PHARMACOTHERAPY AND PSYCHOSOCIAL TREATMENTS FOR ADOLESCENT SUBSTANCE USE DISORDERS

EVIDENCE FROM CLINICAL TRIALS

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Disclosures

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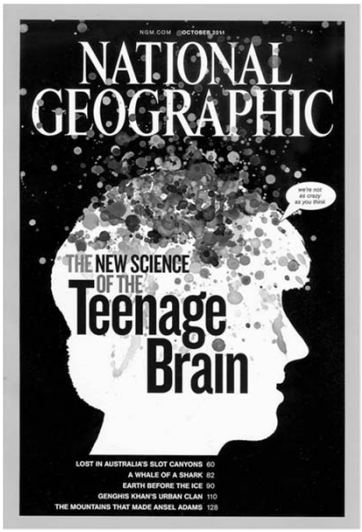
NIH (NIDA, NIAAA)	X

Adolescents and Substance Use

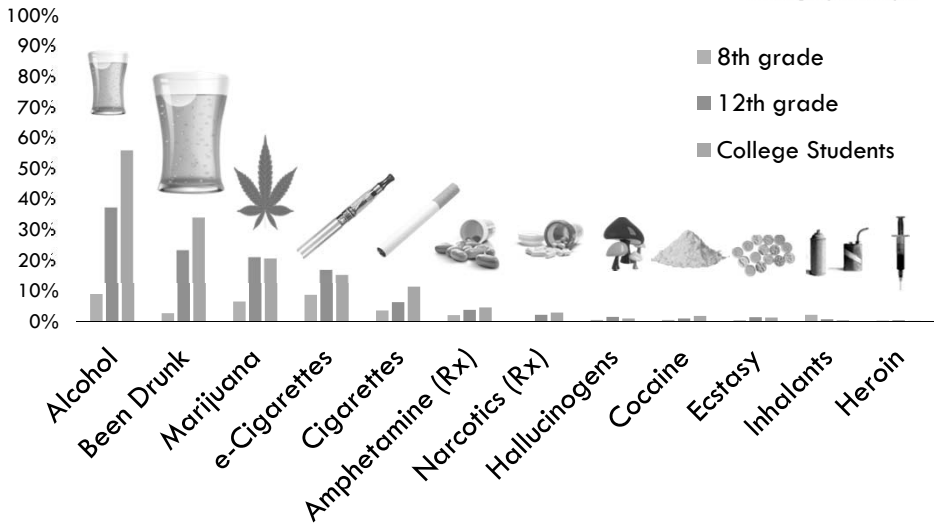


- Critical developmental stage with everything in flux
- "They are always different; they are always the same" – John Peel, BBC Radio 1

Adolescents and Substance Use

- Substance initiation almost always occurs during adolescence (Johnston et al., 2015)
- Adolescent substance users are more prone than adults to developing dependence symptoms and difficulty cutting down (Chen & Anthony, 2003)
- If we can intervene effectively during adolescence, we may provide a much larger impact on substance use disorder (SUD)-related morbidity and mortality than if we solely focus on treatments for adults

Past 30 Day (Current) Use



Johnston et al., 2015

What should we do?

- Multifaceted efforts to reduce the public health burden of adolescent substance use
  - Learn more about the heterogeneous antecedents, contexts, and consequences of adolescent substance use, to better understand what is normative and what is high-risk
  - Provide science-informed education (global), prevention (global), screening (global), and treatment (targeted, with intensity/modality based on severity, impairment, etc.)

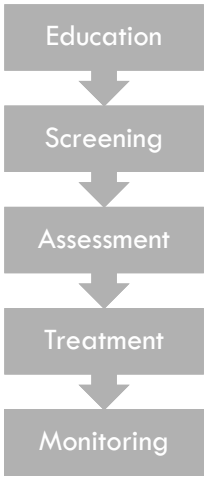
What's being done clinically?

- The large majority of adolescents with SUD do not access treatment at all
  - May not recognize the problem
  - Parents/guardians may not be aware
  - Limitations in available treatment, coverage, etc.
  - Stigma
- Adolescents with SUD are more likely to have legal/juvenile justice involvement than treatment involvement
- Even when accessing treatment, most do not receive evidence-based care

Overall Strategy in Clinical Practice

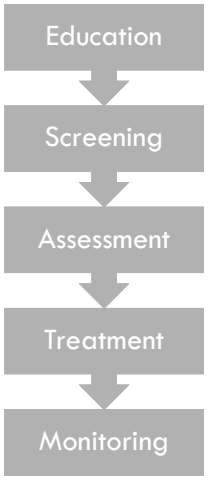
Education
Screening
Assessment
Treatment
Monitoring

Ground Rules on Confidentiality



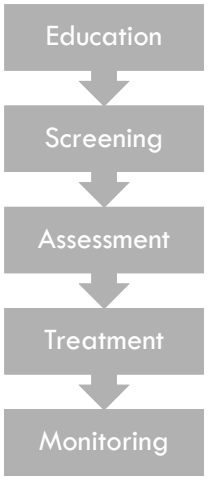
- Before pursuing discussion about substance use, you must establish ground rules with the patient on confidentiality.
- State laws vary, but in general adolescents may keep substance use assessment and treatment confidential from their parents/guardians.

