# **Clinical Guidelines:**

# Pharmacologic Treatment of Attention Deficit and Hyperactivity Disorder (ADHD) in Children and Adolescents

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# 1. BACKGROUND

Community Behavioral Health (CBH) is committed to working with our provider partners to continuously improve the quality of behavioral health care for our shared population. Whenever possible, this is best accomplished through the implementation of evidence-based practices, as well as those informed by nationally recognized treatment guidelines, while respecting the need for individualized treatment.

The following are medication prescribing standards, adapted for the CBH Network from national treatment guidelines. They are intended to guide providers in aligning their practices with the best available scientific evidence to help members with ADHD access state-of-the-art care.

To assess quality of care, CBH will be collecting several standardized metrics. These metrics come either from the Healthcare Effectiveness Data and Information Set (HEDIS), a set of measures used by many major health care organizations for quality improvement or are measures of clear clinical priority in our network. While CBH will be collecting specific data related only to guidelines that have been issued to the network thus far, the use of empirical guidelines and practice parameters is encouraged in all prescribing.

CBH expects providers to follow these guidelines in addition to all other relevant CBH, state, and federal regulations and standards, including CBH prescribing Bulletins (e.g., Provider Bulletin 07-07: Screening for and Treatment of the Components of Metabolic Syndrome), the Department of Behavioral Health and Intellectual disAbility Services (DBHIDS) Practice Guidelines for Resiliency and Recovery-Oriented Treatment, and the DBHIDS Network Inclusion Criteria (NIC) Standards for Excellence.

Note further that the following are guidelines for the pharmacologic treatment of ADHD. CBH and DBHIDS encourage a biopsychosocial and recovery- and resiliency-based approach to treatment; in each case, these guidelines for medication treatment should be but one part of a robust, multidisciplinary treatment approach that involves high-quality psychosocial treatment, collaboration with physical health providers, and inclusion of families and other supports.

# 2. PURPOSE

CBH has updated its guidelines for the treatment of ADHD in children and adolescents to reflect the most recently published evidence-based practice parameters available: those of the American Academy of Pediatrics (AAP), issued in 2019<sup>1</sup>. The current guidelines include references to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5-TR), published since the last iteration of the guidelines in 2011. The update includes the addition of a key action statement regarding the treatment of comorbid conditions. Also notable is the addition of a supplemental article on systemic barriers to the care of children

<sup>&</sup>lt;sup>1</sup> Wolraich ML, Hagan JF, Allan C, et al. AAP Subcommittee on Children and Adolescents with Attention Deficit/Hyperactive Disorder. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. 2019;144(4):e20192528.



and adolescents with ADHD. The AAP subcommittee included representatives from the American Academy of Child and Adolescent Psychiatry (AACAP). AACAP Clinical Practice Guidelines for ADHD are pending and will replace the <u>AACAP Practice Parameters for ADHD</u><sup>2</sup>. CBH encourages its network providers to remain current with the state of evidence-based practice parameters and to incorporate these into the clinical care offered. These guidelines reflect the best scientific evidence available to guide treatment delivery and should be considered the standard of care in the CBH Network. Resources including further details on behavioral treatments related to these guidelines for providers may be accessed in the <u>AAP Clinical Practice</u> Guidelines.

# 3. PRACTICE GUIDELINES (ADAPTED FROM AAP GUIDELINES)

#### 3.1. Assessment

Any child four through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity should receive an evaluation for ADHD. To make a diagnosis of ADHD, the prescribing physician should confirm and document that DSM-5-TR criteria have been met (including documentation of impairment in more than one major setting). This diagnosis should be informed primarily by reports from parents or guardians, teachers, and other school and mental health clinicians involved in the child's care. Parent and teacher behavior rating scales (e.g., the ADHD Rating Scale-IV, the Child Behavior Checklist, the Vanderbilt ADHD diagnostic scales, and the Conners rating scales) may be helpful in clarifying the diagnosis.

