MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

ADHD & Substance Use Disorders

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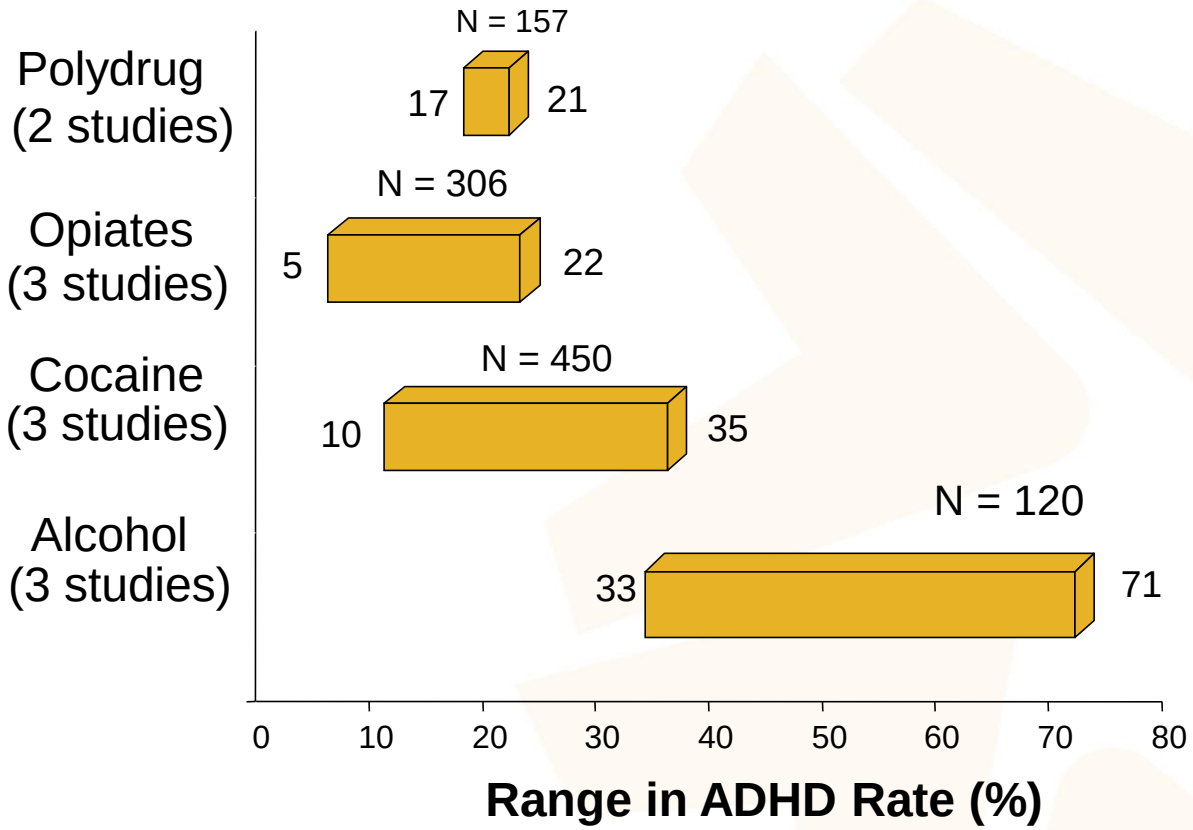
Faculty Disclosure

. Timothy Wilens, M.D. has served as a consultant, or has received grant support from the following

- **Arbor, 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 (eg, substance use disorders)**

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 SUD

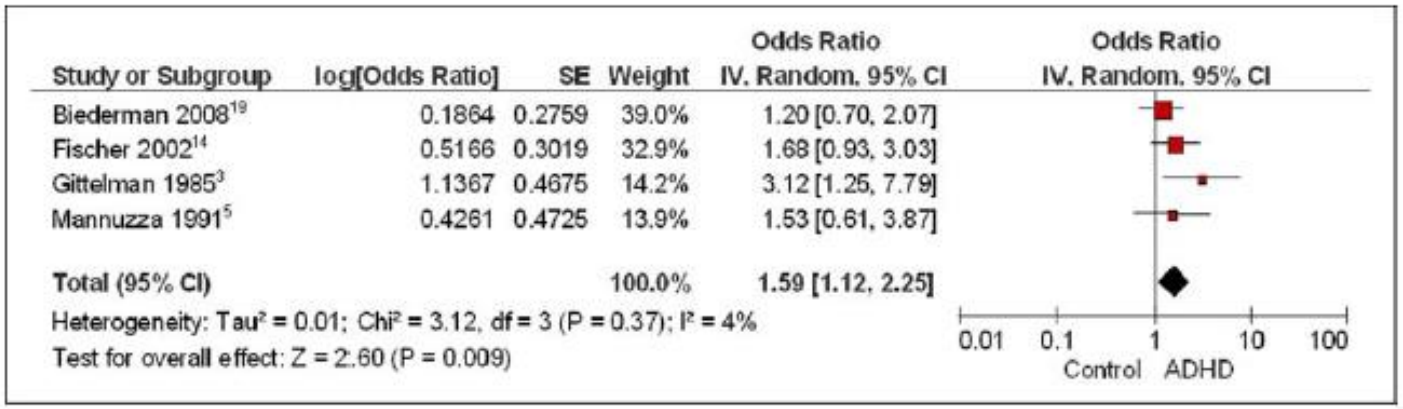


FIGURE 4 Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and psychoactive substance use disorder. Note: Results from a meta-analysis comparing ADHD versus control subjects for psychoactive substance use disorder. CI = confidence interval.

