Medication Assisted Treatments: Focus on Alcohol and Opioid Use Disorders

Elinore F. McCance-Katz, MD, PhD
Professor of Psychiatry
University of California San Francisco
State Medical Director
California Dept. of Alcohol and Drug Programs
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Learning Objectives:

Review some of the basics of substance abuse treatment that can be accomplished in multiple medical settings: primary care, other medical settings, mental health settings, and AOD programs

- Pharmacotherapy for alcohol use disorders
- Office based treatment of opioid dependence
How to Rapidly Screen for Alcohol Problems

Single Question with high sensitivity/specificity:

- In the past year, have you had any times when you had 5 (for women, 4) or more drinks at one sitting?

- If yes, explore drinking, offer advice for cutting back or stopping, if evidence of dependence refer to substance abuse treatment facility.

- Note: a single question does not make a diagnosis, but indicates a need for further screening.
1.) What is your age? ____ yrs

2.) Are you (mark one):  O  Male  O  Female
    O  Transgender

3.) Do you sometimes drink beer, wine, or other alcoholic beverages?  O  Yes  O  No
    O  Decline to answer

If yes, please answer questions 3a and 3b, and continue

(One standard drink is any of these below)

3a.) On average, how many drinks do you have?
    _______ drinks per day and _______ drinks per week

3b.) In the past year, have you had: 5 or more drinks (men) or
    Or 4 or more drinks (women) in one day?
    O  Yes    O  No    O  Decline to answer

4.) In the past year, have you used a prescription drug for non-medical reasons?
    O  Yes    O  No    O  Decline to answer

5.) In the past year have you used an illegal or recreational drug?
    O  Yes    O  No    O  Decline to answer
**ALCOHOL:** Confirm amount of alcohol use with patient.

| Male patient had 5+ drinks/day; female or any patient 65+ had 4+ drinks/day? | O Yes | O No |
| Frequency: __________ |
| Male patient averages > 14 drinks/week; female or any patient 65+ averages > 7 drinks/week? | O Yes | O No |

**DRUGS:** Follow up on patient “Yes” responses on items 4 and/or 5, above.

1. “*Please tell me the name of the illicit drug(s) and/or prescription medication used for non-medical reasons.*”
2. “*How often do you use it?*”

**CLASSIFY USE:** Does pt meet DSM-IV Substance Abuse/Dependence Criteria? *(see criteria on reverse)*

| Pt is: | O Not at risk | O At risk | O Substance Abusing | O Substance Dependent |

**ADVISE:** “*You are drinking/using more than is medically safe. I strongly recommend that you cut down (or quit), and I’m willing to help.*”

**“Are you willing to consider making changes with your substance use?”**

| Maybe | O Conducted Brief Intervention? | O Established Rx contract? | O Completed CURES report? |

Pt. meeting DSM-IV criteria for sub. abuse or dependence should be scheduled for follow-up & offered referral to specialty care. *Treatment Assistance Program (TAP): 415-503-4730* “*Let’s set up a follow-up appointment so we can check back in about this.*”

**Comments:**

| O Referred to specialty care/outside prog. | O Arranged f/u care w/ me or other DGIM | O Provided Educational Materials/Self-help info | O Meds Provided |
Use of Medication Treatments to Treat Alcohol and Opioid Use Disorders

Pharmacotherapy Review
General Considerations for SUD Pharmacotherapy

Alcohol
- Acute withdrawal (usually done inpatient)
- Relapse Prevention - Yes

Opiates
- Acute withdrawal (often done inpatient, but can be outpatient procedure)
- Relapse Prevention - Yes
When to Consider Pharmacotherapy

Consider Precipitant To Treatment And Severity of Associated Medical/Psychiatric/Psychosocial Problems

- Family
- Employment
- Financial
- Medical
- Legal
- Psychiatric Comorbidity (*including risk for harm to self or others*)
- Relapse Potential/Failed Abstinence Based Treatment in Past

The higher the acuity or severity; greater need for use of medication treatment (if there is an appropriate medication intervention available)
Maintenance Medications To Prevent Relapse To Alcohol Use (FDA approved)

- Disulfiram
- Naltrexone (oral and injectable)
- Acamprosate
Clinical Guidance on Use of MAT

Clinical Guidance materials available from SAMHSA:

- TIP 49 Incorporating Alcohol Pharmacotherapies into Medical Practice
  

- SAMHSA Advisory: Naltrexone for Extended Release Injectable Suspension for Treatment of Alcohol Dependence
Disulfiram

How it Works: Blocks alcohol metabolism leading to increase in blood acetaldehyde levels; aims to motivate individual not to drink because they know they will become ill if they do

Disulfiram/ethanol reaction: flushing, weakness, nausea, tachycardia, hypotension
- Treatment of alcohol/disulfiram reaction is supportive (fluids, oxygen)

Side Effects:
- Common: metallic taste, sulfur-like odor
- Rare: hepatotoxicity, neuropathy, psychosis
Disulfiram

Contraindications: cardiac disease, esophageal varices, pregnancy, impulsivity, psychotic disorders, severe cardiovascular, respiratory, or renal disease, severe hepatic dysfunction: transaminases > 3x upper level of normal

