

**Team#1 Knowledge Tracker:  
ADHD 101**



This doc functions as a collection point for all our team’s questions, research, and exploration regarding everything ADHD.

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## **1. ADHD OVERVIEW**

### **A. What Is ADHD?**

Attention-deficit/hyperactivity disorder (ADHD) is a **chronic neurodevelopmental condition** characterized by persistent patterns of **inattention, impulsivity, and/or hyperactivity** that interfere with daily functioning. It affects children and adults, impacting academic, occupational, and social life, with symptoms often continuing into adulthood.

*(Sources: DSM-5, NIMH)*

### **B. Epidemiology**

- **Global Prevalence:** ~5-7% of children, 2.5-4% of adults
- **U.S. Prevalence:** 9.8% of children, 4.4% of adults (CDC estimated adult ADHD population at 15.5 million in 2023)
- **Gender Differences:** More frequently diagnosed in boys (~2:1 in childhood), but girls may be underdiagnosed due to symptom differences

*(Sources: CDC, APA, NIMH)*

### **C. Pathophysiology & MODs**

- **Neurotransmitter Dysregulation:** Dopamine/norepinephrine imbalances in the prefrontal cortex can affect attention and impulse control
- **Brain Structure Differences:** Smaller volume in key regions linked to executive function
- **Genetic Factors:** Highly heritable (~74%), with genes like DRD4, DAT1 implicated
- **Environmental Influences:** Prenatal nicotine exposure, low birth weight, early adversity

*(Sources: NIMH, JAACAP)*

### **D. Presentations**

- **ADHD – Predominantly Inattentive Type (ADHD-PI):** More common in females, often overlooked
- **ADHD – Predominantly Hyperactive-Impulsive Type:** More common in younger children
- **ADHD – Combined Type:** Most prevalent, with a mix of both symptom groups

*(Sources: DSM-5, NIMH, CHADD)*



## **E. Symptoms**

### **1) Inattentive Symptoms**

- Easily distracted, trouble focusing on tasks
- Difficulty following instructions or completing assignments
- Often forgetful and misplaces items
- Avoids tasks requiring sustained mental effort

### **2) Hyperactive-Impulsive Symptoms**

- Fidgeting, restlessness, difficulty staying seated
- Interrupting conversations, talking excessively
- Acting without thinking, difficulty waiting turns

### **3) Emotional and Executive Dysfunction**

- Difficulty regulating emotions, quick mood swings
- Poor time management, procrastination
- Struggles with long-term planning and organization

*(Sources: DSM-5, NIMH, CHADD)*

## **F. Often Overlooked Symptoms & Unseen Burdens**

- **Rejection Sensitivity Dysphoria (RSD):** Intense emotional pain from perceived rejection
- **Executive Dysfunction:** Time blindness, task initiation difficulties, emotional regulation
- **Masking & Burnout:** Many, especially women, hide symptoms, leading to late diagnosis
- **Sleep Dysregulation:** Strong link to delayed sleep phase syndrome (DSPS)

*(Sources: ADHD 2.0, Journal of Psychiatric Research)*



## G. Diagnosis

### How ADHD is Diagnosed

- **Clinical Assessment:** Diagnosis is made by evaluating symptoms based on **DSM-5 criteria**
- **Symptoms must:**
  - be persistent
  - impair daily functioning
  - be present in multiple settings (*ex. home, school, work*)
  - appear before age 12 (*for diagnosis in children*)
- **Symptom Categories:**
  - Inattention: Difficulty sustaining focus, forgetfulness, disorganization
  - Hyperactivity-Impulsivity: Fidgeting, excessive talking, difficulty waiting turns
- **Evaluation Process:**
  - Patient/Caregiver Interviews: gathering behavioral history from multiple sources
  - Standardized Rating Scales: completed by parents, teachers, patient
  - Rule Out Other Conditions: Screening for anxiety, depression, learning disabilities
- **Key Consideration:** ADHD can present differently in adults, often with more executive function deficits than hyperactivity

