Addiction and ADHD: Complex issues in Diagnosis and Treatment

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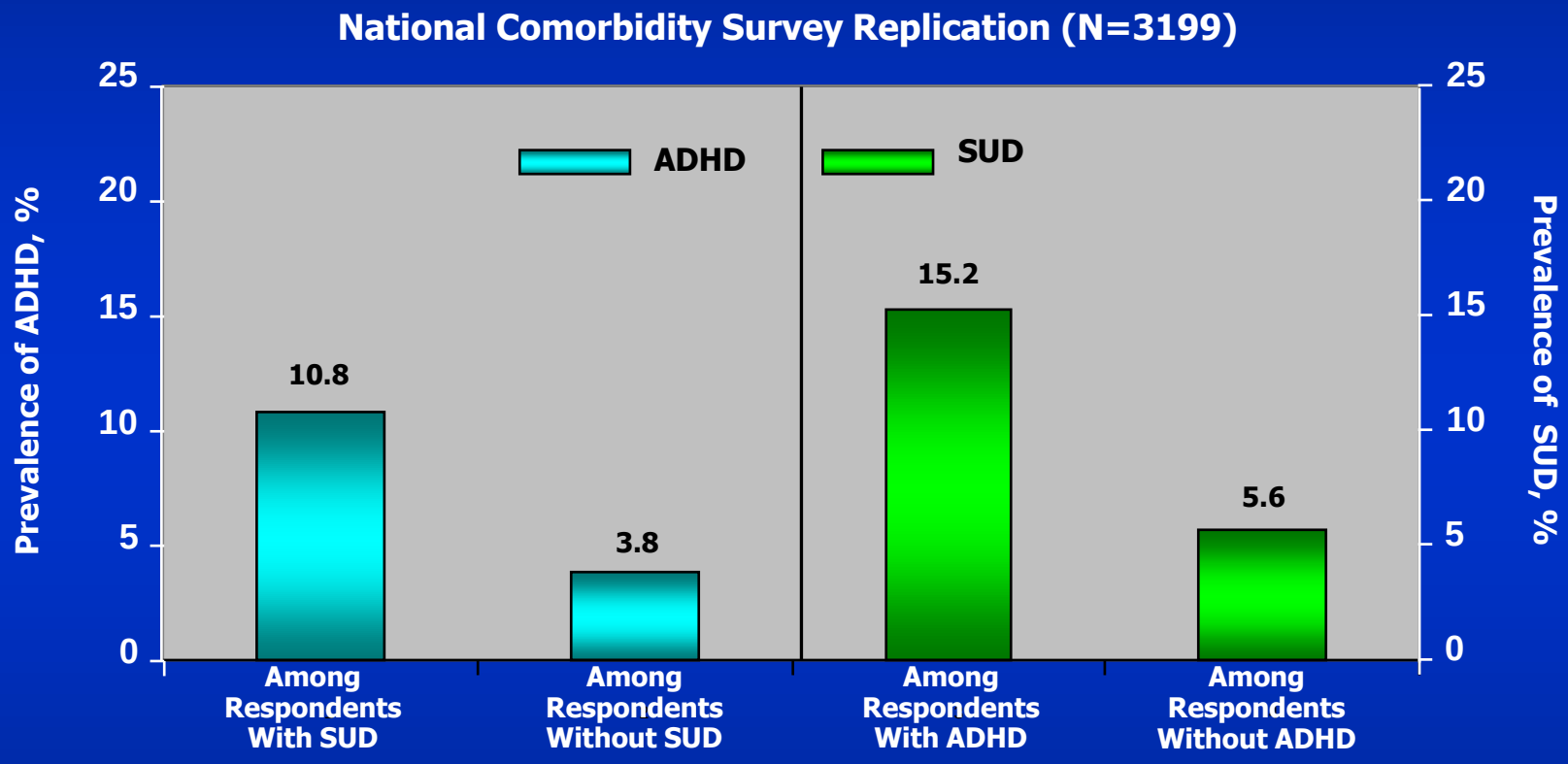
Comorbidity of adult ADHD and SUD in adults: epidemiologic data



(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 Abusers	10-15%
Clure, 1999	136 Cocaine and/or Alcohol Abusers	15%
King, 1999	125 Methadone Patients	17%
Schubiner, 2000	201 Substance Abusers	24%
Daigre, 2009	80 Various	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%**

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 Assumptions

- Standard treatments for ADHD do not work in active substance users
- Even if treatments work for ADHD, they do not impact on the substance use disorder
- Active substance abusers will misuse and divert their medications
- Often there are numerous psychiatric comorbidities making it even harder to effectively treat individuals with ADHD and SUDs

Clinical Conundrums for the Experienced Clinician

- Escalating dosing of stimulants/running out early
- Managing diversion/misuse risk
- Difficulty determining whether stimulant treatment is yielding a benefit in a patient with co-occurring ADHD and SUD

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. 2011	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

There is no need for therapeutic nihilism

- **Meta-analysis with Adults with SUDs** (Cunill et al., Psychopharm, 2015)
- **13 outpatient trials,** (including 1 single-blind).
  - Mixed results were obtained: while pharmacological interventions modestly improved ADHD symptoms, no beneficial effect on drug abstinence.
  - The strength of the recommendation of pharmacological treatment for co-occurring ADHD and SUD is therefore modest.

Pharmacologic Treatment of ADHD and Drug Dependence:

(Carpentier and Levin, 2016)

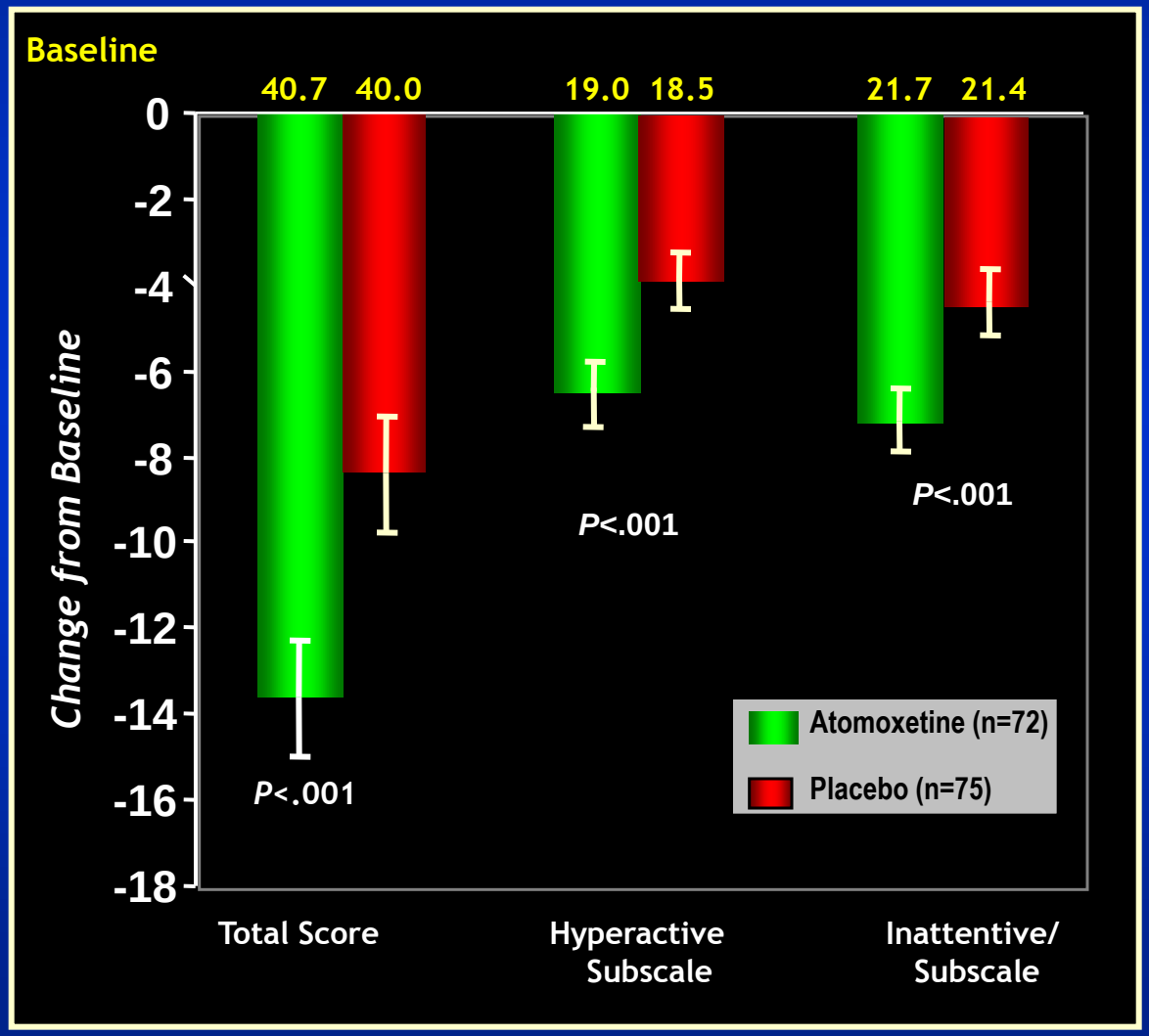
- **Limitations with many of the studies in the meta-analysis (including mine)**
  - Many studies had high drop-out rates. Not addressed
  - Outcome for substance use, based on a very short period
  - Studies may have clearly under-dosed. Used formulations with poor bioavailability
  - Combined all the trials looking at atomoxetine or stimulants. May be differentially effective based on drug of abuse. (Pure noradrenergic agents might be problematic for THC abusers; Stimulants might be better for cocaine/amphetamine)
  - Did not include 2 recent trials, high dose stimulants.

