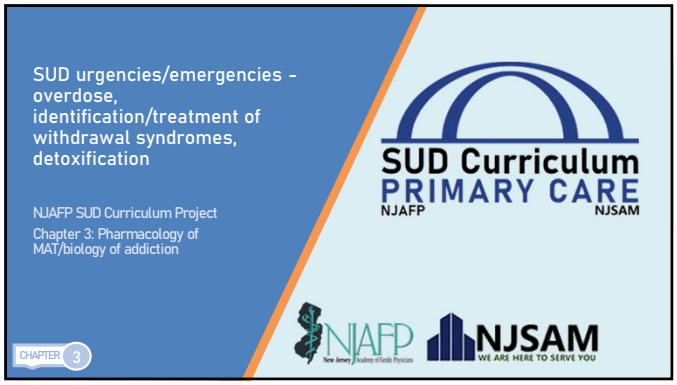
SUD urgencies/emergencies - overdose, identification/treatment of withdrawal syndromes, detoxification
NJAFP SUD Curriculum Project
Chapter 3: Pharmacology of MAT/biology of addiction
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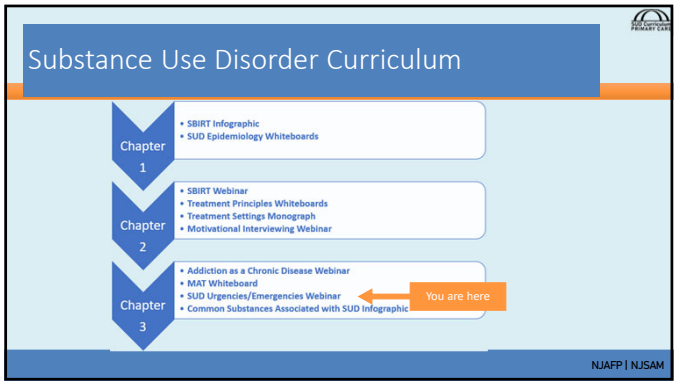
Substance Use Disorder Curriculum
Chapter 1
• SBIRT Infographic
• SUD Epidemiology Whiteboards
Chapter 2
• SBIRT Webinar
• Treatment Principles Whiteboards
• Treatment Settings Monograph
• Motivational Interviewing Webinar
Chapter 3
• Addiction as a Chronic Disease Webinar
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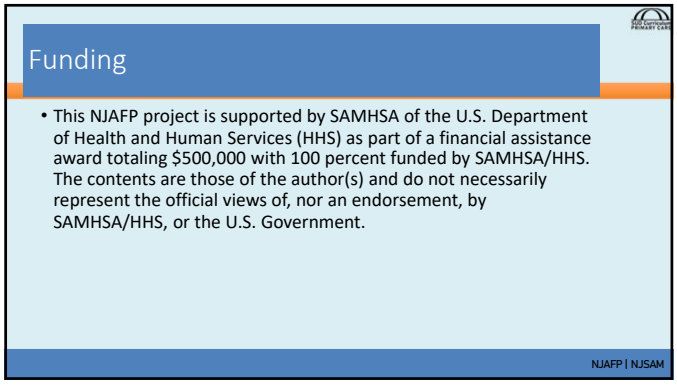
Funding
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3

Disclosures

The following individuals have no relevant financial relationships with ineligible companies to disclose:

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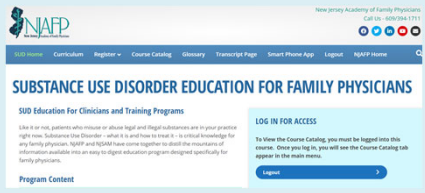
- Lee Radosh, MD, FASAM, FAAFP

4

Following this Presentation….