Likelihood (OR) to Develop Cigarette Smoking

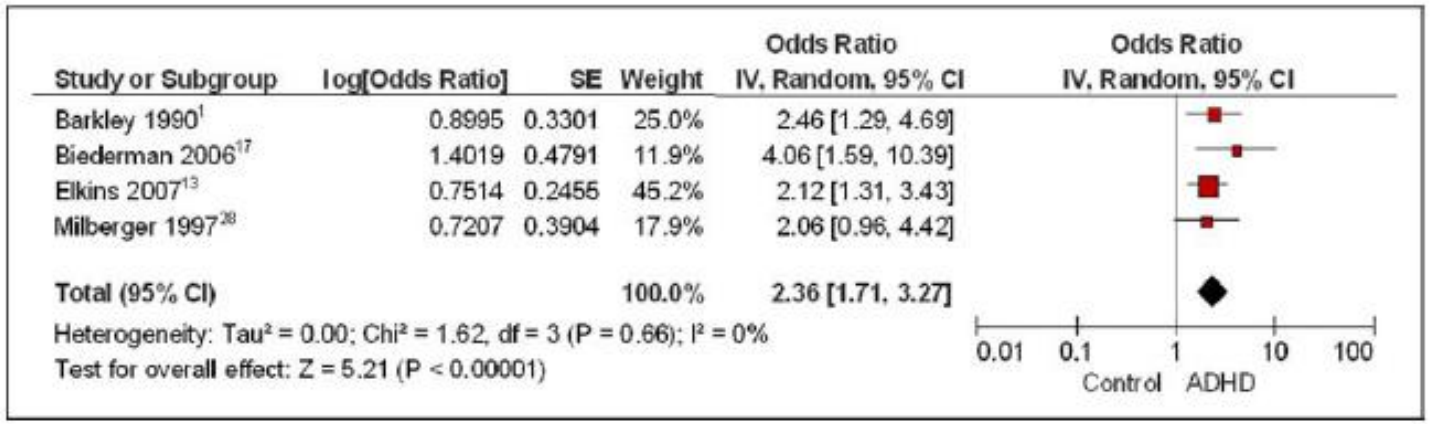


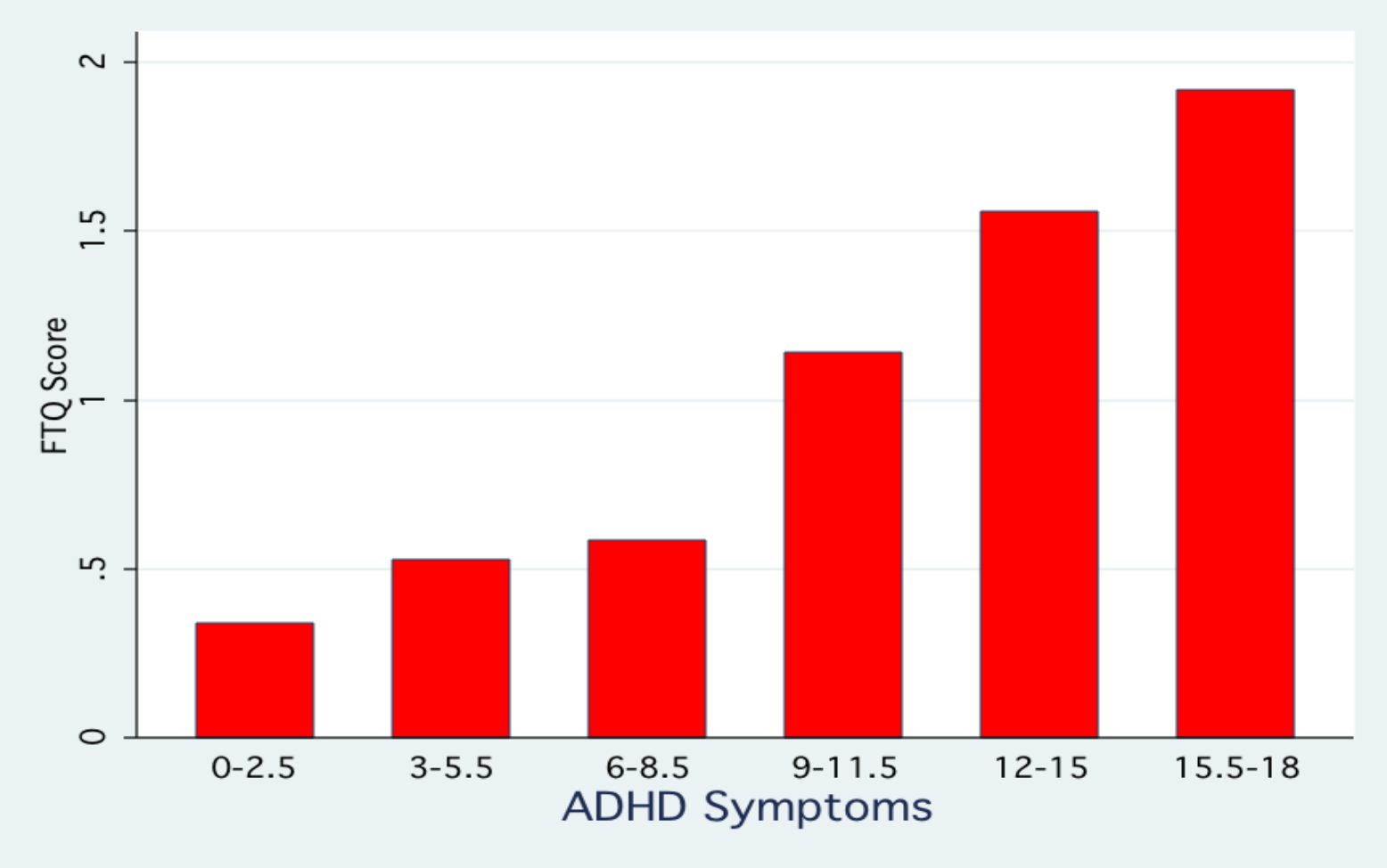
FIGURE 6 Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and nicotine use. Note: Results from a meta-analysis comparing ADHD versus control subjects for nicotine use. CI = confidence interval.

