# *ADHD and Stimulants*

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# Faculty Disclosure

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- **US Food and Drug Administration, NSPHS: NIH (NIDA)**
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- **Clinical care: MGH, Bay Cove, Gavin Foundation, Major/Minor League Baseball**
- **(Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford); ADHD Across the Lifespan (Cambridge), Update in Pharmacotherapy of ADHD (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)**

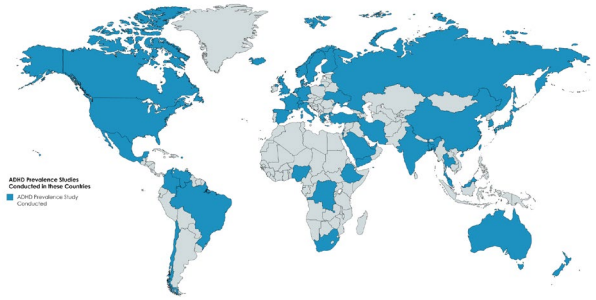
# Overview of ADHD

- ADHD prevalence
  - 8- to 15-year-olds: 6-9%
  - 18- to 44-year-olds: 4-5%
- Associated with chronic course
  - Circa 75% persistence into adolescence
  - Circa 50% persistence into adulthood
- High rates of psychiatric comorbidity
- Impairment in multiple domains
- Diagnosis by DSM V criteria
  - Combined, Inattentive, Hyperactive subtype
- Responds well to treatment

Froehlich TE, et al. *Arch Pediatr Adolesc Med*. 2007;161(9):857-864. Kessler RC, et al. *Am J Psychiatry*. 2006;163(4):716-723. Wilens TE, et al. *Postgrad Med*. 2010;122(5):97-109; Faraone et al, *Nature Neuroscience*, 2015. Adler, Spencer, Wilens ADHD In Children and Adults, Cambridge Press, 2016.

# The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder

Stephen V Faraone, Tobias Banaschewski, David Coghill, et al.




## Abstract

**Background:** Misconceptions about ADHD stigmatize affected people, reduce credibility of providers, and prevent/delay treatment. To challenge misconceptions, we curated findings with strong evidence base.

**Methods:** We reviewed studies with more than 2000 participants or meta-analyses from five or more studies or 2000 or more participants. We excluded meta-analyses that did not assess publication bias, except for meta-analyses of prevalence. For network meta-analyses we required comparison adjusted funnel plots. We excluded treatment studies with waiting-list or treatment as usual controls. From this literature, we extracted evidence-based assertions about the disorder.

**Results:** We generated 208 empirically supported statements about ADHD. The status of the included statements as empirically supported is approved by 80 authors from 27 countries and 6 continents. The contents of the manuscript are endorsed by 366 people who have read this document and agree with its contents.

**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.

**Keywords:** ADHD; Brain; Course; Diagnosis; Genetics; Outcome; Treatment.



› Neurosci Biobehav Rev. 2021 Sep;128:789-818. doi: 10.1016/j.neubiorev.2021.01.022. Epub 2021 Feb 4.

# Diagnosis of ADHD

- Developmentally inappropriate symptoms
  - 6/9 Symptoms of Inattention, Hyperactivity or Combination
  - 5/9 if ≥ 17 years of age (adult)
  - 95% of cases are either combined or inattentive subtype
- Age of onset ≤ 12 years
- Not accounted for by other disorder
  - Can make diagnosis of Autism Spectrum and ADHD
- Diagnosis Clinically Derived
- Rating Scales Helpful (Parent, School)
  - WHO – ADHD (ASRS) (https://add.org/adhd-test/)
  - DSM V, Conners, Brown, Other Scales

# ADHD Assessment

- **Life history**
- **Self-report adequate for adults**
- **Mental status exam**

- **Assess for comorbidity (psychiatric, cognitive, psychosocial, medical)**
- **Rating scales: measuring core and broad features (see next)**
- **Medical history review; cardiac and neurologic status, blood pressure/pulse**
- **If medical history is unremarkable, laboratory or neurological testing is not indicated**

Pliszka S; AACAP Work Group on Quality Issues. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921. Huang H et al. Harvard Review of Psychiatry: 3/4 2020 - Volume 28 - Issue 2 - p 100-106

## Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist

| Patient Name | | Today's Date | |
|---|---|---|---|

| Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment. | Never | Rarely | Sometimes | Often | Very Often |
|---|---|---|---|---|---|
| 1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done? | | | | | |
| 2. How often do you have difficulty getting things in order when you have to do a task that requires organization? | | | | | |
| 3. How often do you have problems remembering appointments or obligations? | | | | | |
| 4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started? | | | | | |
| 5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time? | | | | | |
| 6. How often do you feel overly active and compelled to do things, like you were driven by a motor? | | | | | |
| | | | | | Part A |
| 7. How often do you make careless mistakes when you have to work on a boring or difficult project? | | | | | |
| 8. How often do you have difficulty keeping your attention when you are doing boring or repetitive work? | | | | | |
| 9. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly? | | | | | |
| 10. How often do you misplace or have difficulty finding things at home or at work? | | | | | |
| 11. How often are you distracted by activity or noise around you? | | | | | |
| 12. How often do you leave your seat in meetings or other situations in which you are expected to remain seated? | | | | | |
| 13. How often do you feel restless or fidgety? | | | | | |
| 14. How often do you have difficulty unwinding and relaxing when you have time to yourself? | | | | | |
| 15. How often do you find yourself talking too much when you are in social situations? | | | | | |
| 16. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves? | | | | | |
| 17. How often do you have difficulty waiting your turn in situations when turn taking is required? | | | | | |
| 18. How often do you interrupt others when they are busy? | | | | | |
| | | | | | Part B |

WHO ADHD Screener https://add.org/wp-content/uploads/2015/03/adhd-questionnaire-ASRS111.pdf

# Adults with ADHD Under-report Their Childhood Symptoms

Article

## Accuracy of Adult Recall of Childhood Attention Deficit Hyperactivity Disorder

Salvatore Mannuzza, Ph.D.
Rachel G. Klein, Ph.D.
Donald F. Klein, M.D.
Abrah Bessler, Ph.D.
Patrick Shrout, Ph.D.

