Kentucky School of Alcohol and Other Drug Studies 2017

Medication-Assisted Treatment for Adolescents

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Objectives

- Describe how medication-assisted treatment fits into the context of overall addiction treatment, including for adolescents
- Recognize some advantages and limitations of medication-assisted treatment among special populations (dual diagnosis, pregnancy) of adolescents
- Discuss pharmacotherapy for treatment of opioid use disorder, tobacco use disorder, and alcohol use disorder

Overview

- Overview of Medication-Assisted Therapy
- Lunch
- Pharmacotherapy for Opioid Use Disorder
- Small group case discussions
- Pharmacotherapy for Tobacco Use Disorder
- Break
- Small group case discussions
- Pharmacotherapy for Alcohol Use Disorder
- Small group case discussions
- Wrap-Up

Medication-Assisted Therapy

Long-Term Pharmacotherapy for Substance Use Disorders

- Doesn't cure substance dependence
  - Helps reduce drinking or episodes of use
  - Achieve longer abstinence
- Works for a proportion of patients
- Goals
  - Increase time to relapse
  - Reduce intensity of binge if relapse occurs

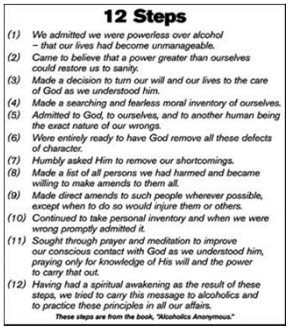
Clinical Use of Pharmacotherapy

- Part of comprehensive plan that addresses psychological, social, & spiritual needs
- Do not use in place of counseling
- Works best in combination with psychosocial support

Behavioral Treatment

- Essential component of addiction treatment
- Multiple modalities available
- Multiple settings
  - Outpatient is most common
- Can be used alone or with pharmacotherapy

12-Step Groups



12 Steps

(1) We admitted we were powerless over alcohol – that our lives had become unmanageable.
(2) Came to believe that a power greater than ourselves could restore us to sanity.
(3) Made a decision to turn our will and our lives to the care of God as we understood him.
(4) Made a searching and fearless moral inventory of ourselves.
(5) Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.
(6) Were entirely ready to have God remove all these defects of character.
(7) Humbly asked Him to remove our shortcomings.
(8) Made a list of all persons we had harmed and became willing to make amends to them all.
(9) Made direct amends to such people wherever possible, except when to do so would injure them or others.
(10) Continued to take personal inventory and when we were wrong promptly admitted it.
(11) Sought through prayer and meditation to improve our conscious contact with God as we understood him, praying only for knowledge of His will and the power to carry that out.
(12) Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics and to practice these principles in all our affairs.

These steps are from the book, "Alcoholics Anonymous."

- Narcotics Anonymous
  - Based on Alcoholics Anonymous
- Group format
- Anonymous
- No cost
- No affiliations or endorsement
- Different groups have different characteristics

Other Addiction Counseling

- Motivational Enhancement
- Cognitive-behavioral Therapy
- Relapse Prevention
- Network therapy
- Family therapy
- Supportive psychotherapy
- Twelve-Step facilitation
- Rational Recovery
- Matrix Model
- Medication Management
- Brief Intervention

Factors to consider

- Whether to add long-term pharmacotherapy
- No pharmacotherapy for most classes of abused drugs
  - Stimulants
  - Hallucinogens
  - Inhalants
  - Marijuana

- Cost
- Availability
- Side effects
- Other meds taken
- Motivation

Adherence

- Medication must be taken consistently to be effective
- Challenging with long-term pharmacotherapy for addiction
  - Many are not immediately rewarding
- Requires sustained motivation
  - Counselors and advocates help with this

What is the endpoint?

