



Definitions and Overview of ADHD

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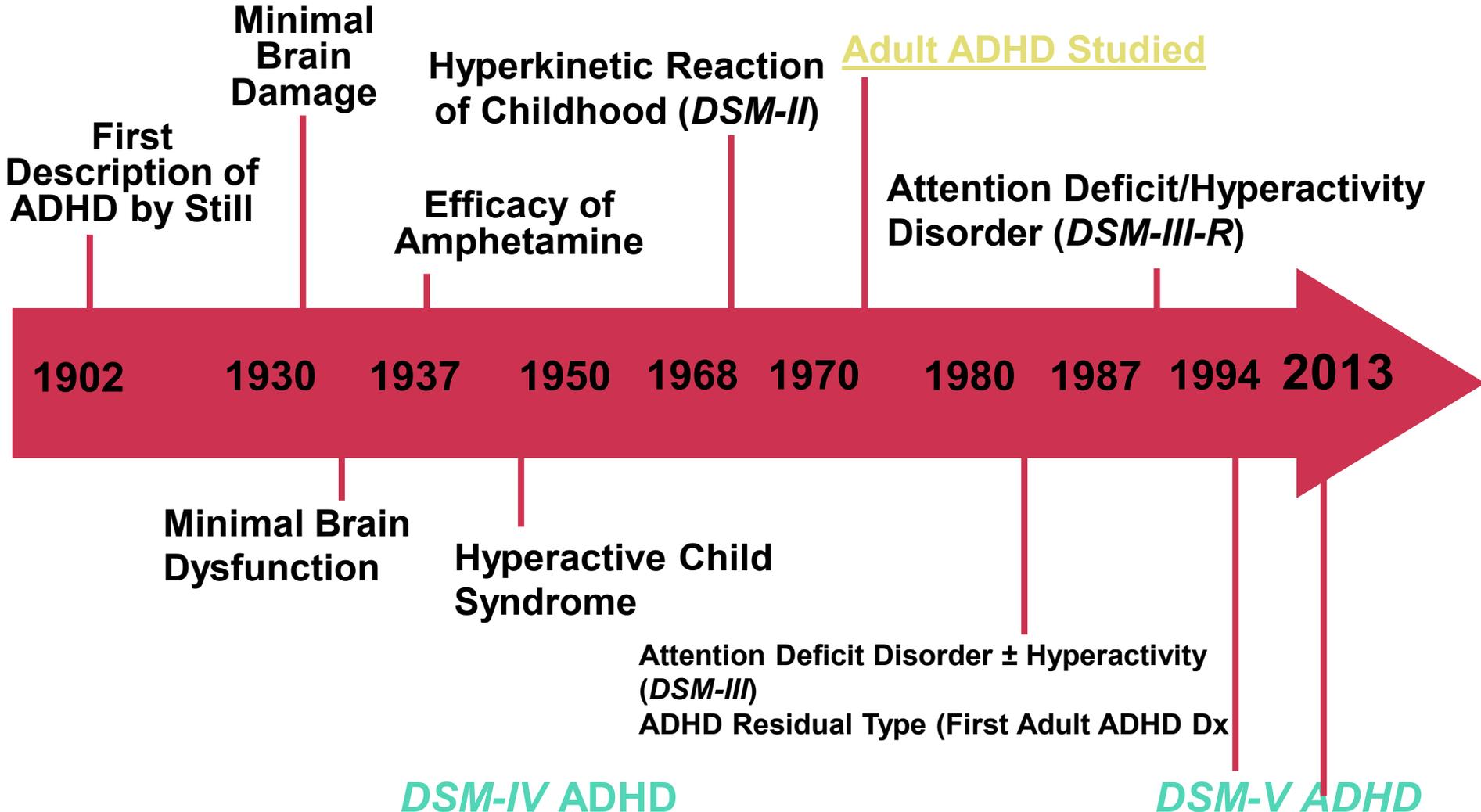
Massachusetts General Hospital

Disclosures 2020-2021

My spouse/partner and I have the following relevant financial relationships with commercial interests to disclose:

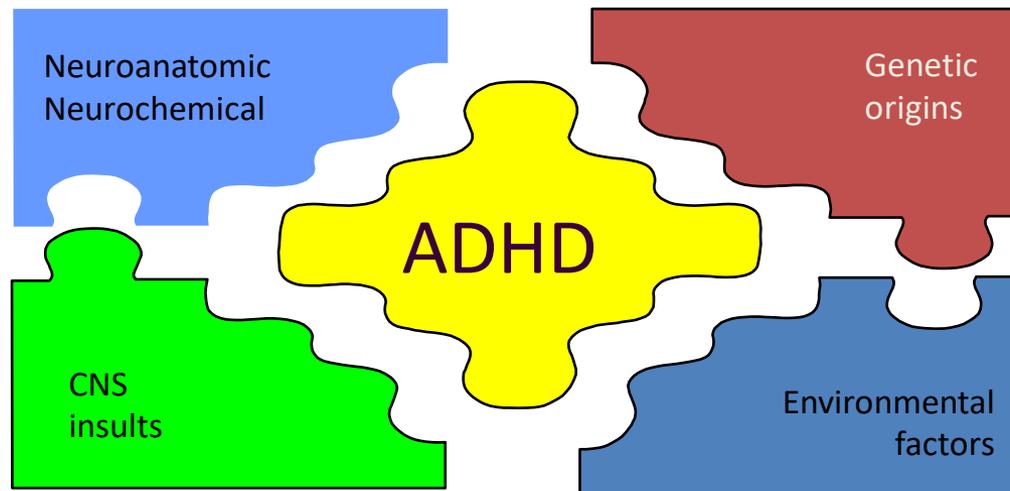
- *Research support:* Genentech, Headspace Inc., Pfizer Pharmaceuticals, Roche TCRC Inc., Sunovion Pharmaceuticals Inc., Takeda/Shire Pharmaceuticals Inc., and Tris.
- *Consulting fees:* Akili, Avekshan LLC, Jazz Pharma, and Shire/Takeda
- *Honorarium for scientific presentation:* Tris
- *Royalties paid to the Department of Psychiatry at MGH, for a copyrighted ADHD rating scale used for ADHD diagnoses:* Biomarin, Bracket Global, Cogstate, Ingenix, Medavent Prophase, Shire, Sunovion, and Theravance
- Through Partners Healthcare Innovation, I have a partnership with MEMOTEXT to commercialize a digital health intervention to improve adherence in ADHD.

