

# Alcohol Use Problems: Recommendations for Medical Management

AOAAM Essentials in Addiction Medicine

# Disclosures

- none

# Objectives

- To have a better understanding of the origin of co-morbid illness.
- To understand some of the more common presentations.
- To understand the basic principals of treatment of the co-morbid patient.

# Objectives

Attendees will have a better understanding of:

- The developmental components of alcohol use problems.
- The commonly used medication assisted withdrawal techniques.
- The importance of monitoring and encouraging ongoing treatment at the appropriate level of care of these patients.

# Introduction

- Epidemiology
  - Co-Morbid
  - Medical Morbidity and Mortality
- Neurobiology of Alcohol
  - Behavioral
  - Pharmacokinetics
- Patterns of drinking
- Screening for alcohol use disorders
- Treatment
  - MET
  - “The Steps”
  - Relapse Prevention
  - Pharmacological
- Treatment in a Chronic Illness Paradigm

# Co-Morbid Alcohol Problems

- The third leading cause of death in the United States, behind tobacco, poor diet and physical inactivity (obesity)
- The second leading cause of disability and disease burden in the United States
- Associated with 41% of traffic deaths,
- 29% of suicides, which constitute the leading causes of death among persons aged 15 to 35 years.

# Alcohol and Health

- **Health risks:** Excessive alcohol consumption
- Cancer
  - pancreas
  - Mouth
  - Pharynx
  - Larynx
  - esophagus
  - Liver
  - breast cancer
- Pancreatitis
- Sudden death in people with cardiovascular disease
- Stroke
- Brain atrophy (shrinkage)
- Cirrhosis of the liver
- Miscarriage
- Fetal alcohol syndrome in an unborn child, including impaired growth and nervous system development
- Injuries due to impaired motor skills
- Suicide
- Heart muscle damage (alcoholic cardiomyopathy) leading to heart failure

# Co-Morbid Alcohol Problems

- 13.5% of the US population had experienced an alcohol disorder during their lifetime
- A third of those people have had at least one other psychiatric diagnosis, this number is even higher among women.
- 22% of mood disordered patients have an alcohol use disorder, 17.9% anxiety patients, 73.6% of antisocial patients.

# Alcohol and Health

- Health benefits: Moderate alcohol consumption
  - Reduce your risk of developing heart disease, peripheral vascular disease and intermittent claudication
  - Reduce your risk of dying of a heart attack
  - Possibly reduce your risk of strokes, particularly ischemic strokes
  - Lower your risk of gallstones
  - Possibly reduce your risk of diabetes

# Problem drinking

- How much is “too much”
  - Causes or elevates the risk for alcohol related problems, or
  - Complicates management of other health problems
- There are increased risks for alcohol-related problems for...
  - Men who drink more than 4 standard drinks in a day or more than 14 in a week
  - Women who drink more than 3 standard drinks in a day or more than 7 per week.

# Problem drinking

- About 3 in 10 adults drink at levels that elevate health risks
- Among heavy drinkers, 1 in 4 has alcohol abuse or dependence.
- All heavy drinkers have a greater risk of hypertension, gastrointestinal bleeding, sleep disorders, major depression, hemorrhagic stroke, cirrhosis of the liver, and several cancers.

# Problem drinking

- Heavy drinking often goes undetected
  - Patients with alcohol dependence received the recommended quality of care only about 10 percent of the time.

# Screening and Brief Intervention

- Patients are likely to be more receptive, open, and ready to change than you expect
  - Most patients don't object to being screened for alcohol use by clinicians and are open to hearing advice afterwards
  - Most primary care patients who screen positive for heavy drinking or alcohol use disorders show some motivational readiness to change
  - Those who have the most severe symptoms are often the most ready to change.

# Screening and Brief Intervention

- Brief interventions can promote significant, lasting reductions in drinking levels in at-risk drinkers who are not alcohol dependent.

