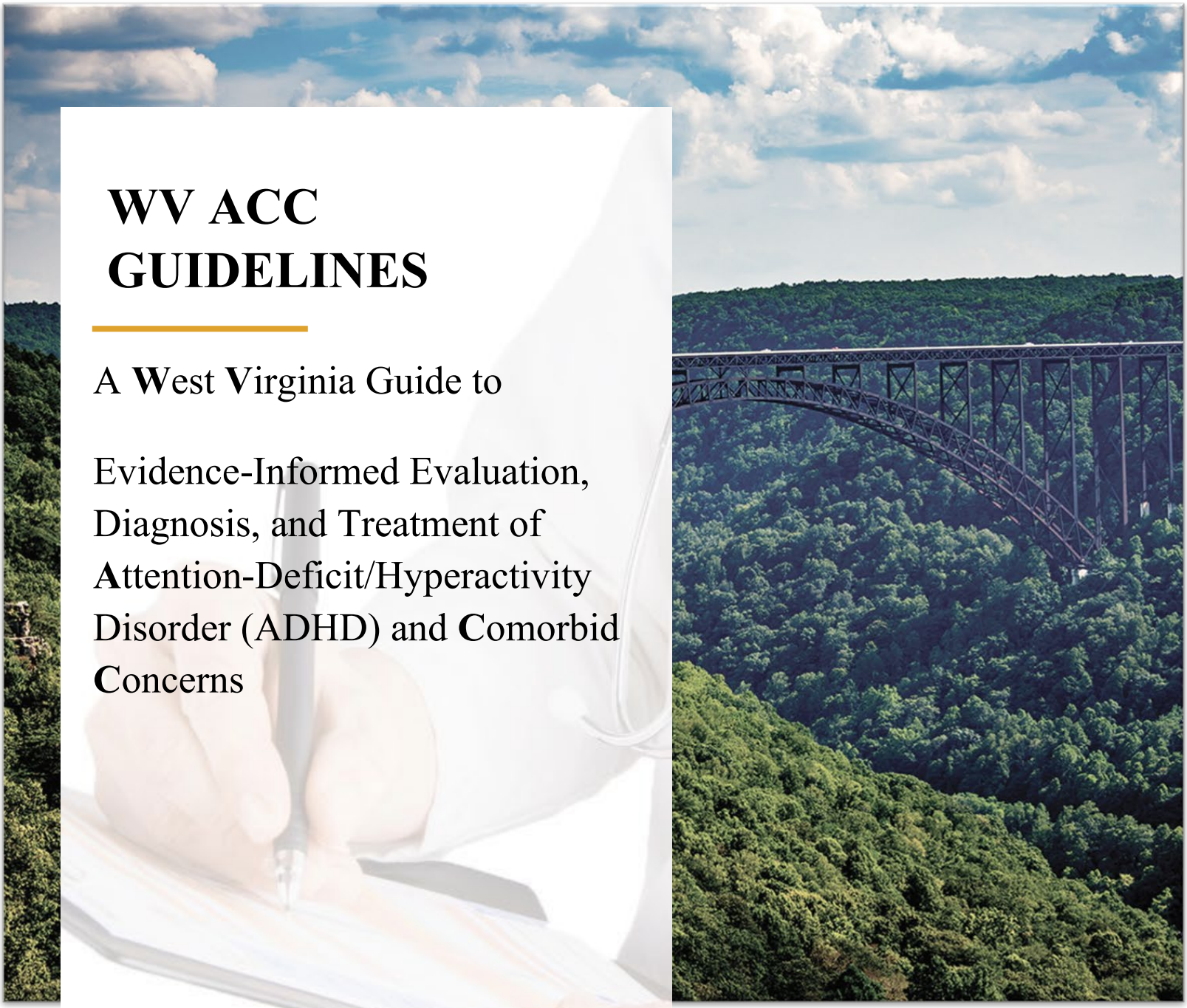

WV ACC GUIDELINES

A **W**est **V**irginia Guide to

Evidence-Informed Evaluation, Diagnosis, and Treatment of **A**ttention-Deficit/Hyperactivity Disorder (ADHD) and **C**omorbid **C**oncerns

2024

WV ACC Guidelines

A West Virginia Guide to Evidence-Informed Evaluation, Diagnosis, and Treatment of ADHD and Comorbid Concerns

West Virginia Department of HEALTH

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Disclaimers

General disclaimer:

This content is not intended to address all possible diagnosis methods, treatments, follow up, drugs or their related contraindications or side effects. Standards of practice change as new data becomes available. Therefore, it is strongly recommended that practitioners independently assess and verify diagnosis, treatments, and drugs for each individual patient. The authors of the WV ACC guidelines assume no liability for any aspect of treatment administered by a practitioner with the aid of this publication.

Drug disclaimer:

The authors do not endorse or recommend the use of any particular drug mentioned in this publication. Before prescribing a new drug to a patient, practitioners are advised to check the product information accompanying each drug to ensure it is appropriate for a specific patient and to identify appropriate dosage, contraindications, side effects, and drug-to-drug interactions.

Standard of care disclaimer:

This publication is not intended to establish a standard of care applicable to practitioners who treated patients diagnosed with ADHD. “Standard of care” is a legal term, not a medical term, which refers to the degree of care a reasonable practitioner would exercise under the same or similar circumstances. The standard of care is a continuum and does not imply optimal care. Practitioner discretion and clinical judgment are paramount and this publication is only intended to aid practitioners’ judgment, not to serve as a substitute for said judgment.

CONTENTS

ACRONYMS

AACAP	American Academy of Child and Adolescent Psychiatry
AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
ABCT	Association for Behavioral and Cognitive Therapies
ACE	Adverse Childhood Experiences
ACOG	American College of Obstetricians and Gynecologists
ADA	Americans with Disabilities Act
ADHD	Attention-Deficit/Hyperactivity Disorder
APA	American Psychiatry Association
APA	American Psychological Association
ASAA	American Sleep Apnea Association
ASD	Autism Spectrum Disorder
BPMT	Behavior Parent Management Training
CADDRA	Canadian ADHD Resource Alliance
CDC	Centers for Disease Control and Prevention
CHADD	Children and Adults with Attention-Deficit/Hyperactivity Disorder
CBT	Cognitive Behavioral Therapy
CIM	Complementary and Integrative Medicine
DEA	Drug Enforcement Agency
DREDF	Disability Rights Education & Defense Fund
DSM-5	Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition
DSM-5-TR	Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition, Text Revision
ER	Extended-Release
EEOC	Equal Employment Opportunity Commission

F2F	Face-to-Face
FDA	Food and Drug Administration
HHS	Department of Health and Human Services
HOPS	Homework, Organizational, and Planning Skills
HRSA	Health Resources and Services Administration
IAPMO	International Association of Plumbing and Mechanical Officials
IDEA	Individuals with Disabilities Education Act
IEP	Individualized Educational Program
KFF	Kaiser Family Foundation
LDA	Learning Disabilities Association of America
NAS	Neonatal Abstinence Syndrome
NASP	National Association of School Psychologists
NCHS	National Center for Health Statistics
NCQA	National Committee for Quality Assurance
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NICE	National Institute for Health and Care Excellence (UK)
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health
NIMH	National Institutes of Mental Health
NSCH	National Survey of Children's Health
OTC	Over-the-Counter
PCIT	Parent Child Interaction Therapy
PFC	Prefrontal Cortex
SAMHSA	Substance Abuse and Mental Health Services Administration
SAT	Student Assistance Teams
SBIRT	Screening, Brief Intervention and Referral to Treatment

SST	Social Skills Training
SUD	Substance Use Disorder
TBI	Traumatic Brain Injury
UDS	Urinary Drug Screening
UDT	Urinary Drug Test
U.S.	United States
WVDE	West Virginia Department of Education
WVDHHR	West Virginia Department of Health and Human Resources/ West Virginia Department of Health (as of 01/01/2024)

Executive Summary

Attention-deficit/hyperactivity disorder (ADHD) is a chronic neurodevelopmental disorder with symptoms of inattention and/or hyperactivity and impulsivity that is one of the most common neurobehavioral disorders in children both nationally and especially in West Virginia. Symptoms such as the inability to keep focus, excessive movement, and hasty acts can range from mild to severe. Treatment of ADHD symptoms requires comprehensive care that can be complex and multi-faceted. This chronic condition is lifelong and can negatively affect academic achievement, well-being, social interactions, relationships, and employment. Approximately 70% of children diagnosed with ADHD will continue to have symptoms through adolescence, and about half will continue to experience symptomatic impairment into adulthood. Adults who received a childhood diagnosis of ADHD are more likely to experience comorbid psychiatric disorders, display higher rates of antisocial behaviors, and may be at an increased risk for early death (Barbaresi et al., 2013). Untreated ADHD in youth is associated with a higher risk of accidental injury, risk-taking, and sensation-seeking behavior (Assayag et al., 2022; Hodgkins et al., 2011a; Shoham et al., 2016). Therefore, there is a strong need for knowledgeable clinicians and other individuals involved in patient care to provide continuous care and resources for patients with ADHD and their families. A multidisciplinary approach including, but not limited to, primary care, mental health specialists, and the educational system and supporting staff is encouraged to ensure appropriate diagnosis and management of ADHD and any other potential coexisting conditions. Unfortunately, some patients and families may struggle to access multidisciplinary care in many areas of West Virginia due to the abundance of rural settings and the limited number of specialists practicing within the state.

Striking trends have been observed in West Virginia regarding the diagnosis of ADHD and the corresponding prescribing of stimulants, a first-line treatment for some age groups with ADHD. The 2019 estimated prevalence of ADHD for children in West Virginia ages three to 17 years was 13.2%, much higher than the national average of 8.6%. Given this high prevalence, it is not surprising that the number of stimulant medications prescribed within the state was similarly elevated. It was noted in the Maternal and Child Health Services Title V Block Grant: West Virginia, FY2019 Annual Report that, for some counties in West Virginia, up to one in four children within certain age groups were prescribed a stimulant (West Virginia Department of Health and Human Resources [DHHR], 2020a). Prescription stimulants are considered the first-line pharmacological treatment for ADHD for certain age groups where appropriate; however, their use is not without risk. Stimulants have the potential to cause adverse effects and should be

prescribed only after a comprehensive evaluation has been completed, an appropriate diagnosis rendered, and a plan of care developed. Of note, behavior management is first-line therapy for children under six years of age and an integral part of first-line therapy for children six to 18 years of age. Despite these recommendations, behavior management/therapies are often underutilized. The evidence for nonpharmacological interventions is extensive and should be considered for each patient.

Stimulants are Schedule II-controlled substances due to their risk for "abuse," dependence, and potential for diversion (Drug Enforcement Agency [DEA], 2022). West Virginia has had the highest drug overdose death rate in the nation since 2014, and in 2020, the state saw a record high of 81.4 drug overdose deaths per 100,000 people (Centers for Disease Control and Prevention [CDC], 2022a). Further in 2019, drug overdose deaths involving psychostimulants, mostly illicit, resulted in the loss of 16,000 lives, an increase nationally of 28% from 2018 to 2019 (Kariisa et al., 2021). This increase in overdose deaths is mainly due to the increased use of illicit psychostimulants (methamphetamine and cocaine) rather than the therapeutic use of prescription stimulants in the context of the treatment of ADHD. Recent studies yielded no evidence that stimulant treatment was associated with increased or decreased risk for later frequent use of alcohol, marijuana, cigarette smoking, or other substances used for adolescents and young adults with childhood ADHD (Molina et al., 2023). However, 1.8%, or approximately 5.1 million, of the United States (U.S.) population aged 12 years and older misused prescription stimulants in 2020, and 0.3%, or approximately 758,000 people, had a prescription stimulant use disorder (National Institute on Drug Abuse [NIDA], 2020). While there is a growing misuse of prescription stimulants, clinicians should not be deterred from using them in patients with legitimate medical needs and appropriate diagnoses. Instead, this underscores the importance of adequate education and training in evaluating, diagnosing, and treating ADHD. Both untreated ADHD and treatment without an accurate diagnosis of ADHD carry associated risks. It is imperative that prescribers utilize prescription stimulants for appropriate patients at appropriate doses and strive to ensure compliance, effectiveness, and tolerability through ongoing monitoring.

When examining the high rate of children diagnosed with ADHD in West Virginia, the increased prevalence is likely due to many factors. Prenatal exposure to nicotine through maternal smoking during pregnancy, low birth weight, and prematurity are all known risk factors for ADHD which the state ranks first, seventh, and third in the nation, respectively. Exposure to prenatal substances resulting in developmental symptoms has the potential for ADHD

misdiagnosis in the absence of a comprehensive neurodevelopmental and neuropsychological evaluation. One recent study suggested that ADHD may be overdiagnosed and overtreated, especially in cases with milder symptoms (Kazda et al., 2021). Various factors, such as socioeconomic status, race, and access to health insurance, were shown to be correlated with the potential for overdiagnosis. Given that many of these factors are present across Appalachia, it is possible that overdiagnosis may be contributing to the elevated prevalence of ADHD in West Virginia, or West Virginia simply has a higher prevalence of ADHD. While additional research is needed to further understand the cause of the increased prevalence of ADHD in West Virginia, this increase nonetheless emphasizes the need for clinician education in this focus area.

While the high percentage of children diagnosed with ADHD is certainly a key factor in driving the high rate of stimulant prescribing, it is not the only impetus. Many individuals are prescribed a psychostimulant without a corresponding diagnosis of ADHD. In fact, a global trend has been documented for the prescribing of stimulants to both children and adults, with a significant percentage (38% and 55%-66%, respectively) not having a corresponding ADHD diagnosis (Sibley, 2018). While some stimulants have a U.S. Food and Drug Administration (FDA) indication for other conditions, such as narcolepsy or binge eating disorder, these health conditions likely represent a very small percentage of those receiving the medications, considering the lower presence of these disease states (1.2% past year prevalence of binge eating disorder and 9.9 persons per 100,0000 per year with narcolepsy (Hudson et al., 2007; Scheer et al., 2019)). It is suspected that the use of stimulants for enhancement of cognitive function to increase academic performance is becoming more prevalent (Sibley, 2018). Off-label prescribing describes when medications are given to treat non-FDA-approved conditions or symptoms, and stimulants are sometimes utilized for off-label treatment of behavioral disorders. There is concern that this off- label use of prescription stimulants for behavioral disorders is especially prevalent in certain populations, such as those in foster care, where regular healthcare and consistent caregivers may not be present. In West Virginia, the number of children in foster care and non-traditional households continues to grow. While more research is needed to further clarify these trends both at the national and state levels, it is evident that education regarding the evaluation, diagnosis, and treatment of ADHD is needed, including accurate diagnostic measures, the inclusion of evidence-based behavior management strategies, and the appropriate use and safety of prescription stimulants. In an attempt to provide a statewide resource for ADHD in West Virginia, a panel of experts from across the state convened to create a state-wide guideline for ADHD assessment, evaluation, and treatment. These materials are intended to serve as a resource for clinicians and other individuals involved in caring for patients with ADHD in West Virginia.

Supplemental information, reference materials, and tools for use in the evaluation, diagnosis, and treatment of ADHD were developed and are included. West Virginia clinicians and others involved in the care of patients with ADHD will have access to resources created using evidence-based research, current national and international guidelines, and expert recommendations for best practices to utilize in the assessment and ongoing care of their patients with ADHD across their lifespan. This panel comprises the following multidisciplinary team.

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Guideline Development

The expert panel's first working assumption is that this guideline was assessed as a whole, and no elements of the document were assessed individually. The second assumption is the expert panel convened on the direction of the guideline from a clinical perspective. A list of the national and international organizational clinical practice guidelines, practice parameters, and recommendations reviewed in the drafting of this document are listed in the following table. In scenarios where there was conflicting guidance among major publications, the expert panel consolidated the evidence and used clinical judgment and experience to arrive at the contents of this document. Third, this guideline was intended to be an additional resource for clinicians and those involved in the care of patients with ADHD, and its purpose is to guide evaluation, diagnosis, treatment, and monitoring of low-complexity patients and evaluation, diagnosis, and treatment of high-complexity patients while awaiting specialist care. This guideline is not intended to replace adequate education and continuing education for ADHD but rather to enhance an existing knowledge base.

Organization	Guideline/Practice Parameter/Recommendations
American Academy of Child and Adolescent Psychiatry (AACAP)	Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention- Deficit/Hyperactivity Disorder 2007©
American Academy of Family Physicians (AAFP)	Diagnosis and Management of Attention- Deficit/Hyperactivity Disorder in Adults 2012© Adult ADHD Toolkit©
American Academy of Pediatrics (AAP)	Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents 2019©
American Psychiatry Association (APA)	Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) 2000© Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR) 2022©
American Psychological Association (APA)	Guidelines for the Practice of Telepsychology©
Association for Behavioral and Cognitive Therapies (ABCT)	Practice Parameters
Canadian ADHD Resource Alliance (CADDRA)	Canadian ADHD Practice Guidelines 4.1 Edition 2020©
Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)	Recommendations
National Association of School Psychologists (NASP)	Practice Parameters
National Institute for Health and Care Excellence (NICE)	Attention-Deficit/Hyperactivity Disorder: Diagnosis and Management 2019©
Society for Developmental and Behavioral Pediatrics (SDBP)	Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder 2020©

West Virginia's Disparity in Care of ADHD

The evaluation, diagnosis, and treatment of ADHD should include a comprehensive, patient-centered approach that can include multiple levels of care and specialties, particularly for patients exhibiting a higher level of symptomology and impairment. West Virginia currently suffers from a shortage of behavioral health services to meet this need. Compounding its challenges, West Virginia has also been identified as having a significantly higher prevalence of ADHD in children three to 17 years of age than the national average, 13.2% versus 8.6%, respectively, in the 2019 National Survey of Children's Health (NSCH) (DRC, 2019). There are several factors contributing to both this increased prevalence and, ultimately, disparity of care for patients with ADHD in West Virginia, one of the most rural and poverty-stricken states in the country (Kaiser Family Foundation [KFF], 2022).

Rural Landscape

West Virginia is the third most rural state in the nation, and a significant contributing factor to the disparity of care for patients with ADHD in West Virginia is the large number of people living in rural areas (DHHR, 2018a). Of its 55 counties, 44 are considered to be rural, with two-thirds of the state's population living in one of these rural areas (Rural Health Information Hub, 2022). Unfortunately, the rural nature makes access to clinicians and other individuals involved in care more challenging, as both general and specialized clinicians are often located outside of these areas in more urban or suburban locations.

Patient travel requirements to healthcare professionals are a challenge in West Virginia. Many patients and families lack acceptable transportation, and public transit remains unavailable in many areas. Even among those with reliable transportation, poor road conditions caused by inclement weather or lack of upkeep further contribute to attendance-related challenges at appointments. It is common for patients in West Virginia to drive hours to see their nearest primary care clinician. Not only does this increased travel requirement contribute to clinician accessibility issues, but it also limits the interactions that a clinician can have with the patient or their family members. Such time and observational constraints can sometimes oblige clinicians to make clinical judgements based on limited information, elevating the possibility of a misdiagnosis as well as limiting opportunities for appropriate monitoring and follow-up. While telemedicine has increased access to some behavioral health specialists, broadband availability is still not available in many rural communities around West Virginia.

Increased Poverty

West Virginia has a poverty rate of 16.8%, compared with the national average of 12.8% (KFF, 2022). When reviewing the 20-year (1997-2016) trends in diagnosed ADHD in U.S. children and adolescents, a significant correlation was noted between lower family income and increased diagnosis of ADHD (Xu et al., 2018). While correlational data should not be confused with causational data, it is possible the correlation is in part due to difficulties in educational and employment attainment and decreased access to healthcare. The increased proportion of the population living below poverty income levels is another factor likely leading to higher rates of ADHD in West Virginia. In areas where the poverty rate is higher, citizens experience greater challenges to secure basic needs, and taking time off work for an appointment can be difficult or impossible. As a result, patients may not receive a proper diagnosis or undergo the appropriate monitoring needed after diagnosis to be successful with their treatment plan.

Abundance of Non-Traditional Households

Another disparity that disproportionately affects West Virginia is the number of children being raised in non-traditional households. More than 2.5 million children in the United States are being raised by "grandfamilies," or households where the primary caregivers are not the biological parents (Generations United, 2022). These families are typically led by grandparents or other members of the extended family. West Virginia ranks third in the nation for the number of "grandfamilies," with 51.2% of grandparents raising their grandchildren. In some counties of West Virginia, this number is up to 83% and unfortunately, the number of "grandfamilies" continues to increase in West Virginia (United States Census Bureau, 2019). Preschool–aged and school-aged children in grandparent-headed households were found to be more likely to have ADHD than children in parent-headed households in a study on family well-being, likely due to the adverse childhood experiences (ACEs) and physical stress associated with the reasons for kinship care (Rapoport et al., 2020). At times, the symptomatic behaviors present in patients with ADHD can be difficult to handle for caregivers, and grandparents are often not prepared physically or emotionally for the challenge. Additionally, generational knowledge gaps exist regarding mental health and its surrounding stigma.

West Virginia had over 7,200 children in foster care in 2020 (Kids Count Data Center, 2022), and this figure continues to grow. Of West Virginia's foster population, 51% enter as a result of parental substance use, well above the national average of 38% (Williams et al., 2022). The prevalence of ADHD among children in foster care is much higher than the general population; children in foster care are three times more likely to have a diagnosis of ADHD, with

one in four children in foster care having received a diagnosis of ADHD compared with one in 14 children in the general population (26% versus 7%) (Danielson et al., 2015). Furthermore, nine out of 10 foster children have experienced a traumatic event at least once. Many times, it is this trauma that leads to the child entering foster care, and this correlation of entry into foster care with ADHD is multifaceted. First, ADHD has a genetic component, and a parent having ADHD could have contributed to the difficulties with raising the child through impairments leading to difficulty maintaining employment, substance use, and/or other co-occurring mental health conditions affecting daily living, to name a few. Additionally, the trauma that the child experienced could lead to inattention or hyperactivity that can be confused for symptoms of ADHD, and the trauma is left untreated due to the misdiagnosis of ADHD (Children and Adults with Attention- Deficit/Hyperactivity Disorder [CHADD], 2017a). Trauma would be considered an ACE that ultimately could affect the function of the child's brain, leading to an actual diagnosis of ADHD. For further information on ACEs and ADHD, please see the section titled "Pathophysiology of ADHD - ACEs and Pathophysiology."