*(Sources: DSM-5, APA, AAP, CDC, NIMH)*

### Challenges in Diagnosing ADHD

- **Symptom Overlap with Other Conditions:**
  - ADHD symptoms mimic anxiety, depression, autism, and learning disabilities
  - Misdiagnosis or missed diagnosis is common
- **Variability in Presentation:**
  - Symptoms change with age (*ex. hyperactivity in childhood may shift to restlessness in adulthood*)
  - Presents differently in girls vs. boys (*girls often show more inattentive symptoms, leading to underdiagnosis*)
- **Subjective & Context Dependent Diagnosis:**
  - No definitive lab test available
  - Diagnosis relies on self-reporting, clinical interviews, and behavioral assessments

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- Consistency of symptoms hard to assess (*they must be present in multiple settings*)
- **Compensatory Strategies Mask Symptoms:**
  - High-IQ individuals or those with strong coping mechanisms may go undiagnosed until adulthood
  - Many adults are diagnosed late due to years of masking or misattributing struggles
- **Social & Cultural Biases:**
  - ADHD is sometimes dismissed as:
    - laziness (*“ADHD doesn’t exist—you’re just being lazy!”*)
    - lack of discipline (*“You just need to try harder!”*)
    - faulty personality traits
  - Underdiagnosis in minority groups due to:
    - lack of access to specialists
    - cultural stigma

*(Sources: DSM-5, APA, CDC, NIMH, CHADD, JAMA)*

### H. Patient Burdens & QOL Issues

ADHD isn’t just about being "hyper" or "distracted." It impacts every part of life—often leading to stress, frustration and lower overall life satisfaction.

#### 1) Academic Struggles

- Difficulty with focus and task completion:  
ADHD makes it hard to stay engaged in lectures, complete homework, and follow multi-step instructions.
- Poor time management:  
Many students with ADHD struggle with deadlines and procrastination, leading to rushed/incomplete work.
- Lower grades and higher dropout rates:  
ADHD is associated with lower academic performance, repeated grades, and increased risk of dropping out of school.
- Challenges with traditional learning methods:  
Many people with ADHD learn better through hands-on/interactive methods rather than lectures/memorization.

★ **Impact:** Students may feel frustrated, misunderstood, or "lazy" when, in reality, their brain processes info differently.

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💡 **Need:** ADHDers need structured, interactive, and personalized learning approaches to thrive.

*(Sources: DSM-5, CDC, NCLD, Barkley2014)*

## 2) Workplace Challenges

- Time management and organization issues:  
Adults with ADHD often struggle with lateness, meeting deadlines, prioritizing tasks, and keeping track of responsibilities.
- Job performance inconsistencies:  
Some days, they may be highly productive, while other days, they struggle to complete even simple tasks.
- Higher job turnover and instability:  
Research suggests adults with ADHD are more likely to change jobs frequently or get fired due to performance issues.
- Difficulty with workplace relationships:  
Impulsivity can lead to interrupting others, missing social cues, or struggling with authority figures.

🌟 **Impact:** They underperform relative to their intelligence/capabilities, leading to lower wages and career dissatisfaction.

💡 **Need:** ADHDers need structured workflows, external accountability, and accommodations to thrive in their career.

*(Sources: HBR, CHADD, Biederman2006)*

## 3) Social & Emotional Impact

- Struggles with relationships:  
Difficulty listening, impulsivity, and forgetfulness can make romance/friendship/family-bonds challenging.
- Low self-esteem and self-doubt:  
Years of criticism for being "lazy" or "not trying hard enough" can lead to chronic self-doubt and a negative self-image.
- Increased risk of anxiety and depression:  
The emotional toll of ADHD can lead to coexisting mental health conditions. Studies show:
  - 50% develop an **anxiety** disorder

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- 30-50% develop depression
- Emotional dysregulation:  
Many with ADHD experience intense emotions which can feel overwhelming and hard to control.

★ **Impact:** They can tend to loneliness, relationship breakdowns, and feelings of failure, even when trying their best.

