Adult ADHD in the Context of Substance use disorders

R. Tyler Reidenbaugh, MD

Disclosures



There's a race of men who don't fit it, a race that can't stay still...



Questions

- Who has it and why?
- What are the consequences of not treating?
 - Cost
 - ► Academic
 - Vocational
 - ► Relational
 - Judicial/Legal
 - Personal, on the daily



Questions

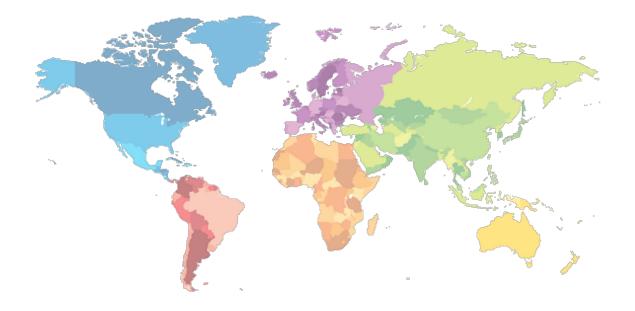
- What are the relationships with other psychiatric disorders?
- What are is the relationship with SUDs?
- Is it helpful or harmful to persons with ADHD and StUD with prescriptions stimulants?
- Would I be placing a person with a history of Stimulant Use Disorder at risk of relapse by providing prescription stimulants?



Epidemiology

- ← Children & Adolescents: 5.9 (2012) \rightarrow 9.8 (2022)
- ← Adults: up to 4.4% (10-11 million)
- ◆ ADHD is more common in males than females (12.9% vs. 5.9%)
 - 4:1 predominantly hyperactive presentation
 - 2:1 predominantly inattentive presentation

Am J Psychiatry. 2006;163(4):716.; Br J Psychiatry. 2007;190:402.; Acta Paediatr Suppl. 2004;93(445):55.; Pediatrics. 2010;125(1):75. Epub 2009 Dec 14.; J Clin Child Adolesc Psychol. 2018;47(2):199. Epub 2018 Jan 24.; Pediatrics. 2019;144(4); MMWR Suppl. 2013;62(2):1.; J Am Acad Child Adolesc Psychiatry. 2014 Jan;53(1):34-46.e2. Epub 2013 Nov 21.; J Atten Disord. 2014;18(7):563. Epub 2012 Sep 5.; J Atten Disord. 2015;19(9):741. Epub 2013 Dec 11. Courtesy of Reinhardt, M.



Genetics

Heritability Index is estimated to be 76%

The risk of ADHD in parents and siblings of children with ADHD in increased 2-8x

~60% of childhood ADHD persists into adulthood

van Emmerik-van Oortmerssen K, van de Glind G, van den Brink W, Smit F, Crunelle CL, Swets M, Schoevers RA. Prevalence of attention-deficit hyperactivity disorder in substance use disorder patients: a meta-analysis and meta-regression analysis. Drug Alcohol Depend. 2012 Apr 1;122(11-2):11-9, doi: 10.1016/j.drugalcdep.2011.12.007. Epub 2011 Dec 30. PMID: 22209385.



Adult Expression of ADHD

Hyperactivity

- Restlessness
- Verbosity
- Constant activity

Impulsivity

- Ending relationships
- Quitting jobs
- Overreacting
- Interrupting
- More driving violations
- Financial difficulties

Inattention

- Procrastinating (stacking)
- Difficult decision making
- Poor time management
- Difficulty organizing activities and prioritizing
- Accidents

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Medscape Medical News

First US Adult ADHD Guidelines Finally on the Way?

Alicia Ault April 11, 2024





COMING SOON!

American Professional Society of ADHD and Related Disorders (APSARD) and the American Psychiatric Association (APA) are collaborating to formulate guidelines.