In the evaluation of a child for ADHD, assessment should be completed for comorbid conditions, including emotional or behavioral (e.g., anxiety, depressive, oppositional defiant, conduct, or trauma-related disorders, substance use), developmental (e.g., learning and language disorder, autism spectrum disorders), and physical (e.g., tics, sleep apnea) conditions. These evaluations must be done by appropriately trained and licensed personnel. The presence of a comorbid condition may alter the treatment of ADHD in some cases.

## 3.2. Cultural and Social Determinants of Health

Recent evidence suggests that African American and Latinx children are less likely to have ADHD diagnosed and are less likely to be treated for ADHD. Special attention should be given to these populations when assessing comorbidities related to ADHD and during ADHD treatment.

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<sup>&</sup>lt;sup>2</sup> Pliszka, Steven. AACAP Workgroup on Quality Issues. <u>AACAP Official Action, Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder</u>. Journal of the American Academy of Child and Adolescent Psychiatry. 2007;46(7): 894-921.



### 3.3. Prescribing & Treatment Guidelines

Recommendations for treatment of children and adolescents with ADHD vary by age:

1. For preschool-aged children (defined by the AAP as children 4-5 years of age), the AAP recommends implementing evidence-based parent- and/or teacher-administered behavior therapy (e.g., Parent Child Interaction Therapy) as the first line of treatment. The AAP recommends methylphenidate as the first line medication if behavioral interventions do not provide significant improvement and there is moderate to severe functional impairment. The AAP notes that methylphenidate is not FDA-approved for the treatment of ADHD in preschool-aged children but has the most robust evidence to support its use in this population. Short-acting amphetamine/dextroamphetamine and dextroamphetamine are FDA-approved to treat ADHD in children as young as three years of age. The AAP does not recommend amphetamines as first line medication for ADHD in this population as they report that the criteria for FDA approval at the time does not meet current standards for approval. The AAP does not recommend diagnosing or treating children younger than four years of age with ADHD based on insufficient data, except for parent training in behavior management for ADHD-like symptoms with significant impairment.

In areas where evidence-based behavioral treatments are not available, the clinician needs to weigh the risks of starting medication at an early age against the harm of delaying diagnosis and treatment.

2. For elementary school-aged children (6-11 years of age), the clinician should prescribe FDAapproved medications for ADHD (see Table 1 in Section 5.) and/or evidence-based parent and/or teacher-administered behavior therapy as treatment for ADHD, preferably both. The evidence is particularly strong for stimulant medications and sufficient but less strong for atomoxetine, extended-release guanfacine, and extended-release clonidine (in that order). The school environment, placement, and supports should be a part of a comprehensive treatment plan and often includes an Individualized Education Program (IEP) or Section 504 plan. c. For adolescents (12-18 years of age), clinicians should prescribe FDA-approved medications for ADHD (see Table 1) with the assent of the adolescent and may prescribe behavior therapy as treatment for ADHD, preferably both. Stimulant medications are highly effective in reducing core ADHD symptoms in adolescents.

The school environment, program, or placement should be a part of a comprehensive treatment plan and often includes an IEP) or Section 504 plan.

The prescriber should initiate and titrate the doses of medication for ADHD to achieve the maximum benefit with minimum adverse effects.

# 3.4. Medication Side Effect Monitoring

Prescribers are encouraged to monitor heart rate (HR) and blood pressure (BP) in youth taking stimulant medication. Non-stimulant ADHD medications may also impact HR and BP. Clinicians are advised to obtain the youth's and family's cardiac history prior to initiation of ADHD medications. The AAP recommends

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further cardiac evaluation prior to initiation of treatment if risk factors are present. Prescribing guidelines for stimulants and atomoxetine include monitoring height and weight at baseline and periodically during treatment.

