Medication Management of Adults with ADHD: Clinical & Epidemiological Perspectives

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Potential Conflicts of Interest

Columbia University
George Washington University
Michigan State University
National Institute on Drug Abuse
National Institute of Mental Health
New York State Office of Mental Health
Ohio State University
Rutgers University
Substance Abuse and Mental Health Services Administration
University of California, San Francisco
Vanderbilt University
Yale University

Overview

Medication treatment of adults with ADHD: efficacy and patterns of use

Groups at risk of stimulant misuse

Clinical assessment: focus on potential for stimulant misuse

Shared decision making in medication management

First Principles of Treatment and Support
Adults with ADHD

Offering adults with ADHD multimodal treatment and support:

Non-pharmacological interventions

Strategies for lifestyle changes (sleep, diet, relaxation, physical activities)
Cognitive behavioral interventions where it is available

Pharmacological treatments

Australian Evidence-Based Clinical Practice Guideline for ADHD, 2022.

Cognitive Behavioral Therapy for Adults with ADHD Partially Responsive to Stimulants

Design: Adults, mean age 42-44 years, with ADHD partially responsive to medications randomly assigned to 12 weekly sessions of cognitive behavioral therapy or relaxation with educational support.

End of treatment, 3-months

	CGI-S Response		ADHD Rating Scale Response	
CBT (n=43)	53%	*p*=.01	67%	*p*=.002
Education/Relaxation (n=43)	23%		33%	

Long-term Outcomes (mean, SD)

	6-month CGI-S	12-month CGI-S	6-month ADHDRS	12-month ADHDRS
CBT	3.05 (1.31)	3.21 (1.24)	13.51 (7.70)	13.39 (8.49)
Education/Relaxation	3.43 (1.19)	3.69 (1.26)	16.20 (9.81)	16.97 (10.72)

Safren SR, et al., *JAMA* 2010. Response defined as 1- or 2-point decrease in CGI-S (severity) and not meeting ADHD criteria; ADHD rating scale response defined as ≥30% decrease from baseline.