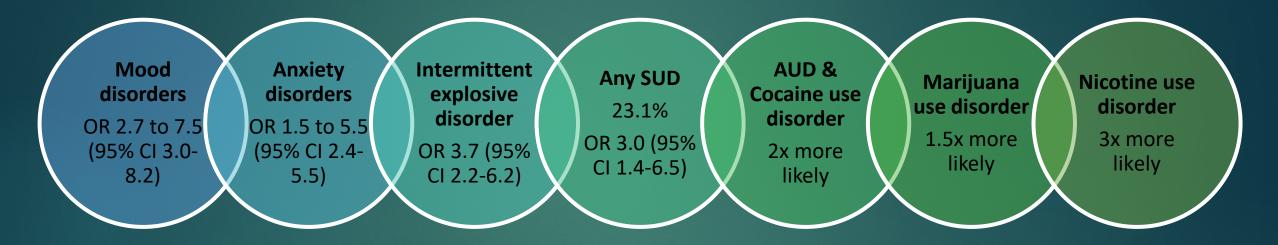
To be released this fall???

ADHD is highly co-morbid with many DSM disorders

Psychiatric Comorbidities in Adults

Condition	w/ADHD	w/o ADHD
Social Phobia	29.3%	7.8%
Specific Phobia	22.7%	9.5%
Bipolar Disorder	19.4%	3.1%
MDD	18.6%	7.8%
PTSD	11.9%	3.3%
GAD	8.0%	2.6%
Alcohol Dep	5.8%	2.0%
Drug Dep	4.4%	0.6%

ADHD Comorbidity



- A dose-response relationship exists the more ADHD symptoms, the more # of comorbidities
 - ADHD + ≥3 comorbidities: OR 7.2 (95% CI 5.1-10.2)
- The rate of comorbidities + ADHD in adults ↑ with age
 - 个 age = 个 likelihood of anxiety, depression, SUD & antisocial personality disorder

Am J Psychiatry. 2006;163(4):716.; Can J Psychiatry. 2009 Oct;54(10):673-83.; J Clin Psychiatry. 2004;65 Suppl 3:3-7.; Br J Psychiatry. 2007;190:402.; Drug Alcohol Depend. 2012 Apr;122(1-2):11-9. Epub 2011 Dec 30. With Permission of Michellel Reinhardt

Healthcare-related Financial Burden (2000)

- ▶ 1.6B for the treatment of ADHD
- ▶ 12.1B for the treatment of co-morbidities

Vocational losses

► 3.7B

Birnbaum, H. G., Kessler, R. C., Lowe, S. W., Secnik, K., Greenberg, P. E., Leong, S. A., & Swensen, A. R. (2005). Costs of attention deficit–hyperactivity disorder (ADHD) in the US: excess costs of persons with ADHD and their family members in 2000. *Current Medical Research and Opinion*, *21*(2), 195–205. https://doi.org/10.1185/030079904X20303

Childhood

- Academic underachievement
- ► Grade retention
- ► Social rejection

Adult

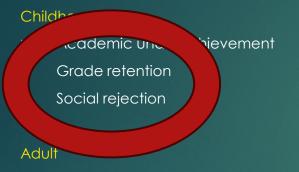
- ► Higher college dropout rates
- Poorer job performance
- Difficulty sustaining employment
- ▶ Lower wages than peers of similar intelligence

Cost to productivity and work loss

- ▶ 1.2B, women
- ▶ 2.26B men

Beauchaine TP, Ben-David I, Bos M. ADHD, financial distress, and suicide in adulthood: A population study. Science Advances. Nov 8, 2019, vol 6, 40.

Matza LS, Paramore C and Manishi Prasad. A Review of the economic burden of ADHD. Cost Effectiveness and Resource Allocation 3, 5 (2005).



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Contribution to Criminality

• 47% v 24% arrests

- 42% v 14% convicted
- 15% v 1% incarcerated

Accidents

38% v 18% accident rate for adults with ADHD

Mannuzza S, Klein RG, Moulton JL 3rd. Lifetime criminality among boys with attention deficit hyperactivity disorder: a prospective follow-up study into adulthood using official arrest records. Psychiatry Res. 2008 Sep 30;160(3):237-46. doi: 10.1016/j.psychres.2007.11.003. Epub 2008 Aug 15. PMID: 18707766; PMCID: PMC2581455.