Prenatal Exposure

Certain in utero substance exposures have been associated with the development of ADHD in offspring, and some of these exposures due to maternal substance use are common in West Virginia. Smoking and consuming alcohol during pregnancy are associated with an increased risk of developing ADHD (Pagnin et al., 2019; Schmitt & Romanos, 2012). In 2018, 24.9% of mothers in West Virginia reported smoking cigarettes during their last trimester of pregnancy (March of Dimes, 2022). A study reviewing the use of alcohol in late pregnancy found that 8.1% of mothers in West Virginia consumed alcohol in the last month of pregnancy (Umer et al., 2020). Furthermore, prenatal exposure to illicit drugs is associated with an increased risk of ADHD in exposed offspring, with opioids carrying the highest risk (Garrison- Desany et al., 2022). In 2018, 49.6% of hospitalized newborns in West Virginia were diagnosed with neonatal abstinence syndrome (March of Dimes, 2022). All of these in utero substance exposures can lead to prematurity and/or low birth weight, which have been associated with all forms of ADHD (Pettersson et al., 2015). Therefore, given West Virginia's high rates of maternal substance use, a correlation between increased substance exposure and its increased prevalence of ADHD likely exists. For a more thorough review of prenatal exposure relating to ADHD, please see the "Pathophysiology- Prenatal Substance Exposure in West Virginia" section of the guideline.

Lack of Specialized Mental Health Professionals

In addition to West Virginia having a high prevalence of ADHD, the disparity of care is further complicated by the lack of specialized mental health professionals, with West Virginia having 45% fewer than the national average (DHHR, 2018a). According to 2015 data, of the 55 counties in West Virginia, there were 36 counties with zero psychiatrists, 22 counties with zero pediatricians, and three counties with zero psychologists per 10,000 children. These types of professionals all play a significant role in the appropriate assessment, evaluation, and treatment of ADHD. In West Virginia, there is an average of 16.7 family medicine physicians per 10,000 children per county, yet only 1.7 and 3.6 psychiatrists and pediatricians, respectively (Centers for Disease Control and Prevention, 2022a). There is also a shortage of social workers. The state of West Virginia has a vacancy rate of 27% for social workers, with certain counties surpassing 50% in unfilled positions (DHHR, 2021). More recent data from the American Academy of Child and Adolescent Psychiatry (AACAP) indicates there are now 46 counties without a child and adolescent psychiatrist and only 10 child and adolescent psychiatrists per 100,000 children in West Virginia (AACAP, 2022). Furthermore, West Virginia was ranked number one in a national survey by *Mental Health America* for the number of adults with a mental health illness who reported unmet need for treatment (Reinert & Nguyen, 2022). Due to decreased access to behavioral health services, the majority of ADHD cases are diagnosed and managed by general medical clinicians (primary care, family medicine, and pediatricians) who already bear a significant caseload. The limited number of clinicians and resources make appropriate evaluation, diagnosis, and treatment even more challenging and can lead to additional health inequities. The higher caseloads can also lead to higher levels of clinician stress and the potential for physical and mental illness for those treating these patients.

Trust in Healthcare

West Virginia is the only state to be completely contained within the Appalachian region, and it has been shown that Appalachians tend to lack trust in medical professionals. A survey examining the perceptions of Appalachians regarding their healthcare satisfaction found residents of the Appalachian region to be less satisfied with the quality of care and information they received from healthcare professionals than patients in other areas of the country (Morrone et al., 2021). “Appalachian culture is more relational than contractual” further depicts the Appalachian viewpoints, including healthcare (Elder et al., 2022). The need for an established relationship between patients and medical professionals creates a challenge and further emphasizes the disparity of healthcare in West Virginia, including in the care of patients with ADHD. There is

likely distrust in the medical community, and it may take time for clinicians to get to know their patients and establish a trusting relationship. Patients may be unwilling to share or even seek treatment for family issues or problems, such as child behavioral issues that may warrant an evaluation for ADHD. Therefore, clinicians and other individuals involved in the care of West Virginians should have a sensitivity and awareness to the Appalachian culture to build this ongoing relationship and trust by being more "down to earth" and authentic, which may help overcome some of the disparity of healthcare in West Virginia (Elder et al., 2022).

Clinicians Overcoming Disparities of Care in West Virginia

Due to a longstanding shortage of mental health specialists in West Virginia, primary care and other healthcare clinicians assume care for the majority of patients with mental health disorders, including those with ADHD. The care of patients with ADHD often requires a great deal of time to be spent with patients, family members, and/or caregivers in the development of a treatment plan, with ongoing continuous monitoring as well as frequent communication regarding continuity of care with family members, teachers, and others. Additionally, the clinical complexity of some patients along with the frequent need to treat using stimulant medications can lead some healthcare clinicians and other individuals involved in the care of patients with ADHD to feel apprehensive about treating this population. The American Academy of Pediatrics (AAP) recognizes that there is a relative lack of training for developmental-behavioral and mental health conditions, including ADHD, during pediatric residency training (Wolraich et al., 2019). The organization Children and Adults with Attention Deficit/Hyperactivity Disorder (CHADD) has also noted the importance of patients with ADHD working with a professional who has clinical expertise in the diagnosis and treatment of ADHD (CHADD, 2023a). Primary care clinicians are trained in residency to diagnose and treat ADHD. The AAP recommends a patient be referred to a specialist if the primary care clinician is not trained or experienced in making the diagnosis or initiating treatment in children and adolescents (Wolraich et al., 2019). The American Academy of Family Physicians (AAFP) advises that there is not a specific point where referral of adults presenting with symptoms of ADHD is generally recommended, but referral to behavioral health services should occur based on other comorbidities for which the family physician would generally refer, including significant depression or anxiety, symptoms that are often a function of ADHD, and other major disabilities affecting daily function (Post & Kurlansik, 2012). Due to clinician shortages in West Virginia, patients can wait months to be seen during these referrals, making this option less than ideal for patients, especially those with more severe symptoms impacting their daily living. In these cases, the treatment of the patient falls to the primary care

clinicians until appropriate referrals and evaluations can be made.

Treatment of ADHD can include use of prescription stimulants as first-line pharmacologic treatment in most age groups for appropriate candidates (Wolraich et al., 2019). Prescription stimulants carry a Schedule II classification by the Drug Enforcement Agency (DEA). Schedule II drugs are defined as medications with acceptable medical uses but that have "high potential for abuse, with use potentially leading to severe psychological or physical dependence" (DEA, 2022). The DEA's classification of stimulants has led to apprehension among clinicians, as well as patients, families, and caregivers of individuals with ADHD, regarding their use in the treatment of ADHD in both children and adults. As mentioned, stimulants are considered to be first-line pharmacological therapy in patients who are six years of age and older and candidates for use by all reputable state, national, and international guidelines, including this guide; the benefit and efficacy of stimulants in the context of treatment of ADHD is well-supported in the literature when there is appropriate monitoring and follow-up. Despite the evidence that patients with ADHD can benefit from prescription stimulants, some clinicians may still be apprehensive to treat using these agents, and some patients/families/caregivers may express concerns regarding their use in treatment. However, use of these agents for a documented, legitimate medical need with appropriate monitoring and follow-up is the mainstay of treatment for many patients with ADHD in which clinicians (primary care, family medicine, and pediatricians) play a central role.

Clinicians and other individuals involved in the care of patients with ADHD in West Virginia face multiple challenges in the treatment of patients' mental health disorders, including ADHD. Due to West Virginia's elevated rates of ADHD, coupled with shortages of clinicians and multiple identified disparities, a significant healthcare gap exists, including in the treatment of ADHD. Primary care clinicians are most readily available to patients, particularly in rural areas, and therefore assume the role of evaluating, diagnosing, and treating West Virginians with ADHD, even in more complex cases while referrals to specialists are pending. The proper evaluation, diagnosis, and careful oversight of treatment remains critical. As a result, there is a need to significantly increase access to evidence-based, effective treatment through outreach and training for primary care clinicians, school-based mental health providers, and other community partners. Educational and reference materials should be readily available to support healthcare clinicians and other individuals involved in patient care in the evidence-based evaluation, diagnosis, treatment, and monitoring of patients with ADHD.

Increasing Access to Specialists – TeleMental Health

Access to both general and specialized mental healthcare is limited in West Virginia due to a large portion of residents living in rural and other underserved locations (Saloner et al., 2019). To assist in alleviating this documented mental health burden, telehealth has been proven as a viable, evidence-informed, and cost-effective method of reaching a population that has commonly gone without adequate care (Hubley et al., 2016; Zhou et al., 2020). Telehealth can be viewed as an umbrella term encompassing the use of technology to augment or replace traditionally face-to-face (F2F) healthcare services, whether provided live (i.e., synchronous [video, telephone]) or non-live (i.e., asynchronous [email, texting]). Among numerous other uses, these modalities can be harnessed by psychologists, psychiatrists, physicians, counselors, social workers, or other healthcare team members for general wellness visits, diagnostic evaluations, management of chronic conditions, discussion of test results, mental health counseling, medication checks, clinician-to-clinician consultation, and the training of healthcare students. Telehealth holds many benefits over traditional F2F methods, including the ability to provide services in various languages, reduce wait times, reduce the need for emergency room visits, increase access for patients with disabilities that limit travel to appointments, provide flexible scheduling, and increase access to specialized healthcare services (Shore, 2020). The convenience of telehealth that allows clinicians to reach patients "where they are" has been shown to not only reduce no-shows but also produce higher patient satisfaction. For those individuals feeling hesitant toward mental health services, it can also act as a foot-in-the-door to showcase what such healthcare services can offer in a familiar and comfortable environment.

While use of telehealth for mental health services has increased for some time, a notable increase in its utilization was observed during the COVID-19 pandemic (Kisicki et al., 2022). For example, psychologists estimated that roughly 85% of their total work transitioned to technology-enhanced care as compared with 7% prior to the pandemic (Pierce et al., 2021). While the degree of usage may decrease as some patients return to in-office visits following the public health emergency, the significant use of telehealth has proven its value for continuation (Mishkind et al., 2021).

A literature review of telemedicine use in the treatment of ADHD found that while more studies are needed, telehealth is a viable option to provide expert consultation and access to treatment, especially in rural areas with less access to healthcare services. Some benefits included low attrition, greater symptomatic and functional improvements than children in standard treatment, high adherence to the AAP guidelines using empirically supported scales and being valued by its users (Spencer et al., 2019). Coinciding with increased usage and research

suggesting that telehealth services can provide outcomes equivalent to F2F delivery for a range of populations, the American Psychological Association, American Psychiatric Association, American Medical Association, American Counseling Association, AAP, and National Association of Social Workers have all supported the development, study, training, and use of telehealth to assist in patient care (Shigekawa et al., 2018).

To ensure optimal services, clinicians should consider common barriers to telehealth prior to initiating the services (Kisicki et al., 2022). First, each clinician should review both their state and federal regulatory requirements in an effort to foster an ethical, legal, safe, and evidence-informed practice. Among the telehealth-specific knowledge that a clinician must hold, clinicians should consider their own level of telehealth knowledge and areas for improvement, the role of confidentiality, types of data security, means of evaluating a patient's appropriateness for receiving telehealth services, strategies for setting up an office or other room for virtual meetings, methods of preventative crisis planning, and means of updating and supplying telehealth-specific informed consenting practices. Before initiating a telehealth visit, a patient must have access to some form of device to allow for effective communication with the clinician, preferably with video capabilities. Similar to the clinician, a patient should also consider finding or creating a private, quiet, distraction-free environment for the services to ensure maintained confidentiality (Perle, 2021). Should video not be a viable option due to limited broadband internet access, telehealth services can be performed over the telephone (Pierce et al., 2021).

-Telehealth and Psychosocial Interventions

Regarding the evaluation, diagnosis, and treatment of ADHD specifically, improved access to mental and behavioral health services through telehealth-providing mental health specialists should be viewed as a means of providing evidence-informed care to the general population, especially to rural communities. Delivery of telehealth in the treatment and management of ADHD is on the rise (Howie et al., 2022; Wosik et al., 2020). For example, there has been an upturn in literature supporting the implementation of behavioral parent management training (including Parent Child Interaction Therapy [PCIT]) via telehealth. Traditional F2F training sessions are being replaced by training videos and show positive results. One study looking at telehealth PCIT used in two- to seven-year-old children showed that the group benefited from improved parenting skills and had improved child behaviors and a high level of "excellent responders" (Ros-DeMarize et al., 2021). Other studies conducted in the telehealth setting examining the effectiveness of Group Triple P, an evidence-based parenting program, and Barkley's

Defiant Children, a behavioral intervention, yielded comparable outcomes (Ros- DeMarize et al., 2021).

-Telehealth and Controlled Substance Prescribing

While there are benefits of increased use of telehealth services, patient safety is an area of concern, especially when controlled substances are prescribed. If a telehealth clinician is compliant with state and federal regulations, medications, including controlled substances, can be prescribed to patients using telehealth services for legitimate medical needs. Even with in-person visits, when controlled substances are prescribed, concerns of misuse or diversion are forever present due to their addictive properties and misuse potential, which can cause hesitation around the prescribing of these medications. Nervousness around prescribing controlled substances, especially class II controls, via telehealth is a viable concern. Consequently, there are additional regulatory requirements and general best practices to mitigate the associated risks. Both federal and state laws dictate the dispensing and/or mailing of controlled drugs. It is not uncommon for telehealth clinicians to be restricted by the company for which they work, sometimes prohibiting Schedule II drugs from being mailed or banning their prescribing altogether. Patients with ADHD can be negatively affected by these prescribing restrictions as first-line treatment for most patients with ADHD comprises a regimen involving a prescription stimulant medication. Clinicians should always reference applicable state and federal regulations to ensure their prescribing practices are compliant.

-Telehealth Selection

While some benefits of telehealth are indisputable, there are also some drawbacks. First and foremost, it is important to ensure use of a reputable telehealth company with qualified clinicians. With the COVID-19 pandemic, a multitude of online platforms advertising telehealth became available to the public. An ADHD diagnosis requires an extensive evaluation, and a considerable amount of time is put into gathering the patient's medical and social history. Caution should be used with telehealth services that do not provide details on their diagnostic criteria, do not indicate where they are licensed, and do not provide cross-site data. In addition, a telehealth service should not diagnose or provide treatment, including medication, without viewing the patient, as parents/families/caregivers can report incorrect information that would otherwise be used in the evaluation. In July

2022, the U.S. Department of Justice charged 36 companies with fraud for a variety of schemes involving telehealth services that led to $1.2 billion in medical fraud charges. The assistant director of the Federal Bureau of Investigation's Criminal Investigative Division warns, "fraudsters and scammers take advantage of telemedicine and use it as a platform to orchestrate their criminal schemes" (King, 2022).

Another downside to telehealth is lack of communication between clinicians. Many online clinicians are seeing the patient for the first time and do not have records from previous clinicians and those individuals involved in the care of the patient (Vivlio Health, 2021). This can be a result of the many electronic health record products in use across the country and the lack of interoperability between them (Beardsley, 2022). Past medical history and current diagnoses are often reported by the patient and can be inaccurate or misinterpreted. It is imperative to obtain appropriate records from previous clinicians before continuing or starting treatment for ADHD. If these records cannot be obtained, a full evaluation, according to the Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition, Text Revision (DSM-5-TR) criteria, should be performed. See the "Evaluation and Diagnosis" section of this guideline for information.

Ultimately, telehealth can not only bring much needed ADHD-specific diagnostic, psychosocial, and pharmacological services to underserved populations but promote social justice, reinforce the importance of cultural factors, and infuse ADHD-related psychology knowledge in training, education, and continuing education for both clinicians and the general population. However, telehealth services should only be provided by reputable clinicians. As always, the proper evaluation and diagnosis of ADHD is imperative to the appropriate treatment of the patient.

Pathophysiology of ADHD

ADHD is a neurodevelopmental disorder characterized by developmentally inappropriate levels of inattention, hyperactivity, and/or impulsivity, which impair an individual's ability to function in different settings (Magnus et al., 2023). Research over the last 30 years has established potential neurochemical and physiological origins of ADHD, but they are not yet definitive (Chisholm-Burns et al., 2021). In addition to genetic imbalances in catecholamine metabolism, which appear to be the primary cause of the disease, diffuse abnormalities in the brain have been associated with cognitive and functional deficits (Chisholm-Burns et al., 2021; Millichap, 2008). These abnormalities lead to a lack of state regulation and periodic attentional lapses.

ADHD tends to be familial and is considered a heterogeneous disorder, with the majority of patients suffering comorbid complications from other psychiatric disorders (Albrecht et al.,

2015; Farone & Biederman, 2017). Frontostriatal circuits, which connect the frontal lobe with the basal ganglia and mediate motor, cognitive, and behavioral functions, show hypometabolism and less activity in this area of the brain (Abramovitch et al., 2013; Morris et al., 2016). The basal ganglia, which contains a high density of dopamine receptors, is also smaller in some individuals with ADHD (Rege, 2022).

Catecholamines, including dopamine, norepinephrine, and epinephrine, are hormones produced by the brain, adrenal medulla, and nerve tissues that act as neurotransmitters in response to stress. During times of stress, the "fight or flight" cascade is activated, with dopamine converting to norepinephrine and then to epinephrine, promoting alertness, increasing blood flow to skeletal muscle, and opening the airways (Fryburg et al., 1995). Lower levels of dopamine and norepinephrine in individuals with ADHD can lead to abnormal cravings for behaviors that stimulate dopamine release, such as drug misuse, risky sexual activities, or gambling (Blum et al., 2008; Sigurdardottir et al., 2016).

Dopamine deficiency in the prefrontal cortex (PFC) and overactivity of striatal dopamine transporters contribute to the symptoms of ADHD (Russell et al., 2000; Volkow et al., 2001). The anterior cingulate cortex (ACC), a region involved in cognitive control, affect allocation, inhibition, decision-making, and drive, is smaller in patients with ADHD compared to those without the disorder (Amico et al., 2011; Makris et al., 2009; Mercadante & Tadi, 2022). Patients with ADHD have demonstrated weaker function and structure of the dorsolateral PFC, which is responsible for regulating attention, behavior, emotion, and inhibition (Arnsten, 2009). Poor scores on executive functioning tests, particularly in areas involving inhibition, switching, set shifting, updating, and sustained attention, are correlated with ADHD (Bayard et al., 2020). Functional imaging has revealed delayed maturation of the dorsolateral PFC and ACC by approximately three years in patients with ADHD (Bayard et al., 2020).

Genetics can also be a risk factor for the development of ADHD. The heritability of ADHD has been estimated to be 76% to 80% (Bukstein, 2022; Fliers et al., 2005). Thus, there is an elevated prevalence of ADHD in children with mothers and fathers with ADHD, and the rate of hyperactivity among siblings with the disorder is higher than the general population (Farone & Biederman, 2017). Among parents with ADHD, 84% have at least one child diagnosed with ADHD and 52% have two or more diagnosed children (Farone & Biederman, 2017). One study targeting families with ADHD found that among children whose ADHD persisted into adulthood, 16.3% had a parent with ADHD and 24.4% had a sibling with the disorder. By comparison, in children whose ADHD is remitted before adulthood, only 10.8% had a parent with ADHD and 4.6% had a sibling with the same diagnosis. This finding suggests that children with ADHD persisting into adulthood are more likely to have a genetic origin for their disease (Farone &

Biederman, 2017).

ADHD is often misdiagnosed as another neurodevelopmental disorder, leading to substantial morbidity (Marangoni et al., 2015). Many of these other disorders have similar pathophysiology that includes a neurochemical imbalance. Adding to the dilemma of similar pathophysiology, most have one or more overlapping symptoms, making differentiation difficult. Psychiatric disorders that are commonly misdiagnosed as ADHD (and vice versa) are oppositional defiant disorder, conduct disorder, anxiety, depression, autism spectrum disorder (ASD), sleep disorders, developmental coordination disorders, learning disabilities, and trauma (Gnanavel et al., 2019). In addition to differentiation, comorbid conditions can also be of concern. Ten percent to 92% of patients with ADHD also have one or more comorbid conditions (Gnanavel et al., 2019). The 2007 NSCH found that 33%, 18%, and 16% of children with ADHD had one, two, or three or more coexisting conditions, respectively (Larson et al., 2011). Therefore, a thorough evaluation and attentive consideration of comorbid disorders is vital to an accurate diagnosis of ADHD.

Additional considerations regarding the pathophysiology of ADHD include ACEs, prenatal substance exposure, acetaminophen use during pregnancy, traumatic brain injury (TBI), certain infections, and toxic metal exposure. Information on each of these topics is provided below.

ACEs and Pathophysiology

ACEs are potentially traumatic events that happen before adulthood and can have lasting negative effects on a person's health and wellbeing. Exposure to these toxic stressors has been shown to alter an individual's molecular and genetic makeup and modify how the neurological, immune, and endocrine systems develop and function (Boullier & Blair, 2018). These changes are similar to the neurological changes seen in the pathophysiology of ADHD. Cumulative stressors (such as ACEs) lead to molecular and genetic changes. Acute stress promotes a normal, adaptive response in the body that maintains stability, also known as allostasis. This stress response is regulated by the sympathetic-adrenal-medullary and hypothalamic-pituitary-adrenal neuroendocrine axes. When a stress stimulus activates the system, the body responds within seconds and releases catecholamines in the tissues and end organs to create a fight-or-flight response. As a result, a cascade of events occurs, such as increased heart rate and blood pressure, splanchnic vasoconstriction, muscular vasodilation, bronchial dilation, and finally a release of glucocorticoids (mainly cortisol) from the adrenal cortex. Chronic stress over extended periods of time increases this allostatic load, resulting in psychological dysfunction due to a sustained stress response. This dysfunction occurs across multiple systems, causing altered brain structure and function, chronic basal inflammation, impaired cellular immunity, and abnormal glucose handling

(Ridout et al., 2018).