ADHD: Timeline of Definitions



ADHD: Etiology

ADHD is a heterogeneous behavioral disorder with multiple possible etiologies



Diagnosis of ADHD

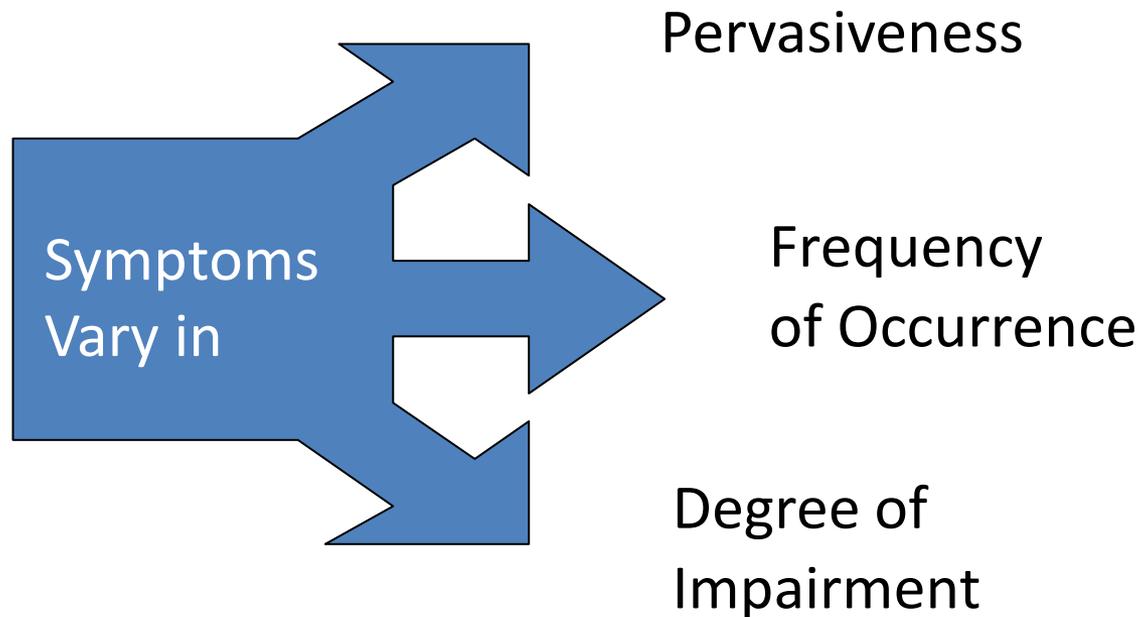
- Diagnosis is based on clinical assessment of symptoms, associated impairment and age of onset
- No test is available
- Symptoms are subjective, as well as developmentally and context sensitive

ADHD: Core Symptom Areas

Inattention

Impulsivity/Hyperactivity

ADHD: Variation in Symptoms



ADHD: DSM-5 Criteria

Inattention

Six or more of the following – manifested *often*:

- Inattention to details/
makes careless mistakes
- Difficulty sustaining
attention
- Seems not to listen
- Fails to finish tasks
- Difficulty organizing
- Avoids tasks requiring
sustained attention
- Loses things
- Easily distracted
- Forgetful

Symptoms of Inattention Often Manifest Differently in Adults

DSM IV Symptom Domain

- Difficulty sustaining attention
- Does not listen
- No follow through
- Can't organize
- Loses important items
- Easily distractible, forgetful



Common Adult Manifestation

- Difficulty sustaining attention
 - Meetings, reading, paperwork
- Paralyzing procrastination
- Slow, inefficient
- Poor time management
- Disorganized

ADHD: DSM-5 Criteria

Impulsivity/Hyperactivity

Six or more of the following – manifested *often*:

Impulsivity

- Blurts out answer before question is finished
- Difficulty awaiting turn
- Interrupts or intrudes on others

Hyperactivity

- Fidgets
- Unable to stay seated
- Inappropriate running/climbing (restlessness)
- Difficulty in engaging in leisure activities quietly
- “On the go”
- Talks excessively

Symptoms of Hyperactivity Can Manifest Differently In Adults

DSM IV Symptom Domain

- Squirms and fidgets
- Can't stay seated
- Runs/climbs excessively
- Can't play/work quietly
- “On the go” / “Driven by motor”
- Talks excessively



Common Adult Manifestation

- Workaholic
- Overscheduled/overwhelmed
- Self-select very active job
- Constant activity
- Talks excessively

American Psychiatric Association. 1994. 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