Individuals with ADHD have a 2-fold increase in premature death vs non-ADHD peers.

Medication initiation for persons with ADHD is associated with:

- Lower risk of all cause mortality (hazard ratio [HR], 0.79; 95% CI, 0.70 to 0.88)
- And unnatural cause mortality (2-year mortality risk, 25.9 per 10 000 individuals vs 33.3 per 10 000 individuals; risk difference, -7.4 per 10 000 individuals; 95% CI, -14.2 to -0.5; HR, 0.75; 95% CI, 0.66 to 0.86)
- No difference for natural cause mortality

Catalá-LópezF, HuttonB, PageMJ, etal. Mortality in persons with autism spectrum disorder or attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. JAMA Pediatr. 2022;176(4):e216401. doi:10.1001/jamapediatrics. 2021.6401

Li, Lin, et al. "ADHD pharmacotherapy and mortality in individuals with ADHD." JAMA 331.10 (2024): 850-860.



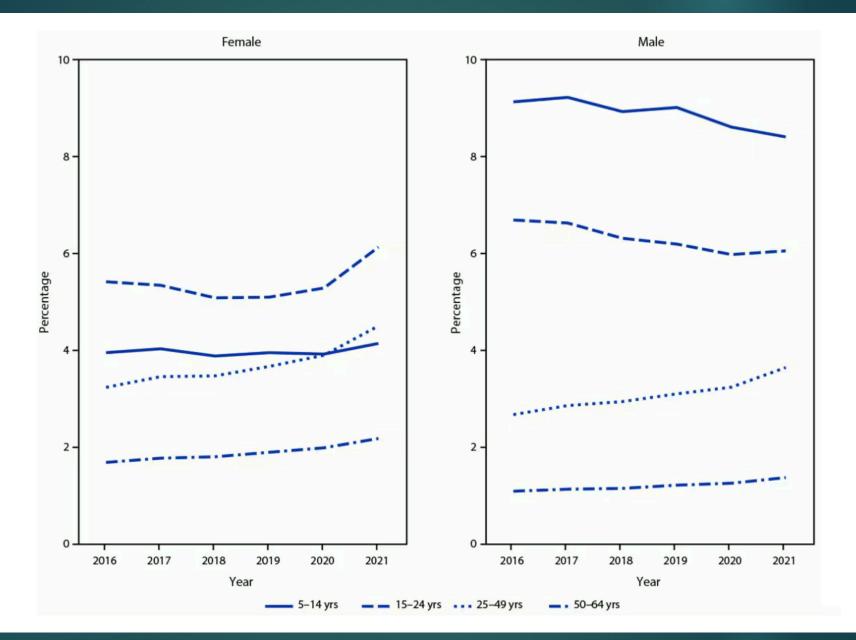


Morbidity and Mortality Weekly Report (*MMWR*)

Trends in Stimulant Prescription Fills Among Commercially Insured Children and Adults — United States, 2016–2021

Weekly / March 31, 2023 / 72(13);327-332

Melissa L. Danielson, MSPH¹; Michele K. Bohm, MPH²; Kimberly Newsome, MPH¹; Angelika H. Claussen, PhD¹; Jennifer W. Kaminski, PhD²; Scott D. Grosse, PhD³; Lila Siwakoti, MPH²; Aziza Arifkhanova, PhD²; Rebecca H. Bitsko, PhD¹; Lara R. Robinson, PhD¹ (<u>VIEW AUTHOR AFFILIATIONS</u>)



Why the Trend?





INCREASED RECOGNITION

GLOBAL PANDEMIC THAT SHIFTED WORKS AND STUDENTS INTO ISOLATED ENVIROMENTS AVAILABILITY (PROMOTION)

The New York Times

The Hazards of Prescribing A.D.H.D. Drugs Online

Buzzy start-ups promising easy access to mental health medication found an eager market on social media. Should anyone be looking for treatment on TikTok, though?