Avoid alcohol and alcohol containing foods

Clinical Dose: 250 mg daily (range: 125-500 mg/d)

Adherence: problem; but if drug is taken it works well (Fuller et al. 1994; Farrell et al. 1995); good idea to start in a substance abuse treatment program
Pharmacotherapy of Alcohol Dependence: Naltrexone

- Oral Naltrexone Hydrochloride
  - Dose: 50 mg per day

- Extended-Release Injectable Naltrexone (Garbutt et al, JAMA 2005)
  - 1 injection per month/ 380 mg
Naltrexone Delays the Onset of Relapse to Alcohol
Naltrexone

Potent inhibitor of mu opioid receptor binding

- may explain reduction of relapse
  - because endogenous opioids involved in the reinforcing (pleasure) effects of alcohol
- May explain reduced craving for alcohol
  - because endogenous opioids may be involved in craving alcohol
Naltrexone Safety

- Can cause hepatocellular injury in very high doses (e.g. 5-10 times higher than normal)
- Contraindicated in acute hepatitis or liver failure
- Check liver function before, q1 month for 3 months, then q 3 months
- Caution about ibuprofen and other non-steroidal anti-inflammatory agents
  - may have additive hepatic effects

VA/DoD CPG SUDs, www.oqp.med.va.gov/cpg/SUD/SUD_Vase.htm
Naltrexone Safety

Other contraindications

- concomitant opioid analgesics (naltrexone will block analgesic effect)
- opioid dependence or withdrawal
- hypersensitivity to naltrexone
- Medical conditions requiring opioid analgesics
- pregnancy (Category C)

Main adverse effects:

- gastrointestinal upset
- abdominal pain
- nausea
- vomiting
- headache
- dizziness
Does Naltrexone Alter Alcohol Effects?

• Within-subject design (n=23) to investigate naltrexone effects (0, 50 and 100 mg qd) in combination with alcohol (0, 0.5 and 1 g/kg)
• Chronic dosing (at least 3 and up to 7 days before alcohol challenge)
• Naltrexone significantly increased subjective ratings of sedative, and unpleasant/sick effects and decreased ratings of liking, best effects and desire to drink
• Alcohol ingestion significantly increased self-reports of intoxication, including high, drunk and feel effects of alcohol or drugs

(McCaul et al. Neuropsychopharmacology, 2000)
Alcohol Relapse Prevention
Medications: Acamprosate

- **How it works**: Acamprosate is an amino acid derivative of taurine that stabilizes glutamatergic neurotransmission altered during withdrawal (Littleton 1995);
- Impact is anticraving, reduced protracted withdrawal
- Effective in reducing relapse to alcohol use in studies leading to FDA approval
- Not effective in Project COMBINE (JAMA 2006, 2008)
- Consider for those with liver impairment; those who fail other treatments
Alcohol Relapse Prevention

Medications: Acamprosate

- Side Effects: Diarrhea (up to 16%), nausea, itching (up to 4%)
- Contraindications: severe renal disease (creat cl < 30 ml.min); mod. Renal disease (creat cl 30-50-ml/min: 1-333 mg pill 3 times daily); h/o allergy to acamprosate
- No abuse liability, hypnotic, muscle relaxant, or anxiolytic properties
- Dose: 2 g daily (2-333 mg pills three times/d)
  - Recommended length of treatment: 1 year
How to Select a Medication for Alcohol Use Disorders

- **Disulfiram**: when the patient is committed to no further drinking; heavy consequences of relapse
- **Naltrexone**: for the patient who wants to cut back or get help for craving
- **Acamprosate**: naltrexone doesn’t work, patient needs opioid analgesia; disulfiram not an option
What about Opioid Addiction?

Increasing use of opioids to treat chronic pain

Rate of addiction and misuse may be underestimated; recent literature estimates: 4-26% have OUD; of those without OUD 10% misuse

Rates of Prescription Pain Medication Abuse

Nonmedical use of prescription medications (past month, 2010): 7 million
Opioids (4.4 million), CNS depressants, stimulants

- Prescription pain medication misuse now second only to marijuana
- Treatment admissions (led by addiction to prescription pain medications): 4 fold increase 2004-2008
- 98% increase in ED visits 2004-2009

Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older: NSDUH 2010

Source Where Respondent Obtained

- One Doctor: 79.4%
- More than One Doctor: 3.3%
- Bought/Took from Friend/Relative: 14.8%
- Free from Friend/Relative: 55%
- Drug Dealer/Stranger: 4.4%
- Bought on Internet: 0.4%
- Other: 6.5%

Source Where Friend/Relative Obtained

- One Doctor: 17.3%
- More than One Doctor: 3.3%
- Free from Friend/Relative: 55%
- Bought/Took from Friend/Relative: 7.3%
- Drug Dealer/Stranger: 4.9%
- Other: 3.5%

Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.

