

Treatment of People with Substance Use Disorder: Overview Alcohol, cannabis and tobacco



APA guidelines 2018 and more

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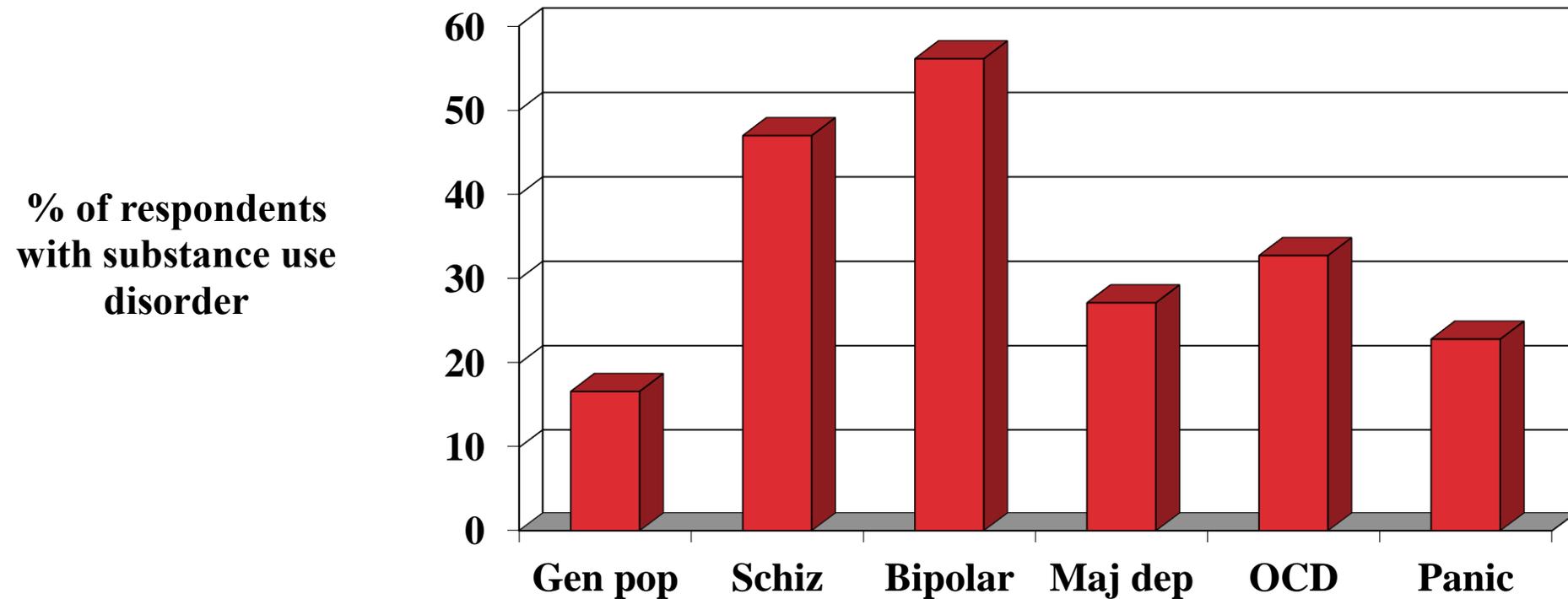
Case – Max

- Max is a 32 year old single man who works as a chef at a fine restaurant. He presents to his primary care provider with severely sprained right ankle. His blood pressure is elevated and he smells faintly of alcohol and tobacco smoke. He says he fell last night coming home after a night with the boys at the bar.
- Family history – father died of MI, mother has diabetes and depression
- Substance history – started drinking at 16, heavy cocaine use during college, now occasional marijuana, 10 tobacco cigarettes/day

