

# Advanced Concepts: ADHD - One Child Many Trajectories

S. Sutton Hamilton, MD



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Dr. Hamilton is a graduate of Duke University, Durham, North Carolina, and earned his medical degree at the University of Pittsburgh School of Medicine in Pennsylvania. He completed his internship and family medicine residency at Franklin Square Hospital, Baltimore, Maryland, where he served as chief resident. At the University of Cincinnati, Ohio, he completed a fellowship in faculty development and received additional training in developmental pediatrics and adolescent medicine. Prior to joining the faculty of Inspira Family Medicine Residency, he served as assistant program director at Blackstone Family Practice Residency in Virginia. Dr. Hamilton's clinical interests include the evaluation and management of children who have attention-deficit/hyperactivity disorder (ADHD), learning difficulties, and emotional/behavioral problems. He has been published in *American Family Physician* and *UpToDate* on the topics of developmental pediatrics and emotional/behavioral problems. He obtained his Drug Abuse Treatment Act (DATA) waiver and treats individuals who have opioid use disorder.

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# Learning Objectives

1. Recognize common problems that develop among children with a history of ADHD as they become adolescents and young adults.
2. Explain how current research suggests treatment for children can attenuate risk for serious adolescent and adult psychopathology.
3. Describe the apparent paradox of adult onset ADHD in the absence of a history of childhood ADHD and list appropriate diagnostic pathways for the proper assessment of such individuals.

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# Audience Engagement System



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## Childhood ADHD and adult outcomes



## FMX 2019: ADHD: One Child, many trajectories

**More plainly:** What are the long term implications, risks, associated with childhood onset ADHD?

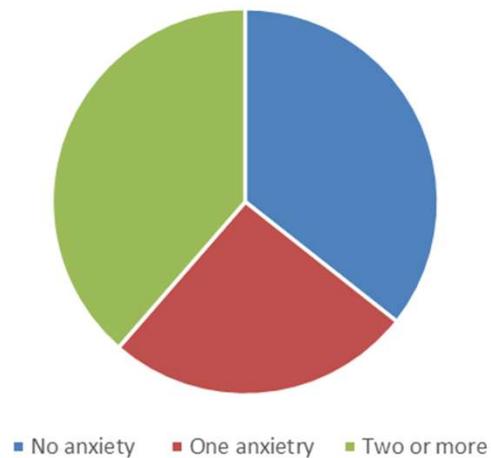
**More importantly:** what can we do as physicians to bend this trajectory in a more favorably direction and mitigate risk?

## ADHD and Anxiety ( in childhood )

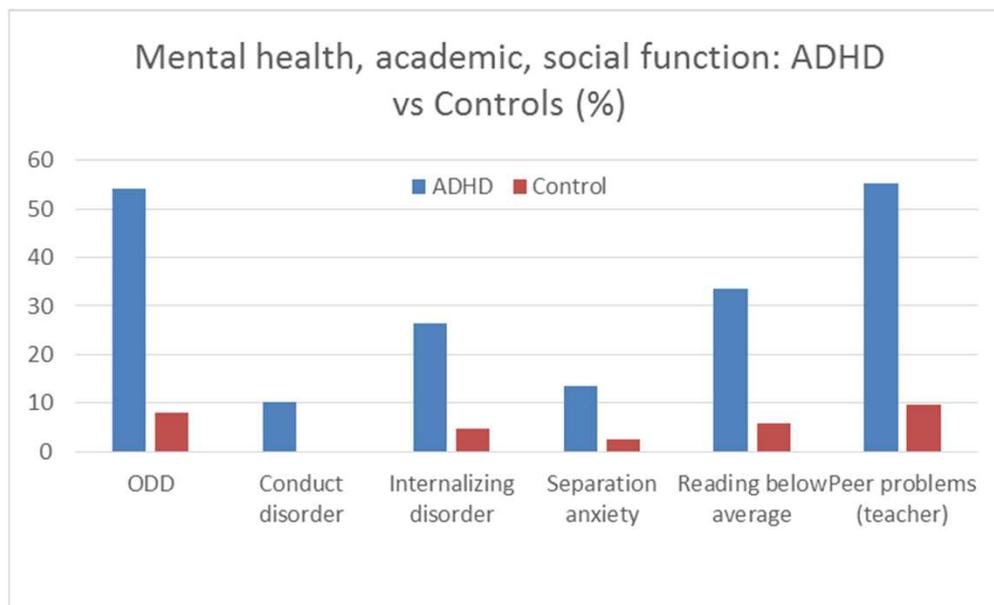
- ▶ ADHD and anxiety commonly co-occur (unclear mechanism)
- ▶ Approximately 25-50% suffer from at least one anxiety disorder.
- ▶ Children with co-existing anxiety tend to be less impulsive, but have more attentive, cognitive and executive skill issues.
- ▶ Co-existing anxiety associated with lower quality of life.