Symptoms of Impulsivity Often Manifest Differently In Adults

Impulsivity in adulthood often carries more serious consequences

DSM IV Symptom Domain

- Blurts out answers
- Can't wait turn
- Intrudes/interrupts others

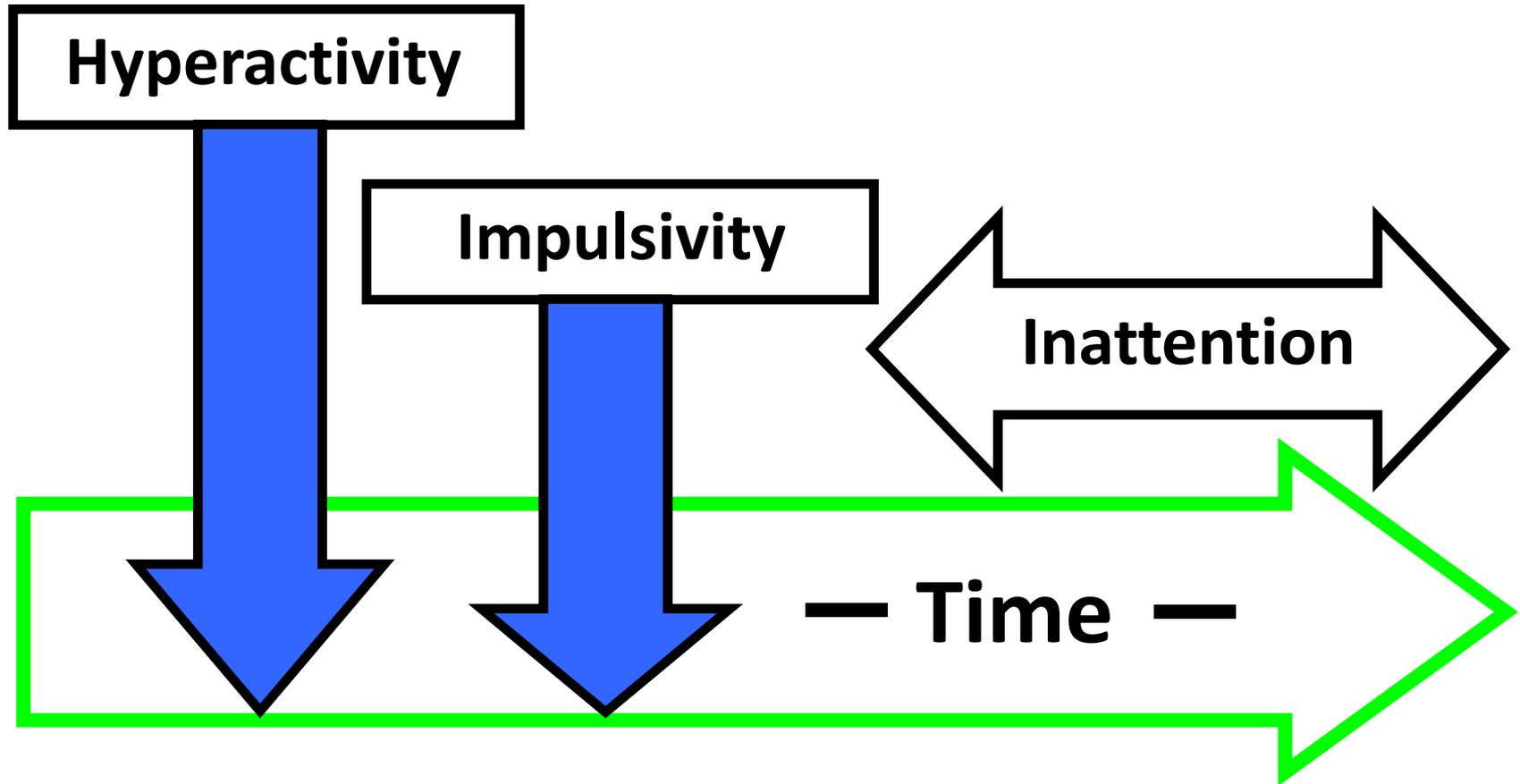


Common Adult Manifestation

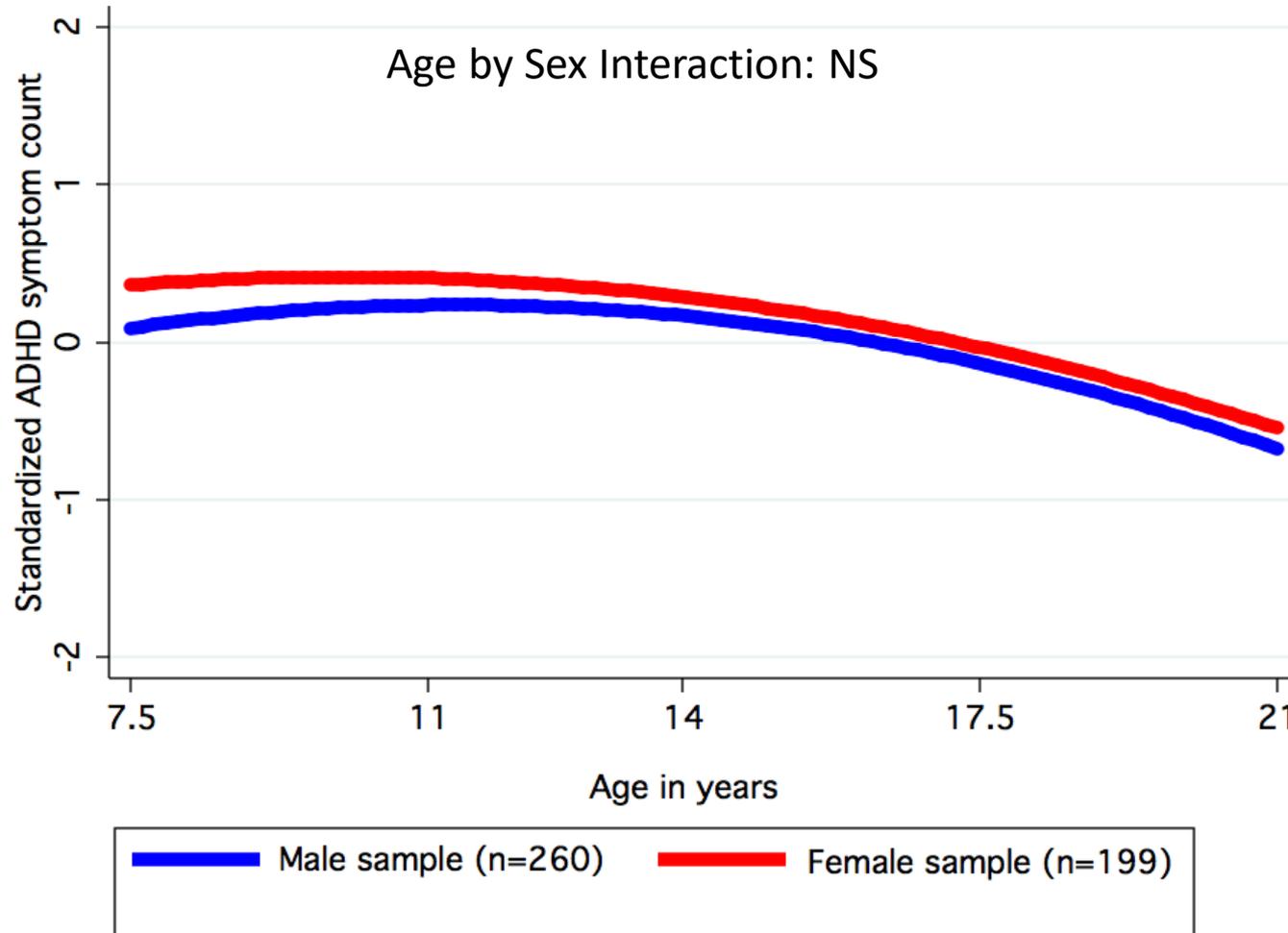
- Low frustration tolerance
 - Losing temper
 - Quitting jobs
 - Ending relationships
 - Driving too fast
 - Addictive personality

American Psychiatric Association. 1994. 83-85., ADHD in Adulthood 1999, Weiss, Hechtman and Weiss