H Share full article



Elizabeth D. Herman for The New York Times



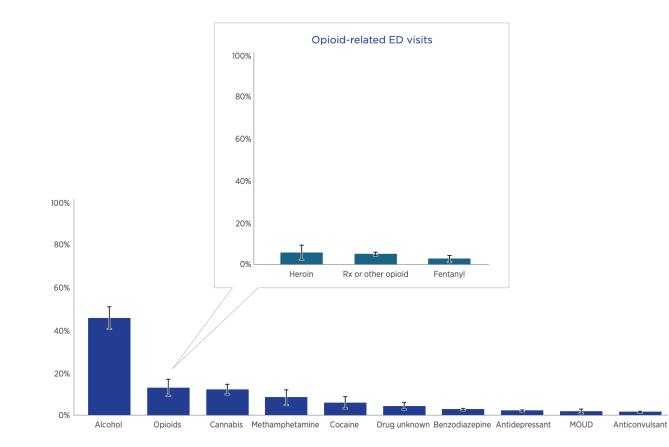
Diversion



Among high school students prescribed stimulants: 15% shared, 7% sold meds to other students 61.5% of college students prescribed ADHD meds shared/sold those meds at least once

2

At a medical school, 25% of students had been offered stimulants without a presciption Among adults prescribed methylphenidate, 44% diverted and 29% misused



Drug Abuse Warning Network (DAWN)

Substance Abuse and Mental Health Services Administration. (2023). Drug Abuse Warning Network: Findings from Drug-Related Emergency Department Visits, 2022 (HHS Publication No. PEP23-07-03-001). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/.

Cannabis	м	Methamphetamine					
CANNABIS		C	Cocaine				
Alcohol		м	Methamphetamine				
COCAINE				METHAMPI	HET	AMINE	
Heroin		Ca	nnabis	Cannabis		Fentany	
HEROIN	BENZODIAZE PINE		Rx or other Opioid		FENTANYL		
Cocaine Alcohol			Cannal	nnabis		Methamphetamin	
Alcohol Fentar	Rx or other OPIOID				Her	oin	

Drug Abuse Warning Network

Substance Abuse and Mental Health Services Administration. (2023). Drug Abuse Warning Network: Findings from Drug-Related Emergency Department Visits, 2022 (HHS Publication No. PEP23-07-03-001). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/.

ADHD and Stimulant Use Disorder

51 pts with methamphetamine use disorder Screened with Wender-Utah Rating Scale

70% Screened Positive for ADHD

Jaffe, Craig, et al. "A comparison of methamphetamine-dependent inpatients with and without childhood attention deficit hyperactivity disorder symptomatology." *Journal of Addictive Diseases* 24.3 (2005): 133-152.

ADHD and Stimulant Use Disorder

Patients who screened positive for ADHD had higher rates of methamphetamine use in the previous 30 days



Jaffe, Craig, et al. "A comparison of methamphetamine-dependent inpatients with and without childhood attention deficit hyperactivity disorder symptomatology." *Journal of Addictive Diseases* 24.3 (2005): 133-152.

Co-Occurence of ADHD and SUD

Any substance use disorders (SUDs), odds ratio 3.0 (95% CI 1.4-6.5)

A meta-analysis of 29 studies of adults with an SUD, the lifetime prevalence of ADHD was 23.1 percent

Among treatment seeking individuals the prevalence of ADHD is 19 – 27%

Kessler et al Kessler et al 2006, van Emmerik-van Oortmerssen et al 2012.