Sciberras E, et al. Anxiety in Children with Attention-Deficit/Hyperactivity Disorder. Pediatrics 2014; 133:801-08

Co-existing anxiety disorders



Sciberras E, et al. Anxiety in Children with Attention-Deficit/Hyperactivity Disorder. Pediatrics 2014; 133:801-08



Efron D et al. Functional Status in Children With ADHD at Age 6-8: A Controlled Study. Pediatrics 2014; 134:e992-1000

## Predictors of emotional problems in adulthood among children with ADHD

- ▶ High comorbidity (  $p < .001$  )
- ▶ High ADHD symptom severity (  $p < .001$  )
- ▶ Harsh discipline (  $p < .001$  )
- ▶ Possessive / protective parenting style (  $p < .001$  )
- ▶ Lack of parental affection (  $p < .001$  )

Roy A, Hectman L, Arnold LE et al. Childhood predictors of adult functional outcomes in the Multimodal Treatment Study of ADHD (MTA). J Am Acad Child Adolesc Psychiatry 2017; 56:687-695

## Poll Question 1

Which of the following is NOT true about young children with ADHD?

- ▶ A. Anxiety is commonly co-occurring.
- ▶ B. It is common for a child with ADHD to meet criteria for more than one anxiety disorder
- ▶ C. Anxiety has not been associated with significant reduction in quality-of-life in children with ADHD.
- ▶ D. Children with anxiety are less impulsive than other children with ADHD.

## ADHD in childhood and subsequent anxiety in adolescence, young adulthood

	ADHD - symptom persisters	ADHD Symptom desisters	Control Group	Odds Ratio (persisters vs. desisters)
Emotional lability (parent report)	1.50	.58	.44	
Emotional lability (self-report)	.91	.46	.42	
Anxiety	14.2%	5.0%	8.1%	3.1
Depression	7.8%	1.8%	3.4%	4.6
Deaths	10 (persisters+ desisters)		1	

Hectman et al. Functional Adult Outcomes 16 Years After Childhood Diagnosis of Attention-Deficit/Hyperactivity Disorder: MTA Results. J Am Acad Child Adolesc Psychiatry 2017; 56:687-95

## ADHD: Natural History

	ADHD - SX persistent	ADHD- SX remission	Control Group
Completed college	8.0%	17.8%	37.1%*
Public assistance	22.2%	9.6%	3.2%
Substance use disorder	38.5%	28.7%	26%

Hectman L et al. Functional Adult Outcomes 16 Years After Childhood Diagnosis of Attention-Deficit/Hyperactivity Disorder: MTA Results. *J Am Acad Child Adolesc Psychiatry* 2017; 56:687-95

## What factors in childhood affect the persistence of ADHD into adulthood?

	Increase in likelihood of persistence (OR)	As a percentage	
Childhood co-morbidity	1.15	15%	
Parental mental health problems	1.35	35%	
Parental marital relationship problems	1.36	36%	
Appropriate parental discipline	0.61	-39%	

Roy A, Hechtman L, Arnold LE, Sibley MH, Molina BS, Swanson JM, Howard AL; MTA Cooperative Group. Childhood Factors Affecting Persistence and Desistence of Attention-Deficit/Hyperactivity Disorder Symptoms in Adulthood: Results From the MTA. *J Am Acad Child Adolesc Psychiatry*. 2016 Nov;55:937-944

## Is childhood ADHD a marker for adult criminality?

- ▶ What are the societal and patient-related implications?
- ▶ What is the effect of treatment in weakening the correlation between childhood ADHD and adult criminality?