**Objective:** Although reports of childhood status are necessary for making a diagnosis of adult attention deficit hyperactivity disorder (ADHD), systematic investigation of the accuracy of retrospective self-reports has been limited. This study examined accuracy of adult recall of childhood ADHD.

**Method:** Participants were from a controlled, prospective 16-year follow-up of children with ADHD. At a mean age of 25 years, 176 probands (85% of the 207 subjects in the initial cohort) and 168 non-ADHD comparison subjects were interviewed by clinicians who were unaware of the subjects' childhood status. Subjects were asked about specific childhood ADHD behaviors, and the diagnosis of childhood ADHD was retrospectively established.

**Results:** Seventy-eight percent of the probands and 11% of the comparison subjects were identified as having childhood ADHD. Six symptoms demonstrated high discriminating power in differentiating the subject groups: distractibility, concentration difficulties, complaints of inattention, acting before thinking, being on the go, and fidgeting/squirming. When findings were adjusted for the prevalence of ADHD in the general population, the power of prediction was low. Positive predictive value was 0.27, i.e., of all adults retrospectively given a diagnosis of childhood ADHD, only 27% would be correctly identified. As expected, positive predictive value increased with increases in the estimated prevalence of ADHD.

**Conclusions:** Retrospective diagnoses of childhood ADHD made on the basis of self-reports will in most cases be invalid in settings such as epidemiological surveys and primary care facilities. Greater accuracy can be expected in settings in which childhood ADHD is frequent. The results stress the importance of obtaining contemporaneous information on childhood symptoms in establishing a childhood history of ADHD. Future directions and implications for DSM-V are discussed.

*(Am J Psychiatry 2002; 159:1882–1888)*

## Table 3 Number of ADHD childhood symptoms reported by participants (self-rating) and their parents

From: The Accuracy of Retrospective Recall of Childhood ADHD: Results from a Longitudinal Study

| | Parent rating in childhood (FBB-ADHS) [a] | Retrospective parent rating (FEA-FFB) [b] | Retrospective self-rating (FEA-FSB) [c] |
|---|---|---|---|
| | *n* = 55 | *n* = 49 | *n* = 53 |
| 0–2 ADHD symptoms | *n* = 0<br>0.0% | *n* = 5<br>10.2% | *n* = 9<br>17.0% |
| 3–5 ADHD symptoms | *n* = 3<br>5.5% | *n* = 7<br>14.3% | *n* = 8<br>15.1% |
| ≥ 6 ADHD symptoms | *n* = 52<br>94.6% | *n* = 37<br>75.5% | *n* = 36<br>67.9% |
| Number of ADHD symptoms | *M* = 15.00<br>*SD* = 5.06 | *M* = 12.10<br>*SD* = 6.78 | *M* = 8.70<br>*SD* = 5.69 |

Home > Journal of Psychopathology and Behavioral Assessment > Article

## The Accuracy of Retrospective Recall of Childhood ADHD: Results from a Longitudinal Study

Open access | Published: 07 December 2020
Volume 43, pages 413–426, (2021) Cite this article