- Please return to the course page for CME information and references



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SUD urgencies/emergencies – overdose, identification/treatment of withdrawal syndromes, detoxification

Lee Radosh, MD, FASAM, FAAFP
Lee.radosh@towerhealth.org

6

Overdose background statistics

- From 1999–2018, almost 450,000 people died from an overdose involving any opioid, including prescription and illicit opioids (CDC.gov)
- This rise can be outlined in three distinct waves

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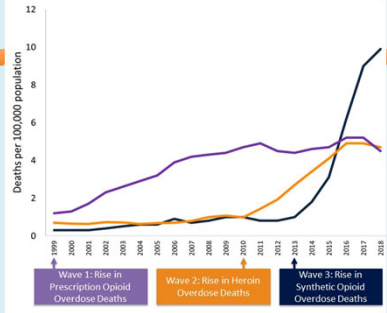
Wave in rise of opioid overdose deaths

1990s
- Increased prescribing of natural and semi-synthetic opioids and methadone since at least 1999

2010
- Rapid increases in overdose deaths involving heroin

2013
- Significant increases in overdose deaths of synthetic opioids illicitly manufactured fentanyl
- The market for illicitly manufactured fentanyl continues to change
- Can be found in combination with heroin, counterfeit pills, and cocaine



CDC. https://www.cdc.gov/drugoverdose/epidemic/index.html

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Signs and symptoms of an opioid overdose

- Breathing can be dangerously slowed or stopped, causing brain damage or death
- Important to recognize the signs and act FAST
- Distinguish between:
  - Potentially life-threatening overdose vs.
  - "Nodding off" (patient is almost unarousable yet breathing/ oxygenation is fine)
- When in doubt, err on the side of caution and assume an overdose

- Signs/symptoms can include:
  - Small, constricted "pinpoint pupils"
  - Falling asleep or loss of consciousness
  - Slow, shallow breathing
  - Choking or gurgling sounds
  - Limp body
  - Pale, blue, or cold skin

CDC. https://www.cdc.gov/drugoverdose/patients/materials.html

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Naloxone overview

- Opioid antagonist
- Designed to rapidly reverse an opioid overdose (OD)
- Can very quickly restore normal respiration
  - NOT used for methamphetamines, cocaine, benzodiazepines OD
- People given naloxone should be observed:
  - Constantly until emergency care arrives, and
  - At least 2 hours by medical personnel after the last dose of naloxone to make sure breathing does not slow or stop again
- Can cause withdrawal symptoms
  - Rapid heart rate, sweating, nausea, vomiting, fluctuations in blood pressure and tremor
  - May be very uncomfortable, but not life-threatening
  - Patient may be agitated/aggressive

NIDA. https://www.drugabuse.gov/publications/drugfacts/naloxone

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"Naloxone is that stuff that you stick through the heart, like in that movie *Pulp Fiction*, right?"

- "No, while naloxone does have an injectable form, it is never injected into the heart . . .
- The injectable form of naloxone is injected either intravenous or intramuscularly . . .
- However, the dramatic difference between the character overdosing and the character after receiving the medicine that is depicted in the film is a possible scenario with naloxone"

National Harm Reduction Coalition. https://harmreduction.org/issues/overdose-prevention/overview/overdose-faqs/

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11

FDA-approved Naloxone formulations

1. Injectable
   - Professional training required
2. Auto-injectable (trade name, Evzio)
   - Prefilled auto-injection device - makes it easy for families or emergency personnel to inject naloxone quickly into the outer thigh
   - Once activated, the device provides verbal instruction to the user describing how to deliver the medication (like automated defibrillators)
3. Nasal Spray (trade name, Narcan)
   - Prefilled, needle-free device that requires no assembly
   - Sprayed into one nostril while patients lay on their back

NIDA. https://www.drugabuse.gov/publications/drugfacts/naloxone

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Naloxone and Pennsylvania

- Act 139 (2014) provides immunity from prosecution for those responding to and reporting overdoses
- "Family , friends and individuals at risk of opioid overdose can access this medication from a pharmacy by obtaining a prescription from their family doctor or by using the standing order . . . issued by Rachel Levine, M.D., Secretary of Health."
- Covered by insurance and/or can get for free in most counties through organizations

PA DOH. https://www.health.pa.gov/topics/disease/Opioids/Pages/Naloxone.aspx

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Naloxone and New Jersey

- "State law allows physicians to prescribe Naloxone (Narcan ®) to anyone in a position to assist others during an overdose (e.g., bystanders). This is called third party prescribing."
- "The Department of Health will issue a standing order to any licensed pharmacist in good standing with the New Jersey Board of Pharmacy to dispense naloxone."

