

**Wait, what did you say?**

**Adult ADHD**

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**Disclosure**  
 Heather Huang, MD

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company which could be considered a conflict of interest.

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**ADHD**

- ADHD is a **developmental** disorder of **executive dysfunction**
- Onset in childhood
- Abnormal development of brain circuits resulting in symptoms of:
  - Inattention
  - Hyperactivity
  - Impulsivity



**Executive Functions**

- Memory
- Attention
- Language
- Reasoning
- Decision-making
- Task execution (praxia)

**Prevalence of ADHD Across Ages**

- 6-9% of children worldwide have ADHD
- By age 25:
  - 15% have persistent symptoms, meeting full diagnostic criteria
  - 50% meet subthreshold criteria (partial remission), and demonstrate impairment
- **2-4% of the adult population**

Faraone & Biederman. Psychol Med 2006; 36: 159-165. Fayyad et al. Cross-national prevalence and correlates of adult ADHD. Br J Psychiatry. 2007. Kessler et al. the prevalence and correlates of adult ADHD in the US: results from the National Comorbidity Survey Replication. Am J Psych. 2006. Simon et al. Prevalence and correlates of adult ADHD disorder: Meta-analysis. Br J Psych. 2009. Viding 2017. Exploring DSM-5 ADHD criteria beyond young adulthood. Johnson et al 2015. ADHD medication use among teens and young adults. Renouf. C et al. 2016. Prescribing trends of ADHD medications in UK primary care.

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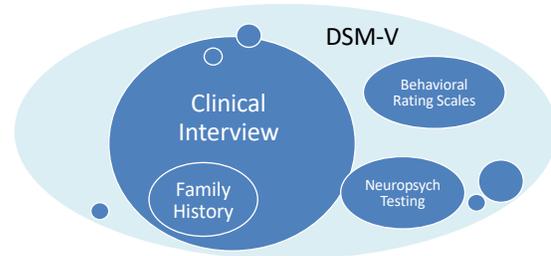
### Adult ADHD

- Adult ADHD is the persistence of childhood ADHD symptoms into adulthood
- Late onset ADHD – Controversial
  - Onset in adolescence, adulthood
  - Are these late onset, vs missed diagnosis, vs mis-diagnosis of another condition (e.g. medical – OSA, TBI; psychiatric – depression, anxiety)

Sibley et al. Am J Psych 2018

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Diagnosis is CLINICAL. There is no test (blood, imaging, or psychological) that can make the dx.



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### Clinical Interview

- Current symptoms
- Previous / Childhood symptoms
- Medical & psychiatric history
- Family history
- Social history

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### DSM-V: ADHD Behavioral Criteria

**A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development.**

**9 possible symptoms for inattention and 9 possible symptoms for hyperactivity-impulsivity**

Adolescents and adults (≥17): Five or more Symptoms have been present for at least 6 months, and are inappropriate for developmental level

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### Inattention

- Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
- Often has trouble holding attention on tasks or play activities.
- Often does not seem to listen when spoken to directly.
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., loses focus, side-tracked).
- Often has trouble organizing tasks and activities.
- Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).
- Often loses things necessary for tasks and activities (e.g. school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
- Is often easily distracted
- Is often forgetful in daily activities.

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### Hyperactivity and Impulsivity

- Often fidgets with or taps hands or feet, or squirms in seat.
- Often leaves seat in situations when remaining seated is expected.
- Often unable to play or take part in leisure activities quietly.
- Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
- Is often "on the go" acting as if "driven by a motor".
- Often talks excessively.
- Often blurts out an answer before a question has been completed.
- Often interrupts or intrudes on others (e.g., butts into conversations or games)
- Often has trouble waiting turns.

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### DSM-V: ADHD Subtypes

- ADHD-inattentive type
- ADHD-hyperactive/impulsive type
- ADHD-combined type

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### DSM-V: ADHD Functional Criteria



Before the age of 12



More than 1 setting

School/work, home, relationships (friends or relatives), social situations



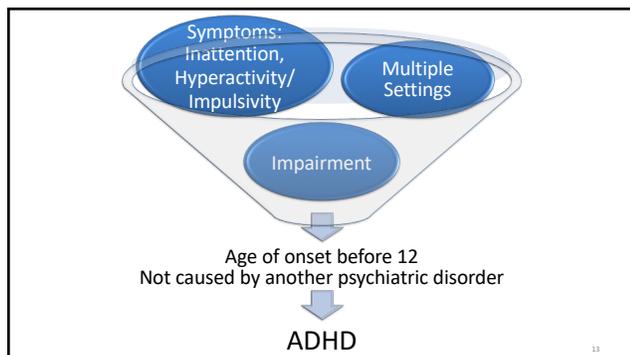
Clear evidence that symptoms cause impairment



