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PROFESSIONAL WORKSHOP: Mental Health Practice during the COVID-19 Pandemic: Applying What We Know about Response to Disasters

Friday, July 24, 2020, 9:00 am – 11:00 pm, Online Broadcast, Presented by: Victor Welzant, PsyD

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Learning Objectives

- Recognize the factors complicating the diagnosis of Attention-deficit hyperactivity disorder (ADHD).
- Describe barriers that reduce the likelihood of providing treatment in substance users.
- Appraise the current treatment literature regarding Attention-Deficit Hyperactivity Disorder (ADHD) and Substance Use Disorders (SUD).

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ADHD and Substance Use Disorders: Diagnostic and Treatment Quandaries

Sheppard Pratt Grand Rounds
July 22, 2020

Frances R. Levin, MD
Kennedy-Leavy Professor of Psychiatry at CUMC
Chief, Division on Substance Use Disorders
Department of Psychiatry
Columbia University Irving Medical Center/
New York State Psychiatric Institute

Financial Disclosure

Support: Research/Salary/Training Support

- Federal:
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  - Substance Abuse and Mental Health Services Administration (SAMHSA): Collaborative Strategies for Training Health Professionals H79 TI081968; Opioid Strategic Targeted Response-Technical Assistance H79 T1080816
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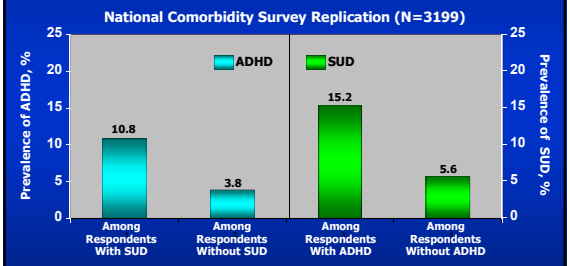
- Major League Baseball (Consultant)
- Scientific Advisory Board Member (unpaid): Novartis, Alkermes, Indivior

Comorbidity of Adult ADHD and SUD in Adults: Epidemiologic Data

(Kessler RC, et al. *Am J Psychiatry*. 2006; 163(4): 716-723)



Prevalence of Adult ADHD in Substance Abusers Seeking Treatment: DSM-IV and Structured Interview*

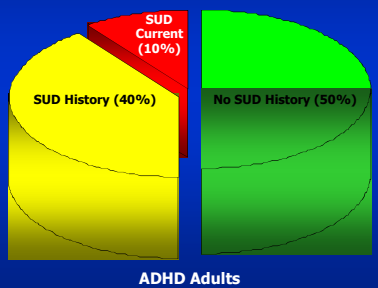
Author, Year	Population	ADHD
Levin, 1998	281 Cocaine Abuse/Dependence	10-15%
Clure, 1999	136 Cocaine/Alcohol Abuse/Dep	5%
King, 1999	125 Methadone Maintenance	17%
Schubiner, 2000	201 Substance Abuse/Dep	24%
Daigre, 2009	80 Various Abuse/Dep	20%

*Van Emmerik-van Oottmerssen et al., 2012: Meta-analysis of 29 Studies, Nicotine as primary drug of abuse not excluded: Also combined childhood diagnosis and adult diagnosis; **Overall 23.1% (CI: 19.4-27. 2%)**

Van de Glind et al., 2013: **DSM-IV prevalence rate was 5-31%, average 14%**; DSM-V criteria 8-33%, average 17%

SUD in ADHD Adults Presenting for Treatment

(SUD rates from Wilen TE, et al., *Am J Addict*, 1998; 7(2); 156-163)



Making the Diagnosis of Adult ADHD

- **A persistent pattern of inattention or hyperactivity/impulsivity that interferes with functioning or development and consists of:**
  - ≥6 symptoms (≥ 5 if adult or adolescent at least age 17) of inattention and/or hyperactivity/impulsivity present for ≥6 months (negatively impacts on social and academic/occupational activities and inconsistent for developmental level).
- **Several inattentive or hyperactive-impulsive symptoms present before age 12**
- **Several symptoms present ≥2 settings**
- **Clear evidence that symptoms interfere with, or reduce the quality of, social, academic or occupational functioning**
- **Symptoms do not happen only during the course of schizophrenia, or another psychotic disorder; and are not accounted for by another mental disorder**

Diagnostic and Statistical Manual of Mental Disorders. Washington, DC, American Psychiatric Association, 2013.

Symptoms of Hyperactivity Often Manifest Differently in Adults

Hyperactivity often changes to inner restlessness

DSM Symptom Domain	Common Adult Manifestation
Squirms and fidgets	Workaholic
Can't stay seated	Overscheduled/overwhelmed
Runs/climbs excessively	Self-select very active job
Can't play/work quietly	Constant activity leading to family tension
"On the go"/"Driven by motor"	Talk excessively
Talk excessively	

American Psychiatric Association 1994, 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Symptoms of Impulsivity Often Manifest Differently in Adults

Impulsivity in adulthood often carries more serious consequences

DSM Symptom Domain	Common Adult Manifestation
Blurts out answers	Low frustration tolerance
Can't wait turn	Quitting jobs
Intrudes/interrupts others	Ending relationships
	Driving too fast
	Losing temper
	Addiction