Conduct disorder and severe mood dysregulation increases SUD risk in ADHD.

OR = odds ratio.

Charach A, et al. *J Am Acad Child Adolesc Psychiatry*. 2011;50(1):9-21.

ADHD Symptoms are Directly Related to Higher Smoking Scores



FTQ = Fagerström Tolerance Questionnaire.

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

t = 5.00, *P* < .001

A More Complicated Course of SUD is Associated with ADHD

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

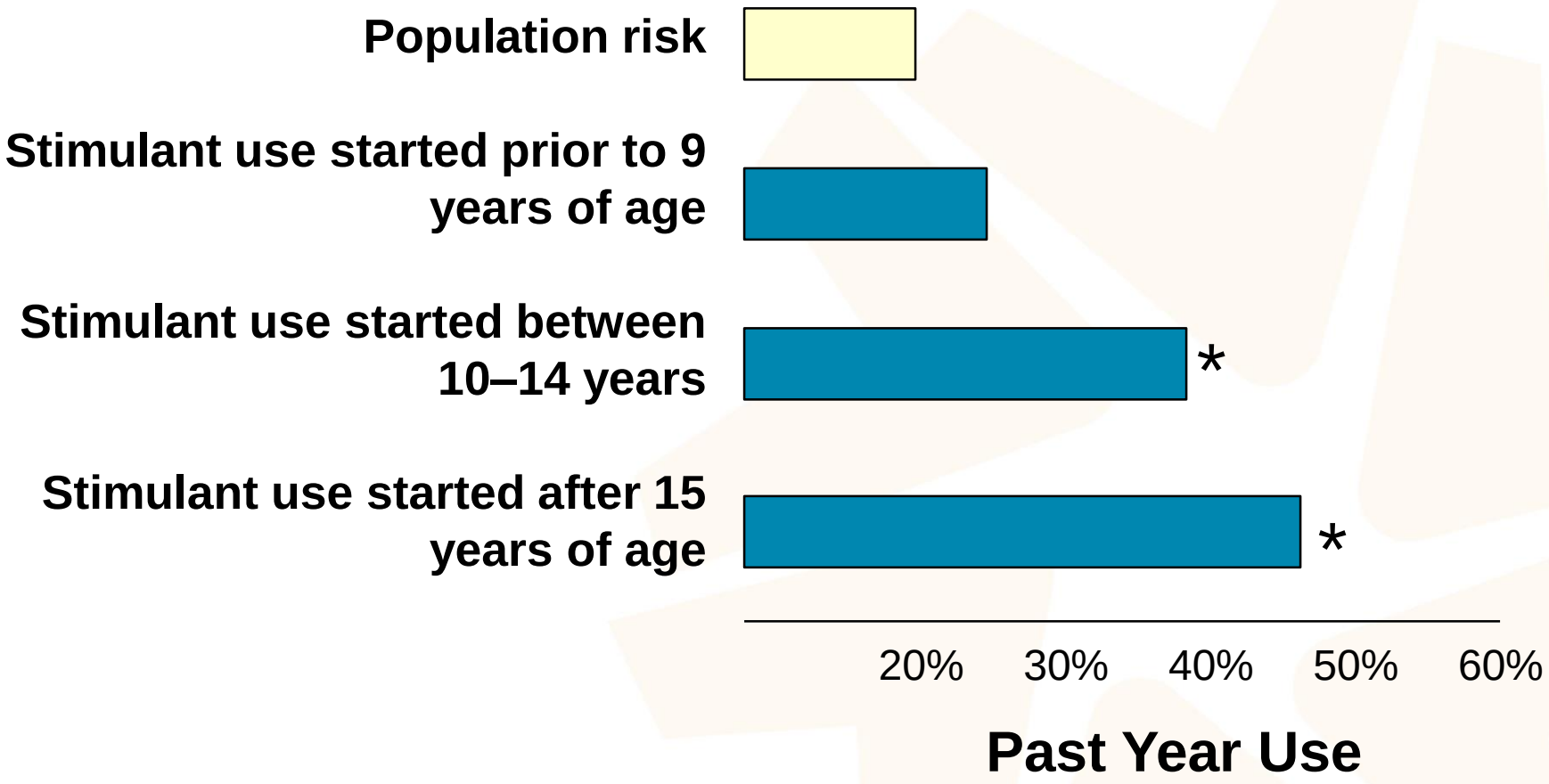
Carroll KM, et al. *Compr Psychiatry*. 1993;34(2):75-82. Schubiner H, et al. *J Clin Psychiatry*. 2000;61(4):244-251. Levin FR, et al. *Drug Alcohol Depend*. 1998;52(1):15-25. Levin FR, et al. *Addict Behav*. 2004;29(9):1875-1882. Wilens TE, et al. *Am J Addict*. 1998;7(2):156-163. Wilens TE, et al. *Am J Addict*. 2005;14(4):319-327.

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, 2020 Psychiatric Research)

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.

