National Academies Sciences, Engineering, and Medicine

Adult Attention Deficit/Hyperactivity Disorder: Diagnosis,
Treatment, and Implications for Drug Development
A Workshop December 12, 2023

Medication Options for Adults with ADHD: Risks and Benefits

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Who is Prescribing What in Adult ADHD?

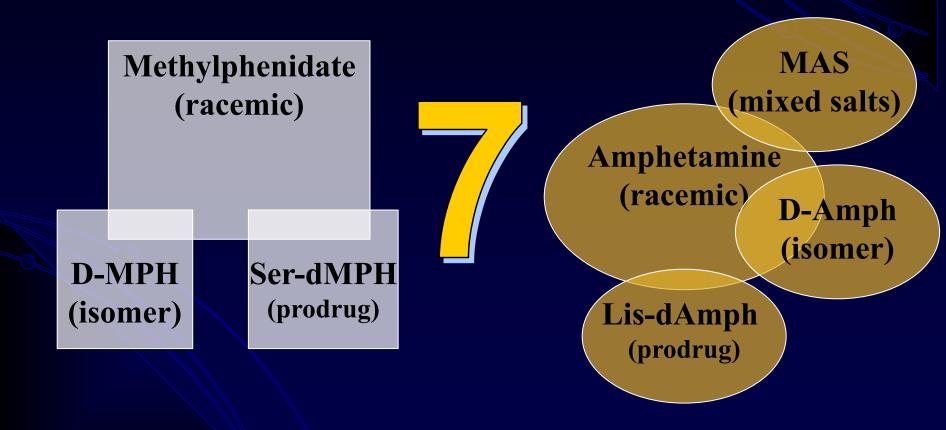
IOVIA ADHD TRX Feb 2020

- Total ADHD Market
 - 61% is adults; 39% is children
- Adult prescriptions:
 - 79% Amph; 13% MPH; 8% Non-stimulants
- Prescription by Specialty (ADHD all ages)
 - 49% by PCPs/NPs
 - 30% by psychiatrists
 - 19% by pediatricians

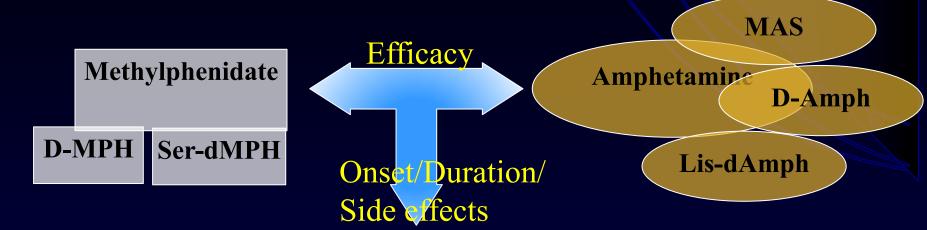
Number of Stimulant Preparations?

>30

Number of Stimulant Compounds?



ADHD Medications



Delivery System Technology

Beaded

(IR/ER ratio, double/triple beaded)

OROS (osmotic release)

Microparticles (liquid, dissolvable tabs, chewables)

Patch



Monotherapy

Adjunctive

Guanfacine ER Clonidine ER not FDA for adults)

Treatment Guidelines

"If stimulant medication is prescribed, a positive response *does not confirm* the diagnosis of ADHD."

Medication response does not make a diagnosis

In fact, 30% of ADHD adults do not have a beneficial response to the first stimulant. They may respond to an alternative stimulant.

Zametkin, A and Ernst, M. Problems in the Management of Attention Deficit-Hyperactivity Disorder. JAMA, Jan. 7, 1999,40-46. Rapport et al. Science, 1987. Rapport, et al. *Archives of General Psychiatry*. 1980;37:933-946.

Benefits

No Diagnosis or Treatment

No record of diagnosis

No pharmacy record

No impact on insurance candidacy

No impact on eligibility for occupational pursuits (military, law enforcement, licensing-pilot, others)

No positive drug screen for ADHD stimulant meds

No reporting of diagnosis

Diagnosed +Treatment

Psychological

Reduced risk of some negative outcomes

Reduce risk of SUD

Improved social relationships

Improved academic/occupational performance

Reduced societal economic costs

Risks

No Treatment

Increased risks of:

Tobacco/substance use

Early pregnancy/STDs

Academic underachievement

Criminal behavior

Car accidents

Multiple jobs

Financial debt

Premature death

Increased economic costs

Treatment

Psychological-if diagnosed incorrectly

Medication effects- stimulant vs non-stimulants

Side-effects

Psychosis

Cardiovascular effects

Misuse for performance

Misuse with other substances (alcohol)

Use for a "high"

Diversion to others

Long-Term Cardiovascular Effects of Medications for ADHD

- "Meta-analytic evidence² from randomized clinical trials (RCTs) shows that amphetamine or atomoxetine use is associated with statistically significant but, on average, small increases in systolic and diastolic blood pressure (BP, ≤5mm Hg) and heart rate (≤10 beats per minute), and methylphenidate may lead to small increases in BP."
- "A minority (5%-15%) of individuals can experience larger increases. The average duration of the trials included in this meta-analysis was 4 months."

