



Pharmacology for Alcohol & Opioid Use Disorders

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Disclosures

Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.

Take home points

- Your attitude and language around substance use disorders can make an important difference to patients.
- Virtual care is different, imperfect, and necessary in times of increasing use.
- Medications can be an effective tool towards improving outcomes for SUDs.
- Please get an X-waiver for buprenorphine prescribing. <https://pcssnow.org>

Agenda

- Talking to patients about SUD and medications
- Virtual care
- Pharmacology for opioids
- Pharmacology for alcohol

Avoid language with implicit stigma

Stigma: “an attribute, behavior, or condition that is socially discrediting”

- “Addict” or “Person with a substance use disorder”
- Are tox screens “positive” or “dirty”?
 - (Is an elevated A1c “dirty”?)

Why discuss this?

- Stigma can push people away from treatment.

Substance use disorders are a biological disease

Brain disease vs Bad choices: FALSE dichotomy

Why discuss this?

- Shame is incredibly common and complicates recovery.
- Medicalizing can normalize their experience.
- Can improve willingness to consider medications.

Substance use disorders are chronic


Think DM, hypertension or epilepsy (not infections)

Why discuss this?

- People fantasize about ‘cure.’
- It will always require some management.
Sometimes a lot of attention, at others little.

Taking medications does not mean 'substituting one drug for another'

STEP 1 Admit Powerlessness



We admitted we were powerless over our addiction - that our lives had become unmanageable

Can you live life according to your own values?

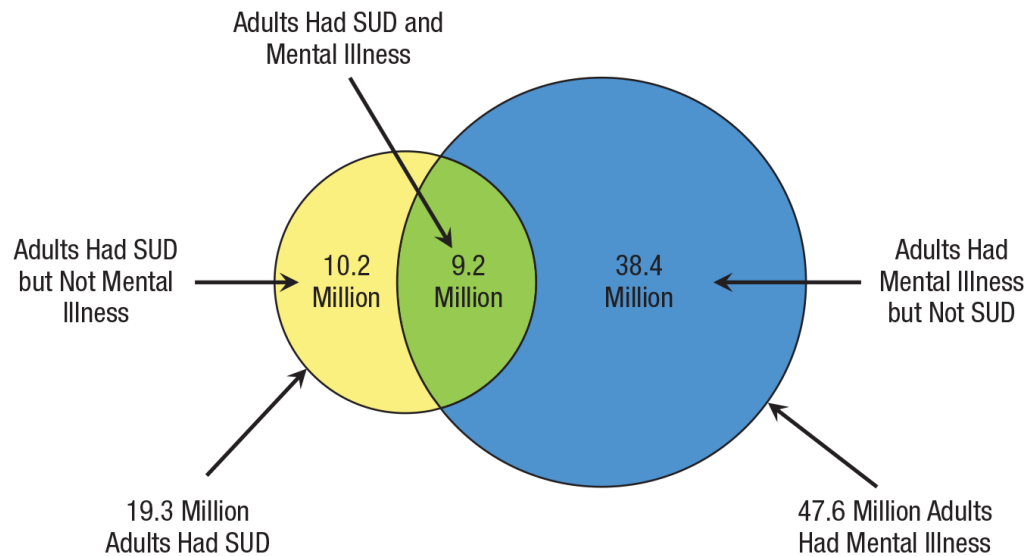
- sustainable with the substance?
- sustainable with medication?

Why discuss this?

- Stigma against medications
- Explore meaning of “addiction”

Diagnose and treat psychiatric comorbidities

- Self-medication hypothesis
- Should you treat SUD first or treat mental health issues first? Treat concurrently.



57.8 Million Adults Had Either SUD or Mental Illness

Agenda

- Talking to patients about SUD and medications
- **Virtual care**
- Pharmacology for opioids
- Pharmacology for alcohol

SUD increases risk of COVID-19

- SUD over-represented among those hospitalized with COVID-19
 - 15.6% of COVID-19 sample vs 10.3% of all hospitalized patients
- Recent SUD ↑'s COVID-19 risk: Adj OR=8.7
 - Recent OUD: Adj OR=10.2
- Lifetime SUD ↑'s COVID-19 risk: Adj OR=1.46
 - Recent OUD: Adj OR=2.42

Outpatient care in the age of COVID-19

- Increased need
 - CDC: 13% having started or increasing substance use to cope with COVID-related stresses
- Adoption of video-based or telephone-based virtual care
- Relaxation of toxicology screens

