

ADHD: Analysis, Statistics, Treatment Approaches and Shortage

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ABSTRACT

One of the most prevalent forms of neurodevelopmental disorders is attention deficit hyperactivity disorder, also known as ADHD. The phrase “neurodevelopmental” has to do with the way the brain grows and develops. With noticeable symptoms and disability that last throughout adulthood, ADHD is frequently chronic. ADHD symptoms include impulsivity (hurried, thoughtless movements), hyperactivity (excessive movement that is inappropriate for the situation), and inattention (inability to maintain concentration). This article overviews analysis and statistics, explores the treatment options.

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Introduction and Overview

One of the most prevalent neurodevelopmental diseases in children seeking therapy is attention-deficit/hyperactivity disorder (ADHD) [1]. It usually becomes evident when hyperactivity manifests by age seven, though it can also occur in very young preschoolers. It could take a child's encounter with the demands of primary school to show signs of inattention or attention deficit [2]. It has a high prevalence of co-occurring mental health issues, including conduct disorder, mood and anxiety disorders, oppositional defiant disorder (ODD), and drug and tobacco use disorders [3].

There are Three Ways in which ADHD can Present itself Depending on the Individual's most Substantial Symptoms

- **Predominantly Inattentive Presentation:** The person finds it difficult to stay organized, complete tasks, pay attention to details, or follow directions or conversations. “They tend to avoid or dislike tasks that require prolonged mental effort. They tend to avoid or dislike tasks that require prolonged mental effort. The individual tends to become easily distracted or forget essential details related to their daily routine.
- **Predominantly Hyperactive-Impulsive Presentation:** The individual cannot sit still, fidgets, talks excessively, and displays impulsive behavior. Children may engage in constant running, jumping, or climbing. Someone impulsively interrupts others, grabs things from people, or speaks at inappropriate times. It is hard for the person to wait their turn or listen to directions. A person with impulsiveness may have more accidents and injuries than others.
- **Combined Presentation:** Inattentiveness, distractibility, and hyperactive, impulsive conduct are characteristics of this most common type of ADHD [4].

Diagnosis

To be diagnosed with ADHD, a child must have shown symptoms before the age of 12 [5]. Children up to the age of 16 are diagnosed with ADHD if they have displayed at most minuscule six

persistent symptoms of inattention and six persistent symptoms of hyperactivity-impulsivity for a minimum of six months.

Inattention Symptom as Per DSM-5

1. Their work, schoolwork, and other activities often require them to pay closer attention to details or make careless mistakes (e.g., they need to pay attention to more information; their work needs to be revised) [6].
2. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
3. Often does not seem to listen when spoken to directly (e.g., the mind seems elsewhere, even without any obvious distraction).
4. Frequently disobeys orders and neglects to complete tasks at work, school, or household chores.
5. Often needs help organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; better time management; failure to meet deadlines).
6. Avoids or finds it difficult to complete tasks that call for prolonged mental effort, such as homework or schoolwork; for older teens and adults, this can include creating reports, filling out forms, and reviewing lengthy papers.
7. Often needs to gain things necessary for tasks or activities.
8. Extraneous stimuli frequently cause the youngster to become easily distracted (for older teens and adults, this may include irrelevant ideas).
9. Often needs to be more mindful in daily activities.

Hyperactivity and Impulsivity, as Per DSM-5

1. The person frequently moves their hands or feet or wiggles in their seat.
2. Often, leave seats when remaining seated is expected (e.g., leave their place in the classroom, in the office, or another workplace).
3. They frequently rush around or climb in improper places. (Note: In adolescents or adults, it may be limited to feeling restless).
4. It is often difficult for the person to engage in leisure activities

- or play quietly.
- They act like they're "driven by a motor" and are frequently "on the go" (i.e., find it challenging to sit still for long periods, including during meetings at restaurants); others may find them agitated or challenging to follow.
 - Frequently talks too much.
 - Frequently answers questions before they are fully asked (e.g., finishing others' sentences; impatient for a turn in discussion).
 - They often require assistance in waiting for their turn. (e.g., while waiting in line).
 - Frequently interrupts or intrudes on other people (e.g., butts into games, talks, or activities; begins using other people's belongings without permission; for adults and teens, may trespass into or take over other people's activities).