Not be caused by other mental disorders

E.g. mood, anxiety, schizophrenia, psychosis, pervasive developmental disorder

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### Current Symptoms - Impairment

- Occupational and educational settings
  - Do you have problems getting along with bosses or co-workers?
  - How are your performance reviews?
  - Have you changed jobs a lot? Why were you changing jobs so often?
- Relationships
  - Ask about divorce, marriages, problems in relationships.
  - Do you have problems w parental responsibilities (e.g getting kids ready for school, homework, meals)?
- Driving
  - Do you feel you're a good driver? Do others think you're a good driver?
  - Have you had your license revoked? Or repeatedly gotten pulled over for speeding?

Mannuzza S, Klein RG. Child Adolesc Psychiatr Clin N Am. 2000;9(3):711-726. Murphy K, Barkley RA. Compr Psychiatry. 1996;37(6):393-401. Klein RG, et al Archives of general psychiatry. 2012;69(12):1295-303. Park K, et al. Clin Psychol Rev. 2017 Aug;56:25-39. Parental ADHD symptoms and parenting behaviors: A meta-analytic review. Young S, et al. Psychol Med. 2015 Jan; 45(1): 247-258.

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### Educational Hx & Surrogate Assessment of Childhood Sxs and Impairment

- Higher rates of:
  - Poor performance (lower GPA and class ranking)
  - Grade retention
  - Tutoring, special ed classes/IEP
  - Reading disability
  - Disciplinary actions (being suspended or expelled)
  - Dropping out
- Fewer enter college
  - Those who do have a lower graduation rate
- Educational history
  - What were your grades like in elementary, middle, and high school?
  - Were you ever diagnosed with a learning disability, or had to take special ed classes?
  - Were you ever held back?
  - Did you ever have any disciplinary problems, or been suspended?
  - Psychosocial stressors

Biederman et al. 1996; Barry et al. 2002; Loe & Feldman 2007, LeFevre et al. 2002

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### Medical History

- Conditions that can mimic ADHD symptoms
  - Thyroid, obesity, metabolic syndrome, chronic illness, OSA
  - Hearing/vision impairment
  - Learning disorders
  - Cognitive impairment (TBI, dementia, CVA)
- Medications
  - Sedatives (e.g. benzodiazepines, narcotics)

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## Psychiatric History

- Poor concentration is a symptom of many psychiatric disorders
  - Screen using PHQ9, GAD7
- >50-75% of adults w ADHD have at least 1 psychiatric disorder.
  - Up to 20-30% - Anxiety disorder
  - Up to 33% - Depression
  - Alcohol (17-45%) and drug (18-30%) dependency
  - 30-70% have a learning disability
  - Up to 20% - Antisocial personality disorder

Kooij SJ et al. European consensus statement on diagnosis and treatment of adult ADHD: The European Network Adult ADHD. BMC Psychiatry. 2010; Wilens et al. ADHD and the substance use disorders: The nature of the relationship, subtypes at risk, and treatment issues. Psychiatr Clin North Am. 2006.

## Family & Social History

- ADHD has a high heritability rate
  - Fhx of ADHD is a strong predictor for ADHD (Parent, sibling, child with ADHD)
- Social/Environmental
  - Stressful home/work environment
  - Abuse, family dysfunction
- Substances
  - Alcohol, illegal drugs
  - Excessive caffeine, sugar, nicotine
  - Repeat assessment 2-3 months after abstaining

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## Supplemental Information:

### Collateral

- Collateral history from partner, family members, friends, employer/co-workers
  - Current or childhood symptoms

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## Supplemental Information:

### Rating Scales

- Assess current or childhood symptoms
- Screening tools. Not diagnostic.
- Helpful to rule out ADHD if negative
- Adult ADHD Self-Report Scale (ASRS).
  - Assesses current symptoms
  - High NPV – 98%
- Wender-Utah
  - Assesses past symptoms (retrospectively assess childhood ADHD)
  - Recall bias can be a problem

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### Neuropsychological Testing

