Addiction Medicine: What’s new for primary care
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How to talk so our patients listen, and listen so our patients talk.

1. Raise the subject
   - Screening results can serve as a convenient way to start the conversation.
   - Ask permission to talk about the health issue

   Thanks for answering our screening questions about smoking. Would you mind taking a few minutes to talk with me about it?

2. Provide feedback
   - If the nurse screened the patient, and the screen is positive, ask “What do you think is a safe limit on how much alcohol you should drink?”
   - And if that limit is below what they reported on screening, develop that discrepancy.
   - Point out the fact that the patient’s behavior puts him or her at risk. Provide quick and basic information.
   - Explore connections between the behavior and patient specific health issues (e.g., risky drinking and injury).

3. Offer Advice
   - Provide direct advice that is appropriate to the severity of the problem.

   I’d like you to consider limiting your drinking to not more than 4 drinks in one day. What are your thoughts about that?
### 4. Enhance motivation

- Help the patient resolve ambivalence and build motivation.
- Pros and cons:
  - What are some of the good things about your drinking [or drug use]?
  - What are some of the not-so-good things?
- Use open-ended questions.
  - “Could you tell me more about your pattern of drinking?” instead of “How much do you drink?”
- Affirm the patient’s strengths.
  - And that means seek them out. Listen to your patient.
- Use reflective listening.
  - “So drinking helps you relax and enjoy time with your friends. On the other hand,…”
- Support the patient’s self-efficacy.

### 5. Negotiate a plan

- Summarize the discussion.
- Changing the patient’s behavior is the patient’s job, not ours.
- But we can help them move toward change.
  - Invite the patient for a follow-up visit.
  - Think small steps. A little success is better than a big failure.

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### Medication Assisted Treatment for Substance Abuse

Putting It All Together

https://adept.missouri.edu/resources.aspx
The Big change in addiction medicine?
- These diseases are medical diseases.
- Done are the days when we should say
  - "You drink too much. Go to AA."  
  - "Our social worker will help you schedule an appointment with a drug treatment program."
- Treatment involves both psychosocial therapy and pharmacotherapy.

Psychosocial therapy
- One-off brief intervention
  - 11% to 12% of hazardous drinkers moderate their drinking to safe levels.
  - That’s a number needed to treat (NNT) of 8 to 9.
- People with substance use problems often have psychiatric comorbidities and many social problems.
  - These are chronic problems.
    - A one-time brief intervention is sufficient for some.
    - For others, it’s only the first conversation.

Identify and diagnose
- How do you find out if your patient has hypertension?
  - Screening
  - And?
- Simple screening questions will identify most hazardous or harmful substance use.
- Diagnosis requires thoughtful and thorough assessment.
  - It might be done over several visits. Just like hypertension.

Tobacco
- Nicotine replacement therapy
  - Doubles the success rate in quitting smoking.
  - Start with one 21 mg/day patch for patients smoking a ppd.
  - Using patch + gum works better.
    - Increase the dose, even up to two 21 mg/day patches if craving for smoking persists.
  - E-cigs? The jury’s still out.
    - Might help some smokers reduce harm.
    - Might entice kids to start.

Tobacco: prescription options
- Bupropion (Wellbutrin®, Zyban®, and generics)
  - Doubles success rate.
- Varenicline (Chantix®)
  - Lower dose, a half of the 1 mg tab BID, works almost as well as standard 1 mg BID, with lower cost and fewer side effects.
  - Increases quit rate 2 to 4-fold.
  - Nausea. Take with food.
  - Risk of depression and suicide probably not increased.
  - But no med works for most smokers. It takes time.

Cytisine? Maybe someday
- Like varenicline, another nicotinic receptor partial agonist
- Derived from Cytisus laborinum (golden rain acacia).
- Increases quit rate 4 fold.
- Hasn’t yet been compared to varenicline head-to-head.
- Not yet available in the U.S.
  - But one can buy Tabex® online ($42 for 100, taken 2 to 5 per day).
Quitting smoking improves mental health

- Meta-analysis in BMJ in 2014
- Anxiety and depression both improved. Effect sizes were small to moderate, about the same as with antidepressant meds.
- Caveat: Association doesn’t prove causation.

Alcohol use disorders

- Excellent evidence of efficacy
  - Naltrexone oral or IM
  - Acamprosate
- Good evidence
  - Topiramate
- Some evidence
  - Gabapentin

Naltrexone (Revia® and generics orally, Vivitrol® IM)

- 50 mg daily
  - Can start with ½ tab for the first few days.
  - One study increased dose to 100 mg daily. We don’t know if the higher dose is better than 50 mg daily.
- Side effects
  - Nausea. Maybe minimized by starting lower, taking with food.
  - As an opioid antagonist, makes treating acute severe pain (e.g., from trauma, pancreatitis) more challenging.
  - Number needed to treat (NNT) = 12 for return to heavy drinking.

Naltrexone’s cost

- Oral
  - Cost = $4 a pill
- Injection
  - 380 mg IM once every 4 weeks (Vivitrol®)
  - $1,200 a shot
  - Manufacturer offers a coupon for up to $500 co-pay at www.Vivitrol.com.

Acamprosate (Campral®)

- 333 mg, two TID
- Cost $6 a day. No generic
- Side effects:
  - Diarrhea
  - Compliance with TID dosing
  - Renally cleared, so OK with moderate liver disease.
  - Lower dose if GFR 30 to 60, 333 mg TID
  - Don’t use if GFR < 30.

Acamprosate

- NNT = 12 to prevent return to any drinking.
- Doesn’t improve outcomes to use acamprosate and naltrexone together
Which one?