Maternal chronic stress is detrimental to a fetus in utero. Psychological stress pre-programs functional parameters, such as hormonal levels, neural activity, and other measurable factors, to abnormal levels, inducing postnatal maladaptation. This pre-programming can induce postnatal maladaptation, leading to difficulties or challenges in adjusting to life after birth (Veru et al., 2014). As maternal cortisol is increased, it is transported across the placenta, entering fetal circulation and altering fetal stress architecture (Keenan et al., 2018). Cortisol also activates the promoter region in the placenta, stimulating corticotropin-releasing hormone, which further increases glucocorticoid (cortisol) release (Keenan et al., 2018).

Children with ACEs and/or in utero exposure related to maternal chronic stress have also been shown to have shorter leukocyte telomere lengths (LTL) (Entringer et al., 2011). Telomeres are structures at the end of chromosomes that are responsible for preventing nucleolytic degradation and unnecessary recombination, repair, or intrachromosomal fusion (Shammas, 2011). Shorter LTLs adversely affect the immune and endocrine system and are direct predictors of age- related disease onset and mortality (Shammas, 2011).

There are three categories of ACEs: abuse, neglect, and household dysfunction. Abuse events include any physical, emotional, or sexual abuse. Neglect events can include both physical and emotional neglect. Homelessness or starvation are examples of physical neglect, whereas isolation or shaming would constitute emotional neglect. Household dysfunction includes situations with drug use in the home, an incarcerated parent, or someone in the home with a mental health condition (CDC, 2022b). Experiencing four or more of these traumatic events as a child has been associated with a higher likelihood of developing chronic diseases, such as mental health disorders (including ADHD), cancer, kidney disease, heart disease and myocardial infarction, asthma, chronic lung disease, hypertension, dyslipidemia, diabetes, digestive diseases, and more (Gilbert et al., 2015; Lin et al., 2021). Almost 80% of children aged five to 15 years of age with an ADHD diagnosis report experiencing at least one ACE, and approximately 50% report two or more (Lugo-Candelas et al., 2021). The CDC reports women and certain racial/ethnic minority groups are at an increased risk of experiencing four or more types of ACEs (CDC, 2021a). In West Virginia, approximately 55.8% of adults report experiencing at least one ACE. The most common ACE in West Virginia is substance misuse in the home (28%), followed by parental separation/divorce (26.6%) and verbal abuse (22.7%) (DHHR, 2018b). Additionally, household income is correlated with ACEs. In West Virginia, adults had an 8.1% chance of experiencing four or more ACEs if the household income was $75,000 or more but a 23% chance if the household income was $15,000 or less (DHHR, 2018b).

Acetaminophen Use During Pregnancy

In 2018, a systematic review, meta-analysis, and meta-regression analysis found that prenatal exposure to acetaminophen was associated with an increased risk for ADHD, ASD, and hyperactivity symptoms (Masarwa et al., 2018). The analysis included seven cohort studies of over 132,000 mother-child pairs, with 61,601 drug exposures (Masarwa et al., 2018). Findings were statistically significant for risk of developing ADHD (relative risk [RR]=1.34 [95% confidence interval (CI),1.21-1.47]) and ASD (RR=1.19 [95% CI,1.14-1.25]) after fetal exposure to acetaminophen (Masarwa et al., 2018). Of note, the authors point out the evidence is based on observational studies, and clinical trials are needed to further evaluate the safety of acetaminophen in pregnancy (Masarwa et al., 2018). Literature since 2018 has continued to support these findings. Researchers at Johns Hopkins University Bloomberg School of Public Health collected umbilical cord blood from 996 births, of which 257 were included in the sample due to acetaminophen exposure. By the average age of 8.9 years, for those with intrauterine acetaminophen exposure, 25.8% of the children had been diagnosed with ADHD, 6.6% with ASD, and 4.2% with both (Ji et al., 2020). Their research found that only 32.8% of children with exposure to acetaminophen were neurotypical (Ji et al., 2020). These results suggest that intrauterine acetaminophen exposure may significantly increase the risk of developing childhood ADHD and ASD. A large meta-analysis examining European studies yielded similar results (Alemany et al., 2021). While research is ongoing, the use of acetaminophen in pregnancy should be discussed with a physician, especially in families where the development of ADHD is a concern.

Prenatal Substance Exposure in West Virginia

Another significant risk factor in the development of ADHD is substance exposure in utero. Risks for development of attention disorders include maternal illicit substance use, including nicotine, alcohol, cannabis, opioids, methamphetamine, and cocaine. Neonatal abstinence syndrome (NAS) occurs when infants have been exposed to drugs in the womb prior to birth. The average rate of NAS in West Virginia is much higher than the national average, especially considering some exposures do not lead to NAS. A study conducted between 2020 and 2022 by researchers at West Virginia University revealed nearly one in eight infants born in West Virginia were exposed to opioids, stimulants, and/or cannabis in utero. Opioid and stimulant exposure rates were 10 times higher than national rates. Preterm birth was significantly associated with stimulant exposure. Cannabis was the most prevalent substance exposure, affecting 7.9% of infants. Additionally, 4.4% of infants were exposed to opioids, while 2.1% had been exposed to

stimulants. The study also observed that over 10% of the infants experienced exposure to at least one of these substances, with 1.7% exposed to two substances and 0.3% exposed to all three. The research indicated a 40% increased risk of preterm birth among infants exposed to stimulants alone, and a 70% increased risk when exposed to both stimulants and cannabis. Moreover, concurrent exposures to opioids and cannabis almost doubled the risk of infants born small for their gestational age, and the mean birth weight of infants exposed to these substances decreased by 200 to 500 grams. Another notable finding was that 20% of women in the study smoked during pregnancy, and of the infants exposed to substances in utero, 64.2% were also exposed to maternal smoking. Throughout the duration of the study, the number of newborns exposed to substances in utero exceeded 4,000, highlighting the significance and impact of this issue (Umer et al., 2023).

The effects of the ongoing drug epidemic with use of non-prescription or the misuse of prescription medication has been observed and documented through various age groups. After birth, when drug exposure has ceased, an infant may experience withdrawal symptoms. NAS can occur from exposure to opioids, cocaine, alcohol, and other drugs. In 2017, the rate of NAS was found to be 50.6 per 1,000 live births per year for West Virginia residents and as high as 107 cases per 1,000 live births in a single county (DHHR, 2018b). Since 2014, West Virginia has had six times the national average rate of NAS per 1,000 birth hospitalizations each year (U.S. Department of Health and Human Services, n.d.). This ongoing drug use in pregnancy has resulted in a much higher rate of in utero drug exposure in West Virginia, especially considering that not all babies exposed to drugs in utero develop NAS. As a result of the high prevalence of intrauterine drug exposure in West Virginia, the effects of certain substances on a child's development and behavior should be reviewed, especially in the context of evaluation, diagnosis, and treatment of ADHD.

-Alcohol Consumption During Pregnancy

Fetal alcohol exposure has been shown to decrease the size of many areas of the brain, including the cerebellum, and may lead to overall microcephaly and a decrease in white matter. This decrease in white matter impairs the brain's cellular connectivity (O'Neil, 2010). Fetal alcohol syndrome can range in symptoms from facial and limb development effects to cognitive delays or impairment; hence, there is a spectrum of disorders that fall under this term. No level of alcohol use during pregnancy has been deemed as safe (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2021). Fetal alcohol exposure has been shown to have serious neurobehavioral effects in the fetus,

including deficits in attention, memory, verbal fluency, reaction time, executive functioning, and motor learning (Ross et al., 2015). Fetal alcohol spectrum disorders can be characterized by learning difficulties and deficits in controlling emotions and impulsivity and communicating. Individuals with fetal alcohol spectrum disorders are more likely to have ADHD, depression and anxiety, and problems with hyperactivity, conduct, and impulse control (NIAAA, 2021). In fact, ADHD is the most commonly reported mental health diagnosis in those with fetal alcohol spectrum disorders, and it is suspected that fetal alcohol spectrum disorders are underdiagnosed in individuals with ADHD due to lack of information regarding exposure and fear of stigma (Peadon & Elliott, 2010).

-Nicotine/Tobacco Use During Pregnancy

Nicotine exposure in utero correlates with lower epinephrine and norepinephrine levels in the cord blood of infants. These neurotransmitters are important to the autonomic function that may play a role in ADHD. Nicotine has also been shown to suppress levels of dopamine at receptor sites in infants (Blood-Siegfried & Rende, 2010). In the United States, West Virginia has the highest proportion of women who smoke during pregnancy (approximately 30%) (CDC, 2022b). Prenatal tobacco exposure has been associated with increased activity, inattention, and behavioral problems. It has also been shown that symptoms of conduct disorder were observed at greater rates in children (seven to 15 years old) who were exposed to tobacco during fetal development (Cornelius & Day, 2009). Furthermore, maternal smoking during pregnancy significantly predicted symptoms of oppositional defiant disorder and can be predictive of the severity of hyperactive-impulsive and conduct disorder symptoms (Langley et al., 2007). With the high prevalence of smoking during pregnancy in West Virginia, clinicians and other individuals involved in the care of pregnant patients using tobacco should consider prevention measures such as counseling and referral to services for tobacco cessation. Fetal exposure to nicotine should be considered when evaluating and diagnosing children for ADHD and other potential coexisting conditions.

-Cannabis Use During Pregnancy

In utero cannabis exposure is associated with altered connectivity of the caudate nucleus and cerebellum, which may result in increased impulsivity and attention deficits. In addition, it disrupts anterior insula connectivity, potentially affecting motivation and

decision making. Tetrahydrocannabinol (THC), the psychoactive ingredient in cannabis that causes a high, changes dopamine development, altering emotional regulation (Grewen et al., 2014). Cannabis is the most commonly used recreational drug during pregnancy. The overall effects on fetal and child development are yet to be reported, but a recent study showed that intrauterine cannabis exposure led to increased cortisol, anxiety, aggression, and hyperactivity in young children (Rompala et al., 2021). Some of these symptoms can overlap with ADHD or other coexisting conditions. Additionally, prenatal cannabis exposure may lead to interference in proper brain maturation in children, which can lead to cognitive deficits as well as depression, hyperactivity, inattention, and impulsivity. The prevalence of affective disorders, such as anxiety and depression, and ADHD resulting from prenatal cannabis use can vary based on the duration and intensity of maternal use while pregnant; therefore, appropriate and timely interventions are important for mothers and their children to minimize risks (Roncero et al., 2020).

-Opioid Use During Pregnancy

Opioids freely cross the placenta and induce change in fetal catecholamine, glutamate, and acetylcholine neurotransmitter levels (Grecco & Atwood, 2020). The most affected parts of the brain are the PFC, amygdala (important in brain connectivity related to decision making and reward reinforcement), and hippocampus (helps promote functions requiring attention and cognition) (Plessen et al., 2006; Walhovd et al., 2007). Prenatal opioid exposure has been found to significantly increase the risk of ADHD symptoms in childhood. A meta-analysis of seven studies found that children with prenatal opioid exposure had a positive association with hyperactivity/impulsivity, inattention, and combined ADHD scores. Combined ADHD scores were also positively associated with prenatal opioid exposure in preschool- and school-age children (Schwartz et al., 2021). The main opioid exposures in the included studies of the meta-analysis included heroin, methadone, and/or buprenorphine, but a limitation was that all studies had polydrug use, including additional illicit substances. In a study of five- to 12-year-old children, in utero heroin exposure was associated with high rates of inattention, hyperactivity, and behavioral problems but not cognitive impairment. Additionally, intellectual development of those children was found to be influenced by a child's environment, which can improve developmental outcomes (Ornoy et al., 2001). Overall, fetal opioid exposure can lead to an increased prevalence of ADHD and behavioral problems, and treatment of opioid use disorders and pain during pregnancy should be carefully considered and monitored due to

fetal and maternal risks and benefits (Ross et al., 2015).

-Methamphetamine Use During Pregnancy

Prenatal methamphetamine exposure reduces blood flow through the placenta and alters caudate nucleus and thalamus development in the fetus. Asymmetrical caudate nucleus development has been linked to ADHD (Schrimsher et al., 2002). Methamphetamine also suppresses levels of dopamine and norepinephrine in the fetal brain (Thompson et al., 2009). While there is a great need for additional research to fully assess the effects of maternal methamphetamine use during pregnancy, some effects of methamphetamine intrauterine exposure on child development have been documented. In three- and five-year-old children, increased emotional reactivity and anxious/depressed problems were present. At five years of age, externalizing and ADHD problems were observed at higher rates in children exposed to methamphetamine. Additionally, heavy prenatal methamphetamine exposure is associated with increased attention problems by five years of age (LaGasse et al., 2012). Prenatal methamphetamine exposure was also shown to be associated with deficits in behavioral and emotional control as well as deficits in executive functioning in five-year-old and six and a half-year-old children, respectively (Abar et al., 2013). At seven and a half years of age, prenatal exposure to methamphetamine was found to be associated with behavior problems. Notably, early adversity, which can be a consequence of prenatal methamphetamine exposure, was identified as a strong determinant of these behavior problems (Abar et al., 2013).

-Cocaine Use During Pregnancy

Cocaine use during pregnancy affects several regions of fetal brain development, including the amygdala, caudate nucleus, and PFC. Cocaine is inhibitory of the reuptake of monoamine neurotransmitters and leads to a concentration of dopamine, serotonin, and norepinephrine within the synaptic cleft (Ross et al., 2015). Prenatal cocaine exposure has been associated with deficits in language performance; more specifically, more severe exposure leads to greater deficits (Bandstra et al., 2004). In children aged five and seven years with prenatal cocaine exposure, impairments in attention processing are observed. At age five, increased omission errors and response times for target tasks are observed in those with prenatal cocaine exposure, and in patients seven years of age, decreased consistency in performance was observed (Accornero et al., 2007). In a study of nine-year-

olds, higher levels of prenatal cocaine exposure were found to be associated with disruptive behaviors, including aggression and delinquent behaviors. When rating aggressive behaviors, children were 1.3 times more likely to be rated as aggressive with each increased unit of prenatal cocaine exposure. The likelihood of delinquent behavior ratings doubled with each unit of prenatal cocaine exposure (McLaughlin et al., 2011). Overall, exposure can lead to both attention and emotional dysregulation in children, especially with higher levels of exposure (Rompala et al., 2021; Ross et al., 2015).

Overall, more data on prenatal drug exposure and its role in ADHD development is needed; however, numerous studies indicate the probability for an associated increased risk for ADHD, related symptoms, or coexisting conditions with overlapping symptoms. A limitation of many studies attempting to focus on the effects of a single substance is the inability to eliminate confounding variables, such as polysubstance use, that may influence the overall results. However, it is evident that a correlation exists between substance exposure during pregnancy and increased cognitive, behavioral, and attention problems. Therefore, as a prevention measure, women should be counseled and/or referred for additional treatments if needed during pregnancy to address substance use and the potential effects on the fetus. While this prior exposure may not change the treatment plan for ADHD, it is a crucial factor to consider during the comprehensive evaluation and diagnosis of children presenting with attention and behavioral problems.

Other/Secondary Causes of ADHD

Secondary causes of ADHD (not to be confused with secondary symptoms) refer to the development of ADHD during or after an infection, event, or exposure. The majority of studies on ADHD exclude patients with ADHD resulting from a secondary cause, limiting the evidence. As a result, little is known about its etiology, though it is likely due to diffuse neuronal changes from injury or immune response. Children and adults with secondary causes of ADHD may respond differently to ADHD medications than patients with a primary diagnosis of ADHD. It has been suggested that medications to treat ADHD may be less effective for this population, and adverse effects, especially agitation, may be more pronounced. Below are examples of secondary causes of ADHD.

-Traumatic/Anoxic Brain Injury

Traumatic brain injury (TBI) usually results from a violent blow or jolt to the head.

Research has shown that children with a serious brain injury are more likely to develop ADHD. A study from 2018 found that one in five children with TBI will develop ADHD (Narad et al., 2018), and newer literature suggests one mild brain injury before age five yields a 64% increase in the risk of developing ADHD (Wimberley et al., 2022). Furthermore, the disorder may not develop for several months or years following the injury (Narad et al., 2018; Tramontana et al., 2021). Patients with TBI tend to display similar deficits in attention, behavior, and mood (Tramontana et al., 2021).

Anoxic brain injury is the result of some birth injuries. Birth injuries can be caused by many situations, including positional issues (such as baby being breech), babies of large size, assisted delivery devices, unusual pelvis shape, nuchal cord, amniotic level problems, and more. There has been an association between birth injuries and the development of mental health disorders, including ADHD. In a study looking at birth complications in children with ADHD, there was a significantly higher rate of neonatal complications in the ADHD cohort compared with their unaffected siblings (Ben Amor et al., 2005). A study in 2013 looking at in utero exposure to hypoxic conditions and ADHD found that children exposed to ischemic-hypoxic conditions were associated with increased odds of ADHD across all race and ethnicity groups (Getahun et al., 2013). They also found that birth asphyxia, respiratory distress syndrome, and pre- eclampsia were all independently associated with ADHD (Getahun et al., 2013).

-Toxic Metal Exposure

Even at small amounts, toxic heavy metals are harmful to neurological development and have been correlated with ADHD or ADHD symptoms. With toxic metal exposure, specifically lead, neural connectivity is disrupted, and neurotransmitter release is decreased. Lead is thought to be substituted for calcium and zinc at the neuronal synapse, interfering with normal neurotransmission. Overall, there is “miswiring” of the central nervous system, with impaired programming of cell-to-cell communication (Goyer, 1996). A study in 2018 found that children exposed to heavy metals, especially lead, cadmium, and antimony, were at an increased susceptibility to development of ADHD. It was noted that higher levels of metal exposure correlated with worsening ADHD symptoms (Lee et al., 2018).

Lead exposure is particularly concerning in West Virginia. More than half of the current housing in West Virginia was built prior to 1980, when homes were regularly manufactured with lead paint (DHHR, 2022a). Many dwellings were repainted, but lead

paint still poses serious health risks when not properly removed (Minnesota Department of Health, 2022). Lead paint resides in the walls (interior and exterior), carpet, windows, trim, and even the soil around the home (Minnesota Department of Health, 2022). Children are at greater risk of lead poisoning than adults due to their exploratory nature and propensity to put objects in their mouth (DHHR, 2022a).

Another source of lead exposure is through the use of lead pipes. While lead pipes were banned in the 1980s, numerous homes built in the early 1900s still contain this toxic metal (Leffler, 2021). Between 2015 and 2019, 447 children in West Virginia presented with elevated lead levels in their blood (DHHR, 2022a), and it is estimated that 20,000 households in West Virginia have lead service lines (Olson & Stubblefield, 2021). A press release in 2021 indicated that the water supply in Clarksburg, West Virginia, was found to have water levels tens to hundreds of times higher than the federal standard, prompting the U.S. Environmental Protection Agency to issue an order for the water board to find an alternative source of drinking water (Kelly, 2021). Recent national infrastructure investments are underway to address the lead pipe exposure (International Association of Plumbing and Mechanical Officials [IAPMO], 2022), but at this time, it is still a concern in West Virginia.

In response to this increased possibility of lead exposure in West Virginia, the West Virginia Bureau for Public Health strengthened their screening efforts by implementing the Childhood Lead Screening Rule, which requires healthcare clinicians to conduct a blood screening test on all children before the age of six years. This test indicates elevated levels of lead in accordance with CDC recommendations (Amjad, 2022). The Rule, in conjunction with West Virginia State Code §16-35, states that all children should receive the screening test at one year of age and then again at two years of age. Children aged 36- 72 months should also be screened if they did not receive previous testing. Children with blood levels above 5 µg/dL should have a follow-up test within three months, and the information and results should be provided to the parent/family/caregiver (Amjad, 2022). Therefore, clinicians should be able to utilize this testing as a means of assessing possible lead exposure association with ADHD symptomology. Clinicians should ensure all children under the age of six years have been screened for lead exposure, including those patients presenting with ADHD symptoms.

-Infections

Studies focusing on the relationship between illness and ADHD are very limited,

but a study out of Turkey found a statistically significant correlation between children infected with measles, mumps, and rubella and the development of ADHD (Bekdas et al., 2014). The study proposes that children with viral cerebellitis experience immune changes in their brain tissue, which may contribute to the development of ADHD symptoms. These immune changes could involve the interaction of major histocompatibility complex (MHC) proteins with cytokines like interleukin-1 (IL-1) and interleukin-6 (IL-6), affecting learning, memory, and synaptic structures. The study also suggests the potential involvement of genetic polymorphisms in mediating the effects of these mechanisms (Bekdas et al., 2014). It has been suggested that there may be an association between the Epstein-Barr virus and ADHD symptoms in children. However, a 2022 study conducted did not find evidence supporting this association (Wang et al., 2022). More studies are needed to evaluate the direct effects that viruses can have on brain tissue and the subsequent development of ADHD. When evaluating a patient for a possible ADHD diagnosis, previous infective exposures should be considered in the past medical history.

ADHD has extensive pathophysiology affecting multiple parts of the brain and its physiological processes. Altered catecholamine handling appears to be the primary cause of symptomology (Chisholm-Burns et al., 2021). Genetic predisposition, in utero exposure to toxic agents, and ACEs can be possible predictors of disease (Bukstein, 2022). ADHD is considered a familial disorder with high heritability, estimated to be between 76% to 80% (Bukstein, 2022; Fliers et al., 2005). Exposure to harmful substances in utero, such as illicit drugs and alcohol, is strongly associated with an impaired stress response, abnormal behavior, and deficits with executive functioning (McLaughlin et al., 2011; Rompala et al., 2021; Ross et al., 2015).