💡 **Need:** Access to tools like therapy to help improve self-awareness, communication, relationships, and mental health

*(Sources: NIMH, Kessler2006)*

### 4) Financial Burden

- Higher healthcare costs:  
People with ADHD often require specialized support which can be expensive.
- Impulsive spending:  
Impulse control issues can lead to poor financial decisions, overspending, and difficulty saving money.
- Workplace inefficiencies:  
ADHD-related productivity losses and unemployment cost businesses est. \$140 billion annually in the U.S.
- Legal and financial troubles:  
Poor organization can lead to missed bill payments, overdraft fees, or tax issues.

★ **Impact:** Struggles with financial instability can make it harder to feel secure and plan for the future.

💡 **Need:** Access to tools like automation and financial planning tools to help gain control over finances

*(Sources: CDC, CHADD, Barkley2010)*

### I. Possible Role of Smart Phones/Tech & Social Media in ADHD

- **Increased ADHD Symptom Visibility:** Social media algorithms reward/reinforce impulsivity and distractibility
- **Attention Fragmentation:** Constant notifications and short-form content may worsen focus
- **Potential Benefits:** Digital tools like ADHD apps can aid organization, focus, and time management

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*(Sources: Journal of Attention Disorders, APA)*

## 2. **ADHD TREATMENT LANDSCAPE**

### A. Treatment Goals

Currently available treatments focus on **symptom management** and **functional improvement**, primarily aiming to:

- improve attention and focus
- decrease impulsivity and hyperactivity
- support emotional regulation
- reduce risk of coexisting mental health conditions

*(Sources: AAP, APA, NICE, CDC, CHADD, MGH)*

### B. Standard of Care

ADHD management typically involves a multimodal approach.

- **Medication:**
  - First-line: Stimulants (ex. methylphenidate, amphetamines)
  - Second line: Non-stimulants (esp. for those who cannot tolerate stimulants)
- **Behavioral Therapy:** including Cognitive Behavioral Therapy (CBT) and behavioral interventions for coping strategies
- **Lifestyle Adjustments:** like encouraging exercise, diet changes, and mindfulness practices
- **Coaching & Support Systems:** ADHD coaches and executive function training can improve daily life skills.

*(Sources: AAP, NICE)*

### C. ADHD Medications

#### Stimulants:

#### 1) Adderall

- Generic: (amphetamine/dextroamphetamine)
- Company: Takeda

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- FDA-approved in 1996
- MOA: Increases dopamine & norepinephrine availability
- Efficacy: Improves focus & impulse control in ~70% of patients

### 2) Concerta

- Generic: (methylphenidate ER)
- Company: Janssen
- FDA-approved in 2000
- MOA: Dopamine/norepinephrine reuptake inhibitor
- Efficacy: Extended time-released throughout day to significantly reduces inattention and impulsivity
- Website: [concerta.net](http://concerta.net)

### 3) Daytrana

- Generic: (methylphenidate transdermal system)
- Company: Noven Pharmaceuticals
- FDA-approved in 2006
- MOA: Transdermal patch that delivers methylphenidate through the skin, increasing dopamine and norepinephrine activity in the brain
- Efficacy: Provides steady ADHD symptom control throughout the day; offers a non-oral option for patients who have difficulty swallowing pills
- Website: [daytrana.com](http://daytrana.com)

### 4) Vyvanse

- Generic: (lisdexamfetamine dimesylate)
- Company: Takeda
- FDA-approved in 2007
- MOA: Prodrug converted to dextroamphetamine, increasing dopamine & norepinephrine availability
- Efficacy: Sustained symptom control for  $\leq 14$  hrs, with reduced potential for abuse due to prodrug formulation

### 5) Evekeo

- Generic: (amphetamine sulfate)
- Company: Arbor Pharmaceuticals

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- FDA-approved in 2014
- MOA: Racemic mixture of amphetamine salts that enhances dopamine & norepinephrine activity
- Efficacy: Studies indicate that it helps sustain attention and reduce disruptive behaviors throughout the day
- Website: [evekeo.com](http://evekeo.com)