Outpatient care in the age of COVID-19

Benefits

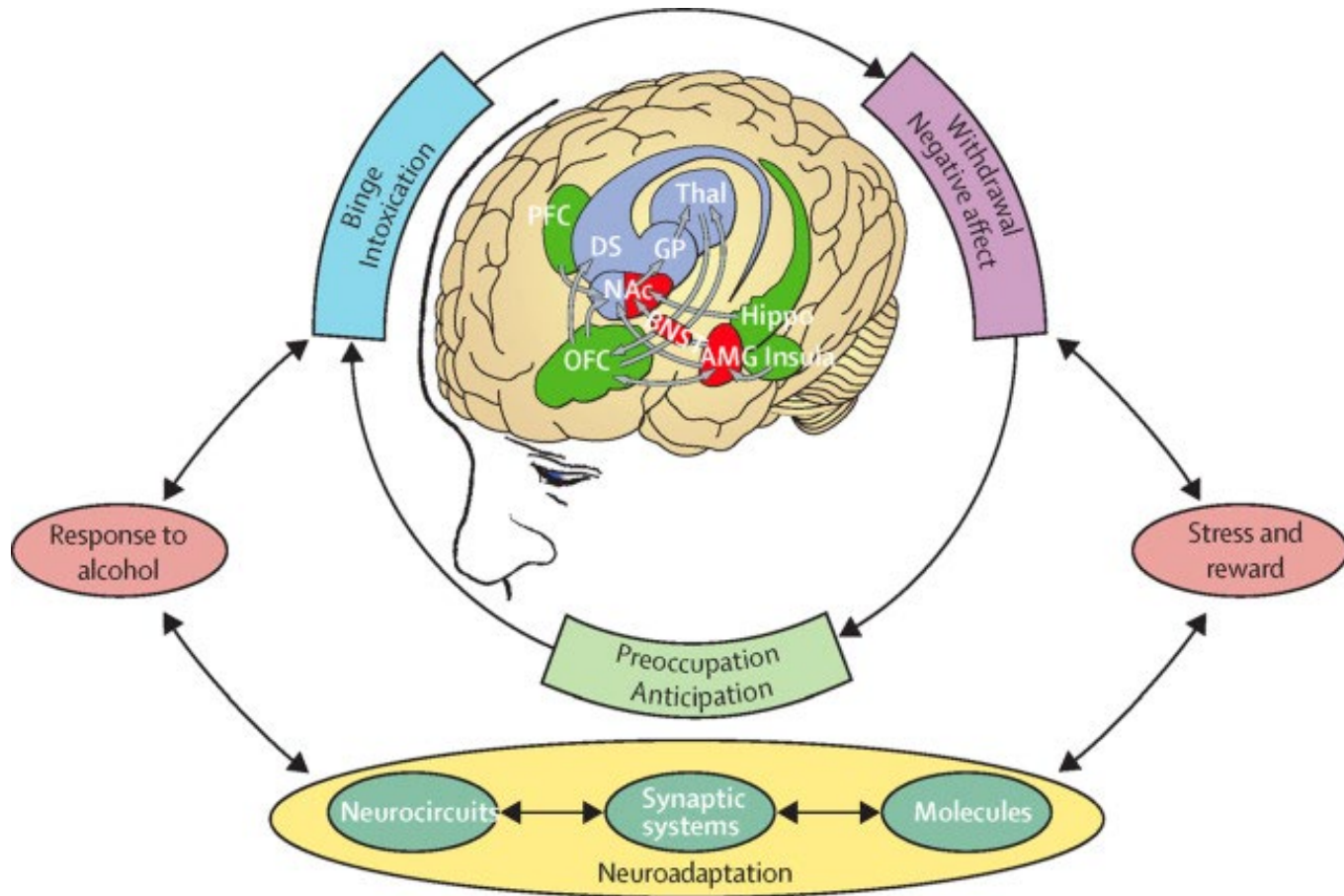
- Decreased no-show rates
- Can increase access
- COVID-19 fear can promote change

Challenges

- Lack of privacy
- Lack of internet / phone access
- Increased need for services
- Worsening of comorbidities
- Clinician isolation
- Insurance coverage for virtual care long-term?

Agenda

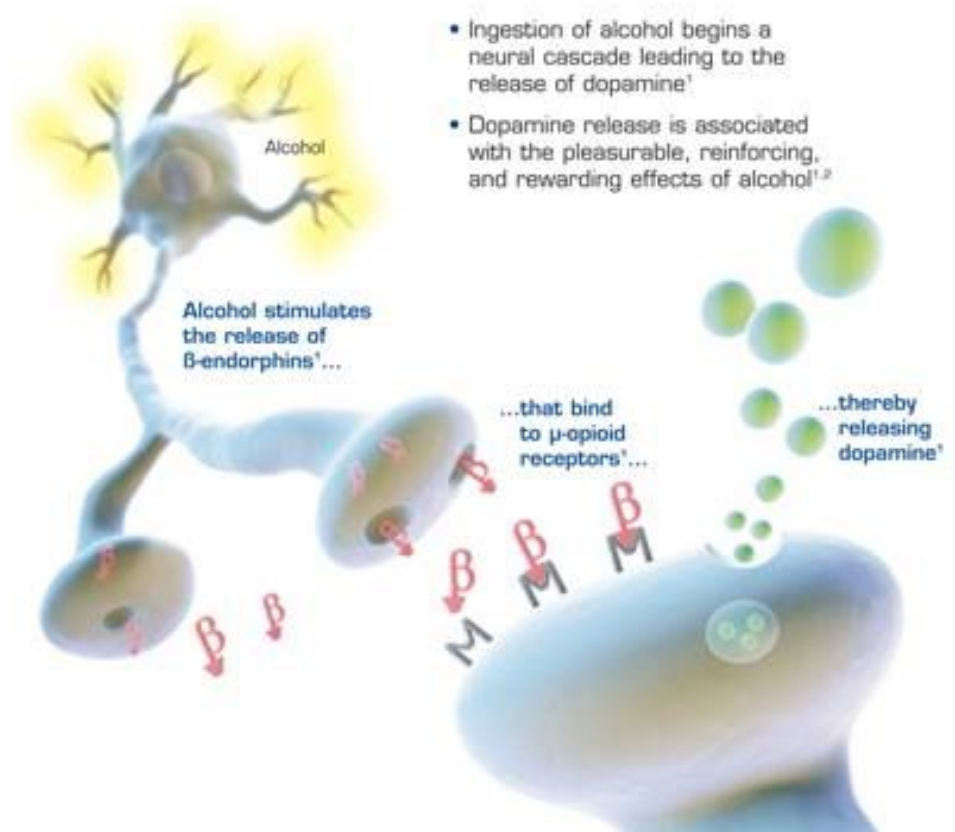
- Talking to patients about SUD and medications
- Virtual care
- **Pharmacology for opioids**
- Pharmacology for alcohol



