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Alcohol Use Disorder & Its Treatment

1. What is Risky Use of Alcohol?

- **Sometimes referred to as "hazardous use," "at-risk use," or "heavy drinking;" Alcohol consumption that puts one at risk for health consequences;** not severe enough to be an alcohol use disorder though individuals with Risky Use may develop an Alcohol Use Disorder.
- Risky use defined
    - **Men < 65 y/o**
        - **On average >14 drinks per week**
        - **> 4 drinks on any day**
    - **Women and adults > 65 y/o**
        - **On average > 7 drinks per week**
        - **> 3 drinks on any day**
    - **Binge drinking: Associated with acute injuries due to intoxication**
        - **Men-5 standard drinks within 2 hours**
        - **Women-4 standard drinks within 2 hours**
    - **What is a "drink"?**
        - **An accurate history can be tricky to obtain from patients.**
          Standard drink is: 12 ounces of beer; 5 ounces of wine, 1.5 ounces of liquor

2. Who is at particular risk for an Alcohol Use Disorder?

- Younger adults
- Males: 2-3x's M vs F
- Native Americans
- Adults with significant disability, other substance use disorders, or a mood disorder

3. What are common screening methods that can be used?

- SBIRT recommends the AUDIT-C
    - **How often do you drink alcohol?**
      How many drinks do you typically have when you drink?
      How often do you have 5 or more drinks on one occasion?
- Could use CAGE screen
- **Biological markers that may indicate problematic alcohol consumption are elevated liver enzymes. Elevated GGT in conjunction with increased MCV, is highly sensitive for alcohol intake above normal parameters**

4. What are the Treatment Goals?

- Research studies suggest a small number of patients may be able to resume normal or controlled drinking. This is an area of controversy. Controlled drinking is probably more likely for people with a mild disorder, not for a more severe disorder. Advocates for a harm reduction approach argue that for some patients this is an achievable aim which reduces risk to patients.
- Psychosocial treatment short term goals:
    - Support adherence to medication for Alcohol Use Disorder
    - Promote participation in other psychosocial services
    - Involve family, community, and employment resources
- Overall goals (short and long term)
    - Encourage and support abstinence (or reduction in alcohol use)

5. What Treatment Options are available?

Continuing Care Approach to Treatment

- Recognition that addiction is often chronic and relapsing.
- Emphasizes modifications in the intensiveness of treatment and the monitoring as the illness waxes and wanes over time.

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A. Psychosocial Interventions

- Brief Intervention
  - **Effective treatments for non-dependent, at-risk alcohol use;**
  - **The BI part of SBIRT (Screening, Brief Intervention, Referral to Treatment)**
- Motivational interviewing
  - Counseling technique for eliciting behavioral change by helping patient explore and resolve ambivalence about substance use and move through the stages of change (especially if pt in pre-contemplation and contemplation stages)
  - May be used in a Brief Intervention
- Cognitive Behavioral Therapy
  - Structured, goal directed form of psychotherapy in which patients learn how their thought processes contribute to their behavior.
  - Increased cognitive awareness is combined with techniques to help patients develop new and adaptive ways of behaving which in turn leads to changes in their thoughts and emotions.
  - CBT is found to have modest positive effect on outcomes for alcohol and other drug dependence compared to controlled conditions and no treatment
- Residential Treatment
  - 24 hour, drug and alcohol free environment
  - Wide variety of clinical services provided and treatment models
  - No well-designed research trials that compare effectiveness of residential treatment to lower levels of care
- Mutual Help Groups
  - AA (Alcoholics Anonymous) and other 12 step programs
  - Working towards abstinence through group sharing and support

B. Pharmacotherapy for Alcohol Use Disorder

- Several medications can be used to treat moderate-to-severe Alcohol Use Disorder leading to reduced heavy drinking and increased days of abstinence; there is little evidence for the effectiveness of medication in treatment of Risky alcohol use or mild Alcohol Use Disorder.
- Ideal patient for treatment with medication
  - Current, heavy use and ongoing risk for consequences from use
  - Motivated to reduce alcohol intake
  - Prefer medication along with, or instead of, psychosocial intervention
  - No medical contraindications to the individual drug

First line medications

- Naltrexone
  - **Mechanism of Action: Exerts effects by blockade of the mu-opioid receptor.** Endogenous opioids are involved in the expression of alcohol's reinforcing effects
  - **May be started while patient is still drinking**
    - disulfiram (Antabuse) needs to be started in abstinent patients;
    - acamprosate (Campral) ideally is used once abstinence is achieved
  - **Decreases alcohol cravings**
  - **Cannot be given to patients taking opioids**
  - **Contraindicated in patients with significant liver disease**
    - **May cause liver enzyme elevation; periodically monitor liver enzymes during naltrexone treatment**
  - **Available in long acting injectable (depot) form of Vivitrol** (cost issues, is expensive)