FDA Approved Medications for ADHD

Stimulants*

- Amphetamine based
- Methylphenidate based

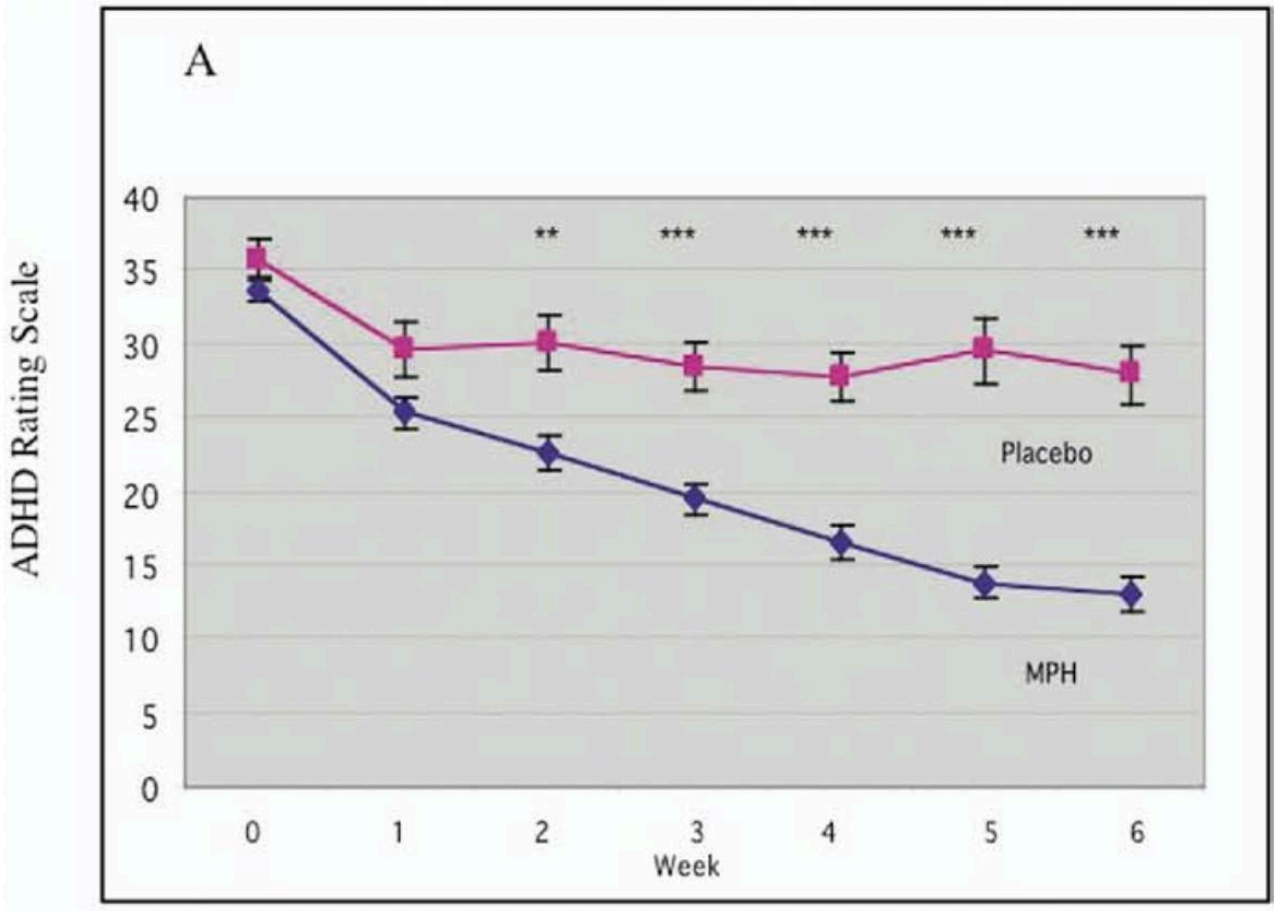
Non-Stimulants

- Atomoxetine (SNRI)
- Viloxazine ER (SNRI)
- Guanfacine XR** (alpha 2A adrenergic agonist)
- Clonidine XR** (alpha 2A adrenergic agonist)

*DEA Schedule II: Drugs that have a high potential for abuse that may lead to severe psychological or physical dependence. Black box warnings.

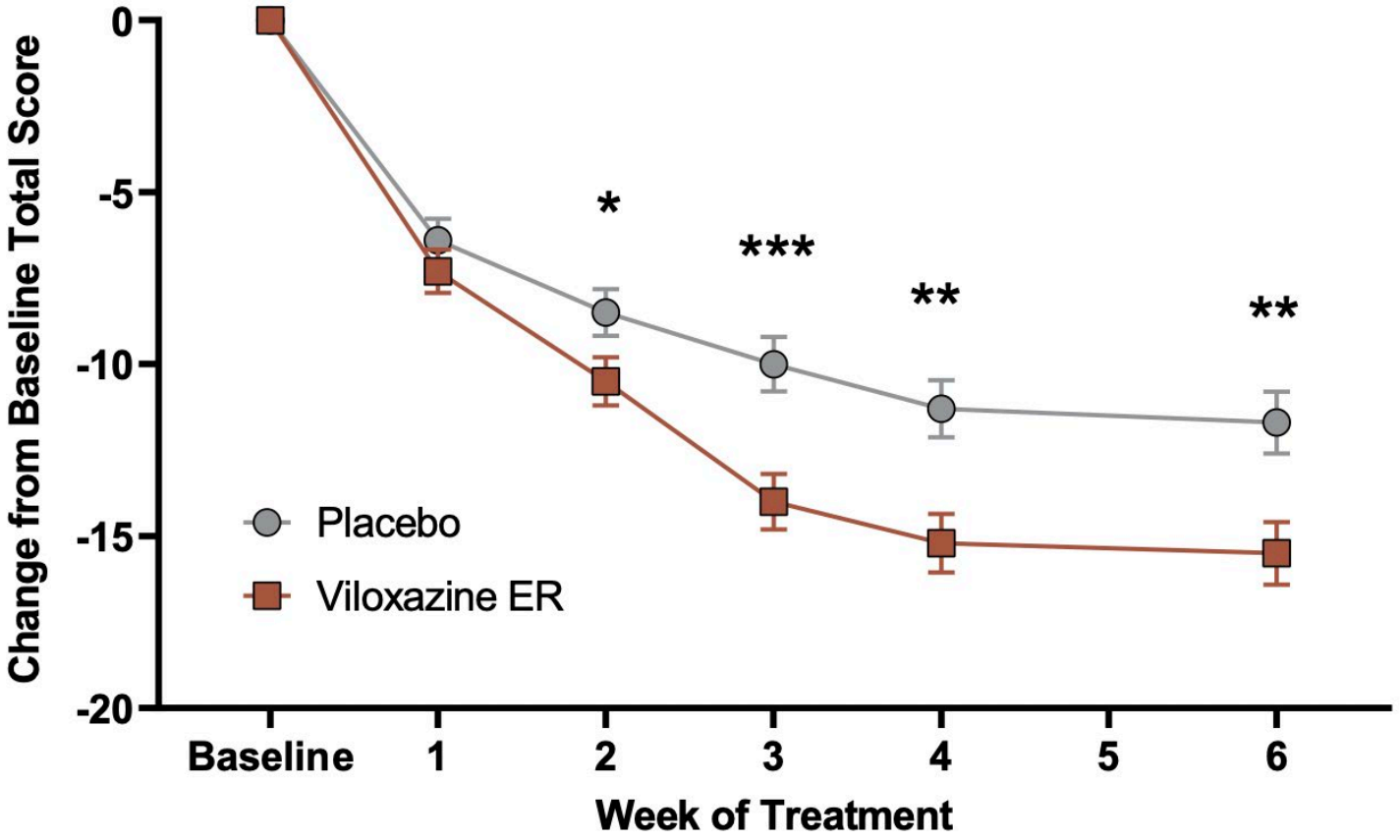
**Not approved for use in adults with ADHD

