



POMA
Substance Use Disorder
Education Series
LIVE WEBINAR

Session I

“MAT and the Disease Model of Addiction” – Karen Arscott, DO
 “The Management of Withdrawal and Overdose” – Eric Millie, DO

1

Drug Withdrawal/ Overdose

Eric J Millie DO

2

Objectives

Upon completing this lecture, the learner should:

- Recognize common trends in substance use disorder and how they pertain to morbidity/mortality on a national level
- Describe therapeutic interventions to assist patients with withdrawal from various substances of abuse
- Incorporate treatment strategies and clinical decision making when faced with a potential drug overdose

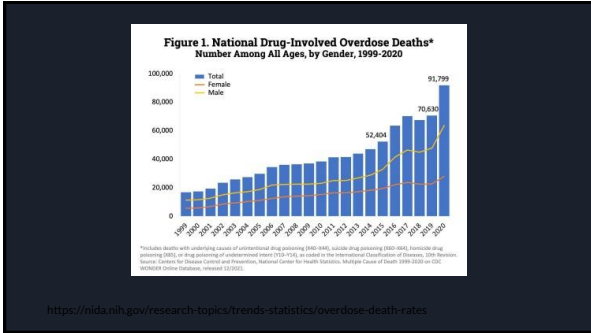
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Substance Use Disorder Statistics

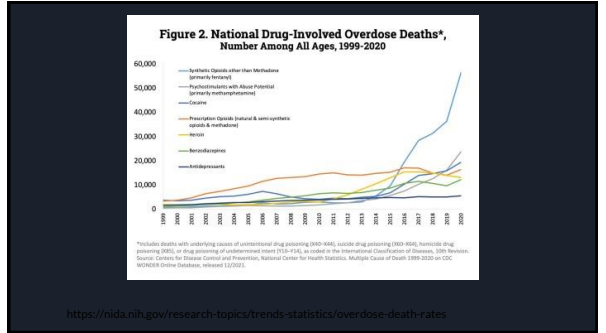
From the National Center for Drug Abuse Statistics and the CDC:

- 50% of individuals over the age of 12 have used an illicit substance
- Over 932,000 people have died of drug overdose since 1999 (over 1 million now)
 - 75% of overdose deaths in 2020 involved opiates, number is growing
 - Deaths involving stimulants (ie methamphetamine) are growing +/- concomitant opiate use

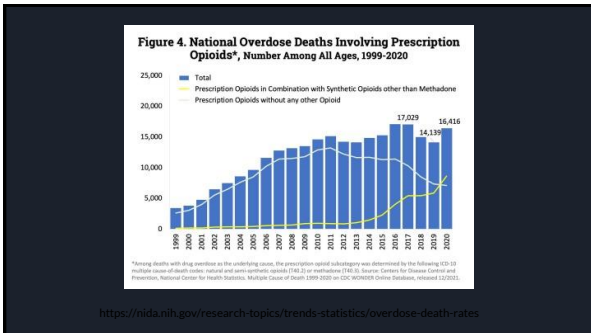
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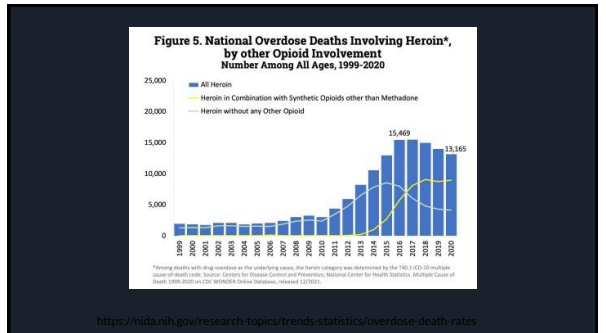
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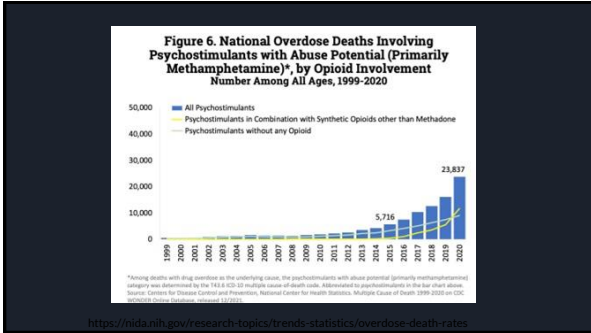
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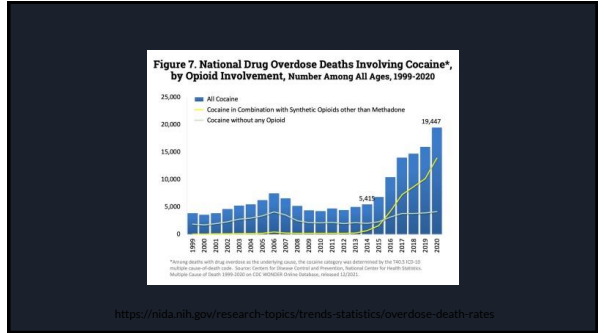
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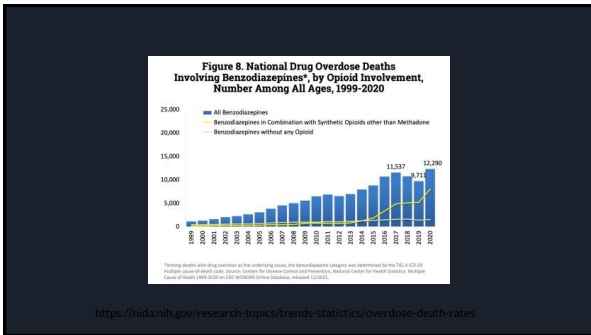
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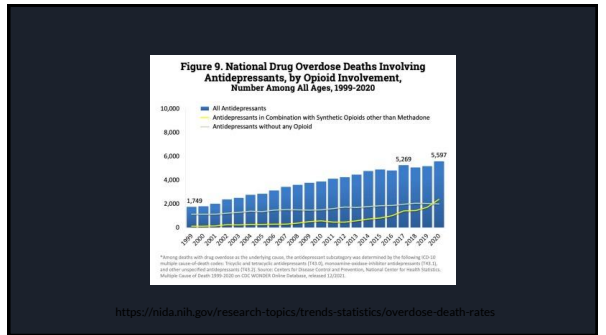
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12