Download PDF

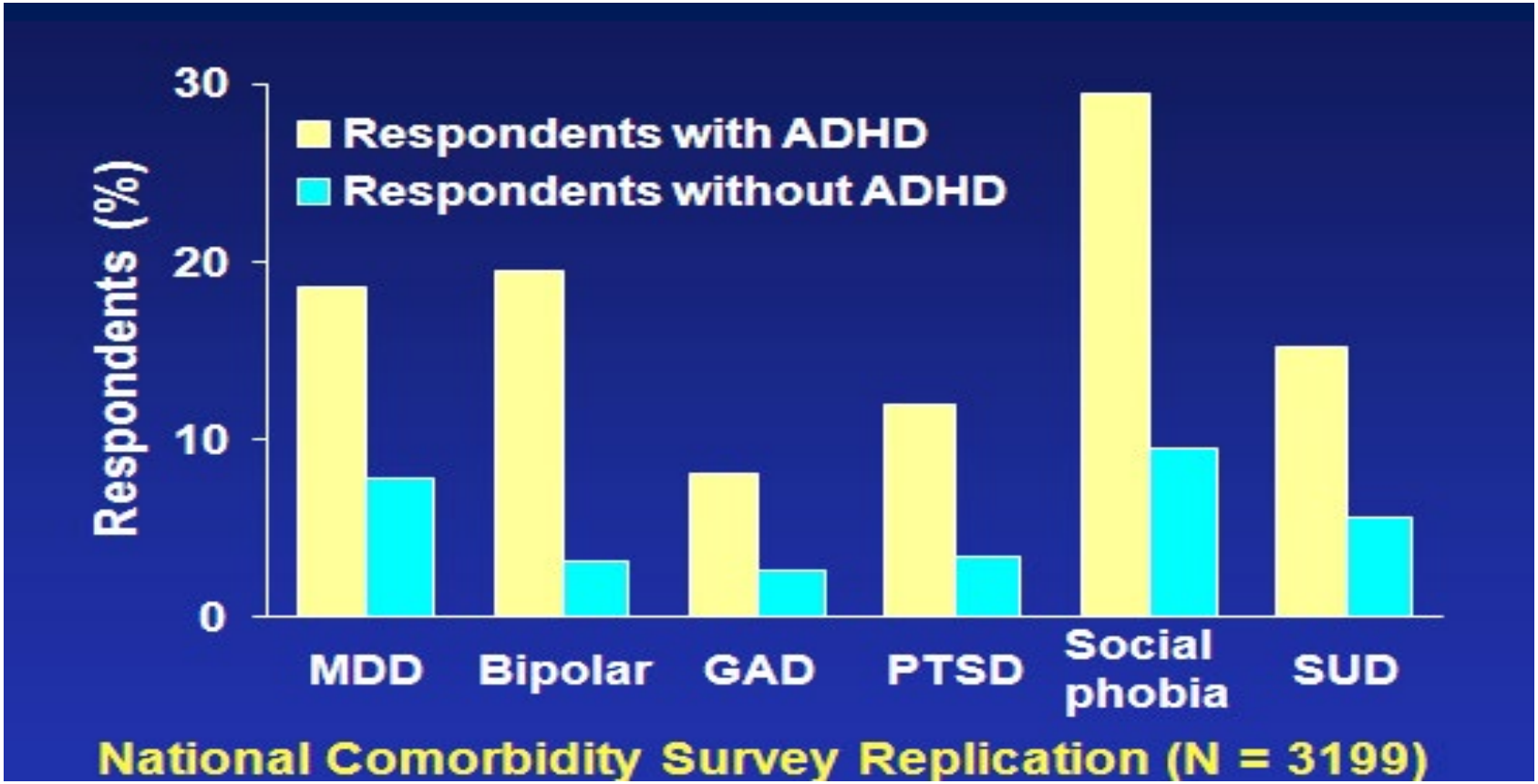


Elena von Wirth, Janet Mandler, Dieter Breuer & Manfred Döpfner



### Abstract

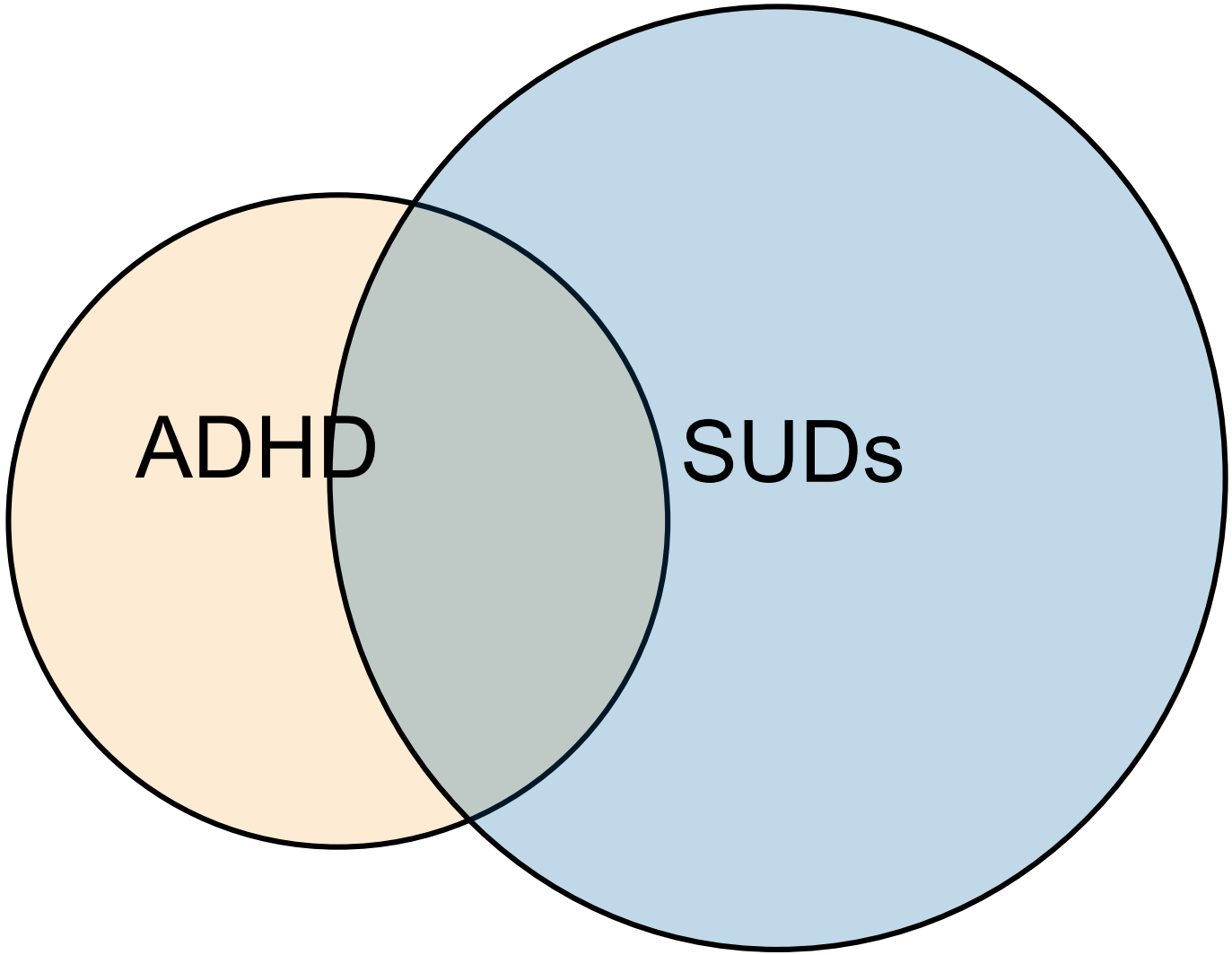
Attention-deficit/hyperactivity disorder (ADHD) is a childhood-onset condition that may continue into adulthood. When assessing adult patients, clinicians usually rely on retrospective reports of childhood symptoms to evaluate the age-of-onset criterion. Since inaccurate symptom recall may impede the diagnosis and treatment of ADHD, knowledge about the factors influencing retrospective reports is needed. This longitudinal study investigated (a) the accuracy of retrospective symptom ratings by adult participants with a childhood diagnosis of ADHD (self-ratings) and parents or significant others (proxy ratings), and (b) the influence of current ADHD symptom severity and ADHD-associated impairments on retrospective symptom ratings. Participants ($N = 55$) were members of the Cologne Adaptive Multimodal Treatment (CAMT) study who had been referred and treated for ADHD in childhood and were reassessed in adulthood (average age 27 years). Participants' retrospective self-ratings were substantially lower than, and did not correlate with, parents' ADHD symptom ratings provided at study entry, while retrospective symptom ratings provided by proxy respondents correlated moderately with parents' childhood ratings. In addition, participants were more likely to underreport childhood symptoms (79%) and more frequently denied the presence of three or more childhood symptoms (17%) compared to proxy respondents (65% underreporting, 10% false-negative recall). Proxy respondents' symptom recall was best predicted by childhood ADHD, while participants' symptom recall was best predicted by current ADHD symptom severity. ADHD-associated impairments were not correlated with symptom recall after controlling for childhood ADHD. Together, these findings suggest a recall bias in adult patients and question the validity of retrospective reports, even in clinical samples.