Methylphenidate for Symptoms of Adults with ADHD



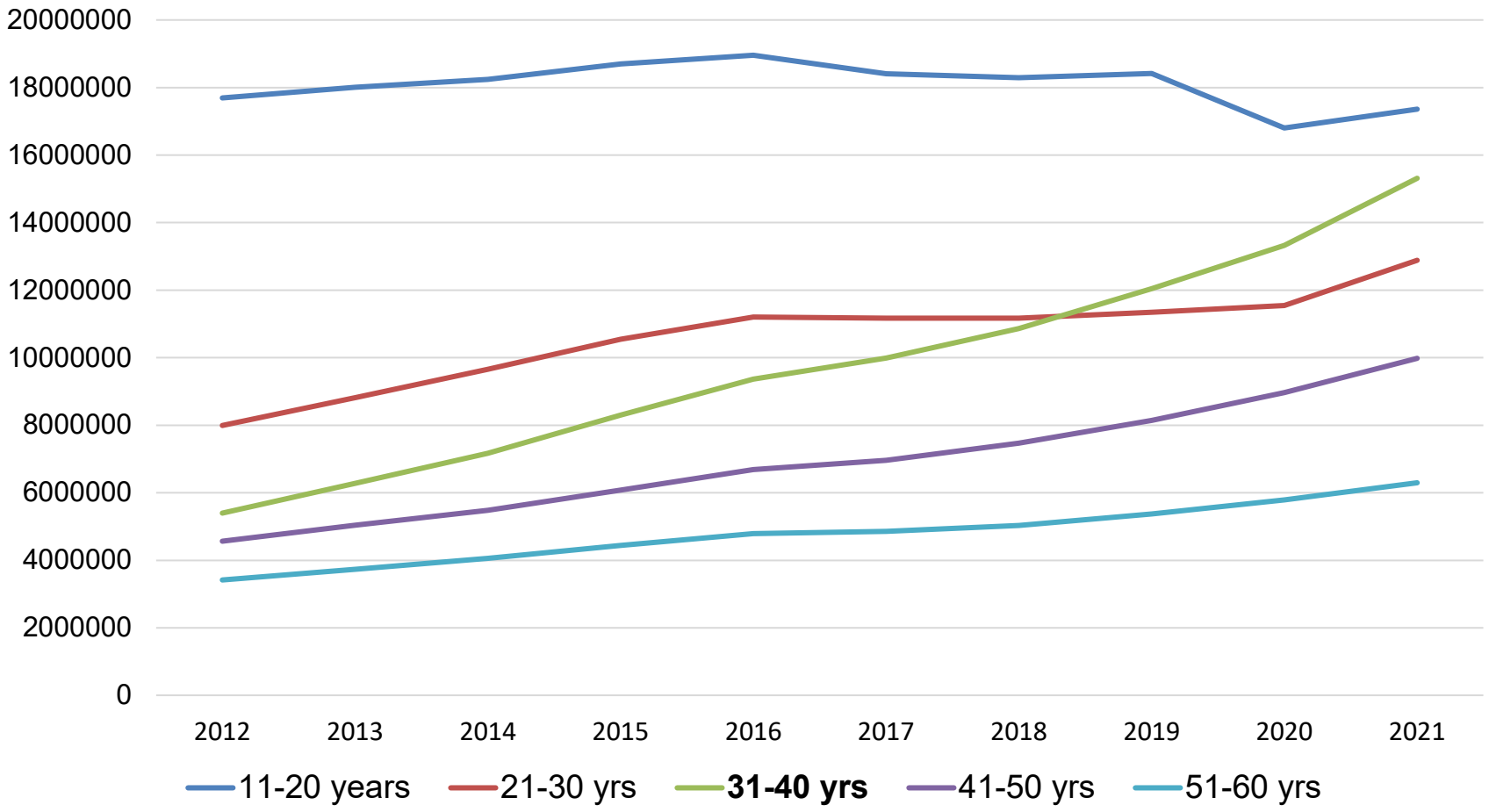
Spencer T et al, *Biol Psych* 2005, Ages 19 to 60 years, MPH=104, placebo=42, Double blinded randomized controlled trial, **p<.001, ***p<.0001, MPH titrated over 3 weeks to 1.0 mg/kg/day TID dosing.