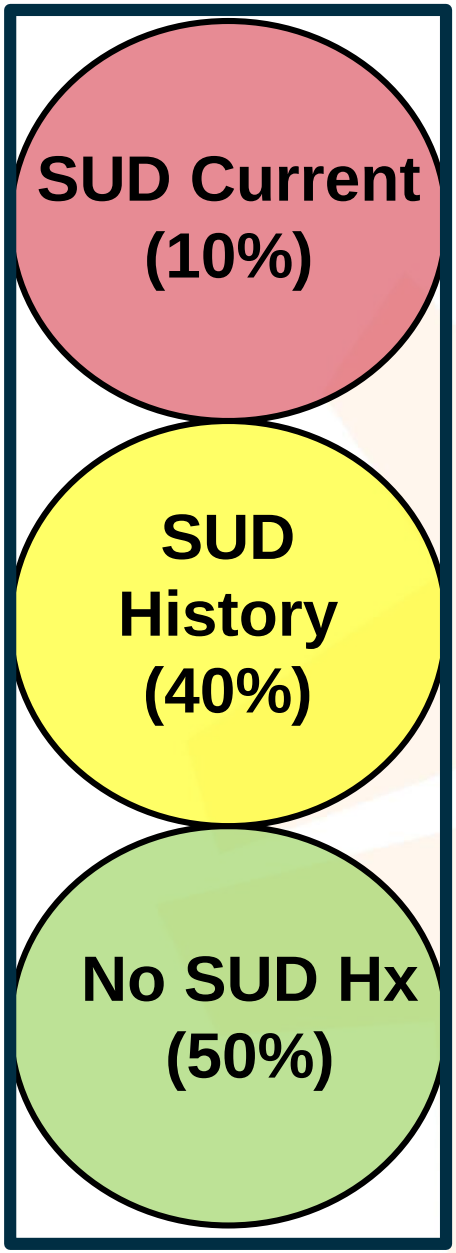
Diagnostic Dilemmas in ADHD and SUD

- Overlap symptoms of SUD in ADHD
  - Intoxication or withdrawal (30% worsening of ADHD)
  - 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 (eg, 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.

SUD in ADHD Adults Presenting for Treatment



ADHD ADULTS

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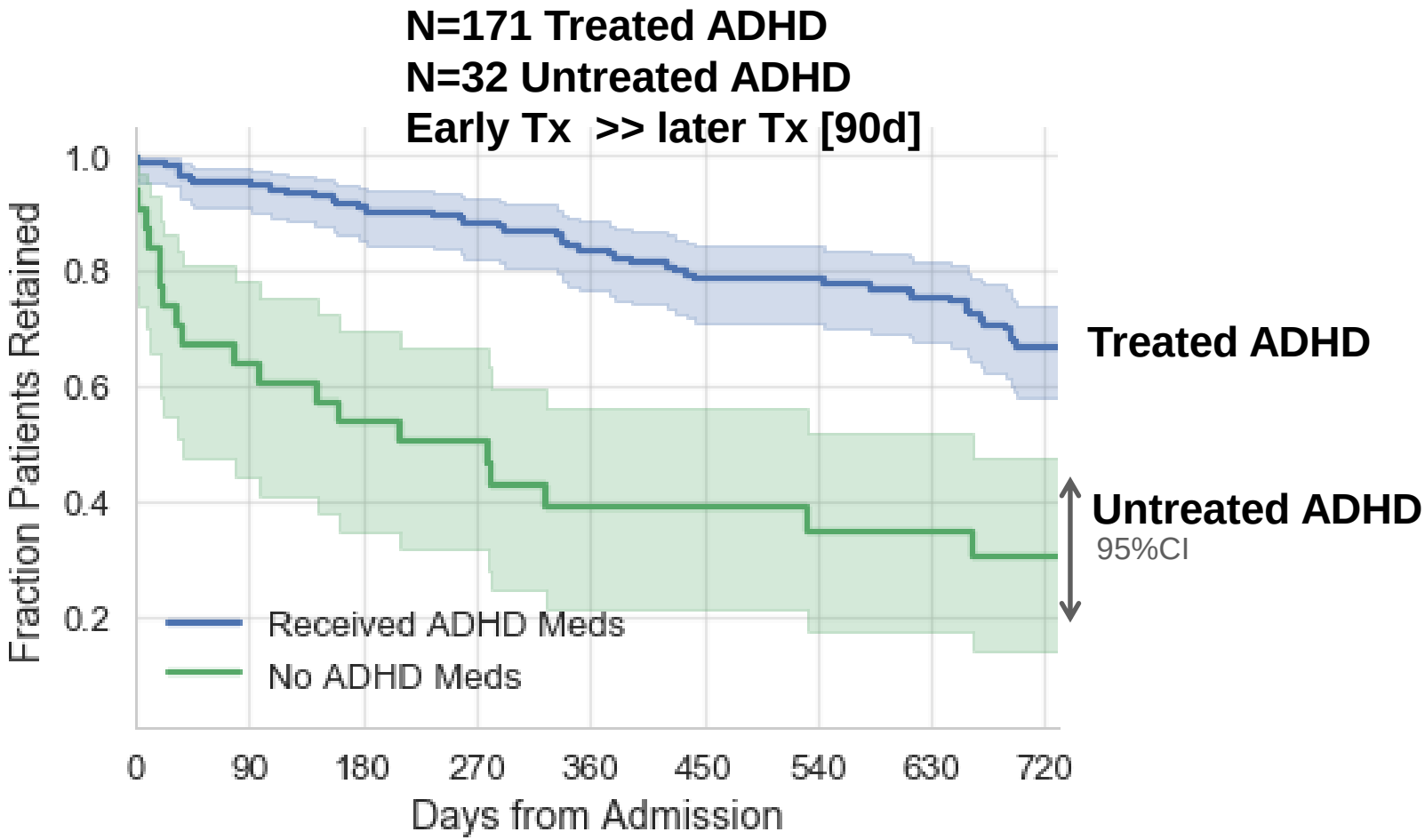
Wilens TE, et al. *Am J Addict*. 1998;7(2):156-163.

