



ADHD and Substance Use Disorders (SUD)

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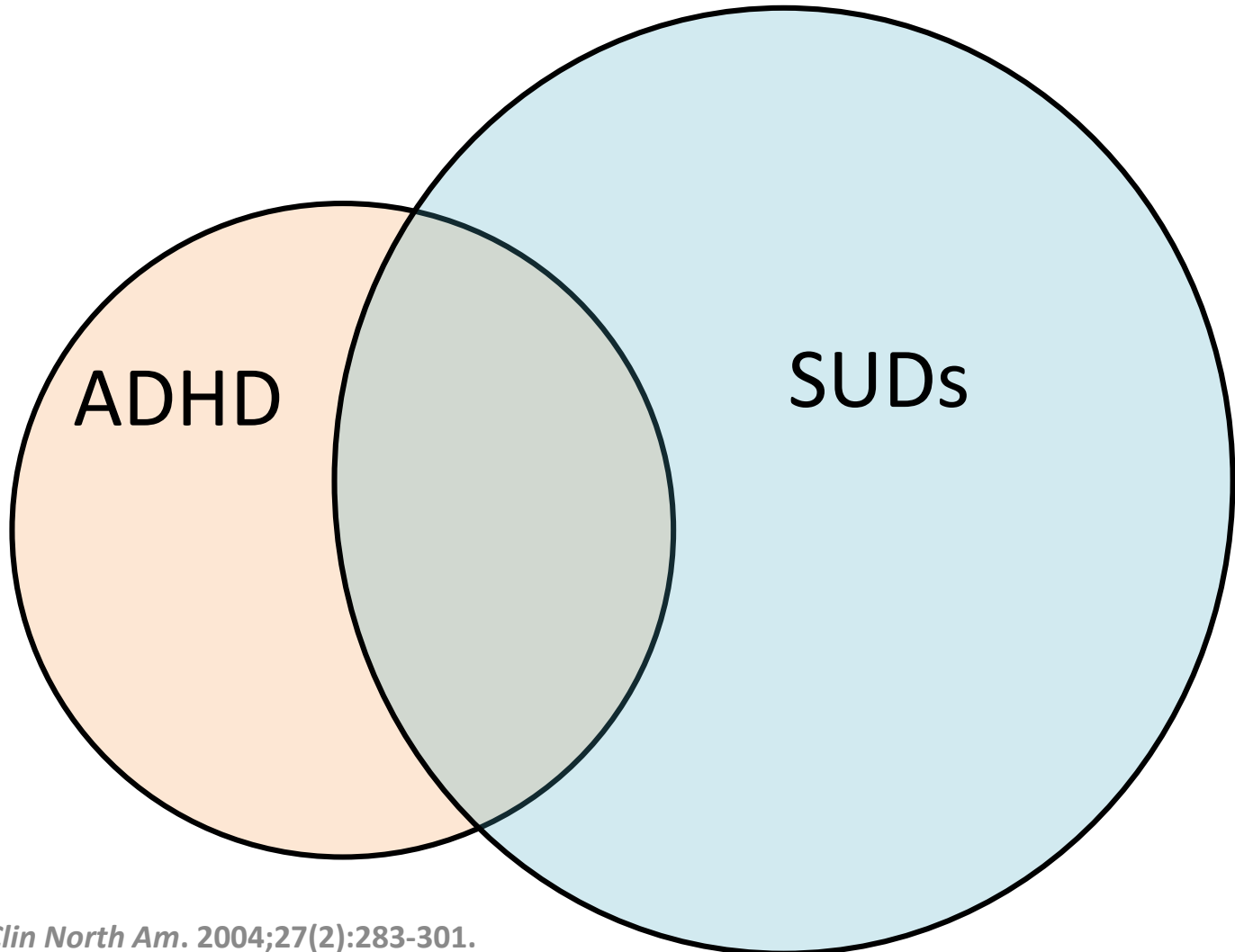
Faculty Disclosure

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- Kempharm, Otsuka, NIH (NIDA), Ironshore, Vallon
- Licensing agreement with Ironshore (Before School Functioning Questionnaire)
- Clinical care: MGH, Bay Cove Human Services, Gavin/Phoenix, National Football League (ERM Associates), Major/Minor League Baseball
- (Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford); ADHD Across the Lifespan (Cambridge) , MGH Comprehensive Clinical Psychiatry (Elsevier), MGH Psychopharmacology and Neurotherapeutics (Elsevier)

Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (e.g., substance use disorders)

Overlap between ADHD and SUDs

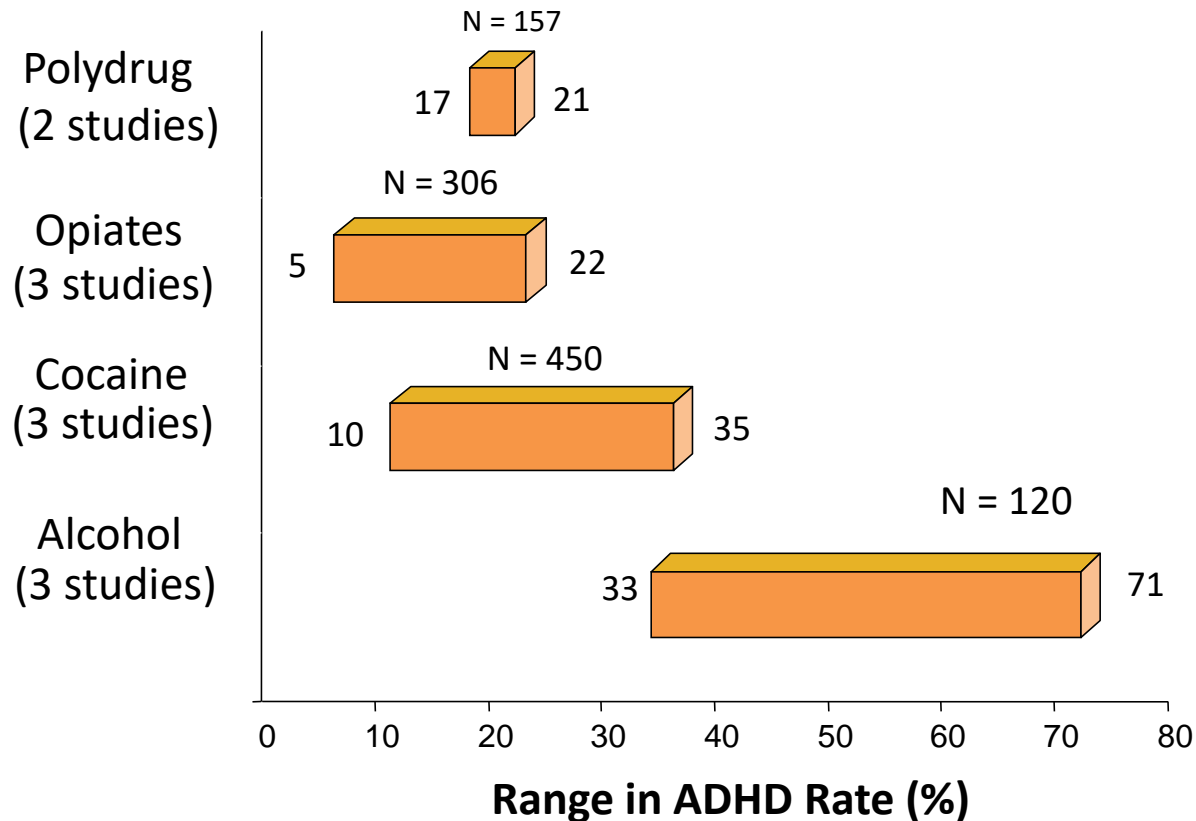


Wilens TE. *Psychiatr Clin North Am.* 2004;27(2):283-301.

van Emmerik-van Oortmerssen K, et al. *Drug Alcohol Depend.* 2012;122(1-2):11-19.