- Not necessary for routine dx of ADHD
- Purpose is to objectively assess the individual's cognitive functions and identify areas of impairment
- Does NOT diagnose ADHD
  - No unique cognitive profile for patients w ADHD
- Support conclusions based on history
  - Can be helpful if the clinical assessment is inconclusive
- Expensive

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### Physical Exam

- Very low-quality evidence to support any of the following:
  - Baseline vitals: weight, BP, pulse
  - EKG screening prior to initiating stimulants
  - Routine laboratory testing (e.g. thyroid studies, LFTs)

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### Treatment

- First: Treat comorbid psychiatric dx
- Goal: Improve symptoms, optimize functional performance
- Psychotherapeutic strategies
- Medication
- Accommodations: Educational, Vocational

### Psychotherapeutic Strategies

- Psychoeducation
- Cognitive behavioral therapy
  - Time management, organization, planning
    - Daily structure and maintaining a daily schedule
    - Use of lists
  - Environmental restructuring
    - Keeping distractions to a minimum
    - Setting small, reachable goals
    - Limiting choices
- Books: Mastering Your Adult ADHD, Driven to Distraction

Young JL et al, Adult ADHD Diagnosis, Management, and Treatment in the DSM-5 Era. Prim Care companion CNS disord. 2016.  
Mongia et al. CBT for adults with ADHD: A review or recent RCTs. Curr Psych Rep. 2012.

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### Vocational/Educational Accommodations

- Wisconsin Department of Workforce Development (DVR)
- Illinois Department of Human Services – Vocational Rehabilitation
- UW-Madison McBurney Disability Resource Center
- Suggest new students go to the university website and search “disability services”
- U.S Department of Education
  - Students with ADHD and Section 504: A Resource Guide(2016)
  - Know Your Rights: Students with ADHD (2016)
  - Identifying and Treating Attention Deficit Hyperactivity Disorder: A Resource for School and Home 2008

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### Medication

Stimulants	Non-Stimulants
<ul style="list-style-type: none"> <li>• Methylphenidate</li> <li>• Amphetamine</li> <li>• Combination</li> </ul>	<ul style="list-style-type: none"> <li>• Atomoxetine</li> </ul>

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### Stimulants

- First-line medication for the treatment of ADHD
- Increase catecholamines (NE, DA) in the brain
- Similar efficacy between all of them
  - 70% of pts respond to the 1<sup>st</sup> stimulant tried
  - 90-95% respond to the 2<sup>nd</sup> one tried
- Similar side effect profile
- Different pharmacokinetic and pharmacodynamic profiles

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### Methylphenidates

	Methylphenidate	Dexmethylphenidate	
Immediate 4 hrs	IR	Focalin IR	2-3x/day, 4 hr apart Not impacted by food
Intermediate 6-8 hrs	Ritalin SR Metadate ER Methylin ER	Focalin XR	2x/day dosing OR 1x/day + IR dosing
Long acting 8-10 hrs	Ritalin LA Metadate CD Atpensio XR Daytrana (patch) Concerta (10-12 hrs)		1x/day  Daytrana – 9 hrs on, rotate site daily to prevent rash.

### Notes on Long-acting Methylphenidate

- Peak concentration is slowed down by a high-fat meal
- Ritalin LA and Focalin XR have 2 peaks in concentration, mimicking IR BID dosing
  - 50% of the drug is released immediately, 50% released 4 hrs later.
- Metadate CD releases 30% immediately and 70% over the remaining time
- Focalin XR, Metadate CD, Ritalin LA: Capsules that can be opened and sprinkled onto food. Do not chew beads.
- Concerta: Longest acting. 22% of the drug is released immediately, and the rest is released at a controlled rate. Cannot be crushed/broken

Briars et al. A review of pharmacological management of attention-deficit/hyperactivity disorder. *J Pediatr Pharmacol Ther* 2016.