MGH Study: Treatment of ADHD Improves Retention in Treatment



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

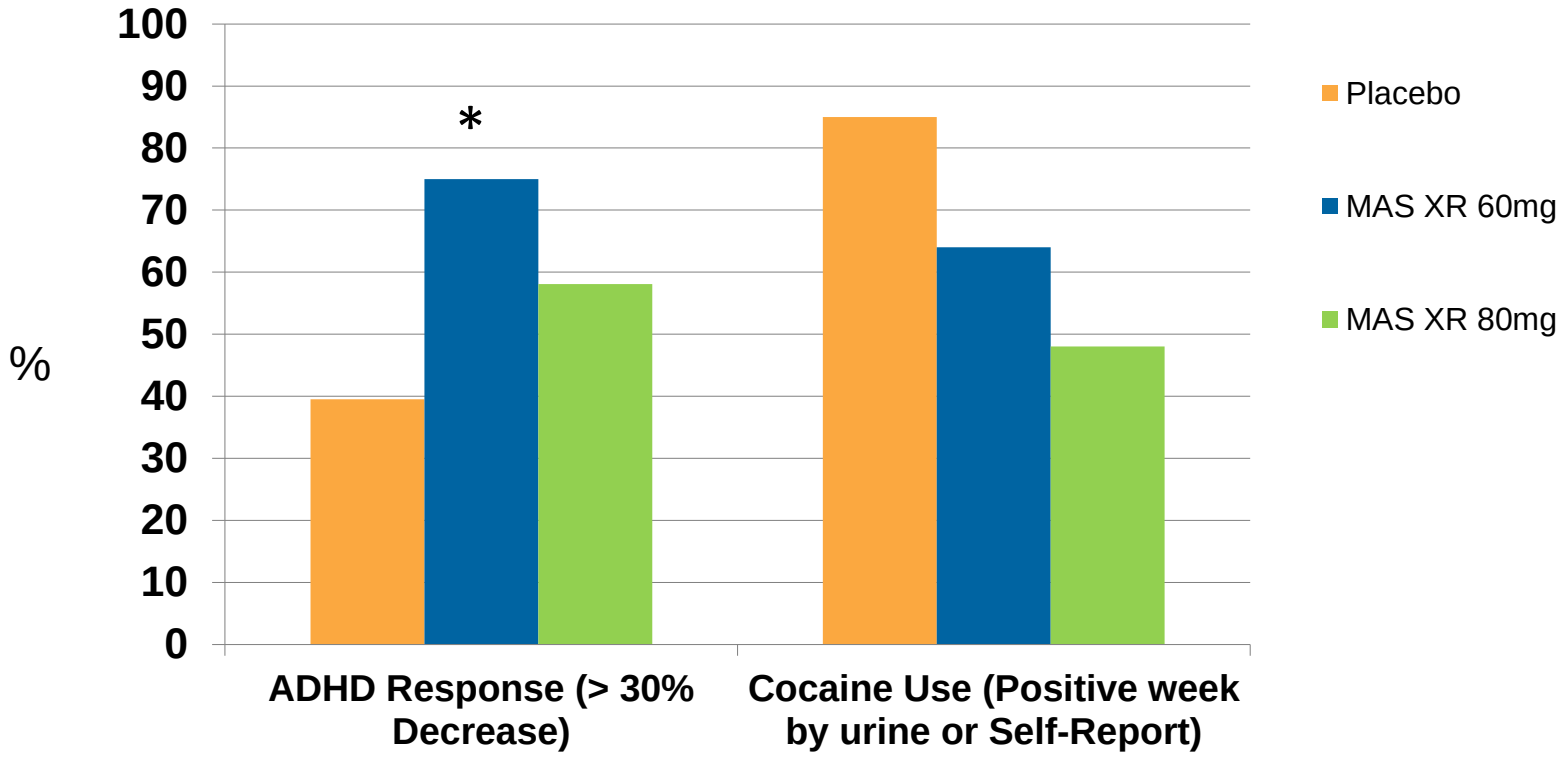
Double-Blind Studies of Stimulants to Treat Current Substance Abusers with ADHD

- 6 Studies
  - 1 study in adolescent substance abusers administered pemoline
  - 2 studies in adult cocaine abusers administered IR or SR MPH
  - 1 study in adult methadone maintenance patients administered SR MPH or SR-bupropion
  - 1 study in adults with briefly abstinent amphetamine abusers given OROS MPH
  - 1 RCT with high-dose MAS XR showing improvement
- Efficacy (vs placebo)
  - No overall improvement in SUD (trend to improvement in 1 study)
  - 2 studies suggest benefit in reducing ADHD symptoms on some measures but not others
  - 1 study showing improvement in ADHD and SUD (high-dose MAS XR)
- Safety
  - No serious adverse events
  - No worsening of SUD
  - No evidence of diversion

IR = immediate release; MAS XR = mixed amphetamine salts; RCT = randomized controlled trial; SR = sustained release.

Schubiner H, et al. *Exp Clin Psychopharmacol*. 2002;10(3):286-294. Riggs PD, et al. *J Am Acad Child Adolesc Psychiatry*. 2004;43(4):420-429. Levin FR. Personal Communication. 2006. Konstenius M, et al. *Drug Alcohol Depend*. 2010;108(1-2):130-133.

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



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

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

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)