Koob & Volkow, 2016

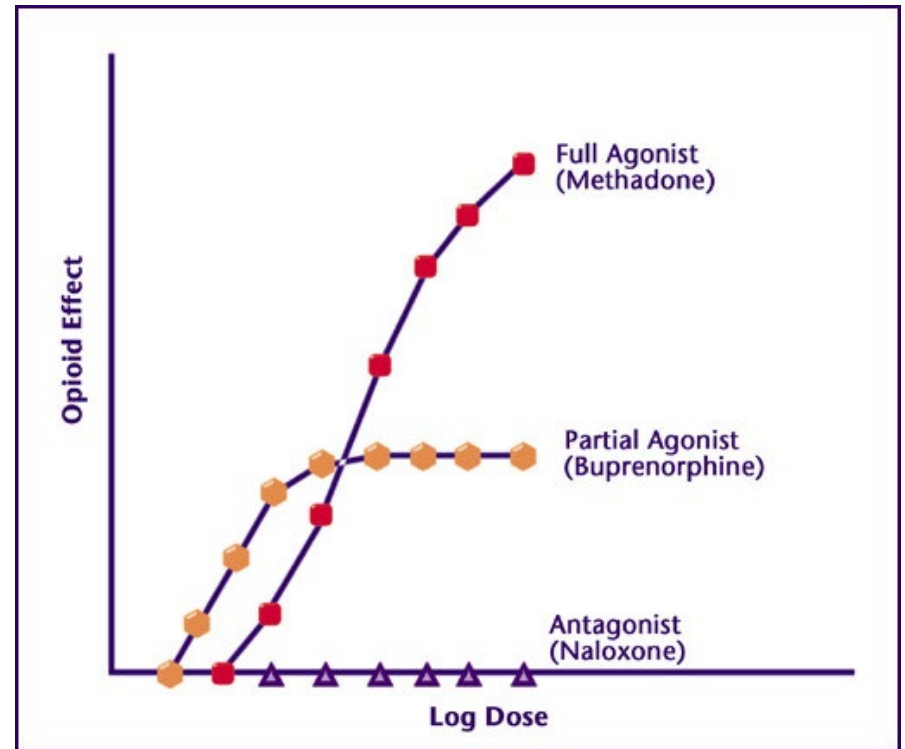
A closer view of reward circuitry

- GABA-ergic receptors upstream of dopamine neurons
- Release of endogenous opioids onto μ -opioid receptors cause dopamine release