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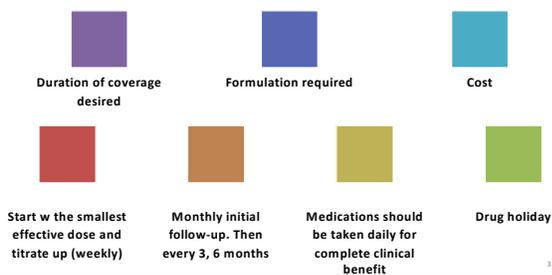
### Amphetamine

- Adderall, Dexedrine, Vyvanse
  - Dexedrine (Dextroamphetamine) – IR and XR (4-6; 6-8 hrs)
  - Adderall (Dextroamphetamine + amphetamine) – IR and XR (4-6; 8-10 hrs)
  - Vyvanse (Lisdexamphetamine) – 10 hrs
- Can be opened and placed on food
- Delay in absorption of ~2.5 hrs if taken w a high-fat meal

Briars et al. A review of pharmacological management of attention-deficit/hyperactivity disorder. *J Pediatr Pharmacol Ther* 2016.

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### General Strategies for Stimulant Use



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### Titration Examples

	Adderall XR 10-20mg daily	Ritalin 5-10mg daily	Focalin XR 10-20mg daily	Vyvanse 30mg daily
Week 1 • Start at a low dose. Allow patient to self-titrate at low dose.				
Week 2 • If needed, advance dose weekly.	Adderall XR 30mg daily	Ritalin 20mg daily	Focalin XR 30mg daily	Vyvanse 40mg daily
Week 3	Adderall XR 40mg daily	Ritalin 30mg daily	Focalin XR 40mg daily	Vyvanse 50mg daily
		... etc...		
I continue to titrate if needed to a max dose of...	60mg daily	60mg daily	40mg daily	70mg daily

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### Stimulants: Adverse Effects

- Generally dose dependent
- Most common
  - Appetite suppression +/- weight loss
  - Sleep disturbances
- Other
  - Abdominal discomfort
  - Headaches, irritability, anxiety
  - Conflicting data on growth impact
    - 1-2 cm height loss that is sustained, but dependent on dose/duration of tx
  - Stimulants may worsen tics
    - Tics affect 2-12% of the general population, and about 20% of patients w ADHD
    - Presence of tics is not a contraindication for stimulant use

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### Stimulants: Adverse CV Effects

- Small increases in HR and BP; significant elevations are rare.
  - Initial titration phase
  - Responsive to dosing/timing adjustments
  - SBP  $3.5 \pm 11.8$ mmHg, DBP  $4 \pm 8.5$ mmHg
  - HR  $4.5 \pm 10.5$ bpm
- No association b/wn stimulant use (at prescribed doses to tx ADHD) and serious CV events
  - QTc prolongation
  - Torsades
  - Sudden cardiac death
  - MI or stroke

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### Stimulants: Adverse CV Effects

- All pts should be screened for BP, HR, CV problems
- Use caution in patients with a h/o, Fhx of, or RF for CVD
- Do NOT use stimulants or atomoxetine in patients with serious heart problems or in which  $\uparrow$  in HR/BP would be problematic
- No evidence to support EKG screening prior to stimulant use
- Monitor BP and HR only if underlying medical condition that would be compromised by increases in BP or HR
- Investigate any abnormalities immediately

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### Non-Stimulants: Atomoxetine

General	<ul style="list-style-type: none"> <li>• Selective NE reuptake inhibitor               <ul style="list-style-type: none"> <li>• results in increased DA and NE in PFC</li> </ul> </li> <li>• As effective or less effective than stimulants in RCT (depending on the stimulant/formulation)</li> </ul>
Dosing	<ul style="list-style-type: none"> <li>• Starting dose: 40mg daily.</li> <li>• Max dose: 100mg daily (1-2x/day dosing).</li> <li>• Can be stopped abruptly. No need to taper.</li> </ul>
Response	<ul style="list-style-type: none"> <li>• 1-2 wks for an initial response</li> <li>• 4-6 wks for full therapeutic effect</li> <li>• May continue to have improvement for up to 2 months</li> </ul>
Side effects	<ul style="list-style-type: none"> <li>• Relatively well tolerated.</li> <li>• SE = somnolence, dry mouth, GI upset/nausea (esp if dose advanced too quickly), reduced appetite (tends to improve over time), increase in HR or BP</li> <li>• Case reports of severe liver injury</li> <li>• Black box warning – potential to increase SI</li> </ul>

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## When to Refer?