Ground Rules on Confidentiality



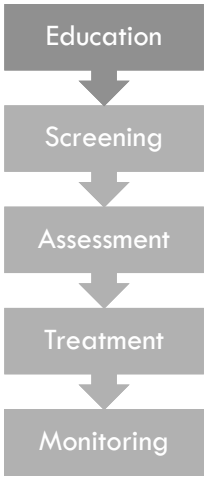
- Patients should be made aware of their right to confidentiality, but must also know the limits (e.g., suicidality, homicidality, acute danger related to substance use).
- In many situations, sharing information with parents/guardians may be beneficial for the adolescent, but the adolescent must be agreeable.

Ground Rules on Confidentiality



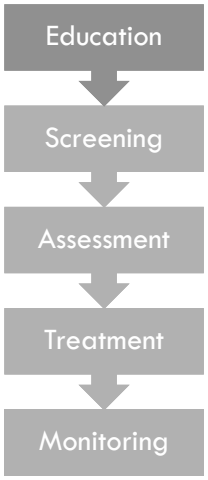
- Key examples
  - Urine drug testing
    - Sharing results with parents/guardians may help the adolescent regain trust and privileges lost due to substance use.
  - Family therapy
    - Sharing details of substance use may help family appropriately engage in and respond to family-based interventions.
- Regardless, the adolescent must agree to this before you proceed.
  - Otherwise, you breach confidentiality and erode therapeutic trust. (Weddle & Kokotailo, 2005.)

Education



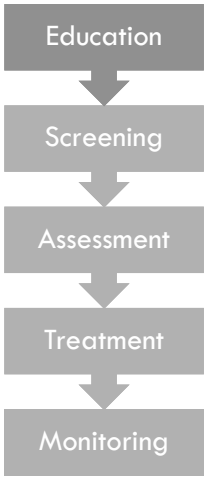
- This should be be provided to all patients (young and old, substance using and not), though the message should be developmentally appropriate.
- Objective, practical information is critical to offset widespread misinformation.

Education



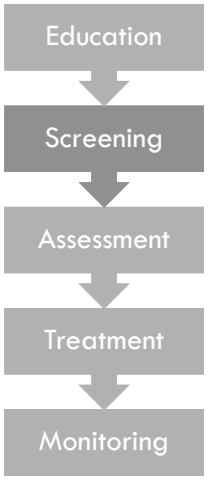
- Adolescents are often very receptive to clear, objective information from a trusted medical provider.
- Be careful to avoid exaggerated, sensationalistic warning messages.
- Focus instead on science-based material that is relevant to adolescents.
  - Substance use and the developing brain.

Education



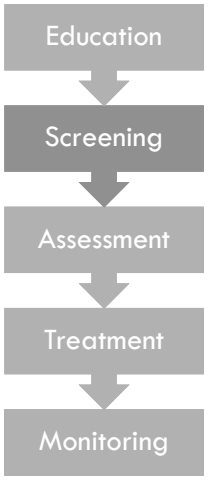
- Good sources of free educational information (for children, adolescents, families, and clinicians):
  - National Institute on Drug Abuse (NIDA) for Teens
    - http://teens.drugabuse.gov/
  - The Partnership at Drugfree.org
    - http://www.drugfree.org/

Screening



- Whether or not you suspect substance use, routine substance use screening is essential for all adolescent patients.
- A number of screening tools have been validated for adolescents, most commonly for use in the primary care setting.
- CAGE (Cut down, Annoyed, Guilty, Eye-opener) questionnaire is *not* useful with adolescents.

Screening



- Start with a simple screen regarding frequency of use (e.g., never, once or twice, monthly, weekly, daily, almost daily) over the past year (Levy, et al., 2014.)
  - Tobacco products
  - Alcohol
  - Marijuana
  - Illegal drugs (such as cocaine or Ecstasy)
  - Prescription drugs that were not prescribed for you (such as pain medication or Adderall)
  - Over-the-counter medications (such as cough medicine) for nonmedical reasons
  - Inhalants (such as nitrous oxide)
  - Herbs or synthetic drugs (such as salvia, K2, or bath salts)
- Positive responses can be followed up with further questions on patterns of use, binge episodes, associated impairment, etc.