Substance Use Disorder

Criteria for Substance Abuse Disorders

- Loss of control over the substance
- Neglecting other parts of your life because of substance use
- Continuing to use, even when it causes problems in relationships
- Using substances even when it puts you in danger
- Having to use larger amounts or for longer
- Having to use more of the substance to get the same effect
- Experiencing withdrawal symptoms

<https://www.cdc.gov/ncbddd/mentalhealth/pamphlets/2018/5-criteria-for-substance-use-disorder-21926>

13

| | DSM-IV Abuse ^a | | DSM-IV Dependence ^b | | DSM-5 Substance Use Disorders ^c |
|--|---------------------------|----------------|--------------------------------|---|--|
| Hazardous use | X | } ≥1 criterion | - | } | X |
| Social/interpersonal problems related to use | X | | - | | X |
| Neglected major roles to use | X | | - | | X |
| Legal problems | X | | - | | - |
| Withdrawal ^d | - | } ≥3 criteria | X | } | X |
| Tolerance | - | | X | | X |
| Used larger amounts/longer | - | | X | | X |
| Repeated attempts to quit/control use | - | | X | | X |
| Much time spent using | - | | X | | X |
| Physical/psychological problems related to use | - | | X | | X |
| Activities given up to use | - | | X | | X |
| Craving | - | - | - | X | |

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3767415/>

14

Addiction vs Dependence

| | |
|--|--|
| <p>Addiction:</p> <ul style="list-style-type: none"> - Compulsive use of a substance despite negative consequences - Addiction does not affect every person who is repeatedly exposed to a substance - Combination of genetic and environmental factors - Physical changes in the brain | <p>Dependence</p> <ul style="list-style-type: none"> - Body functions normally only in presence of substance - Leads to tolerance with repeated exposure - Stopping exposure leads to withdrawal |
|--|--|

15

Drug Withdrawal

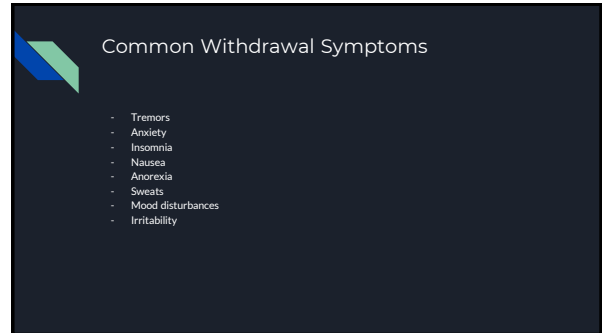
What Drugs can cause withdrawal symptoms:

- CNS Depressants: Alcohol, Benzodiazepines, Barbiturates, Opiates
- CNS Stimulants: Cocaine, Amphetamine, Methamphetamine
- Marijuana
- Nicotine

16



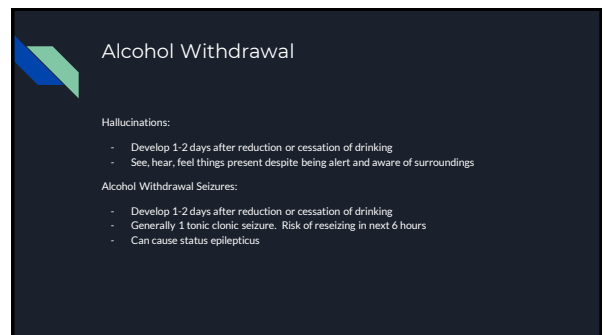
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18



19



20

Delirium Tremens

- Develops 1-4 days after cessation or reduction of alcohol consumption
- Preceded by autonomic signs (elevated HR, elevated temp, elevated BP, elevated agitation)
- Not the simple "shakes" common with alcohol withdrawal
- 5% of patients with DT die from metabolic, cardiovascular, or infectious cause

21

Delirium Tremens: Risk Factors

- Severity of alcohol use disorder
- Length of alcohol use disorder
- Previous episode of DT
- Abnormal liver function
- Concomitant acute illness
- Older age
- More severe withdrawal symptoms

22

Clinical Institute Withdrawal Assessment for Alcohol – revised (CIWA-Ar) scale

| Symptoms | Range of scores |
|-----------------------------------|---|
| Nausea or vomiting | 0 (no nausea, no vomiting) – 7 (constant nausea and/or vomiting) |
| Tremor | 0 (no tremor) – 7 (severe tremors, even with arms not extended) |
| Profuse/sweats | 0 (no sweat visible) – 7 (drenching sweats) |
| Anxiety | 0 (no anxiety, at ease) – 7 (acute panic states) |
| Agitation | 0 (normal activity) – 7 (constantly trashes about) |
| Tactile disturbances | 0 (none) – 7 (continuous hallucinations) |
| Auditory disturbances | 0 (not present) – 7 (continuous hallucinations) |
| Visual disturbances | 0 (not present) – 7 (continuous hallucinations) |
| Headache | 0 (not present) – 7 (extremely severe) |
| Orientation/clouding of sensorium | 0 (oriented, can do serial additions) – 4 (Disoriented for place and/or person) |

23

CIWA-Ar Tool

Score Grading

- Less than 8 = mild withdrawal
- 8-15 = moderate withdrawal
- >15 = severe withdrawal, potential for adverse outcomes

Score interpretation

- CIWA-Ar <8: No pharmacologic treatment necessary
- CIWA-Ar 8-15: May be appropriate to prevent development of adverse outcomes
- CIWA-Ar >15: Treatment indicated

Mirajello A et al. Identification and Management of Alcohol Withdrawal Syndrome. *Drugs*. 2015 Mar; 75(3):329-353.
Kaltman S, Bharadwaj B. Clinical management of alcohol withdrawal: A systematic review. *Int Psychiatry J*. 2013 Jul-Dec; 22(2):100-108.

24

Alcohol Withdrawal Treatment

- Mainstay of treatment = long acting benzodiazepines (diazepam, lorazepam, chlordiazepoxide)
- Benzo and alcohol cross tolerant: tolerant of one, tolerant of the other
- Deficiency of one can be treated with addition of other agent
- Reduces development of DT and withdrawal seizure
- Fixed dose vs symptom triggered dosing
- Lorazepam for those with significant liver disease

Other medications used in treatment of alcohol withdrawal include: clonidine, phenobarbital, carbamazepine

25

Opioid Withdrawal

- Nausea/vomiting
- Diarrhea
- Insomnia
- Anxiety
- Fever
- Tachycardia
- Sweating
- Cramping
- Chills
- Elevated BP