Furthermore, ACEs are linked to chronic health conditions and can affect how the body responds to adversity (Ridout et al., 2018). Awareness of the risk factors of ADHD, preventable or non-preventable, will aid in appropriate evaluation and diagnosis, guide treatment and mitigation of symptoms, and possibly allow for prevention measures for future generations. It is critical for healthcare clinicians and other individuals involved in the care of patients with ADHD to promote positive parenting skills and advocate for support of parents/families/caregivers. Focusing on prevention and early intervention will improve the future mental and physical health of children and adults in West Virginia.

Evaluation and Diagnosis

Primary care clinicians play a significant role in identifying ADHD in children and clarifying lingering ADHD symptom-related issues present in adults. In children, routine visits for preventive care can lead to earlier diagnosis and intervention of not only ADHD but other possible coexisting conditions or alternative diagnoses. While these early encounters may allow for patient or caregiver concerns to be addressed as well as observations of the patient, not all primary care clinicians feel prepared to appropriately evaluate, diagnose, or provide interventions for ADHD. For example, the AAP recommends that for patients between the ages of four and 18 years, a pediatrician or primary care clinician initiates an evaluation and treatment for ADHD and other coexisting conditions, but it is acknowledged that some primary care physicians may not be trained and experienced to successfully diagnose or treat ADHD. If the primary care clinician is not trained or experienced, it is recommended that the patient be referred to an appropriate subspecialist for treatment (Wolraich et al., 2019). For adult patients, the AAFP does not make a specific recommendation for referral as they state it is at the clinician's discretion. However, the AAFP does suggest a referral based on other comorbidities for which the clinician would typically refer, such as anxiety and depression, symptoms that can be a function of ADHD (issues with organization and planning, marital problems, etc.), and other major disabilities affecting daily function (Post & Kurlansik, 2012).

The majority of ADHD diagnoses are made in childhood, but there is a subset of patients who are diagnosed in adulthood (American Psychiatric Association, 2022a). Adults may present with unique circumstances. The AAFP states that adults may retain some, but not all, of their symptoms from childhood, indicating partial remission. Historical recollection of symptoms by adults is required as the symptoms listed in the DSM-5-TR must have been present prior to 12 years of age. For this reason, the DSM-5-TR criteria are not as stringent for adults as they are for children; rather than requiring six DSM-5-TR symptoms of inattention and/or hyperactivity/impulsivity as is needed for a diagnosis in childhood, only five are required for adults (Post & Kurlansik, 2012). However, accurate recollection of childhood symptoms can present a challenge for an accurate diagnosis of ADHD in adults.

Training in evaluation, diagnosis, and treatment of ADHD is important to ensure an accurate diagnosis with an appropriate, effective, and tailored treatment plan to foster the highest achievable outcomes. A comprehensive evaluation for ADHD may require multiple office visits in order to critically evaluate a patient's medical, developmental, educational, and psychosocial histories in efforts to clarify the presence or absence of symptoms meeting the DSM-5-TR criteria for ADHD. Assessment tools from multiple informants (e.g., patient, caregivers, teachers,

employers, spouses) can supplement and validate both verbal histories and available documentation, clarify current symptoms, determine the severity and settings of the symptoms, and determine the presence of symptoms beyond those related to ADHD. A diagnosis of ADHD should only occur following the review of all assessment results, histories, and observations to rule out other possible causes of the inattention and/or hyperactivity/impulsivity (e.g., anxiety, mood, sleep, medication side effects, substance use).

If a patient or caregiver is reporting symptoms suggestive of a possible ADHD diagnosis, evaluation should begin with an initial interview to assess the presence of specific ADHD-related symptoms and how they are interfering with activities of daily living by socially, emotionally, or behaviorally impacting academic, social, familial, or work performance. More specifically, interviews with the patient and family/caregiver/spouse (i.e., collateral individuals) should be conducted to systematically assess and document the patient's symptoms in order to evaluate the accuracy of a possible diagnosis of ADHD or another condition with overlapping symptoms. A thorough interview with the patient can supplement collateral reports and allow for an inventory and description of the patient's self-observed symptoms. During a visit, the clinician can monitor the patient and make behavioral observations. Observation of the patient can identify relevant symptomology as well as encourage further inquiry into the patient's distress from their symptoms, awareness of their behaviors, and ability to control their behaviors. By gathering collateral reports, self-reports, and observations during this initial process, the clinician can begin to see if the DSM- 5-TR criteria for ADHD, provided below, is consistent with the patient's symptomology, prompting a full assessment for ADHD before a diagnosis is made.

The assessment and evaluation of adult patients for ADHD presents unique challenges. Although ADHD persists into adulthood for a large subset of the population, it has been traditionally viewed as a childhood disorder (Culpepper & Mattingly, 2010). As mentioned, the DSM-5-TR diagnostic criteria require patients to have symptoms before the age of 12 years, which can be challenging for adults to recall. The criteria also require symptoms to significantly impact at least two areas of life, and as patients grow into adulthood, compensatory mechanisms can make their symptoms less intrusive. As with the childhood population, ADHD symptoms are often masked by comorbid psychiatric conditions and symptom overlap, further complicating the diagnosis. The concern for prescription drug misuse and diversion is also more prevalent in the adult population, especially young adults aged 18 to 25 years (Post & Kurlansik, 2012). Therefore, there may be additional considerations regarding evaluation and diagnosis of adult patients who present with ADHD symptomology.

Listed below are a few suggested questions that can be presented during the interview process to inquire about a patient's symptomology. Interviews should be utilized to verify the

patient's number and type of symptoms that may correspond to the symptoms for ADHD in the DSM-5-TR Attention-Deficit/Hyperactivity Disorder Diagnostic Criteria, provided below.

- What symptoms are present?
- When do symptoms occur?
- In what situations do the symptoms occur?
- What was the age of onset of symptoms?
- What is the duration of symptoms?
- Is there anything which lessens the symptoms?
- How do the symptoms impact activities of daily living?

Upon collection of symptom information, the DSM-5-TR criteria should be compared to the patient's symptoms to determine if they are consistent with an ADHD diagnosis. The DSM-5-TR criteria are listed below, but it should be noted that there are various overlapping symptoms with other possible coexisting conditions, which are further detailed in this document. Therefore, ensure the symptoms present are not due to a potential coexisting condition to ensure an accurate diagnosis.

DSM-5-TR: Attention-Deficit/Hyperactivity Disorder Diagnostic Criteria (American Psychiatric Association, 2022, Text Revision)

DSM-5-TR: Attention-Deficit/Hyperactivity Disorder Diagnostic Criteria

A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least six months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

   Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).

b. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).

c. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).

d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).

e. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).

f. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).

g. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

h. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).

i. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least six months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

a. Often fidgets with or taps hands or feet or squirms in their seat.

b. Often leaves a seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).

c. Often runs about or climbs in situations where it is inappropriate. (**Note:** In adolescents or adults, it may be limited to feeling restless.)

d. Often unable to play or engage in leisure activities quietly.

e. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).

f. Often talks excessively.

g. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for their turn in conversation).

h. Often has difficulty waiting his or her turn (e.g., while waiting in line).

i. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).

j. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.

k. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

l. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

m. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

Specify whether:

- **(F90.2) Combined presentation:** If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past six months.

- **(F90.0) Predominantly inattentive presentation:** If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past six months.

- **(F90.1) Predominantly hyperactive/impulsive presentation:** If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past six months.

Specify if:

- **In partial remission:** When full criteria were previously met, fewer than the full criteria have been met for the past six months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

- **Mild:** Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.
- **Moderate:** Symptoms or functional impairment between "mild" and "severe" are present.
- **Severe:** Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

NOTE: On March 18, 2022, the DSM-5 was updated to the DSM-5-TR. The following criterion reflects the updated ADHD diagnostic criteria in the DSM-5-TR. For a list of changes made to the ADHD diagnostic criteria, see APPENDIX 1.1: DSM-5 TO DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter.

Bio-Psycho-Social Assessment

In addition to review and documentation of the patient's symptoms, a bio-psycho-social assessment should be conducted with the patient and family/caregiver to document possible risk factors for ADHD or other potential coexisting conditions, additional potential underlying sources of the reported symptoms, or contributing causes of symptoms. Many of the items to include in the bio-psycho-social assessment are included below. This list is not intended to be exhaustive but provides examples of common inclusions.

-Complete physical examination

- Measurement of height, weight, head circumference (children), and vital signs
- Complete neurologic examination to rule out neurological disorders such as head injuries or seizure disorders
- Communication skills
- Behavioral observation
- Focus on thyroid examination to rule out thyroid abnormalities and assess thyroid hormone levels

-Medical history

- Gestational age at birth
- Birth injuries
- Developmental history
  - Children-Developmental milestones
  - Adults-Helps establish symptoms that occurred in childhood
- Hearing or visual impairment
- History of exposure (e.g., toxic metals, prenatal substance exposure)
- Thyroid abnormalities
- Sleep disturbances
- Tic disorders
- Medications
- Head trauma
- Loss of consciousness
- Co-occurring mental health symptoms (e.g., anxiety, depression, trauma)
- Current and past medications

-Family history

- Medical history
- Behavioral health
  - Drug use
  - Criminal behavior
- Mental health
- History of ADHD

-Social history

- Family situation
- Peer relationships
- Trauma
- Stressors

-Patient behavioral patterns and family expectations

- Information regarding onset, course, and functional impact of symptoms
- What the patient or family has tried to address the challenges

-Academic/employment history

- School absences
- Academic performance
- Accommodations (e.g., 504 plan) or modifications (e.g., individualized education program [IEP]) in school
- Work absences
- Work performance

-Substance use

- Current use
- Historical use

-Current eating/toileting (as appropriate for age)

-Sleep

- Duration
- Quality

- Symptoms of sleep apnea

-Strengths and talents

Assessment

(see APPENDIX 1.2: Assessments for Children and APPENDIX 1.3: Assessments for Adults)

If the patient's history (medical, family, academic, etc.), symptomology, and observations are suggestive of an ADHD diagnosis according to DSM-5-TR criteria, a formal assessment via a validated assessment tool and/or more targeted interview may be conducted to confirm the diagnosis and rule out other possible diagnoses. A validated and normed rating scale is encouraged, as it aids in evaluating ADHD and other comorbidities. There are various assessments that can be utilized to assist with categorization of the patient's in-home, in-class, or at-work behaviors and symptoms. Broadband and narrowband assessments are used in practice, and use of both types of assessments is recommended to clarify both targeted and broader symptomology. The assessments vary in cost (some are available free of charge), time of completion, validated age range, reporter (e.g., self, caregiver, spouse, teacher), and norming/comparison types. While the assessments are often easy to administer, clinicians should have appropriate training on result interpretation, as each may differ with regard to scoring, outcome, and scale interpretation. These diagnostic evaluation tools should not be used in isolation to make a diagnosis. Rather, they should be used in conjunction with interviews and observations to not only ensure DSM-5-TR criteria for ADHD are met but ensure that other non-ADHD conditions are not creating similar symptoms. Using anxiety as an example, a high score on an inattention scale of a rating form may occur due to anxiety creating similar symptoms as ADHD-related inattention. However, the elevated inattention scale score in this scenario is related to anxiety and will decrease with anxiety alleviation. A summary of the available assessments and interviews are provided below, and additional information on each of the individual scales is available in APPENDIX 1.2: Assessments for Children and APPENDIX 1.3: Assessments for Adults. These measures are those that are available and recommended at the time of this publication. It is important to note that measures are often updated, and new measures are developed and may be appropriate to use.

-Clinical Interviews

(see APPENDIX 1.2: Assessments for Children and APPENDIX 1.3: Assessments for Adults)

During a thorough evaluation for ADHD and possible coexisting conditions, a clinical interview is likely to be an integral part of the process. Some of the scales from previously mentioned assessments may be integrated into the interview along with information regarding the patient's reported symptomology. There are several types of interviews utilized to identify markers, clarify sequencing and timeframes, and evaluate settings of challenges and intensity/frequency/duration of symptoms. Types include semi-structured, structured, or unstructured interviews.

-Structured Interviews

Structured interviews are typically scripted with yes/no questions to allow for navigation through the interview to questions pertaining to the reported symptomology. More detailed items may be addressed as the interview continues and symptoms are identified. This style of interview provides standardized ratings of the patient's responses. The most common structured interviews utilized are diagnostic interviews, which usually measure the specific criteria for mental disorders as defined in the DSM-5-TR. Use increases the coverage of disorders that may otherwise be overlooked in less standardized approaches and decreases the variability among interviewers (Lilienfeld & Cautin, 2015). Due to the clear question set, an advantage of a fully structured interview is that it can be delegated to a technician, assistant, or patient/caregiver, if needed. However, these interviews are quite time consuming, and offer the least flexibility in how the questions are asked.

Examples for children:

- Children's Interview for Psychiatric Syndromes (ChIPS and P-ChIPS)©
- Diagnostic Interview Schedule for Children-IV (DISC-IV)©
- Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-KID D)©

Examples for adults:

- Conners' Adult ADHD Diagnostic Interview for DSM-IV™ (CAADID™)
- Mini-International Neuropsychiatric Interview – Adult Version©

-Semi-Structured Interviews

Semi-structured interviews assist the clinician with initial probing questions regarding symptomology that may allow for more detailed questions or conversation to be presented by the clinician upon response from the patient. There is typically a general outline that the clinician can follow and explore diagnostic principles, sometimes limiting the flexibility in questions (Kollins & Sparrow, 2010). Questions do not have to be asked verbatim, as in a structured interview. In semi-structured interviews, the clinician uses specified initial questions but has the ability to augment or modify follow-up questions. These interviews require experienced clinicians to perform the interview and make diagnoses (Lilienfeld & Cautin, 2015). Due to the level of detail, this type of interview can be quite time consuming, so clinicians should plan accordingly.

Examples for children:

- Child and Adolescent Psychiatric Assessment (CAPA)©
- Kiddie-Schedule for Affective Disorders and Schizophrenia for School-aged Children Present and Lifetime (K-SADS-PL) ©

Examples for adults:

- Adult ADHD Clinical Diagnostic Scale (ACDS)©
- Young Adult Psychiatric Assessment (YAPA) ©
- The Diagnostic Interview for ADHD in Adults (DIVA-5)©

-Unstructured Interviews

Unstructured interviews are free-flowing conversations between the clinician and respondent, with no parameters for specific topics, allowing ample opportunity to gather clinical information (Lilienfeld & Cautin, 2015). The flow, sequence, and content are largely guided by the clinician's theoretical model, view of psychopathology, training, knowledge base, intuitions, and interpersonal style as well as the nature of the responses (Lilienfeld & Cautin, 2015). The benefit of this interview style is the ability to form a strong therapeutic relationship with the patient. However, the unstructured nature of the interview can lead to loss of information needed for an accurate diagnosis.

-Broadband Assessments

Broadband assessments can be used to assess symptoms of attention, hyperactivity, and impulsivity related to other behavioral and mental health conditions that may overlap with ADHD. Symptoms and behaviors relating to academic or occupational performance, executive functioning, peer relationships, and additional potential coexisting conditions can be evaluated with use of a broadband assessment. It is important to review the symptoms/conditions for which the assessment has been validated to ensure the one administered to the patient aligns with reported patient symptoms, behaviors, and suspected conditions. A few examples of broadband assessments that can be used to evaluate ADHD are listed below.

Examples for children:

- Achenbach System of Empirically Based Assessment System (ASEBA)©
    - Child Behavior Checklist (CBCL)©
- Barkley Functional Impairment Scale (BFIS-CA)©
- Behavioral Assessment for Children-3rd Edition (BASC-3)©
- Conners Comprehensive Behavior Rating Scale (CBRS)®
- Pediatric Symptom Checklist (PSC)©

Examples for adults:

- Achenbach System of Empirically Based Assessment System (ASEBA)©
- Minnesota Multiphasic Personality Inventory-3 (MMPI-3)©
- Personality Assessment Inventory (PAI)©

-Narrowband Assessments

Narrowband assessments focus specifically on the diagnosis of ADHD. The questions or reported observations tend to emphasize ADHD symptoms of inattention, hyperactivity, and impulsivity. The majority of the available narrowband assessments use the DSM-5-TR criteria for ADHD. Listed below are a few examples of narrowband assessments for children and adults.

Examples for children:

- Vanderbilt Scales©
- Conners 4™
- ADHD Rating Scales (ADHD-RS-5)©
- Brown Attention-Deficit Disorder Scale®
- Swanson, Nolan and Pelham (SNAP-IV)

Scale

Examples for adults:

- Conners Adult ADHD Rating Scales-Observer-reported/Long version (CAARS-O:L)©
- Conners Adult ADHD Rating Scales-Self-reported (CAARS-S:R)©
- Barkley Adult ADHD Rating Scale-IV (BAARS-IV)©
- Adult ADHD Self-Report Scale Symptom Checklist (ASRS-DSM-5)©

Gender and Age Disparities in ADHD Diagnosis

The diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) reveals a gender disparity, with boys having nearly twice the amount of ADHD diagnoses compared to girls (Bitsko et al., 2022). When evaluating patients for ADHD, understanding gender differences in symptomology is crucial as it may affect the type of ADHD presentation. Although ADHD subtypes are not gender-specific, discernible differences exist. Females tend to exhibit more internalizing symptomology, often presenting as predominantly inattentive (Rucklidge, 2010). Conversely, males generally display more externalizing symptomology, presenting as predominately hyperactive/impulsive (Gershon & Gershon, 2002). These externalized symptoms, whether attributable to ADHD or other behavioral conditions like oppositional defiant disorder or conduct disorder, are more likely to cause classroom disruptions (Furzer et al., 2022).

These gender-based differences in symptom presentation often lead to a disparity in referrals for ADHD assessments. Specifically, females may be under-referred while males are over-referred. Teachers without special education training have a tendency to overestimate the severity of ADHD symptoms in males and underestimate them in females. However, it is important to recognize that while age plays a role in ADHD assessments, the gender disparities in referrals remain significant (Furzer et al., 2022). In a study where participants assessed fictional academic profiles of children, teachers consistently demonstrated a tendency to refer boys more frequently than girls for ADHD evaluations. The gender discrepancy in referrals becomes most

pronounced when the child exhibits hyperactivity as the sole symptom, without accompanying inattention or aggression (Sciutto et al., 2004). This highlights a potential referral bias in ADHD evaluations, emphasizing the need for equitable assessments across genders.

The age of children compared to their classroom peers affects referral rates, with notable gender implications. One research study based in British Columbia, Canada showed that boys with birthdays close to the enrollment cut-off date (December) have a 30% higher probability of receiving an ADHD diagnosis and a 41% higher probability of receiving a prescription for medication to treat ADHD compared to peers born in January. For girls born in December, the differences were even more pronounced: they were 70% more likely to be diagnosed with ADHD and 77% more likely to receive a prescription for ADHD medication than their January-born counterparts (Morrow et al., 2012). Age, coupled with gender, significantly influences ADHD referral and diagnosis, underscoring the importance of considering both factors in the assessment process.

Alternative Diagnoses or Possible Coexisting Conditions

- see Appendix 1.5: Overlapping Symptoms with Attention-Deficit/Hyperactivity Disorder (ADHD)

While this guideline's focus is on the evaluation and diagnosis of ADHD, primary care clinicians should consistently screen for comorbid conditions when evaluating a patient for ADHD per the recommendations of the expert panel and all reputable ADHD guidelines. In a parent-reported survey, nearly two-thirds (63.8%) of children with ADHD also had at least one coexisting condition (Danielson et al., 2018). When looking at adults with ADHD, approximately 60% to 70% had a coexisting condition (Piñeiro-Dieguez et al., 2016). Due to this high prevalence of ADHD with other coexisting conditions, The Society for Developmental and Behavioral Pediatrics (SDBP) developed additional assessment and treatment recommendations for children and adolescents with "complex ADHD". Complex ADHD, as defined by the SDBP, is "ADHD co-occurring with one or more learning, neurodevelopmental, or psychiatric disorders" (Barbaresi et al., 2020).

It is important to examine both the possibility of an alternative diagnosis as well as the possibility for a coexisting condition when an ADHD diagnosis is being considered. There are multiple conditions that create overlapping symptoms that could lead to a misdiagnosis. An improper diagnosis creates the potential for delayed or inappropriate treatments (both psychosocial and pharmacological), increasing the chances of harm as well as an individual or family using a finite number of resources that were not applied to appropriate interventions. These considerations should be taken into account when creating a treatment plan for patients with ADHD, overlapping

symptoms, and/or coexisting conditions. If a primary care clinician does not believe they have ample training and experience in methods of appropriately evaluating and treating patients with ADHD and/or the coexisting conditions, the patient should be referred to a specialty clinician to co- manage the patient's care through development of an interprofessional, multimodal treatment plan (Barbaresi et al., 2020; Wolraich et al., 2019). Appropriate and thorough evaluation of patients who present with behavioral or attention issues allows for timely treatment and, ultimately, improvement of symptoms to improve function. Depending on the severity of the patient's symptoms, serious impairment in daily life, including academic achievement, daily responsibilities, and employment expectations, can occur without successful management.

Symptoms of ADHD are often confused and misdiagnosed for other disorders. While the following list of conditions is not fully comprehensive, it is meant to give clinicians reference during the differential diagnosis process. A chart with the overlapping symptoms is available in APPENDIX 1.5 Overlapping Symptoms with Attention-Deficit/Hyperactivity Disorder (ADHD). It is extremely common for patients with ADHD to have more than one condition, as many of the disorders listed below coexist with ADHD. The clinician will have to evaluate the symptoms and discern whether they are caused by ADHD alone, another disorder altogether, or multiple disorders, which is not an easy task. The conditions are listed below in no particular order in terms of clinician focus and present the prevalence in the general population as well as the prevalence in those with a diagnosis of ADHD. Also, as a reference, APPENDIX 1.4: Screening/Assessment Tools for Attention-Deficit/Hyperactivity Disorder (ADHD) and Related Conditions lists screening tools, most accessed at no charge, for the majority of these conditions to assist in the diagnostic process.