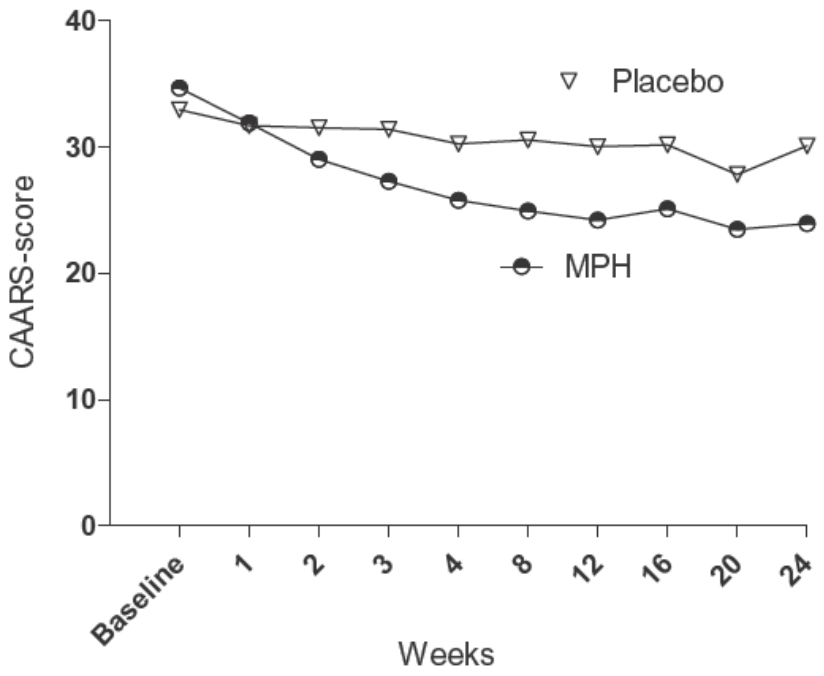
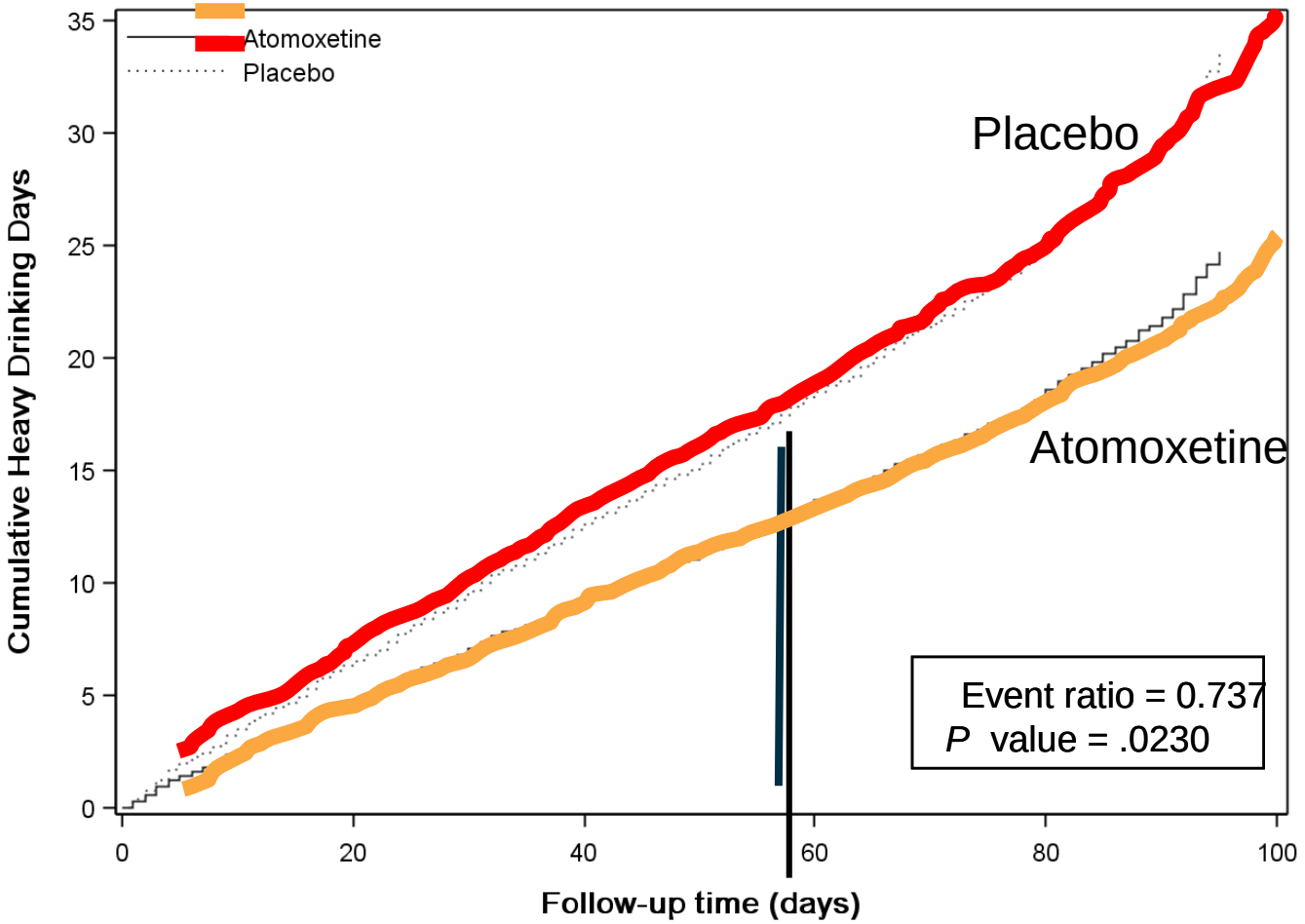


Figure 2. Change in self-rated ADHD symptoms (95% CI:-13.78 to -1.91, *P*=0.011).

Konstenius M, et al. *Addiction*. 2014;109(3):440-449.

Atomoxetine Improves Outcome in Recently Abstinent Adults



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.

Child and Adolescent Disorders (T Benton, Section Editor)

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

Courtney A. Zulauf [1], Susan E. Sprich [2], Steven A. Safren [3] 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-oc…odate recent…he treatm…e high risk fo…DHD across…ains disco… treatment alone does not appear to be particularly effective in treating SUD in currently active substance 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.