**Among respondents aged 18-44 years with ADHD, comorbid disorder within previous 12 months. For all comparisons, *P*<0.05.**

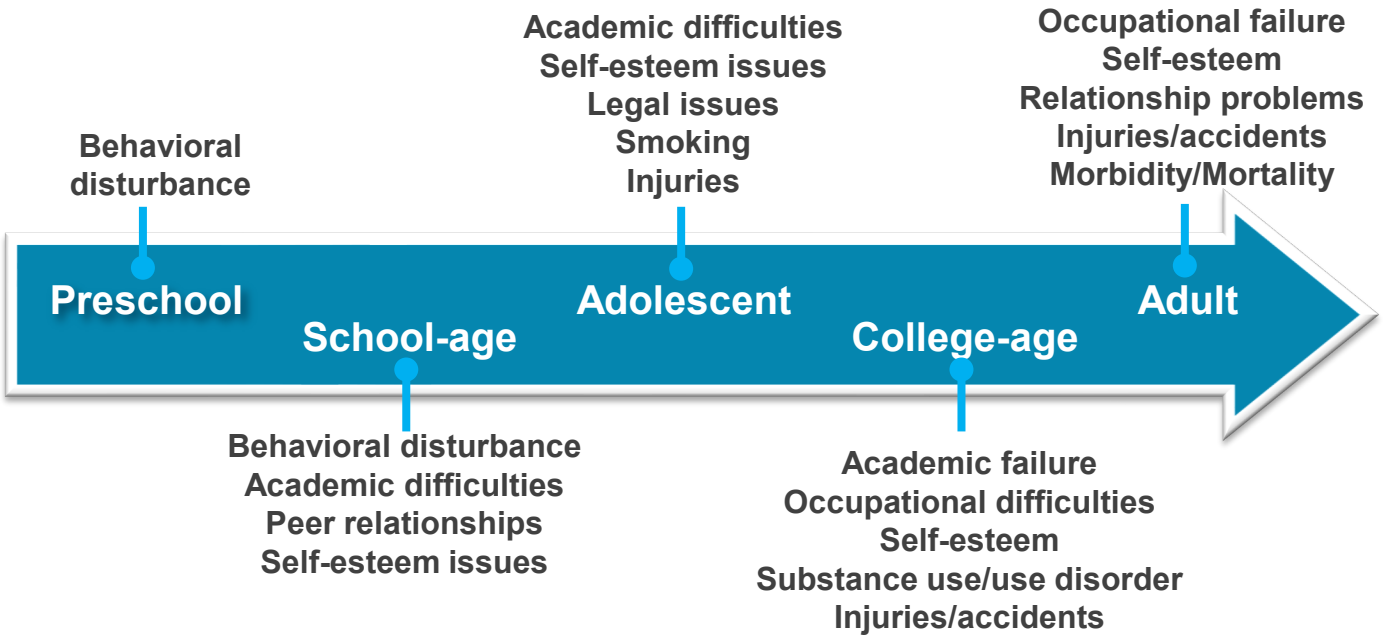
**Kessler RC et al. *Am J Psychiatry*. 2006;163(4):716-723.**

# Overlap between ADHD and SUDs



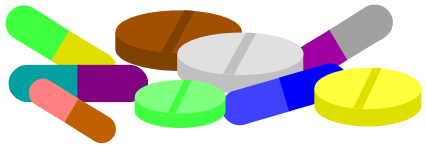

**Wilens TE. *Psychiatr Clin North Am*. 2004;27(2):283-301. van Emmerik-van Oortmerssen K, et al. *Drug Alcohol Depend*. 2012;122(1-2):11-19.**

# Developmental Impact of Untreated ADHD




Pliszka S. AACAP Work Group on Quality Issues. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921.
Brown TE, et al. *Postgrad Med*. 2010;122(5):42-51.
Adler, Spencer, Wilens ADHD in Children and Adults, 2015, Cambridge Press.

# Pharmacological Treatment



- **Stimulants** ← FDA Approved
  - Methylphenidate
  - Amphetamines
- **Noradrenergic agents** ← FDA Approved
  - Atomoxetine
  - Viloxazine XR
- **Alpha Agonists** ← FDA Approved
  - Guanfacine (XR)
  - Clonidine (XR)
  - Guan XR or Clon XR + stimulants ← FDA Approved
- **Antidepressants**
  - Bupropion
  - Tricyclics
- **Combination/others**
  - Modafinil
  - Memantine

Newcorn & Wilens, Child Adolesc Psych Clin N Am, Elsevier Press 2022. www.drugs.com

# Methylphenidate (MPH) in ADHD

| Medication | Starting Dose | Maximum Dose* | Duration |
|---|---|---|---|
| Ritalin IR® | 5 mg QD/BID | 2 mg/kg/day | 4 hr / BID |
| Focalin® | 2.5 mg QD/BID | 1 mg/kg/day | 4–5 hr / BID–TID |
| Focalin XR® | 5 mg QD | 1 mg/kg/day | 10–12 hr QD |
| Daytrana® | 10 mg | | 6–16 hr |
| Concerta® | 18 mg QD | 2 mg/kg/day | 12 hr / once |
| Metadate CD® | 20 mg QD | | 8 hr / once |
| Ritalin LA® | 20 mg QD | | 8 hr / once |
| Quillivant XR® | <10 mg QD | | 12 hr / once |
| Quillichew ER® | <10 mg QD | | 8 hr / once |
| Cotempla XR-ODT® (disintegrating tab) | 8.6 mg QD | 51.8 mg | 12 hr / once |
| Aptensio XR® | 10 mg QD | 2 mg/kg/day | 12 hr / once |
| Adhansia XR® | 25 mg QD | | 12 hr / once |
| Jornay PM® (delayed release) | 20 mg QD | 100 mg | 12 hr / once |
| Azstarys™ (serdexMPH, MPH) | 26.1/5.2 mg QD | 52.3/10.4 mg | 13 hr / once |

*May exceed FDA approved dose.