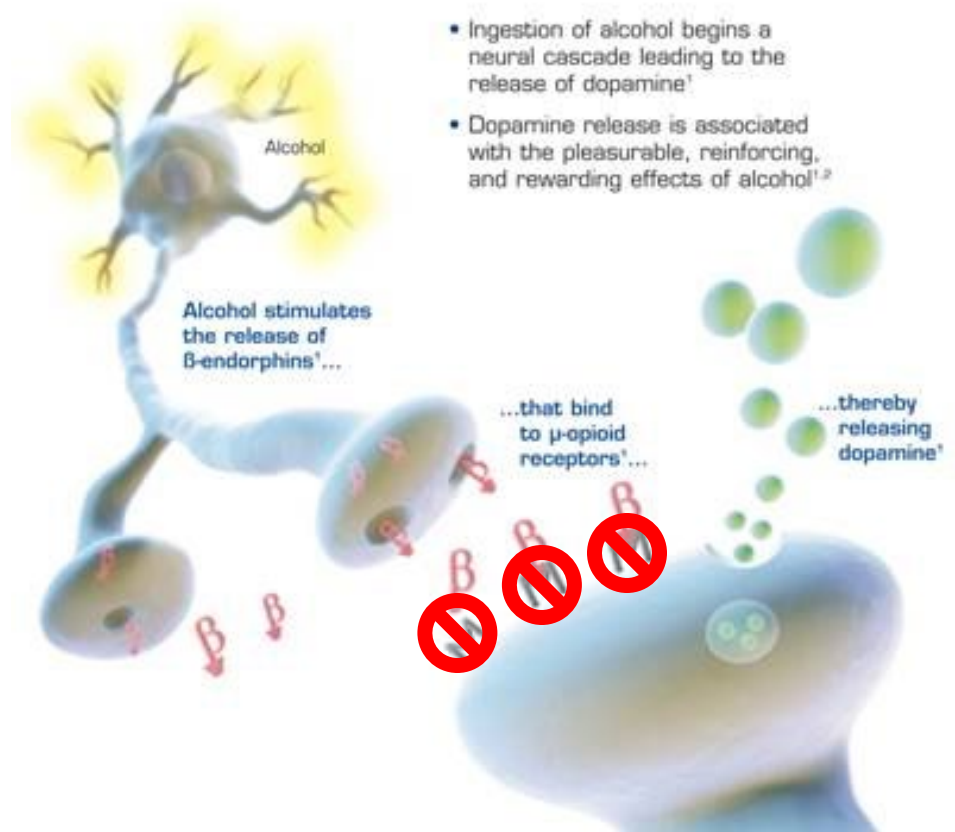
FDA Approved Options

- Naltrexone
- Buprenorphine
- Methadone



Naltrexone: mechanism

- Opioid receptor blocker interferes with dopamine release



Naltrexone: efficacy (opioids)

- Oral naltrexone not effective for abstinence or retention
 - Driven by non-adherence
 - Forcing adherence improved outcomes
- XR-naltrexone increased abstinence, decrease cravings, improved retention
 - Most patients discontinue within 6 months
 - Challenge to induce patients on naltrexone, perhaps aided by naltrexone-aided detox.

Naltrexone

Dosing

- First dose 7-10d after short-acting opioids (up to 14d after buprenorphine/methadone)
- 25mg for first 6 days (with food to mitigate side effects). Then increase to 50mg
- 380mg qMonth injectable

Side effects

- Nausea / ↓ appetite
- Headaches
- Elevated LFTs (rare)
 - Baseline and within first month

Contraindications

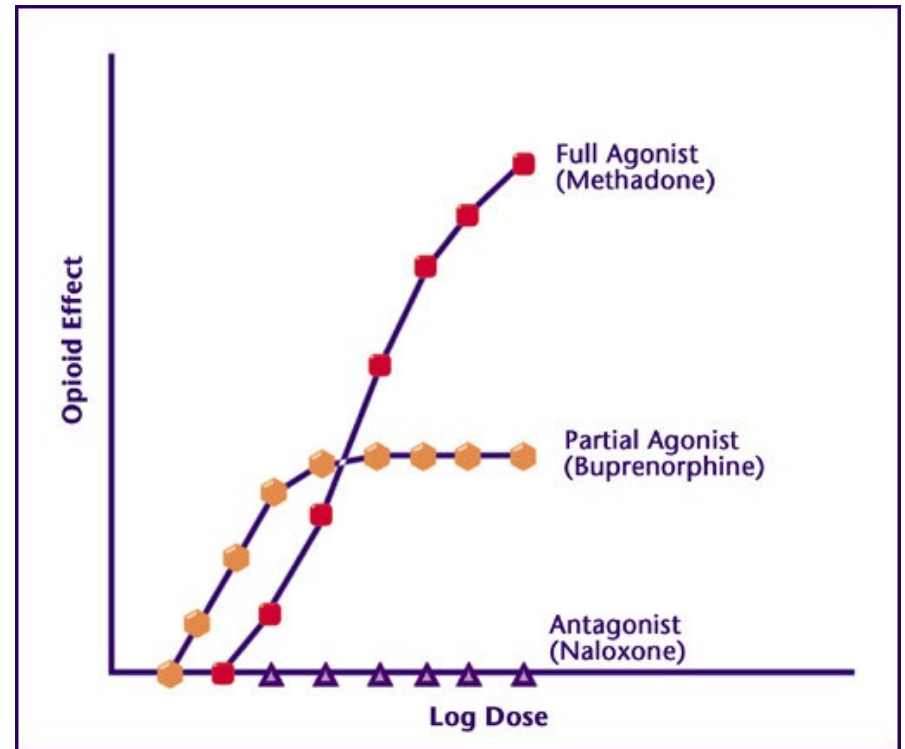
- Opioid dependent
- LFTs >3x normal

Pearls

- There exist naltrexone-assisted detox protocols to allow XR-naltrexone at day 7.
- Need to plan ahead for surgery

Buprenorphine mechanism

- Partial agonist at μ -opioid receptor
- Very small K_d (tight binding to μ -OR)
- Antagonist at κ -opioid receptor (antidepressant effect?)



Buprenorphine - effectiveness

- All doses retain in treatment better than placebo
- Doses \geq 16mg per day suppress illicit use
- Reduces all-cause mortality (4.3 vs 9.5 deaths/1000 person-years in vs out tx)

Mattick, Breen, Kimber, & Davoli, 2014;
Sordo et al., 2017

Buprenorphine

- Office-based dosing
- Formulations
 - Sublingual: bup/nal (tab), Suboxone (film), Subutex (tab), Zubsolv (tab)
 - Intramuscular (q30 days): Sublocade
 - Subdermal (q6 months): Probuphine
 - Transdermal: Bunavail
- Naloxone prevents injection (little absorption)
 - Buprenorphine only (Subutex) if pregnant

Buprenorphine

Dosing

- 2-32mg daily
- Can split doses
 - Analgesic benefits 6-8 hours
- Doses 16+mg daily shown to decrease positive tox screens.