- **Acamprosate (Campral)**
  - Mechanism of Actions: Proposed anti-drinking mechanism is modulation of glutamate neurotransmission.
  - **Multiple meta-analyses show reduction in alcohol consumption compared to placebo, a reduced rate of returning to drinking, and an increased cumulative abstinence duration.**
  - While useful for Alcohol Use Disorder, not found to have a significant effect on Risky/Heavy Drinking.
  - **Excreted mostly unchanged by the kidneys; contraindicated in patients with renal failure but can be used safely in patients with liver disease.**

Second line medications

- Disulfiram (Antabuse)
  - **Mechanism of Action: Inhibits aldehyde dehydrogenase and prevents metabolism of alcohol's primary metabolite, acetaldehyde. Acetaldehyde accumulation in the blood causes unpleasant effects.**
  - **Needs to be started in abstinent patients**
    - After stopping the medication, the duration of drug's activity may be as long as 2 weeks.
  - Study suggests disulfiram is most effective when routinely taken under supervised conditions;

Off label/not FDA approved

- Topiramate (Topamax)
  - Some studies show it decreases alcohol use in patients with moderate-to-severe Alcohol Use Disorder.
- Gabapentin (Neurontin)
  - Some studies support use in treatment of patients with moderate-to-severe Alcohol Use Disorder;

C. Combining medications

- Offers possibility of more effective treatment but research trials have shown mixed results. Medication combination no more effective than naltrexone alone.

D. Medications vs Psychosocial Treatments

- Are no clinical trials that directly compare medications to psychosocial interventions

E. Combining Medication with Psychosocial Treatments

- Evidence is mixed as to whether the combination of medication and psychosocial treatment is more effective than medication alone.
- Studies have generally not found that combination of CBT and medications for moderate-to-severe Alcohol Use Disorder to improve outcomes versus either intervention individually

Opioid Use Disorder Treatments

Opioid Use Disorder:

- Those with an opioid use disorder typically use heroin 2-6 times per day
  IV use is rapid, most efficient means to produce euphoria; IV use, most heroin overdoses. More overdoses than intranasal, smoking, or PO
  Intranasal use is rapid enough to produce euphoria
  Smoking is the fastest route for delivering the drug to the brain

- Intoxication
  - **Natural or synthetic opioids, act at 1 of the 3 main opioid receptor systems (mu, kappa, delta)**
  - **Central nervous system depressant effects**
    - **Activation of mu receptors in the CNS results in depressant effects (respiratory depression), analgesia, and miosis. Also have the potential to cause euphoria.**
  - **Signs of Opioid Intoxication**
    - **Pinpoint pupils, drowsiness, slurred speech, impaired cognition**
- Tolerance
  - **Many users start out using heroin to get high but then need larger and larger amounts to get the same effect; Gets to the point where they must use simply to avoid withdrawal**
- Withdrawal
  - **Watering eyes, runny nose, yawning, muscle twitching, hyperactive bowel sounds, piloerection**

- Typically a chronic, relapsing illness associated with significantly increased morbidity and mortality
  - Mortality: increased mortality vs. general population, primarily due to overdose and trauma

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Treatment Options

- Often require long term treatment to prevent relapse: In general, abstaining from heroin for at least one year suggests a favorable prognosis for remaining abstinent again for a significant period of time.
- **First line treatment: an opioid agonist: methadone or buprenorphine**
  - Suppress craving and withdrawal symptoms
    Block effects of other opioids
    Studies show association of treatment duration with lower rates of mortality
  - Buprenorphine is preferred over methadone due to it being safer than methadone
  - Methadone tends to be more efficacious than buprenorphine
- **First line alternative: naltrexone PO and LAI (long acting injectable)**
  - If highly motivated pt;
  - If medication use can be supervised;
  - If pt in occupations that do not permit opioid agonist treatments
- Non-Medication options for long term treatment
  - Individual or group addiction counseling
  - Participation in mutual help groups such as Narcotics Anonymous

Opioid Agonist Medication Treatment

- **Methadone**
  - **long acting opioid agonist, binds to mu receptors**
  - also reduces euphoric effects of subsequent opioid use
  - treatment associated with reduction in spread of HIV
  - Adverse effects
    - Cardiac arrhythmias: qTc prolongation
    - Hyperalgesia-chronic use may result in increased sensitivity to pain within a month of starting chronic therapy
    - Potential for overdose-since full agonist, higher risk for OD vs. partial agonist buprenorphine
      Significantly higher risk of abuse and lethal overdose compared with buprenorphine
    - Drug-drug interactions-based on p450 system; many meds may induce or inhibit