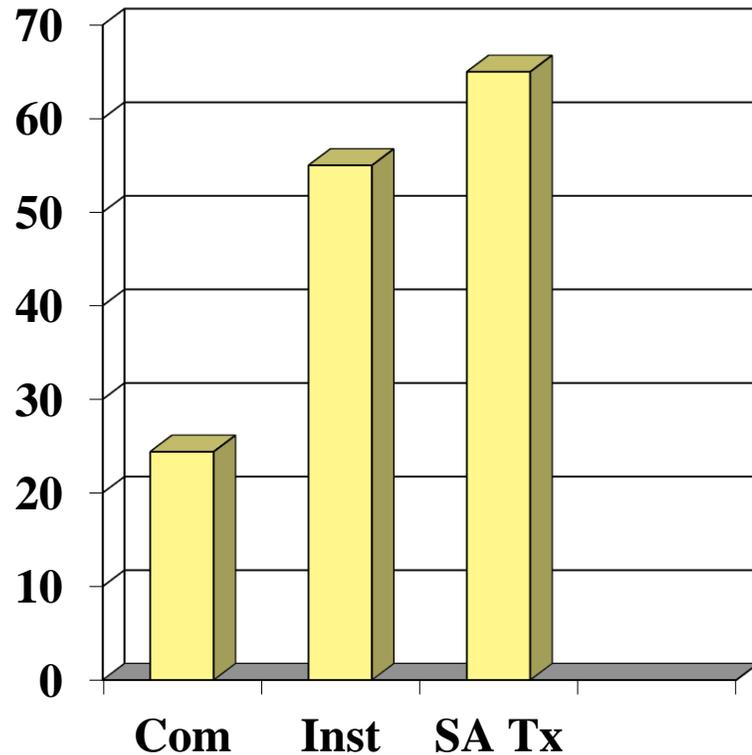
Overview

- Epidemiology of alcohol, cannabis and tobacco use disorders
- Comorbidity between SUD and mental illnesses
- Health impacts of specific substance use disorders
- Screening, assessment and treatment planning for people with substance use disorder
- Pharmacotherapy for alcohol, cannabis and tobacco use disorders

Lifetime prevalence of substance use disorders in gen pop and in people with mental illness (ECA study)



Prevalence of mental illness in people with alcohol disorder in different settings



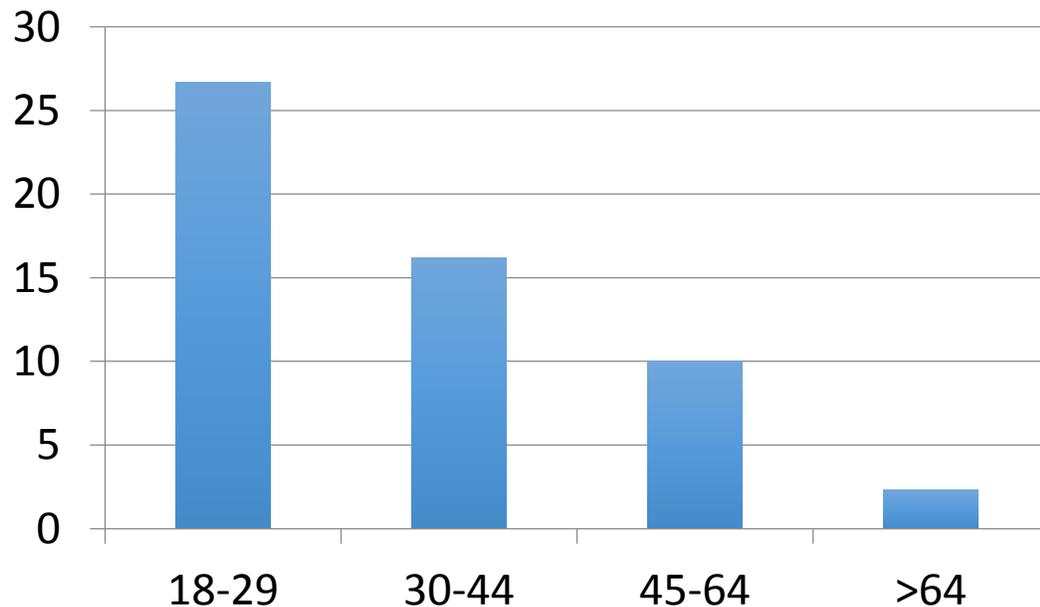
- In community, 24.4% have mental illness
- In institutions, 55% have mental illness
- In substance abuse treatment, 65% have mental illness

Patterns of Alcohol Use Disorder

NESARC-III, 2012 Survey (Grant et al, 2015)

