WELCOME to the

Substance Use ECHO

Session will start in less than 15 minutes

For educational and quality improvement purposes, we will be recording this video-session

By participating in this clinic you are consenting to be recorded –
we appreciate and value your participation

If you have questions or concerns, please email

ECHO@hitchcock.org

Attendance

- Spoke participants
- Hub participants

Please type your name, organization into chat

Please turn video on

Respect Private Health Information

To protect patient privacy, please only display or say information that doesn't identify a patient or that cannot be linked to a patient.

- **Names:** Please do not refer to a patient's first/middle/last name or use any initials, etc.
- **Locations**: Please do not identify a patient's county, city or town. Instead please use only the patient's state if you must.
- **Dates:** Please do not use any dates (like birthdates, etc) that are linked to a patient. Instead please use only the patient's age(unless > 89)
- **Employment:** Please do not identify a patient's employer, work location or occupation.
- **Other Common Identifiers:** Patient's family members, friends, co-workers, phone numbers, e-mails, etc.

Treatment of People with Alcohol Use Disorder

Assessment and pharmacotherapy based on 2018 APA guidelines

Mary.f.brunette@dartmouth.edu

March 2020

Conflict of Interest Disclosure Statement

No Conflicts of Interest

2. Main Take Home Points

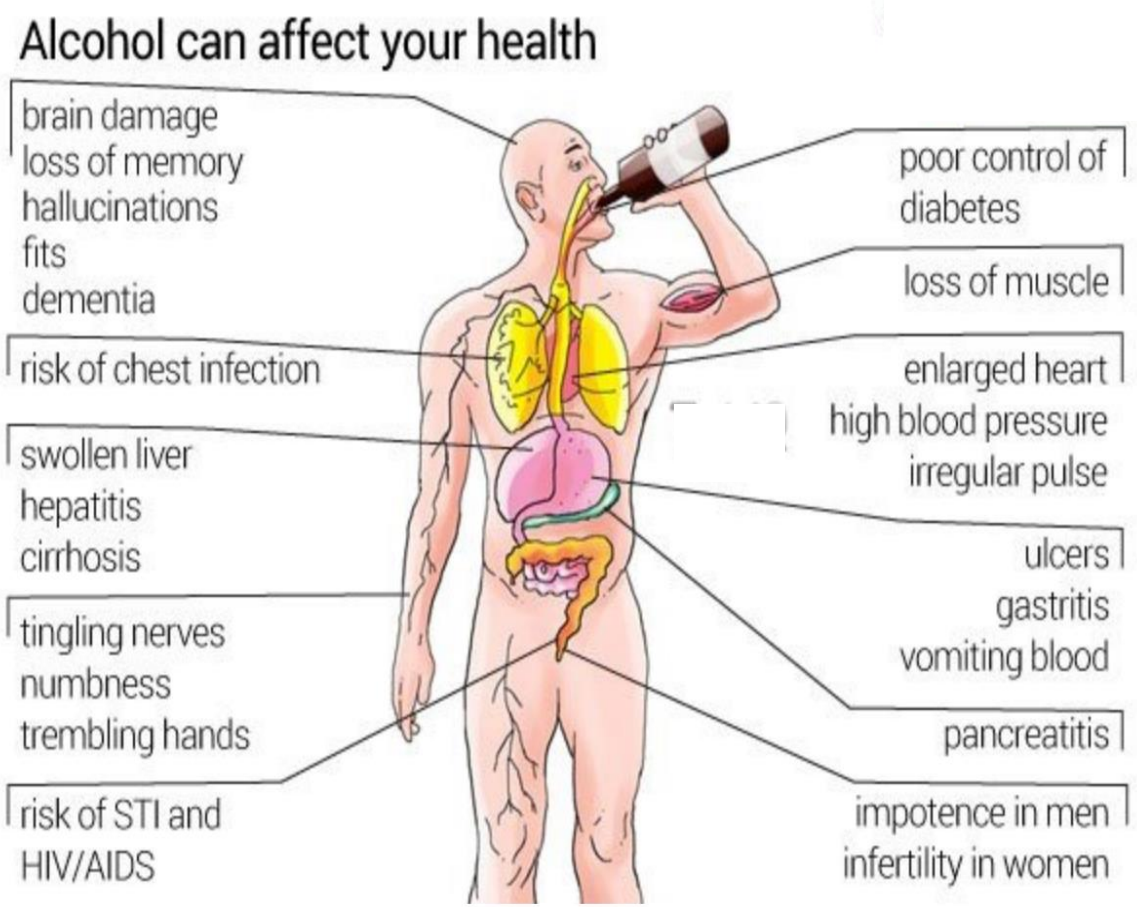
- Medications are effective for reducing drinking in people with moderate to severe alcohol use disorder (AUD)
- Medications can be combined with other therapeutic approaches