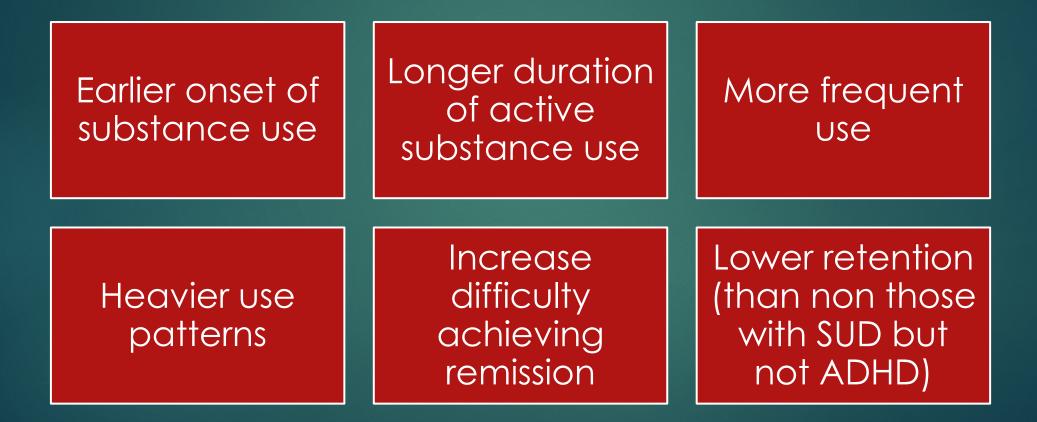
Co-Occurence of ADHD and SUD

Persons with adult ADHD have poorer outcomes and higher risk of relapse then patient w/o ADHD

The multiple psychiatric comorbidities further complicate successful outcomes

Persons with substance use disorders are less likely to receive to treatment for ADHD.

Consequences of co-occurring ADHD and SUD



Wilens TE, Biederman J, Mick E. Does ADHD affect the course of substance abuse? findings from a sample of adults with and without ADHD. Am J Addict. 1998;7(2):156–163; Levin FR, Evans SM, Vosburg SK, et al. Impact of attention-deficit hyperactivity disorder and other psychopathology on treatment retention among cocaine abusers in a therapeutic community. Addict Behav. 2004;29(9):1875–1882; Carroll KM, Rounsaville BJ. History and significance of childhood attention deficit disorder in treatment-seeking cocaine abusers. Compr Psychiatry. 1993;34(2):75–82.

Psychostimulants and Substance Abuse

Does untreated ADHD increase the risks of developing a Substance use disorder?

YES

Does treatment of a patient (child/adolescent) with a psychostimulant predispose them to later substance use or development of SUD?

Does stimulant treatment for ADHD reduce the risk of SUDs or decrease use of substances of abuse?

YES

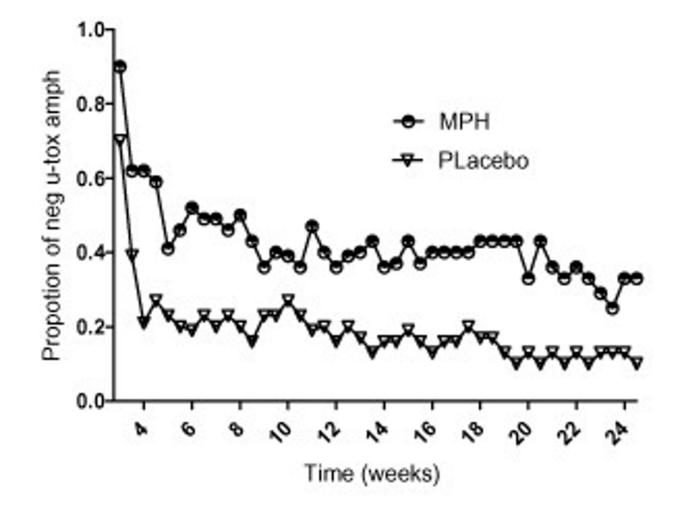
MPH for Co-Occurring ADHD and Amphetamine Use Disorder

56 patients with ADHD and amphetamine use disorder

27 pts received MPH at 96 to 180 mg/day

27 pts received placebo

Konstenius, M., Jayaram-Lindström, N., Guterstam, J., Beck, O., Philips, B. and Franck, J. (2014), MPH for adults with ADHD and SUD. Addiction, 109: 440-449. https://doi.org/10.1111/add.12369



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Subjects with co-occurring ADHD and cocaine use disorder 60 mg

80 mg

Placebo

Levin FR, Mariani JJ, Specker S, Mooney M, Mahony A, Brooks DJ, Babb D, Bai Y, Eberly LE, Nunes EV, Grabowski J. Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jun;72(6):593-602. doi: 10.1001/jamapsychiatry.2015.41. PMID: 25887096; PMCID: PMC4456227.