-Anxiety Disorders

- Prevalence in the general population:
    - Children aged three-17 years in 2019: 9.4% (Bitsko et al., 2022) (lifetime prevalence in adolescents aged 13-18 years: 31.9% [Kessler, et al., 2005])
    - Adults aged 18 and older in 2019: 15.6% (National Center for Health Statistics (NCHS), 2020)
- Prevalence within the population with ADHD:
    - Children: 25% to 32.7% (Kessler et al., 2006) (Larson et al., 2011)
    - Adults: ~50% (American Academy of Family Physicians [AAFP],2022a)

Distinguishing factors: One of the core symptoms of many anxiety disorders is difficulty concentrating or maintaining attention. Individuals with anxiety are inattentive because their focus is turned inward by worry or rumination. In contrast, those with ADHD struggle with inattention and distractibility because their attention is drawn outward by novel stimuli or excessively held by pleasurable activities. Additionally, individuals with anxiety often engage in restless behaviors that can mimic hyperactivity. Anxiety is often related to triggers (phobias, social separation, generalized about situations, etc.) that can create a level of inattention or jittering like ADHD. Addressing the anxiety or triggers through medications, therapy, or both, can significantly alleviate or eliminate the symptoms altogether, depending on the severity of symptoms, which differs some from ADHD. A neurodevelopmental history can help clarify the diagnosis and distinguish between anxiety and ADHD, especially in adolescents and adults.

-Depressive Disorders (Unipolar or Bipolar)

- Prevalence in the general population:
    - Children: 3.2% (Ghandour et al., 2019)
    - Adolescents aged 12-17 years of age in 2020: 17% (National Institute of Mental Health (NIMH), 2022a)
    - Adults aged 18 years or older in 2020: 8.4% (NIMH, 2022a)
- Prevalence within the population with ADHD:
    - Children: 16.8% (Danielson et al., 2018)
    - Adults: 18.6% (McIntosh et al., 2009)

Distinguishing factors: Individuals with depressed mood frequently experience poor concentration. However, the symptoms of depression are episodic rather than continuous, and diminished concentration will occur alongside other depressive symptomology such as changes in sleep patterns, appetite, feelings of guilt, and anhedonia (the inability to experience pleasure). The symptoms of ADHD, on the other hand, are not episodic and are present at some level most or all the time.

-Bipolar Disorders (Mania or Hypomania)

- Prevalence in the general population:
    - Children: 1% (Moreno et al., 2007)
    - Adults: 1%-4% (Cerimele et al., 2014)

- Prevalence within the population with ADHD:
    - Children: 22% (Singh et al., 2006)
    - Adults: 20% (Brus et al., 2014)

Distinguishing factors: Increased energy, poor concentration, distractibility, and impulsivity are core symptoms of manic or hypomanic mood states. However, elevated mood states occur as discrete episodes that are a change from the patient's baseline behavior. In contrast, those with ADHD display symptoms on a more continuous basis. Further, those with mania or hypomania will display other symptoms consistent with their mood disorder, such as grandiosity, decreased need for sleep, racing thoughts, or risk-taking behavior out of the norm from their baseline.

-Autism Spectrum Disorder

- Prevalence in the general population:
    - Children: 2.5% (Kogan et al., 2018)
- Prevalence within the ADHD population:
    - Children: 13.7% (Danielson et al., 2018)

Distinguishing factors: Individuals with ASD display symptomology that involves impairment in social skills, communication, restricted interests, and repetitive behaviors. There can be broad differences in symptom severity within this group, but a formal evaluation for ASD is strongly recommended for all children demonstrating ASD features due to the benefits of early intervention at home and in school. Many symptoms of ASD can look similar to those seen in ADHD, with some distinct differences. For example, patients with ADHD tend to lose focus easily on activities of little interest, whereas those with ASD do not, but communication or social skill deficits in ASD can be mistaken for inattentiveness (Ashinoff & Abu-Akel, 2021). Patients with ASD usually do not shy away from activities that require sustained attention as would be expected in patients with ADHD, but a strong desire to preferentially engage with restricted interests can be misinterpreted as lack of attention or distractibility (CHADD, 2023b). Patients with ASD do not usually display the same type of impulsive behaviors as those with ADHD. For example, patients with ADHD tend to talk excessively, have a strong need to be in constant motion, and may even appear uncomfortable if they are not moving. Patients with ASD will not usually display these characteristics, but stereotyped behaviors can be misunderstood as

hyperactive behavior (Neff, 2023). Additionally, patients with ADHD tend to easily forget important information and may misplace their belongings often, which is not a hallmark sign of ASD (Rapport et al., 2022). Children with ASD can also have ADHD.

-Trauma and Stressor-Related Disorders

- Prevalence (posttraumatic stress disorder) in the general population:
    - Children: 15.9% in trauma-exposed youth (Alisic et al., 2018)
    - Adults: 20% of trauma-exposed adults (CHADD, 2017b)

Distinguishing factors: Individuals with trauma-related disorders often struggle with attentiveness and sustained concentration. This can be due to recurrent and intrusive memories, dissociative states that negatively impact awareness of situations or surroundings, or diminished interest in activities. Trauma-related symptoms, by definition, have onset following a traumatic event and are often triggered or worsen following exposure to reminders of the event. In contrast, ADHD symptoms may worsen under certain situations but are mostly non-contextual.

-Learning Disorders

- Lifetime prevalence in the general population:
    - Children: 10% (Altarac & Saroha, 2007)
- Prevalence within the population with ADHD:
    - Children: 30%-50% (Learning Disabilities Association of America [LDA], 2003)

Distinguishing factors: Children with specific learning disorders are often inattentive when engaged in learning activities related to their area of disability. However, they do not show attention deficits with other tasks and they are not more hyperactive or impulsive than their peers. In contrast, by definition, children with ADHD struggle with symptoms across more than one setting. ADHD is commonly comorbid with learning disorders.

-Oppositional Defiant Disorder

- Prevalence in the general population:
    - Children: 3.3% across cultures (Canino et al., 2010)

- Prevalence within the population with ADHD:
    - Children: 35% (healthychildren.org staff, 2017)

Distinguishing factors: Those with oppositional defiant disorder (ODD) display argumentativeness and defiance toward adult authority figures solely out of a desire to resist conforming to rules or demands. The child with ADHD, on the other hand, is more likely to resist requests related to academic or mentally demanding tasks. Alternatively, failure to follow through with tasks in ADHD can be secondary to forgetfulness, distractibility, or impulsivity. Annoying others is common to both conditions, but for those with ODD, this behavior is typically deliberate. In those with ADHD, the annoyance may be more of an unintended consequence of their symptoms. ADHD and ODD commonly co-occur.

-Intellectual Disability

- Prevalence in the general population:
    - Children: 1.19% (Zablotsky et al., 2017)
    - Adult: 1.1%-1.3% (Anderson et al., 2019)
- Prevalence of ADHD in those with an intellectual disability:
    - Children: 9%-16% (Ageranioti-Bélanger, et al., 2012)
    - Adults: 8.7%-20.4% (Al-Khudairi et al., 2019)

Distinguishing factors: Individuals with intellectual disability can struggle with attention if placed in academic settings that are not commensurate with their intellectual level. Outside of these settings, however, their ability to focus will be on par with their mental age, not necessarily their chronological age. Those with ADHD will struggle with attentional tasks across multiple settings, to include non-academic situations.

-Sleep Disorders

- Prevalence in the general population:
    - Children: Up to 50% (Carter et al., 2014)
    - Adults: 25% (American Sleep Apnea Association [ASAA], 2022)
- Prevalence within the population with ADHD
    - Children: 25%-50% (Wajszilber et al., 2018)
    - Adults: 25%-50% (Wajszilber et al., 2018)

Distinguishing factors: Sleep disorders, such as insomnia, sleep-disordered breathing, circadian rhythm sleep disorders, narcolepsy, and others, can lead to insufficient sleep or sleep fragmentation. This lack of sufficient sleep can result in disturbances of mood, behavior, and attention that can resemble many of the symptoms of ADHD. Attentional and behavioral symptoms that chronologically begin after onset of the sleep disorder are unlikely to be related to ADHD. ADHD and sleep disorders often co-occur, sometimes as a consequence of stimulant therapy or due to poor bedtime routines seen with many children who have ADHD. If, when the sleep disorder is addressed or the patient gets adequate sleep, the symptoms resolve, then an ADHD diagnosis is likely inaccurate.

-Substance Use Disorders

(see APPENDIX 3.3: Screening Tools for Substance Use: Adolescents and APPENDIX 3.4: Screening Tools for Substance Use: Adults and APPENDIX 3.2: National Institute on Drug Abuse (NIDA) Screening Tools Chart)

- Prevalence in the general population:
    - Adolescents: 11.4% (Swendsen et al., 2012)
    - Adults: 7.8% (McCance-Katz, 2018)
- Prevalence within the ADHD population:
    - Adolescents: 10% (Molina et al., 2013)
    - Adults: 15.2% (Substance Abuse and Mental Health Services Administration [SAMHSA], 2015)

Distinguishing factors: Use of many substances, either prescription or illegal, can cause similar symptoms to ADHD, during either intoxication or withdrawal states. For example, alcohol intoxication can cause inattentive and impulsive behavior, while intoxication with stimulants, such as cocaine or methamphetamine, can lead to hyperactivity and impulsivity. A comprehensive list of substances and their effects is well beyond the scope of this document, but if substance misuse is infrequent, then hyperactive, impulsive, and inattentive symptoms should mostly be confined to periods of misuse or withdrawal. However, differentiating ADHD from substance use can be challenging if use is very frequent. It is possible that a patient presenting with ADHD symptomology does not have ADHD in the presence of illicit substance use. A clear history of onset of ADHD symptoms prior to the onset of drug use or during sustained periods of sobriety is key. Furthermore, urine drug testing for substance use can be considered when substance use is

suspected, and the patient may not be forthcoming with information regarding use.

Presentation and Treatment of ADHD Across the Lifespan

Symptoms:

Although ADHD often persists into adulthood, symptomology may change as the patient ages. For example, younger children (especially males) are more likely to demonstrate and be diagnosed with the hyperactive/impulsive presentation of ADHD than older children. In a study examining age-related differences in behavioral symptoms and neuropsychological function, a significant reduction was found in the severity of hyperactive and impulsive symptoms with age (Bramham et al., 2012). While some symptoms decrease with age, others may increase. Adult patients report higher levels of inattention as they age, and new symptoms, such as poor memory, poor job performance, and time blindness, may emerge (Bramham et al., 2012; CHADD, 2020a). Therefore, symptoms of adult ADHD may not present as clearly as symptoms do in children with ADHD. Symptoms such as impulsiveness, agitation, and difficulty paying attention may still be present; however, symptoms such as hyperactivity may decrease as the patient ages (AAFP, 2023a). As a result, many children who presented with a hyperactivity/impulsivity presentation earlier in life may later present with a combined type presentation, the type of ADHD found in 62% of adults (Wilens et al., 2009).

Several reasons for these changes in symptomology have been proposed; many patients are well-managed by adulthood, have developed better habits, or have learned new coping techniques as they aged (CHADD, 2020a). Reduction in some of these symptoms as one ages can often be confused with "growing out of it", but statistically, 50%-86% of ADHD cases diagnosed in childhood will continue into adulthood with some level of impairment (CHADD, 2020a). Interestingly, adult patients with less severe symptoms who no longer meet DSM-5-TR criteria for an ADHD diagnosis still have abnormally small caudate nuclei (CHADD, 2020a), suggesting that while the symptoms of ADHD have improved, the physical brain differences remain. Some adults may no longer meet the criteria for an ADHD diagnosis but still have impairment in social, academic, or occupational functioning, which is referred to as "ADHD in partial remission" (SAMHSA, 2016).

Strengths of ADHD

While the symptoms of ADHD may present challenges for patients in structured settings like classrooms and work environments, the neurodivergent nature of ADHD does not preclude

individuals from demonstrating positive behaviors and talents. The behavioral characteristics of ADHD should not be looked at in a binary form but instead be viewed as existing on a spectrum or continuum. Some adults with ADHD may exhibit particular strengths or inventive characteristics, contrasting with the daily challenges presented by their condition (Sedgewick, 2019). Some of these strengths are likely adaptations developed through various treatment modalities, enabling patients to succeed in their daily lives. 'Low-needs ADHD' is characterized by individuals who meet the full diagnostic criteria for ADHD yet maintain a relatively high level of functionality, even though the disorder continues to significantly impair certain areas of their daily lives (Lesch, 2018). Adults with ADHD have been found to exhibit divergent thinking, a cognitive process integral to developing novel ideas and inventive solutions to problems (White & Shah, 2006). Other potentially positive aspects of ADHD symptoms and adaptations could include creativity, hyperfocus, intuitive understanding, and empathy. Therefore, individualized care of patients with ADHD can allow for maximum outcomes, especially when both daily challenges and a strength-based approach are implemented.

Treatment:

-Comorbid Conditions

As previously mentioned, the prevalence of comorbidities (e.g., anxiety, mood disorders, learning challenges) in patients with ADHD is high, with more than 50% of patients having a comorbid disorder and one in seven patients having three or more (Mattingly et al., 2021). There can be a significant amount of symptoms that overlap with ADHD. In addition to identifying comorbidities, clinicians should also assess for and address non-compliance with treatment. Mental health professionals should be vigilant in their treatment approach in this population to ensure that coexisting conditions are identified during the evaluation and diagnosis process. Clinicians and other individuals involved in the care of patients with ADHD and comorbid conditions should ensure that both the ADHD and comorbid conditions are adequately treated.

-ADHD and Early Intervention

While substantial research has shown the efficacy of both pharmacological and nonpharmacological therapy for ADHD, little information exists regarding the appropriate or optimal sequence of treatment. Uncertainty remains on whether the clinician should initiate the patient on behavioral therapy, a medication regimen, or a combination of both. It

is important to remember these recommendations will not apply to every patient. As always, it is necessary to individualize care based on the patient's symptomology, past medical and social history, and comorbid conditions.

The CHADD organization recommends that behavioral treatment begin at diagnosis (CHADD, 2016). Research consistently shows that early intervention (both pharmacological and nonpharmacological) improves overall neuropsychological, academic, behavioral, and social functioning (Tarver et al., 2015). Children who are diagnosed and treated (pharmacologically and/or non-pharmacologically) before school age have less chance of expulsion from pre-kindergarten and/or kindergarten (McGoey et al., 2002). Further, children utilizing nonpharmacological interventions *early* were more likely to delay pharmacological treatment or avoid it altogether (DuPaul & Kern, 2011). Early nonpharmacologic intervention in high-risk children (such as children with a family history of ADHD) reduced the incidence of ADHD-related symptomology by school age (Rappaport et al., 1998). Despite the overwhelming evidence for treatment, especially early treatment, only 11% of adults with an ADHD diagnosis reported receiving treatment in the last 12 months, and 77% of children with a current ADHD diagnosis are treated (CDC, 2022c; Kessler et al., 2006). It is imperative that patients who are appropriately diagnosed with ADHD as well as other coexisting conditions are treated promptly, without delaying therapy.

In order to properly identify and foster early intervention, research has identified eight risk markers in infants that should be monitored by clinicians due to their association with the development of ADHD (Gurevitz et al., 2012). Identifying risk markers in infancy allows for earlier intervention and treatment if needed. These risk factors include mothers of advanced maternal age, mothers with lower education, a family history of ADHD, family history of social problems, decreased head circumference percentile, delay in motor development, delay in language development, and/or difficult temperament (Mattingly et al., 2021).

-Adults with ADHD

The impact of ADHD into adulthood can be significant for those afflicted with the disorder as it can affect an individual's ability to remember details, control behavior, listen to instructions, and get along with others at work, school, or home (AAFP, 2023b). The estimated prevalence of ADHD in adults over the last 15-30 years is around 4%-5% of the adult population (Kessler et al., 2006). Symptoms of adult ADHD may not present

as clearly as symptoms do in children with ADHD. Symptoms such as impulsiveness, agitation, and difficulty paying attention may still be present; however, other symptoms, such as hyperactivity, may decrease as the patient ages (AAFP, 2022a). Adults afflicted with ADHD may find themselves experiencing difficulty performing tasks such as maintaining a house, developing stable relationships, and sustaining positive work performance (AAFP, 2022a).

The appropriate diagnosis and treatment of adults with ADHD is important for reducing a number of quality of life and mortality risk factors, such as motor vehicle accidents, poor academic/work performance, increased mortality rates from unnatural causes, criminal behavior, and suicidal behavior (AAFP, 2022a). Adults presenting with ADHD symptoms can often require multiple visits to gather enough evidence for diagnosis (AAFP, 2023c).

Age Based Treatment Recommendations:

-Preschool-Aged Children – < 6 Years of Age

The AAP recommends avoiding a diagnosis in patients under 4 years of age. For parents of children, four to six years of age with ADHD, behavioral parent management training and classroom behavioral interventions are recommended as first-line therapy (Wolraich et al., 2019). If behavioral interventions have not provided significant improvement, or if the child is a more imminent harm to themselves, methylphenidate may be considered for patients over four years of age (Wolraich et al., 2019). The clinician needs to weigh the risks of starting methylphenidate against the harm of delaying diagnosis and treatment before the age of six years in areas in which evidence-based behavioral treatments are not available (Wolraich et al., 2019). Although amphetamines have FDA approval for use in preschool-aged children with ADHD and have been suggested to be as equally efficacious as methylphenidate, they may present with a greater number of adverse effects (Faraone, 2018). For example, in a comparative review of amphetamine and methylphenidate, amphetamine caused more insomnia and loss of appetite (Arnold L. E., 2000).

-Elementary School-Aged Children – Age 6 Years to 12th Birthday

The AAP recommends school-aged children be prescribed an FDA-approved medication along with parent training in behavior management and/or behavioral classroom

interventions (Wolraich et al., 2019). All school-aged children should receive educational interventions and school accommodations, such as environmental and behavioral support.

-Adolescents – Age 12 Years to 18th Birthday

The AAP recommends adolescents be prescribed an FDA-approved medication, with the adolescent's assent. Of note, the recommendation for assent should be considered with respect to the adolescent's developmental age and/or degree of any cognitive disability. The primary care clinician is encouraged to prescribe evidence-based training interventions and/or behavioral interventions (Wolraich et al., 2019). Adolescents should receive educational interventions and individualized instructional support. Psychosocial treatments that focus on life and organizational skills often help reduce symptom-based impairment.

-Transition of Adolescents to Adulthood

Transition from the teenage years into adulthood can be difficult for any adolescent, but for many individuals with ADHD, this period of life can be especially challenging. It can be a time of new found freedom with less restriction from parents/family/caregivers. It is also a time when most individuals are making decisions regarding future careers and educational goals. Statistically, two-thirds of teens with ADHD will continue to experience significantly impairing symptomology into adulthood, and those teens with ADHD are at higher risk of lower educational attainment, job difficulties and social problems. Teens transitioning to adulthood are also at higher risk for driving challenges, becoming parents at a younger age, and acquiring sexually transmitted infections. For these reasons, continued treatment during this delicate time is crucial. Clinicians and other individuals involved in the care should prepare for this transition well before the age of consent, counseling the patient and parents/family/caregivers on the importance of awareness and continued treatment. With proper treatment, many teens with ADHD go on to become successful, productive adults (CHADD, 2022a).

-Adults – 18 Years of Age and Older

The AAFP and the Canadian ADHD Resource Alliance (CADDRA) recommend pharmacological management of ADHD as first-line therapy (Canadian ADHD Resource Alliance, 2021; Post & Kurlansik, 2012). A retrospective study in 2009 compared

atomoxetine, long-acting stimulants, intermediate-acting stimulants, short-acting stimulants, bupropion, and alpha-2 adrenergic agonists. This study found that atomoxetine and long-acting stimulants were more likely to result in monotherapy unless the patient had a hyperactive component of ADHD (Pohl et al., 2009).

Although there is clear evidence supporting nonpharmacological treatments to address impairments associated with ADHD in adolescents and children, there remains very limited evidence supporting their use for adults with ADHD. More specifically, evidence for adults suggests mixed results without identified randomized trials. Even among those studies, adding stringent and highly structured cognitive behavioral therapy to pharmacological treatments produced varying results (De Crescenzo et al., 2017). In patients who have not met their goals with cognitive behavioral therapy (CBT) and other psychotherapies, which often do not address the core components of ADHD, applied skill-based accommodations such as organizational and planning tactics have been successful additions to medication.

A summary of the above treatment recommendations is listed below for quick reference:

Preschool-aged children (<6 years):*

A. Primary care clinicians (PCC) should prescribe evidence-based behavioral parent training in behavior management (BPMT) and/or behavioral classroom interventions.

B. In patients greater than four years of age, methylphenidate may be considered if there is no significant improvement with behavioral interventions and there is continued moderate to severe disturbance.

C. In areas in which evidence-based behavioral treatments are not available, the clinician needs to weigh the risk of starting medication before the age of six years against the harms of delaying treatment.

*Of note, the AAP advises to avoid a diagnosis of ADHD prior to the age of four years.

Elementary School-aged children (age 6 years to 12th birthday):

A. PCC should prescribe FDA-approved medications for ADHD along with BPMT and/or behavioral classroom interventions.

B. Educational interventions and instructional support are a necessary part of the treatment plan.

Adolescents (age 12 years to 18th birthday):

A. PCC should prescribe FDA-approved medications for ADHD.

B. PCC is encouraged to prescribe evidence-based training interventions and/or behavioral interventions.

C. Educational interventions and instructional support are a necessary part of the treatment plan.

Adults (age 18 years of age and older):

A. FDA-approved stimulants (for those determined to be candidates for use of prescription stimulants) or atomoxetine are considered first-line treatments for ADHD after coexisting mental health and substance use disorders are treated.

i. Consider long-acting stimulants for all patients who are candidates for stimulants due to lower misuse and diversion potential.

ii. Consider a nonstimulant (atomoxetine, bupropion, clonidine/guanfacine) with recent substance use or history of substance use disorder.

B. Without sufficient symptom improvement, consider adjusting the dose or trying alternative medications (TCAs, modafinil, etc.).