**Meta-analysis:**  
15,442 individuals with ADHD from 9 distinct (international) samples.

	RR	95% CI	p=	
Arrest	2.2	1.3 - 5.5	.002	
Conviction	3.3	2.1 - 5.2	.001	
Incarceration	2.9	1.9 - 4.3	.001	

Mohr-Jensen C et al. A meta-analysis and systematic review of the risks associated with childhood attention-Deficit hyperactivity disorder on long-term outcomes of arrests, convictions, and incarcerations. Clin Psychol Rev. 2016; 48:32-42

## ADHD and criminality: Nationwide (Denmark)

- ▶ Studies show childhood ADHD associated with 2-3 fold increased risk of arrest, conviction and incarceration
- ▶ Nationwide Danish study with 4231 youth with ADHD diagnosis, control group of 19,295 ( without ADHD)
- ▶ History of conviction: ADHD group = 32%; control group conviction rate 15.6%
- ▶ Hazard ratio associated with ADHD = 2.4 ( entire sample ); HR = 2.4 (male ) and **4.7 ( female)**

Mohr-Jensen C et al. Attention-Deficit/Hyperactivity Disorder in Childhood and Adolescence and the Risk Of Crime in Young Adulthood in a Danish Nationwide Study. J Am Acad Child Adolesc Psychiatry. 2019; 58:443-452

## ADHD and Criminality: Can medication attenuate the correlation? Mohr-Jensen et al. 2019

- ▶ Periods of ADHD medication use were associated with significant risk reduction (20%) for conviction and incarceration.
- ▶ While receiving medical treatment HR - 0.8
- ▶ No association was found between treatment with SSRI with respect to conviction / incarceration
- ▶ Suggests it's the medication itself, and medical adherence is not a confound.

Mohr-Jensen C et al. Attention-Deficit/Hyperactivity Disorder in Childhood and Adolescence and the Risk Of Crime in Young Adulthood in a Danish Nationwide Study. J Am Acad Child Adolesc Psychiatry. 2019; 58:443-452

## Poll Question 2

What is the advantage of inter-individual comparison?

- ▶ A. It eliminates confounds.
- ▶ B. It reduced many person-specific confounds.
- ▶ C. It reduces the need for long study duration.
- ▶ D. It increases study applicability compared with a randomized controlled study.

## ADHD and Criminality: Can medication attenuate the correlation? Lichtenstein et al. 2012

- ▶ Compared with nontreatment period, treatment was associated with a 20-30% reduction in conviction.
- ▶ A “within-patient” analysis accounts for confounds that remain present in individual ( e.g. genetic, early environmental factors).
- ▶ Whereas stimulant discontinuation was associated with increased incarceration, no correlation was found with SSRI discontinuation.
- ▶ “Inverse relationship between ADHD treatment and incarceration, conviction.”

Lichtenstein P et al. Medication for Attention Deficit-Hyperactivity Disorder and Criminality. N Engl J Med 2012; 367:2006-14

## ADHD and risk for substance use disorder (SUD) in adulthood.

- ▶ Twice as likely to smoke ( OR = 2.08)
- ▶ Three times as likely to report nicotine dependence ( OR 2.82)
- ▶ Nearly twice as likely to meet diagnostic criteria for alcohol abuse or dependence ( OR 1.74)
- ▶ Approximately 1.5 times as likely to meet criteria for marijuana use disorder ( OR = 1.58)
- ▶ Twice as likely to develop cocaine abuse or dependence ( OR = 2.05)
- ▶ Approximately 2.5 times as likely do develop SUD overall ( OR = 2.5)

Lee SS et al. Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and Substance use and abuse/dependence: a meta-analytic review. Clin Psychol Rev 2011; 31:328-41

## ADHD and SUD

- ▶ Prescribing methods to reduce prescription abuse and diversion
  - ▶ Medication secured by parent who observes administration.
  - ▶ Use of long-acting stimulants including especially
    - ▶ Osmotic-controlled release delivery system (OROS methylphenidate)
    - ▶ Prodrug lisdexamphfetamine
    - ▶ Non-stimulants such as Guanfacine XR and Atomoxetine

## Does childhood treatment with stimulants reduce risk for substance use disorder in adulthood?

- ▶ Swedish registry: 26,249 men and 12,504 women who had ever received an outpatient diagnosis of ADHD.
- ▶ Approximately 50% age 8-15 years, 30% 16-25 years.
- ▶ Databases allowed for within-individual comparisons between when a given person is
  - (a) taking stimulant versus
  - (b) periods where the individual was off medication.