- Your comfort levels
  - Making the diagnosis
  - Prescribing the medication
- Extreme dysfunction due to ADHD symptoms
- Previous treatment failures
- Psychiatric comorbidities
  - Suicidal or homicidal
  - Psychosis
  - Needing diagnosis clarification on other psychiatric disorders (e.g. PTSD, bipolar, personality disorders)
  - Substance abuse

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## Summary

- ADHD is a developmental disorder of executive dysfunction that can result in impairing symptoms of inattention and hyperactivity/impulsivity.
- Adult ADHD refers to the persistence of ADHD symptoms into adulthood.
  - Up to 2/3 of children with ADHD will have some ongoing symptoms as an adult.
- Psychiatric comorbidity is common

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## Summary

- Diagnosis is clinical and can be supported by rating scales and/or neuropsych testing
- ADHD is not the most common reason for poor concentration in adults
- Treatment options include:
  - Psychopharmacology – Stimulants, Atomoxetine
  - Psycho-education, psychotherapy, behavioral strategies
  - Education/vocational accommodations

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Questions?

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## Supplemental Slides

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## Peripartum Considerations

- Women with ADHD are more likely than those without to:
  - Experience problems with sleep and chronic pain
  - Have impairment in daily activities
  - Have substance/alcohol use disorders, MDD, GAD
- Two small studies suggest adverse effects of ADHD in women on their:
  - Parental self-esteem
  - Ability to parent effectively - problem-solve during child-rearing and monitor their child's behavior

Banks T, et al. J Child Fam Stud. 2008;17(1):28-43.  
Marraccini ME, et al. Journal of midwifery & women's health. 2017;62(6):684-95.

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## Peripartum Considerations

- Limited data on the possible effects of ADHD medications used in pregnancy and with breast-feeding.
- “The drugs used for the treatment of ADHD are apparently not teratogenic, but due to paucity of data, especially on the long-term neurodevelopmental outcome, the treating physician should reconsider the need of treatment during pregnancy. If needed, methylphenidate, amphetamines and bupropion are preferred drugs.”

Ornoff A. Pharmacological Treatment of Attention Deficit Hyperactivity Disorder During Pregnancy and Lactation. Pharm Res. 2018.

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## Abuse Potential – Black Box Warning

- 1 out of 5 students w ADHD are asked to give, sell, or trade their medications
  - Stimulant misuse is seen in up to 9% of grade + high school students ...
  - ... and up to 35% of college-age individuals
- 6.6% of US adults (16 million) used prescription stimulants (2015-2016)
  - 68% (11 million) used these medications without misuse
  - One in three users (31.2%) reported misuse at least once
  - 2.7% had a prescription stimulant use disorder
- Most common source = friends and family members (56.9%)
- Most common reason for misuse = direct stimulant effect to improve performance (78%)
  - Nonmedical use of prescription stimulants is not associated with performance improvement

Harstead E, et. ADHD and substance abuse. Am Acad Ped, 2014. Compton et al. The American Journal of psychiatry. . 2018. Vol175(8), p. 743-750. Arria AM, et al. Addict Behav 2013; 38: 1643–1650. Arria AM, et al. Addict Behav 2017; 65:245–249.

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### Controlled Substance Agreements

- Establishes clear expectations between the patient and provider
  - Lost/stolen prescriptions
  - Early refills
  - Excessive alcohol use
  - Illicit drug use
  - One prescribing provider/pharmacy
- Consider review every 1-3yrs
- Random urine drug screen
  - At least yearly
  - Can also help assess compliance with medication

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### ADHD and Comorbid Substance Use Disorder

- Does pharmacologic tx of ADHD reduce the risk for substance abuse?
  - Tx of ADHD sx's may reduce the risk of developing SUDs
    - 85% reduction in risk of SUDs in youth w ADHD.
    - Those treated at a younger age less likely to use than those w delayed tx
  - Systematic review of meta-analysis: Pharmacological tx of ADHD in pts w comorbid SUDs:
    - ADHD sx's improve compared to placebo
    - No benefit on substance use outcomes
  - 2 RCTs show that using robust dosing of stimulants (OROS-MPH up to 180mg daily, Adderall XR 80mg daily), having a larger effect on ADHD sx's, was a/w drug abstinence
- Decisions about the type of pharmacological intervention and when to begin tx should be based on safety

Cunill R et al. Pharmacological treatment of ADHD w co-morbid drug dependence. Psychopharm. 2015. Luo et al. Towards Precision Addiction Tx - new findings in comorbid substance use and ADHD. Curr Psychiatry Rep. 2017. Harstad E, et. ADHD and substance abuse. Am Acad Ped. 2014. Biederman J, et al. Pharmacotherapy of ADHD reduces risk for SUD. Pediatrics. 1999;104(2).

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