- Naltrexone might work better in reducing heavy drinking in non-abstinent alcoholics.
- Acamprosate might work better in helping patients maintain abstinence.

Topiramate (Topamax® and generics)

- 25 mg ramped up to 200–300 mg per day
  - Generic costs $1 to $2 per day. Tablets can be split, but are unstable, so don’t.
- Side effects
  - Dygeusia
  - Anorexia
  - Cognitive slowing
- Some studies suggest it works, to some extent.

Gabapentin. 12-week clinical trial

- One study found that adding gabapentin 400 mg TID for 6 weeks to naltrexone 50 mg daily improved drinking outcomes.
- But they also found that naltrexone + placebo didn’t work any better than double placebo. And that just isn’t consistent with a wealth of other research on naltrexone.

Disulfiram (Antabuse® and generics)

- 250 mg per day.
- Might buy you some time, but it works by threat.
- Compliance with daily dosing is the challenge.
- Consider directly observed therapy by the patient’s spouse or significant other.

For alcoholism + depression

- Sertraline + naltrexone was better, both for depression and for drinking, than either med by itself or the two placebos.
- NNT of 3 to 4
- Single study. We don’t have studies (yet) on other SSRIs.
For alcohol withdrawal
- Gabapentin (Neurontin®) 400 mg TID in a tapering schedule
  - Might be as effective as a benzo, but not much evidence yet.
  - Fewer side effects
  - Lower likelihood of return to heavy drinking
  - Good option with milder withdrawal.
  - Drug of first choice for outpatients.

Methamphetamine
- Topiramate
  - Modest effects only with secondary outcomes in one RCT.
  - Mirtazapine (Remeron®)
    - One RCT done in San Francisco health dept in MSM
    - 30 mg daily
    - NNT = 3 to get negative weekly urines

Marijuana
- The good, the not-so-good, and the UNKNOWNS.
- Medical marijuana?
  - Little evidence.
  - What happened in 1776? Dried foxglove leaves to treat CHF
- Recreational marijuana?
  - See especially Dr. Volkow’s article in NEJM.
    - 9% of regular users get addicted to it.
    - Regular use by adolescents cuts IQ by 6 points.

Pharmacotherapy for marijuana
- N-acetylcysteine 600 mg, two BID
- Placebo: The inside of placebo blister packs was sprinkled with NAC.
- Available OTC as a supplement
- Contingency management: Participants were paid $5 for each appt they kept + $5 for each drug-free urine.
  - Plus a weekly 10-minute visit with the doc or PA.

How well did NAC work?
- NNT = ~7

Gabapentin for marijuana dependence
- 400 mg TID versus placebo
For cocaine, some meds might help

- N-acetylcysteine 1200 mg BID reduces cocaine craving
- Some preliminary evidence for
  - Ondansetron
  - Topiramate
  - Modafinil
  - Disulfiram (as a dopamine agent)
  - etc...
- But no good evidence for any pharmacotherapy. Stay tuned.

The most efficacious pharmacotherapies

- Are those for opioid use disorders
  - Methadone
  - Buprenorphine

Buprenorphine

- Partial mu agonist = there’s a ceiling on its effects (~24-32 mg/d)
- Very potent: 1 mg SL = 40-50 mg oral morphine
- Usually given as buprenorphine + naloxone in a 4:1 ratio (Suboxone®, etc).
  - The naloxone prevents IV misuse.
  - Costs $8 per (trade-name) Film, and typical dose is BID-TID.
  - Generics cost exactly the same—at least for now.
  - But plain buprenorphine 8 mg (generic) costs less, though prices vary widely.

Efficacy of buprenorphine

- Randomized clinical trial of counseling
- With buprenorphine, 49% stayed clean, w/ or w/o counseling.
- When the med was stopped after 3 months, that proportion dropped to 9%.
- Number needed to treat
  - \[ \frac{1}{(49\% - 9\%)} = \frac{1}{0.4} = 2.5 \]

Drawbacks to buprenorphine

- Getting off it may be difficult.
  - But the current federal guideline says, p. 58: Maintenance therapy with buprenorphine “may be indefinite.”
  - Compare this to other meds for brain disorders, like depression or epilepsy.
  - The physician has to be specially "certified" by SAMHSA to prescribe buprenorphine for addiction.
Methadone

- Full agonist at the $\mu$ receptor.
- Relatively cheap.
  - But methadone maintenance programs in Missouri all require cash payment at each visit. About $400 a month.
- Once-a-day dosing for treating addiction
  - q8h in treating pain
- Reduces illicit opioid use and HIV-risk behaviors.
- Possibly reduces criminal behavior.

But ...

- Wildly variable half-life
  - Across the population, varies from 5 hours to 5 days.
- Plethora of drug-drug interactions
- In treating addiction, methadone can be prescribed and dispensed only in federally licensed methadone maintenance programs.
  - Or for inpatients by any doc with a DEA number
- Missouri has 4 methadone clinics.

Naltrexone

- An opioid antagonist, naltrexone blocks the effects of opioids, including the euphoria, analgesia, et al.
- But as with disulfiram for alcohol, oral naltrexone is just too easy to stop taking.
- 380 mg naltrexone IM every 4 weeks is attractive
  - To us clinicians, that is. Not so much to patients. Not at all to insurance companies.

Does IM naltrexone work for opioid addiction?

- Two head-to-head RCT’s of IM naltrexone versus buprenorphine are underway (in U.S. and in Norway).
  - Nothing yet on methadone vs naltrexone.
- For now, the best evidence we have is expert opinion:
  - IM naltrexone appears to work, reducing craving by the second month on medication.
  - These experts say that, in their experience, IM naltrexone blunts craving as well as buprenorphine.