  Methadone Administration
  - Dosing can vary widely among patients and doses do not correlate well with blood levels
  - Relatively low dose (20-30 mg) can attenuate acute opiate withdrawal but is usually not effective at suppressing craving and blocking the effects of other opioids
  - Dosing for opioid addiction differs significantly from doses used to treat chronic pain
  - Patients who take alcohol or benzodiazepines are more likely to become sedated and have risk of respiratory depression

- **Buprenorphine**
  - **Partial mu agonist with high affinity for the mu-opioid receptor; can displace full agonist opioids from the receptor and precipitate opioid withdrawal; thus pts need to be abstinent from opioid use for a sufficient period before starting this treatment**
  - **With naloxone (an opioid antagonist)**
    - **Buprenorphine is typically given in combination with naloxone in its oral form because naloxone has poor oral bioavailability and has little to no activity when administered sublingually; If given parenterally though, naloxone can precipitate withdrawal; this prevents people from attempting to abuse the combination drug by crushing the tablets and dissolving them for IV injection.**
  - Like methadone, considerable variability among patients in the dose given and blood levels produced
    - Not detected by the standard urine drug screen; needs specialized assay to detect.
  - Adverse consequences
    - Respiratory depression is typically negligible from buprenorphine alone; is seen when used in combination with other substances, especially alcohol and/or benzodiazepines
    - Lower potential for overdose than methadone
    - Can precipitate opioid withdrawal; thus pts need to be abstinent from opioid use for a sufficient period before starting this treatment

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Opioid Antagonist treatment

- Naltrexone: Prevents users from experiencing opioid intoxication or physiologic dependence
- Used for maintenance treatment and to prevent relapse in opioid use disorder

Cocaine Use Disorder

Treatment of Stimulant Use Disorders (cocaine, methamphetamine, amphetamine)

- **No medications have been shown in randomized trials to be consistently efficacious for stimulant use disorders.**
- Only psychosocial interventions have proven efficacy in reducing stimulant use, but these treatments alone are insufficient for many patients.

Cocaine Mechanism of Action

- **Enhances dopamine activity by blocking the monoamine (dopamine, norepinephrine, serotonin) pre-synaptic re-uptake pumps.**
- Cocaine's psychological effects and abuse liability are due to enhancement of brain dopamine activity especially in the corticomesolimbic dopamine reward circuit.
  - **Intoxication effects include: increased energy, alertness, and sociability; elation or euphoria; decreased fatigue, decreased need for sleep, decreased appetite.** (Sounds like a manic episode!)

Cocaine and psychiatry related disorders

- Current cocaine users twice as likely to have symptoms of depression or anxiety as non-users
  With increased dose, duration of use, or more efficient route of administration
  - Dysphoric mood, panic attacks,
  - Also grandiosity, impaired judgment, suspiciousness/paranoia/psychosis
    - In cocaine use disorder:
      80% patients report psychotic symptoms
      Visual & tactile hallucinations >> auditory hallucinations

- Associated with variety of movement disorders
  - Sterotyped behaviors, acute dystonia, choreoathetosis, and akathisia, buccolingual dyskinesias, Tardive dyskinesias
  - Cocaine users are at increased risk of acute dystonic reactions from antipsychotic medications

- Chronic use
  - Associated with cognitive impairment; will persist for at least several weeks of abstinence.
  - **Cessation of heavy use results in withdrawal syndrome with prominent psychological features (depression, anxiety, anhedonia, fatigue, increased appetite, increased sleep) but usually mild physical symptoms.**
    - Usually resolves in 1-2 weeks without treatment.

Urine Drug Testing

	Detection window for Urine test	
Amphetamines	2-3 days	
Cocaine	2-3 days	May be positive for up to 2 weeks after chronic heavy use
Marijuana	1-7 days	May be positive for 1 month with chronic moderate to heavy use
Opiates	1-3 days	
Phencyclidine	7-14 days	

Substance Induced Psychosis

- Psychosis may result from use of prescribed stimulants, alcohol, cocaine, PCP and other hallucinogens, methamphetamines, designer drugs (synthetic cannabinoids--K2, Spice) or withdrawal of alcohol or benzodiazepines
- Most instances of drug induced psychosis the substance is detectible; however cases of persistent psychosis for days or weeks after a drug is cleared have been described (especially with hallucinogens and amphetamines)