*May exceed FDA approved dose.

*Update in the Pharmacotherapy of ADHD, Child Adolesc Psych Clin N Am, Newcord & Wilens (eds), Elsevier Press, 2022* www.drugs.com. US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. www.accessdata.fda.gov/scripts/cder/daf/.

# Amphetamine (AMPH) in ADHD

| Medication | Starting Dose | Maximum Dose* Usual Dosing | Duration |
|---|---|---|---|
| Adderall® | 2.5–5 mg QD | 1.5 mg/kg/day | 6 hr / BID |
| Adderall XR® | 2.5–5 mg QD | | 12 hr / QD |
| Vyvanse® | 30 mg QD | | 12–14 hr / QD |
| Mydayis® | 12.5 mg QD | 50/25 mg (adult/adolescent) | To 16 hr / QD |
| Dexedrine Tablets® | 2.5–5 mg BID | 1.5 mg/kg/day | 3–5 hr / BID–QID |
| Evekeo® | 2.5–5 mg BID | | 3–5 hr / BID–QID |
| Dexedrine Spansule® | 5 mg QD | | 6 hr / QD–BID |
| Dyanavel® XR (suspension) | 2.5–5 mg QD | 1.5 mg/kg/day | 13 hr / QD |
| Adzenys XR-ODT® (disintegrating tab) | 6.3–12.5 mg QD | 12.5 mg (adolescents) | 12 hr / QD |
| Xelstrym (Patch) | 4.5 mg | | 12 hr/ QD |

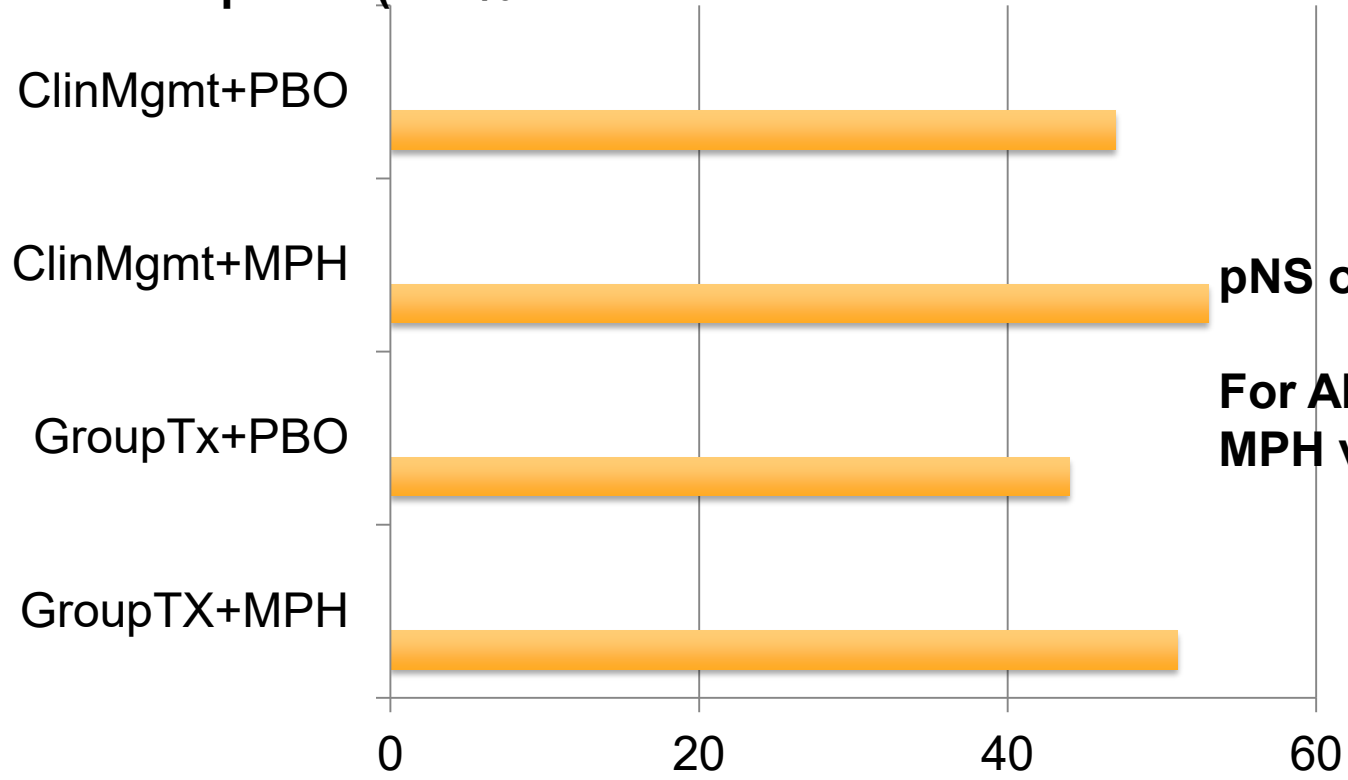
*May exceed FDA approved dose.

. *Update in the Pharmacotherapy of ADHD, Child Adolesc Psych Clin N Am, Newcord & Wilens (eds), Elsevier Press, 2022* www.drugs.com. US Food and Drug Administration. Drugs@FDA: FDA Approved Drug Products. www.accessdata.fda.gov/scripts/cder/daf/.