26

Table 1. Typical Withdrawal Characteristics of Various Opioids

| Opioid | Half-Life (Adults) | Onset of Withdrawal Symptoms After Exposure | Onset of Withdrawal Symptoms After Prenatal Exposure | Typical Duration of Withdrawal |
|---------------|---------------------|---|--|--|
| Heroin | 2-6 min* | 6 h | 24-48 h | 8-10 days |
| Methadone | 8-150 h (mean 35 h) | 24-96 h | 48-72 h | 10-14 days, secondary withdrawal as long as 6 mo |
| Buprenorphine | Mean 37 h | 6-24 h | 36-60 h | Milder withdrawal than other opioids. Usually resolves within 7 days, but may be prolonged in neonates |
| Morphine | 1.5-7 h | 8-12 h | ND | 7-10 days |
| Oxycodone | 3-5 h | 6-12 h | 36-72 h | 7-14 days, secondary withdrawal as long as 6 mo |
| Hydrocodone | 7-9 h | 8-12 h | 24-96 h | 5-14 days, secondary withdrawal as long as 6 mo |
| Fentanyl | 11-36 h (mean 21 h) | 3-5 h | ND | 4-5 days |

* Heroin is metabolized to morphine-6-glucuronide and morphine.
 min: minute; ND: no data available.
 Source: *Reference 6, 5, 11, 12, 14, 16, 18, 25.*

<https://www.upharmacist.com/article/acute-opioid-withdrawal-identification-and-treatment-strategies>

27

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

COWS Clinical Opiate Withdrawal Scale

| | | |
|---|--|--|
| Timing of Pain Scale 0 No pain 1 Mild to moderate pain 2 Moderate to severe pain 3 Severe pain 4 Pain more than 12h | Respirations 0 Normal 1 Mildly depressed 2 Moderate 3 Severe 4 Tachypnea or hyperpnea 5 Multiple episodes of hiccups or vomiting | CGT (past week last 24 hours) 0 No CGT 1 Mild 2 Moderate 3 Severe 4 Multiple episodes of hiccups or vomiting |
| Energy level (12 hours not assessed by the caregiver or patient) 0 No report of chills or sweating 1 No report of chills or sweating 2 Flushed or abnormal sweating 3 Flushed or abnormal sweating or chills 4 Flushed or abnormal sweating or chills 5 Flushed or abnormal sweating or chills 6 Flushed or abnormal sweating or chills | Thirst (abstinence of opiate for 24 hours) 0 No thirst 1 Mild thirst 2 Moderate thirst 3 Severe thirst 4 Multiple episodes of hiccups or vomiting | Thirst (abstinence of opiate for 24 hours) 0 No thirst 1 Mild thirst 2 Moderate thirst 3 Severe thirst 4 Multiple episodes of hiccups or vomiting |
| Tolerance (other opiate drug assessment) 0 Able to do 10h 1 Unable to do 10h 2 Unable to do 10h 3 Unable to do 10h 4 Unable to do 10h 5 Unable to do 10h | Thirst (abstinence of opiate for 24 hours) 0 No thirst 1 Mild thirst 2 Moderate thirst 3 Severe thirst 4 Multiple episodes of hiccups or vomiting | Thirst (abstinence of opiate for 24 hours) 0 No thirst 1 Mild thirst 2 Moderate thirst 3 Severe thirst 4 Multiple episodes of hiccups or vomiting |
| Pupil size 0 Pupil pin-point or normal size for room light 1 Pupil pin-point or normal size for room light 2 Pupil pin-point or normal size for room light 3 Pupil pin-point or normal size for room light 4 Pupil pin-point or normal size for room light 5 Pupil pin-point or normal size for room light | Adrenaline (abstinence) 0 None 1 Mild 2 Moderate 3 Severe 4 Multiple episodes of hiccups or vomiting | Adrenaline (abstinence) 0 None 1 Mild 2 Moderate 3 Severe 4 Multiple episodes of hiccups or vomiting |
| Diarrhea or loose stools (patient not having pain previously, only the additional symptoms assessed - cannot be assessed if patient is in pain) 0 No diarrhea or loose stools 1 Mild diarrhea or loose stools 2 Moderate diarrhea or loose stools 3 Severe diarrhea or loose stools 4 Multiple episodes of hiccups or vomiting | Diarrhea (abstinence) 0 None 1 Mild 2 Moderate 3 Severe 4 Multiple episodes of hiccups or vomiting | Diarrhea (abstinence) 0 None 1 Mild 2 Moderate 3 Severe 4 Multiple episodes of hiccups or vomiting |
| Empty stomach (Nausea/vomiting or loss of appetite or anorexia) 0 No empty stomach 1 Mild empty stomach 2 Moderate empty stomach 3 Severe empty stomach 4 Multiple episodes of hiccups or vomiting | Empty stomach (Nausea/vomiting or loss of appetite or anorexia) 0 No empty stomach 1 Mild empty stomach 2 Moderate empty stomach 3 Severe empty stomach 4 Multiple episodes of hiccups or vomiting | Empty stomach (Nausea/vomiting or loss of appetite or anorexia) 0 No empty stomach 1 Mild empty stomach 2 Moderate empty stomach 3 Severe empty stomach 4 Multiple episodes of hiccups or vomiting |