Prevalence:
Lifetime 29.1%, Past year 13%

Past year AUD by age group



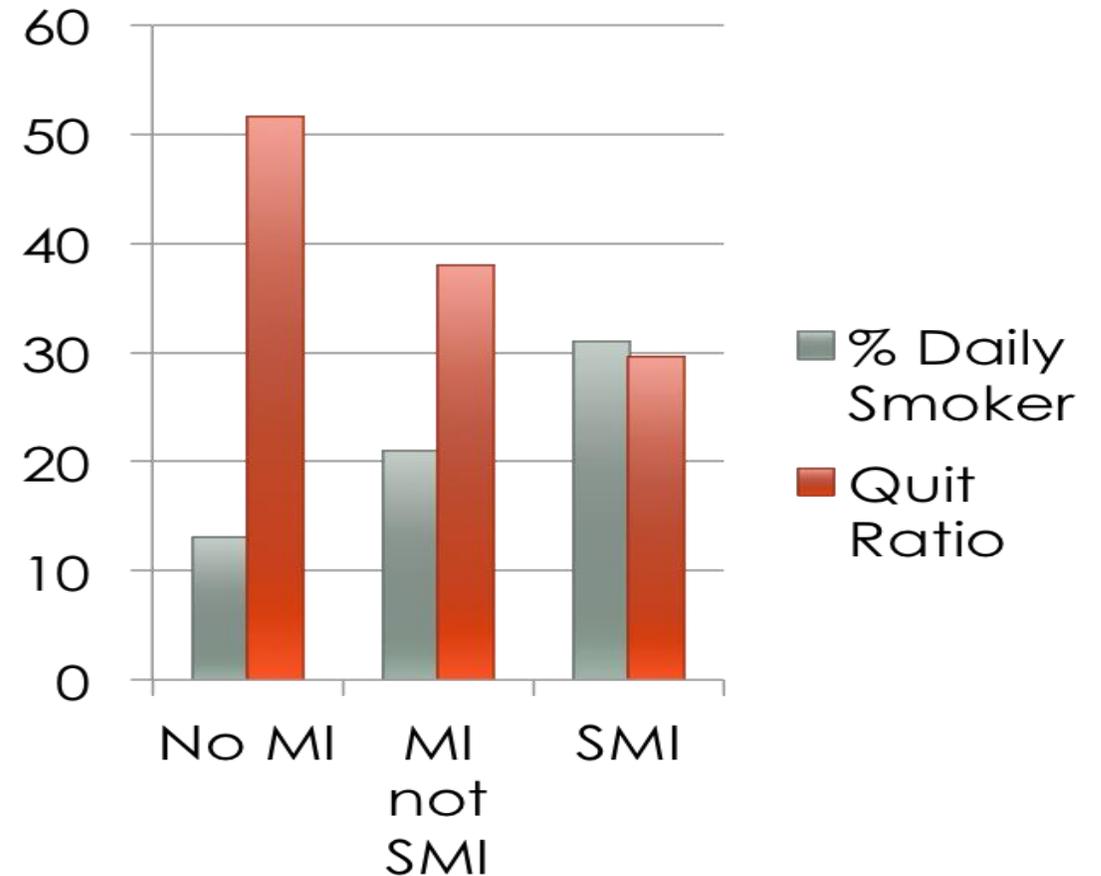
Past year prevalence demographics

- Male 17.6%, Female 10.4%
- Black 14%, White 14%
- Native American 19.2%
- Asian, Pacific Isl 10.6%
- Hispanic 13.6%
- Urban 14%, rural 10.2%

Recent U.S. daily tobacco smoking

(Glasheen 2014)

- 2008-12 National Surveys on Drug Use and Health
- 229,000 adults ≥ 18
- Established mental illness with SCID telephone interview in subsample
- 14.2% had any MI (AMI)
- 3.9% had severe mental illness (SMI)