Screening

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- CRAFFT (Knight, et al., 2002.) may be used for further exploration of positive responses.
- This tool helps identify adolescents with high-risk substance use requiring further assessment.
- Two versions
  - Clinician administered
  - Adolescent self-report (may be completed in the waiting room)
- Free PDFs available at http://www.ceasar-boston.org/clinicians/crafft.php

The CRAFFT Screening Interview

Part A

During the PAST 12 MONTHS, did you:	No	Yes
1. Drink any alcohol (more than a few sips)? (Do not count sips of alcohol taken during family or religious events.)	☐	☐
2. Smoke any marijuana or hashish?	☐	☐
3. Use anything else to get high? ("anything else" includes illegal drugs, over the counter and prescription drugs, and things that you sniff or "huff")	☐	☐

For clinic use only: Did the patient answer "yes" to any questions in Part A?

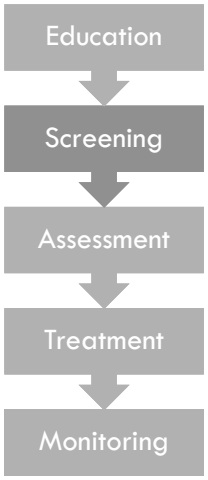
No ☐ → **Ask CAR question only, then stop**

Yes ☐ → **Ask all 6 CRAFFT questions**

Part B	No	Yes
1. Have you ever ridden in a **CAR** driven by someone (including yourself) who was "high" or had been using alcohol or drugs?	☐	☐
2. Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?	☐	☐
3. Do you ever use alcohol or drugs while you are by yourself, or **ALONE**?	☐	☐
4. Do you ever **FORGET** things you did while using alcohol or drugs?	☐	☐
5. Do your **FAMILY** or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?	☐	☐
6. Have you ever gotten into **TROUBLE** while you were using alcohol or drugs?	☐	☐

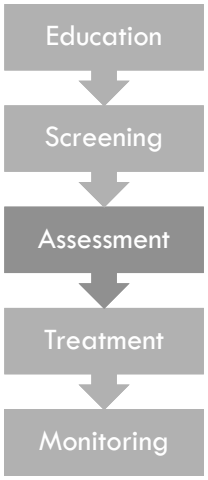
CRAFFT Scoring: Each "yes" response in **Part B** scores 1 point.
A total score of 2 or higher is a positive screen, indicating a need for additional assessment.

Screening



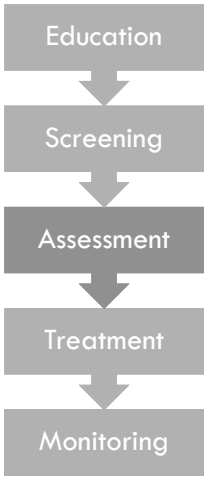
- Don't forget tobacco!
  - Almost all adult smokers started during adolescence.
  - Cigarette smoking remains the leading cause of preventable death in the U.S. and the world.
  - CRAFFT and many other screening tools do not pick up tobacco use.
    - It must be assessed separately (at least ask yes/no and frequency).

Assessment



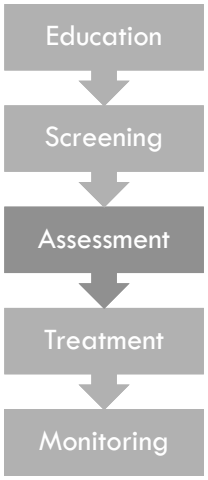
- When either (a) screening suggests high-risk substance use, or (b) an adolescent/family presents with concern regarding substance use, careful assessment is necessary.
- Substance use is heterogeneous, so understanding the specific situation and presentation is critical.

Assessment



- Always provide the opportunity for the adolescent to describe the situation without the parent/guardian present.
- While maintaining agreed-upon confidentiality, involve the parents/guardians in a separate interview to gather collateral information.

Assessment: Diagnosis



- With transition to *DSM-5*, substance abuse and dependence are collapsed into substance use disorder (e.g., Cannabis Use Disorder, Alcohol Use Disorder, Opioid Use Disorder).
  - Mild (meets 2-3 of 11 criteria)
  - Moderate (meets 4-5 of 11 criteria)
  - Severe (meets ≥6 of 11 criteria)

Assessment: Functional Analysis

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Monitoring

- Efficient model to characterize the presenting substance use situation and help identify high-yield treatment strategies