Prescribing of medications for ADHD that are not FDA-approved for this indication is generally discouraged and must proceed according to <u>CBH Provider Bulletin 10-03: Use of Psychotropic Medications in Children and Adolescents (FDA-Approved and Off-Label).</u>

To ensure appropriate titration to optimize symptom control, for appropriate reevaluation of symptoms and functional impact, and to monitor for the emergence of adverse effects, these follow-up intervals are required after the initiation of an ADHD medication:

- One medication management follow-up visit no more than 30 days after the prescription is initiated
- 2. At least two more such visits after the initial 30-day period of medication

# 3.5. Coordination of Care and Engagement

The public children's behavioral health system in Pennsylvania is based on the principles developed through the <u>Department of Human Services (DHS) Child and Adolescent Service System Program (CASSP)</u>. The principles are defined as follows: child-centered, family-focused, community-based, multi-system, culturally competent, and least intrusive/restrictive. Moreover, <u>Philadelphia's System of Care initiative</u>, whose mission is to support the delivery of quality mental health services to children and young adults with complex mental health needs, promotes care that is youth and family-driven, community based, and culturally and linguistically competent<sup>3</sup>. Treatment for ADHD, including pharmacologic interventions, should align with these principles. Youth diagnosed with ADHD should receive evidence-based and holistic care, to include access to resources and services that promote recovery, resilience and thriving. Specifically, care should be characterized by access to behavioral/psychotherapeutic interventions, integration with physical health systems, effective collaboration with child-serving systems including schools and child welfare, peer support, and case management.

Achieving improved follow-up care and the provision of evidence-based care are contingent upon successful engagement of youth and families in care. Providers are encouraged to develop and implement processes that promote engagement and strengthen the therapeutic alliance. The National Alliance on Mental Illness (NAMI) has published **guidance** on promoting a culture of engagement in the mental health system; salient features include principles of shared-decision making, adopting a strengths-based approach, and including natural supports<sup>4</sup>.

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<sup>&</sup>lt;sup>3</sup> Philadelphia System of Care, **System of Care Framework**.

<sup>&</sup>lt;sup>4</sup> National Alliance on Mental Illness (NAMI), Engagement: A New Standard for Mental Health Care



#### 3.6. Safety and Diversion

As with any medication, providers should educate parents and caregivers regarding safe storage practices for ADHD medications. Children should only have access to medications under the supervision of a responsible adult. To minimize the risk of diversion when prescribing stimulant medications, which are classified as Schedule II medications by the Drug Enforcement Agency (DEA), providers should adhere to established state and federal guidelines including querying prescription drug monitoring programs. In situations where the risk of diversion needs to be minimized, providers should consider prescribing long-acting stimulants with a lower risk of abuse potential.

# 4. MONITORING

CBH encourages its providers to maintain robust internal quality management programs to ensure treatment of CBH members adheres to these and other applicable guidelines. In addition to "as needed" reviews of medical records when quality issues arise, CBH will be tracking and sharing the following performance metrics with providers:

- → HEDIS ADD: Follow-up care for children prescribed ADHD Medication, tracked via the National Committee for Quality Assurance (NCQA) HEDIS measure<sup>5</sup>)
  - Initiation Phase: Assesses children between age 6-12 who were diagnosed with ADHD and had one follow-up visit with a practitioner with prescribing authority within 30 days of their first prescription of ADHD medication
  - Continuation Phase: Assesses children between age 6-12 who had a prescription for ADHD medication and remained on the medication for at least 210 days and had at least 2 follow-up visits with a practitioner in the 9 months following Initiation Phase
- Appropriate use of medication for children and adolescents diagnosed with ADHD (will be tracked via claims data to generate percentages of members with ADHD prescribed FDAapproved medications, other medications, and no medication). In addition, providers should maintain documentation of all evaluations and interventions described in these guidelines, whether delivered by the provider or an outside practitioner. CBH and the DBHIDS Network Improvement and Accountability Collaborative (NIAC) will continue to monitor treatment provided to assure that care is consistent with the **DBHIDS NIC Standards for Excellence**.

<sup>&</sup>lt;sup>5</sup> National Committee for Quality Assurance (NCQA), Follow-Up Care for Children Prescribed ADHD Medication (ADD, ADD-E)