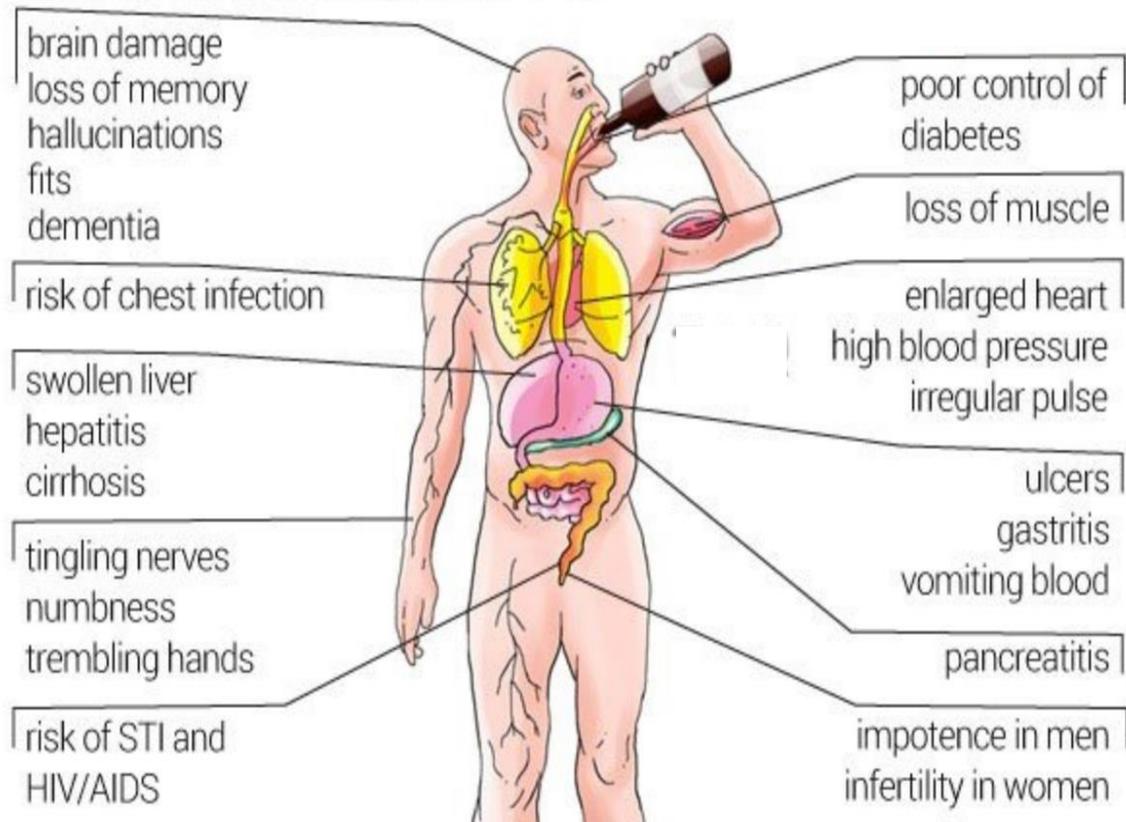


Prevalence summary

- Comorbidity of mental illness and substance use disorders is common
- Providers will encounter co-occurring disorders regularly

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

Alcohol can affect your health



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

Cannabis use disorder impact on mental health: It depends on the product...

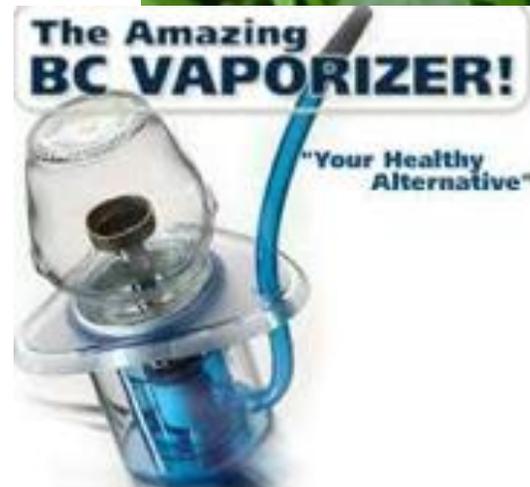
THC - tetrahydrocannabinol

- Addictive
- Increases paranoia, psychosis and anxiety among vulnerable people

CBD – cannabidiol

- Not addictive
- May reduce psychosis and anxiety among vulnerable people

Strength and potency of each component



on
cannabi

Cannabis use disorder impact on health

Effects of short-term use

- Impaired short-term memory, making it difficult to learn and to retain information
- Impaired motor coordination, interfering with driving skills and increasing the risk of injuries
- Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases
- In high doses, paranoia and psychosis

Effects of long-term or heavy use

- Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)
- *Altered brain development
- *Poor educational outcome, with increased likelihood of dropping out of school
- *Cognitive impairment, with lower IQ among those who were frequent users during adolescence
- *Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)
- *Symptoms of chronic bronchitis
- Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