"…Structured therapies may be effective in treating adolescents and young adults with ADHD and SUD…"

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*

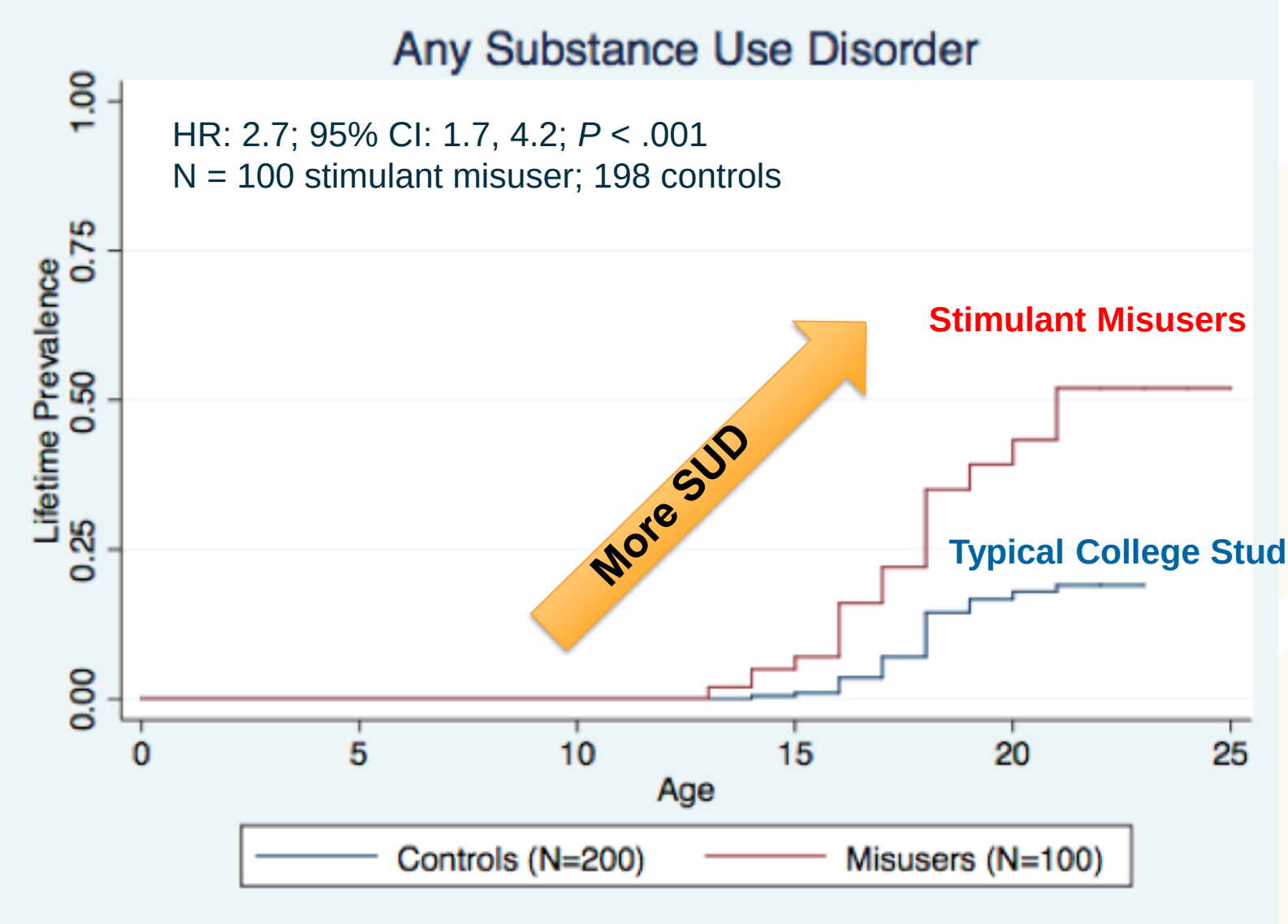
Zulauf CA, et al. *Curr Psychiatry Rep*. 2014;16(3):436.

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.

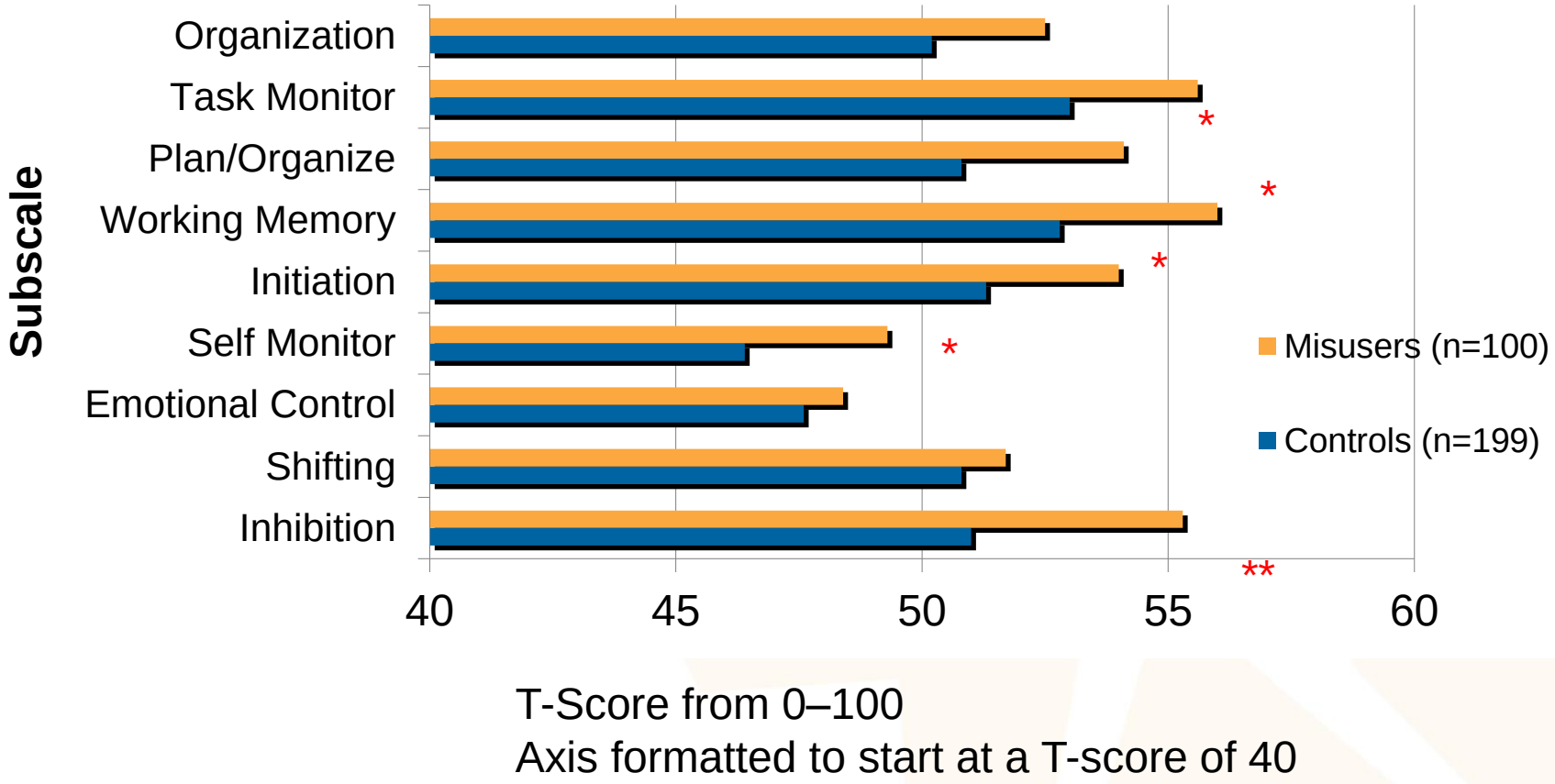
College Stimulant Misusers Have High Rates of SUD