SUD is a Risk Factor for ADHD:

Illustrative Overlap of ADHD in Adults with SUD



Overall, 23% of adults with SUD have ADHD (N = 29 studies)*

Wilens TE. *Psychiatr Clin North Am.* 2004;27(2):283-301.

*van Emmerik-van Oortmerssen K, et al. *Drug Alcohol Depend.* 2012;122(1-2):11-19.

Childhood ADHD is Related to Future Cigarette and SUD

Likelihood (OR) to Develop Cigarette Smoking

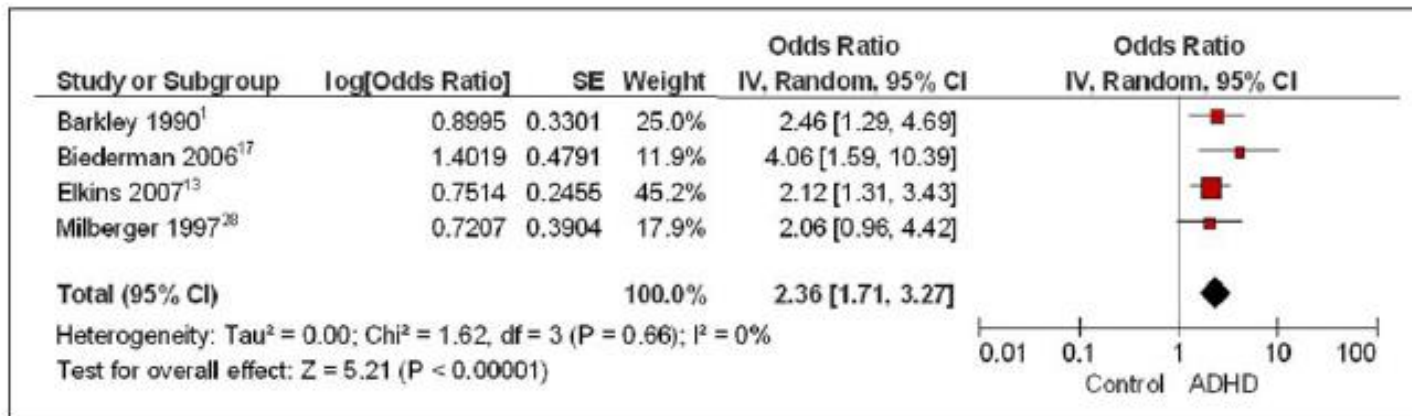


FIGURE 6 Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and nicotine use. Note: Results from a meta-analysis comparing ADHD versus control subjects for nicotine use. CI = confidence interval.

Likelihood (OR) to Develop SUD

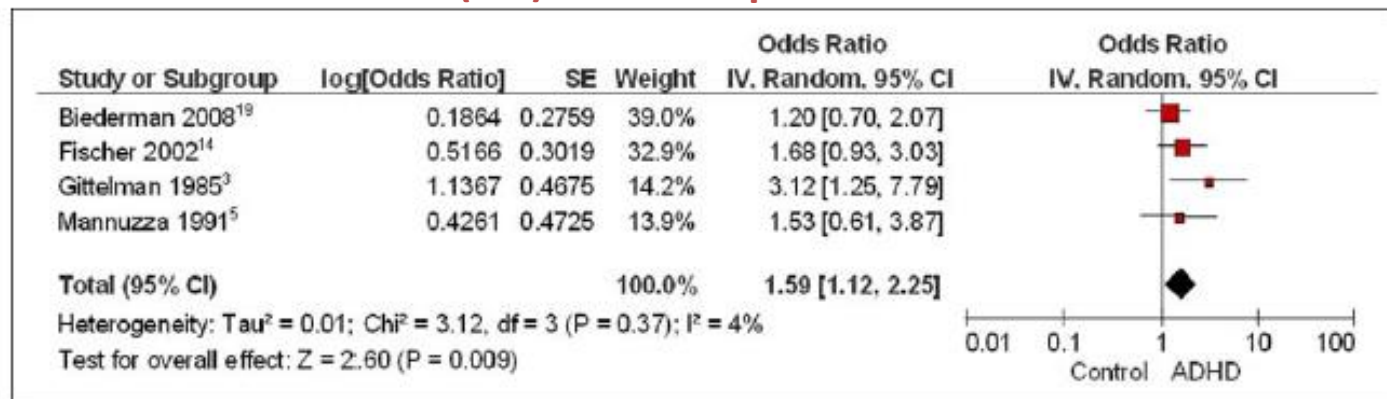
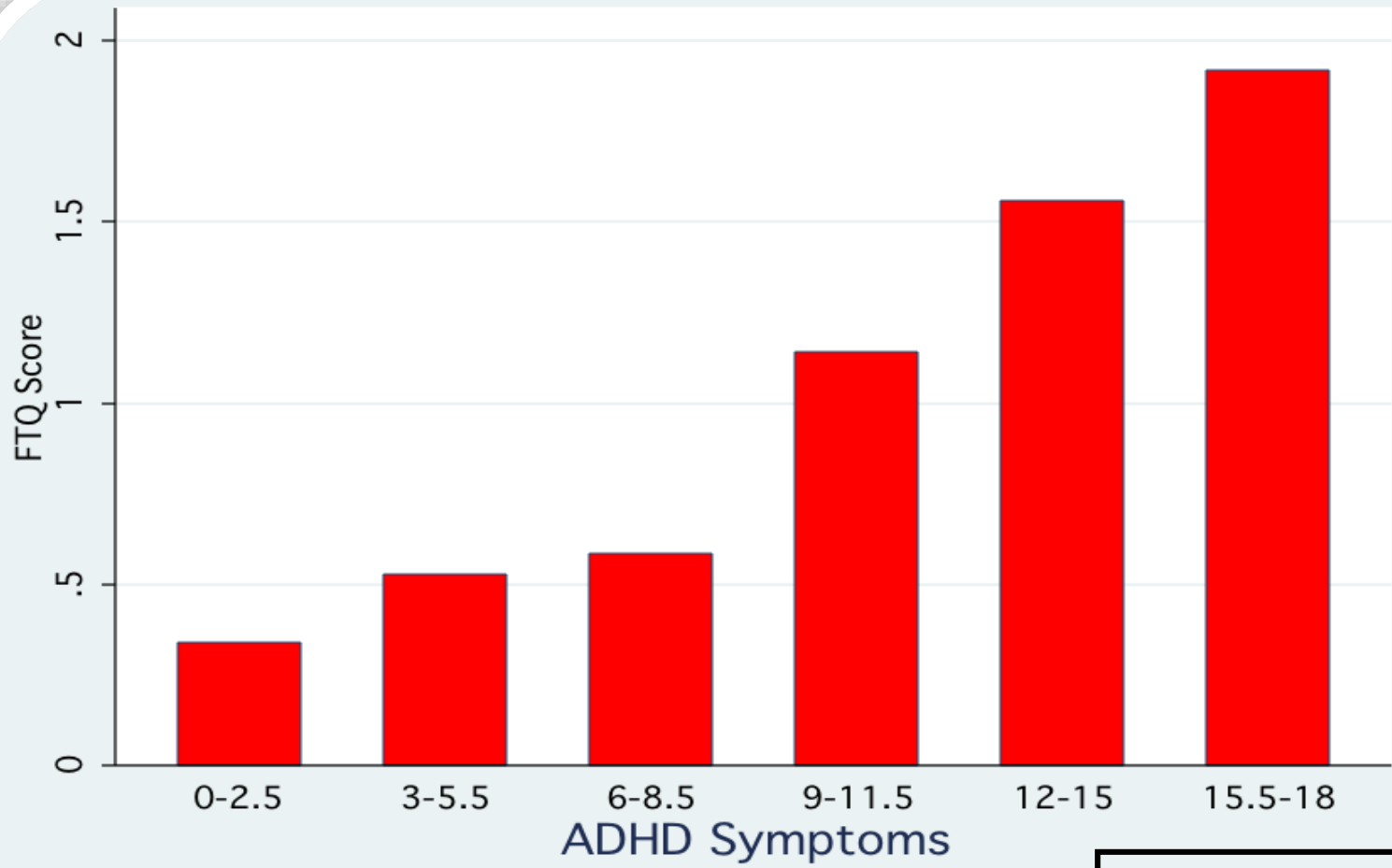


FIGURE 4 Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and psychoactive substance use disorder. Note: Results from a meta-analysis comparing ADHD versus control subjects for psychoactive substance use disorder. CI = confidence interval.