# Screening and Brief Intervention

- Screening
  - A single question about heavy drinking days to use during a clinical interview
    - Do you sometimes drink beer, wine or other alcoholic beverages
      - How many times in the past month have you had 5 (man), 4 (woman) drinks in a day?
  - A standard drink is 14grams of or alcohol
    - 12 oz beer
    - 5 oz wine
    - 1.5 oz liquor

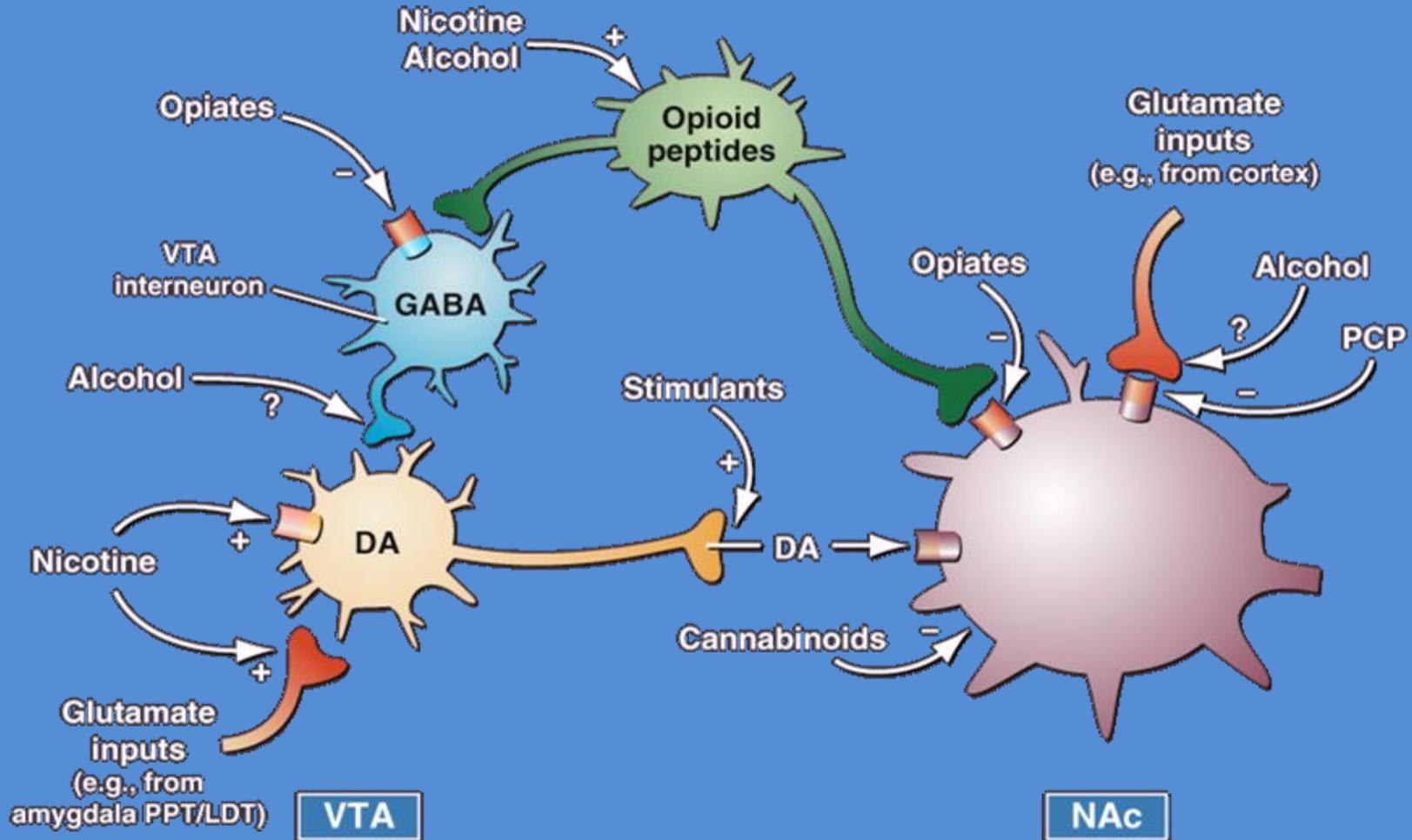
# Screening and Brief Intervention

- The AUDIT – a self report instrument
  - 10-question Alcohol Use Disorders Identification Test (AUDIT) (12), may be used to obtain more qualitative information about a patient's alcohol consumption.
  - Research shows that the AUDIT may be especially useful:
    - Most populations including women, minorities, adolescents and young adults; there is little research in older patients.
    - The AUDIT includes questions of
      - Quantity
      - Frequency
      - Binge drinking
      - Dependence symptoms
      - Alcohol-related problems
  - Positive Screening ( $\geq 8$  for men,  $\geq 4$  for women)

# Neurobiology of Alcohol Intoxication

- Multiple systems involved with selective actions.
  - GABA ( $\gamma$ -aminobutyric acid)
  - Glutamate
  - Opioids
  - Cannaboids
  - Dopamine
  - Serotonin

# Unconditioned Response



# Neurobiology of Alcohol Intoxication

- GABA-A is intimately involved in the intoxicating effects of alcohol (motor impairment and anxiolytic)
- GABA-B is involved in the craving and withdrawal effects of alcohol.