- Duration of most long-term pharmacotherapy is not indefinite
  - Months to years
- Goal is stabilization
  - Flexibility
  - Individualized
  - Allow for relapse

Addiction in Adolescents

- Pattern of use
  - Shorter duration
  - Fewer consequences
- Protection from consequences
  - Family
  - Legal (Juvenile Justice System vs. adult courts)
- Immaturity
  - Don't recognize problem
  - Habilitation, not rehabilitation

Substance Use Disorders in Adolescents

- More difficult to treat
- Higher relapse rates
- Worse outcomes
- Increased risk for injuries and violence

SUD Pharmacotherapy in Adolescents

- Medications that are regular component of adult treatment are not often used in youth
- Lack of FDA approval
- Not a lot of published data
- Youthful experimentation may not lead to full SUD

Opioid Painkillers

Short-acting

- **Tylenol #3 (codeine)**
- **Darvon (propoxyphene)**
- **Vicodin (hydrocodone)**
- **MSIR (morphine)**
- **Percocet (oxycodone)**
- **Dilaudid (hydromorphone)**
- **Fentora (fentanyl)**

Long-acting

- **MS Contin (morphine)**
- **OxyContin (oxycodone)**
- **Opana ER (oxymorphone)**
- **Dolophine (methadone)**
- **Duragesic (fentanyl)**
- **Exalgo (hydromorphone)**

Opioid effects

- Analgesia
  - Dissociation from pain
- Euphoria
  - Dissociation from anything/everything unpleasant
- Sedation
  - Reduction of anxiety
- Slows respiratory rate
- Smooth muscle relaxation
  - Nausea
  - Constipation
- Vasodilation
  - Low blood pressure
  - Headache
- Histamine release
  - Itching
- Cough suppression

Opioid Use in Adolescents

- 2015 data
  - 276,000 adolescents were current nonmedical users of opioid painkillers
  - 122,000 having an addiction to prescription pain relievers
  - 21,000 adolescents had used heroin in the past year
  - 5,000 were current heroin users
- Admissions for opioid addiction treatment have increased

Opioid Use Progression

- Most adolescents who misuse prescription pain relievers are given them for free by a friend or relative
- 4/5 new heroin users started out misusing prescription painkillers
- 94% of people in treatment for opioid addiction said they chose to use heroin because prescription opioids were “far more expensive and harder to obtain.”

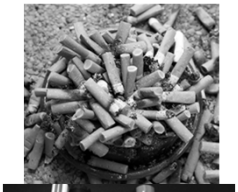
Tobacco

- Cigarettes, cigars, pipes
  - Many different harmful compounds
- Smokeless tobacco
  - “snuff,” “chew”
- Stimulant & relaxes
- Acute effects
  - Vasoconstriction
- Very short-acting, so high-frequency use
  - Very reinforcing

Electronic cigarettes

- Neither designed nor marketed for smoking cessation
- Intentionally attractive to youth with flavorings (bubblegum, etc.)
- Only recently became regulated in U.S.
- Less harmful than tobacco, but more dangerous than air

Smoking rates



- Tobacco & weight
  - Girls concerned about their weight start smoking at higher rates than boys
- 13% of adolescents smoke ½ pack/day
- Up to 24% of girls and 30% of boys have ever used e-cigarette
  - 7- to 10-fold increase from 2011 to 2015

Why is it so hard to quit smoking?

- Nicotine is as addicting as heroin, cocaine, or alcohol
- Stimulation of nicotine receptors in the brain & activation of the dopamine reward system mediate the pleasurable effects and positive reinforcement

Why is it so hard to quit smoking?

- The behaviors of seeking, lighting, & self-administering cigarettes become entrenched in daily routine
- Nicotine has become important in modulation of mood, appetite, energy metabolism, and ability to deal with stress & boredom

Alcohol

- CNS depressant
- Disinhibition
  - Depress inhibitions first
  - Reduce anxiety
  - Fun at parties
- Socially acceptable
- Readily available
  - Not illegal
  - Obtain from older peers

Epidemiology

- Most teens use alcohol occasionally without consequences
  - 80% of high school students have used alcohol
- Problem behavior
  - 35% of 12th graders binge drink at least once a month
  - 4% of adolescents drink daily