Double-Blind Outpatient Studies Using Stimulants/Atomoxetine to Treatment Substance Abusers with ADHD: Overall Summary

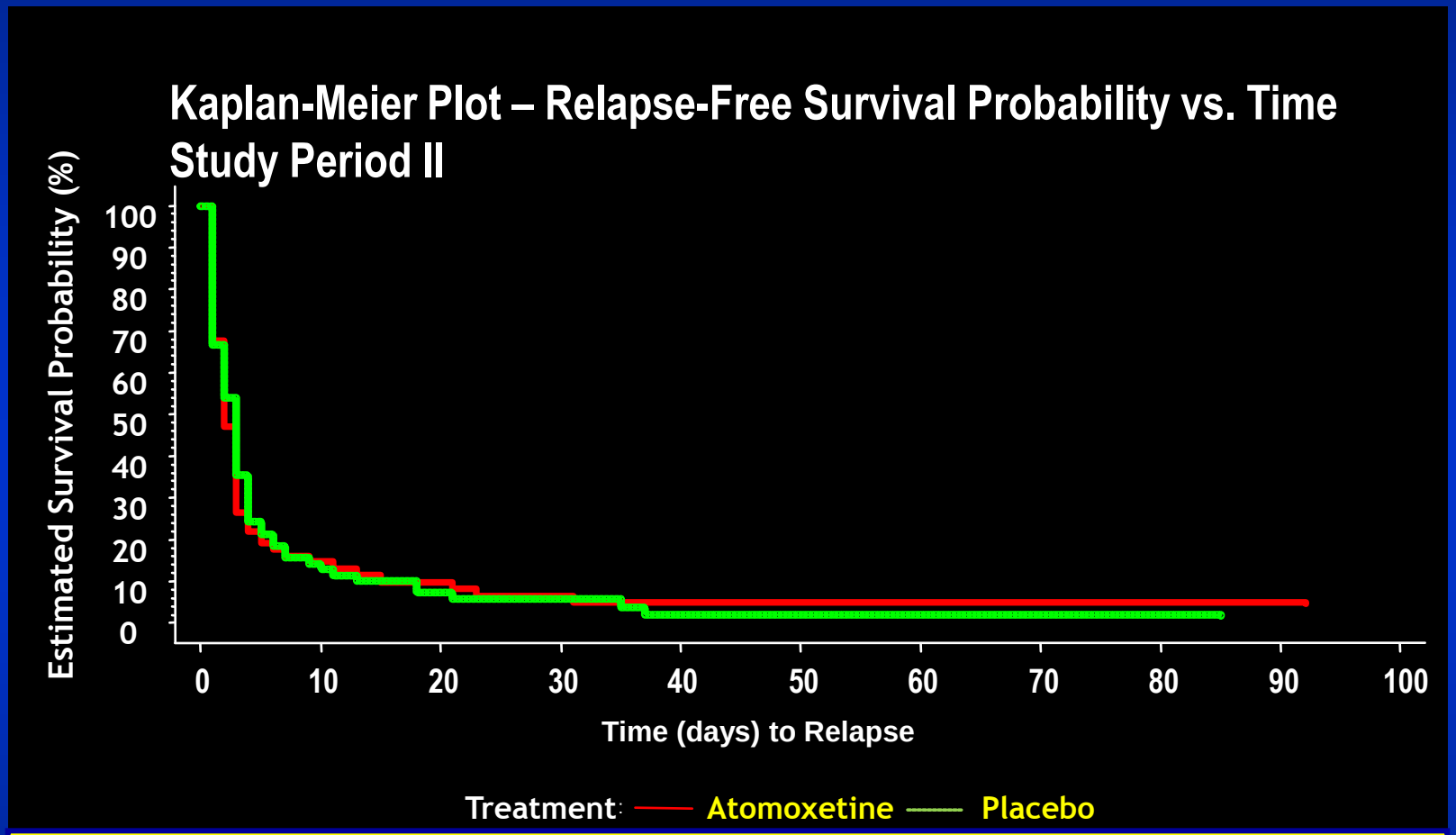
- 15 outpatient double-blind trials, 13 conducted in outpatients
- Most of the outpatient studies have some "signal" in terms of reducing ADHD (9/13 studies) and approximately 40% suggest some benefit in terms of substance use, particularly if there is an ADHD response (6/13).
- Majority of the trials (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)



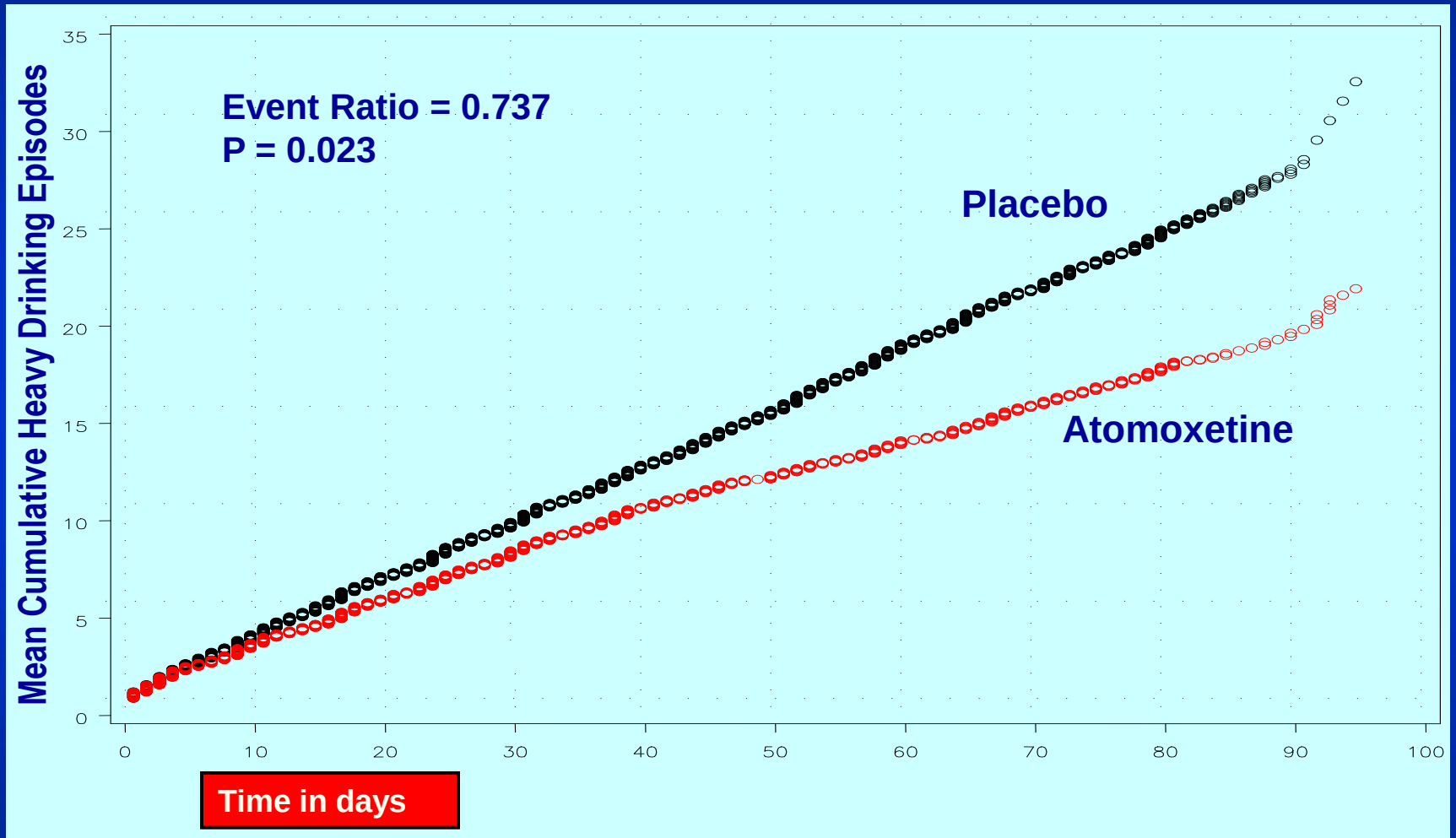
Atomoxetine vs. Placebo in Recently Abstinent Adults with Alcohol Use Disorders: Primary Outcome-Time to Alcohol Relapse