NJ DOH. https://nj.gov/health/integratedhealth/services-treatment/naloxone.shtml

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14

Withdrawal management

- GOAL: provide medical and psychological care of patients who are experiencing withdrawal symptoms as a result of ceasing or reducing use of their drug of dependence
- Withdrawal symptoms vary according to the drug of dependence and severity of dependence

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Opioid withdrawal management

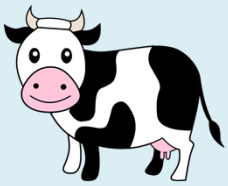
- COWS (clinical opioid withdrawal scale)
- Could be administered 1-2 times daily
- Use the COWS to select an appropriate management strategy as patients go through withdrawal
  - Mild withdrawal symptoms (COWS score 0-8 or 0-10)
    - Symptomatic treatment given
  - Moderate withdrawal symptoms (8-20 or 10-20)
    - Symptomatic treatment along with opioid medications such as buprenorphine or (less commonly) methadone

NIDA. https://www.drugabuse.gov/sites/default/files/ClinicalOpiateWithdrawalScale.pdf

16

Figure 1: Clinical Opiate Withdrawal Scale (COWS)

Sign or Symptom	Score
Heart Rate	< 80 = 0 81-100 = 1 101-120 = 2 > 120 = 4
Sweating	None = 0 Subjective report = 1 Flushed or moist face = 2 Beads of sweat on face = 3 Sweat streaming of face = 4
Restlessness	Able to sit still = 0 Subjective reports of restlessness = 1 Frequent shifting or extraneous movements = 3 Unable to sit still for longer than a few seconds = 5
Pupil size	Normal or small = 0 Pupils possibly larger than appropriate = 1 Pupils moderately dilated = 2 Pupils so dilated that only rim or iris visible = 5
Bone or joint aches	None = 0 Mild diffuse discomfort = 1 Subjective reports = 2 Patient actively rubbing joints or muscles = 4
Rhinorrhea or lacrimation	None = 0 Congestion or moist eyes = 1 Rhinorrhea or lacrimation = 2 Nose constantly running or tears streaming = 4
Yawning	None = 0 Yawning 1-2 times = 1 Yawning > 3 times = 2 Yawning several times per minute = 4
Anxiety or irritability	None = 0 Subjective report = 1 Patient appears anxious = 2 So irritable that cannot participate in assessment = 4
Gooseflesh	Smooth skin = 0 Piloerection can be felt = 3 Prominent piloerection = 5



Taming the SRU. https://www.tamingthesru.com/blog/diagnostics/opioid-withdrawal-therapy

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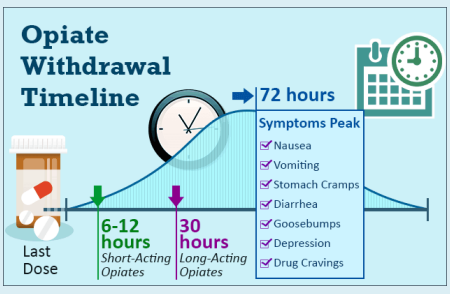

Dr. Stacy Green. https://www.drstacygreen.com/opioid-withdrawal/

18

Symptomatic management overview

- Treatment of opioid withdrawal usually involves treating the symptoms
- These so-called "comfort" medications are (mostly) off-label for opioid withdrawal
- Typically, these are used the first 24 hours since the last opioid dose