# Neurobiology of Alcohol Intoxication

- Opioid system – involved in desire to drink and self administration.
- Cannabinoid CB1 receptors – result in decrease alcohol preference
- Dopamine – Involved in alcohol reinforcement, repeated administration increases dopamine in the nucleus accumbens, involvement in cues.
- Serotonin - reuptake blockade can decrease alcohol intake

# Alcohol Treatment

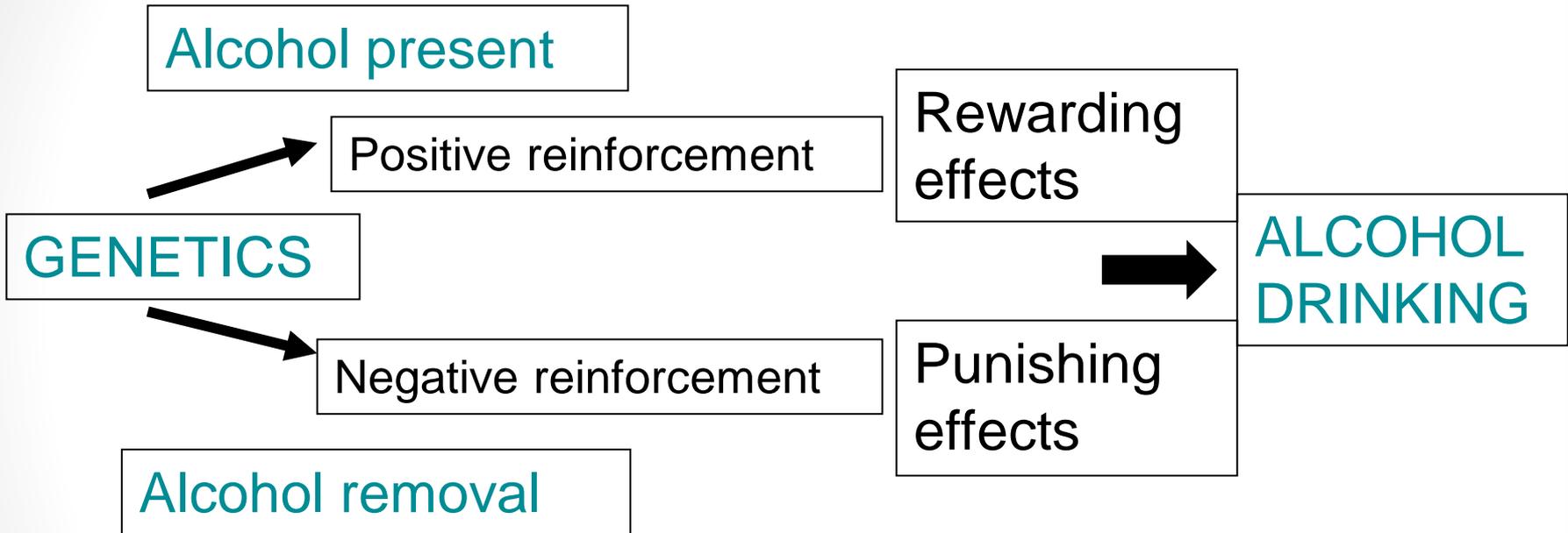


*"I can change! I swear!"*

# Treatment

- Treatment
  - MET
  - “The Steps”
  - Relapse Prevention
  - Family Therapy
  - Social Support

# Reinforcing effects of alcohol



Similar to the early signs of the alcohol withdrawal syndrome.  
Consequence of “opposing neuro-adaptation” in CNS?

