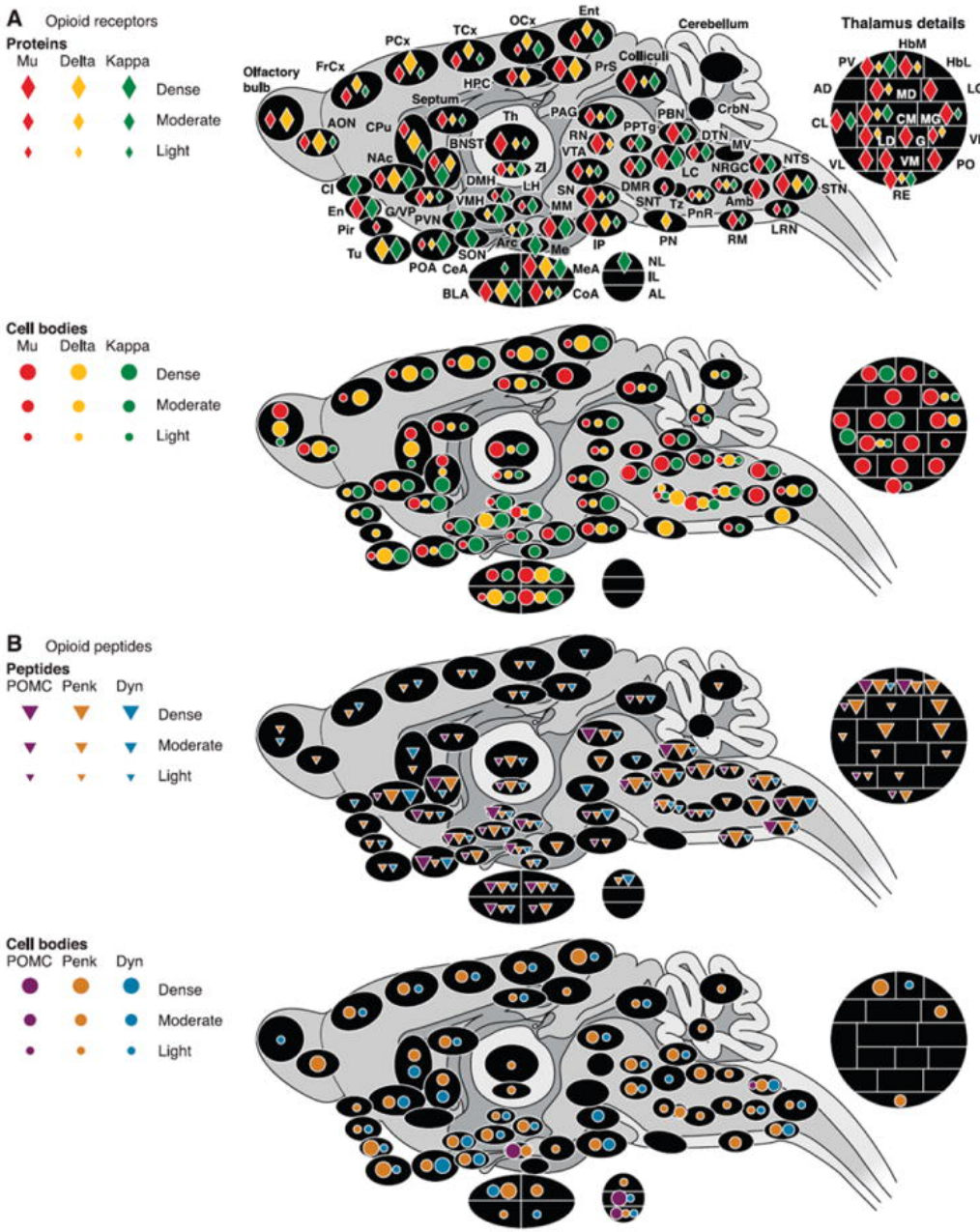
- Major complications
  - QT prolongation → fatal arrhythmias
  - Hypoxia →
    - Myocardial infarction
    - Rhabdomyolysis
    - Seizures
  - Noncardiogenic pulmonary edema and ARDS
  - Aspiration → pneumonitis, pneumonia
  - Needle contamination/soft tissue infection → bacteremia