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19

Commonly utilized comfort medications

- Anti-emetics, such as promethazine
- Analgesics, such as ibuprofen and/or acetaminophen
- Muscle relaxers, such as cyclobenzaprine
- Anti-spasmodics, such as dicyclomine
- Anti-anxiety medications, such as clonidine or propranolol
- Hypnotics, such as trazodone

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20

Clonidine

- Commonly used "comfort" medication
- Alpha-2 adrenergic agonist
- Can provide relief of many physical symptoms of opioid withdrawal
  - Sweating, diarrhea, vomiting, abdominal cramps, chills, anxiety, insomnia, and tremor
- Can also cause drowsiness, dizziness and low blood pressure
- Continue to monitor blood pressure and cease clonidine if blood pressure drops below 90/50mmHg

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Lofexidine

- Approved in 2018 for opioid withdrawal
- The only FDA approved medication for opioid withdrawal
- Like clonidine
- Anecdotally: rarely used

Am Fam Physician. 2019 Mar 15;99(6) 392-394

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Withdrawal treatment with opioid receptor partial agonists (buprenorphine)

- Buprenorphine - best opioid medication for management of moderate to severe opioid withdrawal
- Alleviates withdrawal symptoms and reduces cravings
- Partial opiate agonist
- Should only be given after the patient begins to experience withdrawal symptoms
  - Usually at least 8 hours after last taking heroin/short-acting opioid dose
    - Most providers wait at least 24 hours
  - If given too early can cause "precipitated withdrawal"

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23

Precipitated withdrawal

- Buprenorphine - high affinity for the opioid mu receptor
  - Will displace existing medications (ex, opioid agonist) already on the receptor
- If a patient gets buprenorphine too early in withdrawal (that is, when there is still an agonist on the receptor)
  - As the patient's receptors are replaced with buprenorphine (a *partial* agonist, not *full* agonist) the patient will suddenly feel withdrawal symptoms, sometimes significant
- This is called precipitated withdrawal
- "Going from a 10 to a 3"
  - The patient will feel the difference
- Management tends to be supportive
  - Comfort medications as used for typical opioid withdrawal
  - Continued administration of buprenorphine
    - Can be small, (1-2 mg) frequent (every 1-2 hours) doses
    - Can be 8mg every 2-4 hours
    - These can be helpful to "saturate" the mu receptors to provide some relief

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Withdrawal treatment with opioid receptor agonists (methadone)

- To avoid the risk of overdose in the first days of treatment, methadone can be given in divided doses
  - For example, give 30mg in two doses of 15mg morning and evening
- Can be used for longer acting opioid withdrawal
- Methadone is *occasionally* used, but *uncommon* (buprenorphine MUCH more commonly used)

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Buprenorphine dosing regimens

- Many possible, reasonable dosing regimens for buprenorphine for opioid withdrawal
- Vary based on
  - Environment (how monitored/complex can the regimen be)
  - Baseline symptoms/drug use pattern/tolerance
  - Availability of support
  - Provider/institution/program preferences
- Sample regimen
  - Day 1 - 6 mg
  - Day 2 - 8 mg
  - Day 3 - 10 mg
  - Day 4 - 8 mg
  - Day 5 - 4 mg
- Another sample regimen
  - Day 1 – 8mg
  - Day 2 – 16 mg
  - Day 3 – 8mg
  - Day 4 – 8 mg

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26

Risk of overdose after withdrawal

- All opioid dependent patients who have withdrawn from opioids should be advised that they are at INCREASED risk of overdose due to reduced opioid tolerance, especially if it has been some time (weeks to months) since their last use
- Should they use opioids again, they must use a smaller amount than usual to reduce the risk of overdose
- Review with patients AND families (they can closely monitor)

BMJ. 2003 May 3; 326(7396): 959–960
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC153851/