# 5. APPENDICES

#### 5.1. ADHD and Psychiatric Co-morbidities

Special consideration should be given for the complexities in managing ADHD with co-morbid psychiatric diagnoses. ADHD is often comorbid with Oppositional Defiant Disorder, Conduct Disorder, Mood Disorders, Anxiety Disorders, Substance Abuse disorders, Autism Spectrum Disorder, Intellectual disability, language and learning disorders, and Tic Disorders<sup>6</sup>. Children and adolescents with ADHD and coexisting conditions are at risk for more adverse outcomes. Youth/caregiver preference, symptomatology, the degree of functional impairment, medical/family history, and psychosocial factors should inform treatment planning in this clinical context. Based on the above factors, decisions regarding medication, therapy, and behavioral interventions will vary and should be evidence-based and characterized by psychoeducation, informed consent, and shared decision making. Treating ADHD with psychiatric comorbidities may include using combined therapy (medication with behavioral/therapeutic interventions) as first-line treatment, optimizing drug delivery mechanisms (e.g., prescribing prodrug or long-acting stimulants to reduce the risk of abuse in youth with substance abuse disorders), and prioritizing symptom reduction for the primary diagnosis<sup>7</sup>.

### 5.2. Special Populations: Transition Age Youth

The term transitional age youth (TAY) generally refers to the cohort of individuals spanning the age demographic of older adolescence to early adulthood, approximately 16-25 years of age. This developmental period is characterized by unique challenges and milestones, including separation-individuation, identity formation, vocational and educational transitions, and achieving intimacy<sup>8</sup>. Youth with mental health conditions, including ADHD, are particularly vulnerable during this time given the increased rate of emerging psychiatric illnesses, functional impairment, and significant psychosocial stressors for youth who identify as ethnic and/or sexual minorities, are economically disadvantaged, aging out of foster care, or have multiple system involvement. This cohort of youth must also navigate transitioning from child to adult serving systems of care, including mental and physical health care. According to the AAP and AACAP, a significant percentage of children diagnosed with ADHD will continue to experience symptoms and impairment into adulthood. TAY receiving treatment for ADHD may be at risk of disengaging from treatment and suffering adverse health, educational, and socioeconomic outcomes. Strategies and interventions that may facilitate

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<sup>&</sup>lt;sup>6</sup> Barbaresi WJ, Campell L, Diekroger EA, et al. Society for Developmental and Behavioral Pediatrics, Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder, Journal of Developmental & Behavioral Pediatrics. 2020; 41: S35-S57 doi: 10.1097/DBP.0000000000000770.

<sup>&</sup>lt;sup>7</sup> Austerman, J. <u>ADHD and Behavioral Disorders: Assessment, Management and an update from DSM-5</u>, Cleveland Clinic Journal of Medicine. 2015; 82(1): S2-S7.

<sup>&</sup>lt;sup>8</sup> Martel A & Fuchs CD. <u>Transitional Age Youth and Mental Illness – Influences on Young Adult Outcomes</u>, Child and Adolescent Psychiatric Clinics. 2017;26(2): PXIII-XVII.



continuity of care for TAY include motivational interviewing, peer support, mentorship, case management, shared decision making, and strengthening natural supports9.

# 5.3. Approved Medications for ADHD<sup>10</sup>

#### 5.3.1. Stimulants

Brand Name	Generic Name	Duration	Available Dosage Strengths
	Class: Methylphenidat	te	
Adhansia XR <sup>TM</sup>	methylphenidate hydrochloride – extended-release (capsule)	16 hours	25mg 35mg 45mg 55mg 70mg 85mg
AzstarysTM	serdexmethylphenidate and dexmethylphenidate (capsule)	10+ hours	26.1mg/5.2mg 39.2mg/7.8mg 52.3mg/10.4mg
Aptensio XR <sup>TM</sup>	methylphenidate hydrochloride – extended-release (capsule)	12 hours	10mg 15mg 20mg 30mg 40mg 50mg 60mg
Concerta <sup>®</sup>	methylphenidate hydrochloride – extended-release (tablet)	10-12 hours	18mg 27mg 36mg 54mg 72mg
Cotempla <sup>TM</sup> XR-ODT	methylphenidate extended-release (orally disintegrating tablet)	8-12 hours	8.6mg 17.3mg 25.9mg
Daytrana <sup>®</sup>	methylphenidate (transdermal patch)	10-16 hours	10mg 15mg 20mg 30mg
Focalin <sup>®</sup>	dexmethylphenidate hydrochloride (tablet)	3-5 hours	2.5mg 5mg 10mg
Focalin XR®	dexmethylphenidate hydrochloride – extended- release (capsule)	12 hours	5mg 10mg 15m 20mg 25m 30mg 35mg 40mg
Jornay PM <sup>TM</sup>	methylphenidate hydrochloride – extended-release (capsule)	12+ hours	20mg 40mg 60mg 80mg 100mg
Metadate CD®	methylphenidate hydrochloride – extended-release (capsule)	8 hours	10mg 20mg 30mg 40mg 50mg