Increasing potency of street cannabis and increased emergency room visits

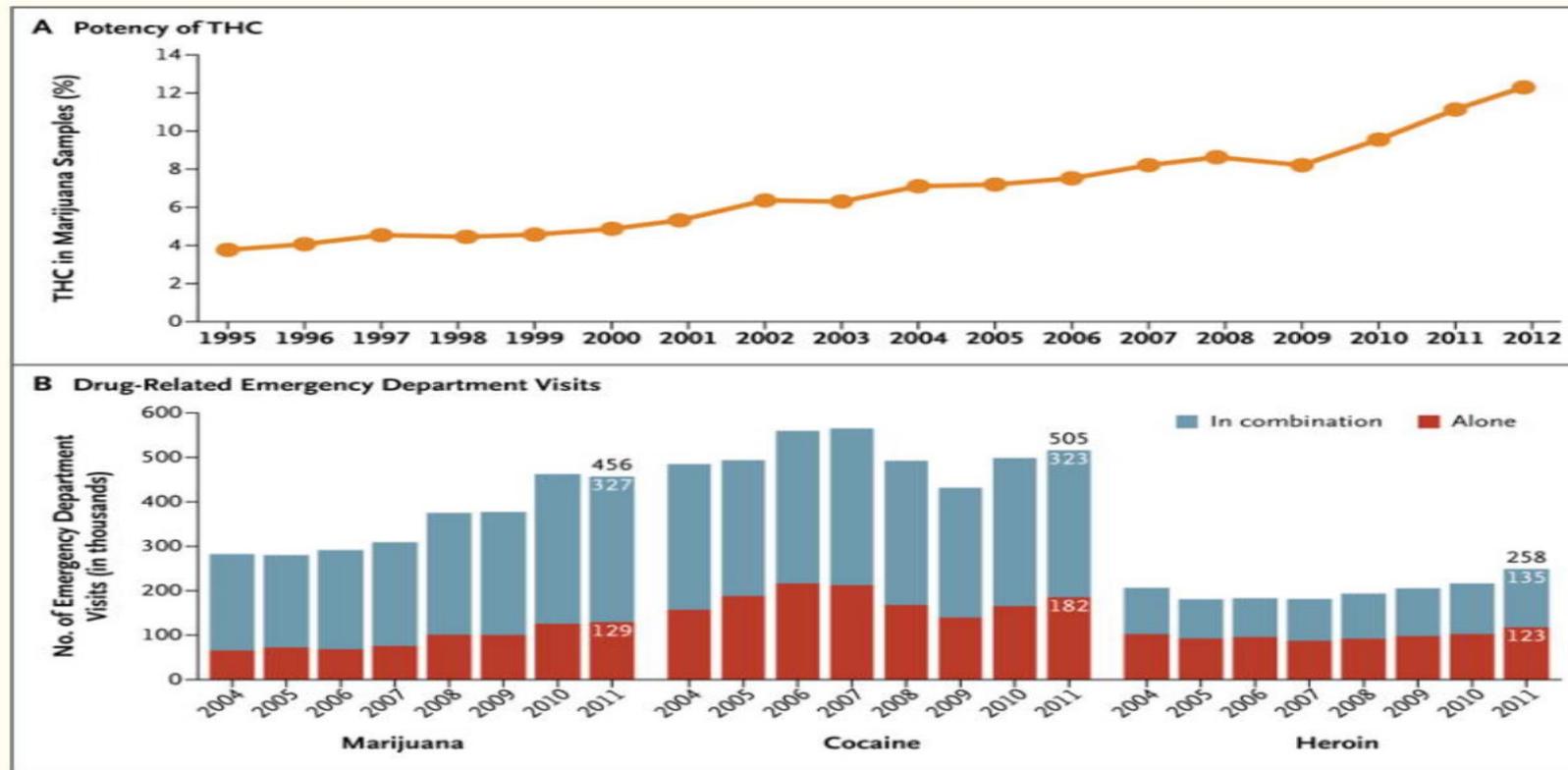
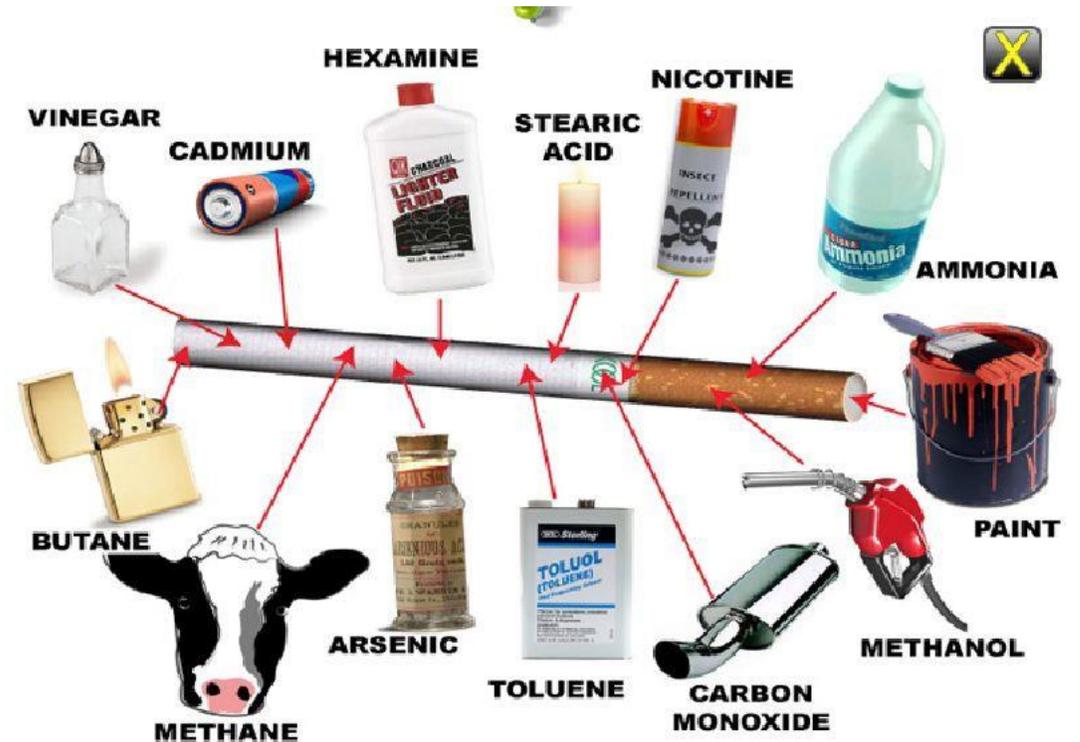