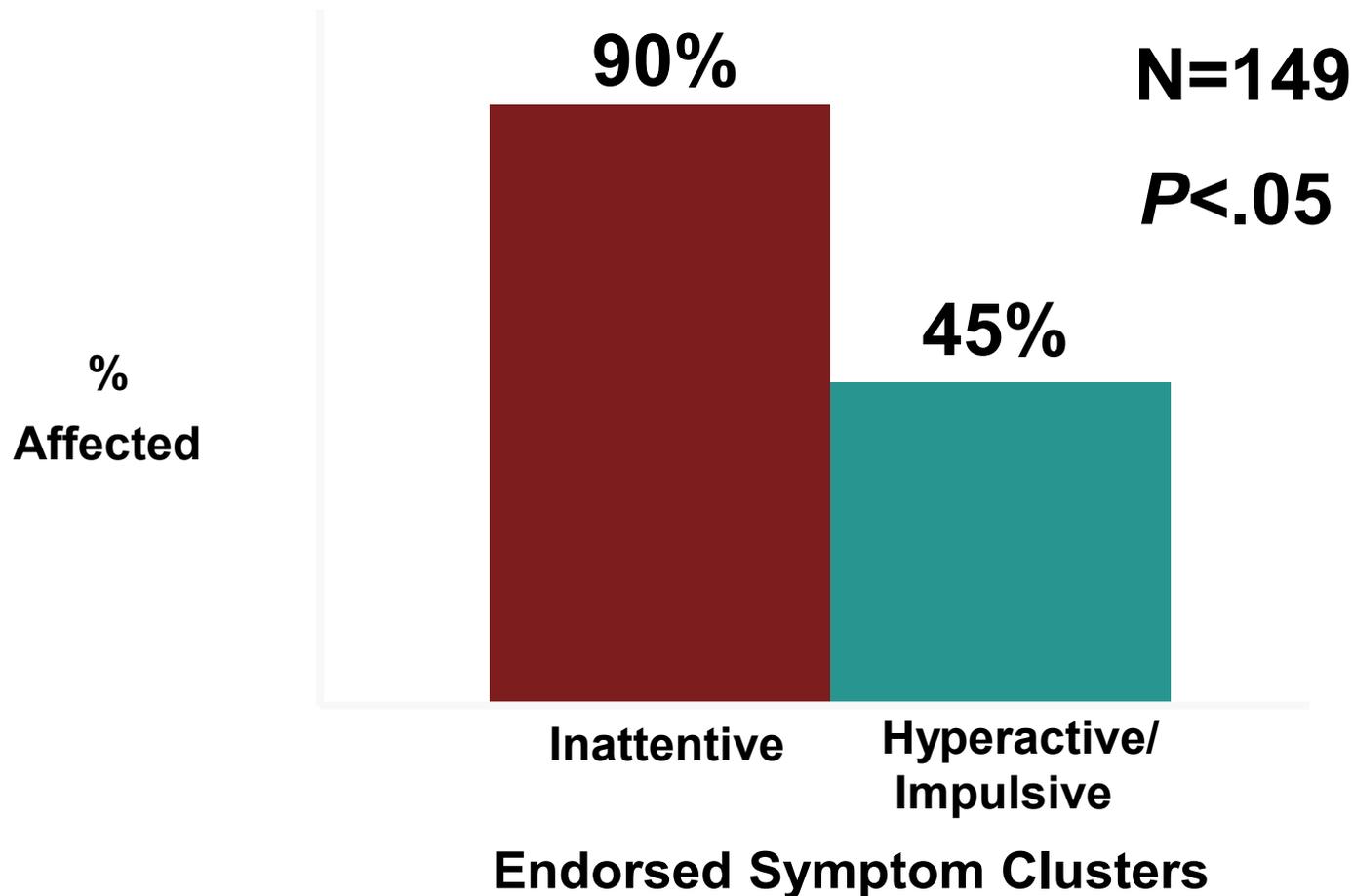
ADHD: Course of the Disorder



Course of ADHD Symptoms Over Time by Sex: A Growth Curve Model



Inattention Drives Presentation of ADHD in Adults



Millstein R et al. *J Atten Disord.* 1997;2:159-166.

Is ADHD a Valid Diagnosis in Adults?

**Comorbidity and
Neuropsychological
Deficits**

**Family-Genetic
Studies**



SYNDROMATIC CONTINUITY

**Imaging
Studies**



**Treatment
Effectiveness**

Impairments

Wender PH. *J Clin Psychiatry*. 1998;59(suppl 7):76-79.
Spencer et al. *J Clin Psychiatry*. 1998;59:59-68.

ADHD Impairment Persists

Childhood	▶▶▶	Adulthood
School failure or underachievement	Becomes	Job failure/underemployment
Multiple injuries	Becomes	Car accidents/injuries
Drug experimentation	Becomes	Addiction
Oppositional defiant or conduct disorder	Becomes	Antisocial personality disorder, criminality
Impulsivity, carelessness	Becomes	Unwanted pregnancy, sexually transmitted disease, divorce
Chronic failure	Becomes	Hopelessness, frustration, giving up

Changes in DSM-5 ADHD

- “Neurodevelopmental” - not “disruptive”
- $\geq 6/9$ inattentive or $\geq 6/9$ impulsive/hyperactive symptoms over last six months (>5 for adults)
- Symptoms caused impairment by age 12 (no longer 7)
- ASDs no longer exclusionary
- No more “subtypes”; Inattentive / Hyperactive-impulsive / Combined are now “Presentations”
- Restricted inattentive subtype: In Appendix, worthy of further study

Diagnosis of ADHD in Adults: Patient Compensation Efforts

Patient attempts to compensate and time invested in the compensation is an important diagnostic indication

Patients usually:

- Set up rigid schedules
- Pursue areas of interest with extreme zeal
- Seek careers/situations with controllable stimuli
- Make use of organizational tools
- Impose own “time-outs” during stimulus overload situations (take walks/disappear)

Diagnosis of ADHD in Adults: Common Clinical Histories

- Difficulties in elementary or secondary school
 - Comments: “not living up to potential,” “spacey,” “hyper”
 - Behavioral issues: “class clown”
- Difficulties in college
 - Incomplete degree or longer time to complete degree
 - Difficulty engaging in further education
- Difficulties at work
 - Underachievement (mixed reviews)
 - Low efficiency: Longer time to complete tasks
- Difficulties at home
 - Poor organization, does not complete tasks
 - Strained relationships with spouse and kids (who also may have ADHD)

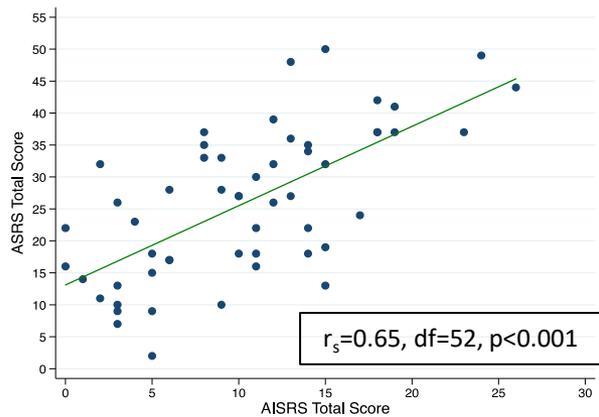
Diagnosis of ADHD in Adults: Validity of Self-Reports

- Self-report reliable and useful in diagnosis of ADHD in adults

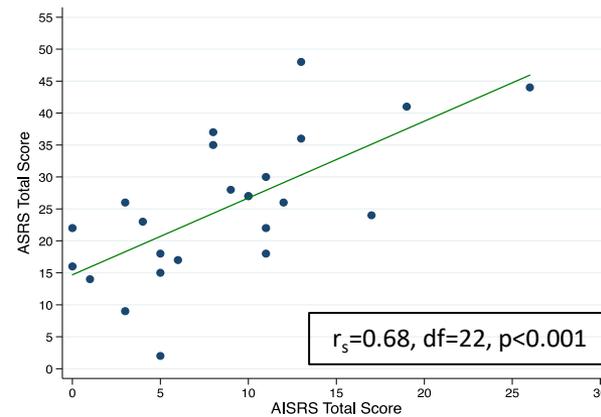
Murphy P, Schachar R. *Am J Psychiatry*. 2000;157:1156-1159; Conners CK. *J Clin Psych*. 1998;59(suppl 7):24-30; ASRS v1.1. Available at: www.adultADD.com/2_2_recognizing/screener.jsp. Accessed November 26, 2003.