A B C

Antecedents → Behaviors → Consequences

Treatment

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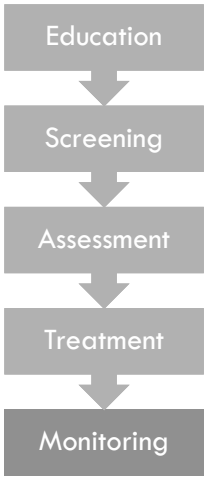
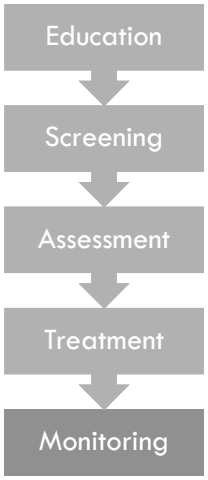
- Psychosocial approaches (for review: Hogue et al., 2014.; Tanner-Smith, et al., 2012.; Waldron & Turner, 2008.; Sussman et al., 2006.)
  - Motivational enhancement (Barnett, et al., 2012.)
  - Cognitive/behavioral therapy (Hendriks, et al., 2011.; Kaminer & Slesnick, 2005.)
  - Family therapy (Rigter, et al., 2013.; Spas, et al., 2012.)
  - Contingency management (Stanger et al., 2015; Stanger & Budney, 2010.)
- Pharmacotherapies
  - *Adjunct to psychosocial treatment*
  - Large trials to date only for opioid, tobacco, and cannabis use disorders – stay tuned for a review of findings!
- Know your limits!
  - Severity and/or acuity may necessitate more intensive care than you can provide in clinic

Monitoring



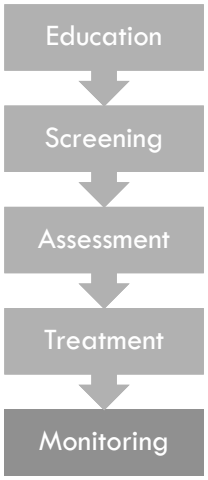
- Urine drug testing is a key component of monitoring, offering objective assessment.
  - Often necessary when trust has been eroded.
  - Can be used as a motivating rather than punitive tool ("clean" result tied to praise and reinforcement).

Monitoring



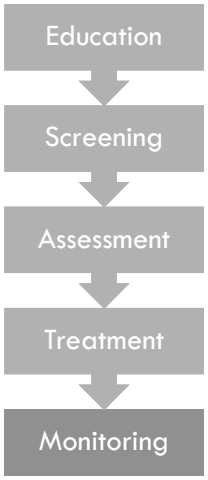
- However, urine testing is not perfect.
  - Most drugs clear within 1-3 days, while cannabinoids can linger for weeks after cessation in heavy, chronic users.
    - Infrequent testing can miss non-daily use of many substances.
  - Not a reliable reflection of how much someone is using.
  - There can be cross-reactivity and false negatives and positives.

Monitoring



- However, urine testing is not perfect.
  - Typical testing does not detect alcohol, tobacco, or designer/synthetic compounds (e.g., K2/Spice).
    - Breathalyzers may be used for alcohol and smoked tobacco.
    - Urine cotinine may be used for tobacco.
    - New (currently send-out) labs can detect K2/Spice.
  - Potential for "cheating," particularly if result is tied to rewards or consequences.
    - Best to use test kits that include pH, specific gravity, and temperature testing.

Monitoring



- Do not dismiss the importance of eliciting self-report.
  - Helps gauge quantity, frequency, and context of use, which can inform psychosocial treatment.
  - Self-report in adolescents is more reliable than you might think.
  - Helps with building rapport.

Monitoring

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- Do not dismiss the role parents can play in this.
  - When framing substance abstinence as a shared goal, parents, and patients can be aligned.
  - Parents can provide "natural" contingent rewards when the patient is doing well.
    - Translates clinic practice of contingency management to the real world.

Monitoring

Education
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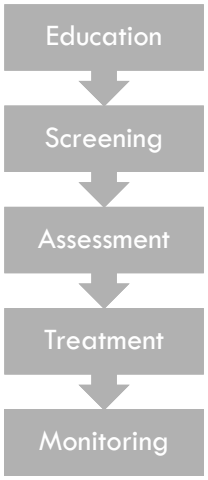
- Must frame both continuously and categorically.

Overall Framework



- Framework
  - Identification
    - Presentation in context of practice that performs routine substance use education and screening.
  - Detail gathering
    - History from patient and family
    - Functional analysis
    - Diagnostic assessment
  - Treatment planning and delivery
    - Efficient components of psychosocial treatments that match needs; pair with treatments targeting comorbid disorders.
    - Pharmacotherapy when indicated by severity/acuity.
  - Monitoring/follow-up
    - Urine testing
    - Self and family report
    - Reinforcement of skills gained with psychosocial treatment
    - Medication management

Medications for SUD?