# Classical conditioning and relapse

## Unconditioned stimulus

Alcohol in brain

## Response

**Reward** – alterations in neurotransmission causing relaxation, euphoria, stress buffering etc.

## Associated stimuli

**Enteroceptive** – mood states that precipitate drinking

**Exteroceptive** – environment, sight of alcoholic drinks, smell and taste of alcohol (or e.g. smoking) etc

Repetition makes the associated stimuli become **conditioned stimuli** and capable of eliciting **anticipation of reward**, i.e. they have become **positively reinforcing** and potential causes of relapse.

# Negative reinforcement in abstinence

## Same UC stimulus

Alcohol in brain

## Different response

Adaptation – *alterations in neurotransmission designed to oppose the effects of alcohol.*

## Same associated stimuli

**Enteroceptive** – mood states that precipitate drinking

**Exteroceptive** – environment, sight of alcoholic drinks, smell and taste of alcohol (or e.g. smoking) etc

In dependence **conditioned stimuli** elicit CNS **adaptation to alcohol** generating “conditioned tolerance” if alcohol is taken and “pseudowithdrawal” if it is not, i.e. they are now **negatively reinforcing** and potential causes of relapse.

# Relapse

## Conditioned stimuli

### Affect & Stress

**Enteroceptive** – mood states that precipitate drinking

**Exteroceptive** – environment, sight of alcoholic drinks, smell and taste of alcohol etc

“Cues” & “Priming”

## Response

Anticipation of reward and pseudowithdrawal simultaneously or sequentially provide **positive and negative reinforcement** for relapse?

# Causes of relapse

- Genetics?
- Boredom
- Peer pressure
- Memories

Not much that drug treatment can do about these; so drugs are never going to be completely effective?

- Cues
- Priming
- Affect
- Stress

Areas where drug treatment may be effective.

- There many triggers to relapse but only a few are drug targets.
- What is it about cues, priming, affect and stress that can induce a relapse?

# Alcohol Withdrawal Treatment

- Alcohol – related seizures
  - Grand mal in 15-23% (Victor M, 1953;Guthrie, 1989)
  - Usually in first 48 hours but may be seen up to 10 days
  - May be multiple, rarely status, may require diazepam 10 mg slow IVP
  - 1st episode or atypical seizure: evaluate for other causes
  - Ongoing pharmacotherapy not indicated for w/d seizures
  - Genetic pre-determinates, past seizure disorder, hx withdrawal seizures, combination alcohol and benzodiazepine withdrawal.

# Alcohol Withdrawal Treatment

- Hallucinosiis
  - Primarily auditory
    - Tactile
    - Visual
  - Typically with intact sensorium

# Alcohol Withdrawal Treatment

- DTs
  - Acute, reversible, organic psychosis; significant morbidity and mortality
  - Usually begins approx. 72 hours; may last 2 - 6 days and sometimes longer
  - Severe AWS symptoms with clouded sensorium
  - Hallucinations w/o insight produce panic and severe agitation
  - Mortality increases with delayed Dx, inadequate Rx, and concurrent medical conditions.

# Alcohol Withdrawal Treatment

- Supportive
  - Quiet
  - Well lit room
- Behavioral
- Nutritional
- Drug Therapy

# Alcohol Assessment

- Clinical Institute Withdrawal Assessment - Ar
  - Ten item scale
  - Rapid assessment
  - Easy scoring 10 signs (0-7) 0-67
  - Administered by medical personnel
  - Patient needs to be communicative
  - Subjective on the part of the patient and the nurse.

# CLINICAL INSTITUTE WITHDRAWAL ASSESSMENT OF ALCOHOL SCALE, REVISED (CIWA-AR)

Patient: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_ (24 hour clock, midnight = 00:00)

Pulse or heart rate, taken for one minute: \_\_\_\_\_ Blood pressure: \_\_\_\_\_

**NAUSEA AND VOMITING** — Ask “Do you feel sick to your stomach? Have you vomited?” Observation.

- 0 no nausea and no vomiting
- 1 mild nausea with no vomiting
- 2
- 3
- 4 intermittent nausea with dry heaves
- 5
- 6
- 7 constant nausea, frequent dry heaves and vomiting

**TREMOR** — Arms extended and fingers spread apart. Observation.

- 0 no tremor
- 1 not visible, but can be felt fingertip to fingertip
- 2
- 3
- 4 moderate, with patient's arms extended
- 5
- 6
- 7 severe, even with arms not extended

**PAROXYSMAL SWEATS** — Observation.

- 0 no sweat visible
- 1 barely perceptible sweating, palms moist
- 2
- 3
- 4 beads of sweat obvious on forehead
- 5
- 6
- 7 drenching sweats