Buprenorphine - Induction

- **Withdrawal**: sx from ↓ opioid availability
- **Precipitated withdrawal**: intense sx from ↓ opioid activity after adding opioid antagonist or partial agonist
- **Bupe induction**: prevent precipitated withdrawal by not starting buprenorphine until opioid activity is low (although patient in some withdrawal)
 - **Microdosing** protocols exist; slow start of bup/nal without withdrawal

Buprenorphine - Injectable

RBP-6000 (Sublocade): q30d at 300mg or 100mg

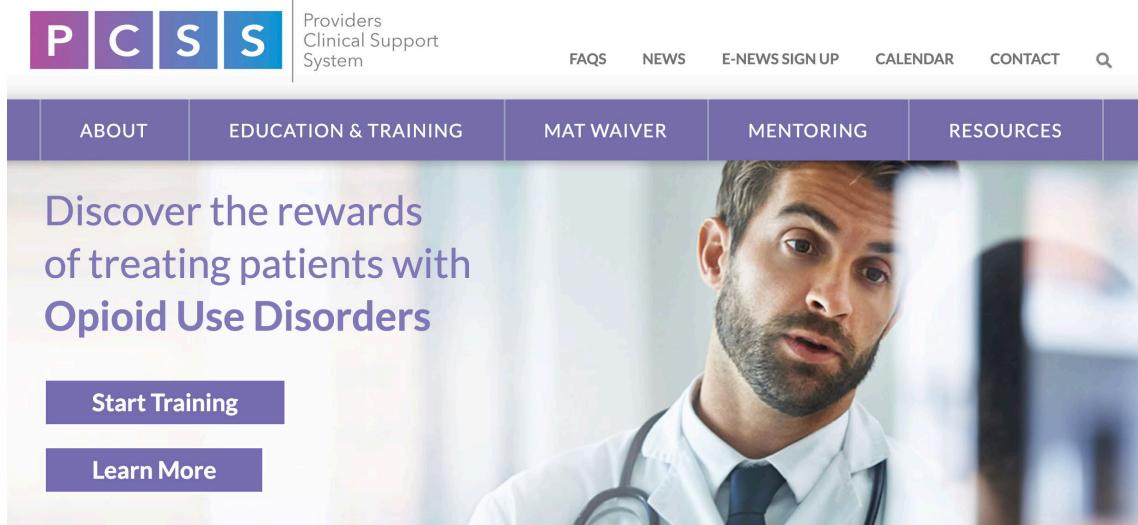
- 300mg/2mo + 100mg / 4 months beat placebo and equivalent to 300mg / 6mo.
- Often requires some amount of supplemental sublingual bup/nal for first few weeks

CAM2038 (Brixadi): weekly or monthly; flexible dosing

- Non-inferior response rates to sublingual bup/nal
- Tentative approval by FDA (as of Aug 2020)

Buprenorphine – Get started

Learn more at <https://PCSSnow.org>



PCSS Providers Clinical Support System

FAQS NEWS E-NEWS SIGN UP CALENDAR CONTACT Q

ABOUT EDUCATION & TRAINING MAT WAIVER MENTORING RESOURCES

Discover the rewards of treating patients with Opioid Use Disorders

Start Training

Learn More

PUBLIC HEALTH UPDATE: As the situation with COVID-19 rapidly evolves, SAMHSA is promoting the use of evidence-based resources and practices related to the virus. PCSS has collected a variety of resources you may find helpful while we all navigate this difficult healthcare crisis. PCSS also offers a discussion forum moderated by addiction specialists where health professionals can post questions and receive answers from clinical experts and other colleagues. For questions or concerns, email pcss@aaap.org.

View Resources

Join Discussion Forum

- Free training re: SUD care
- Online X-waiver training
- Online mentoring
- Free CME

Methadone

Pharmacology

- Variable half-life 24-36 hrs
- Analgesic benefit for 8-12 hrs
- Liver metabolism
 - Induces own metabolism

Methadone

Dosing

- Only at licensed Opioid Treatment Programs (OTPs)
- Can earn “take home” doses
- Typical dose range: 60-120mg once daily

Methadone

Contraindications

- Respiratory compromise
 - Severe COPD, severe OSA
- QTc > 500ms
- Paralytic ileus
- Prescribed benzodiazepines (relative)

Methadone

Whom to refer?

- Need structure of daily dosing
- Chronic pain
 - but recall limited duration of analgesic effect; eventual split dosing?

How to choose MOUD treatment

Injectable Naltrexone vs Buprenorphine/Naloxone

- US: 570 in opioid detox randomized to XR-NTX or Bup/Nal with 24 week f/u
 - Better induction with Bup/Nal (94%) vs XR-NTX (72%)
 - If successfully inducted, similar rates of relapse, positive urines tox screens, adverse events
 - Moderator: Homeless favors XR-NTX; not homeless favors Bup/Nal
- Norway: 159 outpatients randomized to XR-NTX or Bup/Nal with 12 week f/u
 - XR-NTX non-inferior to bup/nal re: retention and superior re: illicit opioid use

Ongoing trials to compare XR-Bup with sublingual Bup/Nal and XR-NTX.