<sup>&</sup>lt;sup>9</sup> Buitelaar J.K. Optimising treatment strategies for ADHD in adolescence to minimise "lost in transition" to adulthood, Epidemiology and Psychiatric Sciences. 2017;26: 448-452 doi:10.1017/S2045796017000154

ADHD Medications Approved by the US FDA. Prepared by Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD), 2023.



Brand Name	Generic Name	Duration	Available Dosage Strengths
Metadate® ER	$methyl phenidate\ hydrochloride-extended-release \\ (tablet)$	8-12 hours	20mg
Methylin® ER	methylphenidate hydrochloride – extended-release (tablet)	8 hours	10mg 20mg
Methylin <sup>®</sup> Oral Solution	methylphenidate hydrochloride (liquid)	3-5 hours	5mg/5ml and 10mg/5ml
QuilliChew ER <sup>TM</sup>	methylphenidate hydrochloride – extended-release (chewable tablet)	8-12 hours	20mg 30mg 40mg
Quillivant XR®	methylphenidate hydrochloride – extended-release (liquid)	8, 10, and 12 hours	25mg/5ml (5mg/ml)
Ritalin®	methylphenidate hydrochloride (tablet)	3-5 hours	5mg 10mg 20mg
Ritalin LA®	methylphenidate hydrochloride – extended-release (capsule)	8 hours	10mg 20mg 30mg 40mg
	Class: Amphetamine		
Adderall <sup>®</sup>	Amphetamine and dextroamphetamine mixed salts (tablet)	4-8 hours	5mg 7.5mg 10mg 12.5mg 15mg 20mg 30mg
Adderall XR®	Amphetamine and dextroamphetamine mixed salts – extended-release (capsule)	8-12 hours	5mg 10mg 15mg 20mg 25mg 30mg
Adzenys ER	amphetamine extended-release oral suspension (liquid)	9-12 hours	3.1mg/2.5ml 6.3mg/5ml 9.4mg/7.5ml 12.5mg/10ml 15.7mg/12.5ml 18.8mg/15ml
Adzenys XR-ODT™	amphetamine extended-release (orally disintegrating tablet)	9-12 hours	3.1mg 6.3mg 9.4mg 12.5mg 15.7mg 18.8mg
Desoxyn®	methamphetamine hydrochloride (tablet)	4-8 hours	5mg
Dexedrine®	Dextroamphetamine-sulfate-(tablet)	4-6 hours	2.5mg 5mg 7.5mg 10mg 15 mg 20mg 30mg
Dexedrine®	dextroamphetamine sulfate – extended-release (tablet)	6-9 hours	15mg
Dexedrine Spansule®	dextroamphetamine sulfate – extended release (capsule)	8-12 hours	15mg



Brand Name	Generic Name	Duration	Available Dosage Strengths
Dyanavel® XR	amphetamine extended-release tablet	8–12 hours	2.5mg 5mg 10mg 15mg 20mg
Dyanavel® XR	amphetamine extended-release oral suspension (liquid)	8-12 hours	2.5mg/ml, 12.5mg/tsp
Evekeo®	amphetamine sulfate (tablet)	4-6 hours	5mg 10mg
Evekeo ODT <sup>TM</sup>	amphetamine sulfate – orally disintegrating (tablet)	4-6 hours	5mg 10mg 15mg 20mg
Mydayis™	mixed salts of a single-entity amphetamine product – extended-release (capsule)	16 hours	12.5mg 25mg 37.5mg 50mg
ProCentra®	dextroamphetamine sulfate (liquid)	4-8 hours	5mg/5ml
Vyvanse®	lisdexamfetamine dimesylate (chewable tablet)	8-12 hours	10mg 20mg 30mg 40mg 50mg 60mg
Vyvanse <sup>®</sup>	lisdexamfetamine dimesylate (capsule)	10-12 hours	10mg 20mg 30mg 40mg 50mg 60mg 70mg
Xelstrym™	dextroamphetamine (transdermal patch)	9 hours	10mg 15mg 20mg 30mg
Zenzedi <sup>®</sup>	dextroamphetamine sulfate (tablet)	4-8 hours	2.5mg 5mg 7.5mg 10mg 15mg 20mg 30mg