# Methylphenidate (MPH) is More Effective vs Counseling/CBT in ADHD in Adults Multisite 1 year Study

**(Philipsen et al. JAMA Psychiatry, 2015:1199-1210)**

**Percent Response (>30% reduction in Observer CAARS ADHD index) at 52 weeks**



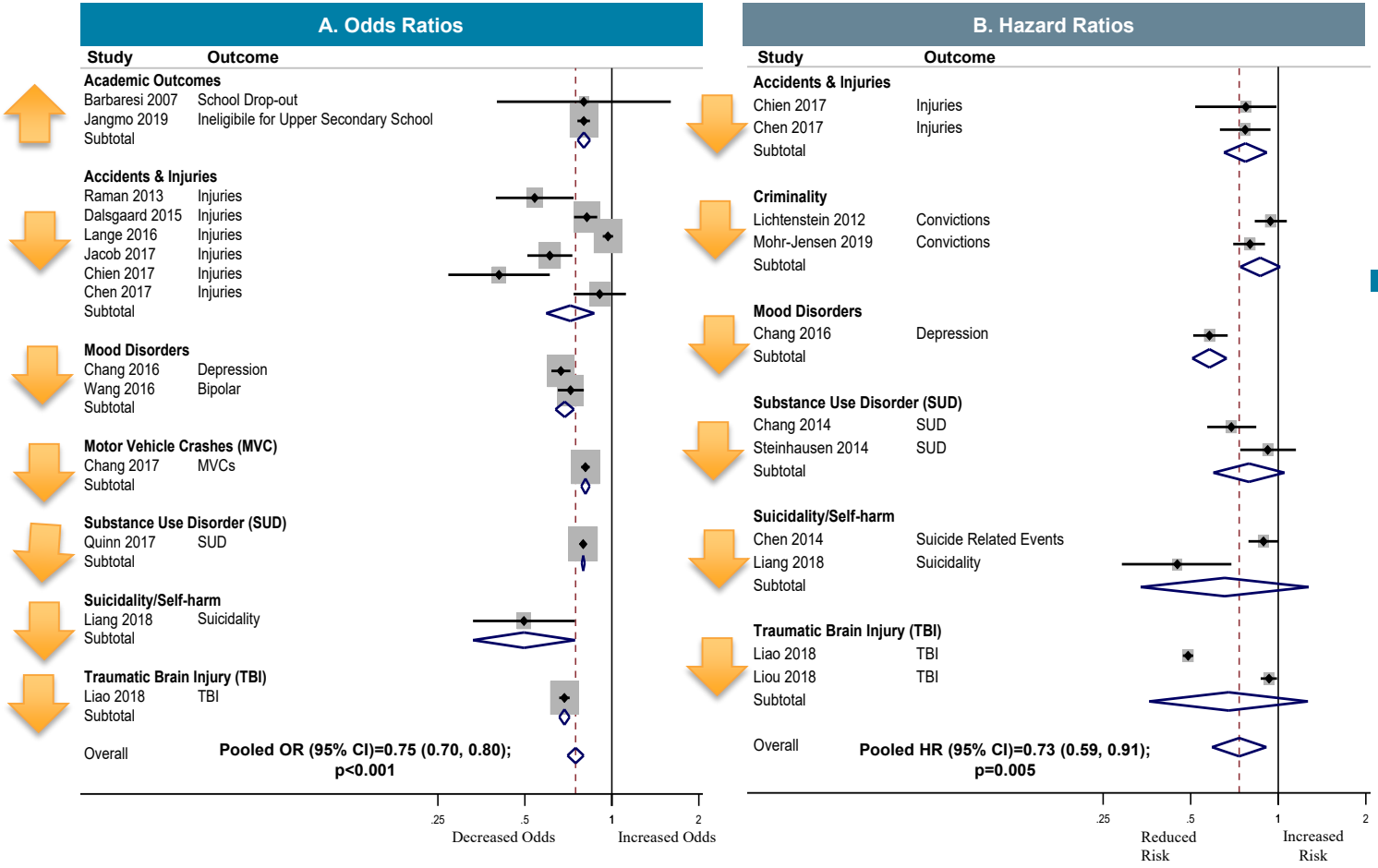

**pNS overall % response;**

**For ADHD index LOCF: MPH vs PBO p<0.001**

**N=419 subjects, 7 German Centers,**
**12 Weeks of weekly treatment then monthly thereafter; Tx to 1 year**
**MPH Dosing to 60 mg/day maximum (or 1.3 mg/kg/day)**

# Long Term Studies of ADHD: Stimulant Treated vs. Untreated

Odds ratios and hazard ratios <1 indicate decreased risk in medicated vs. unmedicated ADHD patients




- (from Boland, et al , Psychiatric Research 2020)