Subjects with co-occurring ADHD and cocaine use disorder 60 mg 75% had >30% j in ADHD symptoms

80 mg 58.1% had >30% ↓ in ADHD symptoms

Placebo 39.5% had >30% 1 in ADHD sx

Levin FR, Mariani JJ, Specker S, Mooney M, Mahony A, Brooks DJ, Babb D, Bai Y, Eberly LE, Nunes EV, Grabowski J. Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jun;72(6):593-602. doi: 10.1001/jamapsychiatry.2015.41. PMID: 25887096; PMCID: PMC4456227. Subjects with co-occurring ADHD and cocaine use disorder

60 mg 17.5% abstinence last 3 weeks

80 mg 30.2% abstinence last 3 weeks

PICCEDO 7% abstinence last 3 weeks

Levin FR, Mariani JJ, Specker S, Mooney M, Mahony A, Brooks DJ, Babb D, Bai Y, Eberly LE, Nunes EV, Grabowski J. Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult Attention-Deficit/Hyperactivity Disorder and Cocaine Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2015 Jun;72(6):593-602. doi: 10.1001/jamapsychiatry.2015.41. PMID: 25887096; PMCID: PMC4456227.

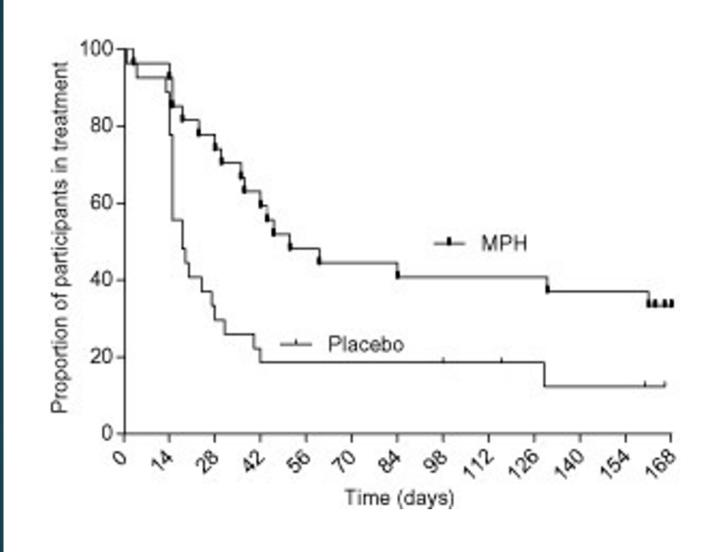
Summary of Treatments

Emerging directions only recently been codified as guidelines

Both trials utilized psychostimulants at the upper end of the therapeutic window

Treatment was significantly structured with a minimum of two participant encounters weekly

Not treatments for stimulant use disorder



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Konstenius, M., Jayaram-Lindström, N., Guterstam, J., Beck, O., Philips, B. and Franck, J. (2014), MPH for adults with ADHD and SUD. Addiction, 109: 440-449. <u>https://doi.org/10.1111/add.12369</u>