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



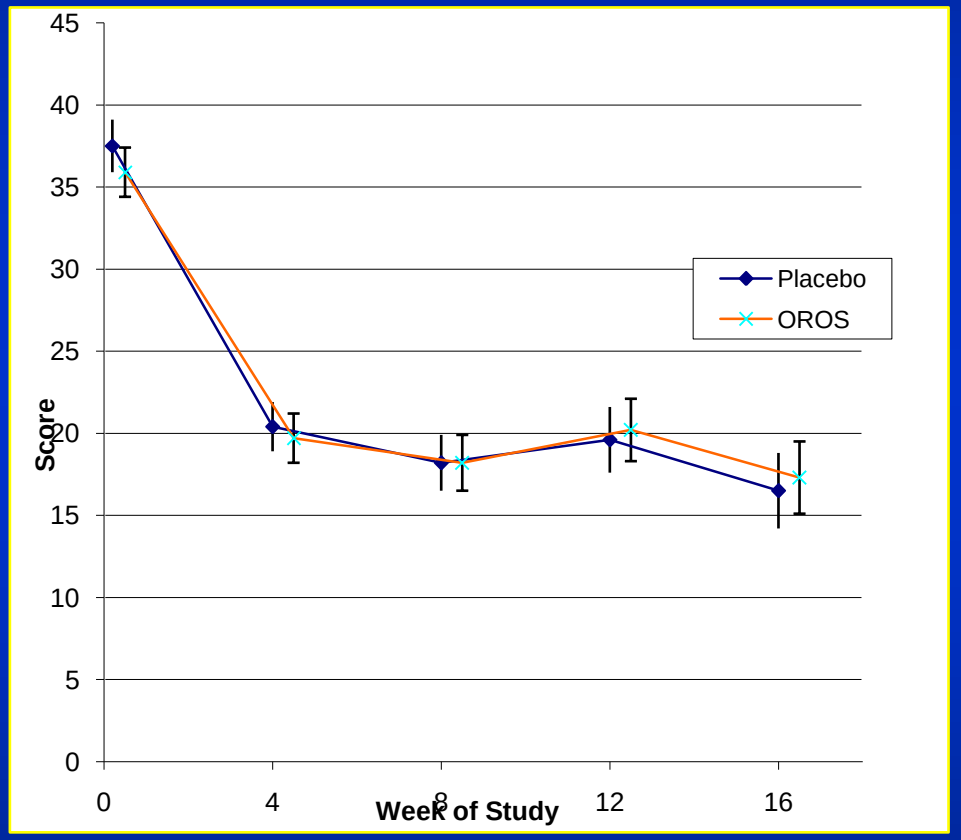
An event ratio of 0.737 indicates that, relative to patients treated with placebo, atomoxetine-treated patients experienced an approximately 26.3% greater reduction in the rate of heavy drinking. Separation occurred at Day 55

(Wilens, et al., 2008)

Adolescent DSM-IV ADHD Checklist by Treatment Group

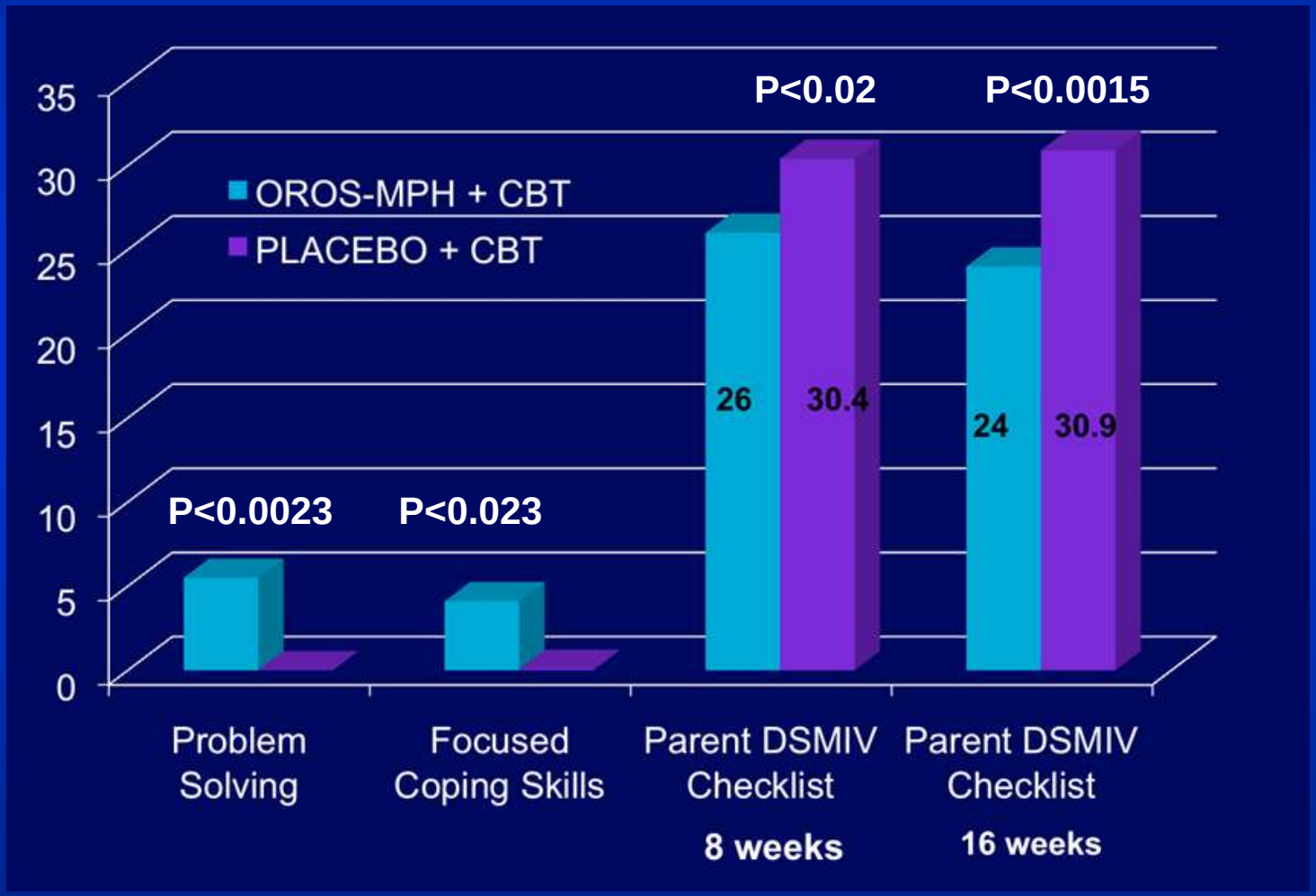
(Riggs et al., 2011)

- 303 adolescents with SUDs, randomized to OROS-MPH or placebo with CBT platform
- 16 week trial, adolescents, ages 13-18 years
- 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

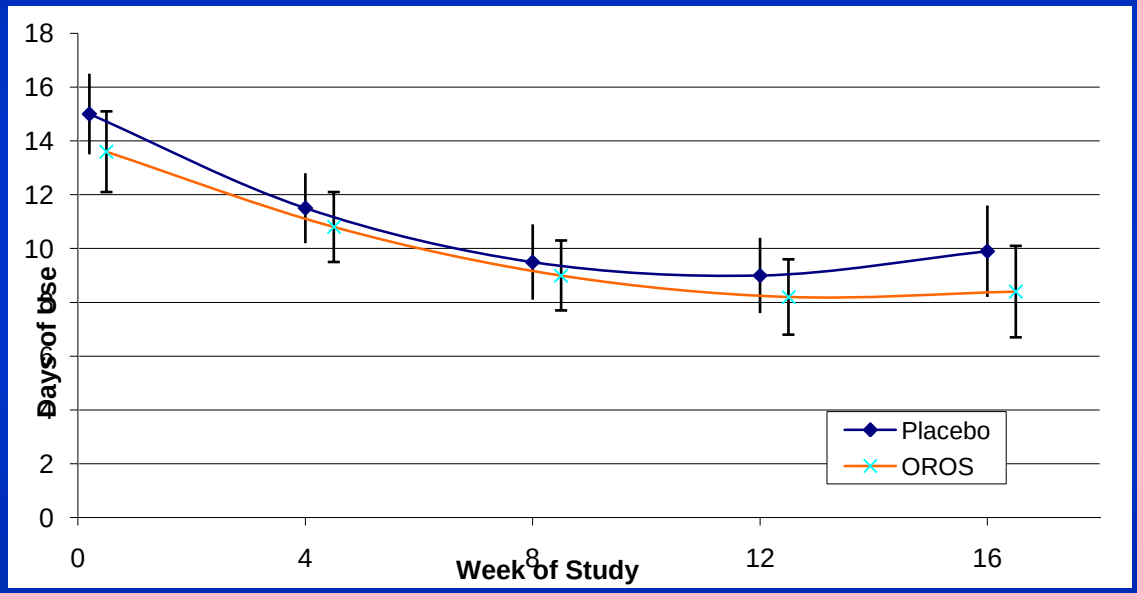
(Riggs et al., 2011)



Primary Substance Use Outcome Past 28 Days of Use

(Riggs et al., 2011)