### 6) Dyanavel XR

- Generic: (amphetamine)
- Company: Tris Pharma
- FDA-approved in 2015
- MOA: Extended-release liquid formulation that enhances dopamine & norepinephrine activity
- Efficacy: Sustained ADHD symptom management, particularly for patients who prefer liquid medications
- Website: [dyanavelxr.com](http://dyanavelxr.com)

### 7) Adzenys XR-ODT

- Generic: (amphetamine)
- Company: Neos Therapeutics
- FDA-approved in 2016
- MOA: Extended-release orally disintegrating, Adderall bioequivalent
- Efficacy: Provides once-daily ADHD symptom control with an alternative to traditional tablets
- Website: [adzenysxrodt.com](http://adzenysxrodt.com)

## Non-Stimulants:

### 8) Strattera

- Generic: (atomoxetine)
- Company: Eli Lilly (formerly) (brand discontinued in 2023 after generic became available in 2017)
- FDA-approved in 2002
- MOA: Selective norepinephrine reuptake inhibitor
- Efficacy: Improves attention & impulse control in patients intolerant to stimulants, with effects building over weeks

### 9) Intuniv

- Generic: (guanfacine extended-release)
- Company: Takeda

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- FDA-approved in 2009
- MOA: Alpha-2 adrenergic agonist that modulates prefrontal cortex activity
- Efficacy: Adjunct therapy that can help manage residual symptoms and reduce stimulant-related side effects

### 10) Kapvay

- Generic: (clonidine extended-release)
- Company: Concordia Pharmaceuticals (formerly) (discontinued after generic became available)
- FDA-approved in 2010
- MOA: Alpha-2 adrenergic agonist that reduces norepinephrine release
- Efficacy: Its gradual MOA makes it beneficial for patients who experience heightened evening restlessness

### 11) Qelbree

- Generic: (viloxazine)
- Company: Supernus Pharmaceuticals
- Expanded FDA-approved in 2022
- MOA: Selective norepinephrine modulator
- Efficacy: Shown to significantly reduce ADHD symptom scores as early as week 2 in clinical studies
- Website: [qelbree.com](http://qelbree.com)

### 12) Onyda XR

- Generic: (clonidine hydrochloride)
- Company: Tris Pharma
- Expanded FDA-approved in 2024
- MOA: Centrally acting alpha<sub>2</sub>-adrenergic agonist; extended-release oral suspension designed for once-daily nighttime dosing to modulate norepinephrine activity in the brain
- Efficacy: particularly beneficial for pediatric patients who prefer liquid medications or require adjunctive therapy to stimulants
- Website: [onyda.com](http://onyda.com)

*(Sources: FDA, APA)*

## D. Adverse Reactions

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### Stimulants

- **Amphetamines & Methylphenidates:**
  - 📄 Examples: Adderall, Vyvanse, Concerta
  - ⚠️ Common Side Effects: Insomnia, appetite loss, increased heart rate, irritability, headaches
  - ⚡ Serious Risks: Heart issues, psychiatric effects (anxiety, aggression, hallucinations), potential for misuse

### Non-Stimulants

- **Atomoxetine:**
  - 📄 Ex: Strattera
  - ⚠️ Nausea, fatigue, appetite loss
  - ⚡ Black box warning: Increased suicidal thoughts in youth, liver toxicity risk
- **Viloxazine**
  - 📄 Ex: Qelbree
  - ⚠️ Sleepiness, nausea, irritability
  - ⚡ Suicide risk, blood pressure elevation, mood swings
- **Alpha-2 Agonists**
  - 📄 Ex: Intuniv, Kapvay
  - ⚠️ Fatigue, dizziness, dry mouth
  - ⚡ Risk of low blood pressure, bradycardia, rebound hypertension if stopped abruptly

### 💡 Key Takeaways

- **Stimulants** are highly effective but carry risks of cardiovascular effects, appetite suppression, and insomnia
- **Non-stimulants** have a lower abuse potential but may cause sedation, mood changes, or blood pressure issues
- **All ADHD medications require:**
  - close monitoring
  - careful dosing
  - patient-specific considerations

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*(Sources: FDA, NIMH, Mayo Clinic, AAP, Clinical Reviews)*