Agenda

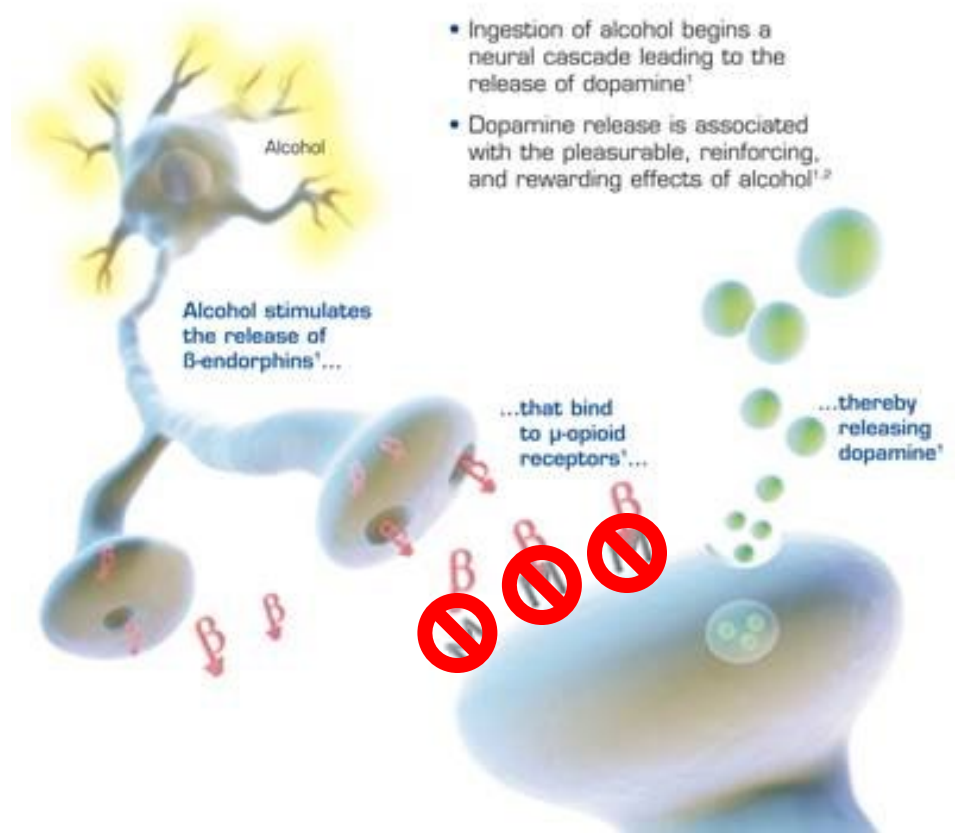
- Talking to patients about SUD and medications
- Virtual care
- Pharmacology for opioids
- **Pharmacology for alcohol**

FDA Approved Options

- Naltrexone
- Acamprosate
- Disulfiram

Naltrexone: mechanism

- Opioid receptor blocker interferes with dopamine release from alcohol



Naltrexone: efficacy (alcohol)

Oral naltrexone

- Reduced heavy drinking (NNT=12)
- Decrease daily drinking (NNT=25)
- Abstinence (NNT=20)
- Decrease cravings

Extended-release (IM) naltrexone

- Similar as naltrexone
- Ongoing clinical trials vs oral naltrexone

Naltrexone (for alcohol)

Dosing

- 50mg daily
- 25mg for first 6 days, with food to mitigate side effects
- 380mg qMonth injectable

Side effects

- Nausea / ↓ appetite
- Headaches
- Elevated LFTs (rare)
 - Baseline and within first month

Contraindications

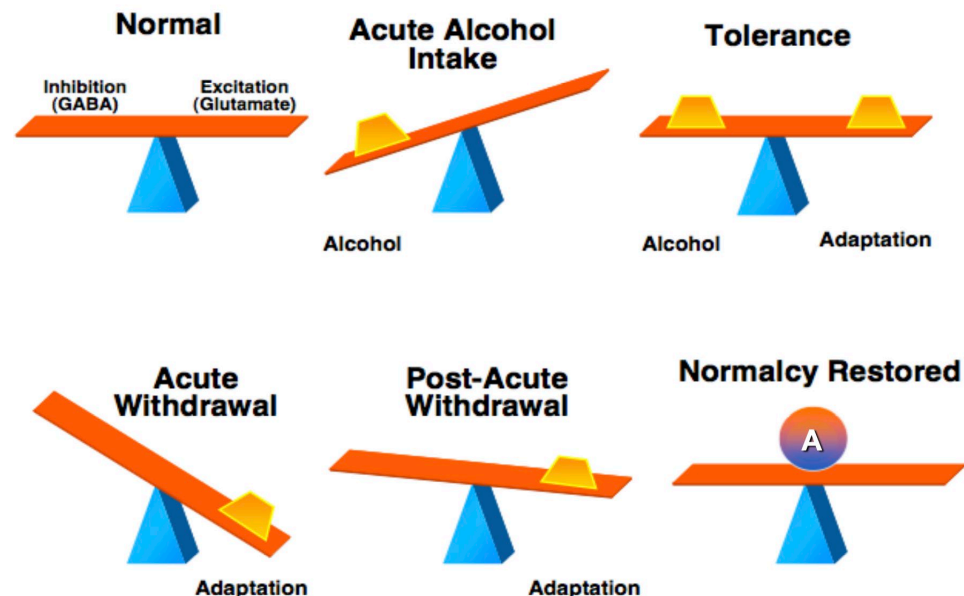
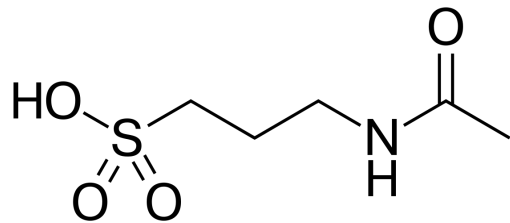
- Opioid dependent
- LFTs >3x normal