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

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

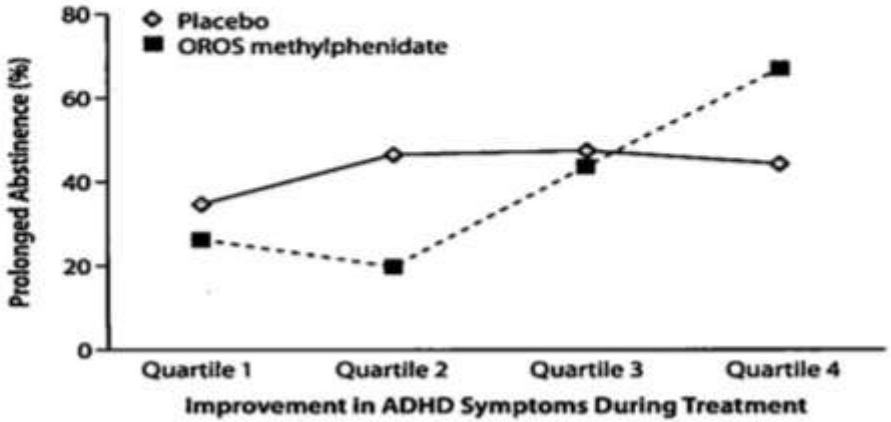
Multi-site placebo-controlled trial evaluating Concerta® (OROS-MPH) for adult cigarette smokers with ADHD

(Winhusen et al., 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 Improvment, Change Score[a] of 14–23 (n = 63)	Quartile 4: Large Improvment, 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

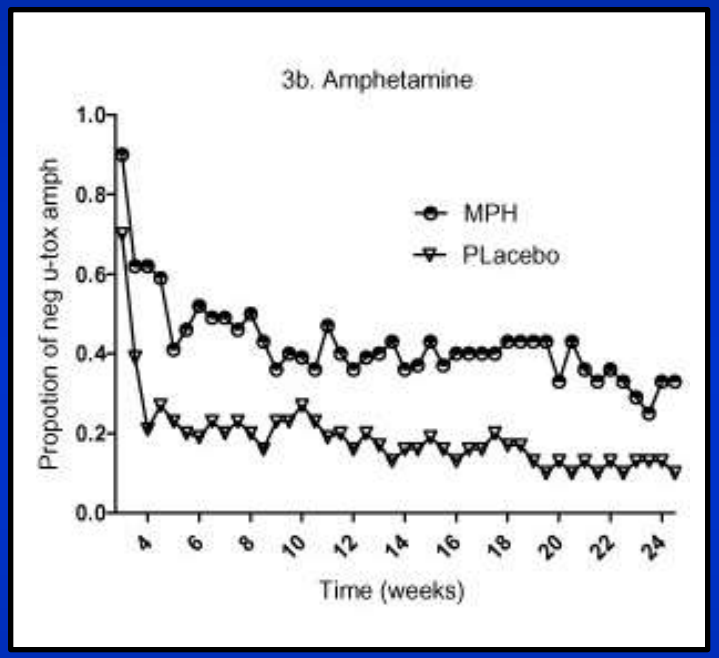
[a]ADHD-RS change scores were calculated as ADHD-RS score at baseline minus score at end of study; values shown are the range of change scores within each quartile (no. of patients per quartile). [b]Tests for pairwise contrasts between treatment groups within each quartile.
Abbreviations: ADHD = attention-deficit/hyperactivity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

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

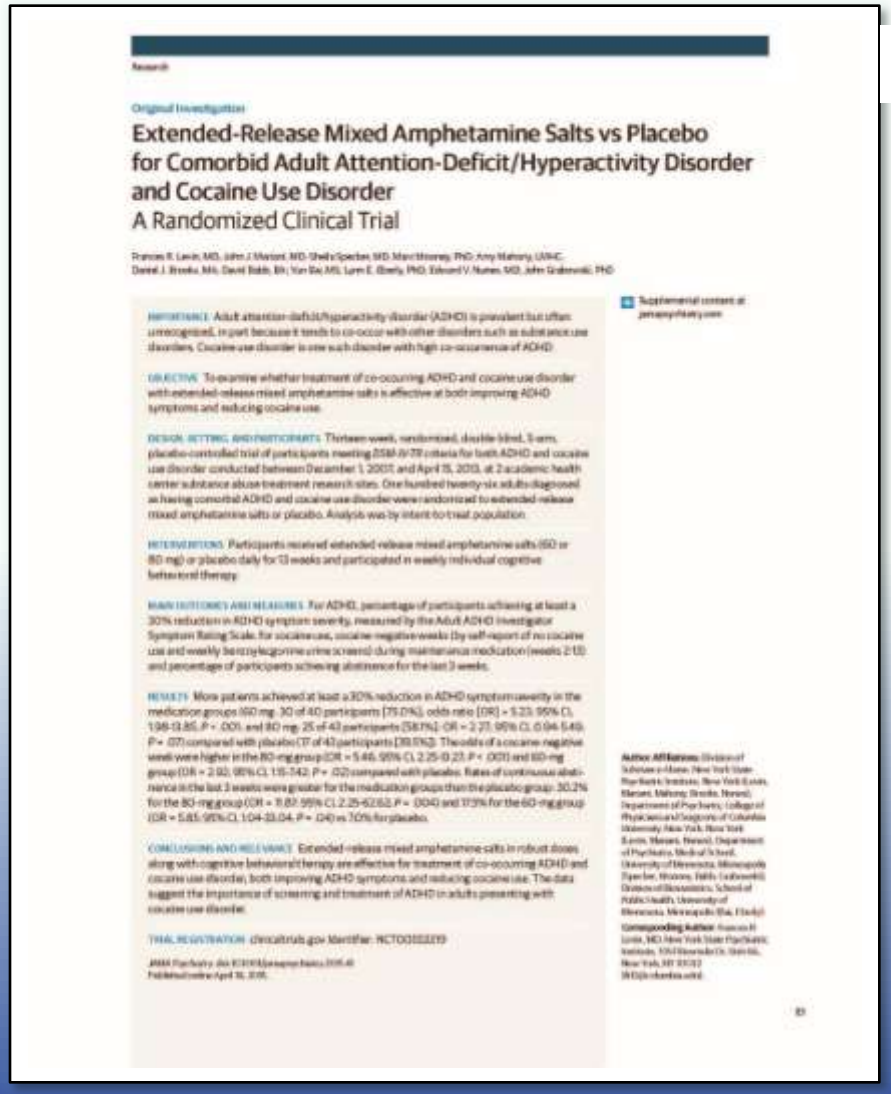
Sustained Release Methylphenidate (OROS-MPH) for ADHD Criminal Offenders with Amphetamine Dependence

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

- **Up to 180 mg/day, with majority on ORO-MPH tolerating the maximum dose**
- **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.



Research

Original Investigation

Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder

A Randomized Clinical Trial

Frances R. Levin, MD; John J. Mariani, MD; Sheila Specker, MD; Marc Mooney, PhD; Amy Mahony, LMHC; Daniel J. Brooks, MA; David Babb, BA; Yan Dai, MS; Lynn E. Eberly, PhD; Edward V. Nunes, MD; John Grabowski, PhD

Supplemental content at jamapsychiatry.com

IMPORTANCE Adult attention-deficit/hyperactivity disorder (ADHD) is prevalent but often unrecognized, in part because it tends to co-occur with other disorders such as substance use disorders. Cocaine use disorder is one such disorder with high co-occurrence of ADHD.

OBJECTIVE To examine whether treatment of co-occurring ADHD and cocaine use disorder with extended-release mixed amphetamine salts is effective at both improving ADHD symptoms and reducing cocaine use.

DESIGN, SETTING, AND PARTICIPANTS Thirteen-week, randomized, double-blind, 3-arm, placebo-controlled trial of participants meeting DSM-IV-TR criteria for both ADHD and cocaine use disorder conducted between December 1, 2007, and April 15, 2013, at 2 academic health center substance abuse treatment research sites. One hundred twenty-six adults diagnosed as having comorbid ADHD and cocaine use disorder were randomized to extended-release mixed amphetamine salts or placebo. Analysis was by intent-to-treat population.

INTERVENTIONS Participants received extended-release mixed amphetamine salts (60 or 80 mg) or placebo daily for 13 weeks and participated in weekly individual cognitive behavioral therapy.

MAIN OUTCOMES AND MEASURES For ADHD, percentage of participants achieving at least a 30% reduction in ADHD symptom severity, measured by the Adult ADHD Investigator Symptom Rating Scale. For cocaine use, cocaine-negative weeks (by self-report of no cocaine use and weekly benzoylecgonine urine screens) during maintenance medication (weeks 2-13) and percentage of participants achieving abstinence for the last 3 weeks.

RESULTS More patients achieved at least a 30% reduction in ADHD symptom severity in the medication groups (60 mg: 30 of 40 participants [75.0%]; odds ratio [OR] = 5.23; 95% CI, 1.98-13.85; $P = .001$; and 80 mg: 25 of 43 participants [58.1%]; OR = 2.27; 95% CI, 0.94-5.49; $P = .07$) compared with placebo (17 of 43 participants [39.5%]). The odds of a cocaine-negative week were higher in the 80-mg group (OR = 5.46; 95% CI, 2.25-13.23; $P < .001$) and 60-mg group (OR = 2.92; 95% CI, 1.15-7.42; $P = .02$) compared with placebo. Rates of continuous abstinence in the last 3 weeks were greater for the medication groups than the placebo group: 30.2% for the 80-mg group (OR = 11.87; 95% CI, 2.25-62.62; $P = .004$) and 17.5% for the 60-mg group (OR = 5.83; 95% CI, 1.04-33.04; $P = .04$) vs 7.0% for placebo.