C. CBT has been shown to be helpful as adjunctive treatment with medication.

D. To monitor for misuse or diversion of stimulants, clinicians should consider using a patient and provider agreement and other risk reduction strategies at their discretion.

Detailed information on the recommended treatment options will be provided in the following sections: Nonpharmacologic Treatment Options and Pharmacological Treatment Options. Also, the information is summarized in APPENDIX 2.4: Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacological Treatment Recommendations.

Risks of Untreated ADHD:

Patients are often aware of the adverse effects of medications used to treat ADHD, but they are rarely familiar with the pitfalls of the disorder if it remains untreated. ADHD can have a

profound effect on a patient's ability to sustain attention and control impulsive behavior, and the consequences of failing to treat ADHD can go well beyond the inability to focus. The aforementioned evidence-based treatment options, both pharmacological and nonpharmacological, are advocated to foster optimal outcomes. When compared with treated patients, evidence suggests long-term outcomes related to academic achievement, social behavior, driving, and substance misuse are poorer in patients who are not treated (AAFP, 2022b). For this reason, patients should be informed of the long-term benefits that the treatment of ADHD can offer.

-Academic Challenges

Academic difficulties are among the most important adverse consequences of ADHD and are common reasons for caregivers to seek treatment for their child. Students with untreated ADHD have increased rates of grade retention (being held back) and lower rates of high school graduation and post-secondary education (AAFP, 2022b). It is well-established that treating ADHD can improve academic performance and test scores in the short term. However, in a large systematic review of 176 studies regarding the long-term (≥2 years) academic effects of ADHD, it was found that academic performance and information learned was improved in patients who received treatment for their symptoms versus those who did not (Arnold et al., 2015).

-Social Challenges

Individuals with ADHD often experience social difficulties, social rejection, and interpersonal relationship problems as a result of their inattention, impulsivity, and hyperactivity (CHADD, 2022b). Untreated ADHD is associated with a lower quality of life (Fleming & McMahon, 2012). Treatment of these symptoms is associated with positive outcomes. A systematic review of 127 studies found that patients with untreated ADHD experienced poorer long-term self-esteem and social function outcomes compared with patients without ADHD. When patients were treated for ADHD, a beneficial response was seen in the majority relating to self-esteem (89%) and social function (77%) outcomes (Harpin et al., 2013).

-Difficulty With Driving

Patients with ADHD have been shown to be at an increased risk for impairment in driving behaviors, traffic crashes and injuries and poorer long-term outcomes related to

driving (AAFP, 2022a; Biederman et al., 2012; Shaw et al., 2012). In a study comparing driving behaviors in young adults (aged 18-26 years) with ADHD, it was found that patients treated with lisdexamfetamine had significantly better scores on the Manchester Driving Behavior Questionnaire, which measures driving errors, lapses, and violations compared with untreated patients (Biederman et al., 2012). A systematic review examining the impact of ADHD on driving behaviors found that 100% of the studies reported driving outcome benefits in the treatment groups (Shaw et al., 2012). Also, a 2017 national cohort study of over 2 million patients found that use of a medication to treat ADHD was associated with a significant reduction in the risk of motor vehicle collisions in both male and female patients (Chang et al., 2017).

-Substance Use Disorder

A commonly expressed concern is that long-term use of stimulant medication may lead to the development of a SUD (Chang et al., 2014). Statistically, children with ADHD, whether treated or not, are at higher risk of developing a SUD (Wolraich et al., 2019). While a 2014 study showed that the treatment of ADHD can have a protective effect against future SUD, a more recent multimodal treatment study of ADHD found that the use of stimulant treatment for ADHD was not associated with an increased or decreased risk of substance use when adjusting for variables that drive increasing substance use over time (Chang et al., 2014; Molina et al., 2023). Additionally, patients with an active SUD can benefit from the treatment of ADHD. Even though they may not be candidates for stimulant therapy, there are additional appropriate pharmacological nonstimulant treatment options. A study reviewing psychosocial outcomes of 60 male patients with ADHD and SUD found that treatment of ADHD resulted in fewer substance use relapses, required less frequent compulsory care, and exhibited higher employment rates than the non-treated group (Bihlar Muld et al., 2015).

-Suicide

Patients with ADHD, regardless of other comorbidities, are at a greater risk of attempting and completing suicide (Shen et al., 2021). A meta-analysis examining the relationship between ADHD and suicide showed a significant association between ADHD and suicide attempts, ideation, plans, and completions (Septier et al., 2019). The effects of medication on suicide risk in patients with ADHD were studied, and the results indicated

lower odds of suicide attempts in those using stimulant medications for treatment (statistical significance was not obtained for nonstimulant medications) (Chang et al., 2020). Data shows that 30% of individuals who took their life had a visit with a healthcare provider within the last seven days, and over half of those individuals were seen within the last thirty days (Ahmedani et al., 2019). Given the timing of the attempt and statistics regarding recent medical treatment, visits with healthcare clinicians can provide an opportunity for potential intervention. The mental health professional shortage has not been positive for this population. In a cross-sectional study of U.S. youth aged five-19 years of age, the suicide rate increased as county levels of mental health professional shortages increased (Hoffmann et al., 2022). Through screening, early identification, intervention, and steady support, available healthcare professionals can significantly lower these devastating numbers (Kemp et al., 2021).

Prevention of suicide can begin with simply asking questions during a healthcare visit. In the past, it was believed that asking a high-risk patient about a suicide attempt could provoke suicidal ideation or attempts. Research has shown this idea to be a fallacy (Dazzi et al., 2014). Inquiring about self-harm actually reduces suicidal ideation and improves mental health treatment, yet most healthcare settings do not routinely screen high-risk patients (Dazzi et al., 2014; National Institute of Mental Health, 2022b). There are numerous resources available to assist healthcare clinicians and other individuals involved in the care of patients with ADHD in suicide prevention, and the Suicide and Crisis Lifeline is available to patients 24 hours a day and can be reached by dialing 988 anywhere in the nation.

In summary, data suggests that the evidence-informed treatments of ADHD as identified in this guide can improve academic outcomes and social behaviors and decrease the risks of driving impairment, substance misuse, and suicide. It is imperative that clinicians and other individuals involved in the care of patients with ADHD to counsel patients on these risks, especially where there is hesitancy to accept treatment.

Implications of Misdiagnosis and Inappropriate Off-Label Prescribing

While there are risks of untreated ADHD, there are also implications or risks when a thorough evaluation and diagnosis have not occurred leading to a misdiagnosis, and further, when treatments are utilized outside of their evidence base without an appropriate indication.

-Misdiagnosis

The consequences of misdiagnosing ADHD or any of its comorbid conditions, which may present similarly, can impose significant burdens on patients, families, and caregivers. This emphasizes the need for a complete and thorough evaluation. An incorrect diagnosis can lead to delayed or inappropriate treatment, both psychosocial and pharmacological, increase the risks of morbidity from untreated conditions, and result in significant opportunity costs in terms of time and financial resources for patients and their families. In the US alone, the medication costs linked to inappropriately diagnosed ADHD were estimated to range between $320 million and $500 million annually (Thomas et al., 2013).

The process of diagnosing a behavioral or developmental condition often carries more than just medical implications. It has the potential to alter how a child is viewed and treated by those around them, from family members to educational professionals. This change in perception, linked with the label of a diagnosis, can significantly influence a child's social interactions and personal development. Individuals diagnosed with ADHD frequently face lower expectations from parents and teachers and are commonly seen as lazier and less intelligent by their peers (Thomas et al., 2013).

Further compounding the issue is the potential erosion of a patient's trust in the healthcare system, along with their enthusiasm to seek future care, due to a diagnostic error (Balogh et al., 2015). The gravity of diagnostic errors is demonstrated in specific situations, such as when prescribing stimulants to individuals with undiagnosed bipolar disorder, which may lead to an escalation of manic episodes, as highlighted by research findings (Viktorin et al., 2016). Absence of a thorough biological history or physical examination may lead to misattribution of symptoms to ADHD, as seen in cases of thyroid disease. For instance, hyperthyroidism symptoms like anxiety, nervousness, irritability, and physical hyperactivity can mimic ADHD. Yet, the administration of dextroamphetamine and certain methylphenidate products is contraindicated in patients with hyperthyroidism, since sympathomimetic stimulation could trigger cardiac arrhythmias or other adverse effects (Lanett Company Inc., 2021; Takeda Pharmaceuticals America, Inc., 2023).

-Off-label Stimulant Use Without Evidence

Stimulants have a long history of being prescribed for a variety of conditions, including narcolepsy, appetite suppression, binge eating, depression, senile behavior, lethargy, and ADHD (Moore et al., 2023). However, the evolution of medical

understanding and treatment options has led to changes in the indications for these medications. With advances in medication classes, a deeper understanding of disorders, enhanced clinical research, stricter regulatory controls, public health initiatives, and the availability of behavioral therapies, the landscape of stimulant prescription has shifted.

Prescribing an FDA-approved drug in a manner not specified by the FDA's approved packaging label, commonly referred to as off-label use, is both legal and a frequent practice in medical care (FDA, 2018). This approach occupies a complex position within the healthcare landscape; when it is anchored in robust clinical evidence and expert consensus, it can significantly improve patient outcomes, particularly in scenarios where existing treatments may be inadequate. Such flexibility affords healthcare providers the ability to customize treatments to the unique needs of their patients, thereby contributing to innovations in medical practice and patient care.

However, such prescribing must be underpinned by careful clinical judgment and a comprehensive understanding of the medication's pharmacology, potential benefits, and risks. The off-label use of stimulants, for instance, is an example where the balance between potential benefit and harm must be carefully considered. While these medications may offer significant benefits when used appropriately, they also carry a risk for misuse, necessitating a cautious and informed approach. Providers should ensure that off-label prescriptions are based on sound scientific rationale and evidence and remain committed to monitoring for efficacy and adverse effects, adjusting treatment plans as necessary. This responsible approach safeguards patient health and upholds the integrity of off-label prescribing as a component of medical practice.

The extent of off-label stimulant use is challenging to quantify. Research indicates a 250% increase in stimulant prescriptions from 2006 to 2016 in the United States, with minimal increases in ADHD diagnoses. The study also noted an increase in new stimulant prescriptions among populations at greater risk for adverse effects, which include older adults, individuals with obesity, and geriatric patients with cardiovascular risk factors, particularly in the years from 2010 to 2020 (Brumbaugh et al., 2022). Another study of ADHD medication prescribing trends for children three to 18 years old found 91.4% of prescriptions for those aged three to five were off-label, decreasing to 21% after age five. Concerns from the authors include the high frequency of alpha agonist prescriptions, the prescribing of large doses, and the use of untested formulations such as clonidine patches in very young children (Panther et al., 2017).

Individuals with ADHD may have comorbid disorders, potentially leading to off-label prescriptions of stimulants for conditions that extend beyond the typical scope of ADHD treatment. Off-label use has been explored in conditions ranging from depression to Alzheimer's-related apathy and autism spectrum disorder, with mixed efficacy results. One study reported that off-label prescribing of stimulants accounts for 57% of the stimulant prescriptions given to patients over 50, and just 37.5% of these off-label prescriptions had a concurrent psychiatric diagnosis, which raises concerns about the appropriateness and potential overuse of stimulants in older populations (Rizvi et al., 2023).

The use of stimulants in the treatment of behavioral and mental health disorders beyond ADHD necessitates careful consideration of the evidence base. In a systematic review and meta-analysis, stimulants had a moderate-to-large effect on oppositional behavior, conduct problems, and aggression in youth with ADHD, whether or not oppositional defiant disorder or conduct disorder was present (Pringsheim et al., 2015). In a small retrospective review, no additional benefit was found from stimulant medication in children under 7 years with disruptive behavior disorders compared to behavioral intervention alone, with stimulants marginally associated with less improvement in conduct disorder (Parsley et al., 2020). This suggests caution against expecting improved outcomes from stimulants for disruptive behaviors and mood issues, emphasizing the need for further research.

For depressive disorders, stimulants can rapidly alleviate symptoms, but evidence supporting their efficacy from randomized controlled trials is limited. Long-term effectiveness in major and bipolar depression requires investigation (Malhi et al., 2016). The evidence for stimulant use in bipolar disorder is inconclusive, with few trials and limitations such as small sample sizes and short follow-up periods. Some international guidelines endorse stimulants as adjunctive treatment for bipolar depression, yet safety and efficacy remain poorly researched (Perugi et al., 2017).

In pure oppositional defiant disorder without ADHD, a clinical trial showed symptom reduction across all stimulant dosages, but without statistical significance, possibly due to the small sample size. This warrants cautious consideration of stimulants and calls for larger studies to confirm efficacy (Spencer et al., 2006).

The relationship between stimulants and anxiety is complex. Anxiety, commonly reported as a side effect, may actually decrease with psychostimulant treatment, as indicated by a meta-analysis that found a lower risk of anxiety compared to placebo (Coughlin et al., 2015). This paradoxical effect suggests that stimulants could improve anxiety symptoms in some individuals, possibly due to better ADHD symptom control, yet an accurate diagnosis is critical.

Finally, the predominant inclusion of ADHD patients in stimulant trials limits the understanding of the medications' direct impact on other behavioral disorders. This inclusion criteria coupled with small sample sizes and short follow-up periods demonstrates the need for more research into the potential indications of stimulants. Clinicians must acknowledge evidence limitations and advocate for more comprehensive research to ascertain the efficacy and safety of stimulants in non-ADHD populations.

The ethical considerations of off-label stimulant prescriptions, particularly for cognitive enhancement in healthy individuals, warrant careful examination. Societal pressures to perform at peak levels academically or professionally may influence individuals to seek such enhancements, initiating ethical debates concerning fairness and informed consent. Healthcare professionals must consider these factors, ensuring that any use of stimulants is judicious and patient-centered, with a clear medical justification overriding any external pressures to conform to performance-enhancing norms (Larriviere et al., 2009; Farah et al., 2004).

Overall, it is crucial that a patient undergo a comprehensive evaluation and diagnosis for ADHD to ensure an accurate diagnosis. The patient and family's preferences for treatment should be considered, and **evidenced-based** strategies should be incorporated into the agreed upon treatment plan, whether pharmacologic, nonpharmacologic, or a combination of both throughout a patient's lifespan, even as symptoms may change.

Nonpharmacologic Treatment Options

Nonpharmacologic options are those interventions that do not include use of pharmaceutical agents. Most nonpharmacologic treatments fall under psychotherapy, a term used when trained mental health professionals assist in changing behaviors to reduce symptoms and/or impairments associated with ADHD and other coexisting conditions. As mentioned,

nonpharmacologic treatment is considered first-line treatment for ADHD in children under six years of age. It is to be utilized in school-aged children and adolescents as an adjuvant treatment to pharmacological treatment agents. In addition, adults are often treated with forms of psychotherapy for ADHD symptom control or improving the level of associated impairment.

Various forms of nonpharmacological treatment options are listed and described below. This is not an exhaustive list of non-pharmacological options, and it portrays the evidence available at the time of this guide's development. With the abundance of terminology used to describe this area of therapeutics, this guideline is intended to help build a shared vocabulary to make treatment modalities more approachable to the general population. For instance, psychotherapy is a term commonly used to define a variety of treatment techniques used by trained mental health clinicians to help a patient identify and change troubling emotions, thoughts, and behaviors (NIMH, 2022a). Numerous forms of psychotherapy are practiced, each with their own goal of therapy. Often, differing terms for psychotherapy are used broadly and interchangeably, leading to confusion over the distinct treatments. Therefore, this reference can be utilized to aid in distinguishing various nonpharmacological treatment modalities for ADHD to ensure appropriate treatment recommendations, referrals, and follow-up occur.

Preschool-aged children (age < 6 years):

First-line

- Behavioral Parent Management Training
- Behavioral Classroom Management
- Combined Behavioral Management Interventions

Second-line

- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Extensive Practice and Feedback

Third-line

- Not applicable (N/A)

Limited Evidence

- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Limited Practice and Feedback

Lacking Evidence

- Social Skills Training

Elementary School-aged children (age 6 to 12th birthday):

First-line

- Behavioral Parent Management Training
- Behavioral Classroom Management
- Behavioral Peer Intervention
- Organizational Training
- Combined Behavioral Management Interventions

Second-line

- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Extensive Practice and Feedback

Third-line

- N/A

Limited Evidence

- Cognitive Behavioral Training
- Modified Behavioral Parent Management Training
- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Limited Practice and Feedback

Lacking Evidence

- Social Skills Training

Adolescents (age 12 to 18th birthday):

First-line

- Organizational Training

Second-line

- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Extensive Practice and Feedback

Third-line

- Behavioral Parent Management Training

Limited Evidence

- Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Limited Practice and Feedback

Lacking Evidence

- N/A

Adults (18 years of age and older):

First-line

- N/A

Second-line

- Cognitive Behavioral Therapy (CBT)

Third-line

- Psychological Counseling/Emotional Therapy
- Use of technological aids

Limited Evidence

- Organizational Training

Lacking Evidence

- N/A

Please see Appendix 2.2: Nonpharmacological Treatments for a summary of the above information.

Behavioral Classroom Management

Description: Based on principles of reinforcement and punishment, behavioral classroom management is an intervention used to educate teachers on strategies designed to improve in-classroom, off-task and disruptive behaviors. The intervention involves teachers learning new skills designed to improve compliance and teacher-child relationships while reducing problematic disruptive behaviors. Skills taught include, but are not limited to, a teacher's strategic use of attention to preventatively bolster positive behavior, use of transition warnings, providing instructions in specific ways to bolster compliance, contingency management, student monitoring, and management of defiance and outbursts.

Age-Based Recommendations:

- Preschool-Aged Children: First-line
- Elementary School-Aged Children: First-line
- Adolescents: N/A
- Adults: N/A

Use in Practice: Behavioral management is one of the most common and efficacious nonpharmacological methods used in the treatment of ADHD-related symptomology within the classroom. The goal is to keep students with ADHD in the classroom, among peers, with minimal distractions and disruptions. Therefore, it is important for teachers to have skills to assist with the management of ADHD symptoms in a manner that is conducive for the classroom. Many studies have concluded that behavioral classroom management is effective for preschool- and elementary-aged children. In a controlled trial in 2021, behavioral classroom management was found to be highly effective in reducing problem behaviors compared with controlled conditions in younger and older children. Decreases in inattentive behaviors, hyperactive and impulsive symptoms, and oppositional defiant behaviors were seen (Staff et al., 2021). In a meta-analysis, classroom interventions reduced off-task and disruptive behavior in children; specifically, consequence-based interventions were more effective than antecedent-based, self-regulation, and combined interventions. Consequence-based interventions include preventative reinforcement of on-task and positive behaviors, reprimands, prizes, or privileges (Bear & Nietzel, 1991; Pfiffner & Haack, 2014). It has been shown that school-age children are very goal-oriented and respond to classroom interventions well when appropriately motivated (Gaastra et al., 2016).

Examples of behavioral classroom management components are listed below:

-Antecedent Techniques

This technique involves the teacher or adult attempting to manipulate the student's antecedents, or stimulus conditions, that favor desired behaviors. It is thought to strengthen the relationship between the stimulus condition and response. For example, if the child is to remain seated during quiet or nap time, providing clear instructions for that expectation, in addition to manipulating the environment to reflect quiet time (e.g., low lights, quiet, lullaby music), will increase the chance of compliance (Staff et al., 2021).

-Consequent Techniques

This technique manipulates the consequences of an action, instead of the environment. For example, if a student is engaging in unacceptable behavior, the teacher will ignore or penalize the behavior. If the behavior is positive, the student is praised or a reward is given. This technique builds off of the Principles of Behavior Theory, which states the frequency of behavior will increase when followed by a perceived positive consequence and decrease when followed by a perceived negative consequence (Staff et al., 2021).

-Common Strategies for Behavioral Classroom Management

There are various strategies utilized in behavioral management of children with ADHD. These include maintaining a routine, setting rules with the students versus posting them, creating stimulating lessons that are more likely to engage students, using positive language, developing healthy relations with students, and adjusting scoring methods (Positive Action Staff, 2021).

Behavioral Parent Management Training

Description: Based on principles of reinforcement and punishment (BPMT) is an intervention used to address child and adolescent off-task and disruptive behaviors. In BPMT, families work with a trained clinician to learn new skills designed to improve compliance and parent/family/caregiver-child relationships while reducing problematic disruptive behaviors. Skills taught within the training include, but are not limited to, an adult's strategic use of attention

to bolster positive behavior, providing instructions in specific ways to bolster compliance, contingency management, and managing defiance and outbursts.

Age-based Recommendations:

- Preschool-Aged Children: First-line
- Elementary School-Aged Children: First-line
- Adolescents: Third-line
- Adults: N/A

Use in Practice: Behavioral therapy for treatment of ADHD refers to a broad range of interventions aiming to change behaviors through environmental (physical or social) modifications. BPMT, also referred to as "parent management training" or "behavioral management parent training", is one of the most well-studied interventions for child mental health disorders. ADHD is an impairment with performance, not necessarily ability; patients do not usually struggle with recognizing inappropriate behavior and are quick to validate appropriate behavior. The challenge lies in the execution of said appropriate behavior due to inattention, hyperactivity, or impulsivity. For this reason, patients benefit from BPMT, as this training provides education to parents/family/caregivers and helps address the difficulties a child or adolescent with ADHD experiences and how their reaction to such experiences can have long-lasting effects. The program is intended to empower parents/family/caregivers to become a proactive, informed decision maker throughout a child's development to maximize function. Through this type of training, parents/family/caregivers are provided with techniques to enhance their child's ability to self-regulate their conduct to improve overall behavior, reduce unwanted behaviors, and provide appropriate consequences when a child fails to meet their goals (Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, 2011). BPMT can address both core behavioral symptoms and functional impairments. BPMT with a mental health professional can be conducted in various settings via multiple means of communication (in-person and telehealth). Those who need more individualized sessions or have children with more severe symptoms can meet individually. There are also group sessions that can provide additional exposure to training in different behavioral situations, offering the support of other parents/family/caregivers with similar experiences. Likewise, there are options for parent training that include the child and improving the quality of the parent/family/caregivers-child relationship. Ultimately, when deciding which type of BPMT session to utilize, parent/family/caregiver availability should be considered, as their participation and engagement is

necessary for effectiveness. However, availability of services and health insurance coverage may restrict options. This type of parental education training prepares parents/families/caregivers to make well-educated decisions for the child and family now, and in the future, improving long-term outcomes (Barkley, 2015).