Statistics

The prevalence estimates of ADHD exhibit variability due to variations in study methodology, age groups under investigation, and evolving diagnostic criteria [7,8]. Millions of kids worldwide have been diagnosed with ADHD. Data from a national survey of parents between 2016 and 2019 estimates children aged 3-17 were diagnosed with ADHD is 6 million. This number includes,

- 3-5 years: 265,000 (2%)
- 6-11 years: 2.4 million (10%)
- 12-17 years: 3.3 million (13%)

Boys are 13 % more likely than girls to receive an ADHD diagnosis; this may be because guys are more prone than girls to exhibit hyperactive behavior, which is readily noticeable and potentially disruptive [9]. Nearly two-thirds of children and adolescents with ADHD who were diagnosed within the last year were on medication, and around half had received behavioral treatment for the disorder. Almost 25% had not had any ADHD treatment [10]. Six in ten children with ADHD also have at least one additional mental, emotional, or behavioral issue, such as depression, autism spectrum disorder, Tourette syndrome, or anxiety, according to a national parent study conducted in 2016 [11].

Treatment

The Journal of Pediatrics released a study examining the various forms of treatment given to American children diagnosed with attention-deficit/hyperactivity disorder (ADHD) between the ages of 4 and 17. For children older than six, experts advise combining medicine and behavior therapy; for younger children, behavior it is advisable to commence therapy as early as possible [10].

Stimulants

Two groups of stimulants, i.e., amphetamine salts and methylphenidate, have been approved by the FDA for the treatment of ADHD in the pediatric population.

- Amphetamine salt:** Through several different methods, amphetamine, a central nervous system (CNS) stimulant, increases dopamine, norepinephrine, and serotonin levels in the synaptic cleft. DAT, NET, and SERT are the monoamine transporters that take up amphetamine through uptake or diffusion into the presynaptic axon terminal. Amphetamine inhibits vesicular monoamine transporter 2 (VMAT2) and disrupts the electrochemical gradients required for vesicular transporter activity once it has entered the presynaptic terminal, increasing the quantities of monoamine neurotransmitters in the cytosol [11].
- Methylphenidate:** Methylphenidate prevents dopamine and norepinephrine (NE) from being reabsorbed by presynaptic neurons. The transporters of neurotransmitters are blocked to

regulate their levels in the synaptic cleft of NE and dopamine. Thus, methylphenidate produces its well-known stimulant action in the prefrontal cortex of the central nervous system (CNS). Methylphenidate seems to speed up neuronal firing rate compared to other drugs (such as amphetamines) that are phenethylamine derivatives. Another factor contributing to elevated dopamine levels is that it is a mild agonist at the 5HT1A receptor [12].

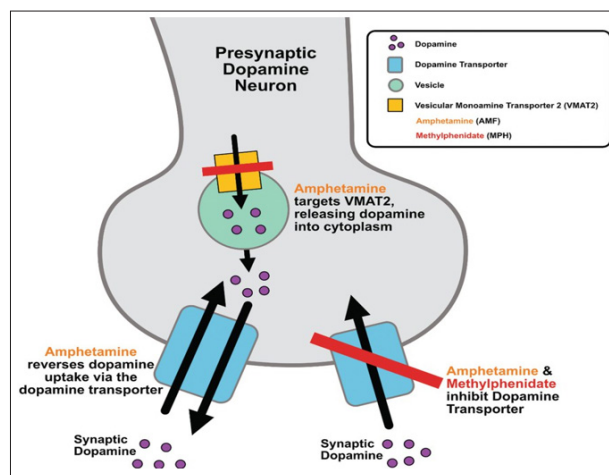


Figure 1: Mechanism of Action [13].

Methylphenidate Formulations

Methylphenidate IR (immediate release)	2.5-20 mg tabs, oral suspension, and chewable 2-3 times a day, 30 min before meal	Contraindication: a) Monoamine oxidase inhibitors (MAOI): min 14 days after discontinuation b) Glaucoma c) Severe hypertension Side Effects: a) Nausea b) Loss of appetite c) Insomnia d) Dizziness e) Headache Monitoring: i. Blood pressure ii. Heart rate
Methylphenidate SR (sustained release)	20 mg SR tablets	
Methylphenidate long-acting (LA) 1/2 IR, 1/2 SR in one capsule	10-40 mg LA capsule	
Methylphenidate ER (extended release)	10-20 mg ER tablets	
Methylphenidate IR-ext rel (Concerta) OROS system	18,27,36,54 mg ER tablets	
Dexmethylphenidate IR	1.5-10 mg tablets	Same as methylphenidate
Dexmethylphenidate ER	5-40 mg Capsule	