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27

Benzodiazepine withdrawal management

- Unlike withdrawal from other substances, withdrawal from benzodiazepines (or alcohol) can be life-threatening
- First step in benzodiazepine withdrawal management
  - Stabilize the patient on an appropriate dose of an equivalent benzodiazepine to be able to safely taper the patient
- Among the most used are diazepam, lorazepam, chlordiazepoxide, oxazepam

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28

Benzodiazepine equivalency

- Many free on-line calculators and related tools are available to help in calculations
- However, calculations and dosages are approximate
  - Clinical judgment and response to treatment is paramount
  - This is fluid: make adjustments

- Some sample equivalents
  - Alprazolam (Xanax) 0.5-1 mg
  - Clonazepam (Klonopin) 1-2 mg
  - Lorazepam (Ativan) 2 mg
  - Chlordiazepoxide (Librium) 25 mg
  - Diazepam (Valium) 10 mg
  - Clorazepate (Tranxene) 15 mg
  - Estazolam (Prosom) 1 mg
  - Flurazepam (Dalmane) 30 mg
  - Oxazepam (Serax) 30 mg
  - Halazepam (Paxipam) 80 mg
  - Temazepam (Restoril) 15 mg
  - Triazolam (Halcion) 0.25 mg
  - Quazepam (Doral) 15 mg

https://www.benzo.org.uk/bzequiv.htm

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29

Alcohol withdrawal management

- Unlike withdrawal from other substances, withdrawal from alcohol (or benzodiazepines) can be life-threatening
- Alcohol withdrawal scale
  - CIWA, Clinical Institute Withdrawal Assessment
  - Depending on scenario, should be administered every 4-8 hours to gauge someone's severity

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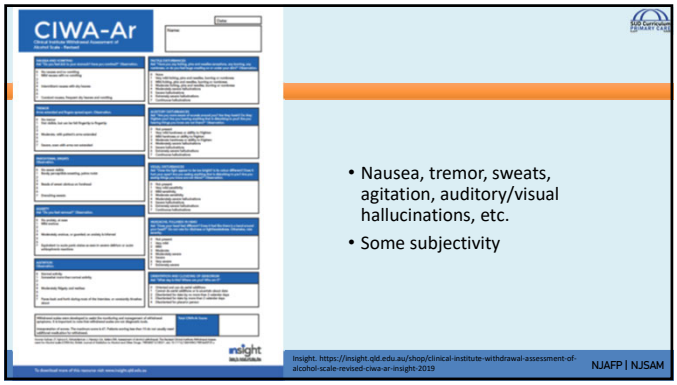
30



31

Mild withdrawal (1-10 CIWA) treatment

- "Mild" varies
  - Some consider 1-4, some 1-7, etc.
- Insomnia - 10-30 mg of po temazepam
- Abdominal cramps – dicyclomine 10-20 mg po qid propantheline 15 mg po tid
- Nausea/vomiting - promethazine po 25-75 mg or metoclopramide 10 mg po or IM as required tid
- Mineral supplementation - folate 1 mg and thiamine 100 mg po daily

ASAM. (2020) *Alcohol Withdrawal Management* https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_2

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32

Moderate withdrawal (CIWA 10-18) treatment

- "Moderate" varies
  - Some consider 5-14, etc.
- Symptomatic treatment like mild withdrawal symptoms treatment
- Add diazepam or chlordiazepoxide taper
  - Often over 7-14 days
- If liver impairment (3X above normal LFT's) use lorazepam or oxazepam
- Some would start benzodiazepines at CIWA 8 or even lower

ASAM. (2020) *Alcohol Withdrawal Management* https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf?sfvrsn=ba255c2_2

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Severe withdrawal (CIWA >=19) treatment

