Medication Assisted Treatment for Substance Abuse in Primary Care

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The Big change in addiction medicine?

- These diseases are rapidly becoming 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 an alcohol and drug treatment program."
- Physicians, P.A.'s, and N.P.'s hold the power of the prescription,
- and these diseases are becoming diseases we can treat with a prescription.

Before we dive into pharmacotherapy …

- Don't forget the power of conversation.
  - "Brief intervention" by a primary care clinician helps about 11% to 12% of hazardous drinkers to moderate their drinking to safe levels.
  - That's a number needed to treat (NNT) of 8 to 9.
  - Well-spoken words have power.

But first …

- Before you can Rx, you need to Dx.
- How do you find out if your patient has hypertension?
  - Screening
- How do you find out if your patient has hazardous or harmful substance use?
  - Screening: See handout

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 may work better.
  - Increase the dose, even up to two 21 mg/day patches if craving for smoking persists.

Tobacco

- Bupropion (Wellbutrin®, Zyban®, and generics)
  - Also doubles success rate.
  - NRT + bupropion together don't work any better than either by itself.
  - Increases seizure risk.
  - 150 mg of the SR once a day for several days, then BID.

Varenicline (Chantix®)

- Standard dosing uses fancy cardboard weekly packs.
- Lower dose, 0.5 mg BID, works almost as well as standard 1 mg BID, with lower cost and fewer side effects.
- Increases quit rate by 2 to 4 times.
- Nausea. Take with food.
- Risk of depression and suicide probably not all that common. Use it, but stay in touch with the patient and arrange close follow up.

Alcohol

- You all know that brief interventions sometimes work for hazardous drinkers.
- And in addition, prescribe medication for patients with alcohol dependence.
- Comorbid anxiety disorders are common, but benzos are risky and don't treat the addiction.

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.

Naltrexone

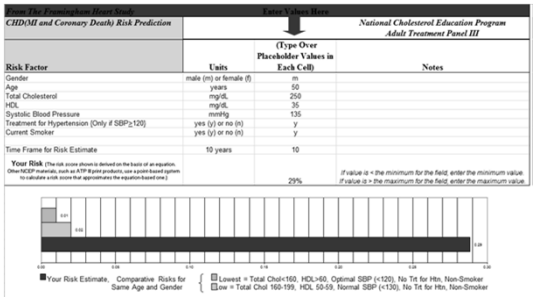
- Oral
  - Cost = $3.50 a pill
- Or injection (if patient tolerates a few days of oral)
  - 380 mg IM once every 4 weeks (Vivitrol®)
  - $1,200 a shot. Insurance hassles.
  - Manufacturer offers a coupon for up to $500 co-pay at www.Vivitrol.com.

Naltrexone

- Compliance makes a difference.
  - Directly observed oral naltrexone 3 times a week (100, 100, 150 mg) may work better than on-your-own at home.
  - That's why some drug courts mandate Vivitrol.
  - But we have little science comparing oral and IM.

Naltrexone

- Number needed to treat (NNT) = 9
- NNT is the number of people who need to be treated for one person to benefit.
  - It's 1 ÷ (rate in control group – rate in intervention group)
  - Or the other way around.
- How does that NNT compare with other treatments we use?
  - How many patients need to be treated with a statin to prevent one CV event in 10 years?



From The Framingham Heart Study — Enter Values Here

CHD(MI and Coronary Death) Risk Prediction — *National Cholesterol Education Program Adult Treatment Panel III*

Risk Factor	Units	(Type Over Placeholder Values in Each Cell)	Notes
Gender	male (m) or female (f)	m	
Age	years	50	
Total Cholesterol	mg/dL	250	
HDL	mg/dL	35	
Systolic Blood Pressure	mmHg	135	
Treatment for Hypertension [Only if SBP≥120]	yes (y) or no (n)	y	
Current Smoker	yes (y) or no (n)	y	
Time Frame for Risk Estimate	10 years	10	
Your Risk (The risk score shown is derived on the basis of an equation. Other NCEP materials, such as ATP 9-point products, use a point-based system to calculate a risk score that approximates the equation-based one.)		29%	If value is < the minimum for the field, enter the minimum value. If value is > the maximum for the field, enter the maximum value.