Chang Z et al. Stimulant ADHD medication and risk for substance abuse. J Child Psychol Psychiatry 2014; 55:878-85

## Does treatment (adolescent, adult) with stimulants reduce risk for SUD?

- ▶ Within-individual comparisons, medication use associated with lower rate of concurrent substance-related events **HR 0.65** (male) **HR 0.69** (female).
- ▶ That is, there was a roughly 30% reduction in SUD events associated with taking ADHD medication.
- ▶ The longer an individual took medication, the lower the risk for substance abuse.

Chang Z et al. Stimulant ADHD medication and risk for substance abuse. J Child Psychol Psychiatry 2014; 55:878-85

## Does treatment in childhood reduce risk for adolescent substance use disorder?

- ▶ Less substance use when:
  - ▶ Stimulant therapy used instead of non-stimulant.
  - ▶ Early age of onset of medical treatment.
  - ▶ Longer duration of medical treatment.

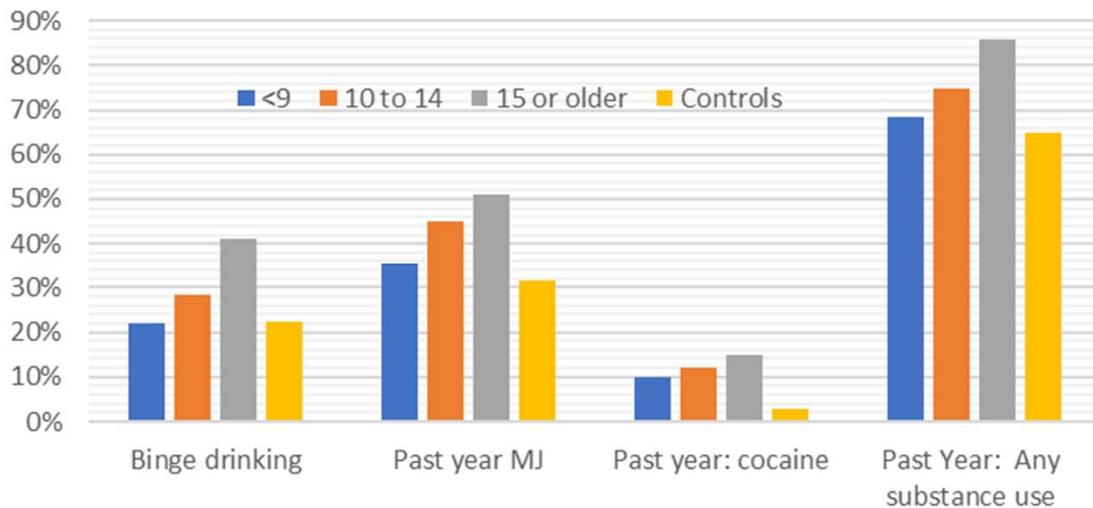
McCabe SE et al. Age of Onset, Duration, and Type of medication Therapy for Attention-Deficit Hyperactivity Disorder and Substance Use During Adolescence: A Multi-Cohort National Study. J Am Acad Child Psychiatry 2016; 55:479-486

## Does the age of initiation of treatment affect long-term outcomes?

Age of stimulant initiation	Binge drinking	Past year MJ	Past year: cocaine	Past Year: Any substance use
<9	22.1%	35.3%	9.9%	68.5%
10-14	28.5%	45.1%	12.2%	74.8%
15 or older	41.1%	51.1%	14.8%	85.7
Controls	22.4%	31.5%	3.0%	65.0%

McCabe SE et al. Age of Onset, Duration, and Type of medication Therapy for Attention-Deficit Hyperactivity Disorder and Substance Use During Adolescence: A Multi-Cohort National Study. J Am Acad Child Psychiatry 2016; 55:479-486

### Age of treatment initiation and substance use



### Poll Question 3

Which of the following statements is true about ADHD and SUD?

- ▶ A. More than one half of children with ADHD describe problematic cocaine use in adulthood.
- ▶ B. Observational data suggests that early treatment of ADHD reduces SUD in adulthood.
- ▶ C. Randomized studies of over twenty year's duration have proven that treatment reduces subsequent SUD.
- ▶ D. Treatment of ADHD in childhood with stimulants likely increases the risk for subsequent SUD or problematic drug use.