Viloxazine for Symptoms of Adults with ADHD



Nasser et al, *CNS Drugs* 2022, N=190 viloxazine, N=184 placebo ,ages 18-65 years, double blind randomized controlled trial, ADHD rating scale, * p<.05, **p<.01, ***p<.001, mean viloxazine dose 504 mg/day.

Stimulant Prescriptions for Adults in the United States



IQVIA analysis prepared for DEA, 2022

Methylphenidate Prescription Patterns by Age

Characteristic	Age 12-17 N=658	Age 18-24 N=198	**Age 25-49** **N=831**
Daily MPH dosage, mean (SD)	34.3 (63.0)	93.9 (218.5)	269.0 (543.3)
Different prescribers (SD)	2.7 (1.6)	2.6 (2.3)	4.2 (5.4)
Different pharmacists (SD)	1.8 (1.0)	2.2 (2.2)	4.0 (5.6)
Benzodiazepines (%)	2%	15%	60%
Non-BZD anxiolytics (%)	4%	6%	14%
Opioid analgesics (%)	6%	12%	39%
OUD maintenance tx (%)	0%	3%	30%

Pauly et al Br *J Clin Pharmacol* 2018 (French prescription data, Provence-Alpes-Cote d'Azur). Opioid maintenance includes high dose buprenorphine or methadone.

Prediction of suspicious methylphenidate prescription use among adults in Denmark

Characteristic	Univariate OR (95%CI)	Multivariate OR (95%CI)
Sex		
Female	0.7 (0.5-1.2)	0.8 (0.5-1.3)
Age, years		
18-24	1.0	1.0
25-49	**3.0 (1.6-5.6)**	**2.5 (1.3-4.7**)
50+	0.8 (0.2-2.7)	0.6 (0.2-2.2)
Formulation		
Extended release	5.1 (3.3-7.9)	4.3 (2.8-6.8)
Immediate release	1.0	1.0
Prescriber		
Specialist	1.0	1.0
General practitioner	3.8 (1.9-7.3)	3.1 (1.6-6.0)
Hospital doctor	4.7 (2.6-8.6)	4.1 (2.2-7.5)

Rasmussen et al., *Pharmaco Epi Drug Safety* 2015, Suspicious ≥4 different MPH prescribers within first Year, **MPH ≥ 3 DDD/day,** cohort, n=20,829, outcome=82 (0.4%). Also controlled for recent use of benzodiazepines, opioids, antipsychotics, antiepileptics, antidepressants, and drugs used for addictive disorders.