- Food and Drug Administration (FDA)-approved in <u>adults</u>:
  - Tobacco Use Disorder
    - Nicotine Replacement Therapy, Bupropion SR, Varenicline
  - Alcohol Use Disorder
    - Benzodiazepines (detox only), Disulfiram, Naltrexone, Acamprosate
  - Opioid Use Disorder
    - Methadone, Buprenorphine/Naloxone (approved down to age 16), Naltrexone
- There are no FDA-approved medications for any other substance use disorder (cannabis, cocaine, methamphetamine, etc.)

Tobacco Use Disorder: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	End of Treatment Abstinence	Post-Treatment Follow-Up Abstinence
Nicotine Replacement Therapy	Hanson, et al. 2003.	10-week RCT *N*=100	Nicotine patch vs. placebo patch	CBT + contingency management (CM)	28% vs. 24% (OR 1.2)	N/A
	Moolchan, et al. 2005.	12-week RCT *N*=120	Nicotine patch vs. Nicotine gum vs. placebo patch/gum	Group-based CBT	*21%* vs. 9% vs. 5% (ORs *4.9* and 1.8)	Week 26: 21% vs. 9% vs. 5% (ORs 4.9 and 1.8)
	Rubinstein, et al. 2008.	8-week RCT *N*=40	Nicotine nasal spray vs. no nasal spray	Brief weekly individual counseling	0% vs. 12%	N/A
	Scherphof et al. 2014.	6- to 9-week RCT *N*=257	Nicotine patch vs. placebo patch	Initial information meeting	14.8% vs. 13.1% [*22.4%* vs. 14.5% in high compliance group (OR *1.09*)]	Week 26: 8.1% vs. 5.7% (OR 1.54) Week 52: 4.4% vs. 6.6% (OR 0.64)

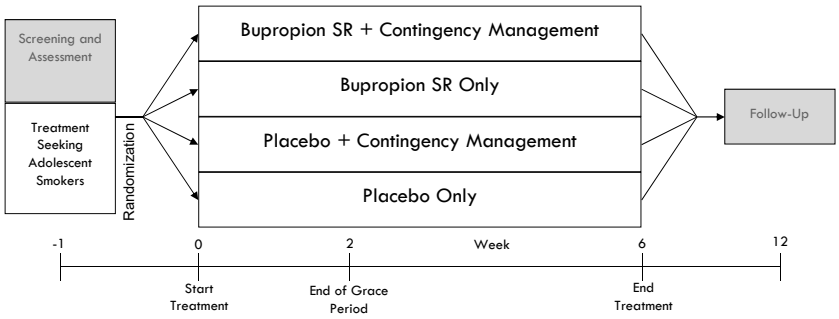
RCTs: Randomized controlled trials

Tobacco Use Disorder: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	End of Treatment Abstinence	Post-Treatment Follow-Up Abstinence
Bupropion SR	Killen, et al. 2004.	10-week RCT *N*=211	Bupropion SR 150 mg vs. placebo	Nicotine patch and group skills training	23% vs. 28% (OR 0.8)	Week 26: 8% vs. 7% (OR 1.2)
	Muramoto, et al. 2007.	6-week RCT *N*=312	Bupropion SR 300 mg vs. bupropion SR 150 mg vs. placebo	Brief weekly individual counseling	*300 mg 14%*, 150 mg 11%, Placebo 6% (ORs *2.6* and 1.9)	Week 26: *300 mg 14%*, 150 mg 3%, Placebo 10% (ORs *1.5* and 0.3)
	Gray, et al. 2011.	6-week RCT *N*=136	Bupropion SR 300 mg vs. placebo, each with or without CM (2x2 design)	Brief weekly individual counseling	*27%*, 8.3%, 10.3%, 9.4%	Week 12: 10.8%, 5.6%, 0%, 6.3%
Varenicline	Gray, et al. 2012.	8-week RCT *N*=29	Varenicline 1 mg BID vs. bupropion XL 300 mg	Brief weekly individual counseling	26.7% vs. 14.3%	N/A

Tobacco Use Disorder:

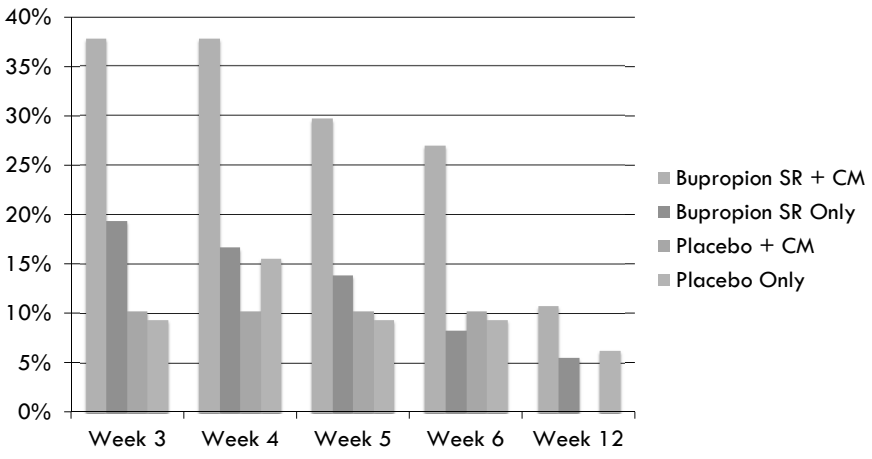
Bupropion/Contingency Management 2x2 Trial