3. What is Alcohol Use Disorder (AUD)?

- **A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following symptoms, occurring within a 12 month period**
- **2-3 = mild AUD; 4-5 = moderate AUD; 6-10= severe AUD**

- Use more than intended
- Desire to cut down or control alcohol us.
- A great deal of time is spent in activities necessary to obtain or use
- Craving, or a strong desire or urge to use alcohol.
- Use resulting in a failure to fulfill major role obligations
- Continued alcohol use despite persistent problems
- Important social, occupational, or recreational activities are given up or reduced because of alcohol use
- Recurrent alcohol use in situations where it is physically dangerous
- Alcohol use is continued despite problems
- Tolerance
- Withdrawal

4. Alcohol impact on health – >14 drinks/week for men, >7 drinks/week for women (USDHHS, 2015)



20-35% of primary care patients have Alcohol Use Disorder

5. Simple Screen and Assessment

- Screen: Do you sometimes drink beer, wine or hard liquer? If yes, how many times in the past year did you have five (four for women) drinks in a day? (Any answer over 0 screens positive, including ‘not sure.’)
- Assessment: Nonjudgemental style, frequency and quantity of alcohol use, biomarkers of alcohol use, all other substances, psychiatric comorbidity

6. Determine treatment goals related to alcohol use

- Provide education on potential value of harm reduction and abstinence
- Elicit patient preferences and motivation for goals:
  - Reduce drinking
  - Avoid drinking in hazardous situations
  - Stop drinking
- Determining goals
  - Helps form therapeutic alliance
  - Provides structure for shared decision making for treatments
  - When determining goals, consider:
    - Legal obligations related to alcohol including DUI
    - Work and home responsibilities?
    - Risk to self and others

7. Develop treatment plan

Once goals are clear, develop treatment plan, to include:

1. Start with either behavioral intervention – cognitive-behavioral therapy – OR pharmacologic intervention. If not effective, combine both.
2. Self help and formal support for maintaining engagement in self-help (AA, etc)
3. Engaging and educating natural supports

8. AUD Treatment - pharmacotherapy

- Pharmacotherapy – Focus on altering reinforcing effects of alcohol use
- Use for people with moderate to severe AUD & heavy drinking

- For people who:
  - Have current heavy use and ongoing risk for consequences from use
  - Are motivated to reduce alcohol use
  - Prefer medication along with or instead of psychosocial intervention
  - Do not have medical contraindications to the individual drug

9. AUD Treatment - pharmacotherapy

- First Line Medications
  - **Naltrexone**
  - **Acamprosate**
- Second Line Medications
  - **Disulfiram**
  - Topiramate
  - Gabapentin
  - Baclofen
  - Nalmefene
  - SSRIs
  - Ondansetron
  - Varenicline

10. Naltrexone – First Line

- Works through blockade of mu-opioid receptors
  - Endogenous opioids involved in modulating expression of alcohol's reinforcing effects
  - Modifies hypothalamic-pituitary-adrenal axis to suppress ethanol consumption.
- Clinical trials found naltrexone to reduce alcohol consumption compared to placebo – tends to reduce heavy drinking among male heavy drinkers
- Can be initiated while individual still drinking
- Cannot be given to patients taking opioids
- Usual dosage:
  - Oral 50mg, 1-2 tablets/day,
  - Injectable Vivitrol 380 mg Q 4 weeks

11. Naltrexone – First Line

- Side effects oral
  - Nausea
  - Headache
  - Dizziness
- Side Effects injectable
  - Nausea
  - Fatigue
  - Decreased Appetite
- 2% increased LFTS – check before and monitor
- Avoid in acute hepatitis or liver failure; those using prescribed opioids or will need to use prescribed opioids
- Naltrexone is also effective as a monitored treatment for people with opioid use disorder who have become abstinent (it will induce withdrawal in those still using)
- Therapeutic response predicted by family hx AUD, strong cravings for alcohol