### E. Companies With ADHD Pipelines

#### 1) Takeda

- History with ADHD: owns Adderall XR and Vyvanse (both widely prescribed)
- Pipeline:
  - Developing next-gen stimulant formulations with smoother symptom control, reduced crash effects, and minimized abuse potential
  - Researching prodrug stimulants with extended-release properties for all-day efficacy

#### 2) Janssen

- History with ADHD: created Concerta
- Pipeline:
  - Investigating ultra-long-acting stimulant meds for full-day symptom relief with minimal rebound effects
  - Researching novel delivery mechanisms to optimize absorption and reduce variability in response

#### 3) Supernus Pharmaceuticals

- History with ADHD: recently launched Qelbree
- Pipeline:
  - Exploring innovative non-stimulant therapies targeting multiple neurotransmitter systems beyond norepinephrine
  - Aiming to improve executive function and emotional regulation while reducing side effects
  - Investigating extended-release formulations and combination therapies to enhance treatment efficacy

*(Sources: Company Reports, ClinicalTrials.gov)*

### F. Companies Advancing Toward FDA Approval

#### • Cingulate Inc.

- Lead Candidate: CTx-1301 (dexamethylphenidate)
- Status: Completed Phase 3 trials; NDA submission planned for mid-2025
- Innovation: Utilizes Precision Timed Release™ (PTR™) technology for true once-daily dosing, aiming to provide consistent therapeutic levels throughout the day without the need for booster doses .

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- **Axsome Therapeutics**
  - Candidate: Solriamfetol (Sunosi)
  - Status: Phase 3 trial (FOCUS) achieved primary and key secondary endpoints in adults with ADHD
  - Mechanism: A dopamine and norepinephrine reuptake inhibitor (DNRI), originally approved for narcolepsy, now being evaluated for ADHD treatment
- **Otsuka Pharmaceutical Development & Commercialization, Inc.**
  - Candidate: Centanafadine (EB-1020)
  - Status: Completed Phase 3 trials
  - Mechanism: Triple reuptake inhibitor targeting serotonin, norepinephrine, and dopamine, offering a novel approach to ADHD treatment
- **Supernus Pharmaceuticals**
  - Candidate: SPN-810 (molindone ER)
  - Status: Phase 3 trials targeting impulsive aggression in children with ADHD
  - Mechanism: A dopamine D<sub>2</sub> receptor antagonist and serotonin receptor modulator, addressing behavioral symptoms associated with ADHD
- **Ironshore Pharmaceuticals**
  - Candidate: HLD200 (delayed-release and extended-release methylphenidate)
  - Status: Undergoing Phase 3 clinical development
  - Innovation: Designed for evening dosing to manage early morning ADHD symptoms in children
- **Shionogi & Co., Ltd.**
  - Product: ENDEAVORRIDE® (digital therapeutic app)
  - Status: Received manufacturing and marketing approval in Japan for pediatric ADHD
  - Innovation: A digital therapeutic developed in collaboration with Akili, Inc., providing an adjunctive treatment option for children with ADHD .

*(Sources: Company Reports, ClinicalTrials.gov, GlobeNewswire, PubMed)*

### G. IPG's ADHD Collaborations

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- **Takeda:** an IPG subsidiary (Shire) co-promoted ADHD meds like Adderall XR, Daytrana, and Vyvanse as recently as 2023
- **Eli Lilly:** an IPG subsidiary (Foote Cone & Belding) contributed to ADHD awareness initiatives tied to Strattera

### 3. **AI & ADHD**

#### A. **AI/Tech Solutions for ADHD**

- **AI-Powered Diagnostic Tools:** AI algorithms could help improve early ADHD diagnosis using behavioral data
- **Therapy Apps:** Apps like **Akili Interactive's EndeavorRx** (an FDA-approved digital therapy) use AI-driven cognitive training
- **Wearable Tech:** Smartwatches with ADHD-focused reminders can help with executive function support.
- **Coaching & Support:** AI-powered chatbots/coaches & personal assistant apps can help manage tasks and provide structure

*(Sources: Nature Digital Medicine, FDA, ClinicalTrials.gov)*