#### 5.3.2. Non-Stimulants

Brand Name	Generic Name	Duration	Available Dosage Strengths
Class: Norepinephrine Reuptake Inhibitor			
Strattera®	atomoxetine hydrochloride (capsule)	24 hours	10mg 18mg 25mg 40mg 60mg 80mg 100mg
Qelbree™	viloxazine extended-release (capsule)	24 hours	100mg 150mg 200mg
Class: Alpha Agonist			
Kapvay®	clonidine hydrochloride – extended-release (tablet)	12-24 hours	0.lmg 0.2mg



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Brand Name	Generic Name	Duration	Available Dosage Strengths
Intuniv <sup>®</sup>	guanfacine hydrochloride – extended-release (tablet)	12-24 hours	lmg 2mg 3mg 4mg

#### 5.4. Additional Resources

- **FDA Medication Guides**
- **ADHD Medication Guide** (Recommended by the AAP)
- **CMS Pediatric Stimulant and Related Medication Factsheet**
- **CMS Pediatric Dosing Chart**
- **AACAP ADHD: Parents' Medication Guide**

#### 5.5. References

- Community Behavioral Health (CBH), Provider Bulletin 07-07: Screening for and Treatment of the Components of Metabolic Syndrome.
- Department of Behavioral Health and Intellectual disAbility Services (DBHIDS), Philadelphia Behavioral Health Practice Guidelines, 2013, or latest version.
- Department of Behavioral Health and Intellectual disAbility Services (DBHIDS), Network Inclusion Criteria Standards of Excellence, February 2019, or latest version.
- → Wolraich ML, Hagan JF, Allan C, et al. AAP Subcommittee on Children and Adolescents with Attention Deficit/Hyperactive Disorder. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. 2019;144(4):e20192528.
- Pliszka, Steven. AACAP Workgroup on Quality Issues. AACAP Official Action, Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-**<u>Deficit/Hyperactivity Disorder.</u>** Journal of the American Academy of Child and Adolescent Psychiatry. 2007;46(7): 2007;46(7):894-921.
- Community Behavioral Health (CBH), <u>Provider Bulletin 10-03: Use of Psychotropic</u> Medications in Children and Adolescents (FDA-Approved and Off-Label).
- National Committee for Quality Assurance (NCQA), Follow-Up Care for Children Prescribed ADHD Medication (ADD, ADD-E).



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- **→** PA Department of Human Services Child and Adolescent Social Service Program (CASSP).
- → Philadelphia System of Care, <u>System of Care Framework</u>.
- National Alliance on Mental Illness (NAMI), <u>Engagement: A New Standard for Mental Health</u> <u>Care</u>.
- ➡ Barbaresi WJ, Campell L, Diekroger EA, et al. Society for Developmental and Behavioral Pediatrics, Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder, Journal of Developmental & Behavioral Pediatrics. 2020; 41: S35-S57 doi: 10.1097/DBP.000000000000770.
- → Austerman, J. <u>ADHD and Behavioral Disorders: Assessment, Management and an update</u> <u>from DSM-5</u>, Cleveland Clinic Journal of Medicine. 2015; 82(1): S2-S7.
- → Martel A & Fuchs CD. <u>Transitional Age Youth and Mental Illness Influences on Young Adult Outcomes</u>, Child and Adolescent Psychiatric Clinics. 2017;26(2): PXIII-XVII.
- ➡ Buitelaar J.K. Optimising treatment strategies for ADHD in adolescence to minimise 'lost in transition' to adulthood, *Epidemiology and Psychiatric Sciences*. 2017;26: 448–452 doi:10.1017/S2045796017000154