Prediction of suspicious methylphenidate prescription use among adults in Denmark

Characteristic (Past 6 months)	Univariate OR (95%CI)	Multivariate OR (95%CI)
Medications for addictive disorders	4.2 (2.3-7.6)	2.1 (1.1-3.9)
Benzodiazepines	3.0 (1.9-4.7)	1.7 (1.0-2.8)
Opioids	2.4 (1.404.0)	1.8 (1.0-3.0)
Antipsychotics	3.0 (1.9-4.8)	1.6 (1.0-2.7)
Antiepileptics	2.8 (1.6-4.7)	1.4 (0.8-2.5)
Antidepressants	1.4 (0.9-2.2)	1.1 (0.7-1.7)

Rasmussen et al., *Pharm Epi Drug Safety* 2015, Suspicious ≥4 different MPH prescribers within first Year and **MPH ≥ 3 DDD/day**, Cohort, n=20,829, outcome=82 (0.4%). Analysis also controlled for patient age, patient sex, MPH formulation, and prescriber type.

Potential for
Non-Medical Use and Diversion of Stimulants

Non-medical use

- *Abuse:* Intentional improper use to experience psychotropic effects (e.g., to get high)
- *Misuse:* Intentional improper use other than to get high, such as taking an additional dose without consulting with a prescriber because the patients believes that his or her symptoms were not adequately controlled.

Non-indicated use: "performance enhancement" or "neuroenhancement"

- *People without ADHD seeking to improve their cognitive, emotional, or motivational functioning (students, workers)*
- *May be medical or non-medical use*

Diversion

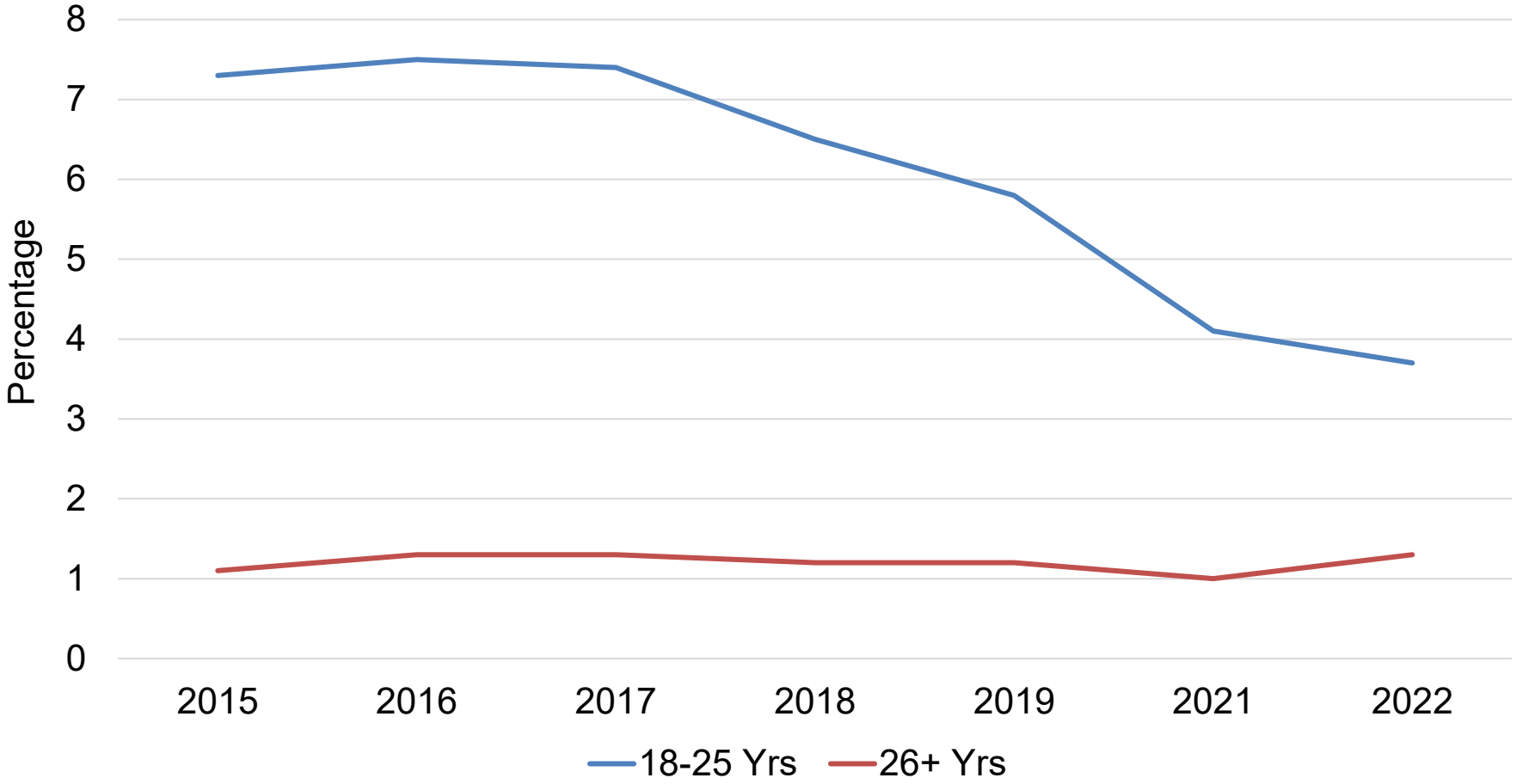
- Unlawful channeling of controlled pharmaceuticals from legal to illegal sources.