Your Risk Estimate. Comparative Risks for Same Age and Gender: Lowest = Total Chol<160, HDL>60, Optimal SBP (<120), No Trt for Htn, Non-Smoker; ow = Total Chol 160-199, HDL 50-59, Normal SBP (<130), No Trt for Htn, Non-Smoker

Acamprosate (Campral®)

- 333 mg, two TID
- Cost $5.50 a day. No generic
- Side effects:
  - Diarrhea
  - Compliance with TID dosing
- If CrCl 30 to 60, 333 mg TID
  - Don't use if CrCl < 30.
- OK with moderate liver disease

Acamprosate

- NNT = 9
- 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 newly abstinent alcoholics.

Topiramate (Topamax® and generics)

- 25 mg ramped up to 200 mg per day
  - One study went as high as 300 mg per day
  - Go up by 25 mg per day or, one study, 25 mg BID.
    - One study used max of 75 mg per day.
  - Generic costs $1 to $1.70 per day. Tablets can be split, but are unstable, so splitting's probably not a good idea.
- Side effects
  - Dysgeusia
  - Anorexia
  - Cognitive slowing (but, hey, it's better than alcohol!)

Disulfiram (Antabuse® and generics)

- 250 mg per day.
- Might buy you some time, but it works by threat. It doesn't treat the chronic brain disease.
- Compliance with daily dosing is the challenge.
- Consider directly observed therapy by the patient's spouse or significant other.

For alcoholism + depression

- Sertraline (Zoloft®) + naltrexone was better, both for depression and for drinking, than either med by itself or the two placebos.
- NNT of 3 to 4

For alcohol withdrawal

- Gabapentin (Neurontin® and generics) 400 mg TID in a tapering schedule
  - As effective as lorazepam (Ativan®) 2 mg TID also tapering schedule
  - Fewer side effects
  - Lower likelihood of return to heavy drinking
- Keep this in mind for inpatients with lower withdrawal severity.
- Consider it the drug of first choice for outpatients.

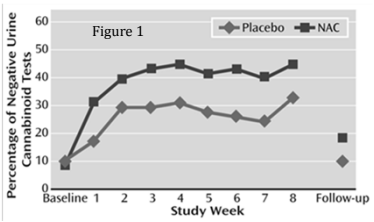
Methamphetamine

- 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

- 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?



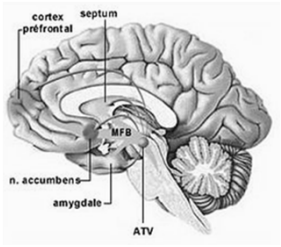
NNT = ~7

Gray KM, Carpenter MJ, Baker NL, et al.
A double-blind randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents.
Am J Psychiatry. 2012;169(8):805-81

What does NAC do?

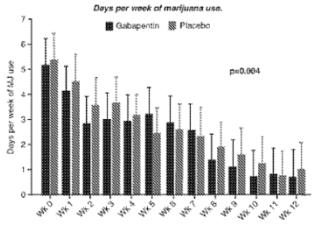
- In animal studies, chronic drug self-administration down-regulates the cystine-glutamate exchanger in the nucleus accumbens.
- Administration of NAC up-regulates this exchanger.
- The output neurons of the nucleus accumbens send axon projections to the ventral analog of the globus pallidus, known as the ventral pallidum (VP). The VP, in turn, projects to the medial dorsal nucleus of the dorsal thalamus, which projects to the prefrontal cortex as well as the striatum.

And just in case you wanted to know …



Gabapentin for marijuana dependence

- 400 mg TID versus placebo



NNT?

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 …
- Stay tuned

Opioid addiction

- 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®).
  - The naloxone prevents IV misuse.
  - Generics are just coming to market.
  - Costs $8 per (trade-name) Film, and typical dose is 2 to 3 / day.

Buprenorphine

- Side effects
  - Those common to all opioids like constipation.
    - Can make migraines worse.
  - Used under the tongue because of extensive first-pass metabolism (the liver chews it up before it can get to the central circulation).
  - Taste is terrible.

Buprenorphine works.

- 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
  - $1 \div (49\% - 9\%) = 1 \div 0.4 = 2.5$

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.
  - But it's not that hard. If Dan Vinson did it, …

Naltrexone

- An opioid antagonist, naltrexone blocks the effects of opioids, including the euphoria, analgesia, et al.
- Like with disulfiram, oral naltrexone is just too easy to stop taking.
  - "I'm doing fine. I don't need this any more."
- 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?

- A head-to-head RCT of naltrexone versus buprenorphine and methadone is planned.
- 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 or methadone.