Methylphenidate IR-ext rel (METADATE CD) beads that dissolve at different rates	10-60 mg ER capsule	iii. Height & weight iv. Mood changes v. Abuse (adults)
Methylphenidate transdermal patch (Daytrana)	1.1 mg/hr 3.3 mg/hr	

Dexmethylphenidate Formulations

Dextroamphetamine and Amphetamine

Dextroamphetamine and amphetamine IR (adderal)	5-30 mg scored tablet	Contraindication: Monoamine oxidase inhibitors (MAOI): min 14 days after discontinuation Glaucoma Severe hypertension Side Effects: Nausea Loss of appetite Insomnia Dizziness Headache Monitoring: Blood pressure Heart rate Height & weight Mood changes
Dextroamphetamine and amphetamine ER (adderal xr)	5-30 mg ER capsule	
Dextroamphetamine IR	5-10 MG tablets	
SR and IR Dextroamphetamine	5,10,15 mg SR capsule	

Lisdexamfetamine (prodrug of dexamphetamine)

Lesdexamfetamine (Vyvanse)	10mg -70 mg capsules	Same as Dextroamphetamine and amphetamine
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Non-Stimulant Medication

Norepinephrine Reuptake Inhibitors

1. **Atomoxetine:** As a norepinephrine reuptake inhibitor, atomoxetine raises synaptic noradrenaline by attaching to the norepinephrine transporter. Norepinephrine transporters regulate dopamine reuptake in the prefrontal cortex since there aren't many dopamine transporters there. As a result, atomoxetine raises dopamine and noradrenaline in the synapses of the prefrontal cortex [14]. Especially during the first few months of treatment, children receiving atomoxetine should be regularly monitored for signs of suicidality, clinical deterioration, and unexpected behavioral changes. Dosing adjustments should also be closely observed.

2. **Qelbree (Viloxazine):** Studies reveal that the mechanism of action of Viloxazine is directly linked to blocking norepinephrine reuptake. Nonetheless, it is remarkable that Viloxazine does not affect norepinephrine release. Studies have shown Viloxazine efficiently blocks norepinephrine transport, which results in elevated norepinephrine levels via reuptake inhibition in the amygdala, nucleus accumbens, and prefrontal cortex. Moreover, Viloxazine somewhat raises dopamine levels in the amygdala, prefrontal cortex, and, to a lesser degree, the nucleus accumbens. The norepinephrine transporter, also in charge of dopamine reuptake, is thought to cause this phenomenon [15]. Children receiving this drug require close monitoring for any signs of clinical deterioration and suicidality.

Alpha Agonist

1. **Kapvay (Clonidine hydrochloride ER tablet):** By stimulating alpha2-adrenergic receptors in the brain stem, clonidine reduces

sympathetic outflow from the central nervous system as well as blood pressure, heart rate, peripheral resistance, and renal vascular resistance [16]. The mechanism of action of clonidine in ADHD is not known.

2. **Intuniv (guanfacine ER):** Inhibiting cAMP synthesis and closing HCN channels, guanfacine activates postsynaptic alpha-2A adrenergic receptors. This increases the effectiveness of pyramidal neurons in the prefrontal cortex (PFC) signaling and enhances working memory and attention. Furthermore, activation of the alpha-2A receptors stimulates the dendritic spines of pyramidal neurons in the medial PFC, which are linked to cognitive processes, including memory and learning [17].

Conclusion

While ADHD is not a brand-new phenomenon, its incidence has sharply grown in recent years. This outcome is not surprising given evolving diagnostic criteria and increasing awareness of the condition among underrepresented populations, particularly women and people of color. Social media and the media have raised awareness of ADHD among the public. Individuals are more inclined to discuss their worries with a doctor, which could lead to more diagnoses. For both pediatric and adult populations with ADHD and concurrent disorders, pharmacotherapy using stimulants is a cornerstone of evidence-based treatment. A thorough assessment of the child and their family, including evaluations for mental health, social skills, cognitive abilities, and education, should come before using stimulants. Before difficulties, chronicity, and social incapacitation, early therapeutic intervention is crucial. Even though the pharmacological treatments for ADHD that are already available have generally good tolerability and reasonably substantial effect sizes (in short-term trials), there is still a need to discover new drugs and enhance existing pharmacotherapeutic techniques.

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