Spearman's Rank Correlations Examining the Association between the AISRS (Clinician) and ASRS (SELF)

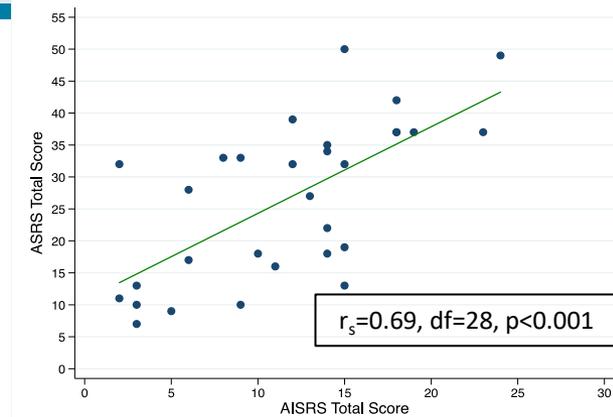
A. Whole Sample (N=54)



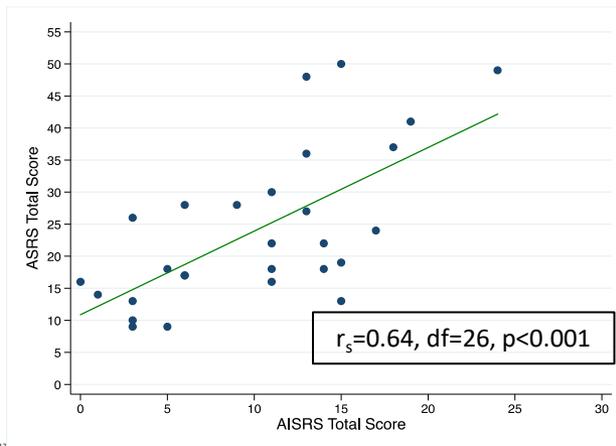
B. Males (N=24)



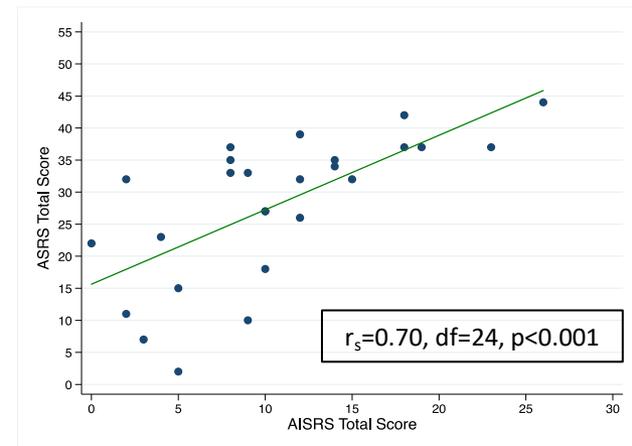
C. Females (N=30)



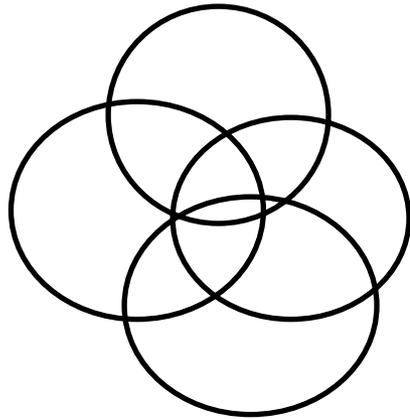
D. Age ≤40 Years (N=28)



E. Age >40 Years (N=26)



Comorbidity in ADHD



Antisocial Disorder (10%)

Major Depressive Disorder (35%)

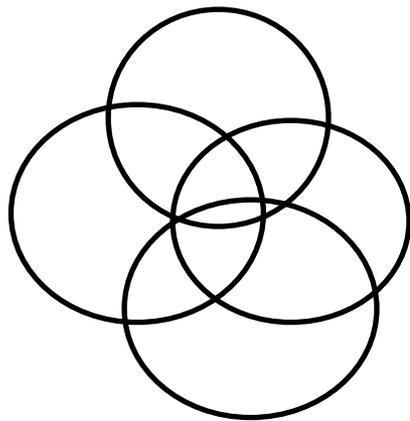
Bipolar Disorder (15%)

Anxiety Disorders (40%)

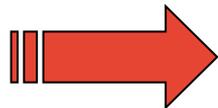
Substance Abuse Disorders (50%)

Shekim WO, et al. *Compr Psychiatry*. 1990;31:416-425.
Biederman J, et al. *Am J Psychiatry*. 1993;150:1792-1798.

ADHD Comorbidity in Other Psychiatric Disorders



<u>Disorder</u>	<u>ADHD Rate</u>
Major Depression ¹	20%
Bipolar Disorder ²	15%
Generalized Anxiety Disorders ³	20%
Substance Abuse ⁴	25%



Re-evaluate refractory patients for ADHD.

1. Alpert, et al. *Psychiatry Res.* 1996.
2. Nierenberg, et al. Presented at: APA; May 18-23, 2002; Philadelphia, Pa.
3. Fones, et al. *J Affective Dis.* 2000
4. Wilens. *Psych Clin N Am.* 2004.