American Psychiatric Association 1994, 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Symptoms of Inattention Often Manifest Differently in Adults

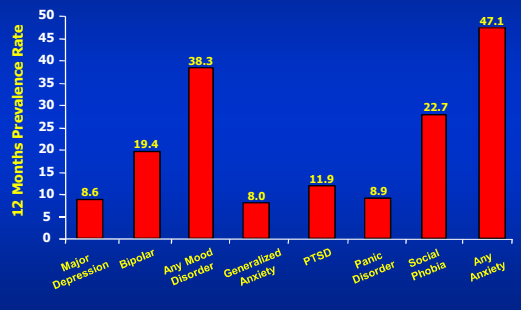
DSM Symptom Domain	Common Adult Manifestation
Fails to give close attention to details	Difficulty sustaining attention
Difficulty sustaining attention	▪ Meetings, reading, paperwork
Doesn't listen	Paralyzing procrastination
No follow through	Slow, inefficient
Can't organize	Poor time management
Avoids tasks that require close attention	Disorganized
Loses important items	
Easily distractible	
Forgetful of Daily Activities	

American Psychiatric Association 1994, 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Making the ADHD Diagnosis: Why is it Difficult in Adults?

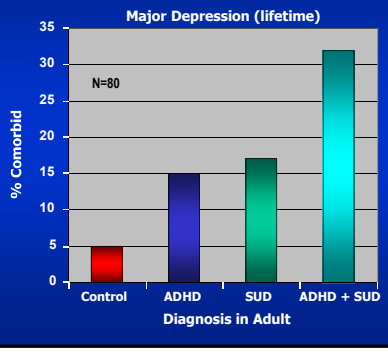
- **It tends to be easier in children and adolescents**
- **Factors Leading to Underdiagnosis**
  - The developmental "appropriateness" of the symptoms (DSM-V provides adult-relevant description of symptoms)
  - The age criterion (maybe less of a problem)
  - Additional psychopathology (overrules and more important than ADHD)

Community Sample of Adults with ADHD



Kessler et al., 2006

Comorbidity in Adults with ADHD + SA



Similar outcomes for ASPD, Anxiety & other disruptive disorder

Wilens et al., *Am J Addiction*, 2005

Diagnosing ADHD in the Presence of Other Psychiatric Comorbidity: Common Diagnostic Quandary

- **Adults with ADHD**
  - Overlap of symptoms can make it difficult to distinguish whether individual has one disorder, two, or multiple disorders
  - ADHD vs. Depression
    - **Common symptoms**: Inattention/concentration, Psychomotor agitation/restlessness, Sleep difficulties
    - **More likely to see with ADHD**: Improvement with structure, chronic work/school impairment, not listening to others, problems with organization, impulsivity
    - **More Likely to see with Depression**: Anhedonia, weight loss/gain, feelings of worthlessness/guilt, fatigue, irritability; disinterest in activities
    - **Unique to depression**: Psychosis, suicidality
    - **Unique to ADHD**: Talkativeness, Constant activity

Levin and Mariani, et al 2012., Psychiatric Clin North Am

Additional Psychiatric Comorbidity

- ADHD vs. Bipolar Illness
  - **Common symptoms**: Hyperactivity, inattention, talkativeness, work dysfunction, impulsivity - but more extreme in bipolar I, harder to distinguish for Bipolar II
  - **More likely to see with Bipolar Illness:** Irritability, Depression, Substance Use/Use Disorders
  - **More likely to see with ADHD:** Improvement with structure
  - **Unique to Bipolar Illness**: Psychosis, suicidality, expansive mood, grandiosity, decreased need for sleep, cyclical symptomatology
  - **Unique to ADHD**: Constant presence of core symptoms
- Disorders tend to run in families
  - If strong family history for bipolar illness, need to closely evaluate for bipolar disorder.

Levin and Mariani, et al., Psychiatric Clin North Am, 2012

Adults with ADHD and Substance Use Disorders: Factor Leading to Underdiagnosis

- **Inability to recall symptoms prior to age 12**
  - Alcohol dependent, opiate-dependent, methamphetamine-dependent have cognitive deficits compared to nonsubstance abusers. (Maxwell et al., 2005; Davis et al. 2002) Deficits shown to persist with abstinent alcoholics (Davies et al., 2005)
  - Early-onset cannabis use (< 17 years old) exhibit poorer cognitive performance compared to late-onset users (Pope et al., 2003).
- **Lack of corroboration from older family members**
  - May have estranged relationships, do not want family to be contacted
  - If parents used alcohol/drugs- Parents can't remember details

Adults with ADHD: Factors Leading to Overdiagnosis

- **Not obtaining adequate longitudinal history**
- **Relying on screening instruments alone**
- **Not ensuring that all DSM-V criteria are met (symptoms in multiple domains/significant impairment)**
- **Learning Disabilities**
- **Desire to get special consideration with test-taking, performance enhancement**

Adults with ADHD and Substance Use Disorders: Factors Leading to Overdiagnosis

- **Ongoing substance use might mimic ADHD symptoms**
  - Acute Effects
    - Cocaine and other stimulants: Restlessness, agitation
  - Withdrawal:
    - Alcohol: Restlessness, agitation
    - Sedative-Hypnotics: Restlessness, agitation
    - THC: Restlessness, agitation, irritability
    - Nicotine: Restlessness, irritability, frustration, anger, difficulty concentrating
    - Cocaine: Psychomotor agitation, difficulties with concentration