ADHD Symptoms are Directly Related to Higher Smoking Scores



$t = 5.00, P < .001$





FTQ = Fagerström Tolerance Questionnaire.

Wilens TE, et al. *J Pediatr.* 2008;153(3):414-419.

A More Complicated Course of SUD is Associated with ADHD

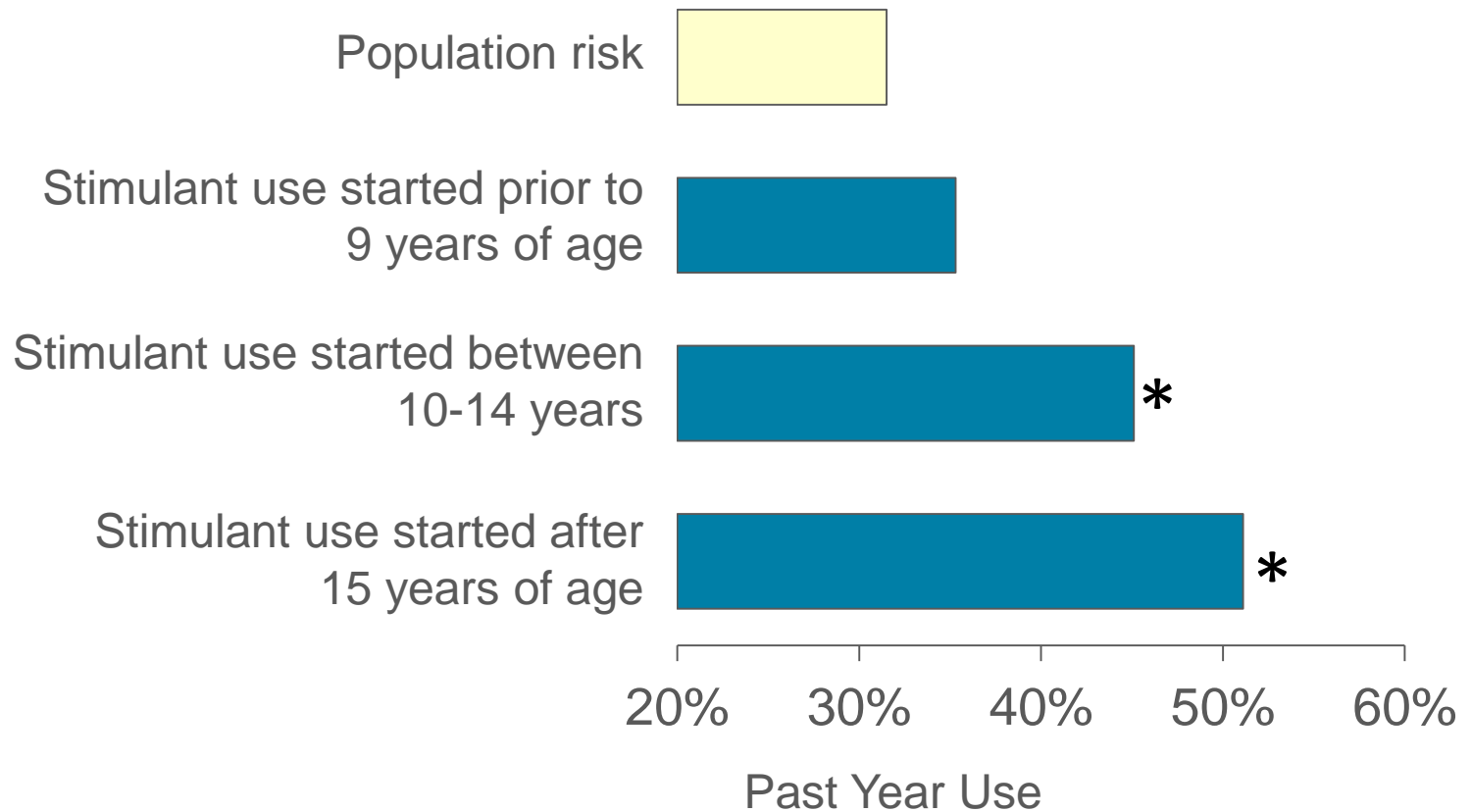
- **More severe SUD**
- **Higher rates of other psychiatric comorbidities (eg, conduct/antisocial disorders)**
- **Less remission from SUD**
- **Longer course of SUD**
- **Lower retention in SUD treatment**

Long-Term Studies of ADHD: Stimulant Treated vs Untreated and Subsequent Substance Use Disorders

Study	Country	Total: N	ADHD: N	Age	Main Findings Tx vs UnTx
Quinn et al. 2017	USA	146,000,000	2,993,887	15–42 yrs	Within group 
Sundquist et al. 2015	Sweden	551,164	9,424	Mean 15 yrs	Between group 
Chang et al. 2014	Sweden		38,753	8–46 yrs	Between group 
Steinhausen et al. 2014	Denmark		20,742	11–20 yrs	Between & Within groups 

(from Boland et al, 2019 Submitted)

Early ADHD Treatment Reduces Marijuana Use



10 Cohorts of high school seniors 2005 to 2014 (N = 40,358; ~10% with ADHD).

* $P < .001$ vs controls.

McCabe SE, et al. *J Am Acad Child Adolesc Psychiatry*. 2016;55(6):479-486.