BPMT is one of the most studied psychosocial interventions and one of the top three most studied evidence-based treatments for ADHD (CHADD, 2017c). BPMT has been tested worldwide in a variety of ethnicities and cultures and consistently shows improved outcomes in preschool- and elementary-aged children (Charach et al., 2013; Feldman et al. 2018; Lai et al., 2018; Yang et al., 2021). Accordingly, BPMT is considered first-line therapy for ADHD in preschool- and elementary-aged patients. Listed below are **some** commonly used therapies and programs utilizing the BPMT approach in the management of ADHD.

-Parent Child Interaction Therapy (PCIT)

PCIT is designed for parents/families/caregivers of young children experiencing social, behavioral, and/or emotional difficulties. PCIT is evidence-based and considered a gold standard treatment option (Parent Child Interaction Therapy (PCIT), 2021). Integrating components of social learning, attachment, developmental theories, and behavioral principles, parents/families/caregivers learn how to adopt an authoritative parenting style in two phases, the Child-Directed Interaction phase, and the Parent-Directed Interaction phase (PCIT, 2021). The Child-Directed Interaction phase focuses on enhancing the parent-child relationship by learning child-centered interaction skills, and the Child-Directed Interaction phase helps build behavioral management skills (PCIT, 2021).

-Barkley's Defiant Children: Manual for Assessment and Parent Training

Barkley's Defiant Children training is a 10-step program taught by trained professionals in individual or group settings. In this training model, parents/families/caregivers learn why certain behaviors occur and how to anticipate them. Praising appropriate behavior, increasing compliant and independent play, implementing a point system and daily report card, and implementing transition plans that address poor behavior are key factors in this model. Peer-reviewed research of this parent training has shown improvements in parental functioning and teacher ratings of attention, aggression, self-control, social skills, and classroom behavior (Anastopoulos et al., 1993; Barkley et al., 2000).

-Helping the Noncompliant Child (HNC)

HNC targets parents/families/caregivers of children aged three to eight years of age who are noncompliant and have related disruptive behaviors. This program aims to improve parent-child interactions (what they believe to be a significant part in the development and maintenance of conduct) and teach parents/families/caregivers how to obtain compliance in their child. The program typically comprises individualized family sessions and involves a series of parenting skills to increase positive attention for appropriate child behavior, decrease attention for mildly inappropriate behavior, and appropriately correct noncompliance. Studies report improvement in home behavior, disruptive behavior, and parental anxiety (Jones et al., 2014; McMahon et al., 2010; Rosenblat et al., 2017; Wells & Egan, 1988).

-Triple-P (Positive Parent Program)

The Triple-P approach is intended for parents/families/caregivers of children from birth to 16 years of age. Rather than a single program, it is a suite of interventions with increasing intensity that offer parenting tips and strategies. Each level is provided online, making it a flexible program for busy families. The program aims to give just enough guidance to encourage self-sufficiency in both individual and group settings.

-New Forest Parent Program (NFPP)

NFPP is designed for children with or at risk of ADHD. Parents/families/caregivers are taught skills to help their child self-regulate and reduce inattentiveness, impulsiveness, and other difficult behaviors. This program is home-based and parent-led, making it a viable choice for busy family schedules.

-The Incredible Years

This online platform is used to train parents/families/caregivers, teachers, and children worldwide through self-study and workshops. The goal of the program is to prevent young children's behavioral problems and promote their social, emotional, and

academic competence. It is designed to work with varying cultures and socioeconomic groups.

Behavioral Peer Intervention

Description: Behavioral peer interventions are strategies designed to encourage appropriate peer interactions. In the intervention, one or more peers are guided by an adult's direct assistance, external cues, and reinforcement to remain on-task and demonstrate positive behavior (e.g., positive social interactions, positive academic performance).

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: First-line
- Adolescents: N/A
- Adults: N/A

Use in Practice: This nonpharmacological method is defined in a comprehensive meta-analysis on psychosocial interventions as "utilizing social skills to encourage appropriate peer interactions" (Fabiano et al., 2021). This intervention trains one or more peers to provide support, assistance, and social cues to students with ADHD in an attempt to keep the child on task, increase academic achievement, and strengthen social skills. The student-peer interactions are often reinforced by the teacher or other adults. This method distinctly differs from social skills training as this is a behavioral intervention rather than a training intervention.

Evidence has demonstrated that peer attention is a functional reinforcer of appropriate and inappropriate behaviors. Functional analysis indicates off-task behaviors sensitive to attention from peers and intervention improves off-task behaviors (Grauvogel-MacAleese & Wallace, 2010). A systematic review and meta-analysis of school-aged children found significant improvements in social behaviors when peer intervention was implemented. Children in the study benefited from the intervention even when they were not taking pharmacological agents to treat ADHD (Cordier et al., 2018).

Cognitive Behavioral Therapy

Description: CBT is an intervention that involves exploring the interconnectivity between a child, adolescent, or adult's thoughts, feelings, and behaviors. Through evaluation, individuals are taught methods of assessing their thoughts (e.g., "being their own detective"), analyzing the thoughts, and modifying any cognitive biases that may lead to maladaptive thoughts. Based on

this method, individuals learn to change their corresponding behaviors that occur in response to triggering events in efforts to foster more positive outcomes.

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: N/A
- Adolescents: N/A
- Adults: Second-line

Use in Practice: A well-established, nonpharmacologic option for the treatment of ADHD is CBT. This method utilizes a therapist who works with an adult student or employee on various strategies to help with difficult situations that may arise in school or work. Also, it can change certain patterns or ways of thinking that can help adults with ADHD manage these situations. It is focused on helping individuals deal with stress and challenges and can be beneficial for adults (Harvard Medical School, 2022). In a systematic review, CBT appeared to have the most benefit compared with other nonpharmacological methods in adults with ADHD (Nimmo-Smith et al., 2020).

Cognitive Behavioral Training

Description: Cognitive behavioral training is a training method (i.e., not a therapy) designed to improve working memory and other brain-related components of executive functioning (i.e., organization, planning). Through repetition of tasks via targeted activities, individuals learn to "strengthen" different brain structures and functions. Strategies are often computerized.

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: Limited evidence
- Adolescents: N/A
- Adults: N/A

Use in Practice: Cognitive behavioral training is a form of psychological treatment where the patient works with a mental health specialist in a structured way for a preset number of sessions (Ditzell & Raypole, 2021). The goal of therapy is to help the patient recognize and revise cognitive habits that affect the patient's productivity and emotional mindset (Ditzell & Raypole,

2021). Cognitive behavioral training is widely used in the treatment of other conditions, such as anxiety and depression, but in the context of ADHD treatment, there is some conflicting evidence that it may or may not have a benefit in therapy.

Some earlier studies were conducted with computer tasks that involved memory, but critics argued these tasks were not very applicable to daily living. Training that involved stimuli and clinician interactions were shown to have the most effect on daily functions (Tamm et al., 2013). A meta-analysis shows that cognitive behavioral training may improve working-memory performance, but it has limited effects on ADHD symptoms (Cortese et al., 2015). Thus, this method is still undergoing research and considered experimental.

In the school setting, cognitive behavioral training focuses on self-control and comprehension skills. Training sets can include working on self-instruction and problem-solving skills. This method has shown to be of little benefit, with only modest clinical importance (Bear & Nietzel, 1991; DuPaul & Eckert, 1994; Dush et al., 1989). Another meta-analysis showed no clinically meaningful difference in patients using cognitive behavioral training, and it is often replaced in the school setting by self-regulation strategies (Fabiano et al., 2021).

Combined Behavioral Management Interventions

Description: Combined behavior management intervention refers to the combination of nonpharmacological behavioral approaches involving both home (i.e., behavioral parent management training) and school (i.e., behavior classroom management) techniques. Implementation across settings fosters consistency for children and adolescents.

Age-based Recommendations:

- Preschool-Aged Children: First-line
- Elementary School-Aged Children: First-line
- Adolescents: N/A
- Adults: N/A

Use in Practice: Nonpharmacological methods are often combined for a multimodal approach. Combined behavioral therapy can involve both home and school interventions. When comparing multicomponent behavioral interventions with standard parent/family/caregiver-focused treatments in elementary school-aged children, greater improvements were seen with the multicomponent versus standard treatments. Teacher ratings for inattention, organizational skills, social skills, and global functioning and parent/family/caregiver ratings of organizational skills were improved

(Pfiffner & Haack, 2014). Due to the improved outcomes, it was highly recommended to use combined therapy in the treatment of ADHD. The largest volume of studies in the comprehensive meta-analysis included the behavioral intervention studies, and when these interventions were combined with contingency management in schools, evidence of improvement was strong (Fabiano et al., 2021).

Combined Training Interventions

Description: Combined Training Intervention programs use two or more nonpharmacologic treatments in the management of ADHD symptoms. For example, some programs combine parent behavior training with CBT or behavioral parent training with behavioral modification training. These interventions can be further broken down into two groups, outlined below, based on the level of practice and feedback the program utilizes.

-Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Extensive Practice and Feedback

Age-based Recommendations:

- Preschool-Aged Children: Second-line
- Elementary School-Aged Children: Second-line
- Adolescents: Second-line
- Adults: N/A

Use in Practice: The Challenging Horizon's Program (CHP) focuses on academic and social functioning through participation in group and individual interventions. Interventions involve extensive practice of new skills, followed by feedback. Students meet with staff several times during the school week to learn new skills for organization, study methods, and social behaviors. The student then implements these skills throughout the week before reconvening to discuss the successes and barriers. These skills are practiced over several months to years; to improve the family dynamic, parenting groups are included in the sessions. Students who received CHP had symptom improvement and less impairment from ADHD than students receiving standard community resources (Evans et al., 2011). Research assessing the effectiveness of the CHP and other similar programs have shown benefits in children and adolescents, which is the primary reason for the classification as second-line therapy.

-Combined Training Interventions Involving the Application of Relevant Skills to Daily Functioning with Limited Practice and Feedback

Age-based Recommendations:

- Preschool-Aged Children: Limited evidence
- Elementary School-Aged Children: Limited evidence
- Adolescents: Limited evidence
- Adults: N/A

Use in Practice: This intervention, while similar to the CHP, involves much less practice and feedback. The program is simply teaching the skills, rather than addressing their success in daily life through feedback. The analysis examining its results only included high school students and had mixed results. One study reported no significant benefits, while others reported improvements in symptom ratings; there were mixed findings related to global indices of functioning (Evans et al., 2018a).

Modified BPMT

Description: Modified BPMT adapts traditional BPMT for specialized populations, including single mothers, specific cultures, and for comorbid challenges (e.g., both ADHD and anxiety).

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: Limited evidence
- Adolescents: N/A
- Adults: N/A

Use in Practice: Modified BPMT programs are adjusted for single mothers or mothers with other risk factors, such as having a diagnosis of ADHD or depression. Literature has shown parental stress and/or lack of stability greatly affects the outcomes of BPMT. In particular, single mothers are at risk for poorer outcomes during and following BPMT. A study compared different training courses and found that more enhanced programs increased the engagement of single mothers compared with traditional programs. However, the enhanced training program was not found to be significantly better and the results were inconclusive whether the treatment effects were maintained (Chacko et al., 2009). Thus, modified BPMT programs are at the experimental level, and more research is needed to secure their place in therapy. On an important note, these

programs are intended to supplement traditional behavioral approaches, not replace them.

An example of a modified BPMT program is outlined below:

-Single Mother Training/Mothers with Depression/Mothers with ADHD

Specialized programs include child participation and are similar to traditional BPMT programs in content, with some enhancements. Altered intake procedures address mothers' expectations for the program and any negative feelings toward the chances of a successful outcome. With solutions developed during intake, practical barriers, such as childcare and transportation, can be resolved to allow for participation in the program. Subsections for coping-modeling, problem-solving, and psychosocial functioning can also be addressed in group settings where participation between mothers to increase support and attendance is encouraged. There are a few variations of this training, such as "Mothers with Depression" and "Mothers with ADHD". The incidence of depression in mothers whose children have ADHD is significantly higher than the general population, so there is a need for these programs (McCormick, 1995).

Organizational Skills Training

Description: Organizational skills training focuses on teaching children and adolescents to better organize home and school materials. Skills taught within the training include, but are not limited to, time management, organization/folder systems, list creation, and self-reinforcement.

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: First-line
- Adolescents: First-line
- Adults: Limited evidence

Use in Practice: Children and adolescents with ADHD often struggle with organizational tasks in school and social activities. Forgetting homework assignments, misplacing items, and struggling with time management are common examples of organizational tasks with which those with ADHD tend to have difficulties. Medications have not been shown to stabilize or improve this skill area, leaving opportunity for non-pharmacological options. With the implementation of formal programs, patients can be trained to focus on school-related tasks and learn time-management

skills. Common themes in this intervention include keeping a calendar of upcoming due dates and self-monitoring progress using checklists. Parents/families/caregivers and teachers are encouraged to practice positive reinforcement when improvements are noted.

Organizational difficulties are most prominent in the school setting among children with ADHD (Langberg et al., 2008). Organizational training has been studied in children, adolescents, and adults and is associated with significant improvements in the organization of materials, homework management, time management, and planning. The benefits are most pronounced in school-aged children, and some research has even shown reduction in ADHD symptoms and gains in academic functioning (Langberg et al., 2008). There are many programs participating in organizational training.

Examples of common organizational suggestions are listed below:

-Organizational Training Suggestions

Some common suggestions to help students get organized are setting up a specific area for schoolwork free of distractions and providing school supplies to stock the study area. Working with the teacher to communicate assignments in a notebook and gentle reminders before assignments are due are also helpful. Scheduling regular times for locker and desk clean out and assisting with organization using color coded folders for specific subjects aids in assignment management. It is also advantageous to set up a reward system for improvements along the way (Low & Lockhart, 2021).

-Homework, Organization, and Planning Skills (HOPS)

Another resource for organizational development designed for students and parents/families/caregivers is an 11-week program called HOPS that has been shown to be effective through teacher reporting of major improvements in behavior and grades (Langberg et al., 2011). This nonpharmacologic approach is an established option with significant benefit to school-age children and adolescents with ADHD.

Psychological Counseling/Emotional Therapy

Description: Psychological counseling and emotional therapy are interventional strategies designed to assist individuals in processing and either overcoming or adapting to emotional and behavioral struggles that result from individual, social, familial, romantic, and/or occupational challenges.

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: N/A
- Adolescents: N/A
- Adults: Third-line

Use in Practice: Many adults with ADHD struggle emotionally, which can affect relationships with peers. Some experience difficulties in situations such as having a boss demanding more work at the last minute or waiting in line for something and becoming impatient (Barkley & Murphy, 2006). These situations have the potential to hinder an adult's environment and negatively affect the relationships around them. Working with a psychiatrist or another trained professional to handle these unpleasant emotions can have a great impact on quality of life in someone with ADHD. This strategy can also guide adults with ADHD with concomitant anxiety or depression since emotional therapy has been shown to be beneficial in these disease states (Harvard Medical School, 2022). There are various forms of psychological counseling, including vocational counseling. It is designed to develop the skills and abilities necessary to perform a specific profession in a productive way. Vocational counseling is aimed at identifying one's strengths and limitations and then matching patients to jobs that highlight their strengths (Barkley & Murphy, 2006).

Social Skills Training

Description: Social skills training (SST) is a series of strategies designed to encourage appropriate social responding among children and adolescents. Skills include, but are not limited to, making appropriate eye contact, initiating conversations, discussing shared interests, employing other conversational skills, turn taking, and respecting personal space.

Age-based Recommendations:

- Preschool-Aged Children: Lacking evidence
- Elementary School-Aged Children: Lacking evidence
- Adolescents: N/A
- Adults: N/A

Use in Practice: Many children with ADHD experience interpersonal challenges. As mentioned before, SST aims to develop appropriate social behaviors in children (Fabiano et al., 2021).

Training follows the notion that teaching a child basic social skills will prepare a solid foundation when adding pharmacotherapy to their treatment plan. Pharmacological treatment options primarily manage hyperactive or inattentive behaviors and have less effect on social factors. SST involves cognitive training, such as teaching the child how to better interpret and understand the emotions of others. These clinician-conducted sessions can be individual or group settings. Lessons may include basic skill sets, such as learning to carry on a polite conversation, or more complex skill development, like dealing with difficult social interactions (Barkley et al., 2000).

The efficacy of this treatment has been challenged. One critique of this approach refers to it as a "train and hope" strategy (DuPaul & Eckert, 1994). Others argue these skills would have no general effect outside of the treatment group setting, and in another study, they were found to be ineffective (Abikoff et al., 2004; Evans et al., 2018a). There is little evidence to support the efficacy of SST in the management of ADHD, but it does show promise in the management of other disease states like anxiety, autism, and aggression disorders. A recent meta-analysis pointed out the lack of data availability in the context of treatment of ADHD, which was a limitation to the evidence (Fabiano et al., 2021). Overall, more analysis is needed to determine its place in therapy.

Use of Technological Aids

Description: Technological aids are tools (usually electronic) that assist patients with ADHD in performing tasks or developing skills. Common aids include electronic timers and alerts on phones or computers for keeping track of time and applications and personal digital assistants (PDAs) that assist with schedules and academic applications, among others.

Age-based Recommendations:

- Preschool-Aged Children: N/A
- Elementary School-Aged Children: N/A
- Adolescents: N/A
- Adults: Third-line

Use in Practice: Patients with ADHD can benefit from technological advancements to assist with symptom management. A variety of applications and tools help patients with the impairments of daily living associated with ADHD. There are tools that help with time management (planners, PDA), writing skills (spell-check and grammar-check), social interaction (electronic tablets and cell phones), and financial management (tax websites, budget planners) (Barkley & Murphy, 2006). Implementing some of these technological aids may benefit adult patients with day-to-day

tasks.

Therapeutic Monitoring and Follow-up of Nonpharmacological Interventions

In addition to medications (see Pharmacological Treatment Options), psychosocial interventions remain a cornerstone of ADHD intervention, especially for children and adolescents. More specifically, major guidelines recommend evidence-based psychotherapy, either as sole or adjunctive treatment, if the patient is under 12 years of age. If the patient is 12 years of age or older, psychotherapy should be strongly considered as adjunctive therapy. Despite these recommendations, implementation of psychotherapy remains low, with some sources suggesting that approximately 50% of children with ADHD seen in practice settings obtain care that matches the treatment recommendations from the AACAP (Hodgkins et al., 2011b). A Vital Signs report showed only 50% of children (approximately 60% of children in the 2-5 years of age group) that were indicated for psychotherapy actually received the services (CDC, 2018). As a result, the CDC issued a report in 2016 calling for more utilization of BPMT (Knopf, 2016). Such trends have persisted over time. In 2019, it was reported that 45% of children evaluated for ADHD did not receive behavioral therapy either during the 120 days prior to or the 300 days following a newly started medication (U.S. Department of Health and Human Services [HHS], 2019). An important component of these evidence-based recommendations for nonpharmacological treatment is monitoring and follow-up. Patients who begin to utilize a nonpharmacological treatment require appropriate monitoring to oversee and sustain both behavioral and emotional gains. Nevertheless, diligent follow-up and monitoring of this population also remains relatively low. Although patient-specific reasons for lack of follow-up can vary (e.g., time considerations, financial considerations, treatment outcome), below are some recommendations and considerations for the clinician's comprehensive monitoring plan specifically relating to any nonpharmacological interventions following the initial diagnosis and start of treatment.

The timing and frequency of visits of nonpharmacological treatment should be considered according to patient-specific factors. Following an initial visit with the mental health clinician providing the recommended psychosocial intervention, new patients should have a follow-up visit within 30 days, and it should preferably be scheduled before the patient leaves the office. For more intensive treatment of symptoms and/or to align with treatment-specific recommendations, more frequent visits are recommended. For example, BPMT can sometimes involve initial behavioral escalation of a child's disruptive behaviors before seeing improvement. Due to this possibility, frequent, ongoing appointments with the clinician (e.g., weekly or biweekly) can allow for ongoing problem-solving and alleviation of the potential symptom escalation. In this case, waiting longer

periods between visits may be detrimental to patient outcomes and function, which could be perceived as a treatment failure leading to premature termination of services.

To foster attendance and participation, a thorough discussion between the clinician and patient (or family) regarding treatment strategies, goals, and realistic expectations for outcomes is essential. Ensuring patients and families understand the treatment strategies has been suggested to be a predictive factor of positive outcomes. A patient who does not understand how a specific strategy will address their unique issues may not benefit as greatly as a patient who has a better grasp of their treatment goals and expected benefits. Additionally, setting patient-specific goals not only helps build clinician-patient rapport, but it also improves patient confidence and self-worth to foster motivation for treatment. With regard to treatment expectations, clinicians should clearly indicate that the general goal of treatment is to minimize the functional impact of ADHD symptoms and to maximize a person's ability to compensate or cope with any remaining difficulties (AAFP, 2023a). Patients and their family should be educated that not all symptoms may be fully alleviated with psychosocial intervention with or without medications. For example, the clinician cannot "fix" a patient's memory, but they can help implement strategies to reduce memory-related impairments. Further, although some symptoms may improve over time during and following psychotherapy, some level of impairment may persist (French, 2017).