Graham et al., *In Principles of Addiction Medicine*, 2003; Miller and Gold, 1998

Adults with ADHD and Substance Use Disorders: Factors Leading to Overdiagnosis

- Relying on screening instruments/computer testing alone (mentioned before)
  - May not take into account impact of ongoing substance use or other psychiatric diagnoses
- Chaotic early childhood
  - Inattentive or impulsive symptoms may be secondary to difficulties at home, no structure
- Desire to get stimulant medication

Assessment of ADHD in Adults with Substance Use Disorders

- Complete a timeline for ADHD symptoms: onset of symptoms, what types of symptoms, did they change over time
- Complete a timeline for substance use, onset of use, heavy substance use, problematic use, and periods of abstinence or reduced use
- Determine presence/absence of ADHD symptoms prior to drug use and during periods of abstinence
- If symptoms not present during abstinence or come and go, not consistent with ADHD diagnosis

Why is Treating ADHD Important in Patients with SUDs?

- Earlier onset of SUD when ADHD present
- A reduced likelihood of going into remission if dependence develops
- If remission achieved, longer time to reach remission
- More treatment exposure, yet do less well in treatment
- Higher rates of other psychiatric comorbidities (e.g., conduct/antisocial disorders)

Carroll, Rounsaville. *Comp Psych.* 1993;34:75-82.; Schubiner, et al. *J Clin Psych.* 2000;61:244-251.; Levin, et al. *Drug Alc Dep.* 1998;52:15-25. Wilens T. *Psychiatr Clin N Am.* 2004;27:283-301.; Wilens T, et al. *Am J Addict.* 1998;7(2):156-63.

Common Treatment Quandaries

- Concern that treating children/young adults either increases the risk of SUDs or, at best, has no effect on subsequent substance use or substance use disorders
- Concern that standard treatments for ADHD will not work in active substance users
- Even if treatments work for ADHD, concern that medications will not impact the substance use disorder or may make things worse
- Concern that active substance users will misuse or divert their medications
- Concern that numerous psychiatric comorbidities, along with ADHD and SUD, will make treatment targeting the ADHD ineffective

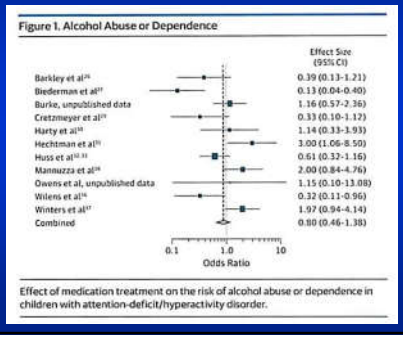
Is ADHD Pharmacology a Risk Factor for Subsequent Substance Use Disorder?

(Humphreys et al., *JAMA Psychiatry*, 2013)

- Concerns that stimulant pharmacotherapy begets SA in ADHD youths growing up
- Meta-analysis conducted in longitudinal studies to examine association between treatment with stimulant medication during childhood and later substance outcomes
- Odd ratios were obtained for lifetime use (ever used) and abuse or dependence status for alcohol, cocaine, marijuana, nicotine, and nonspecific drugs for 2565 participants from 15 different studies
- Aggregate data do not support that stimulants increase substance use or dependence. However, also do not indicate reduced risk as found in earlier meta-analyses
- Limitations: Variable age of onset and duration of stimulant use, variable follow-up; lack of control of comorbidity, those on medication might have more severe symptoms and without medication might have done worse.

Stimulant Medication and Substance Use Outcomes: Meta-Analysis

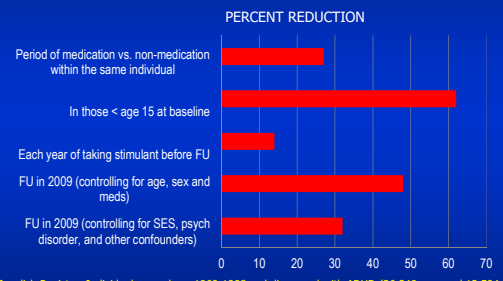
(Humphreys et al., *JAMA Psychiatry*, 2013)



Effect of medication treatment on the risk of alcohol abuse or dependence in children with attention-deficit/hyperactivity disorder.

Among those subjects treated with stimulant ADHD medication, there was a significant reduction in rates of substance abuse

(Chang et al., *J Child Psychol Psychiatry*, 2015)



Swedish Registry: Individuals were born 1960-1998 and diagnosed with ADHD (26,249 men and 12,504 women; circa 50% on stimulant medication in 2006); Authors examined the association between stimulant ADHD medication in 2006 and substance abuse during 2009 (e.g. substance-related crime, hospital visits or death; outcomes : 6% vs 0.5% ADHD vs gen pop)

Psychopharmacologic Treatment of ADHD and SUD: 15 Double Blind Trials, 13 Outpatient