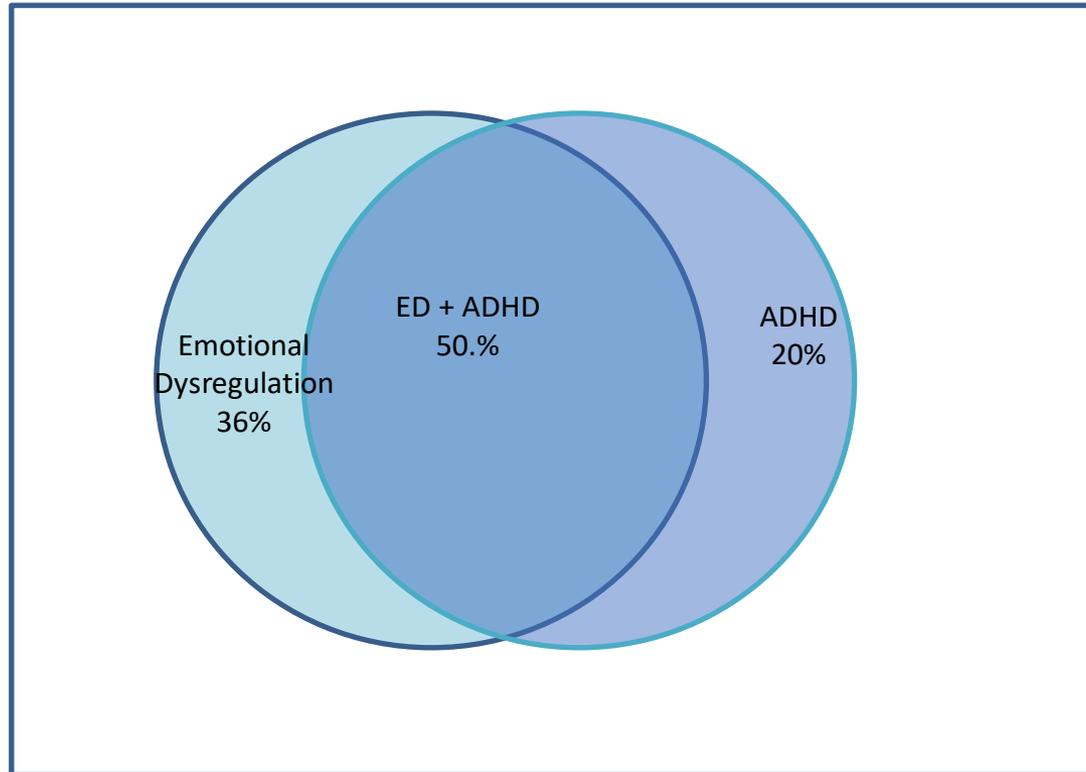
Deficient Emotional Self Regulation

1. Quick to get angry or become upset
2. Easily frustrated
3. Over-react emotionally
4. Easily excited by activities going on around me
5. Lose my temper
6. Argue with others
7. Am touchy or easily annoyed by others
8. Am angry or resentful

Scoring: Never (0), Sometimes (1), Often (2), Very Often (3)

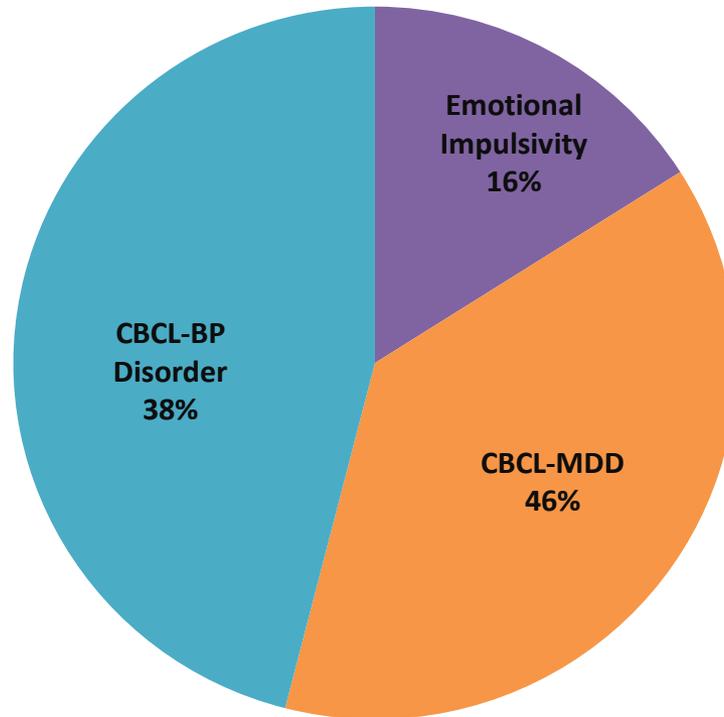
DESR: \geq 95th percentile of total scores in Controls

Overlap between ADHD and Emotional Dysregulation in Youth (N=496)



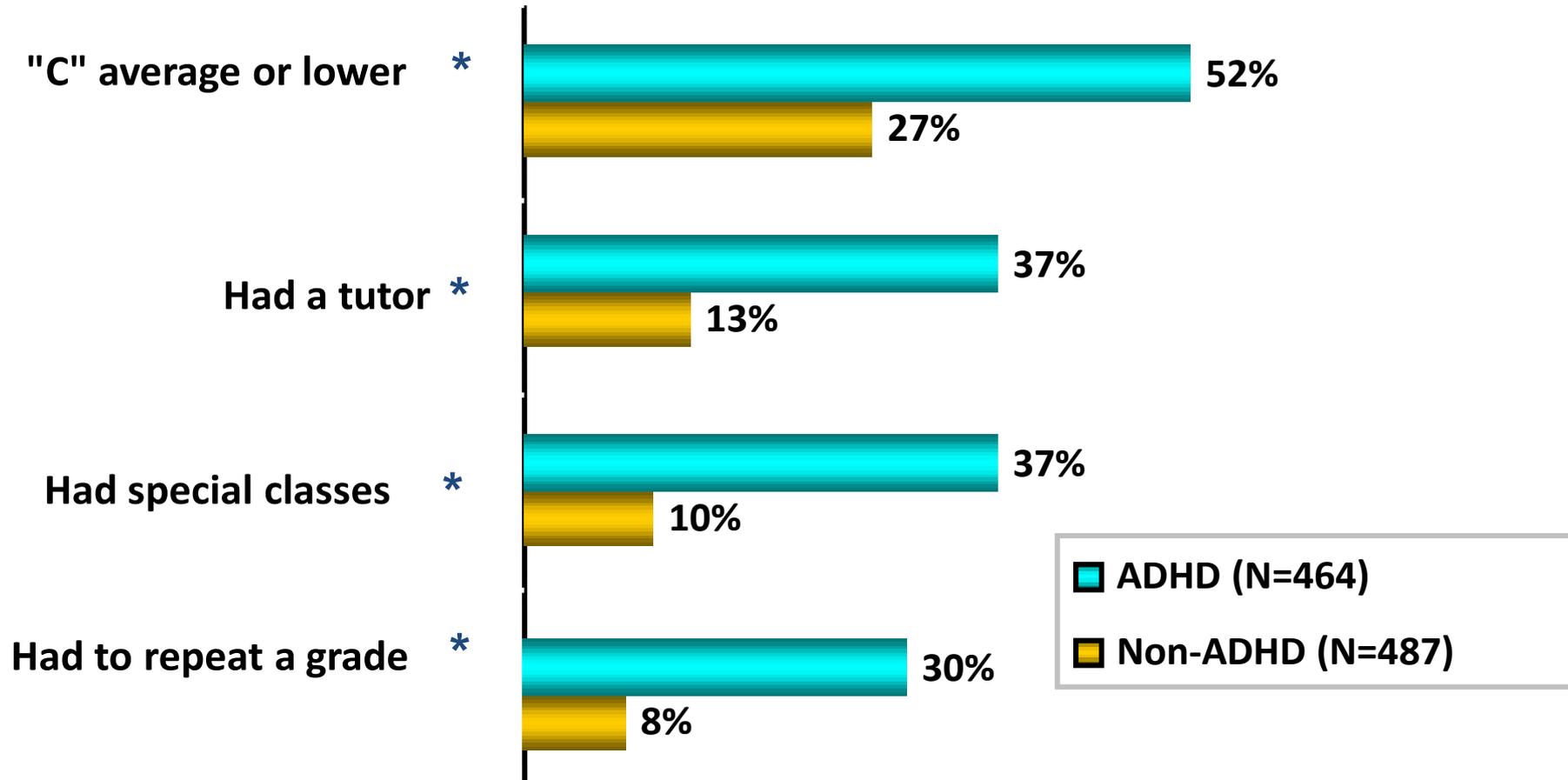
Using CBCL ED definition of $AAA \geq 180$