Figure 1
Increases over Time in the Potency of Tetrahydrocannabinol (THC) in Marijuana and the Number of Emergency Department Visits Involving Marijuana, Cocaine, or Heroin

Elsohley et al, 2014
Drug Abuse Warning
Network, 2011

Tobacco Use Disorder impact on health

- Smoke contains hundreds of toxins
 - Cancers
 - Lung disease
 - Diabetes
 - Cardiac and vascular diseases
 - Poor healing after injury or surgery
- Nicotine in the amounts found in a cigarette
 - Increases blood pressure and pulse
 - Stimulant
 - Not otherwise harmful



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 substance use frequency and severity
 - For alcohol:
 - AUDIT for adults (AUDIT-C short form)
 - CRAFFT for teens

Physiologic biomarkers

APA recommendation for initial eval and ongoing monitoring

For alcohol

- **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

For cannabis

- **Urine THC**
 - Present for days to months due to storage in fat

For tobacco smoking

- **Breath Carbon Monoxide (CO)** is present in any kind of smoke
 - Cigarette smokers usually have breath CO 12-30 ppm
- **Saliva or urine cotinine**
 - Cotinine is breakdown product from nicotine

Determine treatment goals related to substance use

- Provide education on potential value of harm reduction and abstinence
- Elicit patient preferences and motivation for goals:
 - Reduce drinking or drug use
 - Avoid drinking or drug use in hazardous situations
 - Stop drinking or using drugs
- Determining goals
 - Helps form therapeutic alliance
 - Provides structure for shared decision making for treatments

Determine treatment goals continued

Discuss legal obligations related to alcohol or substance use
DUI?

Work and home responsibilities?

Review risk to self and others

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

Case - Max

- After completing the assessment of his ankle, you ask Max more about last night, and about drinking in general. You learn that he drinks 12 beers several nights a week, a 6 pack on other nights, and he drives home after this amount of drinking. Several relationships have “gone south” in the past few years when the girlfriends bugged him about drinking too much. You note he has been hypertensive at other clinic visits and was told to reduce his drinking, which doesn’t seem to have happened. His depression score is in the range of moderate depression, and has not had a period of abstinence so you can’t determine whether the depression is substance induced.
- You let him know that you are concerned about his drinking and feel he has an alcohol use disorder. You note he has depression symptoms, which could be due to drinking. He does not have thoughts of suicide. You advise him that stopping altogether is the healthiest thing he could do. You ask whether he would like some assistance with changing his drinking. After reviewing all of the options with you, he decides to try a medicine. “I’m not a talker,” he says. You also advise him to stop smoking and offer assistance with quitting. He says he is not ready.