12. Acamprosate – First Line

- Modulation of glutamate neurotransmission at metabotropic-5 glutamate receptors
- Meta-analysis found drug to reduce alcohol consumption compared to placebo.
- Can be used once abstinence achieved
- Usual Dosage: 666mg 3x a day after detox and abstinence initiation
- Side effects
  - Diarrhea
  - Nervousness
  - Fatigue
- No hepatic metabolism – safe for people with liver disease
- Contraindicated in low renal function (GFR <30); reduce dose in mild-mod renal impairment
- Good choice for people who use opioids or on opioid replacement therapy
- Therapeutic response predicted by high anxiety, dependence, neg family history, late onset, female gender

13. Disulfiram – Second Line

- Inhibits aldehyde dehydrogenase & prevents metabolism of acetaldehyde
- Discourages drinking by causing unpleasant physiological reaction when alcohol is consumed
- Also effective for cocaine use d/o
- Option for those seeking abstinence who don’t want other options
- Monitoring improves efficacy

- Reaction to drinking on disulfiram
  - Sweating
  - Headache
  - Dyspnea
  - Lowered blood pressure
  - Flushing
  - Sympathetic over activity
  - Palpitations
  - Nausea
  - Vomiting

14. Disulfiram – Second Line

- Initial Dose: 500mg/day for 2 weeks
- Average Dose: 250mg/day
- Side Effects:
  - Fatigue
  - Mild Drowsiness
  - Headache
  - Dermatitis
  - Mild increase in LFT 25%, severe increase 1/20,000
  - Severe: Psychosis & Hepatitis
- Best used for people whose goal is complete abstinence and who are willing to be monitored by family or program

15. Summary

- Medications are effective for reducing drinking in people with moderate to severe AUD
- Medications can be combined with other therapeutic approaches

- Questions, discussion
- Slides on additional important components of alcohol use disorder treatment follow this slide

Simple screens for alcohol use disorder

- Do you sometimes drink beer, wine or hard liquer? If yes, how many times in the past year did you have five (four for women) drinks in a day? (Any answer over 0 screens positive, including ‘not sure.’)

- AUDIT-C (3+women, 4+men)
  - How often do you have a drink containing alcohol?
  - How many drinks containing alcohol do you have on a typical day that you drink
  - How often do you have six or more drinks on one occasion?
- CAGE (2+)
  - Have you ever felt you should **cut down**?
  - Have people **annoyed** you by criticizing your drinking?
  - Have you ever felt bad or **guilty** about your drinking?
  - Have you ever had a drink first thing in the a.m. to get rid of a hangover (**eyeopener**)?

More on Assessment

- Assess for:
  - Alcohol use AND tobacco, other drugs, including prescription and OTC medications used to relax/ get high
  - Potential comorbid psychiatric disorders, suicide and violence risk, medical disorders
  - Use interview with non-judgemental style and open-ended questions to reduce stigma and under-reporting
  - Use other sources of info
- Use quantitative behavioral measure of alcohol use frequency and severity
  - AUDIT for adults (AUDIT-C short form)
  - CRAFFT for teens

Physiologic biomarkers of recent alcohol use

APA recommendation for initial eval and ongoing monitoring

- **Ethyl Glucuronide (EtG)**
  - Conjugate product of alcohol and glucuronide
  - Present in hair and urine for 2-5 days after having a drink
  - False pos UTI (espec in diabetes)
  - False neg in accelerated urine elimination
- **Phosphatidylethanol (PEth)**
  - Product of ETOH interacting with phosphatidylcholine on erythrocyte cell membranes
  - Whole blood biomarker of recent consumption of alcohol
  - Present after daily drinking 2-4 drinks/day for few weeks
  - Remains elevated 2-3 weeks
  - 100% sensitivity

Biomarkers continued

- **CDT – isoform of transferirn, an iron transporting protein formed in the liver**
  - Increased in some genetically prone people with 1 week sustained heavy drinking
  - 60% sensitivity, 95% specificity
  - Elevated after 1 wk heavy drinking, remains high a few weeks
  - False positive with end stage liver disease, pregnancy,

- **Liver enzymes** – AST ALT, GGT – measures liver damage
- **GGT** more alcohol specific but also increases with some medications
  - False pos with obesity, smoking, diabetes, viral hepatitis

- **MCV** - Mean corpuscular volume – elevated with heavy drinking,
  - Remains elevated for 3-4 months

Topiramate – Second Line

- Sulfamate-substituted fructopyranose derivative – found to decrease alcohol use in individuals with alcohol dependence
- Has not been approved for AUD by US FDA
- 2 principal mechanisms that contribute to anti-drinking effects:
  - Antagonizing alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptors & kainite glutamate receptors
  - Facilitating inhibitory GABA(A)-mediated currents at non-benzodiazepine sites on the GABA(A) receptor.