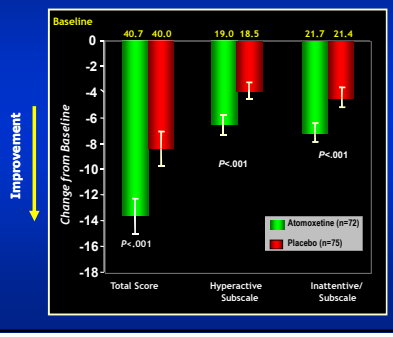
	Sample Size	Drug	RX Use/Results
Schubiner et al., 2002	48	Cocaine	MPH/MIXED for ADHD, Cocaine NEG
Riggs et al., 2004	69	Various	Pemoline/MIXED ADHD, SUD NEG
Carpentier et al., 2005	25	Various	MPH/Inpatient study ADHD NEG
Levin et al., 2006	98	Methad/Cocaine	MPH/Buprop/ADHD and Coc, BOTH NEG
Levin et al., 2007	106	Cocaine	MPH/MIXED for ADHD and Cocaine
Wilens et al., 2008	147	Alcohol	Atomox/ADHD POSITIVE; MIXED Alcohol
Winhusen et al. 2019	255	Nicotine	MPH/ADHD POS; MIXED Smoking
Konstenius et al., 2010	24	Methamph	MPH/ADHD and METHAMP NEG
McRae-Clark et al., 2010	38	Marijuana	Atomox/ADHD MIXED; THC NEG
Thurstone et al., 2010	70	Various	Atomox/ADHD NEG; SUD NEG
Riggs et al., 2011	303	Mostly Marijuana	MPH/MIXED ADHD and SUD
Ginsberg and Lindefors, 2012	30	Various (Mostly Amph)	MPH/Prison Inmates ADHD POS
Kostenius et al., 2013	54	Amphet	MPH/ADHD POSITIVE; SUD POS
Kollins et al. 2014	32	Nicotine	Lisdexamfetamine/ADHS Pos, Nicotine Neg
Levin et al., 2015	126	Cocaine	Mixed Amphetamine Salt XR/ADHD and Coc, BOTH POS

Double-Blind Outpatient Studies Using Stimulants/Atomoxetine to treat adults with ADHD and SUDs: Overall Summary

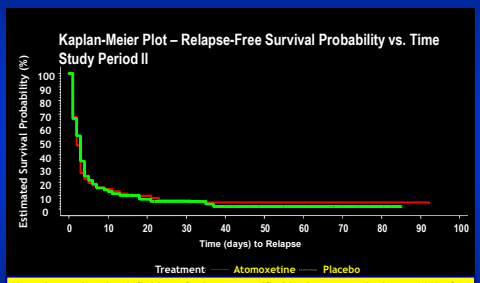
- 15 outpatient double-blind trials, 13 conducted in oupatients
- Most of the outpatient/inpatient studies have some "signal" in terms of reducing ADHD (12/15 studies) and out of the outpatient studies approximately 6/13 (46%) suggest some benefit in terms of substance use.
- Some studies looked at whether response to ADHD associated with reduction to Substance Use (Levin et al. 2007; Riggs et al. 2011; Levin et al. 2018)
- Majority of the trials (inpatient and outpatient, n=9) evaluated methylphenidate, a few evaluated atomoxetine (n=3) or amphetamine formulation (n=2).

Atomoxetine in Adults with ADHD and Recently Abstinent Alcohol Use Disorders: ADHD

(Wilens et al., *Drug Alc Dep* , 2008)



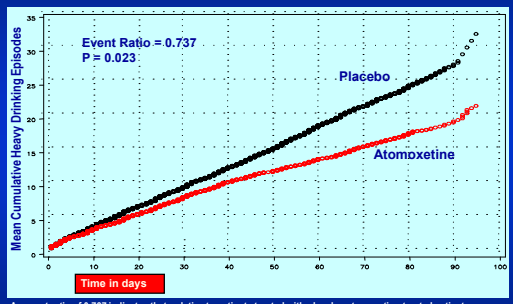
Atomoxetine vs. Placebo in Recently Abstinent Adults with Alcohol Use Disorder: Primary Outcome-Time to Alcohol Relapse



Note that, using the definition of relapse specified in the protocol, almost 90% of subjects had relapsed within 2 weeks.

Wilens et al., *Drug Alc Dep*, 2008

Atomoxetine vs. Placebo in Recently Abstinent Adults with Alcohol Use Disorder and ADHD: Multiple Event Cox Model



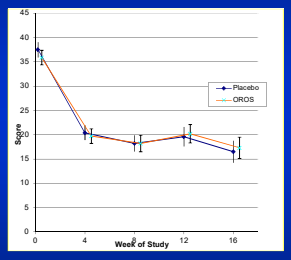
An event ratio of 0.737 indicates that, relative to patients treated with placebo, atomoxetine-treated patients experienced an approximately 26.3% greater reduction in the rate of heavy drinking. Separation occurred at Day 55

Wilens et al., *Drug Alc Dep*, 2008

Double-Blind, placebo controlled OROS-MPH for ADHD Adolescents with DSM-IV SUD

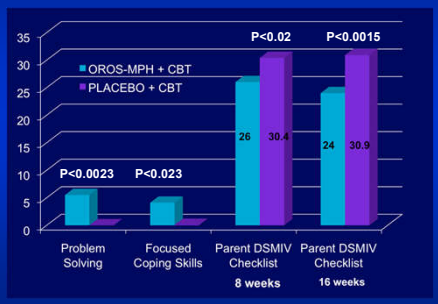
(Riggs et al., 2011, J Am Acad Child Adolesc Psychiatry)

- 303 adolescents with SUDs, randomized to OROS-MPH or placebo with CBT platform
- 16 week trial, adolescents, ages 13-18 years
- ADHD Checklist: A likelihood ratio chi-square test of the treatment effect with three treatment x time terms = 6.7, 4 df; P = 0.1526 for the effect of treatment on ADHD.