Pearls

- Can drink on naltrexone
- Less evidence for prn use, or "The Sinclair Method"
- Stop 48-72 hours before surgery

Acamprosate: mechanism

- Mechanism unclear
- Restores “balance” of excitatory to inhibitory tone
 - mGluR5 antagonist (thereby inhibitory modulator of NMDA-Rs)



Acamprosate: efficacy

Acamprosate

- Maintained abstinence (NNT=8)
- No effect on return to heavy drinking
- Decrease cravings

Acamprosate

Dosing

- 666mg tid (333mg pills)
- 333mg tid initially

Side effects

- Flatulence/diarrhea
- Nausea
- Itching

Contraindications

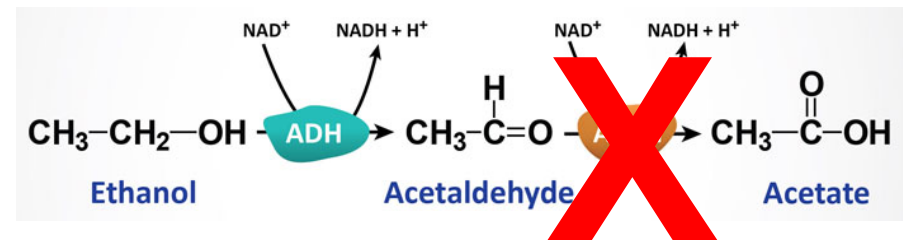
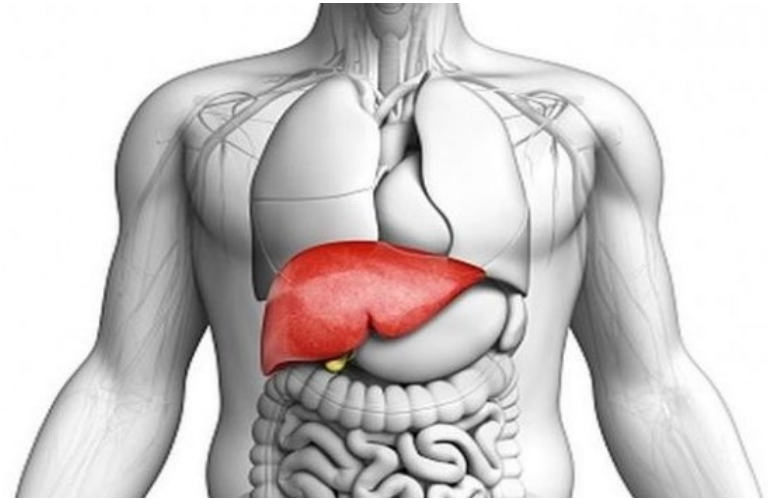
- CrCL <30
- Hypercalcemia
 - TC ≥ 10.3; IC ≥ 5.4

Pearls

- Particularly helpful for negative-emotional state craving (e.g., drinking when sad)
- Can improve alcohol-alterations to sleep architecture
- Best if started while abstinent

Disulfiram – mechanism of action

- Inhibiting acetaldehyde dehydrogenase
- Build up acetaldehyde:
 - Decrease BP
 - Increase HR
 - Sweating
 - Flushing
 - Headaches
 - Vomiting
- Psychological med



Disulfiram - efficacy

- Significantly improved:
 - Abstinence
 - Percentage of abstinence days
 - Time to first drink
- Benefits seen only in open-label trials

Disulfiram

Dosing

- 250-500mg daily
(or ↓ dose or ↓ freq)
- First dose 12+ hrs after last drink
- Disulfiram reaction up to 14d after last dose

Side effects

- Drowsiness (8-10%)
- Garlic/metallic taste
- Fulminant hepatic failure
 - Check LFTs: baseline, 2 weeks, 2 months