Diagnostic Dilemmas in ADHD and SUD

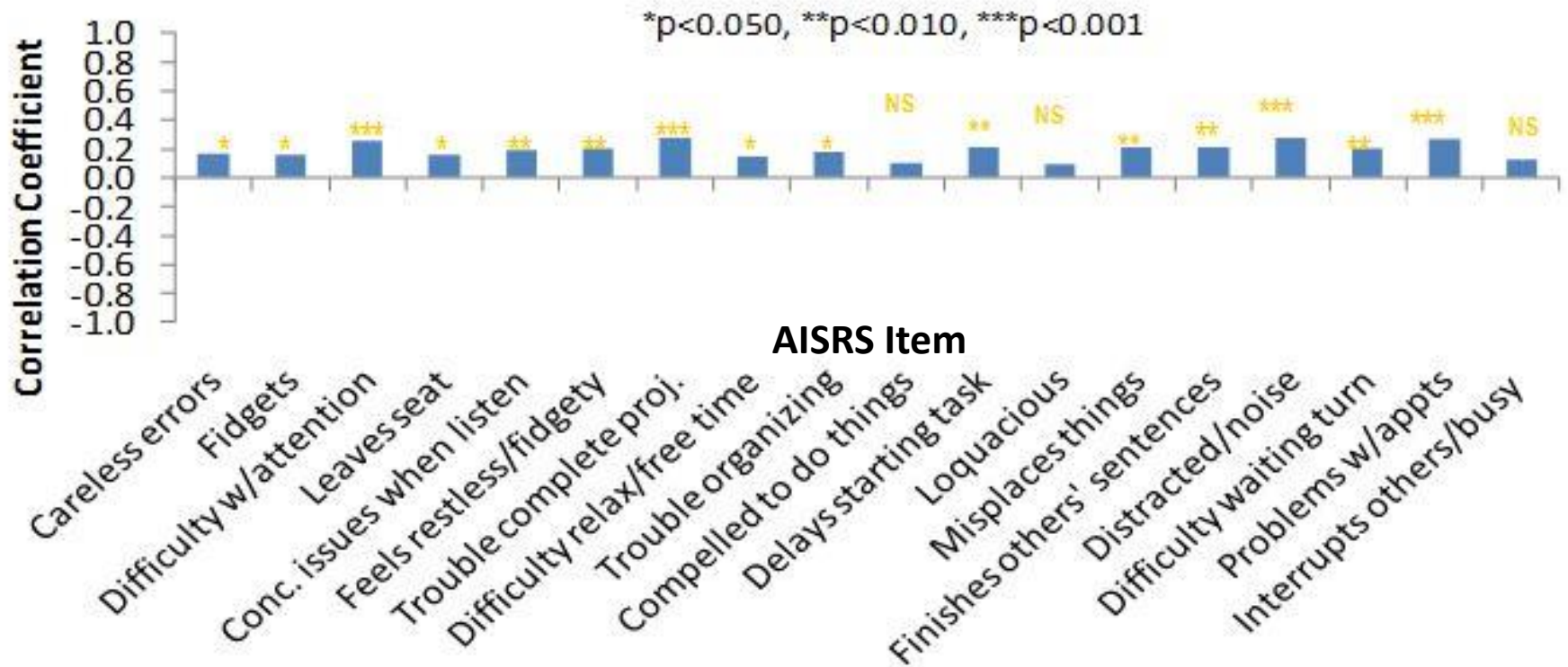
- Overlap symptoms of SUD in ADHD
 - Intoxication or withdrawal
 - Neuropsychological deficits (transient/permanent)
 - SUD “traits” misinterpreted as ADHD (eg, impulsive traits/risk-taking, harm avoidance)
- Other comorbidity (eg, anxiety, disruptive disorders)
- Reliability of retrospective report
- Subthreshold ADHD vs full ADHD
 - Age-of-onset criteria (NOS)
 - Effected domains, inadequate number of symptoms
- Concerns of drug-seeking behavior/rationalization
- Use of rating scales for ADHD helpful (e.g., ASRS)

ASRS = Adult ADHD Self-Report Scale; NOS = not otherwise specified.

Levin FR, et al. *Drug Alcohol Depend.* 1998;52(1):15-25. Riggs PD. *Sci Pract Perspect.* 2003;2(1):18-29. Kaminer Y, et al. *Am J Addict.* 1999;8(2):114-119. Wilens TE, et al. *Curr Opin Psychiatry.* 2011;24(4):280-285. Faraone SV, et al. *Am J Psychiatry.* 2006;163(10):1720-1729. Faraone SV, et al. *Am J Addict.* 2007;16 Suppl 1:24-32.

Current Heavy Alcohol Use Worsens ADHD Symptoms

AISRS Item Scores vs Presence or Absence of Alcohol Abuse* in Placebo Group



*Consumed ≥ 4 alcoholic drinks/day for women, or ≥ 5 drinks/day for men, within 24 hours (cumulative; drink = 1.5 oz liquor, 5 oz wine, 12 oz beer), or ≥ 3 drinks/day for ≥ 1 week (ie, ≥ 7 consecutive days), during the double-blind treatment period (visit 3–14 [baseline to week 12]). *P* values were adjusted for multiple comparisons.

Appts = appointments; Conc = concentration; NS = not statistically significant.

Marijuana (MJ) and ADHD

- **Most common “drug” used/misused in ADHD**
- **Second most common comorbidity in cannabis use disorder**
- **Associated with neuropsychological impairment**
 - Acute effects
 - Chronic - persistent executive dysfunction if initiated early

Wilens et al., J Am Acad Child Adoles Psych: 2011; Am J Addict 2010: 16:14-23

Cooper et al. Eur Neuropsychopharm 2017: 27:795-808

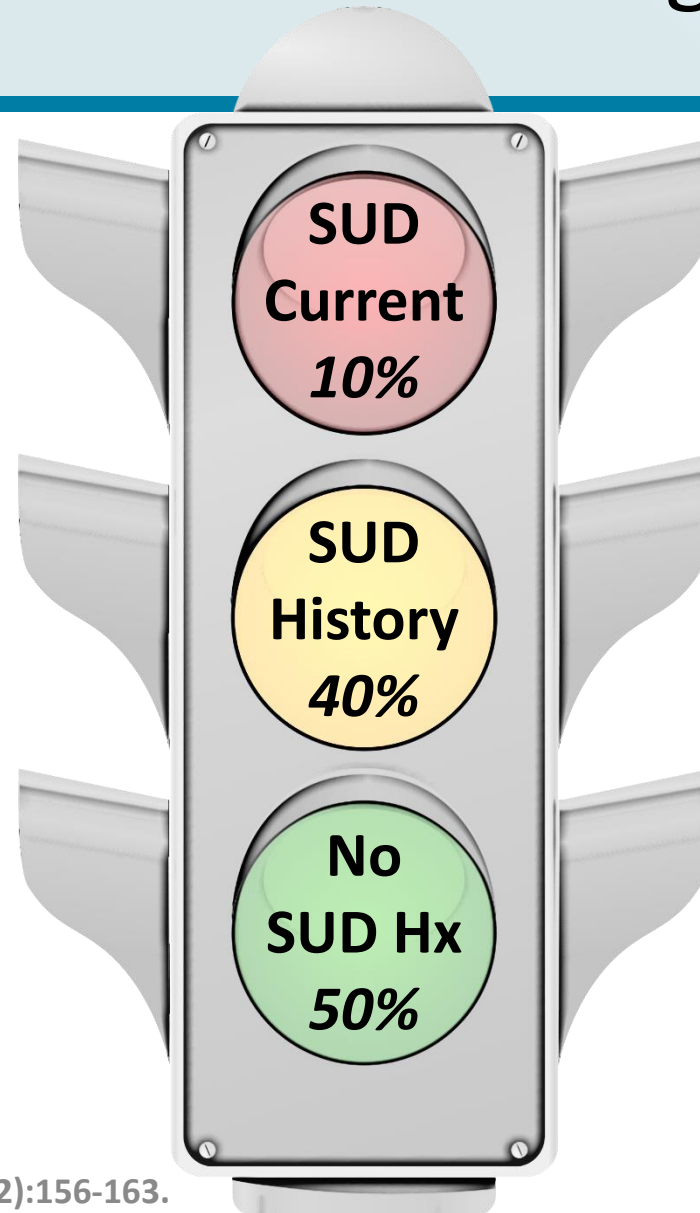
Marijuana (MJ) and ADHD

- **No evidence of more self medication versus non-ADHD**
- **Treatment of ADHD with MJ**
 - Largely case reports
 - RCT of 30 adults with ADHD. Use of oromucosal THC:CBD
 - **Primary outcome: No cognitive or activity improvement;**
 - **Secondary outcomes: Negative to trends to improvement**