Physiology of Intoxication

- Euphoria: central dopamine reward pathways, esp NAcc (mu)
- Sedation: brainstem mu>>kappa
- Respiratory – chemoRs (mu) in brainstem; also forebrain, carotid bodies, vagal nerves; mu>> delta
- Analgesia: spinal and brain mu >> delta, kappa or NOP
- Anxiolysis: noradrenergic inhibition in the locus coeruleus
- GI: mu + delta Rs in myenteric and submucosal plexus
- Anti-tussive: inhibition at medulla (mu > kappa or delta); also PNS and lung (mechanisms less understood)

- Tolerance to euphoria faster than respiratory depression

Physiology of Intoxication



Merrer, et al. Reward Processing Center by the Opioid System in the Brain. *Physiol. Rev.* 2009; 89(4):1379-1412

Pharmacokinetics

- Fentanyl IV:
  - onset immediate, peak minutes, half-life 2-4h
- Heroin:
  - onset immediate, peak <5 min (IV, IN, SQ), half-life 30min
- Hydromorphone IV:
  - onset 5 min, peak 10-20min, half-life 2-3h
- Oxycodone PO:
  - onset 10-15 min, peak 30-60 min, half-life 3-4h
- Hydrocodone PO:
  - onset 10-20 min, peak 30-60 min, half-life 3.5-4.5h

Overdose Risk Factors

- Potency:
  - Potency increases risk of overdose and adverse events[1]
  - Fentanyl > heroin IV > heroin IN > hydromorphone > oxycodone/oxycontin > morphine > hydrocodone > codeine
- IV use (can still OD with oral or insufflation)
- Sporadic use
- Needing help with injection
- Prior overdose
- Concurrent polysubstance use (cocaine, BZDs, sedatives)

1. Murphy, et al. Comparative Rates of Mortality and Serious Adverse Effects Among Commonly Prescribed Opioid Analgesics. Drug Safety, 2018;41:787-795.

Intoxication Management

- Adequate ventilation: Observation only
- Inadequate ventilation (overdose)
  - Naloxone:
    - Standard: 0.4-0.8mg IV (1mg IN), allow 2 min (longer if IN/SQ)
    - Apnea: start at 1-2mg IV
    - If in cardiac arrest, administer ≥ 2mg
    - Consider infusion if high potency/long-acting toxin
  - Repeat dose in 2min if no/partial response
  - Monitor ventilation (end tidal CO2; SpO2 insufficient)
  - Observe ≥ 2-3h after full response (naloxone half-life ~1h)

Acute Opioid Withdrawal: DSM-V

A
- Precipitated (administration of opioid antagonist)

  OR
- Spontaneous (reduction or cessation after heavy use)

B
- PLUS 3 or more symptoms:
  - Nausea or vomiting
  - Dysphoria
  - Muscle aches
  - Rhinorrhea or lacrimation
  - Pupil dilation, sweating or piloerection
  - Fever
  - Yawning
  - Insomnia
  - Diarrhea

C
- Symptoms must cause significant distress or impairment

D
- Cannot be due to another diagnosis

Acute Opioid Withdrawal

- Symptoms
  - GI: **anorexia**, nausea, vomiting, diarrhea
  - Autonomic: **thermoregulation, tachycardia, hypertension**
  - Mood: **Restlessness**, irritability, anxiety, dysphoria
  - Mucocutaneous (lacrimation, rhinorrhea, piloerection)
  - Yawning and sneezing
  - **Pain**

Acute Withdrawal

- Duration:

DRUG	ONSET	PEAK	COMPLETE
Fentanyl (IV)	3–5h	8–12h	4–5d
Heroin (IV)	8–12h	36–72h	7–14d
Morphine (PO)	6–12h	24–72h	5–7d
Methadone (PO)	24–72h	4–6d	14–21d

- Intensity: fast onset/short acting is associated with more intense and earlier discomfort

Post-acute Withdrawal Syndrome

- AKA protracted abstinence and protracted withdrawal
- Prolonged alteration in physiology and mood
- Symptoms
  - Physiologic: temperature, respiration, blood pressure, metabolic rate, heart rate, pupil dilation[1]
  - Prolonged craving
  - Dysphoria, anxiety, mood, insomnia and concentration[2]
- Can last 1 week to 6 months or more

1. The ASAM Principles of Addiction Medicine, 6th Edition, p745-746
2. Protracted Withdrawal. *Substance Abuse Treatment Advisory,* July 2010;9(1). SAMHSA HHS Pub No. 10-4554