Cortese S, Fava C; Long-Term Cardiovascular Effects of Medications for Attention-Deficit/Hyperactivity Disorder-Balancing Benefits and Risks of Treatment. JAMA Psychiatry; November 22, 2023

2. Hennissen L. Bakker MJ, Banaschewski T, et al; ADDUCE consortium. Cardiovascular effects of stimulant and non-stimulant medication for children and adolescents with ADHD: a systematic review and meta-analysis of trials of methylphenidate, amphetamines, and atomoxetine. CNS Drugs. 201;31(3):199-215. doi:10.1007/20263-017-010-7

Benefits of ADHD Stimulant Medication

- Meta-analytic evidence from RCTs demonstrates that stimulants have one of the highest effect sizes, in terms of efficacy, not only in psychiatry but also in medicine overall.¹
- Individuals with ADHD experience significantly fewer unintentional physical injuries, motor vehicle crashes, substance use disorders, and criminal acts, as well as improved academic functioning, during periods when they are taking, compared with periods when they are not taking, methylphenidate.¹

SUD with Prescription Stimulants

- About 10% of individuals in the general population misuse prescription stimulants.
- There is consistent data that extended-release preparation of stimulants have lower abuse liability; and are misused significantly less than immediate release.
- Anyone who misuses prescription stimulants should be queried for substance use disorders (50% rate).
- Non-stimulants have no misuse/abuse potential.

Nonmedical Use of Prescription Stimulants

- U.S. National Poison Data System
- 33,239 retained in study; Jan 2012 December 2016
- Nasal- greater risk of medical admission.
- IV- 21.9 times more likely to die from AMPH vs controls.
- Oral- greater risk of suicide attempts.
- Database doesn't account for cofactors, therefore association is not causality. (i.e. Bipolar and ADHD)

SUD: Divergent Findings by Research Methods

- Animal studies suggest that repeated exposure to stimulants during the sensitive adolescent period was associated with long-term risk of substance abuse (88).
- Clinical follow-up studies suggest that ADHD medication neither protects nor increases the risk of later substance use disorders (89, 90).
- Pharmacoepidemiology studies based on prescription databases have found that ADHD medication was associated with a lower risk of substance-related events up to three years later (64, 66).
- These results might be explained by the differences in the methods of animal, clinical, and pharmacoepidemiology studies.

Chang, Z, et al; Risks and benefits of ADHD medication on behavioral and neuropsychiatric outcomes: a qualitative review of pharmacoepidemiology studies using linked prescription databases. Biol Psychiatry. September 1, 2019; 86(5):335-343. doi: 10.1016/j.biopsych.2019.04.009.

Health Inequities for Appropriate Care and Treatment

- Females- gender bias in mis-diagnosis
- Racial- diagnostic bias by clinicians
- Ethnicities- cultural bias
- Older Age- diagnostic uncertainty/prescription hesitancy
- Rural communities- unavailable (few clinicians with training) or inaccessible (geographical)
- There is a general lack of formal education in professional training programs (psychiatric residencies, psychologists, nurse practitioners, physician assistants, social workers, physicians, pharmacists, mental health therapists)

Clinical Quality Measures

• Assessed 10 clinical measures from electronic health records of 71,310 adult patients diagnosed with ADHD from 2010 to 2020.

Quality Measure	2010	2020
No QMs recorded	52%	10%
2 or more QMs recorded	37%	75%
Treatment with documented DSM 5 ADHD dx	52%	97%
Seen within one month of first prescription	42%	84%
Vitals signs checked before prescription started	11%	24%
Discussed the warnings for medication	31%	29%

Callen EF, et al. J Atten Disorders. 2023. 27(6):575-582.

The Need for Research, Formal Training, and Clinical Education for Adult ADHD

- The APSARD Clinical Practice Guidelines will set a basic clinical standard for the diagnosis and treatment in the U.S.
- Encourage professional training programs to add a focus on adult ADHD to the curriculum.
- Increase research funding on parity with childhood ADHD. NIH's 2023 funding dollars for ADHD: \$5.5 million for adult ADHD, \$78 million for ADHD overall, and for comparison, \$650 million on depression.
- Appropriate funding for the national education of clinicians treating these patients and families.

American Professional Society for ADHD and Related Disorders

- There are international guidelines developed in UK, Canada, European Union, Australia.
- Task Force of 30 national and international researchers and clinicians from psychiatry, psychology, nurse practitioners, nursing, social work.
- The Guideline process has been published in Psychiatric Annuals October 2023 free CME
- Clinical Practice Guidelines development webinar (free CME) Dec 13, 2023



APSARD.org

PSYCH ANNALS



UPCOMING WEBINARS