Cognitive Enhancement: Effects of Single Dose Methylphenidate in Healthy Volunteers (Score Card)

Domain	**Total**	Low Dose	Medium Dose	High Dose
Working memory (k=21)	65%	0%	74%	41%
Processing speed (k=25)	48%	79%	46%	44%
Verbal learning/memory (k=18)	31%	64%	75%	12%
Attention/vigilance (k=87)	29%	37%	32%	38%
Reason/problem solving (k=10)	18%	1%	18%	74%
Visual leaning/memory (k=8)	0%	0%	0%	0%

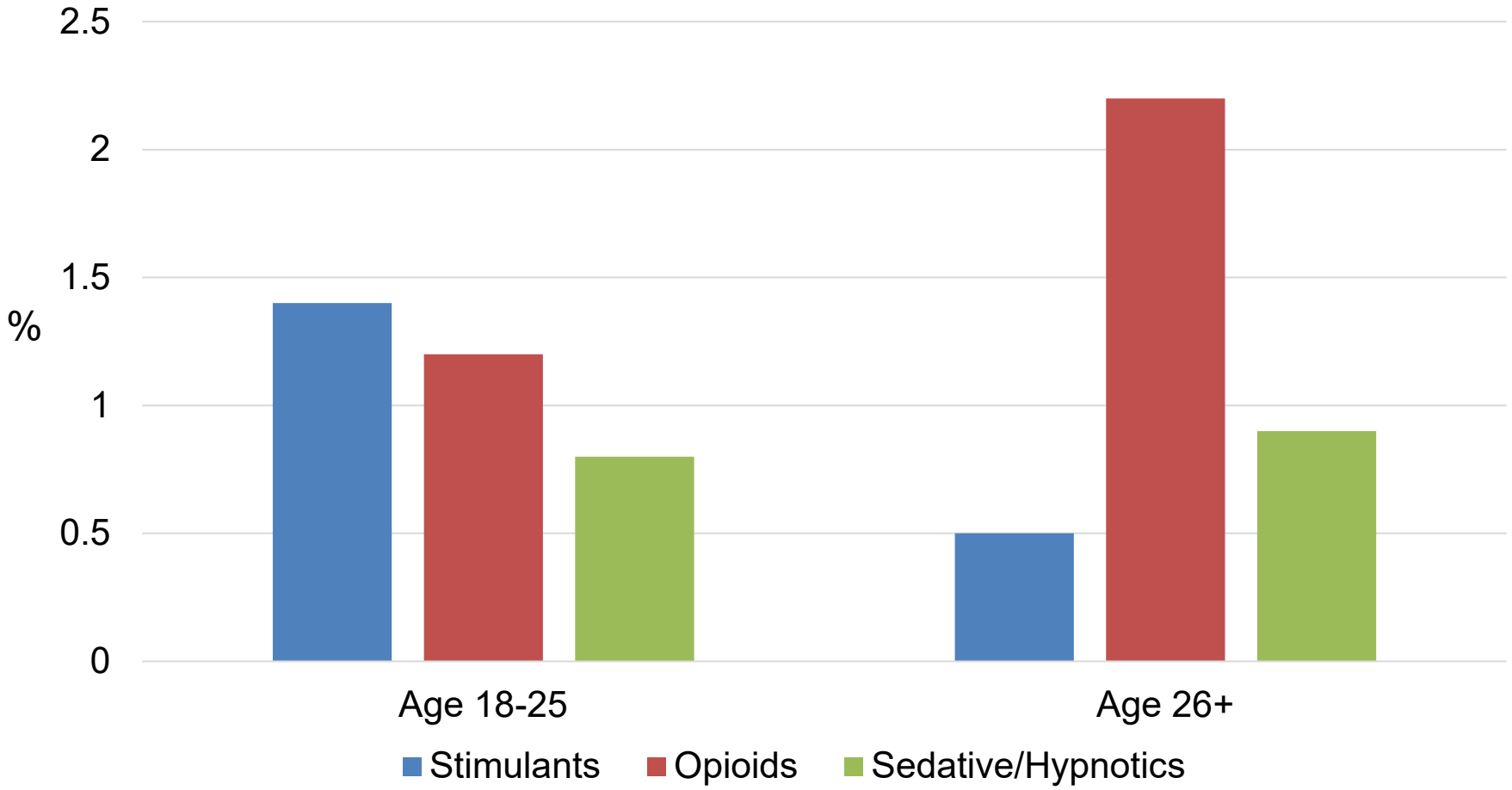
Linssen et al., *Int J Neuropsychopharmacol* 2014. Percentages of studies showing cognitive enhancement in six cognitive domains. Low, medium and high dose were defined as: low: ≤10 mg or ≤0.15 mg/kg; medium: >10 mg, ≤20 mg or >0.15 mg/kg, ≤0.3 mg/kg; high: >20 mg or >0.3 mg/kg.