Score: 0-12 mild, 13-24 moderate, 25-36 moderately severe, more than 36 = severe withdrawal

28

COWS Scoring

- Mild: 12 or less
- Moderate: 13-24
- Moderately Severe: 25-36
- Severe: 37 or greater

29

Opioid Withdrawal Treatment

Methodone

- Mu- and NMDA-agonist
- Slow onset of action, longerr course of action, milder symptoms
- Drawbacks: QT prolongation, CYP450 activation
- Analgesic effect shorter than pharmacologic half life, can lead to respiratory depression if used for pain

Buprenorphine

- Mu-receptor agonist/ antagonist
- More favorable side effect and safety profile than methadone
- Available in many different forms, some of which are abuse deterrent
- Suboxone: buprenorphine/ naloxone combination for withdrawal/ dependence

30

Opioid Withdrawal Treatment

Clonidine

- Helps alleviate symptoms of opioid withdrawal
- Can shorten treatment duration of acute opioid withdrawal
- Limiting factor orthostatic hypotension

31

Chronic Opioid Withdrawal

- Can begin at 6 weeks post acute withdrawal, last up to 26 weeks
- Characterized by inflammation, EEG changes, hypotension, bradycardia, myalgias, and decreased respiratory drive
- Cause for relapse
- Can be mitigated with MAT

32

Sedative-Hypnotic Withdrawal

Symptoms:

- Anxiety
- Insomnia
- Restlessness/ agitation
- Aches and pains
- Hyperacusis
- Coryza
- Nightmares
- Vision changes
- Hyperreflexia
- Ataxia

33

Sedative-Hypnotic Withdrawal

Four categories:

- Symptom recurrence or relapse
 - Symptoms of anxiety/ insomnia return
- Rebound
 - Higher intensity of the symptoms for which benzo written
- Pseudowithdrawal
 - Apprehension leads to symptoms, outside influences factor in
- True Withdrawal
 - Symptoms as described earlier

34

Post-Acute Withdrawal Syndrome

- Symptoms last for weeks to months after discontinuation
- Symptoms often wax and wane
- Irregular, unpredictable, no linear pattern
- Symptoms include:
 - Insomnia
 - Perceptual disturbances
 - Anxiety
 - Sensory hypersensitivities

35

Factors Influencing Sedative-Hypnotic Withdrawal

- Length of treatment
- Dosage
- Long vs short acting
- Potency
 - Alprazolam and Triazolam worst: short acting and potent, develop tolerance quickly
- Concomitant substance use
- Family history (ETOH use)
- Medical comorbidities
- Age (younger better than older)

36

Treatment Approach

- Minimal intervention
 - Deliver simple advice
 - Favorable outcomes in low doses of medication
- Systematic discontinuation
 - Tapering, either on its own or in combination with replacement
 - May need to be done inpatient or medically monitored if patient with underlying mental health or other SUD

37

Other Substance Use Withdrawals

- Stimulants
 - Depression, fatigue, concentration difficulties, anergia, anhedonia
 - Symptoms mild, no hospital, last 1-2 weeks
- Hallucinogens
 - NO WITHDRAWAL
- Marijuana
 - 1/3 of people report symptoms, factor in relapse
- Dissociative Anesthetics
 - 1/3 people report symptoms of withdrawal
 - Anxiety, cravings, compulsions, tremor, insomnia
- Inhalants
 - No significant withdrawal
- "Club drugs"
 - GHB withdrawal similar to sedative-hypnotic withdrawal

38

OVERDOSE

General:

- Assess ABC's
- Try to obtain a history (friends, family, patient, PDMP, etc)
- Labs and Physical Exam findings
- Poison control
- Specific interventions based on above