Gray, K. M., Carpenter, M. J., Baker, N. L., Hartwell, K. J., Lewis, A. L., Hiott, D. W., Deas, D., & Upadhyaya, H. P. (2011). Bupropion SR and contingency management for adolescent smoking cessation. *Journal of Substance Abuse Treatment, 40*, 77-86.

Tobacco Use Disorder:

Bupropion/Contingency Management 2x2 Trial



Tobacco Use Disorder: Adolescent RCTs

- Overall findings are mixed
- Odds ratios (active treatment compared with placebo) vary greatly, but are encouraging at end of treatment
  - Moolchan et al. (Nicotine Patch – OR 4.9)
  - Muramoto et al. (Bupropion SR 300 mg – OR 2.6)
  - Gray et al. (Bupropion SR 300 mg + CM – OR 3.6)
- Post-treatment follow-up odds ratios are less encouraging
- Embedding strong psychosocial/behavioral treatment appears to significantly enhance outcomes

Tobacco Use Disorder: Nicotine Replacement Therapy

- Most positive findings with nicotine patch (Moolchan et al., 2005)
  - 21% end-of-treatment abstinence, compared with 5% for placebo, when added to group-based CBT
  - ≥1 pack cigarettes/day → start with 21mg patch.
  - <1 pack cigarettes/day → start with 14mg patch.
  - Typically continue at least 6 weeks, then step down in dose (e.g., 14mg, 7mg) every 2 weeks, then discontinue

Tobacco Use Disorder: Bupropion SR

- Titrate to 300 mg/day total dose (150 mg qMorning and 150 mg qAfternoon) – lower dosing appears ineffective (Muramoto et al., 2007)
- Combination with behavioral treatment (contingency management) appears to significantly enhance abstinence outcomes (Gray et al., 2011)
- May consider using Bupropion XL for once-daily dosing, though this has not been studied specifically for smoking cessation
- Based on studies to date, consider medication treatment for 6 weeks; longer treatment may be considered on a case-by-case basis

Tobacco Use Disorder: Varenicline

- While varenicline is clearly efficacious in adults, we do not yet have sufficient data to evaluate/support its use in adolescents.
- Two ongoing RCTs are designed to examine varenicline's safety and efficacy for adolescent smoking cessation.
- Adult dosing is 0.5 mg qAM for 3 days, 0.5 mg twice-a-day (BID) for 4 days, and 1mg BID thereafter, for 12 total weeks.

PROJECT QUIT

Alcohol Use Disorder: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	Outcomes
Cyanimide	Niederhofer, et al. 2003.	90-day RCT *N*=26	Cyanimide 200 mg/day vs. placebo	"Additional psychosocial and behavioral treatment" after initial inpatient detoxification	End-of-treatment abstinence 53.8% vs. 15.4%
Disulfiram	Niederhofer, Staffen. 2003.	90-day RCT *N*=26	Disulfiram 200 mg/day vs. placebo		
Acamprosate	Niederhofer, Staffen. 2003. *RETRACTED*	90-day RCT *N*=26	Acamprosate 1332 mg/day vs. placebo		
Naltrexone	Miranda, et al. 2013.	Crossover Study, 8-10 days of each condition *N*=28	Naltrexone 50 mg/day vs. placebo	None (non-treatment-seekers)	Participants were less likely to drink (OR 0.69) or drink heavily (OR 0.54) on study days
	O'Malley et al. 2015	8-week RCT *N*=128 (**young adults**, ages 18-25)	Naltrexone 25 mg/day (+25 mg on anticipated drinking days) vs. placebo	Personalized feedback session and brief counseling every other week	No differences in heavy drinking days or percent days abstinent Naltrexone reduced number of drinks per drinking day (4.9 vs 5.9, p=0.09)

Alcohol Use Disorder: Pharmacotherapies

- Adolescent findings to date are too preliminary/limited to recommend pharmacotherapy for alcohol use disorder
- May potentially consider naltrexone 25-50 mg/day in psychosocial treatment-refractory cases, based on the Miranda and O'Malley findings