- Patients should be in a heavily monitored setting
- May involve VERY large amounts of benzodiazepines
  - Many times greater than would be prescribed for patients in moderate alcohol withdrawal
  - For example, 20mg diazepam (or lorazepam, or other) by mouth every 1-2 hours until symptoms are controlled, and CIWA score is less than 5
  - Sometimes patients get 20, 30, 40 mg lorazepam a day (in addition to "standing" chlordiazepoxide)
- Monitor the patient regularly during this time for excessive sedation
- Initiate anti-seizure precautions
- May also need phenobarbital, other interventions

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34

Delirium Tremens (DT's)

- 1st recognized in 1813
- More than 50% of those with a history of alcohol abuse can exhibit alcohol withdrawal symptoms
- However, only a few (3% to 5%) exhibit symptoms of severe alcohol withdrawal:
  - Profound confusion
  - Autonomic hyperactivity
  - Cardiovascular collapse
- Can occur as early as 48 hours after abrupt cessation of alcohol in those with chronic abuse and can last up to 5 days
- Mortality of up to 37% without appropriate treatment

Rahman A, Paul M. Delirium Tremens. https://www.ncbi.nlm.nih.gov/books/NBK482134/

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35

Issues To Consider in Determining Whether Inpatient or Outpatient Detoxification Is Preferred

Considerations	Indications
Ability to arrive at clinic on a daily basis	Necessary if outpatient detoxification is to be carried out
History of previous delirium tremens or withdrawal seizures	Contraindication to outpatient detoxification: recurrence likely; specific situation may suggest that an attempt at outpatient detoxification is possible
No capacity for informed consent	Protective environment (inpatient) indicated
Suicidal/homicidal/psychotic condition	Protective environment (inpatient) indicated
Able/willing to follow treatment recommendations	Protective environment (inpatient) indicated if unable to follow recommendations
Co-occurring medical conditions	Unstable medical conditions such as diabetes, hypertension, or pregnancy: all relatively strong contraindications to outpatient detoxification
Supportive person to assist	Not essential but advisable for outpatient detoxification

SAMHSA. https://store.samhsa.gov/sites/default/files/d7/priv/sma15-4131.pdf

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36

So . . . what next?

- After the emergency (detox, withdrawal) what next?
- Recovery *begins* after detox/rehab
  - Common misconceptions
    - *"You just got out of rehab? That's great, you're cured"*
    - *"You have a problem with alcohol? Just go to rehab."*
  - Start of a long journey
- Always think next steps
  - CRS (certified recovery specialist), naloxone Rx, MAT, counseling, inpatient rehab, etc.
- "Strike while the iron is hot"

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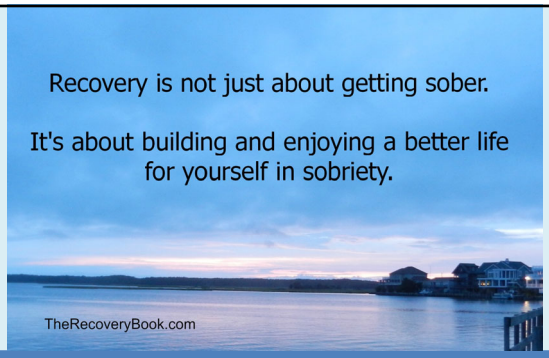
37



https://therecoverybook.com/

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38

Summary

- Know the signs and symptoms of an opioid overdose
- Naloxone – encourage/Rx often
  - When in doubt, administer
- Use tools such as the COWS (for opioids) and CIWA (for alcohol) to help guide withdrawal management
- Consider symptomatic medications ("comfort medications")
- Buprenorphine (Ex, Suboxone) for opioid withdrawal
  - Watch timing – avoid precipitated withdrawal
- Benzodiazepines for alcohol and benzodiazepine withdrawal

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39

Questions are welcome!

Please send any questions for the faculty to shockenberry@njafp.org

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40

Completing this Course

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71 Uhvlghqw/frxuvh frp sdnwhrq z kbeh orjjhg wr |rxu wudqvfulsw

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41

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- Other Physicians: Return to the Course Catalog for more CME accredited SUD courses

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42

43