Alcohol use & abuse

- Prevalence of alcohol disorders highest among young adults
- Risk factors for alcohol dependence
  - Male
  - Younger age
  - Family history
  - Unemployment
  - Dropping out of school

Epidemiology and race

- Black youth have lower rates of substance use than Whites or Hispanics
- Blacks and Hispanics
  - Less likely to drink
  - More likely to have chronic dependence once disorder develops
- Hispanic girls have lower rates of alcohol consumption
  - May mask severity of Hispanic male consumption

Predictive factors

- Factors
  - Age of first use
    - 40% of children who begin drinking before age 15 will develop alcohol dependence
  - Developmental level
  - Frequency of use
    - More important than duration of use
- Predicts more rapid progression

Substance abuse and sexual behaviors

- Risk-taking behavior while intoxicated
  - Unprotected sex may lead to pregnancy
- Drug use causes irregular menstrual cycles, but can still conceive
  - May not realize she is pregnant for several months

Opioids: Effects on fetus

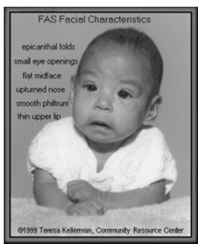
- No known fetal anomalies
- Intrauterine growth retardation
- Neonatal abstinence syndrome
  - Continuous exposure
  - Use up to delivery

Smoking: Effects on fetus

- Most common fetal exposure
- Intrauterine growth retardation
- Higher rates of spontaneous abortion, placenta previa, etc.
- SIDS risk >4x higher
- Nicotine patch better than smoking cigarettes

Alcohol: Effects on fetus

- Fetal Alcohol Syndrome
- Fetal Alcohol Effects
  - Spectrum disorder
- Leading preventable cause of mental retardation
- Encourage abstinence as soon as pregnancy suspected



Medication-Assisted Therapy

- Opioids
  - Prescription painkillers
  - Heroin
- Tobacco
  - Cigarettes
  - Smokeless tobacco
  - Electronic cigarettes
- Alcohol
  - Beer
  - Wine
  - Liquor



Opioid addiction treatments


- Abstinence-based
  - Narcotics Anonymous
  - Residential (with or after detox)
- Behavioral
  - Motivational Interviewing
  - Cognitive-behavioral (CBT)
- Antagonist maintenance
  - Naltrexone
- Opioid maintenance
  - Methadone
  - Buprenorphine

Nicotine Pharmacotherapy

- Replacement
  - nicotine patches
  - nicotine gum
  - nicotine nasal spray
  - lobeline (CigArrest)
- Partial agonists
  - Varenicline (Chantix)
- Antidepressants
  - Bupropion (Zyban)
  - Fluoxetine (Prozac)
- Antagonists
  - mecamylamine
- Deterrent therapy
  - silver acetate

Medications for Alcohol Use Disorder

- Acamprosate (Campral)
- Naltrexone
  - Oral (ReVia)
  - Injection (Vivitrol)
- Disulfiram (Antabuse)

Barriers to medication-assisted treatment in adolescents

- Philosophical opposition
- Compliance issues with medication
  - Irresponsibility
  - Cost
  - Interactions
- Denial of severity
  - Both adolescent & family

Coming off

- Plan ahead
- Support system in place
- Communication between counselor and client
  - Meeting treatment goals
  - Achieved stability
  - Relapse risk factors
- Taper down slowly to avoid withdrawal
- Transition to treatment without pharmacotherapy
  - Treatment doesn't end, just medication prescription

Monitoring for relapse

- Patient report
- Clinical observation
- Collateral information
  - Family
  - Other counselors
  - Probation officer
- Urine drug screening

Relapse: What to look for

- Evasive behavior
- Missing sessions
- Worsening of personal hygiene
- Appears intoxicated
- Hang out with friends who use
- Legal problems
- Reversal of sleep-wake cycle (staying up all night)

Relapse: What to do

- Relapses and remissions are part of any chronic disease process
- Intensify treatment efforts
- Safety issues
  - Overdose risk
- Permission to communicate with others

Questions?