Withdrawal Assessment

- Himmelsbach scale[1] – developed in the '30s and '40s
- Subjective OWS – late 80s, Bronx VA/Mt Sinai
  - Validated, 16-items rated 0-4 by the patient
- Objective OWS – late 80s, Bronx VA/Mt Sinai
  - 13-items rated 0-1
- Clinical Opiate Withdrawal Scale – late 90s
  - validated rapid 11-item rating system to track opioid withdrawal through serial measurements[2]

1. Wesson & Ling, The Clinical Opiate Withdrawal Scale, Jo Psycho Drugs, 2003;35(2):253.

2. Tomkins, et al. Concurrent Validation of the Clinical Opiate Withdrawal Scale (COWS) and Single-Item Indices against the Clinical Institute Narcotic Assessment (CINA) Opioid Withdrawal Instrument. Drug Alcohol Depend. 2009;105(1-2):154.

COWS

- Score at 0, 30, and 120 minutes:
  - Resting pulse
  - Sweating
  - Restlessness
  - Pupil size
  - Bone or joint aches
  - Runny nose or tearing
  - GI upset
  - Tremor
  - Yawning
  - Anxiety or irritability
  - Gooseflesh
- Scored 0-4/0-5 and summed:

MILD: 5-12
MODERATE: 13-24
MODERATELY SEVERE: 25-36
SEVERE: >36

Withdrawal Management

1. Alpha-agonist facilitated (and other supportive care)

2. Opioid agonist therapy

3. Naltrexone assisted (accelerated withdrawal)

4. Ultrarapid opioid detoxification

Withdrawal Management

- Alpha-agonist and supportive care:
  - Alpha-agonists – e.g., clonidine, lofexedine; block noradrenergic output from locus coeruleus
    - Treat most reported withdrawal symptoms
    - Titrate up (by 0.1-0.2mg/d) and taper down (over 5-7d)
  - GI: dicyclomine, loperamide, ondansetron
  - Insomnia: trazodone, quetiapine or zolpidem
  - Myalgias/arthralgias: APAP, NSAIDs
  - Anxiety: hydroxyzine, gabapentin, clonazepam

Withdrawal Management

Opioid Agonist Therapy (full or partial)

- Methadone: controlled withdrawal v MAT
  - Titrate up to a stabilizing dose and then taper
    - Inpatient: 20%/day (1-2 week duration)
    - Outpatient: variable models – 5%/d to 3%/wk[1]
  - Titrate up to stabilizing dose and then continue MAT
- Buprenorphine
  - Titrate up to stabilizing dose (around 16mg) and then taper
  - Various protocols with different timelines

1. Principles of Add Med p 747

Withdrawal Management

- Naltrexone-assisted[1]:
  - Day 1: abstain → withdrawal
  - Day 2: Buprenorphine 2mg q2h up to total dose of 8mg
  - Day 4: start oral naltrexone, titrate to 25-50mg over 1-4d
    - e.g., 1, 3, 6, 12.5, 25, 50mg
  - Day 5-8: 380mg XR naltrexone
  - Dosing based on daily MME/anticipated withdrawal severity
  - Adjuncts: **clonidine, clonazepam**, ibuprofen, trazodone, etc

→ *50-70% successfully initiate XR naltrexone[2]*

1. Sigmon SC, et al. Opioid Detoxification and Naltrexone Induction Strategies: Recommendations for Clinical Practice. Am. J. Drug & Alc. Abuse, 2012, 38. 187-99
2. Sullivan M, et al. Long-acting injectable naltrexone induction: A randomized trial of outpatient opioid detoxification with naltrexone versus buprenorphine. Am J Psychiatry. 2017;174:459–467.

Withdrawal Management

- Ultra-rapid Opioid Detoxification
  - General anesthesia
  - OG or IV infusion of naloxone, naltrexone or nalmefene
  - ~6 hours
  - Discharge at 24-36h
  - Complications: GI, sepsis, CV, thyroid, dysphoria and psychosis, suicide, persistent withdrawal sx (3-4c) death

Conclusions

Intoxication:

- Key OD signs: AMS, RR, miosis, track marks
- OD risk factors: past OD, sporadic use, co-ingestion
- Give naloxone and repeat as needed

Withdrawal:

- Treat withdrawal to prevent relapse
- Rx: alpha agonists + agonist/antagonist therapy
- Provide Rx and emotional support for PAWS

Thank you!