CONCLUSIONS AND RELEVANCE Extended-release mixed amphetamine salts in robust doses along with cognitive behavioral therapy are effective for treatment of co-occurring ADHD and cocaine use disorder, both improving ADHD symptoms and reducing cocaine use. The data suggest the importance of screening and treatment of ADHD in adults presenting with cocaine use disorder.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00333229

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JAMA Psychiatry

FR Levin and coauthors

Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder: A Randomized Clinical Trial

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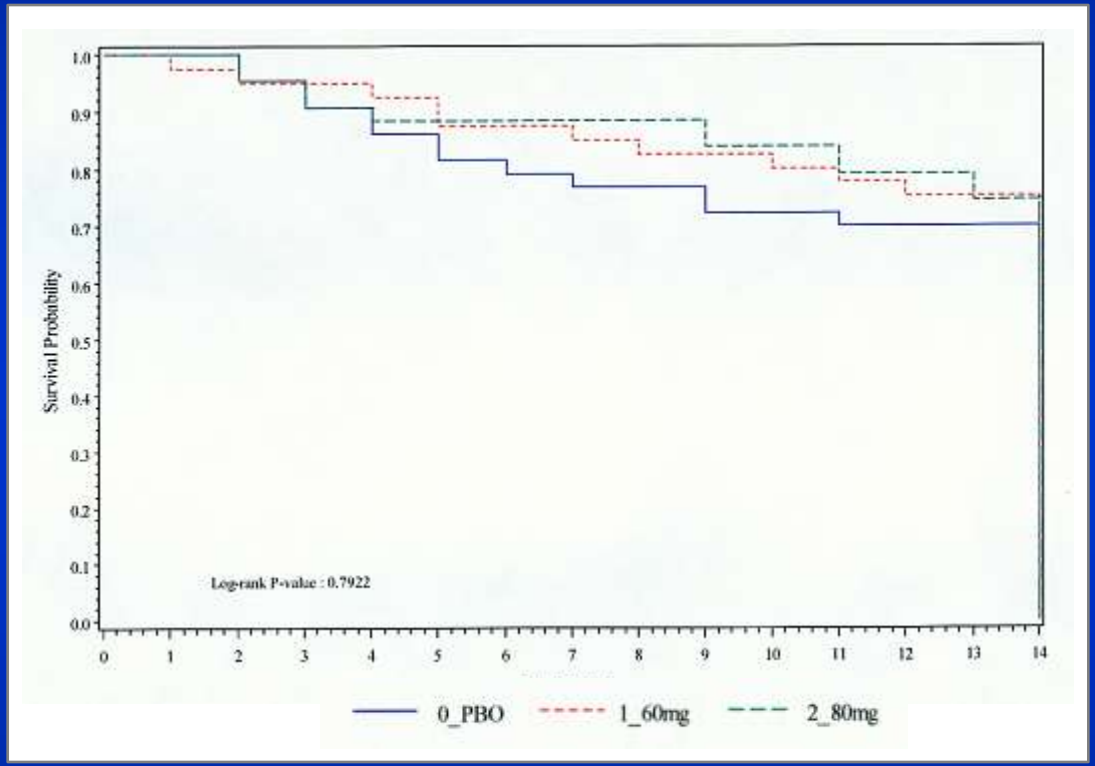
Study Design Overview

- 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

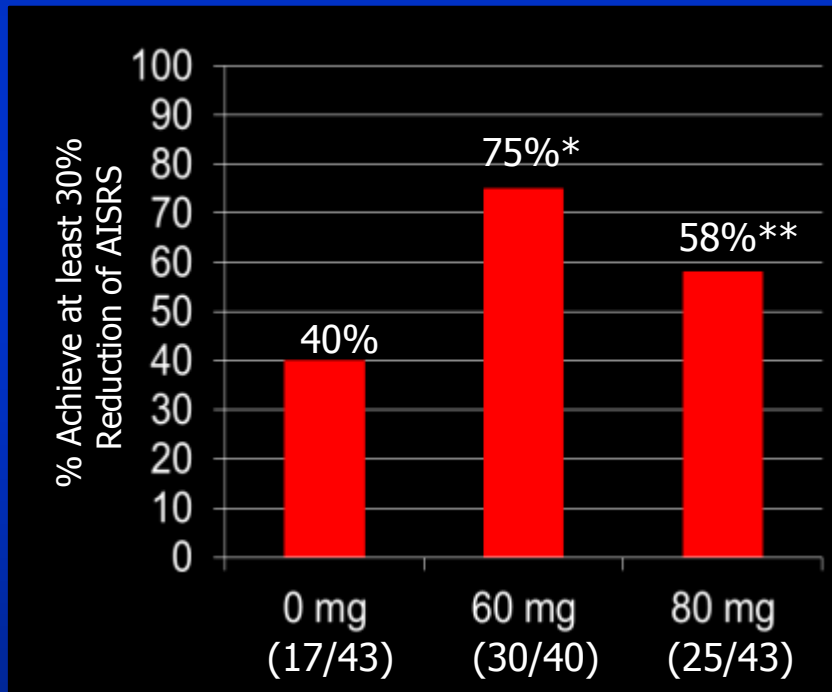
- 139 Entered the trial
- 126 were randomized
- 74% completed the maintenance phase (week 13)