Opioid Use Disorder: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	Outcomes
Buprenorphine	Marsch, et al. 2005.	28-day RCT *N*=36	Buprenorphine vs. Clonidine	Offered thrice weekly counseling and contingency management	64% vs. 32% negative urine opioid tests during treatment 72% vs. 39% retained in treatment
Buprenorphine/ Naloxone	Woody, et al. 2008.	12-week RCT *N*=152	12-week maintenance vs. 14-day detox buprenorphine/ naloxone	Offered weekly individual or group counseling	Less self-reported opioid use during treatment 57% vs. 49% end-of-treatment abstinence 70% vs. 21% retained in treatment

Opioid Use Disorder: Buprenorphine/Naloxone

- Requires physician waiver qualification to prescribe
  - http://buprenorphine.samhsa.gov/waiver_qualifications.html
- Should be prescribed only in the context of counseling and psychosocial support
- Start low (e.g., 2 to 4 mg/day) and gradually titrate in 2 to 4 mg/day increments
- May do a more rapid initial "induction" on first two days of treatment
- Maximum recommended dose is 24 mg/day

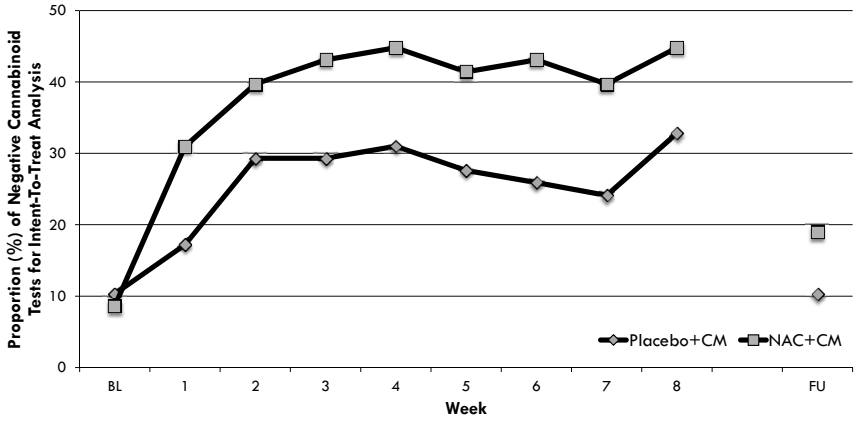
Cannabis Use Disorder: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	Outcomes
N-Acetylcysteine (NAC)	Gray et al., 2012	8-week RCT *N*=116	NAC 1200 mg BID vs. placebo	Contingency management and brief weekly counseling	*41%* vs. 27% negative urine cannabinoid tests during treatment (overall *OR 2.4*) 36% vs. 21% end-of-treatment abstinence
Topiramate	Miranda et al., 2016	6-week RCT *N*=66	Topiramate 200 mg per day vs. placebo	Motivational enhancement therapy	High dropout rate due to tolerability issues; Topiramate yielded greater reduction in use but not abstinence, compared to placebo

Cannabis Use Disorder

N-acetylcysteine (NAC) Trial – Abstinence outcomes

- Intent-to-treat (all randomized participants) with participants assumed to be non-abstinent at any missed visit



Medications for SUD in Adolescents: Summary of RCTs

Medication	Number of Studies and Participants	SUD Indication	Safety/Tolerability	SUD Outcomes
Nicotine Replacement Therapy	3 (total *N*=517)	Tobacco use disorder	Positive	Mixed (most positive for patch)
Bupropion SR	3 (*N*=659)		Positive	Positive at 300 mg
Varenicline	1 (*N*=29)		Positive	Preliminary/ encouraging
Cyanimide	1 (*N*=26)	Alcohol use disorder	Positive	Positive
Disulfiram	1 (*N*=26)		Positive	Positive
Naltrexone	1 (*N*=156)		Positive	Mixed
Buprenorphine (Buprenorphine/Naloxone)	2 (*N*=188)	Opioid use disorder	Positive	Positive
N-Acetylcysteine	1 (*N*=116)	Cannabis use disorder	Positive	Positive
Topiramate	1 (*N*=66)		Negative	Mixed

Medications for SUD in Adolescents: Take Home Points

- *Medications should be used to complement psychosocial treatment.*
- Tobacco use disorder
  - Findings support nicotine patch and bupropion SR 300 mg
- Alcohol use disorder
  - Possible (mixed) support of naltrexone
- Opioid use disorder
  - Findings support buprenorphine/naloxone
- Cannabis use disorder
  - Findings support *N*-acetylcysteine

Psychiatric Medications in Adolescents with SUD

- Nearly all adolescent psychiatric medication trials exclude SUD comorbidity in participants
- This presents several concerns/questions when prescribing these medications in the presence of SUD comorbidity
  - Are they safe?
  - Are they efficacious?
  - Do they have adverse interactions with substances?
  - Do they have effects on substance use (good or bad)?