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Patient Case Presentation

***Please do not attach any patient-specific files or include any Protected Health Information.**

1. Date: Thursday, February 20, 2020
2. Presenter Name: Geoffrey Watters
3. Presenter Organization: University of Wisconsin - Madison
4. ECHO ID: 7042
5. Have you presented this patient during this teleECHO clinic before? ☐ Yes ☒ No

6. Please state your main question for this case: **Given the date/time of patient's last use of opioids, COWS scores, and self-report of withdrawal symptoms, what was the optimal time for initiating buprenorphine therapy in this case?**

Patient Demographic Information:

7. Age: 27
8. Sex: Male
9. Education/Literacy: Graduated high school
10. Income source: Unemployed
11. Social Factors/History:
    - Homeless, sleeping at home of friends' or in abandoned buildings. Living with mother for brief period but not welcome back due to drug use.
    - Release from jail 1/23/2020, pending court date 2/27 for possession charge.
    - Adverse childhood experience: witnessing physical abuse of mother in home by boyfriend.

12. **Substance Use History:**

Alcohol: First use 12 years old progressing to 12-15 beers per day after high school. Alcohol use diminishing after starting regular opioid use. Last use 1 week prior to admission.

Sedatives: Did not endorse use, will continue to assess.

Cocaine: Started smoking crack cocaine 2019, daily use ¼ gram. Last use 2/3/2020.

Stimulants: Denies, except Vyvanse as prescribed in 2014.

Marijuana: First use 11 years old, made me laugh, eat more", using with friends. currently smoking gram per day. History of synthetic cannabinoid use several times resulting in "bad trip", untreated brief psychotic episode(s). Last us 12/2019.

Opioids: Transitioned from alcohol to opioid use when 22 years old, oxycodone 30mg tabs obtained of street. Nasal use of oxycodone leading to nasal heroin and eventually IV heroin starting August 2018. Using heroin alone, up to 1 gram IV per day, last use 2/3/2020. Regularly shares needles; reports HCV diagnosis 12/2018.

Hallucinogens: Mushrooms once in 10/2017 "good trip". Denies LSD, ketamine, ecstasy.

Inhalants: Denies.

Nicotine: Started smoking 15 years old. Pack per day smoker x 7 years.

Caffeine: 2 cups coffee per day.

PDMP was reviewed, last dispensing of buprenorphine 8 mg twice daily on 1/31/2020.

13. <u>Consequences of Substance Use:</u>

- Social/occupational/educational:
  Estrangement from father who used to be primary support.
  Mother and 2 siblings have distanced themselves. "All my supports are completely gone"
  Suspension from school 8th grade, struggles to complete work in school
  Loss of employment
  Loss of apartment, homelessness
  Legal: OWI x3, last in 2015
  Unauthorized use of motor vehicle 10/2019
  Drug possession 8/2019
  Jail with release on 1/23/2020

- Physical (including evidence of tolerance/withdrawal):
  Multiple opioid overdose events, twice since release from jail past 2 weeks (rescue with Narcan by friends)
  Hepatitis C diagnosis 12/2018
  Picking at skin
  No history of abscess infection or infective endocarditis
  Rapid dose escalation with return to using, tolerance
  Using heroin to avoid daily onset of withdrawal symptoms

  * Patient reports was too sick with opioid withdrawal first day of hospitalization to participate in psychosocial interview or attend groups (isolative to room, lying in bed)

Clinical Opioid Withdrawal Scale (COWS)

	2/4 1732	2/4 2330	2/5 0600	2/5 1215	2/5 1810 Bup 8mg	2/6 0225	2/6 0920 Bup 8mg
Pulse							
Sweats		1	2	1			
Restless							
Pupil Size							
Aches	1			1			
Eyes/Nose							1
GI Upset			2	1	3		1
Tremor							
Yawning							
Anxiety				1	1		1
Gooseflesh							
SCORE	**1**	**1**	**4**	**4**	**4**	**0**	**3**

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Vital Signs (2/6 0920)

BP: 132/78
Pulse: 79
Resp: ?
Temp: 36.6 C (97.8 F)

14. Interventions that have been tried:

- Levels of care:
  Residential treatment x 3, twice for alcohol and last for OUD in 2018
  Partial Hospital Program: Non-attendance
  Three additional attempts by patient to engage in treatment past year, but unable to abstain long enough to start outpatient programs
- Medication:
  Buprenorphine/naloxone (diverting to fund heroin, cocaine use?)
  Citalopram, 2-3-month trial 2014, effective
  Lisdexamfetamine, 2 months in 2014 during residential stay, improved concentration
- Support groups in community (12-step/NA)

15.