Heterogeneity of Emotional Dysregulation in ADHD



Educational Impairment in High School

Percentage of Those Who Attended High School



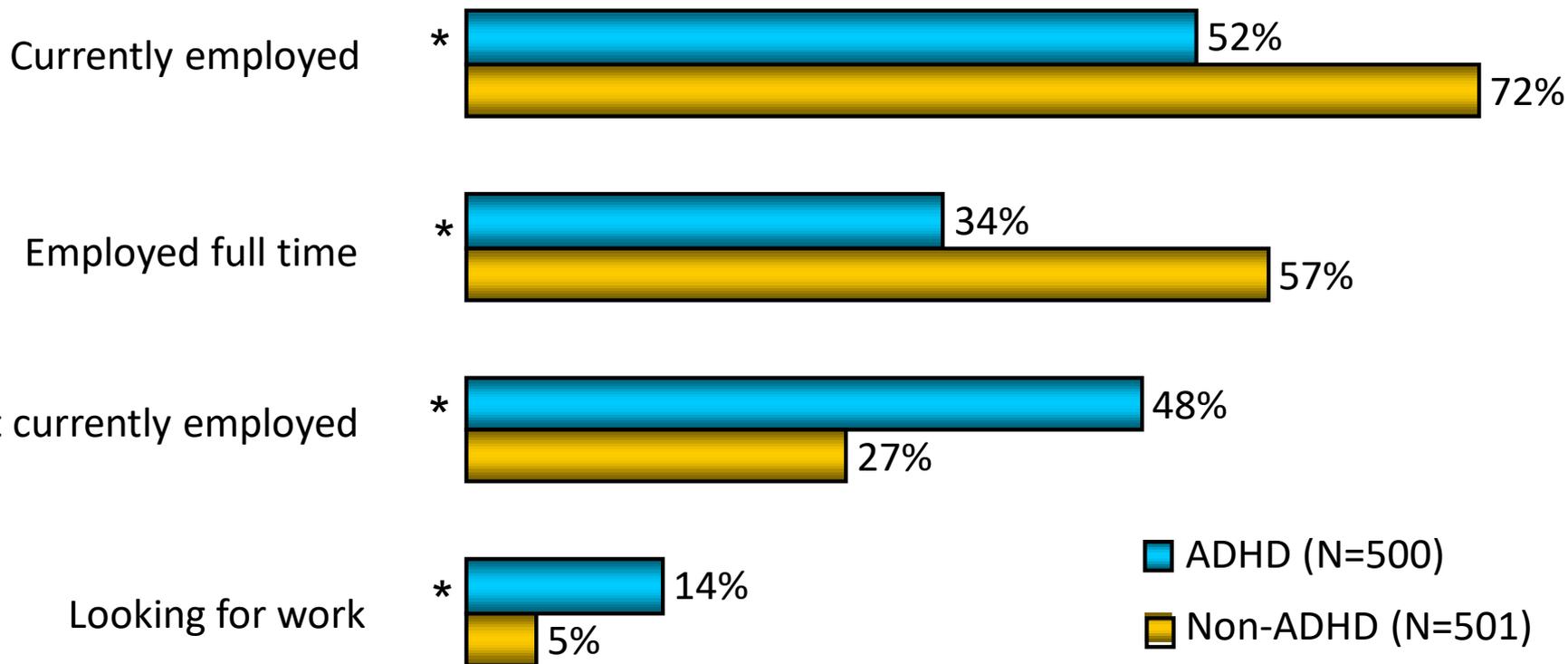
* $p \leq .001$

Biederman et al. *J Clin Psychiatry*. 2006 Apr; 67(4):524-40

www.mghcme.org

Current Employment Status

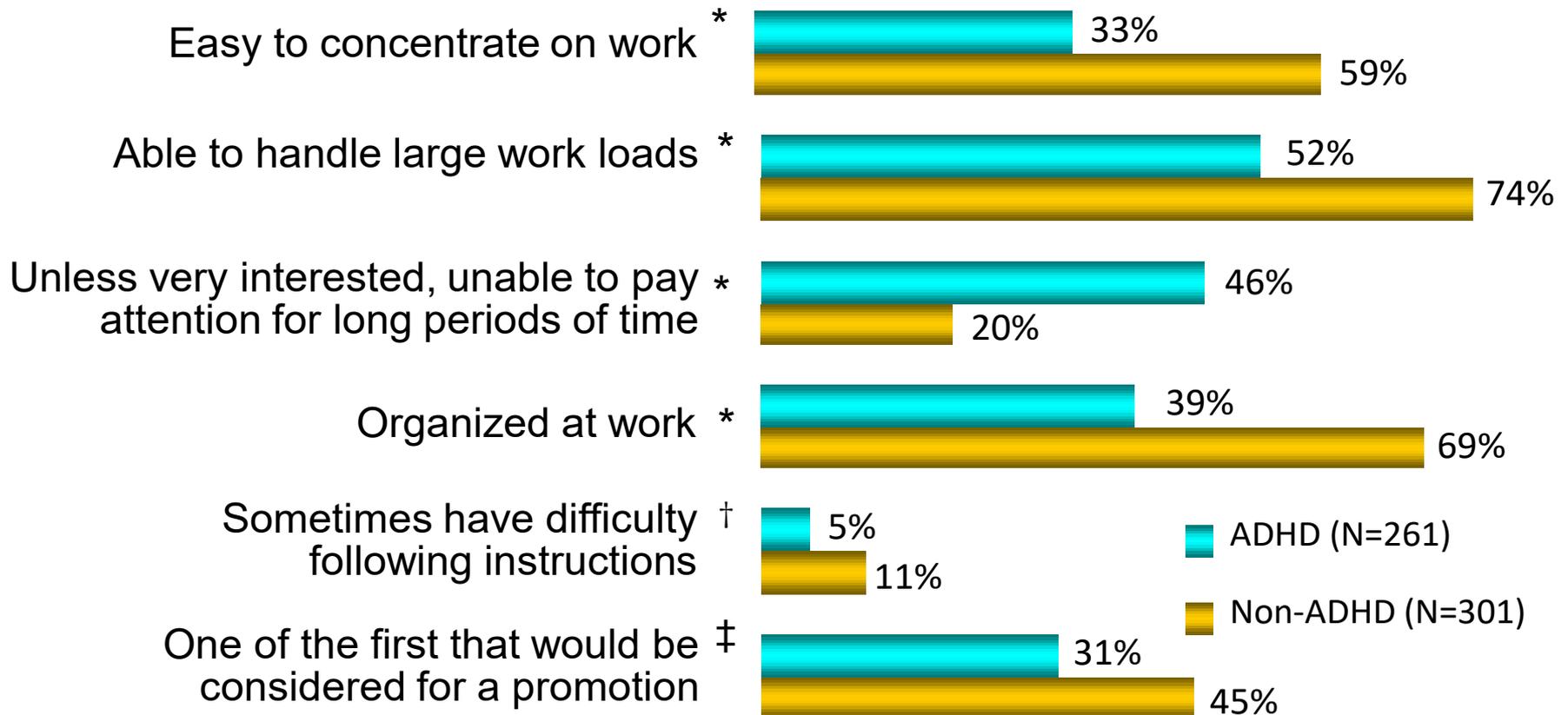
Percentage of Each Group



* $P \leq .001$

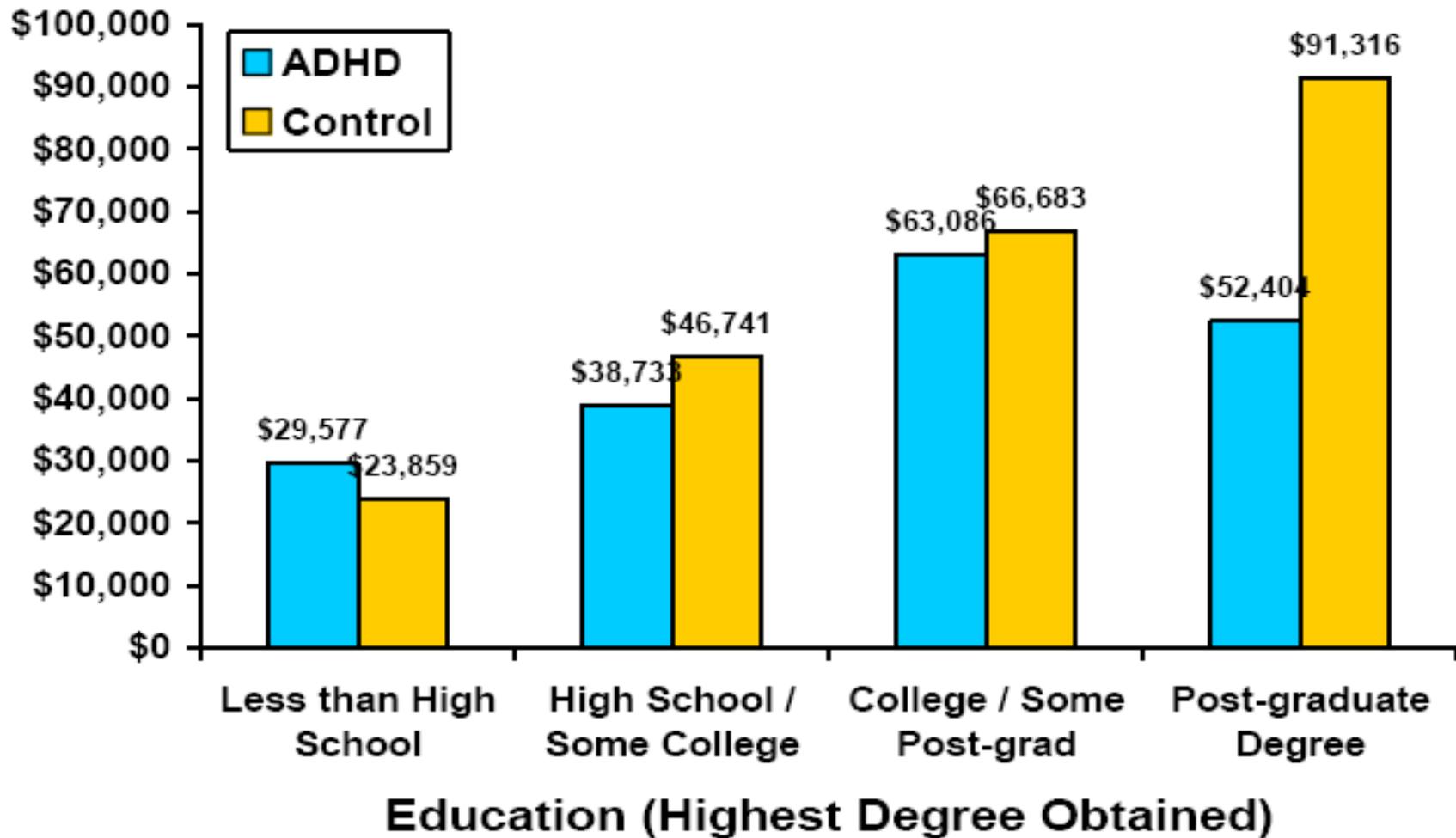
Workplace Impairment

Percentage of Those Employed Who "Strongly Agree"



* $P \leq .001$, † $P \leq .05$, ‡ $P \leq .01$

Average Household Income by Education Level Attained



Poor Adherence to Treatment in ADHD

- Poor adherence occurs despite the well documented morbidity of ADHD, the marked efficacy and safety of stimulants as well as the fact that ADHD symptoms return rapidly when the medication is not taken

The World Federation of ADHD International Consensus Statement: 208 Evidence-based Conclusions about the Disorder

Faraone SV, Banaschewski T, Coghill D, Zheng Y, Biederman J, Bellgrove MA, Newcorn JH, Gignac SM, Aljoudi S, Dalsgaard CM, Hirshfeld DR, Liu J, Mouton RP, Ouakil D, Rubia K, Schweitzer SD, JM, The S, Wang

Methods: We reviewed studies with more than 2,000 participants

Conclusions: Many findings in ADHD are supported by meta-analysis. These allow for firm statements about the nature, course, outcome causes, and treatments for disorders that are useful for reducing misconceptions and stigma.

people who have read this document and agree with its contents.

based assertions about the disorder.

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Faraone et al. *Neurosci Biobehav Rev.* 2021 Feb 4:S0149-7634(21)00049-X.
doi: 10.1016/j.neubiorev.2021.01.022.

ADHD: The Disorder

Symptom domains

- Hyperactivity
- Inattention
- Impulsivity

+

Psychiatric comorbidities

- Anxiety and mood disorders
- Disruptive behavior disorders (conduct disorder and oppositional defiant disorder)

Lead to

Functional impairments

Self

- Low self-esteem
- Accidents and injuries
- Smoking
- Substance abuse
- Delinquency

School / Work

- Academic difficulties, underachievement
- Employment difficulties

Home

- Family stress
- Parenting difficulties

Social

- Poor peer relationships
- Socialization deficit
- Relationship difficulties

Summary

- ADHD is a neurobehavioral disorder with a:
 - Complex etiology
 - Neurobiologic basis
 - Strong genetic component
- ADHD
 - Affects millions of people of both genders
 - Persists through adolescence and adulthood in a high percentage of cases
 - Can have negative impact on multiple areas of functioning
 - ADHD is a highly treatable disorder
 - Adherence to treatment remains very poor