Wilens TE, et al. *J Clin Psychiatry*. 2016;77(7):940-947.

More Executive Dysfunction in Stimulant Misusers

Subscales of the Self-Report Behavior Rating Inventory of Executive Functioning (BRIEF)



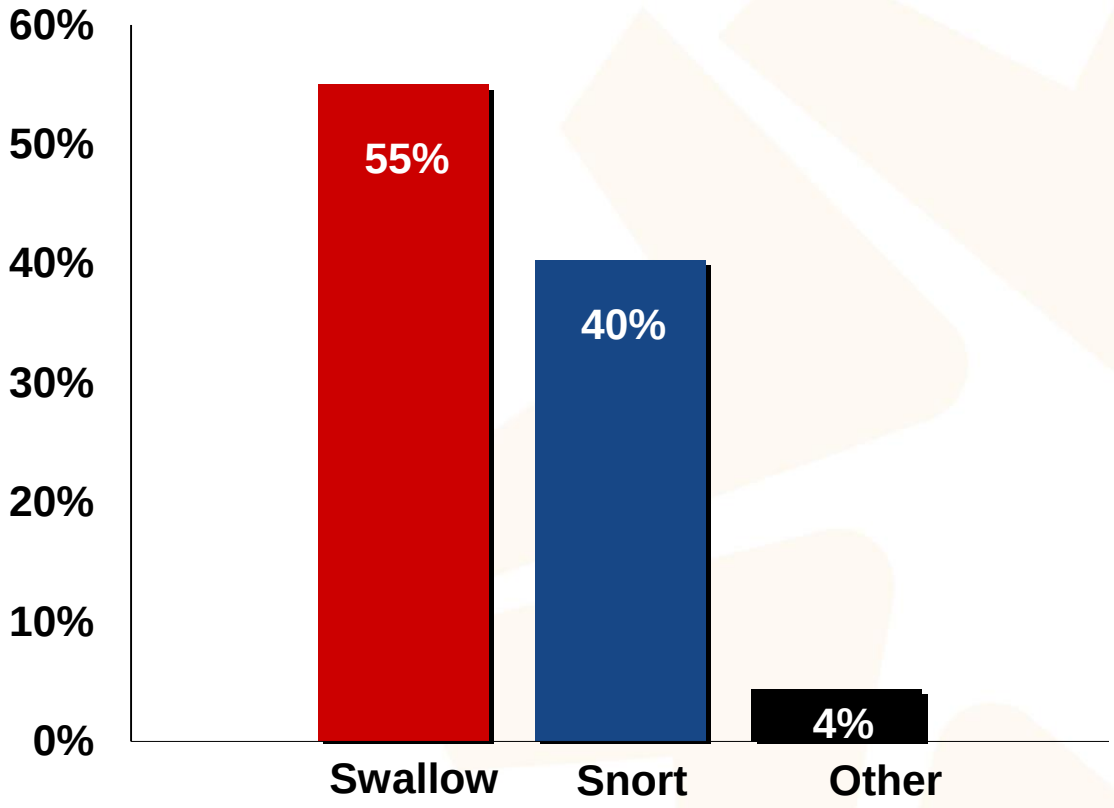
T-Score from 0–100
Axis formatted to start at a T-score of 40

N = 299. *$P < .05$

Wilens TE, et al. *Am J Addict*. 2017;26(4):379-387.

Misuse by Alternative Routes is Common: Snorting is Frequently Reported

Method of Stimulant Misuse by College Students (n = 1025)



Random sample: Anonymous surveys at the University of New Hampshire administered via e-mail and paper, 1025 received out of 5000 distributed, 6.6% diagnosed with ADHD, over 16% of students abuse stimulants.

White BP, et al. *J Am Coll Health*. 2006;54(5):261-268.

Strategies for ADHD and SUD

In context to SUD, ADHD should be treated:

If misuse or less severe SUD, treat ADHD concomitantly (e.g. infrequent MJ use)->brief SUD intervention

More severe SUD --> address SUD (e.g. daily use)

If unable to address or recalcitrant SUD ->use CBT, nonstimulants, extended-release stimulants (may need higher dose), use abuse-deterrent IR stimulants (when available)

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**