**ANXIETY** — Ask “Do you feel nervous?” Observation.

- 0 no anxiety, at ease
- 1 mild anxious
- 2
- 3
- 4 moderately anxious, or guarded, so anxiety is inferred
- 5
- 6
- 7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

**AGITATION** — Observation.

- 0 normal activity
- 1 somewhat more than normal activity
- 2
- 3
- 4 moderately fidgety and restless
- 5
- 6
- 7 paces back and forth during most of the interview, or constantly thrashes about

**TACTILE DISTURBANCES** — Ask “Have you any itching, pins and needles sensations, any burning, any numbness, or do you feel bugs crawling on or under your skin?” Observation.

- 0 none
- 1 very mild itching, pins and needles, burning or numbness
- 2 mild itching, pins and needles, burning or numbness
- 3 moderate itching, pins and needles, burning or numbness
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**AUDITORY DISTURBANCES** — Ask “Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?” Observation.

- 0 not present
- 1 very mild harshness or ability to frighten
- 2 mild harshness or ability to frighten
- 3 moderate harshness or ability to frighten
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**VISUAL DISTURBANCES** — Ask “Does the light appear to be too bright? Is its color different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?” Observation.

- 0 not present
- 1 very mild sensitivity
- 2 mild sensitivity
- 3 moderate sensitivity
- 4 moderately severe hallucinations
- 5 severe hallucinations
- 6 extremely severe hallucinations
- 7 continuous hallucinations

**HEADACHE, FULLNESS IN HEAD** — Ask “Does your head feel different? Does it feel like there is a band around your head?”

- Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
- 0 no present
  - 1 very mild
  - 2 mild
  - 3 moderate
  - 4 moderately severe
  - 5 severe
  - 6 very severe
  - 7 extremely severe

**ORIENTATION AND CLOUDING OF SENSORIUM** —

- Ask “What day is this? Where are you? Who am I?”
- 0 oriented and can do serial additions
  - 1 cannot do serial additions or is uncertain about date
  - 2 disoriented for date by no more than 2 calendar days
  - 3 disoriented for date by more than 2 calendar days
  - 4 disoriented for place/or person

The CIWA-Ar is *not* copyrighted and may be reproduced freely.  
Sullivan, J.T.; Sykora, K.; Schneiderman, J.; Naranjo, C.A.; and Sellers, E.M.  
Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal  
Assessment for Alcohol scale (CIWA-Ar). *British Journal of Addiction* 84:1353-1357, 1989.

Patients scoring less than 10 do not usually need additional medication for withdrawal.

Total CIWA-Ar Score \_\_\_\_\_

Rater's Initials \_\_\_\_\_

Maximum Possible Score 67

# Alcohol Assessment

- Vitals Signs
  - Pulse – Resting  $>90$  bpm
  - Blood pressure – systolic  $> 140$  mmHg
- Consider treatment

# Alcohol Withdrawal Treatment

- Goals
  - Smooth, efficient clinical course
  - No seizures
  - Minimal agitation and discomfort
  - Able to participate in recovery program immediately

# Detoxification from alcohol

- When to use a short half-life sedative
  - Liver disease (patient is jaundiced)
  - Patient is intoxicated and agitated
  - Multiple drugs being used
  - Clinician is uncertain whether the patient has early delirium tremens or early portal systemic encephalopathy

# Alcohol Withdrawal Treatment

- Treatment of AWS – Fixed Dose Regimen
  - Librium 50 / 25 PO Q6hr W/A
  - Ativan 2 / 1mg PO Q6hr W/A
  - Three days meds, one day observation, hold for sedation
  - Ativan 1-2 mg PO or IM prn Symptoms of AWS
  - Ancillary medications

# Alcohol Withdrawal Treatment

- Treatment of AWS – Symptom-driven Regimen
  - Use CIWA scale serially
  - Medicate or observe based on w/d score
  - Pro's: less meds, shorter LOS
  - Con's: requires training, discharge flexibility

# Alcohol Withdrawal Treatment

- Symptom-triggered detoxification
  - Chlordiazepoxide 50 mg for CIWA > 9
  - Repeat CIWA hourly
  - May repeat Chlordiazepoxide q 2 hours CIWA > 9
  - No more than Chlordiazepoxide 300mg in 24 hours