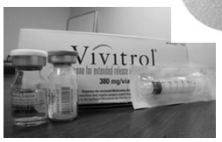
Lunch Time!

Pharmacotherapy for Opioid Use Disorder

Antagonists vs Agonists

- Opioid Antagonists
  - Naloxone (Narcan)
    - Overdose treatment
    - IV, nasal spray
    - Works rapidly
    - Wears off quickly
  - Naltrexone
    - Oral or intramuscular
    - Long-term pharmacotherapy
    - Take regularly for maintenance treatment
- Opioid Agonists
  - Methadone
    - For addiction treatment, restricted to licensed treatment programs
    - Also prescribed for chronic pain management
  - Buprenorphine
    - Office-based opioid treatment (OBOT)
    - Multiple brand names

Naltrexone



- Blocks opioid receptors
  - No effect from using
- Reduces cravings
- Available as
  - Tablets taken daily
  - Intramuscular injection given monthly
- Must be taken to be effective
  - Best when monitored
  - Motivation is key

Oral naltrexone (ReVia)

- Once-daily tablet
- Tablets are much less expensive than injection
  - Generic form available
  - Covered by health insurance
- Requires motivation to take every day
  - Not providing a positive, but preventing a negative
  - Less effective when doses are missed
- No street value

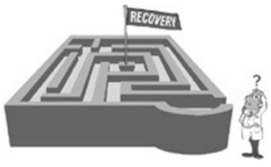
Injectable naltrexone (Vivitrol)

- Intramuscular injection of depot naltrexone given monthly
- Administer in physician office, not at home
- Requires patient motivation
- Advantages of injection
  - Better compliance
  - Less potential for liver toxicity

Naltrexone for Opioid Use Disorder

- Reasonable alternative to opioid agonist maintenance
- May be better for
  - Motivated patients
  - Not using high doses of opioids
  - Concern about diversion
  - Adolescents

Short-term detoxification



- Agonist medication given for <180 days
- Stabilization of withdrawal symptoms and behavior over weeks/months
- Taper over a few months
- Option for those who don't meet criteria for maintenance
- Risk of overdose after tapering off

Opioid Agonist Maintenance

- Long-term pharmacotherapy
- Allows time for full stabilization
  - Establishment of recovery support system
  - Coping skills
  - Employment
  - Stable housing
  - Parenting skills
  - Citizenship
- Indefinite endpoint
- Longer time using often means longer time for full stabilization
- May take a long time to "unlearn" addictive behaviors and work on coping skills
- Months to years
  - Not usually lifelong

Methadone

- Opioid substitution therapy
- Long-acting medication in controlled setting
  - Counseling
  - Social services
- Avoid withdrawal & craving
- Harm reduction
  - Individual
  - Society

Methadone Maintenance

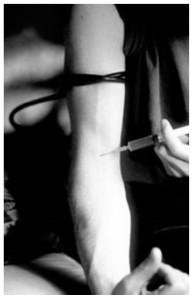
- Use of methadone for >180 days (6 mo.)
- Single daily observed dose
- Highly regulated
  - Narcotic treatment programs must be licensed
- Referral for primary medical services

Methadone

- Long-acting pure opioid agonist
- Requires daily clinic visits, but may get take-home dose privileges
- Significant street reputation
- Also used for pain like other Schedule II opioids

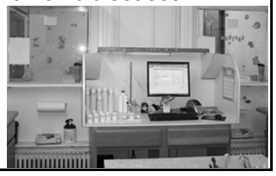
Requirements

- Physical dependence
  - At least 1 year of use
    - Continuous
    - Intermittent
  - Withdrawal signs
- Not physically dependent if just released from
  - Incarceration
  - Hospital
- 18 years old or older



Efficacy of methadone

- There have been many studies and several meta-analyses
- Maintenance superior to detox
- Higher doses (80-100 mg/day) superior to lower doses (50 mg/d)
  - ↓ illicit opioid use
  - ↑ retention in treatment
- Decreases criminal activity
- Reduces spread of HIV
- Results similar to long-term therapy of most chronic diseases



Does methadone get you high?