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

AUD Treatment - pharmacotherapy

- First Line Medications

- Naltrexone
- Acamprosate

- Second Line Medications

- Disulfiram
- Topiramate
- Gabapentin
- Baclofen
- Nalmefene
- SSRIs
- Ondansetron
- Varenicline

Naltrexone – First Line for Alcohol Use Disorder

- 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

Naltrexone – First Line for Alcohol Use Disorder

- 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
- Therapeutic response predicted by family hx AUD, strong cravings for alcohol

Acamprosate – First Line for Alcohol Use Disorder

- 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
- Good choice for people who use opioids or on opioid replacement therapy
- Contraindicated in low renal function (GFR <30); reduce dose in mild-mod renal impairment
- Therapeutic response predicted by high anxiety, dependence, neg family history, late onset, female gender

Disulfiram (Antabuse) – Second Line for Alcohol Disorder

- 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

Disulfiram – Second Line for Alcohol Use Disorder

- 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

Approaches if response to alcohol use disorder 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

Cannabis Use Disorder Pharmacotherapy

- No FDA approved options
- Several promising medications

N-acetylcysteine for Cannabis Use Disorder

- Tested in the treatment of CUD, showing mixed evidence of efficacy
- NAC is available over-the-counter as a dietary supplement and as a prescribed medication for acetaminophen overdose and cystic fibrosis in the US and other countries.
- Efficacy — studies have produced different results, with one trial showing reduced cannabis use with NAC and the other no difference between NAC and placebo
- Side effects — NAC was well tolerated in both trials. No differences between groups were seen in treatment retention rates or proportion of subjects reporting any adverse event compared with placebo
 - The most common adverse events in the first trial were upper respiratory infection, vivid dreams and insomnia

(Gray, et al., 2012; Gray, et al., 2017).

Gabapentin for Cannabis Use Disorder

- A GABAergic agent used in the treatment of seizures and neuropathic pain.
- Efficacy —led to short-term reduction in cannabis use compared with placebo in a clinical trial

(Mason, et al., 2012)

- Side effects —well tolerated
 - The most common adverse events were headache, insomnia, nausea, and depression.
- Administration —titrated to the target dose (300 mg morning and mid-day, 600 mg evening) over four days, maintained for 10.5 weeks, then titrated down over the 12th week.

Cannabinoid agonist for Cannabis Use Disorder

- A small trial of Nabilone in 180 cannabis-dependent adults also found it ineffective in reducing cannabis use

(Hill, et al., 2017)

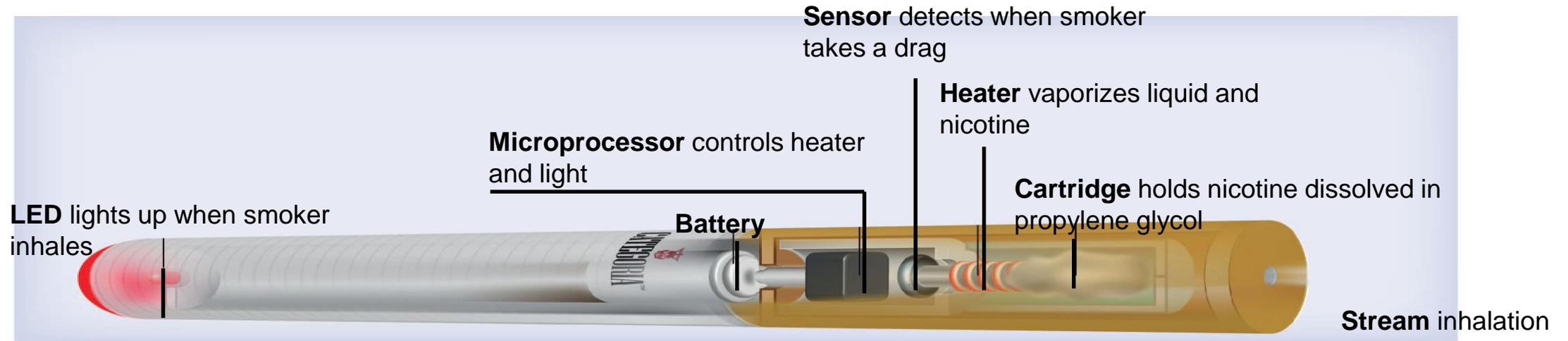
Pharmacotherapy for Tobacco Use Disorder