# Detoxification using short half-life sedatives

- Symptom-triggered detoxification
  - Lorazepam 1 mg for CIWA > 9
  - Repeat CIWA hourly
  - May repeat Lorazepam q 2 hours CIWA > 9
  - No more than Lorazepam 10mg in 24 hours
- Only use lorazepam for detoxification when the patient has significant liver disease or another specific indication

# Maintenance Medications To Prevent Relapse To Alcohol Use (FDA-approved)

- Disulfiram
- Naltrexone (oral and injectable)
- Acamprosate
- Topiramate (no FDA approval)

# Medications approved for Alcohol Anti-Relapse

- **#1. Disulfiram (Antabuse) (1940s)**
- Inhibits breakdown of acetaldehyde (produced in liver by metabolism of alcohol).
- When you drink alcohol you feel sick , flushed, have a pounding headache.

# Disulfiram (Antabuse)

- May be helpful in promoting abstinence for highly motivated patients who are monitored to make sure they take their medication.
- A reasonable choice when abstinence is the desired and necessary goal.
- Standard clinical dose: 250 mg/d (dose needs vary)
- Contraindicated in: psychosis, significant liver disease, esophageal varices, pregnancy, impulsivity

(Barth et al., 2010)

# Medications approved for Alcohol Cravings

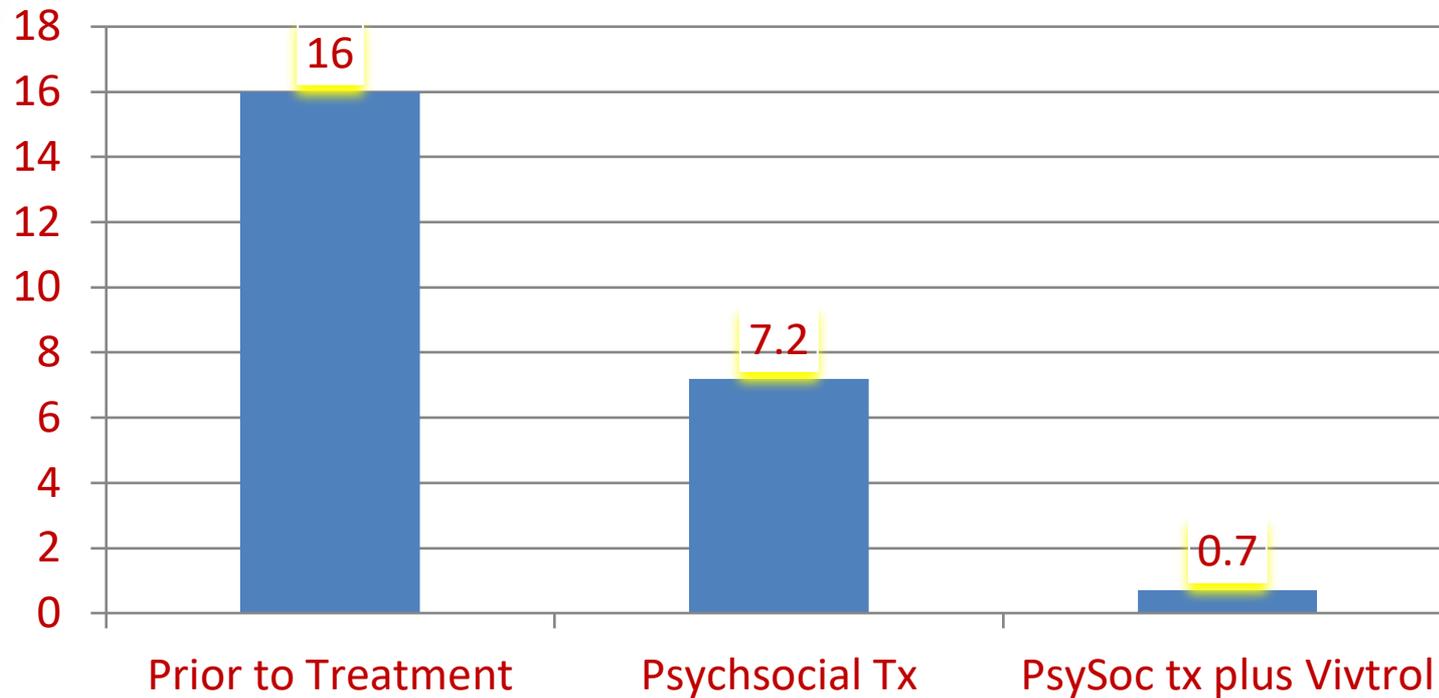
- **#2. Naltrexone (Revia, Vivitrol) (1995, 2004)**
- Relatively mu selective competitive antagonist
- Inhibits endogenous opioid transmitters released by alcohol
- Reduces “rewarding” effects of alcohol and conditioned anticipation of alcohol (i.e. **targets positive reinforcement**).
  - Endogenous opioids are involved in the reinforcing (pleasurable) effects of alcohol and possibly craving
- Long-term compliance oral is not good (maybe some anhedonia), hence value of depot preparation.