- No real euphoria
  - Onset latency
- Does cause sedation
  - Typical opioid effects
  - Reassuring
  - Confused with "high"
- Mix with other drugs
  - benzodiazepines

Methadone and Pregnancy

- Standard of care for opioid-dependent pregnant women
- Stabilization of mother and fetus
  - Medical and social
  - Higher dose in 3rd trimester
- Improves growth of fetus & newborn
- Decreases practice of high-risk behaviors

Methadone forever?

- No specific limit for time on methadone
  - Some states restrict time
- Individual variability
  - Time required to stabilize (drug use, housing, family, job)
  - Long-term clients
- Initial: can't imagine life without *something*
- Stable: able to consider coming off
  - Taper off comfortably over months/years

Buprenorphine

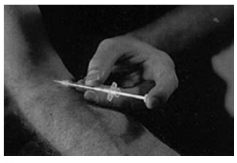
- Alternative to methadone for opioid addiction treatment
- Multiple forms available
  - Combined with naloxone (Suboxone, Zubsolv, Bunavail)
  - Buprenorphine only (Subutex)
- Detox or maintenance
- Long-acting opioid agonist-antagonist

Buprenorphine is an agonist-antagonist

- Binds to opioid receptors in body
- Only activates receptor around 40%, not 100% like other opioids (heroin, methadone)
  - If already in withdrawal, 40% is pretty good
  - If not in withdrawal, dropping from 100% to 40% receptor activation causes withdrawal
- Very low risk of overdose
  - Can OD when combined with sedative (benzos)

Buprenorphine/naloxone

- Combination helps reduce abuse
- Naloxone only active when Suboxone is injected
- Results in withdrawal for users trying to get high
- Buprenorphine alone has similar effect when injected by those who are opioid dependent and not in withdrawal already



What is the right dose?

- Individually determined
  - Based on tolerance, withdrawal
  - Other medications, physical activity level
- Most patients on 12-16 mg daily
  - Over 32 mg/day is less well tolerated

Office-based opioid therapy

- Buprenorphine is less restricted than methadone (Schedule III)
  - Get prescription from pharmacy with refills (up to 6 months)
  - Outpatient physician visits for medication checks as needed
- Addiction counseling is separate, patient may be referred to another provider for this service

Adolescents

- Buprenorphine less age-restricted
  - Can use at age 16
  - Methadone limited to age 18
  - Niche for adolescents who don't qualify for methadone due to age

Study of buprenorphine treatment in adolescents

- Multi-center trial
- Funded by NIDA
- Compared short detox (2 weeks) to maintenance (12 weeks)
- Age 14-21 years old
- Required weekly CBT counseling
- Maintenance group did better
  - Fewer opioid(+) urines
  - Attended more counseling sessions
  - Better retention in treatment
- Detox group used more cocaine and marijuana, and injected more

Buprenorphine and Pregnancy

- Pregnancy Category C
- Use Subutex instead of Suboxone to avoid naloxone
- NAS less intense than with methadone
- Studies ongoing, results encouraging

Referral for treatment

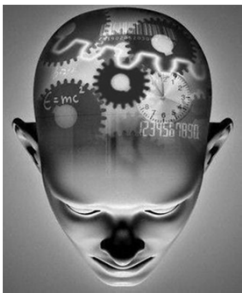
- Opioid dependence
- Available in area
- Ability to afford
- Ability to adhere
- Diversion risk
- Contraindications
- Website:
  - findtreatment.SAMHSA.gov
- Provider locator
- Information for patients and providers

Summary

- Naltrexone helps prevent relapse after detox
- Substitution therapy eliminates withdrawal, cravings, & heroin effects
- Maintenance treatment has been proven to reduce mortality, crime, & spread of infection
- Buprenorphine is less restricted than methadone
- Use buprenorphine for age 16 and up
- Individualized dose and time on maintenance

Questions?