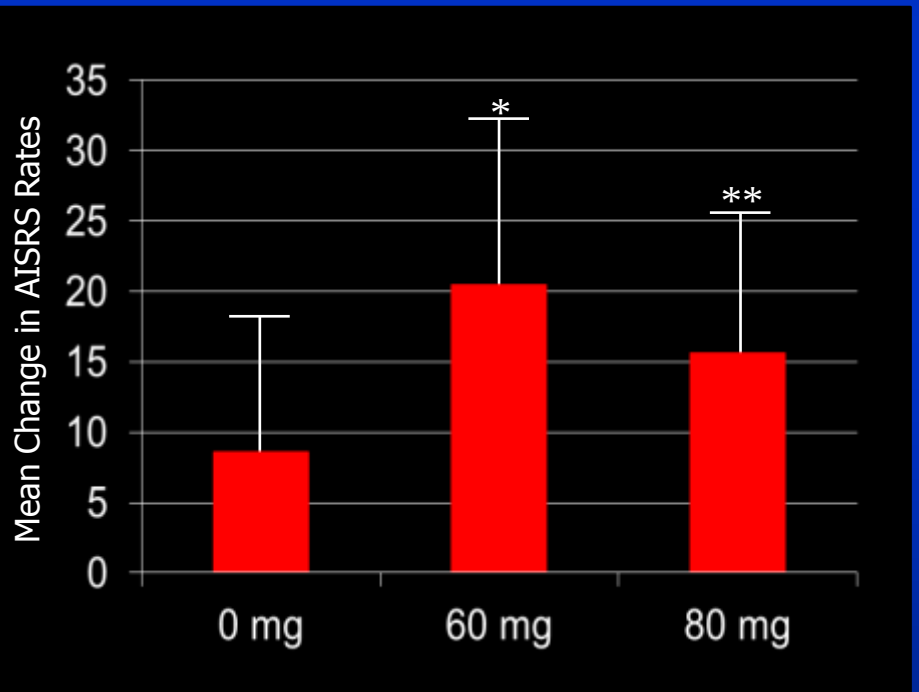


Extended-Release MAS-XR vs. Placebo for ADHD and Cocaine Use Disorder

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

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



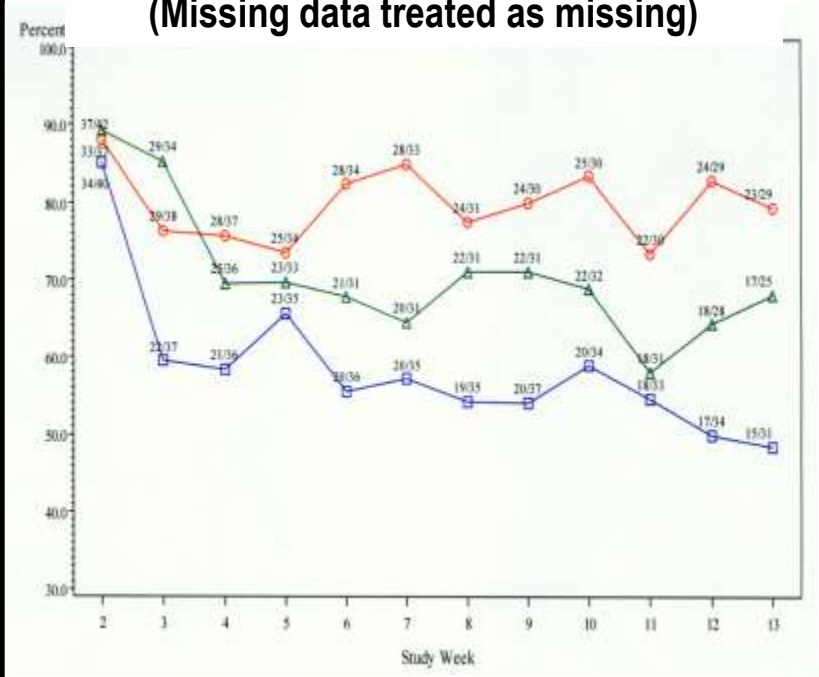


* p = 0.0009
** p = 0.069

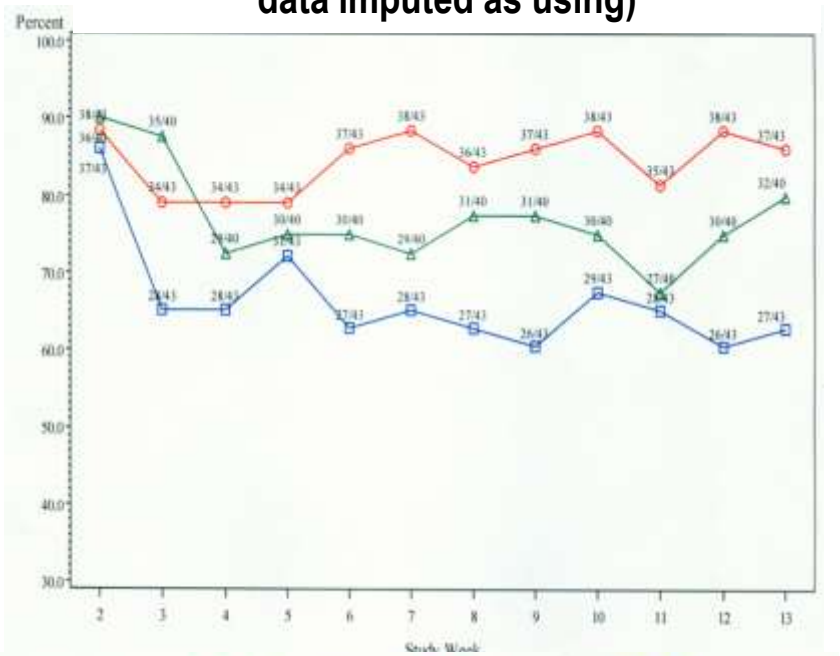
* p = <0.0001
** p = 0.014

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

Cocaine use by treatment group (Missing data treated as missing)



Cocaine use by treatment group (Missing data imputed as using)

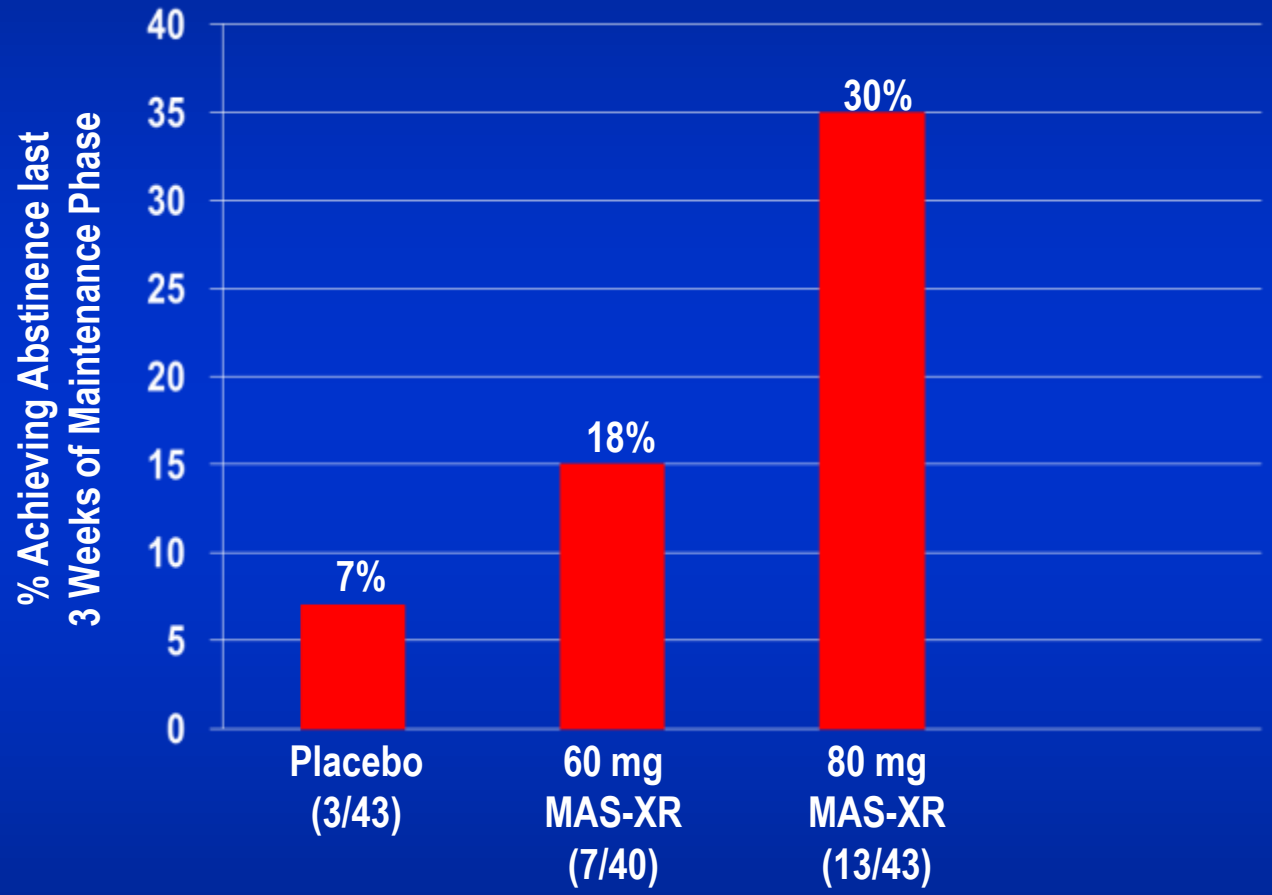


GEE model used to model longitudinal weekly abstinence:

Treatment Group 0_PBO 1_60mg 2_80mg

There was a significant main effect of treatment, with higher abstinence in MAS-XR 80 mg than in PBO (p=0.0002, OR=5.46, CI: 2.25-13.27) and as well as higher abstinence in MAS-XR 60 mg over PBO (p=0.02, OR=2.92, CI: 1.15-7.425). There was also a main effect of study week (p=0.01)

Cocaine Use Outcome

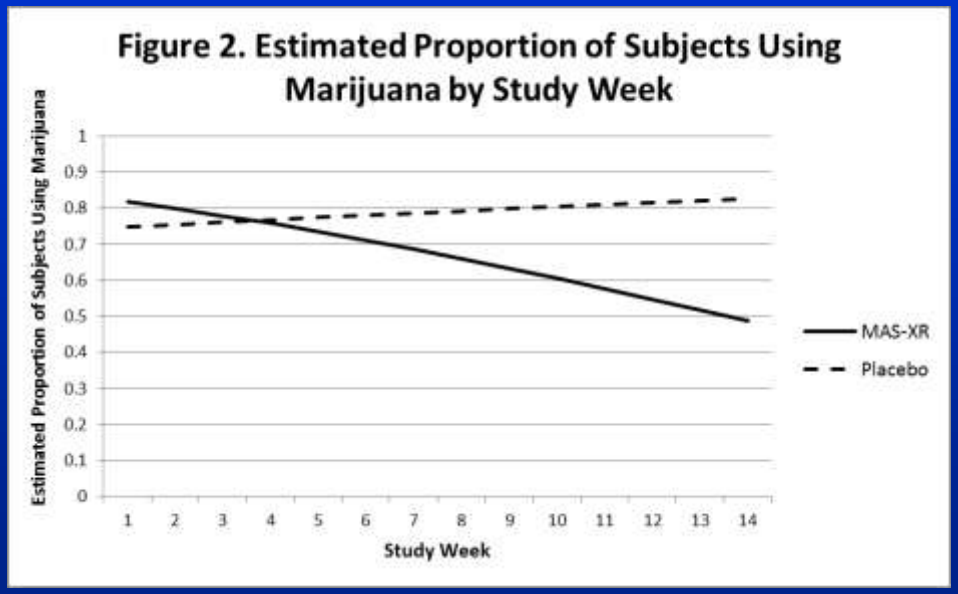


MAS-ER 60 mg vs. placebo (OR=5.85 [CI: 1.04-33.04]; p=0.045)
MAS-ER 80 mg vs. placebo (OR=11.87 [CI: 2.25-62.62]; p=0.004)

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 ($F_{1,658} = 5.39$, $p = 0.0206$), 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)