Secondary ADHD Outcome Measures

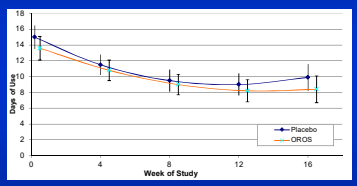
(Riggs et al., 2011, J Am Acad Child Adolesc Psychiatry)



Primary Substance Use Outcome Past 28 Days of Use

(Riggs et al., 2011, J Am Acad Child Adolesc Psychiatry)

The trajectories of past 28 day drug use based on adolescent self-reports did not differ between treatment groups (Chi-square = 3.04, 3 df, p = 0.3855 ; Proc Glimmix). Statistical significant decrease in both groups but no between group differences



- There was a significant reduction in the number of days/past 28 days of non-tobacco drug use in both the OROS-MPH + CBT (mean = -5.1 days; SE = 0.8, p < 0.0001) and placebo + CBT treatment groups (mean= -5.1 days; SE = 0.9, p<0.0001)
- But the difference between groups was not significant based on trajectories of change in past 28 day drug use from baseline to week 16 (Chi-square = 3.7, 3df, p=0.2957; SAS Proc Mixed)

Secondary Drug Use Outcome: Negative Urine Drug Screens by Treatment Group and Treatment Responders

(Riggs et al., 2011, J Am Acad Child Adolesc Psychiatry)

Treatment Group	OROS-MPH + CBT (N=149)	Placebo + CBT (N=-148)	P value
Mean # negative UDS (ITT sample)	Mean = 3.8 (4.9) negative UDS of 11.3 collected	Mean = 2.8 (4.2) negative UDS of 11.7 collected	P= 0.045 Kruskal-Wallis
Treatment Responders Regardless of Medication Grp	**ADHD Responders (CGI-I 1 or 2 at 16 weeks) (N=55)**	**ADHD Non-Responders CGI-I 2 at 16 weeks (N=172)**	
Means # negative UDS (completers)	Mean = 6.2 (5.4)	Mean = 3.1 (44)	P< 0.0001

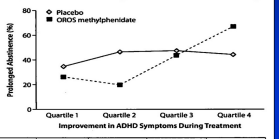
Multi-site placebo-controlled trial evaluating Concerta® (OROS-MPH) for adult cigarette smokers with ADHD

(Winhusen et al., *J Clin Psychiatry, 2010*)

- **Adults with ADHD and nicotine dependence who were interested in quitting**
  - All received nicotine patch and counseling- combination therapy
  - Strengths: Large sample size (n-255), good retention, high compliance, generalizable to various settings
  - OROS-methylphenidate- greater improvement in ADHD symptoms but not nicotine abstinence- compared to placebo

Treating Nicotine Dependence by Targeting ADHD with OROS Methylphenidate: The Role of ADHD Improvement and Treatment Response

Figure 2. Improvement in ADHD Symptoms During Treatment[a] and the Observed Percentages of Patients With Co-Occurring ADHD and Nicotine Dependence (N = 255) Who Achieved Prolonged Abstinence From Smoking



Prolonged Abstinence by Treatment Group	Quartile 1: No Improvement, Change Score[a] < 4 (n = 62)	Quartile 2: Small Improvement, Change Score[a] of 5–13 (n = 66)	Quartile 3: Moderate Improvement, Change Score[a] of 14–23 (n = 63)	Quartile 4: Large Improvement, Change Score[a] ≥ 24 (n = 64)
Placebo, % (n)	34.9 (43)	46.3 (41)	47.4 (19)	44.0 (25)
OROS methylphenidate, % (n)	26.3 (19)	20.0 (25)	43.2 (44)	66.7 (39)
Chi-square[b]	0.44	4.66	0.09	3.21
P	.51	.03	.76	.07

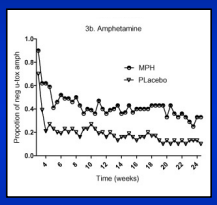
[a]ADHD-RS change scores were calculated as ADHD-RS score at baseline minus score at end of study; values shown are the range of change scores within each quartile (no. of patients per quartile). [b]Tests for pairwise contrasts between treatment groups within each quartile. Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ADHD-RS = ADHD Rating Scale-IV, OROS methylphenidate = osmotic-release oral system methylphenidate.

Nunes, Winhusen, Covey, Levin, et al., 2013, *J Clin Psychiatry*

Sustained Release Methylphenidate (OROS-MPH) for ADHD Criminal Offenders with Amphetamine Dependence

(Konstenius et al., *Addiction*, 2014)

- **Greater improvement in ADHD symptoms for those on MPH. Those that reduced their ADHD symptoms by at least 30%:**
  - **In the MPH group**, 17 patients (**65%**, *n* = 26) compared to seven patients (**27%**, *n* = 26) in the placebo group (*P* = 0.012).
- **Greater proportion of negative drug urines for those receiving MPH compared to placebo (23% vs 16%, *p*= 0.047), including more amphetamine-negative urines (23% vs. 14%, *p*= 0.019)**



Proportion of negative urine-toxicology after release from prison (weeks 3-24) for two treatment groups; methylphenidate (MPH) and placebo over 24 weeks of treatment. Amphetamines negative urines mean difference 95% CI = 0.07 - 0.36.