Wilens et al., J Am Acad Child Adoles Psych: 2011; Am J Addict 2010: 16:14-23

Cooper et al. Eur Neuropsychopharm 2017: 27:795-808

SUD in ADHD Adults Presenting for Treatment



**ADHD
ADULTS**

The Complicated Relationship Between Attention Deficit/Hyperactivity Disorder and Substance Use Disorders

Courtney A. Zulauf¹, Susan E. Sprich², Steven A. Safren³ and Timothy E. Wilens^{1, 4, 5} ✉

Abstract

Adolescents and young adults with substance use disorders (SUD) and attention deficit/hyperactivity disorder (ADHD) are increasingly presenting in clinical practice. The overlap and role of treatment for these co-occurring disorders remains unclear. A review of the literature was conducted to highlight and update

recent research on the high risk for SUD in ADHD across different populations and treatment approaches. Substance

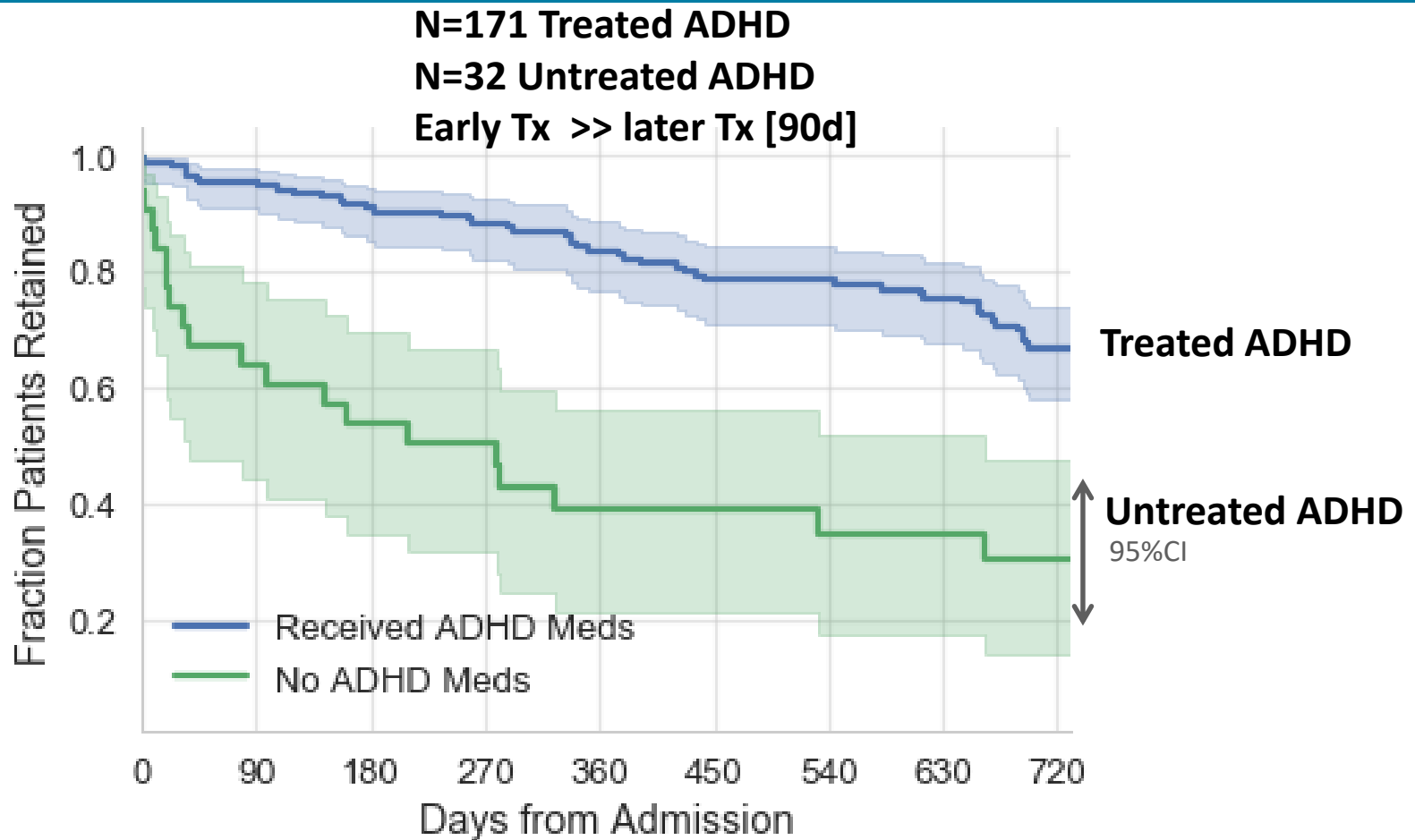
“...Structured therapies may be effective in treating adolescents and young adults with ADHD and SUD...”

abusing individuals with ADHD. Structured therapies may be effective in treating adolescents and young adults with ADHD and SUD. Further controlled trials evaluating the sequence and effect of structured psychotherapies and/or ADHD pharmacotherapy on SUD relapse in these groups are warranted.

Keywords Adolescence – Substance use disorders – Attention deficit/hyperactivity disorder – Stimulants comorbidity – Cognitive-behavioral therapy

This article is part of the Topical Collection on *Child and Adolescent Disorders*

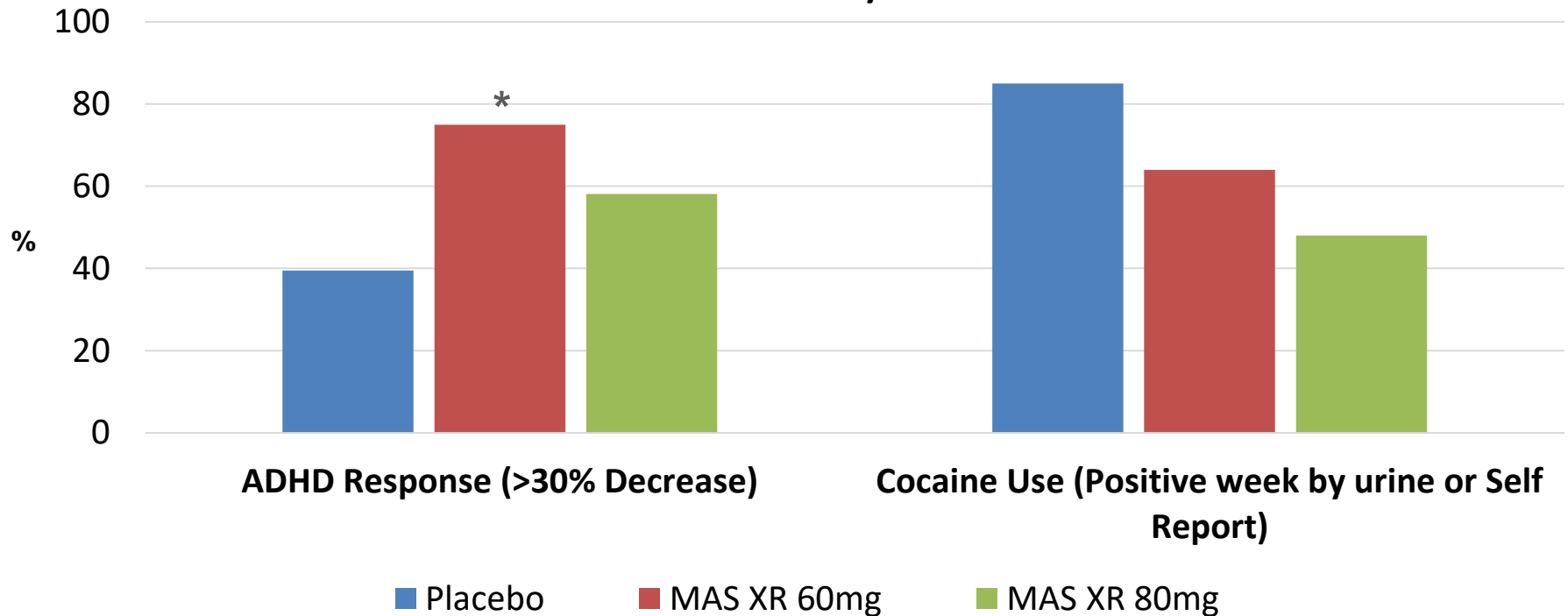
MGH Study: Treatment of ADHD Improves Retention in Treatment



(Kast K, Rao V, Wilens T. J Clin Psych: 2021 In press)

Higher Dose MAS XR is Helpful in ADHD and Cocaine Use Disorder

13-week Randomized Controlled Trial
Diagnosis: Cocaine Use Disorder and ADHD
Treatment: CBT +/- MAS XR



N = 126. * $P < .05$.