Topiramate – Second Line

- FDA approved for treatment of seizure disorders, migraine
- Dosing: should be titrated gradually from 25mg/day -150mg x2/day (max dose) over six weeks to minimize side effects.
- Side Effects:
  - Cognitive impairment
  - Paresthesia
  - Weight Loss
  - Headache
  - Fatigue
  - Dizziness
  - Depression
  - Secondary angle closure glaucoma, metabolic acidosis, hyperammonemic encephalopathy, kidney stones, suicidal ideation and behavior

Gabapentin – Second Line continued

- Indications: Anticonvulsant, neuropathic pain med, restless legs syndrome
- Blocks alpha-d2subunit of voltage-gated calcium channel, indirectly modulating GABA transmission, normalizing stress-induced GABA activation in the amygdala
- RCTs show improved outcomes for people with AUD
- 600 mg TID (1800 mg/day) -
- Well tolerated at low & moderate dosages
- High dosages have side effects of sedation & dizziness

- Subject to abuse by some patients treated for an SUD

Varenicline – Second line

- FDA approved for treatment of tobacco use disorder
- Nicotinic receptor agonist and partial agonist
- Effective for reducing heavy drinking among heavy drinkers
- Titrate 0.5→2 mg/day in BID dosing

Baclofen – Second Line

- Indicated for treatment of spasticity related to MS
- GABA –B agonist
- Mixed results for treatment of AUD found when compared to placebo at 30mg
  - May be more effective at 60mg
- Treatment well tolerated in current trials
  - No abuse liability
  - No serious adverse effects
- Side Effects:
  - Nausea
  - Vertigo
  - Transient Sleepiness
  - Abdominal Pain

Nalmefene – Second Line

- Opioid Antagonist – found to reduce drinking in patients with alcohol dependence - Not available in the US
- Advantages of Nalmefene
  - Absence of dose-dependent liver toxicity
  - Longer-acting effects
  - More effective binding to central opiate receptors
- Side Effects:
  - Nausea
  - Insomnia
  - Fatigue
  - Dizziness
  - Malaise
  - Severe: Psychosis & Disorientation

SSRI – Second Line – Not recommended by APA

- Only found to be effective in treating alcohol dependence in people with a comorbid mood or anxiety disorder.

Ondansetron – Second Line

- Serotonin 5-HT3 receptor antagonist used to treat chemotherapy-induced nausea
- Seen to be selectively effective in two groups
  - Early-onset alcohol dependence
  - Specific genetic variant of serotonin transporter (5-HTT) gene.
- Side Effects:
  - Diarrhea
  - Headache
  - Fever

Approaches if response to pharmacotherapy is poor

- For people with poor response to trial of one medication, adding psychosocial interventions is next step
- Switch: Trial of medication with different pharmacologic profile
- Combining medications offers possibility of more effective treatment for patients who do not respond adequately to a single treatment.
  - Combining treatments with different mechanisms shows the best results
  - Evidence for efficacy is poor

Avoid long term benzodiazepines

- Effective option for treatment of acute withdrawal
- No evidence for any other use of benzos, sedative hypnotics
- Increase risk for behav impairment, sedation, resp suppression, accidental overdose, death
- Use behavioral interventions and SSRIs for anxiety disorders and depressive disorders

Avoid AUD pharmacotherapy for pregnant and breastfeeding women

- Except OK to use benzos for acute withdrawal
- Weigh risks of alcohol exposure to fetus vs. exposure to medication
- Naltrexone is most commonly used during pregnancy - no known risks
- Risks for fetal malformation, greatest in first trimester
  - In order of evidence for risk:
  - Topiramate
  - Acamprosate
- Avoid disulfiram due to potential harm from acetaldehyde
- Acamprosate and gabapentin may be compatible with breastfeeding
- Individualized discussions to weigh harms and benefits

Sign up for Case Presentations

3/24/2020	Pharmacotherapy of OUD	Case 1: Elizabeth Maislen, APRN Case 2:
4/7/2020	Use & misuse of cannabis	Case 1: Case 2:

Reminders:

- Next session March 34th – Pharmacotherapy of OUD (Charlie Brackett)
- Please type your name, organization, and email into chat
- Slides will be posted to the D-H ECHO Connect site