Assumption

- Active substance abusers will misuse and divert their medications

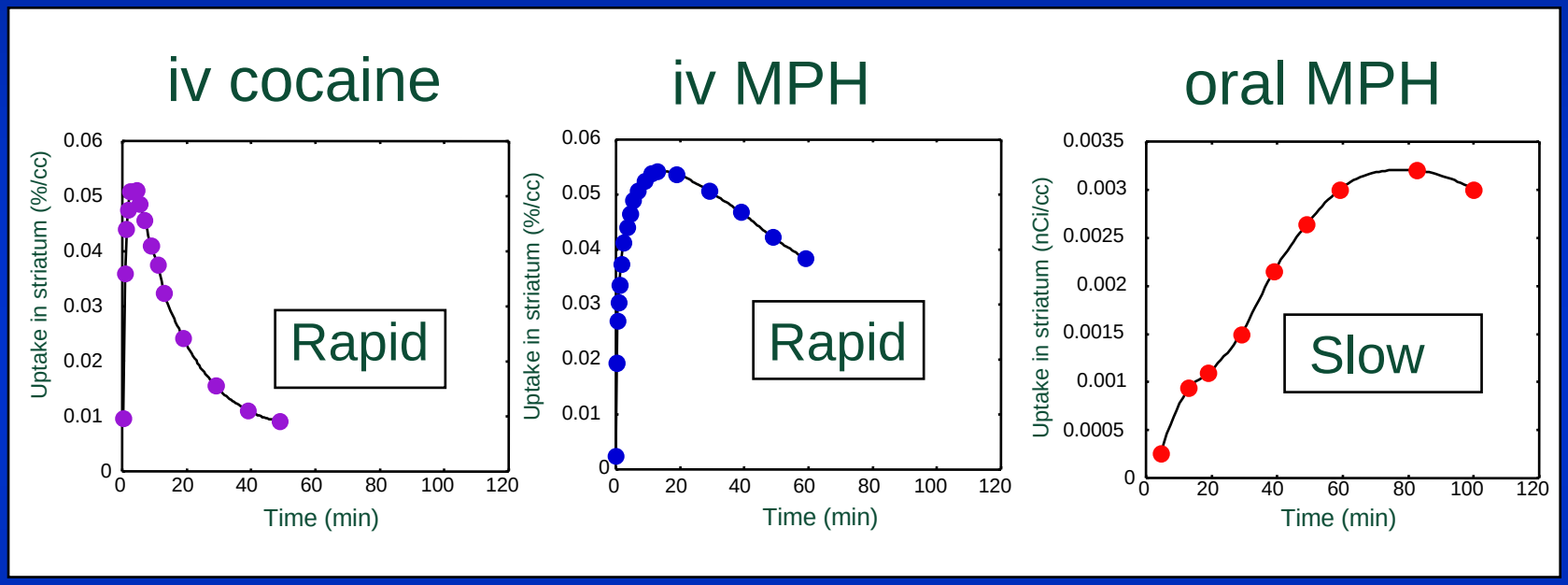
Stimulant Misuse and Diversion

- 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)

Why Risk of Abuse of Prescribed Stimulants in Substance Users seeking treatment is relatively low: Route of administration matters

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



- **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 substantial "high"**

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 lisdexamfetamine or Concerta XL and perhaps Daytrana (methylphenidate patch)

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)

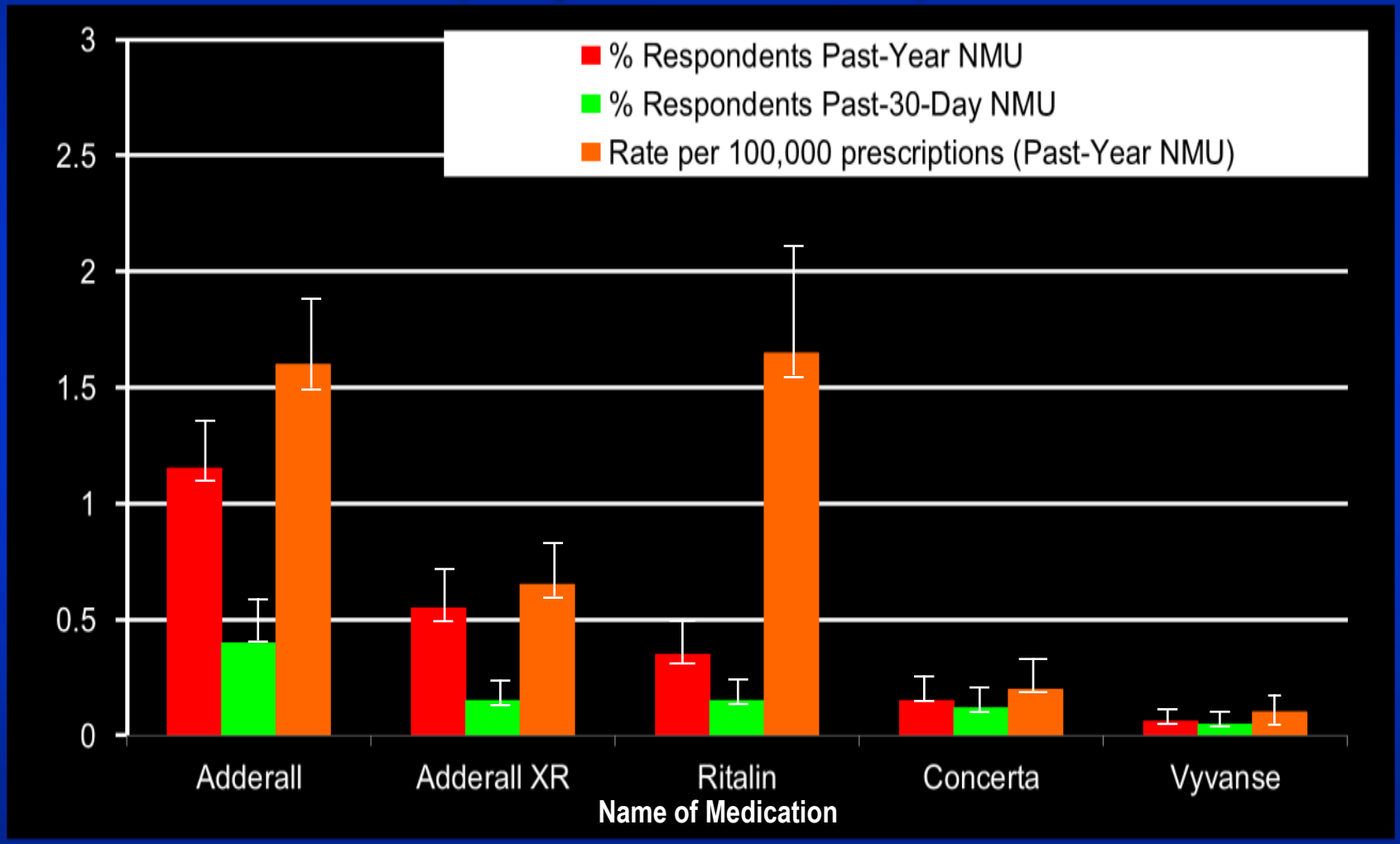


Figure 2. Prevalence of nonmedical use of prescription stimulant compounds: Past year, past 30 days, and past-year rate per 100,000 prescriptions. Note: Vertical bars represent 95% confidence intervals. - NMU = nonmedical use.

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

- **Clinical Experience**
  - Consensus of many clinical investigators that 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.

Medication Abuse Diversion by Treatment Group

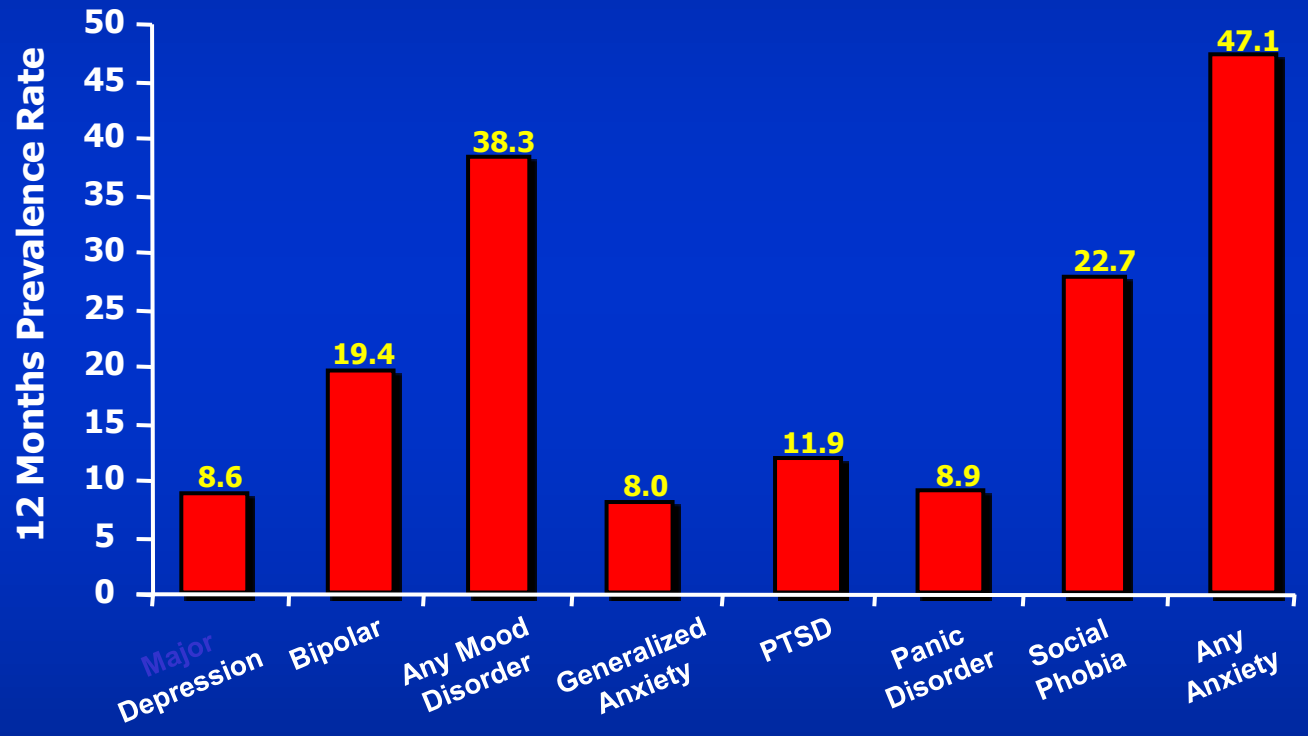
(Winhusen et al. 2010)