CBT = cognitive-behavioral therapy; MAS = mixed amphetamine salts.

Levin FR, et al. *JAMA Psychiatry*. 2015;72(6):593-602.

Methylphenidate for ADHD and Drug Relapse in Criminal Offenders with Substance Dependence:

A 24-Week Randomized Placebo-Controlled Trial

Sample: 54 incarcerated males (mean age = 42 years)

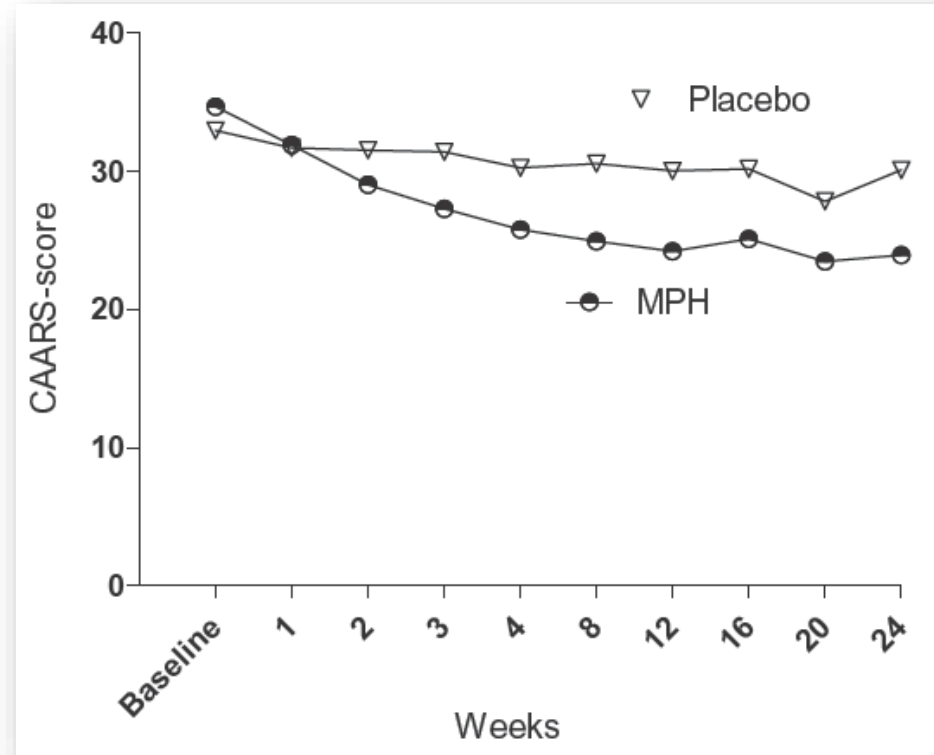
Dose: Start dose 18 mg MPH/placebo titrated over a period of 19 days; mean dose of 108 mg/day

CBT: Individual CBT once weekly for 12 weeks

Measurements: Change in self-reported ADHD symptoms, urine toxicology, retention to treatment

Findings: MPH treated group showed reduced ADHD symptoms ($P=.011$), significantly higher proportion negative urine screens ($P=.047$), and better retention ($P=.032$)

Change in Self-Rated ADHD Symptoms
(95% CI: -13.78 to -1.91, $P=0.011$)



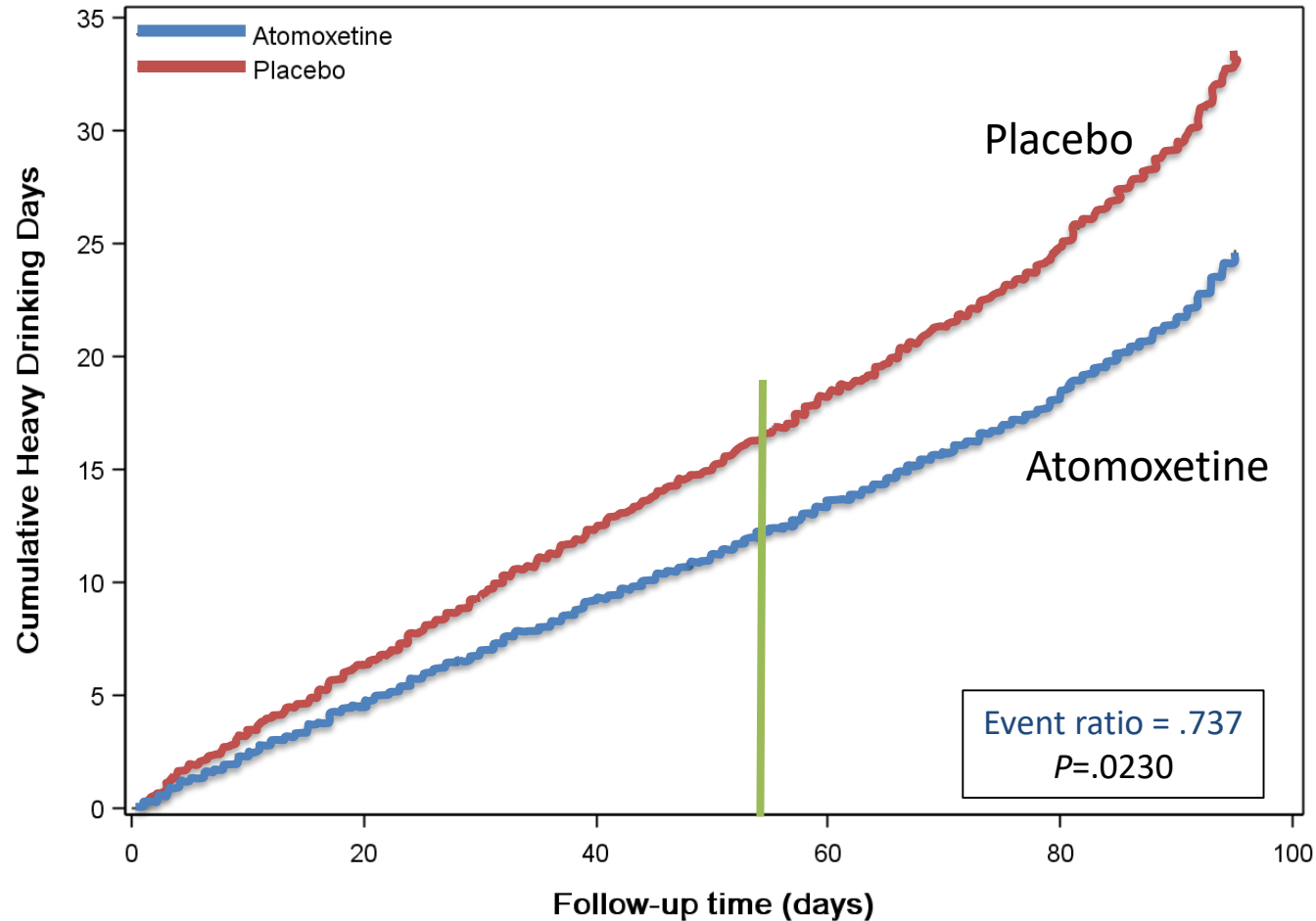
Atomoxetine Improves Outcome in Recently Abstinent Adults

12-week placebo-controlled study
N=147 subjects
Abstinent from 4–30 days

Findings: (ATX vs placebo)

- Improved ADHD Scores
- No differences in relapse rate
- Improved OCD scores
- Improved heavy drinking (shown)

FU study: Few side effects with alcohol



An event ratio of .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 between groups first occurred at day 55.