- **Nicotine Replacement Therapy (NRT)**

- Available in: patch, gum, lozenge, spray
- Patch Dosing: 21 mg/D X 6 wks, 14 mg/D X 2 wks, 7 mg/d X 2 wks (total 10 wks – up to 1 year)
- Lozenge/gum dosing: 2 mg or 4 mg prn craving hourly 8Xday if used with patch, up to 24Xday without patch
- Use patch plus gum or lozenge prn craving – more effective
- Research on higher doses and smoking on patch is safe (Benowitz 1998; Zevin 1998)
 - If smokes $\leq 1/2$ pack/day then start with 14 mg/d patch plus prn gum or lozenge
- Safety/side effects
 - Headache, stomach upset
- Start on quit date – OK to start a month earlier

What about E-Cigarettes?

NOT an FDA-approved approach



- Many types and brands
- Typical cartridge = 2 packs of cigarettes
- Toxins 8-600X lower but most products not tested (Goniewitz, 2014; Rabinowitz 2014)
- Most common among smokers wishing to cut down/quit (Cummins 2014)
- Naturalistic use not associated with different cessation outcomes in SMI cessation studies (Prochaska 2014; Brunette 2014)

Bupropion (Zyban) for Tobacco Use Disorder

- NE and DA reuptake inhibitor
- Dose: 300 mg/day (150 BID) – up to a year
- Interactions: Inhibits 2D6 , metab by 2B6, reduce seizure thresh
 - Consider reduce dose aripiprazole,risperidone, iloperidone
 - Caution with all meds that may reduce seizure threshold
 - Potential interactions with many antidepressants
- Safety/side effects
 - Insomnia, stomach upset, constipation, diarrhea, HTN
- Most effective when used with Nicotine Replacement Patch plus lozenge or gum
- Start 2 weeks before quit date
- Not approved for kids (under 18)

Combination Bupropion/NRT works better than either alone for Tobacco Use Disorder

- Start bupropion 2 weeks before quit date
- Start NRT on quit date or up to a month earlier

Varenicline (Chantix) for Tobacco Use Disorder

- Alpha4beta2 nicotine acetylcholine agonist
- Titrate up from 0.5 mg/day to 1.0 BID over 1 week. 0.5-1.0 mg BID 3-6 months
- Excreted unchanged in urine
- Interactions - no significant
- Safety/side effects: Nausea, diarrhea, headache, neuropsych
- Lower dose to address side effects
- Not studied or approved for kids (under 18)

Tobacco cessation treatment side effects

(remember withdrawal also has effects)

| | Patch | Patch + lozenge | Buprop | Bup + lozenge | Varen* | Placebo* |
|-------------------------|----------|-----------------|-----------|---------------|--------|----------|
| Nausea | 4.3 | 7.9 | 3.8-16* | 5.0 | 52* | 16-19* |
| Sleep dist /Abnl dreams | 11.3 | 9.0 | 12*-16.8 | 10.6 | 15* | 20-22* |
| Local irritation | Skin 15% | Throat 2-7% | Throat 2% | Throat 2-7% | | |
| Irritability | | | 11* | | 12* | 10* |

Smith, 2009; *Nides et al 2006

Case - Max

- You meet with Max monthly for three months while he tries cutting back while on naltrexone. His drinking is reduced by about half. He is less depressed. His hypertension is less severe but persists. He refuses counseling. He is willing to try to cut down his drinking further rather than starting an antihypertensive medication. His goal is to try to limit himself to no more than 3 drinks a day by alternating beer with club soda.
- When asked about his marijuana use, he says he has cut down a bit on that as well and will monitor it with you.
- When asked about his tobacco use, he says he wants to get healthier and is willing to try to quit. You instruct him about using NRT patch with gum and help him call the Quitline.

Summary

- Substance use disorders are common chronic conditions that can be managed in primary care and other medical or psychiatric settings
- Medications are effective for reducing drinking and smoking
- Medications can be combined with other therapeutic approaches
- Behavioral interventions are effective for cannabis and tobacco use disorders
- Combined behavioral and pharmacotherapy are most effective for tobacco use disorders

Thank you – Questions & Discussion



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