Extended Release Mixed Amphetamine Salts for ADHD and Cocaine Dependence

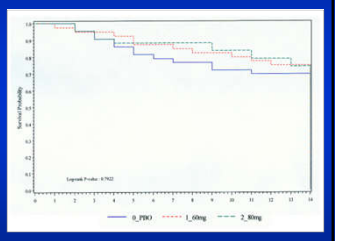
(Levin FR, et al., *JAMA Psychiatry ,2015*)

- **Randomized, placebo-controlled 13-week trial conducted at 2 sites: Columbia University/NYSPI and University of Minnesota**
- **Three times a week visits**
- **MAS-XR 80 mg/day, and MAS-XR 60 mg/day vs placebo or maximum tolerated dose**
- **Weekly individual manualized psychotherapy using cognitive-behavioral therapy/relapse prevention treatment targeting cocaine use and ADHD**
- **Voucher incentives based on attendance and $10/week for return of medication bottles**

Retention

(Levin et al., *JAMA Psychiatry*, 2015)

- **139 Entered the trial**
- **126 were randomized**
- **74% completed the maintenance phase (week 13)**



Extended-Release MAS-XR vs. Placebo for ADHD and Cocaine Use Disorder

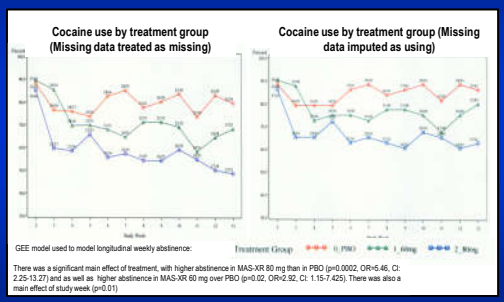
(Levin et al., *JAMA Psychiatry*, 2015)

139 entered, 126 randomized, 74% completed maintenance phase (week 13)

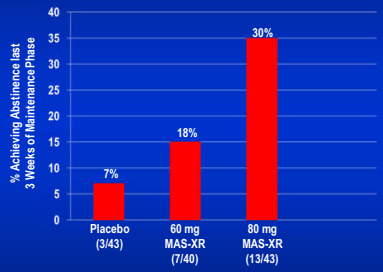
* p = 0.0009
** p = 0.069

* p = <0.0001
** p = 0.014

Cocaine Use by Treatment Group (Self-Report Confirmed by Urine Toxicology)



Cocaine Use Outcome

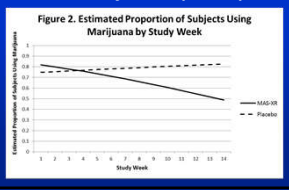


MAS-ER 60 mg vs. placebo (OR=5.85 [CI: 1.04-33.04]; p=0.045)
MAS-ER 80 mg vs. placebo (OR=11.87 [CI: 2.25-62.62]; p=0.004)

MAS-XR increase abstinence for marijuana in patients with co-occurring ADHD and Cocaine Dependence

(Notzon, Mariani, Pavlicova, Glass, Mahony, Brooks, Grabowski, and Levin; Am J Drug Alc Abuse, 2017)

- **Marijuana users were defined as use in the 30 days before study initiation. Marijuana use data were collected with timeline follow-back.**
- **For this analysis, both MAS-XR groups were combined to maximize statistical power, leaving n=20 in the placebo group and n=37 in the MAS-XR group.**
- **Treatment of ADHD and comorbid cocaine use disorders with extended release mixed amphetamine salts is associated with increased weekly abstinence from marijuana compared to placebo**



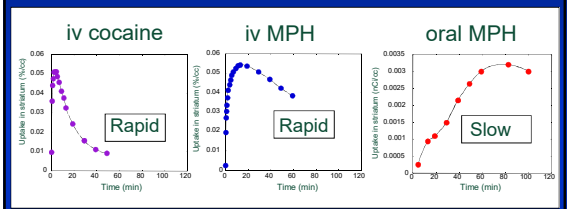
Analysis of the proportion of subjects using marijuana per week revealed significant interaction between study arm and week ($F_{1,638}$ = 5.39, p = 0.0206), indicating significant differential slopes between treatment groups.

Treatment of Co-Occurring ADHD and SUD: Clinical Recommendations

- **Atomoxetine- Shown helpful for abstinent alcohol-dependent individuals, those with tic disorder. High drop-out rate when given to cocaine abusers with ADHD** (Levin et al., 2009).
- **Bupropion ("Off-Label" – not FDA approved for ADHD)**
  - Efficacy in cigarette cessation
  - Useful in comorbid mood disorders
  - Open studies show improved ADHD/SUD/Mood outcome
- **Guanfacine, modafinil, tricyclic antidepressants (Off-label)**
- **Amphetamine or Methylphenidate formulations with stimulant use disorder**

Wilens TE. *Psychiatr Clin North Am.* 2004;27(2):283-301.; Riggs PD, et al., *J Am Acad Child Adolesc Psychiatry.* 1998;37(3):331-2.; Schubiner H. *CNS Drugs.* 2005;19(8):643-55.; Wilson JJ, Levin FR. *J Child Adolesc Psychopharmacol.* 2005;15: 751-763.; Mariani JJ, Levin FR. *Adv Psychiatry.* 2006.