First Case for Group Discussion



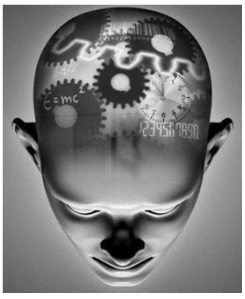
Case #1

- 16 y/o White male
- First tried heroin at age 14
- Snorts $60 of heroin daily for past 10 months
- Longest abstinence: 2 weeks
- Also smokes marijuana, drinks 2-3 beers most weeknights, more on weekends

Case questions

- What type of treatment offers the best chance to prevent relapse?
- Is there any pharmacotherapy that is unavailable to this patient currently?
- In addition to treatment for opioid use disorder, what other issues need to be addressed?

Cases for Group Discussion

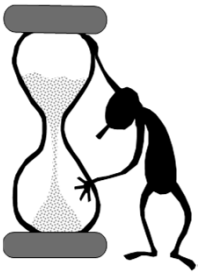


Pharmacotherapy for Tobacco Use Disorder

Nicotine Withdrawal

- craving for tobacco
- irritability, frustration, anger
- anxiety
- difficulty concentrating
- restlessness
- decreased heart rate
- increased appetite or weight gain
- depression
- disrupted sleep
- sedation

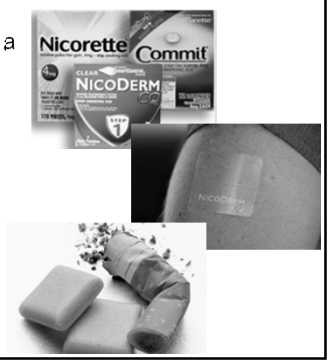
Nicotine Withdrawal



- Begins within 24 hours of last cigarette
- Lasts 2 - 4 weeks
- Tobacco craving & increased hunger may last for 6 months or more

Nicotine replacement therapy

- Always combine with a behavioral therapy program
- Most available OTC
- Reduces harmful effects of tobacco smoking
- Patients should not smoke while using



Nicotine Patch

- Highest success rate of available nicotine replacement pharmacotherapies
- Nicoderm, Nicotrol, Habitrol, Prostep
- Most come in 3 strengths: 21, 14, & 7mg
- Start with 21mg patch for 6 wks, taper to 14 mg for 2 wks, finally 7 mg for 2 weeks
- Use new patch in different spot on upper trunk every 24 hrs

Nicotine Gum

- Nicorette - 2 or 4mg per piece doses
- Requires correct “chewing technique” -- don’t chew like regular chewing gum
- Chew 1 piece for 30 minutes every 1 to 2 hours to prevent nicotine withdrawal
- Chew regularly for first month, then taper off over 6 months

Nicotine Nasal Spray

- Reduces nicotine craving & mimics pleasurable effects of nicotine
- 1 spray in each nostril, up to 40 times in 24 hours
- Use for up to 3 months
- May cause tearing, sneezing, & burning sensation in nose

Bupropion (Zyban)

- Bupropion 150mg sustained release pills
- Works on dopamine & norepinephrine receptors in the brain to decrease withdrawal
- May cause insomnia, anxiety, or seizures
- Prescription includes behavioral program
- Start pills 10-14 days before "quit date"
- Take daily for 3 days, then twice a day
- Continue pills for 8 - 12 weeks

Varenicline (Chantix)

- Nicotine partial agonist
- Start pills 10 days before quit date
  - Increase dose
  - Take for 12-24 weeks
- Includes behavioral program

Efficacy of tobacco cessation products

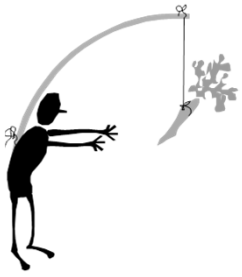
- There have been many studies and several meta-analyses of all products
- Nicotine replacement therapy quit rates are similar with different products
  - Doubles chance of successful quitting
- Combinations are more effective than a single product at a time
- Varenicline
  - Higher rate of continuous tobacco abstinence compared to bupropion & nicotine patch
- Bupropion
  - Quit rates are comparable to nicotine patch