39

Opioid Overdose

- Opioid overdose is a preventable cause of death
- Tolerance to respiratory depression lags behind tolerance to analgesia/ euphoria
- Patients who have completed withdrawal at an increased risk for overdose
- Unsuspected ingestion cause of overdose as well

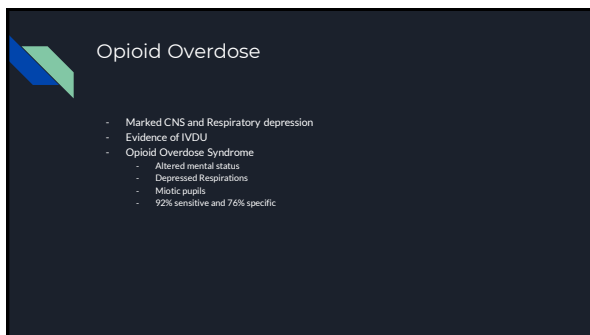
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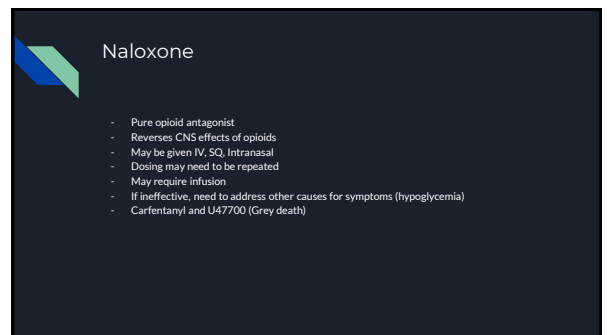
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42



43



44

Sedative Hypnotic Overdose

- Impaired motor activity, slurred speech, and ataxia
- Severe intoxication can induce stupor and coma
- Barbituates can cause respiratory and cardiac arrest at toxic levels
- Benzos rarely lethal alone, but deadly in combination with opioids, barbituates, and alcohol

45

Management of Sedative-Hypnotic Overdose

- ABC's
 - May require ET intubation, cardiac monitoring
- No activated charcoal secondary to risk of aspiration
- Flumazenil not typically used in OD, may perpetuate seizure or cardiac arrest
- Supportive care

46

Alcohol Overdose

Intoxication:

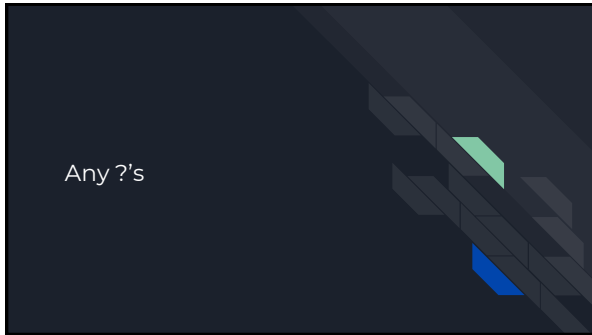
- BAL 0.02%-0.099%: loss of coordination begins, loss of inhibition, change in mood
 - Impairment begins below 0.05%
- BAL 0.10%-0.19%: neurologic impairment
- BAL 0.20%-0.299%: obvious intoxication, nausea, vomiting, ataxia
- BAL 0.30%-0.399%: hypothermia, dysarthria, amnesia, Stage I anesthesia
- BAL 0.40%-0.799%: alcohol coma
 - BAL between 0.60%-0.80% commonly fatal

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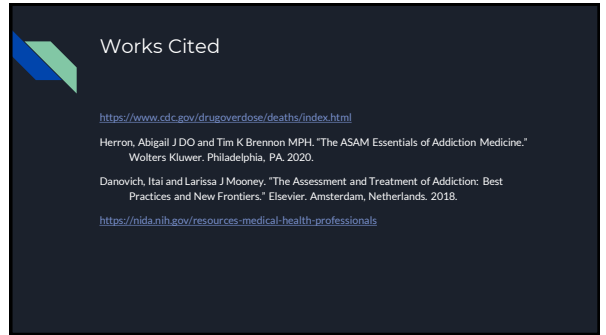
Alcohol Overdose

- Treatment is supportive
- Most will survive with respiratory/ cardiac support
- Need to rule out concomitant drug use (benzo, opioid, TCA)
- Caution about other forms of alcohol (isopropyl, ethylene glycol)
- No antidote

48



49



50