Wilens TE, et al. *Drug Alcohol Depend.* 2008;96(1-2):145-154. Adler L, et al. *Am J Addict.* 2009;18(5):393-401, www.mghcme.org

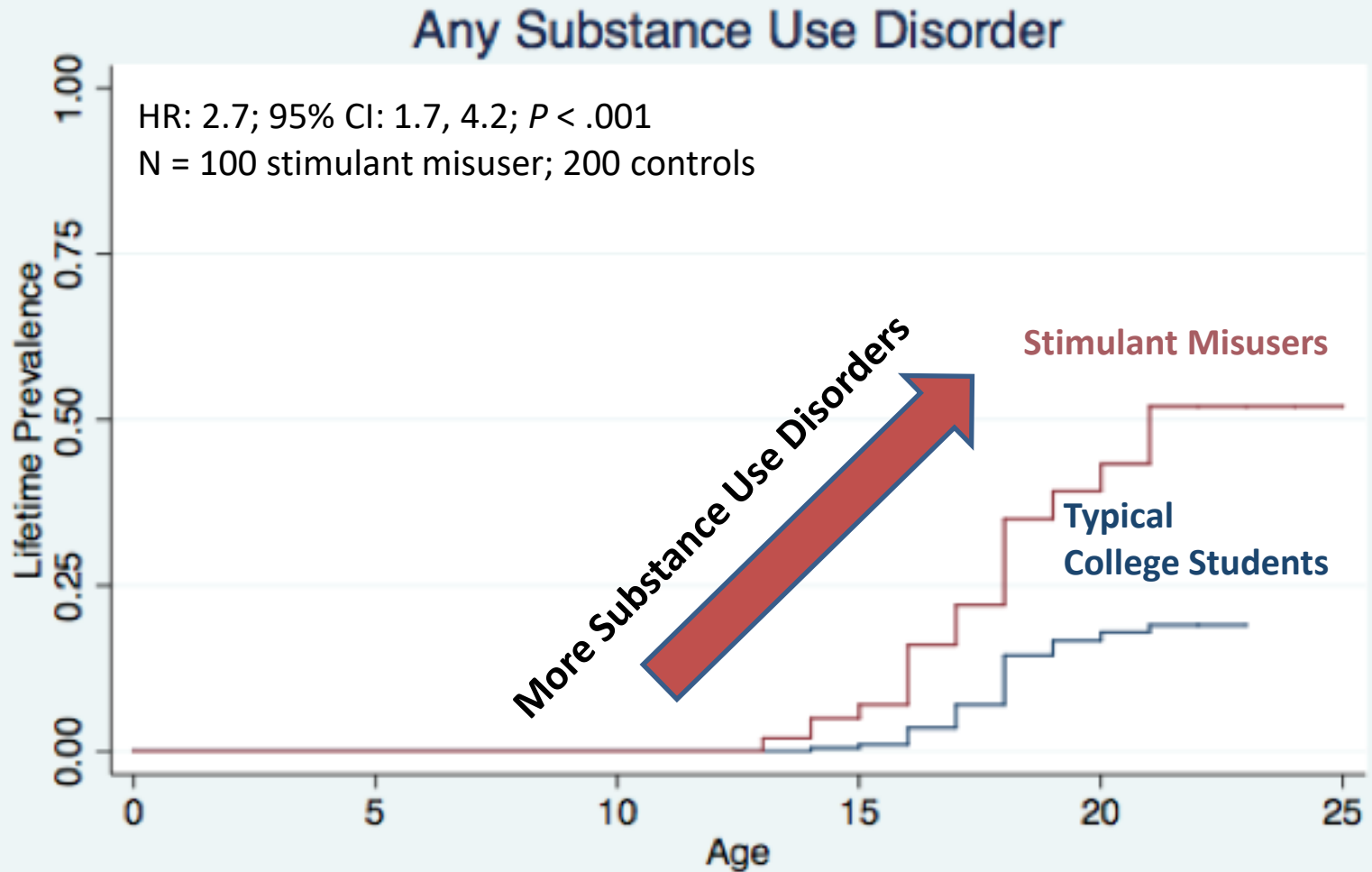
Stimulant Misuse and Diversion

- N > 100 studies; mostly survey studies in college students (80%)
- 10% to 20% prevalence of nonmedical use of stimulants
- 65% to 85% of stimulants diverted from “friends”
 - Majority not “scamming” local doctors
 - Not seen as potentially dangerous
- Motivation typically for concentration/ alertness > getting “high”
- Appears to be occurring in SUD during academic decline
- High rates of full or subthreshold stimulant use disorder in misusers
- High rates of ADHD and neuropsychological dysfunction in stimulant misusers
- More misuse of immediate- vs extended-release stimulant preparations

McCabe SE, et al. *Addiction*. 2005;100(1):96-106. Arria AM, et al. *Subst Abus*. 2008;29(4):19-38. Wilens TE, et al. *J Am Acad Child Adolesc Psychiatry*. 2006;45(4):408-414. Wilens TE, et al. *J Am Acad Child Adolesc Psychiatry*. *J Am Acad Child Adolesc Psychiatry*. 2008;47(1):21-31. Wilens TE, et al. *J Clin Psychiatry*. 2016;77(7):940-947. : Faraone et al. *J Am Acad Child Adoles Psych*, 2019; Wilens et al., *J Attention Disorders* 2020. .