How concerned should we be in making someone high? Rate of Drug Uptake into the brain affects the "High"



- **Cocaine (iv) and methylphenidate (iv) produce a "high" but methylphenidate (oral) does not (10-60 mg)**
- **The slow brain uptake of oral methylphenidate permits effective treatment without a "high"**

Volkow et al., *Arch Gen Psych*, 2007; 1995, *J Neurosci*, 2001

Nonmedical Use and Diversion of ADHD Stimulants Among U.S. Adults Ages 18-49: A National Internet Survey

(Cassidy et al., *J Atten Disord*, 2015)

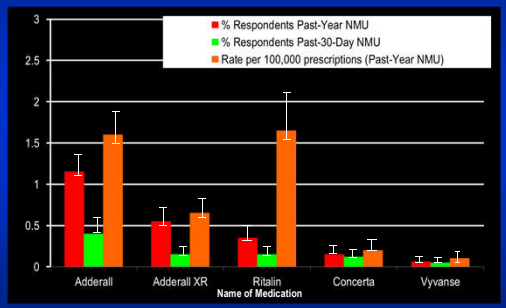


Figure 2. Prevalence of nonmedical use of prescription stimulant compounds. Past year, past 30 days, and past-year rate per 100,000 prescriptions. Note. Vertical bars represent 95% confidence intervals. - NMU = nonmedical use.

Long-Acting Formulations

- More evidence now that we should consider long acting stimulants over immediate release preparations of even atomoxetine which has traditionally been thought of as first line treatment among those with a substance use disorder
- In particular lisdexamphetamine or Concerta XL and perhaps Daytrana

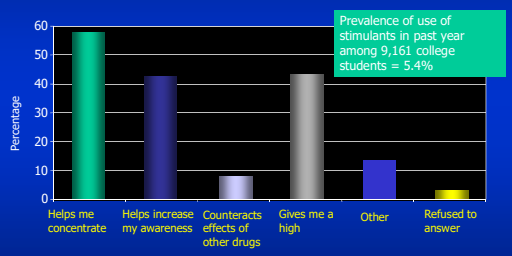
Stimulant Misuse and Diversion

- N=22 Studies (N>113,000 participants); mostly survey studies in college students (80%)
- 10-20% prevalence of non medical use of stimulants
- 65-85% of stimulants diverted from "friends"
  - Majority *not* "scamming" local docs
  - Not seen as potentially dangerous
- Motivation typically for concentration and alertness more so than getting "high"
- Appears to be occurring in substance (ab)users during academic decline
- Increased risk of SUD in stimulant misusers (not causal)

(McCabe and Teeter, Addiction; 2005; Arria et al. Sub Abuse:2007; Wilens et al. JAACAP: 2006, 2008)

Prevalence and motives for illicit use of prescription stimulants in an undergraduate student sample.

What Motivates Undergraduates at One Institution to Use Stimulants Illicitly?

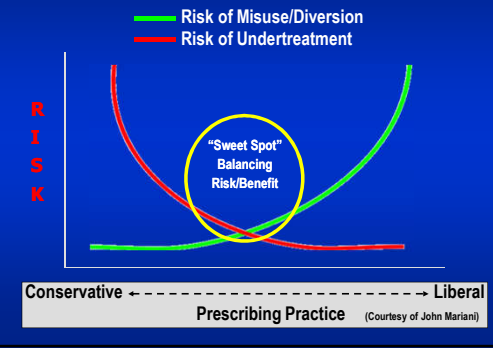


Teter CJ, et al. *J Am Coll Health*. 2005;53(6):253-262.

Stimulant medication abuse in SUD-ADHD patients seeking treatment less than one might expect

- **Clinical Experience**
  - Consensus of many clinical investigators that it abuse of prescribed medications is relatively low, most notable abuse among those with bipolar diathesis
- **None of the clinical trials reported notable diversion or misuse.**
- **Study evaluated misuse/subjective effects of OROS-MPH in 2 CTN trials: Adolescents with SUD and Adults with TUD** (Winhusen et al. 2011)
  - Adolescents with SUDS NOT more likely than adults with nicotine use disorders to describe feeling euphoric with OROS-MPH.
  - Adolescents more likely to lose pills, need replacement pills, than adults BUT among the adolescents, no difference between those taking MPH or placebo.