Past Year Prescription Stimulant Misuse in the United States



Data from SAMHSA's NSDUH. Misuse defined as prescription drug use in any way that is not directed by a doctor. Based on annual nationally representative household sample of approximately 75,000 (all ages ≥ 12 years).

Past Year Prevalence of Prescription Use Disorders United States, 2022



NSDUH, 2022

Principals of Clinical Assessment – Adult ADHD
Integrating a concern for stimulant misuse

Self-report forms

- Adult ADHD Self-Report Scale Screener (ASRS, 18 items)
- Conners' Adult ADHD Rating Scales-Self Report (CAARS, short 26 items)

Clinical Interview

Collateral Information

Childhood Documentation (≤ 12 years, school records, parent reports)

Neuropsychological Assessment (when available)

Include a focus impairment: "interfere with, or reduce the quality of, social, academic, or occupational functioning" (DSM-5)

Assessing Functional Impairment in Adult ADHD
- *Adult Consequences of Inattention, Hyperactivity, and Impulsivity* -

Social Impairment
- Romantic relationships
- Peer relationships
- Parenting
- Educational achievement
- Occupational functioning

Substance Use

Motor vehicle accidents

Other injuries

Risky sexual behavior

Criminal activity

Review: Koshelef et al., *J Atten Dis* 2023

Shared Decision Making
Medication management decisions for adults with ADHD

Whether to initiate pharmacotherapy? Which medication? Dosing?

A model of interactions between clinicians and patients in which both contribute to the clinical decision-making process.

Some evidence suggests shared decision making improves adherence to antidepressant medications for depression.

A. Clinicians present patients with technical information about their condition and benefits/risks of available treatment options.
B. Patients inform clinicians about their goals, values, experiences, and preferences concerning the consequences of the treatment options.

Shared Decision Making
Medication management decisions for adults with ADHD

Shared decision making is especially relevant when:

1. There is more than one reasonable treatment option.
2. When scientific evidence about the safety/effectiveness of treatment options is limited.
3. When treatment options show a similar balance between benefits and risks
4. When patient benefits and risks affect patients or are valued by patients differently

Summary
Medication Management of Adults with ADHD

Consider integrating non-pharmacological interventions with medication management

Weigh stimulant vs. non-stimulant pharmacological options

Evaluate differential clinical effectiveness and risks of misuse

Shared decision making as a process that may improve adherence and clinical outcomes