# 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, J Psychiatric Research, 2020)

# Editorial: Stimulants: Friend or Foe?

Timothy E. Wilens, MD, and Tamar Arit Kaminski, BS

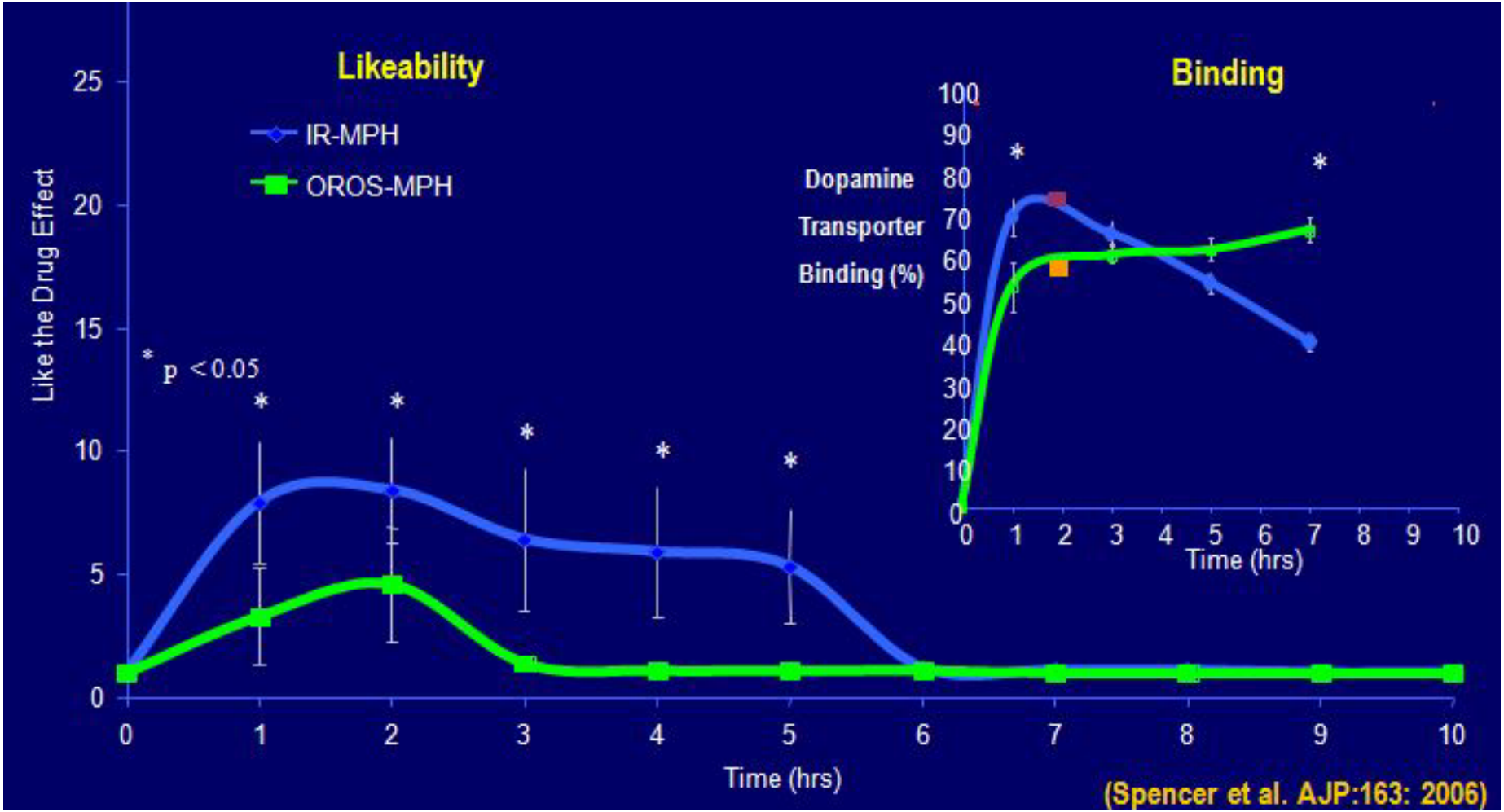
Stimulants remain the treatment of choice for attention-deficit/hyperactivity disorder (ADHD), in part owing to their large effect size within the pharmacotherapeutic repertoire for ADHD—in other words, they are highly effective. When used appropriately, they are also quite safe and actually mitigate the misuse of drugs or alcohol. So, why all the fuss?

Stimulants remain the treatment of choice for attention-deficit/hyperactivity disorder (ADHD), in part owing to their large effect size within the pharmacotherapeutic repertoire for ADHD—in other words, they are highly effective. When used appropriately, they are also quite safe and actually mitigate the misuse of drugs or alcohol. So, why all the fuss?

J Am Acad Child Adolesc Psychiatry 2020;59(1):36-37.

# Stimulant Preparation Linked to Dopamine Transporter Binding and Likeability

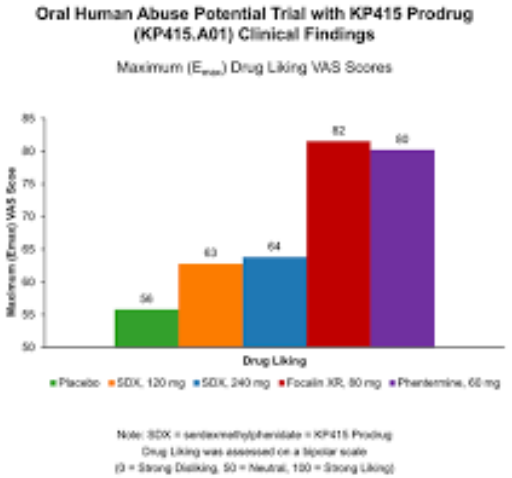
## 40 mg IR-MPH vs 90 mg OROS MPH

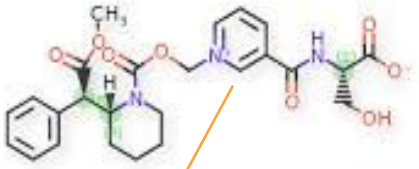


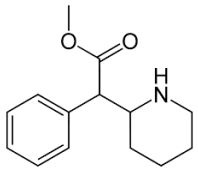

Spencer TJ, et al. *Am J Psychiatry*. 2006;163(3):387-395.