Competing Risks of Controlled Medication RX: Overall Clinical Stability and Optimal Functioning is the Therapeutic Goals



Red Flags to Recognize

- **Escalating Doses**
  - **Symptoms of intoxication or symptoms associated with heavier use (agitation, psychosis, SOB, palpitations)**
- **Running Out Early: Discordant pill count**
  - The PMP Databased is your friend
- Demands for a particular, usually fast acting medication (amphetamine IR)
  - "Extended-release doesn't work for me"
- **Determine why this is happening**
  - Disorganized, losing medication
  - Abusing/Using to get high
    - If bipolar, trying to capture "good feeling," or in early manic episode
  - Dose not enough to achieve therapeutic effect
- **Can always not prescribe if things getting out of control**

Managing Misuse/Diversion for Prescribing Stimulants

- **Limit and keep track of pills**
- **State prescribing databases**
- **Obtain urine toxicology screens (they should only have the type of stimulants you are prescribing)**
- **Frequent patient visits**
- **Preferred use of long-acting agents**
- **Emphasize to patient to take medications regularly, not on a PRN basis**
- **Discussion with patient regarding safe storage and not advertising/sharing medications**
- **Limit-setting: compassionate, yet boundaried**
- **May use a contract outlining the "rules" of treatment**

Treating Adults with ADHD with Additional Psychiatric Disorders

- **There are little empirical data to guide treatment for those that have multiple psychiatric disorders, let alone treatment for ADHD and SUDs without additional psychiatric disorders**
- **The challenge is what to treat first and/or how to treat all of these conditions safely**
- **Generally, if possible, treat what is most clinically impairing first**
- **Overall, both stimulants and atomoxetine seem to work for ADHD even in the presence of additional depression, anxiety disorders and SUDS (Clemow et al. 2017)**

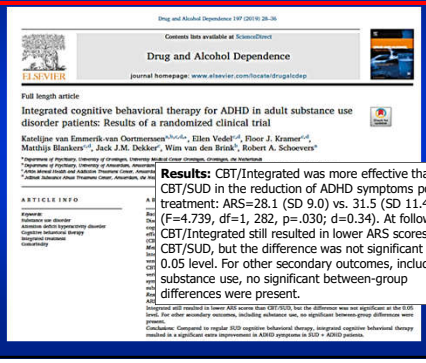
Treating Co-morbidity – Psychosis / Bipolar

- Need to be cautious in treating a patient with ADHD medication if there is a pre-existing psychosis or bipolar illness. Need to discuss the risk-benefit ratio of starting ADHD medication with patients
- If start a stimulant/atomoxetine and psychosis/mania occurs, stop drug and reassess.
  - Clinical experience is may see decreased sleep/need to sleep as first symptom
  - Careful re-evaluation is needed if pre-existing disorders not picked up
- Victorin et al. 2016 (AJP) found that risk of precipitating mania with a stimulant is uncommon if alleviate symptoms first with a mood stabilizer

Clinical Quandary for the Experienced Clinician

- Difficulty determining whether stimulant treatment is yielding a benefit in a patient with co-occurring ADHD and SUD and even more so, with additional psychiatric disorder
  - Carry out structured assessments of ADHD symptoms.
  - Determine the severity of the SUD. Often in severe cases, don't see improvement in ADHD symptoms unless SUD severity is reduced/alcohol-drug use diminishes or psychiatric disorder is addressed
  - If don't see an effect on ADHD symptoms, may need to use higher doses. If you are afraid to use medications in active substance users, underdosing doesn't get you anywhere
  - Look for functional improvements. If there is no improvement in social, occupational, academic settings and still actively using drugs, then no reason to keep prescribing

Integrated cognitive behavioral therapy for ADHD in adult substance use disorder patients: Results of a randomized clinical trial



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Full length article

Integrated cognitive behavioral therapy for ADHD in adult substance use disorder patients: Results of a randomized clinical trial

Katelijne van Emmerik-van Oortmerssen, Eilen Vedel, Floor J. Kramer, Matthijs Blankers, Jack J.M. Dekker, Wim van den Brink, Robert A. Schoevers

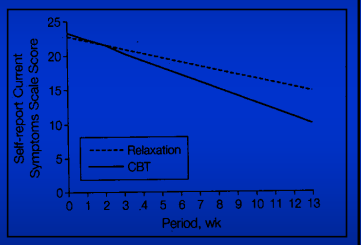
ARTICLE INFO

Results: CBT/Integrated was more effective than CBT/SUD in the reduction of ADHD symptoms post-treatment: ARS=28.1 (SD 9.0) vs. 31.5 (SD 11.4) (F=4.739, df=1, 282, p=.030; d=0.34). At follow-up, CBT/Integrated still resulted in lower ARS scores than CBT/SUD, but the difference was not significant at the 0.05 level. For other secondary outcomes, including substance use, no significant between-group differences were present.

CBT vs. Relaxation with Educational Support for Medication ADHD Adults with Persistent Symptoms

(Safren et al., *JAMA*, 2010)

- 86 patients randomized to 2 behavioral interventions
- Suggests that CBT focusing on ADHD with medication might be superior than medication alone with substance abusers who have partial responses.



What Conclusions Can We Reach?

- Diagnosing ADHD in an Active Substance Users Can Be Done
- Treating children/adolescents/adults reduces risk of substance use and substance use disorders.
- Standard treatments for ADHD can work for active substance users and may reduce substance use
- Active substance users may misuse and divert their medications but if anything, SUD patients in clinical trials ask for dose reductions. In clinical practice, group most likely to misuse/divert- adolescents and emerging adults, particularly if active SUD
- Often there are numerous psychiatric comorbidities making it even harder to effectively treat individuals with ADHD and Substance Use Disorders but it can be done

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