Contraindications

- Severe myocardial disease / coronary occlusion
- Confusion
- LFTs > 3x normal

Pearls

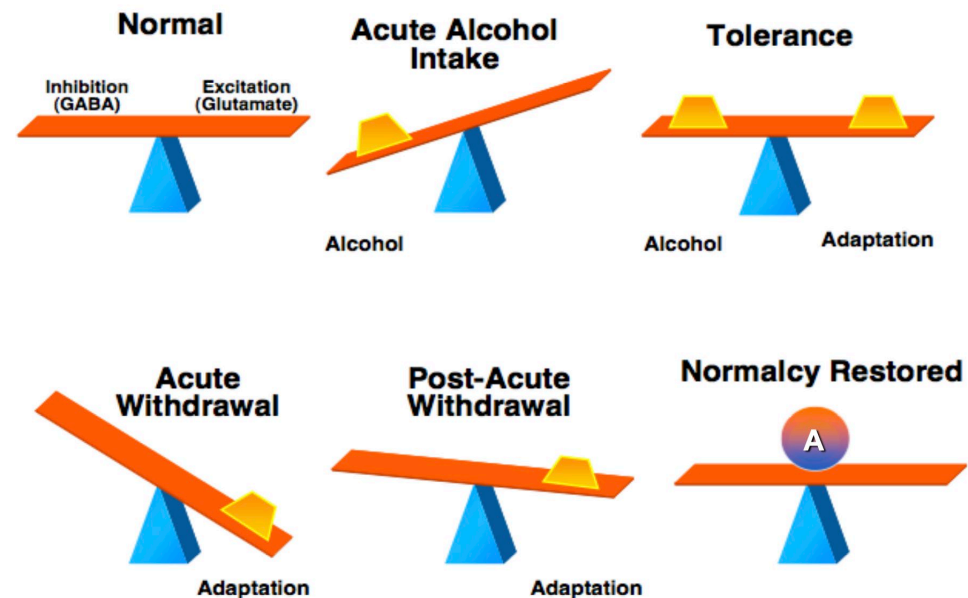
- MUST education on reaction
 - No sauces, perfume, hand sanitizer, etc
- More effective when ingestion is monitored
 - Timothy O'Farrell trust conversations
- Useful to prevent impulsive drinking

Non-FDA Approved Options

- Topiramate
- Gabapentin
- Baclofen
- Valproate
- Ondansetron

Topiramate: mechanism

- Mechanism unclear
- Facilitates GABA_A activity and decreases AMPA and kainate glutamatergic receptors
- Normalizes VTA GABA activity



Topiramate - efficacy

- Decreases % heavy drinking days
- Decreases drinks per drinking day
- Fewer drinking days

- Non-inferior to naltrexone (non-significantly better)
 - Target dose of 300mg in one study; 200mg in another study

Topiramate

Dosing

- 200-300mg divided bid

Side effects

- Cognitive dulling
- Appetite suppression
- Kidney stones

Contraindications

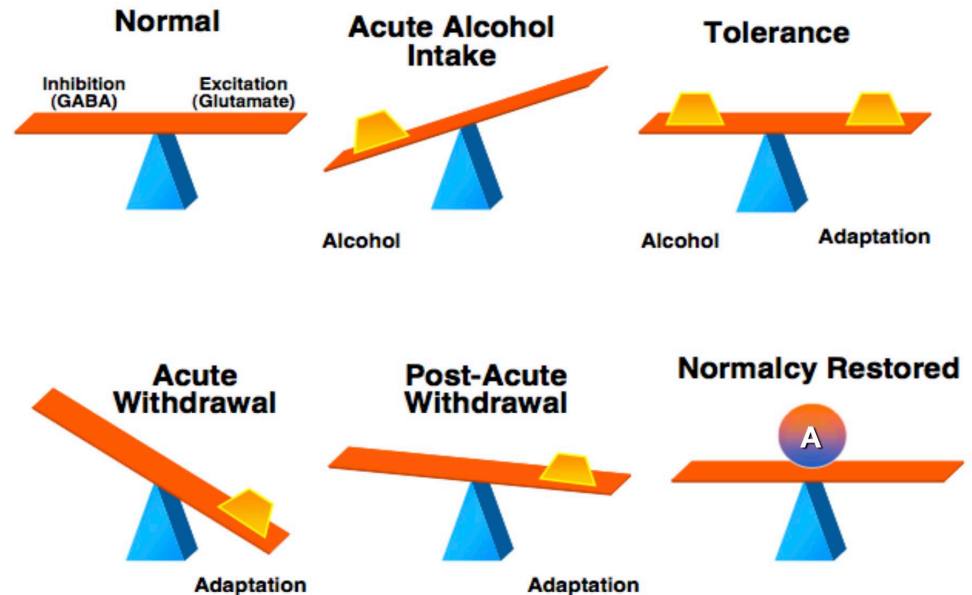
- Previous kidney stones

Pearls

- Increase dose by 25mg per week, until 100mg, then by 50mg per week to avoid cognitive dulling
- Particularly useful if patient desires migraine management and/or weight loss

Gabapentin - mechanism

- Inhibits Voltage-gated calcium channel
- Decrease glutamate release
- (No relation to GABA)



Gabapentin - efficacy

- Decreased number of drinks
- Delayed return to heavy drinking
- Gabapentin enacarbil – no impact on heavy drinking days, abstinence, drinks per week, etc.

Leung, Hall-Flavin, Nelson, Schmidt, & Schak, 2015;
Falk et al., 2019

Gabapentin

Dosing

- 600mg tid
- Higher better?

Side effects

- Sedation

Contraindications

- Renal disease

Pearls

- Start 300mg nightly, rapidly increase to 300mg tid. Then increase to 600mg tid.
- Can be helpful with comorbid anxiety and/or neuralgia

Take home points

- Your attitude and language around substance use disorders can make an important difference to patients.
- Virtual care is different, imperfect, and necessary in times of increasing use.
- Medications can be an effective tool towards improving outcomes for SUDs.
- Please get an X-waiver for buprenorphine prescribing. <https://pcssnow.org>

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