Major Depressive Disorder + SUD: Adolescent RCTs

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	Depression Outcomes	SUD Outcomes
Sertraline (MDD + Alcohol Use Disorder)	Deas et al., 2000	12-week RCT *N*=10	Sertraline vs Placebo	Group CBT	Improvement in both groups (no differences)	Improvement in both groups (no differences)
Fluoxetine (MDD + SUD)	Riggs et al., 2007	16-week RCT *N*=126	Fluoxetine vs Placebo	Individual CBT	Fluoxetine > Placebo in one of two measures	Improvement in both groups (no differences)
Fluoxetine (MDD + SUD)	Findling et al., 2009	8-week RCT *N*=34	Fluoxetine vs Placebo	Treatment-as-usual	Improvement in both groups (no differences)	No significant improvement in either group
Fluoxetine (MDD + Alcohol Use Disorder)	Cornelius et al., 2009	12-Week RCT *N*=50	Fluoxetine vs Placebo	Motivational Interviewing (MI) + CBT	Improvement in both groups (no differences)	Improvement in both groups (no differences)
Fluoxetine (MDD + Cannabis Use Disorder)	Cornelius et al., 2010	12-Week RCT *N*=70	Fluoxetine vs Placebo	MI + CBT	Improvement in both groups (no differences)	Improvement in both groups (no differences)

Bipolar Disorder + SUD

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	Mood Outcomes	SUD Outcomes
Lithium	Geller et al., 1998	6-week RCT *N*=25	Lithium vs Placebo (target lithium level 0.9-1.3 ng/mL)	Weekly interpersonal therapy	Lithium > Placebo (CGAS)	Lithium > Placebo (UDS)

ADHD + SUD

Medication	Publication	Design	Randomized Treatment Groups	Embedded Treatment Received by All Participants	ADHD Outcomes	SUD Outcomes
Pemoline (*no longer indicated due to hepatotoxicity*)	Riggs et al., 2004	12-week RCT *N*=69	Pemoline vs Placebo	None	Pemoline > Placebo	No difference
Methylphenidate Spherical Oral Drug Absorption System (MPH-SODAS)	Szobot et al., 2008	6-week crossover RCT (3 weeks of each treatment) *N*=16	MPH-SODAS vs Placebo	None	MPH-SODAS > Placebo on SNAP-IV and CGI	None
Atomoxetine	Thurstone et al., 2010	12-week RCT *N*=70	Atomoxetine vs Placebo	MI/CBT	No difference	No difference
Osmotic-release Methylphenidate (OROS MPH)	Riggs et al., 2011	12-week RCT *N*=303	OROS MPH vs Placebo	MI/CBT	Mixed [OROS MPH > Placebo on Parent-Reported ADHD Symptoms]	Mixed [OROS MPH > Placebo on Number of Negative UDS]

Psychiatric Medications in Adolescents with SUDs: Summary of RCTs

Medication	Number of Studies and Participants	Psychiatric Indication	Safety/Tolerability	Psychiatric Outcomes	SUD Outcomes
Fluoxetine	4 (total *N*=280)	Major Depression	Positive	Mixed	No Effect
Sertraline	1 (*N*=10)		Positive	No Effect	No Effect
Lithium	1 (*N*=25)	Bipolar Disorder	Positive	Positive	Positive
Pemoline	1 (*N*=69)	ADHD	Positive	Positive	No Effect
Methylphenidate Spheroidal Oral Drug Absorption System (MPH-SODAS)	1 (*N*=16)		Positive	Positive	No Effect
Atomoxetine	1 (*N*=70)		Positive	No Effect	No Effect
Osmotic Release Methylphenidate (OROS MPH)	1 (*N*=303)		Positive	Mixed	Mixed

Psychiatric Medications in Adolescents with SUDs: Take Home Points

- *Medications should be used to complement psychosocial treatment*
- Major Depressive Disorder
  - Most evidence for Fluoxetine
- Bipolar Disorder
  - Only small pilot RCT of Lithium
- ADHD
  - Most evidence for Methylphenidate (OROS MPH or MPH-SODAS)

Medication RCT Take Home Points

- Evidence base for medications in SUD/psychiatric comorbid adolescents is small but growing
- Medications studied to date have generally been well tolerated, and some have yielded significant treatment effects
- Prescribers should combine pharmacotherapy with evidence-based psychosocial treatment
  - There is not, and likely never will be, a "magic pill" for adolescent SUDs and psychiatric comorbidity

Questions?

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