Retention

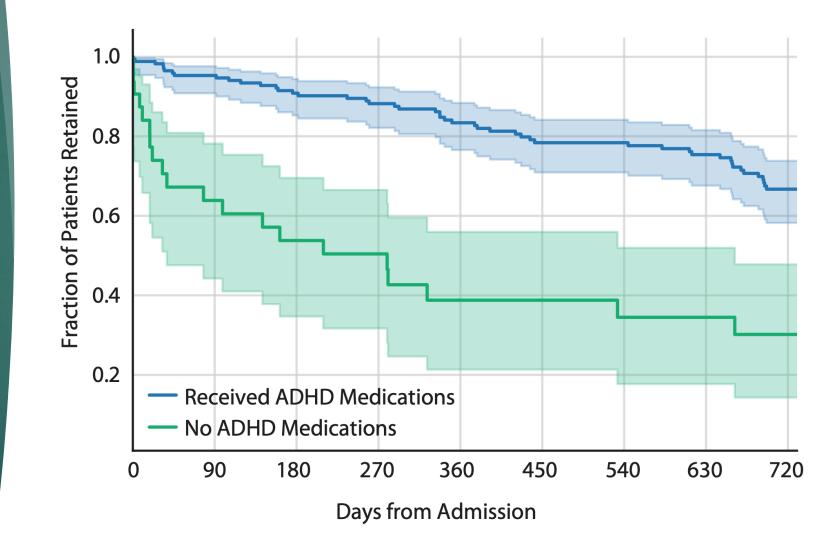
2,163 individuals admitted to outpatient SUD treatment during a 4.5 yr study period

- 203 dx ADHD
- 171 received pharmacotherapy
 - ▶ 63% received non-stimulants; 82% received stimulants
 - ▶ 67% of stimulants given were XR or prodrug formulations
 - Those receiving amphetamine formulations (n=105), 97% were adherent by tox screen
- 32 pts with ADHD received no pharmacotherapy

Kast KA, Rao V, Wilens TE. Pharmacotherapy for attention-deficit/hyperactivity disorder and retention in outpatient substance use disorder treatment: a retrospective cohort study. *J Clin Psychiatry*. 2021;82(2):20m13598.

Retention

Kast KA, Rao V, Wilens TE. Pharmacotherapy for attentiondeficit/hyperactivity disorder and retention in outpatient substance use disorder treatment: a retrospective cohort study. *J Clin Psychiatry*. 2021;82(2):20m13598.



Retention

Those not receiving treatment had 4.9-fold increased risk of attrition

A stimulant trial may increase retention short/long-term

The half-life of retention was 9 months vs 36 months

Deferring treatment may risk early dropout

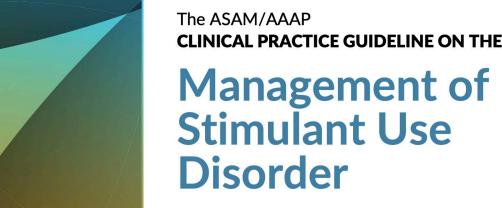
Kast KA, Rao V, Wilens TE. Pharmacotherapy for attentiondeficit/hyperactivity disorder and retention in outpatient substance use disorder treatment: a retrospective cohort study. *J Clin Psychiatry*. 2021;82(2):20m13598.



 Recommend: An assessment of StUD should include screening for ADHD

GUIDELINES

- Addressing ADHD symptoms should be part of tx (low certainty, Strong recommendation)
 - Psychostimulants
 - non-stimulants
 - Behavioral approaches (CM, CRA, CBT)
- When prescribing psychostimulants
 - use extended-release formulations
 - Maintain a level of monitoring consummate with the risk (Clinical consensus, Strong Recommendation)
- For adolescent and young adults
 - Observe administration
 - Counsel on safe-storing and restricted access (Clinical consensus, Strong Recommendation)



Conclusion

Our treatments for stimulant use disorder are modest

- Opiates = great!
- Alcohol = moderate (grossly underutilized)
- Stimulants = we don't have much

THEREFORE

When have known co-morbidity with such a successful treatment it is imperative that we treat.

Take homes

Help for assessing and treating adult ADHD is on the way!

Guidelines are now available for treating combination ADHD and StUD

It can be a challenging patient population

REFER TO PEOPLE LIKE ME