Current Addiction and Mental Health-related Medications:	Medical/Behavioral Health Diagnosis:
• Buprenorphine (Subutex) 8 mg SL BID • Escitalopram 10 mg PO daily • Gabapentin 300 mg PO TID • Nicotine 14 mg/24H transdermal patch daily • Therapeutic multivitamin 1 tab PO daily • Hydroxyzine 25 mg PO TID PRN anxiety • Trazodone 50 mg PO nightly PRN sleep • Clonidine 0.05 mg PO Q6H, PRN • Clonidine 0.1 mg PO Q6H, PRN • Clonidine 0.15 mg PO Q6H, PRN • Clonidine 0.2 mg PO Q6H, PRN • Dicyclomine 20 mg PO Q6H PRN GI cramping • ondansetron 4 mg PO/IM Q6H PRN nausea/vomiting • Loperamide 2 mg PO 4x daily PRN diarrhea • Ibuprofen 400 mg PO Q6H PRN pain	• Opioid use disorder, severe, with substance induced mood disorder [F11.23] • Cocaine dependence [F14.20] • Nicotine dependence [F17.210] • Major depressive disorder, recurrent, moderate [F33.1] • Generalized anxiety disorder [F41.1] • Consider PTSD, mild • Consider ADD

16.

Patient Strengths/protective factors:	Risk factors:
• Identifies reasons for living • Believes he is accountable to family, feels remorse • Resilience to adverse life events • Resourcefulness	• Multiple overdoses • Witnessing overdose of friends • Daily use with high MME • Combining substances • HCV+ • Sharing needles

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	• Poor support system • Unemployment • Homelessness

17. Labs (as indicated), include summary of urine testing or last urine drug screen results:

- 2/7/2020
  Hepatitis C RT-PCR: 682,000 (non-reactive norm)
  AST: 63 (0-40 norm)
  ALT: 128 (0-41)
  HIV: Non-reactive
- 2/5/2020
  Hgb A1C: 5.0
  LDL: 35 (60-129)
  HDL: 42
  Cholesterol: 86
  Triglycerides: 44
- UDS: + OPI, + COC, +THC

18. Patient Goals/Motivations for Treatment:

"I want to live normal again" (return to former life with employment, security).
Wants to re-engage with family.
Verbalizes willingness to follow treatment recommendations.

19. Proposed Diagnoses:

Opioid use disorder, severe, with substance induced mood disorder [F11.23]
Cocaine dependence [F14.20]
Cannabis use disorder, moderate [F12.20]
Major depressive disorder, recurrent, moderate [F33.1]
Generalized anxiety disorder [F41.1]
Nicotine dependence [F17.210]
Chronic viral hepatitis C [B18.2]

20. Proposed Treatment Plan:

1. Continued stabilization of mood at inpatient level of care through use of milieu, group therapy, 1:1 contacts
2. Continued stabilization of opioid withdrawal with buprenorphine 8mg SL BID (transition to BUP-NX formulation after DC)
3. Discontinue COWS
4. SSRI therapy with escitaopram to address mood components
5. Consider prazosin for potential PTSD symptoms, hyper-startle response, sleep disturbance
6. Consider bupropion or atomoxetine to address attentional concerns (23% adults with SUD meet criteria for SUD). Possible secondary benefit with smoking cessation.
7. Discharge to residential program with direct travel from hospital to county human services intake appointment

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By initialing here ___GW____ you have acknowledged that Project ECHO case consultations do not create or otherwise establish a provider-patient relationship between any ECHO clinician and any patient whose case is being presented in a teleECHO clinic.

DSM 5 Criteria for Substance Use Disorder

A use disorder is characterized by maladaptive use resulting in repetitive consequences over the previous 12 months. A minimum of 2-3 criteria is required for a mild substance use disorder diagnosis, while 4-5 is moderate, and 6-7 is severe (American Psychiatric Association 2013)

1. Taking the substance in larger amounts and for longer than intended
2. Wanting to cut down or quit but not being able to do it
3. Spending a lot of time obtaining the substance
4. Craving or a strong desire to use
5. Repeatedly unable to carry out major obligations at work, school, or home due to use
6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by use
7. Stopping or reducing important social, occupational, or recreational activities due to opioid use
8. Recurrent use in physically hazardous situations
9. Consistent use despite acknowledgment of persistent or recurrent physical or psychological difficulties from using
10. *Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. (Does not apply for diminished effect when used appropriately under medical supervision)
11. *Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)

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