Item Scoring Range 1=not at all 10=very much	OROS-MPH (N=144)	Placebo N=141	P value
Medication effective	**6.0 (2.6)**	**4.5 (2.6)**	**P<0.00001**
Like the way medication makes me feel	4.9 (2.4)	4.3 (2.6)	NS
How high do you get on your medication?	2.7 (2.3)	2.1 (1.7)	NS
How depressed do you get on your medication?	2.5 (2.0)	2.0 (1.8)	NS
Crave medication?	1.3 (0.9)	1.4 (1.3)	NS
Crave other drugs?	2.4 (2.5)	2.5 (2.5)	NS
Selling medication to others	3/143 (2.1%)	2/141 (1.4%)	NS
Letting others take their medication	5/143 (3.5%)	2/141 (1.4%)	NS
Taking more than prescribed	6/143 (4.9%)	4/141 (2.8%)	NS
Gotten high on your medication	7/143 (4.9%)	10/141 (7.1%)	NS
Taken medication in a way other than prescribed	3/143 (2.1%)	1/141 (0.7%)	NS
Used drugs or alcohol on days taking study medication	97/143 (67.8%)	102/141 (72.3%)	NS
Reaction to drug/alcohol when taking medication	4/143 (2.8%)	3/141 (2.1%)	NS

Assumptions

- Often there are numerous psychiatric comorbidities making it even harder to effectively treat individuals with ADHD and Substance Use Disorders

Community Sample of Adults with ADHD



Treating Adults With ADHD With Additional Psychiatric Disorders

- Often there are numerous additional psychiatric comorbidities making it even harder to effectively treat individuals with ADHD and Substance Use 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).
- Sometimes patients get more anxious with one stimulant and not another (Dexamphetamine vs. methylphenidate) or less anxious with longer acting preparations or mixed amphetamine salts
- Patients may tolerate atomoxetine better if they have anxiety symptoms and have better relief of anxiety

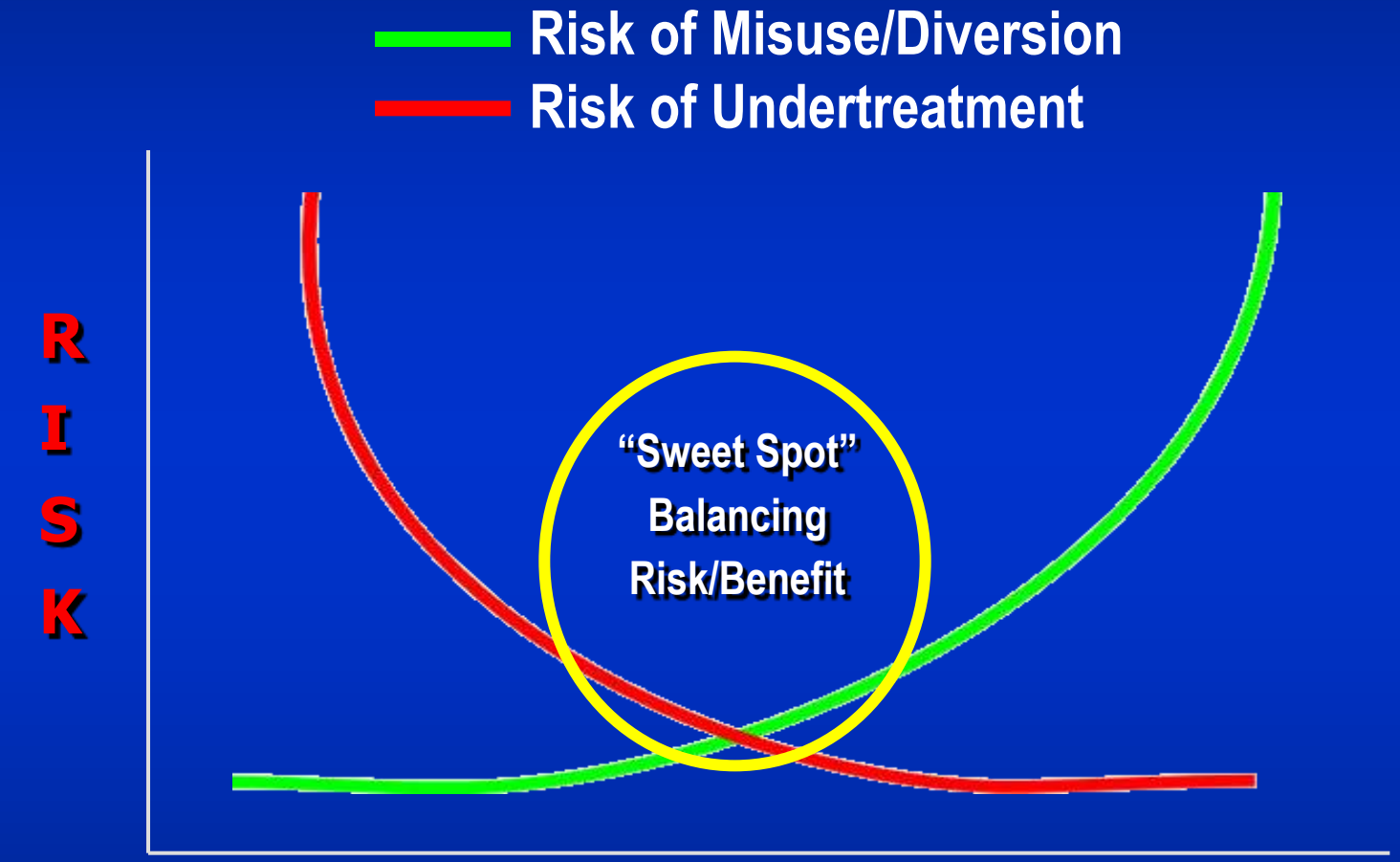
Treating Co-morbidity – Psychosis/ Bipolar Illness

- 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 for 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 Conundrums for the Experienced Clinician

- Escalating dosing of stimulants/running out early
- Managing diversion/misuse risk
- Difficulty determining whether stimulant treatment is yielding a benefit in a patient with co-occurring ADHD and SUD

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



(Courtesy of John Mariani)

Escalating Doses/Running out early

- **First Need to Recognize 'Red flags'**
  - Symptoms of intoxication or symptoms associated with heavier use (agitation, psychosis, SOB, palpitations)
  - Demands for a particular, usually fast acting, medication (amphetamine IR)
  - "Extended-release doesn't work for me"
  - Repeated lost prescriptions
  - Discordant pill count

Escalating Doses/Running out early

- **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 have adequate dose 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
- Look at 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

Clinical Conundrums for the Experienced Clinician

- **Difficulty determining whether stimulant treatment is yielding a benefit in a patient with co-occurring ADHD and SUD**
  - Carry out structured assessments of ADHD symptoms to document improvement.
  - 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
  - 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

Other Treatment Recommendations

- Treatments for ADHD as well as other psychiatric comorbidities include nonpharmacological and pharmacological interventions.
- Nonpharmacological interventions for ADHD encompass a wide-range of interventions including:
  - Behavior therapy
  - Academic intervention
  - family therapy
  - Care coordination have been well studied in children but not adults
  - ADHD Coaches
- First-line treatment for cocaine and cannabis use disorders are psychotherapeutic. Medications are experimental. For SUD, focus on treating withdrawal symptoms or substitution therapies

(Wilens 2004; Riggs 1998; Schubiner 2005; Wilson and Levin 2005; Mariani and Levin 2007; Safren 2006)

Other Treatment Recommendations

- **Non-pharmacologic approaches adjunctively**
  - For SUD: Group and individual psychotherapy (e.g. cognitive-behavioral therapy); Mutual help; Family therapy for adolescents and young adults
  - For ADHD: Cognitive-behavioral therapy, organizational coaches
  - For Major Affective Disorders: Cognitive-behavioral therapy; Interpersonal therapy, Supportive therapy

(Wilens 2004; Riggs 1998; Schubiner 2005; Wilson and Levin 2005; Mariani and Levin 2007; Safren 2006)

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(Wilens 2004; Riggs 1998; Schubiner 2005; Wilson and Levin 2005; Mariani and Levin 2007; Safren 2006)

Conclusions: What Can We Say About Common Assumptions?

- Standard treatments for ADHD do not work in active substance users: Not true
- Even if treatments work for ADHD, they do not impact on the substance use disorder: Depends
- Active substance abusers will misuse and divert their medications: Some individuals will, 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: Yes, but can be done
- Clinical Conundrums can be managed: Escalation of use. Misuse/Diversion, Assessing benefit when multiple psychiatric disorders present

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ANY QUESTIONS?

- THANK YOU!!!