What patients can expect when quitting smoking

- Temporary increase in cough
- weight gain
- nicotine withdrawal symptoms
- pressure from other smokers (esp. if family)

Patient Information

- American Cancer Society
- American Lung Association
- American Heart Association
- U.S. Department of Health & Human Services

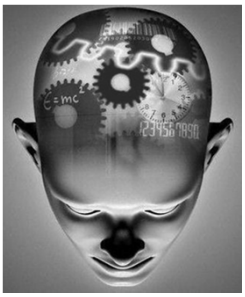


Questions?

Break Time

Please return in 15 minutes to begin small group case discussions for Tobacco Use Disorder

Cases for Group Discussion



Pharmacotherapy for Alcohol Use Disorder

- Acamprosate (Campral)
- Naltrexone (ReVia, Vivitrol)
- Disulfiram (Antabuse)

Acamprosate (Campral)

- Alcohol use disorder pharmacotherapy
- No drug interactions
- Minimal side effects
  - Diarrhea

- Does not treat withdrawal symptoms
- Reduces symptoms of protracted abstinence
  - Insomnia
  - Anxiety
  - Restlessness
- Treat for 12 months
  - Effect sustained for at least 12 months more

Acamprosate in Adolescents

- Limited clinical data on use in adolescents
- Randomized study of 26 subjects age 16-19 with chronic or episodic alcohol use
  - Acamprosate or placebo for 90 days
  - Greater abstinence on acamprosate
- Advantages over disulfiram
  - Well-tolerated
  - No drug interactions

Naltrexone (ReVia)

- Once-daily tablet
- Blocks opioid receptors
  - Reduces pleasurable effects of alcohol
- Reduce craving
- Reduces alcohol slips
  - Prevents escalation to full-blown relapse
- Used for opioids as well as alcohol

Oral naltrexone in Adolescents

- Safe and well-tolerated in open-label trial of 5 adolescents
  - Reduced alcohol consumption and craving
- Randomized trial of 128 subjects age 18-25
  - Reduced drinking intensity (fewer drinks per day)
  - Did not reduce frequency of drinking

Injectable naltrexone (Vivitrol)

- Intramuscular injection of depot naltrexone given monthly
- FDA approved for alcohol and opioids
- Administer in physician office, not at home
- Requires patient motivation

Disulfiram (Antabuse)

- Blocks acetaldehyde dehydrogenase
- Reaction to alcohol
  - Flushing, palpitations, chest tightness
  - Nausea, headache, anxiety
- Avoid slips or relapses
- Affects liver, even without alcohol
- Motivation is necessary
  - Monitored dosing

Disulfiram in Adolescents

- Use in adolescents not formally approved
- Efficacy and side effect information is extrapolated from adult data
- Randomized study of 26 subjects age 16-19 with chronic or episodic alcohol use
  - Greater abstinence on disulfiram
  - No difference in side effects
- Not a preferred agent for adolescents

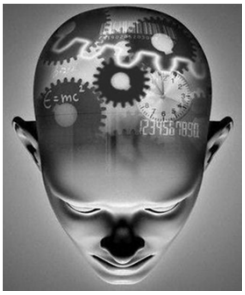
Efficacy of AUD pharmacotherapy

- There have been many studies and several meta-analyses of all products
- Naltrexone
  - Injection: ↓ drinking by 25% more than placebo
  - Pills: ↓ risk of heavy drinking by 17% more than placebo

- Acamprosate
  - ↓ drinking by 14% more than placebo
  - Better for maintenance of abstinence than initiation if not abstinent
- Disulfiram
  - Longer time to 1st drink compared to other meds
  - Reduced overall drinking
  - Only when monitored
    - Less benefit when not monitored

Questions?

Cases for Group Discussion



Thank you!

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