# Naltrexone (Revia, Vivitrol)

- For intense cravings for the rewarding effects of alcohol,
- consistent with findings from a meta-analysis of short-term studies of oral naltrexone demonstrating that naltrexone reduces the rate of relapse to heavy drinking by about 38%.
- study of extended-release injectable naltrexone, reductions in heavy drinking ( $\geq 5$  drinks/day for men,  $\geq 4$  drinks/day for women) with this medication plus counseling were on average 25% greater than reductions with placebo injections plus counseling.

# Naltrexone Injectable - Vivitrol

## Median Drinking Days per Month



Results are from a 6-month, multicenter, double-blind, placebo-controlled clinical trial of alcohol dependent patients. This subset of patients abstinent for 4 or more days prior to treatment initiation

# Naltrexone Safety

- Common AEs:
  - nausea
  - headache
  - injection site reaction (hardening, itching or swelling)
  - *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, q 1 month for 3 months, then q 3 months (this recommendation comes from the VA/DoD guidelines for naltrexone use)
    - “Black Box” warning regarding risk of liver injury was removed from Vivitrol in July 2013.
- Contraindicated if patient on opioid pain medications

<http://www.healthquality.va.gov/guidelines/MH/sud/MedicationsForTheTreatmentOfAlcoholUseDisorderBrochure92816.pdf>

# Pharmacotherapy of Alcohol Dependence: Naltrexone

## ORAL NALTREXONE HYDROCHLORIDE

- FDA-approved dose: 50 mg per day

## LONG-ACTING INJECTABLE NALTREXONE

- Monthly gluteal IM injection of 380 mg; microspheres formulation: better adherence, can be given in doctor's office  
Garbutt et al., 2005
- Prolonged abstinence, reduced # heavy drinking days and drinking days if abstinent 4+ days before treatment initiation  
O' Malley et al., 2007

# Medications approved for Alcohol Anti-Relapse

## #3 Acamprosate (Campral) (2004)

- Indirectly inhibits NMDA receptors for glutamate
- Reduces “withdrawal” weakly, reduces conditioned pseudowithdrawal
- **targets negative reinforcement and conditioning?**
- Long-term compliance good, side effects minimal (except for diarrhea)
- Very non-potent (2g/day) and requires dosing 3x/day. (666mg tablets not popular)

# Acamprosate (Campral)

- Stabilizes glutamatergic neurotransmission altered during withdrawal. Littleton 1995
  - Anticraving, reduced protracted withdrawal
  - No abuse liability, hypnotic, muscle relaxant, or anxiolytic properties
  - Dose: 2 g daily (2 333-mg pills three times/d)
  - Contraindicated: significant renal disease (creatinine clearance <70 ml/min)

# Acamprosate (Campral)

- For patients who feel irritable, anxious, and restless, and who experience sleep difficulties associated with the protracted withdrawal syndrome
- Interferes with the alcoholism-induced hyperexcitation of the glutamate system
- May relieve protracted withdrawal symptoms and reduce negatively reinforcing alcohol cravings
- In a meta-analysis, maintenance of abstinence was significantly improved (88%) with acamprosate.
- Though acamprosate and naltrexone work through different mechanisms, it remains unclear whether they produce additive or synergistic benefits when used in combination.

# How to Select a Medication

- **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

# Alcohol Treatments - Summary

- Patient experiences powerful conditioned responses, positive and negative resulting in a powerless feeling.
- Medications can blunt these responses.
- Watch for more refinement in matching patients and periods of greater neuro-adaptability to treatment choice.
- Consider injectable Naltrexone.
- Watch for new medication.

# Questions?