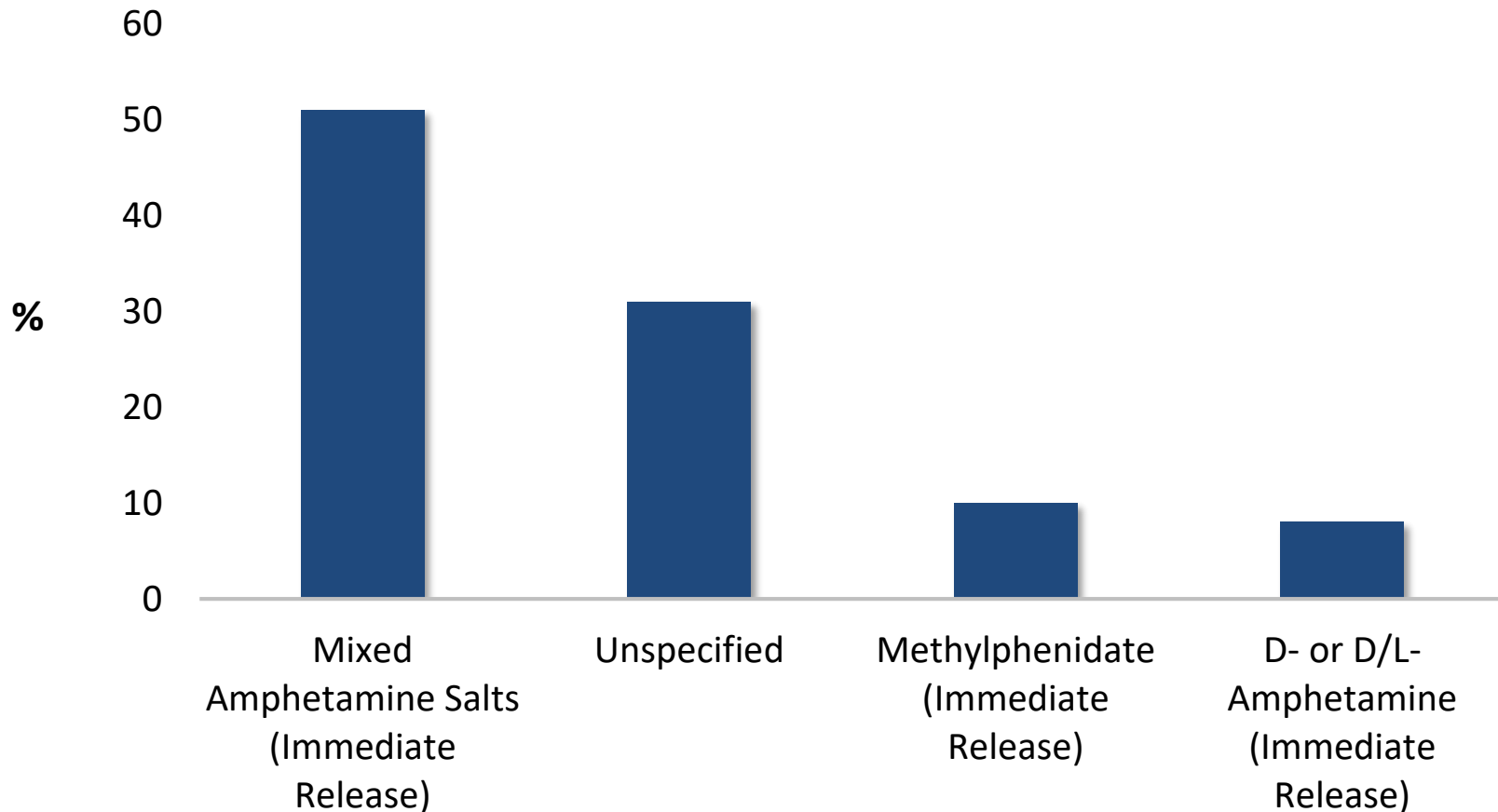


College Stimulant Misusers Have High Rates of SUD

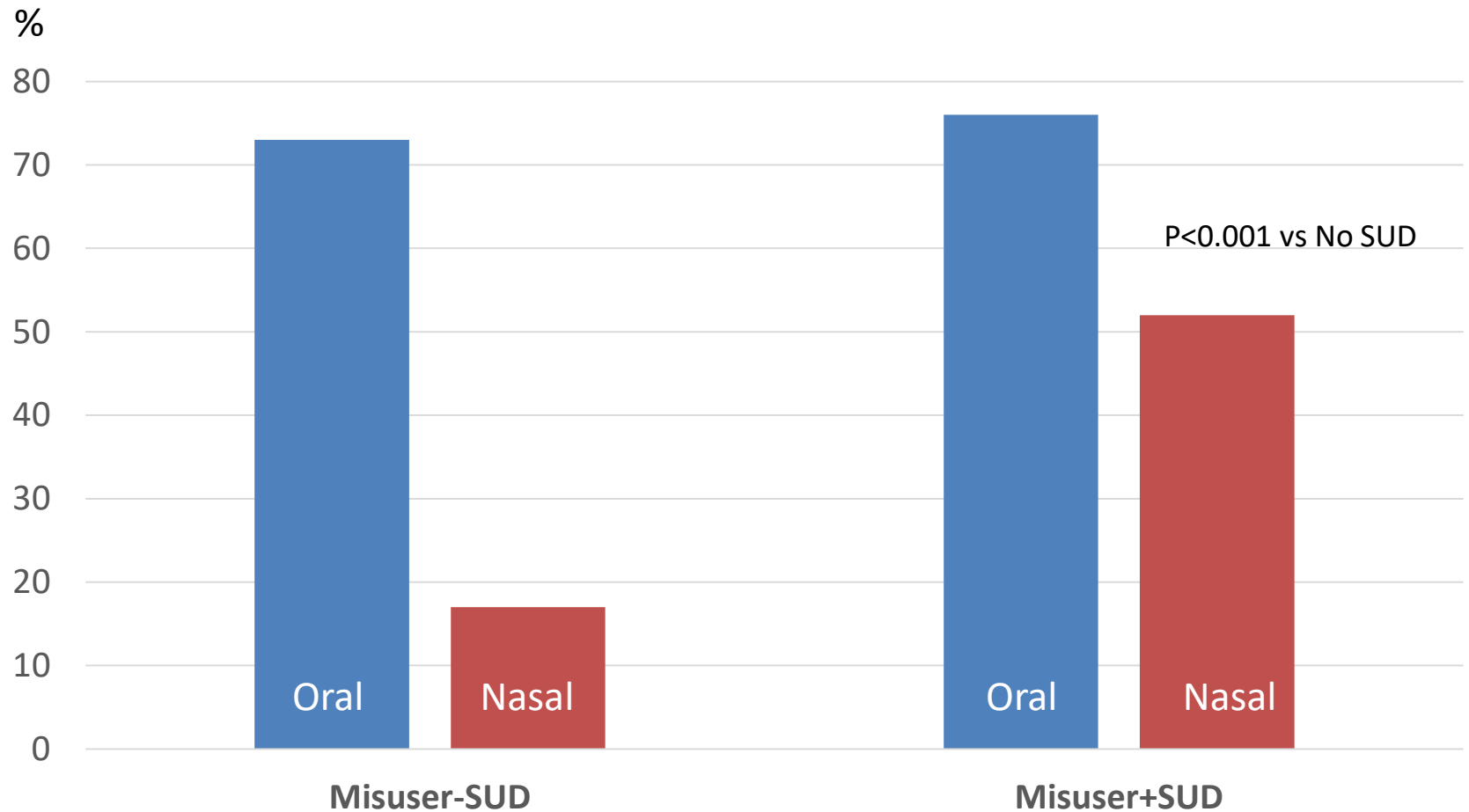


Immediate-Release Stimulants are Preferred by College Students Who Misuse Prescription Stimulants

(n = 39; ~40% have a stimulant use disorder)



Intranasal Misuse of Stimulants is Linked to SUD in College Students (N=100)



Wilens et al. J Atten Disorders, 2020,

Strategies for ADHD and SUD

- In context to SUD, ADHD treatment should be considered
 - If misuse or less severe SUD, treat ADHD concomitantly
 - More severe SUD --> address SUD
 - If unable to address or recalcitrant SUD ->use CBT, nonstimulants, extended-release stimulants (may need higher dose), stay tuned for lower abuse liable stimulants

Wilens and Morrison, ADHD & SUD In *ADHD in Children and Adults*, Cambridge Press, 2015

Kaminski and Wilens, Overlap of ADHD and SUD, in Textbook of SUD, 2019 in press

Impact on Practice

- Since ADHD is a risk factor for cigarette smoking and SUD, teenagers and young adults with ADHD should be queried for both potential problems
- ADHD should be considered in adolescents and adults who smoke cigarettes and/or have SUD
- Treating ADHD helps protect against the onset of cigarette smoking, SUD, and SUD-related criminality
- Strategies exist for management of substance use and use disorder in ADHD
- Since stimulants can be misused, consider extended-release preparations in high risk groups