## Medication use for ADHD and risk for MVA (adults) - Chang Z et al. JAMA Psychiatry 2017

- ▶ US cohort of patients with ADHD ( 2,319,450).
- ▶ Risk of MVA for individuals with ADHD
  - ▶ 44% greater risk in men
  - ▶ 49% greater risk in women
- ▶ “Inter-individual design” used to account for variety of confounds including “confounding by indication.”

## Association Between Medication Use for ADHD and Risk of MVA. Chang Z et al. JAMA Psychiatry 2017

Variable	No. person-months at risk	Number of MVA	Odds ratio: Population:	Within-individual
<u>Men</u>				
-medicated	11,538,041	2250	0.88 (0.84-0.93)	0.62 ( 0.57-0.67)
-unmedicated	12,945,705	3151	1 ( reference)	1 (reference)
<u>Women</u>				
-medicated	14,045,478	2960	0.86 (0.82-0.90)	0.58 (0.53-0.62)
-unmedicated	12,138,441	3134	1 ( reference)	1 (reference)

## Poll Question 4

Which of the following are true about adults with ADHD?

- ▶ A. They are less likely to be involved in motor vehicle crashes.
- ▶ B. Randomized studies show that treatment reduces crashes.
- ▶ C. It's hard to imagine how ADHD could increase the risk of motor vehicle crashes.
- ▶ D. Observation studies show that people are in fewer crashes when they are taking their medication compared with when they are not.

## ADHD and mortality: Dalsgaard S et al. Lancet 2015

- ▶ 1,922,248 individuals followed up to age 32 ( or their death)
- ▶ 44,883 individuals (2-3%) lost to follow-up ( almost entirely due to emigration from Denmark)
- ▶ 32,061 individuals with ADHD ( 1.7% of population)
- ▶ ADHD diagnosis was associated with approximately a doubled mortality rate (mostly in the form of accidents)
- ▶ Girls/women diagnosed with ADHD had greater relative risk for death (3.01 vs. 1.93) compared with boys/men.

Dalsgaard S et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a Nationwide cohort study. Lancet 2015; 385:2190-6

## ADHD and mortality: 32-year prospective cohort study

Cohort	Participants	Person-years	Deaths	Death rate per 10,000 person-years	Mortality Rate Ratio*
	N = 1,922,248	24,907,560	5580	2.24	
ADHD	32,061	183,049	107	5.85	2.07*
No ADHD	1,890,187	24,724,511	5473	2.21	1.0

\* “fully adjusted,” the most conservative estimate. The “crude” MRR = 2.44

Dalsgaard S et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a Nationwide cohort study. *Lancet* 2015; 385:2190-6

## The many potential trajectories for a child with ADHD

- ▶ Randomized studies demonstrate the clear superiority of intensive management with stimulants.
- ▶ Beyond this 14 month randomized study we are reliant on observational studies.
- ▶ While we are reluctant to draw causal inferences, a pattern emerges with these studies:

## The many potential trajectories for a child with ADHD

- ▶ Treatment in childhood correlates with subsequent decreased substance use.
- ▶ This correlation seems “dose dependent” with children who receive a longer duration of more effective therapy, whose therapy is initiated relatively early experiencing the greatest reduction in subsequent substance use.
- ▶ Adults with symptom-remission do better on many important measures, including educational achievement, mental health, SUD.
- ▶ Adults with ADHD, when taking their medication, get in fewer motor-vehicle crashes, have fewer SUD related events and get arrested less frequently.

## Practice Recommendations

- ▶ Recognize that even young children with ADHD often have substantial burden in co-existing conditions (e.g. anxiety, peer problems, ODD).
- ▶ Determine whether or not significant anxiety exists in a child with ADHD.
- ▶ Strive to achieve symptoms resolution for children, adolescents and young adults with ADHD as this correlates with better adult outcomes.
- ▶ Educate families that treatment with ADHD, especially with stimulants, is a research-based means of decreasing subsequent SUD, improving educational outcomes, reducing motor vehicle crashes and reducing ADHD-attributable mortality.

## Contact Information

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## Questions