1 The Other category includes the sources: “Wrote Fake Prescription,” “Stole from Doctor’s Office/Clinic/Hospital/Pharmacy,” and “Some Other Way.”
Clinical Guidance on Use of MAT

- SAMHSA Advisory: An Introduction to Extended-Release Injectable Naltrexone for the Treatment of People with Opioid Dependence
  [Link](http://store.samhsa.gov/product/Advisory-An-Introduction-to-Extended-Release-Injectable-Naltrexone-for-the-Treatment-of-People-with-Opioid-Dependence/SMA12-4682)

- TIP 40 Center for Substance Abuse Treatment. Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs.
  Available from: [Link](http://www.ncbi.nlm.nih.gov/books/NBK64164/)

- TIP 43 Medication Assisted Treatment for Opioid Addiction in Opioid Treatment Programs
  [Link](http://store.samhsa.gov/product/TIP-43-Medication-Assisted-Treatment-for-Opioid-Addiction-in-Opioid-Treatment-Programs/SMA08-4214)
Treatment of Opioid Dependence

Therapeutic Options:
Initial treatment could include a combination of medication treatment plus psychosocial/psychotherapeutic interventions:

Option 1. Inpatient for medical withdrawal followed by:
- Residential or intensive outpatient treatment
- Individual/Group Drug Counseling
What to do if Your Patient Develops a Substance Use Disorder with Prescribed Opioids

Option 2: Medications to prevent relapse:
- Naltrexone (can only be used following medical withdrawal)
- Buprenorphine

Option 3: Some patients may be better suited for methadone maintenance (especially if ongoing opioid analgesia needed but this can only occur in a licensed narcotic treatment program)

Know the options in your community.
Naltrexone (opioid antagonist therapy)

- Block effects of a dose of opiate (Walsh et al. 1996)
- Prevents impulsive use of drug
- Relapse rates high (>80%) following detoxification with no medication treatment
- Dose (oral): 50 mg daily, 100 mg every 2 days, 150 mg every third day
- Injectable naltrexone (380 mg) for opioid dependence now FDA-approved; once a month injection

Who gets naltrexone for opioid addiction?
- Highly motivated
- Does not want agonist/controlled substance
- Some employment requirements
Partial Agonist Treatment (Buprenorphine)

What is agonist therapy?

Use of a *long acting* medication in the same class as the abused drug (once daily dosing)

- Prevention of Withdrawal Syndrome
- Induction of Tolerance

What agonist therapy is not:

- Substitution of “one addiction for another”
Opioid Dependence Maintenance Therapy

Buprenorphine

- Mu opioid receptor partial agonist
- Strong affinity for mu opioid receptors; slow to dissociate
- Schedule III
- Little effect on respiration or cardiovascular responses at high doses
- Induction onto medication when in mild-moderate withdrawal
- Maintenance form: buprenorphine/naloxone combination; except pregnant women: use mono-formulation
- Average dose 8/2-16/4 mg daily (sublingual)
Opioid Dependence
Maintenance Therapy

Buprenorphine

- Can be used for withdrawal treatment or maintenance
- Maintenance treatment more effective than withdrawal treatment
- Mild withdrawal syndrome
- Primary care physicians, psychiatrists, addiction specialists are expected to be providers of this treatment
- Abuse by injection may be a problem
- Drug Interactions: Atazanavir/ritonavir: increases buprenorphine concentrations; rifampin: decreases buprenorphine concentrations; opiate withdrawal possible
- DEA waiver required to prescribe
Methadone Maintenance

Who is appropriate?
- Needs structure of daily dosing/staff evaluation
- Pain and addiction
- Co-occurring mental illness

Characteristics
- Long acting mu agonist
- Duration of action: 24-36 h
- Dose: philosophical issue for many programs
- 30-40 mg will block withdrawal, but not craving
- Illicit opiate use decreases
- 80-120 mg is average therapeutic dose
Why is All of This Important?

Drug and alcohol use disorders affect approximately 10% of Americans.

Substance use disorders are chronic, relapsing diseases that are likely to recur once diagnosed.

Effective pharmacotherapies are available and can be implemented in primary care.

Substance abuse can negatively impact other illnesses present in the patient (e.g.: alcoholic cardiomyopathy, COPD, HIV/AIDS, HCV, other ID) and/or can masquerade as an illness that the patient does not have (e.g.: HTN, seizure d/o, mental disorders).

Can contribute to non-adherence to prescribed regimens, toxicities due to drug interactions.
Clinical Support Systems
Sponsored by Center for Substance Abuse Treatment/SAMHSA

Ask a clinical question...
• Get a response from an expert PCSS mentor
• (888) 5pcss-b-4u (Buprenorphine) (855) 227-2776 (Opioids)

From www.PCSSB.org and www.PCSS-O.org
• download clinical tools, helpful forms and concise guidances (like FAQs) on specific questions regarding opioid dependence, use of buprenorphine, safe/effective use of opioids; information on training and peer support
References

SAMHSA, National Survey on Drug Use and Health, 2008, 2009


VA/DoD CPG SUDs, www.oqp.med.va.gov/cpg/SUD/SUD_Vase.htm


References

2006, 2011 National Survey on Drug Use and Health: National Findings,” SAMHSA.
Office of National Drug Control Policy (ONDCP) www.ondcp.gov