# Prodrug Stimulants are Extended-Release and May Have Lower Likeability and Abuse Liability

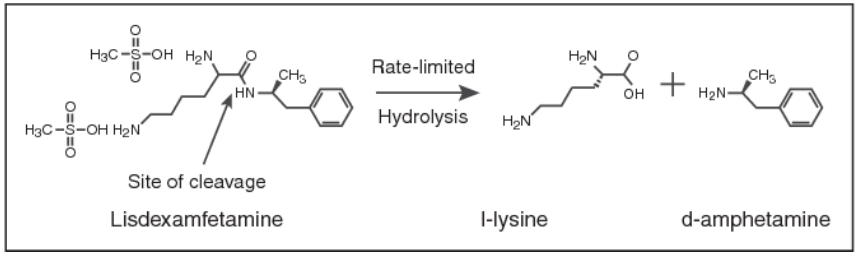
## Serdexmethylphenidate/MPH



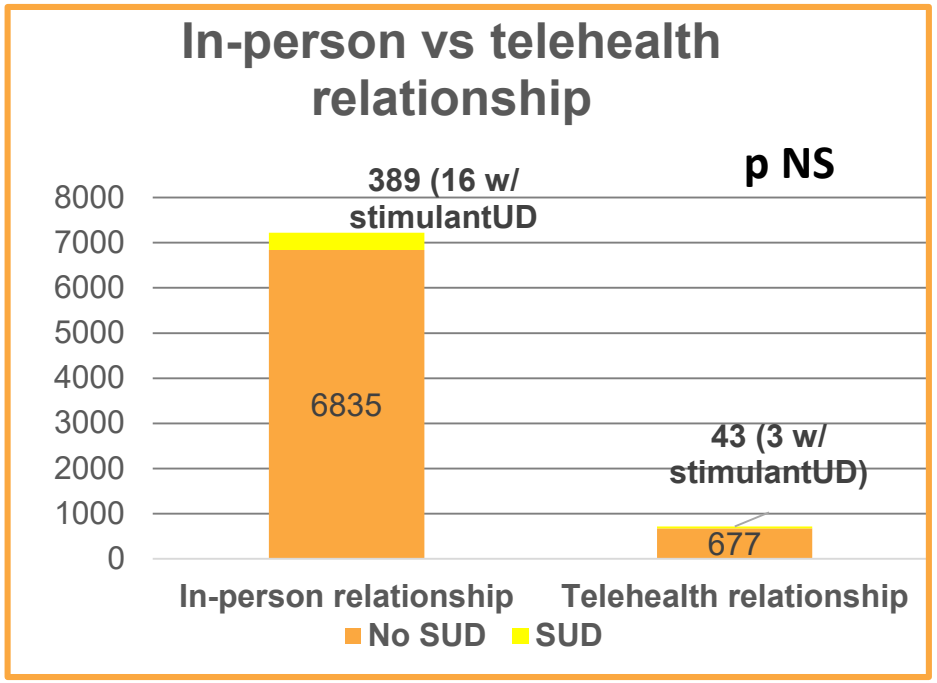




## Lisdexamfetamine



# Telehealth Compared to In Person Experience Does Not Increase Subsequent Stimulant or other SUDs

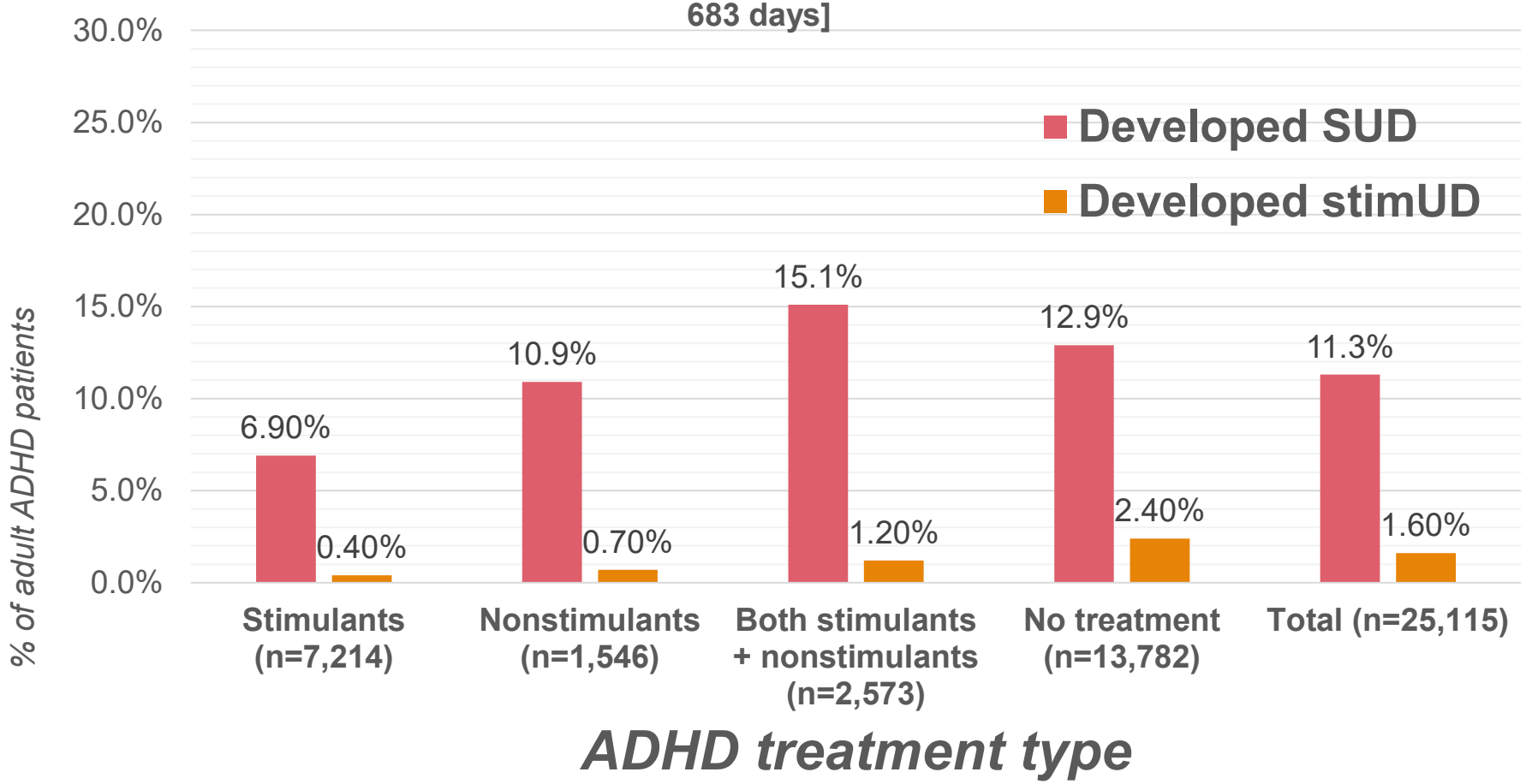
**(N=7944 patients)**




(Rao et al, Am J Psych, 2025)

# Treatment of ADHD in Adults with Stimulants Does Not Increase Stimulant (stimUD) or Substance Use Disorders (SUD)

**[N=25,115 Adults with ADHD, MGB Electronic Health Records, Mean age 31.4 years, f/u mean 683 days]**




**(Rao V et al, Presentation to FDA 3/19/25; in preparation 2025)**

# Summary

- **Since ADHD is a major psychiatric disorder requiring comprehensive diagnostic evaluation and treatment**
- **Medications are among first line treatment for ADHD across the lifespan**
- **Stimulants are the most effective agents for ADHD**
- **Since stimulants can be misused, in high risk groups consider mitigation strategies (e.g. Extended vs Immediate release, education and monitoring)**