To maximize outcomes, clinicians are recommended to track symptomology, impairment, and improvement as the patient proceeds through therapy. Monitoring can occur through direct questioning and questionnaires. While clinicians can directly ask how a patient is feeling or performing, it is suggested that they focus on providing concrete and symptom-specific questions rather than merely asking "How do you feel?". Literature has highlighted many issues with direct questioning (e.g., positive expectancy bias in which they may be trying to appease the clinician). Rather, asking targeted questions about duration, frequency, and intensity of symptoms can allow for gathering of specific information that can be compared with prior reports (e.g., ten 60-minute tantrums per day declined to occasional daily tantrums lasting 5 minutes). In addition to direct questioning, clinicians can use various assessment tools, even those not directly based on the DSM-5-TR, as they can provide valuable insights for symptom tracking and monitoring. Additionally, short versions of rating scales administered throughout treatment conveniently allow for the patient's treatment progress to be monitored and compared as either symptomatic exacerbation or alleviation (Ramsay, 2017). While many of the symptom checklists currently in use are based on DSM-IV criteria, they can be readily adapted to align with DSM-5 criteria. This adaptation involves making necessary adjustments to the age-of-onset criterion, which is now set at 12 years old in the DSM-5, and to the diagnostic thresholds for adult symptom endorsement. For the latter,

the DSM-5 requires endorsement of 5 out of 9 symptoms in either the inattentive or hyperactive/impulsive symptom cluster (Ramsay, 2017). To ensure continuity of care, any data that is collected should be communicated to other healthcare professionals involved in the patient's treatment. It is important to note that while these patient/family/caregiver-reported tracking scales of symptoms can provide objective measurements, they may not always be consistent with practitioner-measured ratings (Gordon et al., 2016; Stuart et al., 2014). If a discrepancy between patient and clinician ratings occurs, a discussion and/or treatment adaptation should result to address why the disagreement exists to help further improve symptoms during treatment. Lastly, it is prudent to monitor for rupture markers, or signs the patient feels uneasy or unsafe due to unintentional circumstances. Helpful rupture markers for the clinician to monitor include, but are not limited to, overt or indirect expression of negative sentiment or hostility, disagreement about goals or therapy tasks, compliance issues, attendance issues, avoidance maneuvers (e.g., becoming oppositional or avoidance of discussing treatment), self-esteem enhancing strategies (e.g., justifying self-actions), and general non-responsiveness to interventions. Should the clinician recognize such challenges, an open discussion may help alleviate concerns or lead to modification of treatments to best help the patient and family.

The aforementioned nonpharmacological treatment recommendations are a part of the comprehensive care of a patient with ADHD. In addition to these services provided by mental health clinicians, education and vocational services are also imperative to maximize function for this population. Provided below is an overview of some of the federal regulations mandating access to additional resources and accommodations for patients with an ADHD diagnosis. Following this overview, there will be a summation of accommodations that could be implemented to further improve function.

Federal Regulations and ADHD

-The Rehabilitation Act/Section 504

The Rehabilitation Act of 1973 allows for every child with a disability to have equal access to an education (U.S. Equal Employment Opportunity Commission [EEOC], 2009). Through this act, many children, including those with ADHD, receive accommodations or modifications. This act is enforced by the U.S. Department of Education through the Office for Civil Rights, and most school systems have at least one coordinator on staff (West Virginia Department of Education [WVDE], 2014). Section 504 of the law defines a disabled person as a person who meets all the following criteria: has, has a record of, or is regarded as having a physical or mental impairment that substantially

limits the student and is expected to continue to majorly affect life activity (Cohen et al., 2017; Disability Rights Education & Defense Fund [DREDF], 2021; WVDE, 2014;).

Students who qualify as disabled are entitled to appropriate accommodations and modifications to eliminate barriers to participation in school and school-related activities. ADHD is one of the leading reasons that a 504 plan for children and adolescents is requested. Examples of some accommodations and modifications include extra time for assignments and tests, reduced volume of assignments, providing exams in shorter segments, highlighting main ideas in texts, providing outlines and practice tests, preferential seating, minimizing distractions, small group instruction, and more (Anzilotti, 2016). Parental/familial/caregiver consent is required before an initial evaluation is completed, but a parent, teacher, counselor, related service provider, school staff, administrator, or community agency can request a section 504 evaluation. Once a child is determined to meet criteria, a 504 plan can be initiated. The 504 plan, which is to be reviewed annually, should contain the student's needs and all accommodations to meet said needs. Since section 504 is a civil rights statute, not a special education statute, county schools receive no additional funding for providing these accommodations (WVDE, 2014).

-Individuals with Disabilities Education Act

The Individuals with Disabilities Education Act (IDEA) governs all special education services for children in the United States. The act is enforced by the U.S. Department of Education through the Office of Special Education Programs (WVDE, 2014). To be covered under this act, the student must be aged 3-21 years and have one or more of the following 13 disabilities: autism, deaf-blindness, deafness, a serious emotional disturbance, hearing impairment, mental retardation, multiple disabilities, orthopedic impairment, specific learning disability, speech or language impairment, traumatic brain injury, visual impairment (including blindness), or other health impairment. “Other health impairment” is defined as an acute or chronic health problem that results in limited alertness with respect to the education environment and adversely affects a child’s education performance; it is under this definition that children with ADHD qualify for the program (Individuals with Disabilities Education Act [IDEA], 2017). As a result of this act, the school is required to provide an Individualized Education Program (IEP) to students with ADHD. The IEP is to be developed by specific participants at an IEP meeting and should operationally define how the school will help the child meet their

needs with measurable and achievable processes (WVDE, 2014). For example, if a student is struggling with class interruptions, the IEP could state "By month three, XXX will reduce his class interruptions from ten per day to two per day. We will achieve this through social reminder queues from peers upon each interruption". Each area for improvement should be listed in this way so that the success of the plan can be accurately measured. The IDEA also requires parent/family/caregiver consent, while clinicians, teachers, or parents/families/caregivers can request an IEP for children with special needs. The IEP is reviewed yearly, and a comprehensive re-evaluation is done every three years to verify the student still meets eligibility.

-The Americans with Disabilities Act

The Americans with Disabilities Act (ADA) is a civil rights law that prohibits discrimination against individuals with disabilities in all places of public life, including schools, jobs, transportation, and all public and private places that are open to the public (Americans with Disabilities Act [ADA], 2022). The ADA's criteria for a disability are consistent with the section 504 requirements. Under this act, public entities must provide services, programs, and activities in the most integrated setting appropriate to the needs of qualified individuals. Accommodations and modifications in policies to avoid discrimination are required unless the entity can demonstrate that an accommodation or modification would alter the nature of their service. To ensure disabled individuals are not excluded from services, programs, and activities, buildings must be accessible to those with disabilities. In addition, auxiliary aids must be provided to individuals at no extra cost to ensure effective communication with individuals with hearing, vision, or speech impairments (HHS, 2013). This act is especially applicable during the transition of school-aged adolescents to the age of consent when they begin to enter the workplace.

ADHD-Related School Services/Resources

As previously mentioned, adequate access to mental health specialists and services continues to be a disparity in many areas of the United States, including West Virginia. However, 90% of youth in America attend public school (Bouchrika, 2022), making public academic institutions a prime target for intervention. It is necessary for clinicians and others involved in the care of patients with ADHD to be aware of potential rights, resources, modifications, and accommodations within the educational system for patients with mental health conditions, including ADHD, to improve access to mental health services and improve

patient outcomes.

This guide will detail some evidence for accommodations and modifications used in the management of ADHD. Another helpful resource is the *West Virginia Parent's Advocacy Guide to Special Education*, which helps caregivers advocate for their child. Additional resources in West Virginia are available online at www.wvadhd.org.

Accommodations and Modifications

Accommodations and modifications depend on the child's specific needs and challenges. Children with ADHD commonly struggle with inattention, distractibility, hyperactivity, impulsivity, and disorganization. Many forms of accommodation exist, most of which are evaluated with case studies. Despite limited evidence, accommodations are generally recommended and readily used based upon specific struggles the student faces.

A systematic review in 2021 examined test accommodations in patients with ADHD and found they are the most common adaptation given to this population. The most common test accommodation was extended time for test takers (Lovett & Nelson, 2021). However, none of the test accommodations had sufficient evidence for support except the "read aloud" technique, where the teacher gives the test orally. This method was tested in two randomized experiments and was shown to improve test performance and grades (Lovett & Nelson, 2021). An older systematic review in 2013 looked at common forms of accommodations for children with behavioral challenges, including ADHD. This study defined choice making (the strategy where students are given the opportunity to select between two equal academic activities), increased task engagement, work productivity, and accuracy. Intra-task simulation, a strategy that adds a task to an already existing task (such as highlighting important text while reading), was found to decrease distracting activity levels during assignments. Shortened task length and having fewer repetitive questions on assignments but covering the same amount of material showed moderate improvement in on-task behavior, but no change was seen in the percentage of correct answers. There were also types of adaptive furniture (furniture that is changed in some way to accommodate an impairment) examined; for ADHD, it is common to see "wiggle chairs" and therapy ball chairs that are thought to help with sensory distractions. The review found that more students remained in their seats and on task with these adaptations, and legible word productivity also increased. Small group instruction, rather than whole group instruction, showed mixed results. Students displayed more on-task behavior but less productivity, measured by the assignment. Time/scheduling changes to allow students more time to complete assignments and exams also showed mixed results. Students had more correct answers per minute, but behavioral

distractions were worse with longer assignments and exams. The response accommodation, providing students with lessons that incorporate frequent opportunities to actively engage and respond to lessons, decreased disruptive behaviors and increased on-task behavior. A few methods had insufficient evidence to conclude efficacy: teacher proximity (placing student closer to the teacher for less distractions), fast-paced instruction (briskly presenting new stimulus, such as flashcard, with shortened time frames for student response before a new stimulus is introduced), and interest incorporation (adding an element of interest to an assignment, such as a favorite cartoon character on a worksheet). The review found extra task simulation (introducing an outside distraction to an activity, such as music or dance) to have negative outcomes. The students were less likely to maintain on-task behavior and displayed increased energy (Harrison et al., 2013).

Elaborating upon work by Harrison, additional accommodations and modifications are available. Some common modifications for distracting classroom behavior are sitting the child next to a positive role model, increasing the distance between desks, using tape around the desk as a physical reminder where the child should remain, allowing the child to borrow notes from other students, having the student help teach the lesson, and using private signals that serve as cues to stay on task. Some students have trouble with incomplete assignments, so accommodations to address this difficulty are allowing extra time to complete the assignment, breaking the assignment up into smaller projects, shortening work periods, orally giving assignment instructions, and checking the students work in 10-minute intervals. For students who easily lose focus, consider using clear verbal signals, like “freeze!", or “one, two, three, eyes on me”, using a laser pointer to illuminate important points, illustrating important topics with pictures, or ringing a bell/playing a chime every time there is an important topic. Furthermore, there are also plenty of accommodations that help students keep track of their work. Some of these include color coding binders to specific subjects, having handouts hole punched in advance to promote using the appropriate folder, using brightly colored paper for homework assignments, appointing certain students as “monitors” to check the status of assignments, or allowing the student to keep a second set of books at home. For students with hyperactivity, keeping them moving is helpful. Some teachers choose to allow the student to run errands and handout papers, allow standing time for the student, provide fidget toys in class to increase concentration, or allow short breaks between assignments. Finally, social accommodations that help students work well with others are encouraging cooperative learning tasks, giving the student a special task in group assignments, assigning a leadership role in group settings, and praising good social behavior among peers.

Although ADHD can be difficult to manage and support academically, the school system is required to offer support systems to help students succeed. With the support, modifications, and accommodations of section 504 and special education services, it is the goal to give students with ADHD the opportunity to accomplish academic milestones with their peers.

Student Assistance Teams

Student Assistance Teams (SAT) are teams made of school staff, commonly an administrator, school counselor, teacher, school psychologist, and/or social worker, that review individual students who have received academic and/or behavioral support and require more assistance (WVDE, n.d.). These teams provide recommendations for additional accommodations and/or other measures to address the struggles the student is facing (WVDE, n.d.). Prior to the first SAT meeting, teachers should have already implemented some classroom modifications. Then, at the SAT meeting, a facilitator leads the group to develop a written plan of action for the student's success (Monongalia County Schools Student Assistance Team, 2022). A follow-up date is then scheduled, and the plan is re-evaluated based on the student's progress (Monongalia County Schools Student Assistance Team, 2022). If the progress is satisfactory, the plan may be continued, but if the progress is unsatisfactory, a plan revision or alternative educational placement may be recommended (Monongalia County Schools Student Assistance Team, 2022).

Additional examples of common school accommodations and interventions can be seen in APPENDIX 2.3: Examples Of Common Recommendations For School Accommodations And Interventions. For School-Focused Resources Specific to West Virginia please visit our website at: https://wvadhd.org/.

Pharmacological Treatment Options

This section reviews pharmacological ADHD treatment options, including FDA-approved medications and medications with literature-supported, off-label use for certain age groups with an ADHD diagnosis. Various patient-specific factors, such as age, patient/family preference, previously successful/failed trialed medications (considering the patient and family's history of medication responses), routes of administration, comorbidities, and side effects, should be accounted for when determining the optimal treatment plan inclusive of a pharmacological option. Careful titration and monitoring of medications should occur to ensure once a medication is started, the dose is appropriately adjusted to balance efficacy and tolerability. There are various side effects that can be mitigated with dose changes, administration with food, appropriate monitoring, or other strategies, but if more serious adverse events occur, the pharmacological

treatment may need to be adjusted or discontinued. Therefore, a comprehensive treatment plan that includes a patient/caregiver/provider-agreed upon regimen, inclusive of pharmacological and/or nonpharmacological options, and extensive patient monitoring for efficacy and side effects is vital to successful management of ADHD symptoms with pharmacological treatments and will allow for individualized treatment selection.

Prior to Starting Medication

Once a patient has met the DSM-5-TR criteria for a diagnosis of ADHD and the decision has been made to start medication by both the patient/caregiver and clinician, the clinician should ensure that the patient/caregiver is thoroughly educated. An explanation regarding the intent to treat the patient's symptoms by improving their ability to focus and enhancing their self-control through medication use should occur at a visit before the medication is initiated. Also, before starting pharmacological treatments, it is prudent to have an honest discussion with the patient/family/caregiver regarding the goals of treatment, specifically addressing the symptoms that drug therapy will likely not improve. For example, medications typically do very little to help with symptoms of disorganization. Emphasizing that there is no "cure" for ADHD can also help the patient set realistic goals for therapy.

Each potential medication for treatment of ADHD has associated adverse effects that will need to be monitored on a continuous basis. A thorough family history and patient evaluation should be conducted prior to initiation of many of the pharmacological options to ensure the appropriate medication for each patient is selected. Potential adverse events associated with the medications used to treat ADHD should be presented in a discussion with the patient/family/caregiver to allow for any concerns to be addressed and taken into consideration in the selection of a medication. To allow for appropriate monitoring throughout care, baseline height, weight, blood pressure, and heart rate should be documented prior to pharmacological management of ADHD. The patient's current medication list should be reviewed to avoid drug interactions with new prescriptions. Finally, the patient or caregiver should be educated on follow-up requirements, including frequency, symptoms, or behaviors to monitor and report; how to assess efficacy of treatment; and what information to bring to follow-up visits (Krull & Chan, 2021). In addition to the detailed information contained within this guide on pharmacological treatment options, the following references are available in the APPENDIX.

- APPENDIX 2.4: Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacological Treatment Recommendations

- APPENDIX 2.5: Attention-Deficit/Hyperactivity Disorder (ADHD) Monitoring and Follow-Up
- APPENDIX 2.6: Attention-Deficit/Hyperactivity Disorder (ADHD) Medications
- APPENDIX 2.7: Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management
- APPENDIX 2.8: Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Conversion Aid
- APPENDIX 2.9: Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy – Drug Interactions

Stimulants

Stimulant medications have been the mainstay of ADHD treatment for decades. Approximately 75% to 80% of children with ADHD will benefit from psychostimulant treatment (Briars & Todd, 2016). Stimulants have been shown to provide clinical benefit in adults with ADHD as well (Post & Kurlansik, 2012). Stimulants are first-line treatment for children over six years of age and adults due to their rapid onset and record of safety and effectiveness for reduction of symptoms of inattention, hyperactivity, and impulsivity in ADHD. However, in cases for children where there is a strong family preference against stimulant medications, concern about misuse or diversion, or a contraindication exists, nonstimulants would then be considered for first-line pharmacological treatment. For adults, the same reasons for choosing or avoiding a stimulant are present, but the AAFP also recommends atomoxetine as a first-line option, which will be discussed later in this guide.

-Dosage Form Considerations

While there are various stimulant formulations available with an FDA-approved indication for treatment of ADHD, there are only two basic types of stimulants: methylphenidates and amphetamines. Each stimulant type is available via pharmaceutical products with various properties that affect their pharmacokinetic and pharmacodynamic profiles. Concerning effectiveness, approximately 40% of patients respond to both amphetamines and methylphenidates, but approximately 40% will only respond to one of the two stimulant categories (Wolraich et al., 2019). Different isomers, salt forms, prodrugs, and delivery systems have been utilized to manipulate the molecules and dosage forms to provide individualized treatment options with regard to effective timing of symptom management and a tolerable side effect profile.

Long-acting formulations are preferred for school-aged children, adolescents, and adults; extended duration of action can prevent school-time administration, allow for

coverage throughout the day, prevent peak and valley effects, and improve compliance. In addition, the extended-release (ER) formulations of stimulants are potentially less likely to be misused than immediate-release (IR) medications due to difficulty in manipulating the dosage form and administering via injection or intranasal routes (SAMHSA, 2015). Short-acting stimulants can be used in situations where an additional dose is required later in the day to extend the duration of the long-acting stimulant, when coverage is only required a few hours a day, or to allow for a more flexible dosing schedule (Canadian ADHD Resource Alliance [CADDRA], 2020). Therefore, the clinician and patient/family/caregivers should consider timing of coverage of target symptoms, side effects, coexisting conditions, formulation required, insurance coverage, and cost when determining the initial pharmacological option in the treatment of ADHD.

-Adverse Events

One of the major adverse reactions associated with the use of prescription psychostimulants is cardiovascular risk with potential for sudden death. Due to the association with sudden death in children and adolescents with cardiac abnormalities and risk for stroke, myocardial infarction, and sudden death in adults, an assessment for personal or family history of cardiac disease (including family history of sudden death, Wolff-Parkinson-White syndrome, hypertrophic cardiomyopathy, and long QT syndrome) should be conducted prior to initiation of psychostimulants. Further evaluation, such as an electrocardiogram, should be performed if any findings are suggestive of cardiac disease prior to psychostimulant use, and a cardiac evaluation should be immediately conducted if chest pain, syncope, or other cardiac symptoms occur with the use of stimulants (Drug Facts and Comparisons online, 2021a). Studies have shown that use of stimulant medications does not increase the risk of serious cardiovascular events in children and adults without cardiac concerns (Bélanger et al., 2009; Habel et al., 2011).

Other adverse events that can occur with use of psychostimulants include decreased appetite and the potential for suppression of growth, insomnia, psychiatric risk, stomach pain, sleep disturbances, tics, and headaches, although this list is not exhaustive. The patient's height and weight should be regularly monitored at appointments to monitor the effects of stimulants on appetite and growth. Dosage form or dose adjustments and/or medication changes may be required if the patient is at risk for these adverse effects to be detrimental to their health and growth. Adjustments to the pharmacological regimen may also be necessary if the patient is not able to get the necessary sleep to function or to

prevent worsening of side effects from the use of prescription stimulants. New onset psychosis has also been associated with prescription stimulant use in the context of ADHD treatment, with an incidence rate of approximately 1 in 660 patients and a slightly increased risk with use of amphetamines over methylphenidate (Moran et al., 2019). Due to the potential for the multiple adverse effects mentioned and possibly others, clinicians should appropriately screen and regularly monitor patients to assure stimulant use is both safe and effective in the management of ADHD. Dose reductions, dosage form adjustments, medication discontinuations, and other adjustments may be necessary before finding the optimal treatment regimen. Prescription stimulants can cause physical dependence after use over time, so tapering the medication can prevent withdrawal symptoms upon discontinuation of the medication.

-Potential for Diversion and Misuse

Prescribers of prescription stimulants should be prepared to incorporate additional monitoring parameters and consideration of patient-specific factors into their practice when prescribing these medications. The DEA classifies prescription stimulants as Schedule II controlled substances due to their ability to cause physical dependence and the potential to be highly addictive. The AAP recommends monitoring adolescents for signs of misuse and diversion of prescription stimulants, and the AAFP directs practitioners to assume all adult patients are at risk of misuse, diversion, or having their medication stolen (AAFP, 2022b; Wolraich et al., 2019). While prescribers should consider the potential for diversion, both initially and in maintenance therapy, there is no current evidence that prescription stimulant use for the treatment of ADHD leads to an increased or decreased risk for substance use later in life (Molina et al., 2023). Prescribers should not let this concern prevent them from using prescription stimulants for patients with a legitimate medical need, such as ADHD. This approach applies once the patient has been evaluated as a suitable candidate for stimulant therapy and a plan for ongoing substance use monitoring has been established.

Clinicians can utilize multiple strategies to ensure the safe and effective use of prescription stimulants in patients with ADHD. Prior to prescribing a stimulant and periodically throughout treatment, an assessment for risk of misuse should be conducted, and patient-specific factors that may limit prescription stimulant use should be reviewed. The AAP and AAFP recommend monitoring for signs of misuse and diversion throughout treatment, with periodic assessments (Post & Kurlansik, 2012; Wolraich et al., 2019). It is also recommended that prescribers consider the use of patient-provider agreements and

regular follow-up visits when prescription stimulants are prescribed to adults with ADHD to adequately monitor for adherence to the patient-provider agreement (Post & Kurlansik, 2012). Patient/family/caregiver education, including the risks of physical dependence, potential for diversion, and safe medication storage, should be completed and should include warning the patient of potential peer requests to share medications (prescription stimulants or other medications) for cognitive enhancement or other non-medical uses. Parents/families/caregivers should directly administer the medication to children, and adolescents should be monitored for early or late fills. Further discussions should include the avoidance of alcohol, tobacco, and other illicit substances as they could interact with the medication or cause additional attention issues, and concerns of efficacy or adverse events should be reported (Krull & Chan, 2021).

For patients who have a higher risk for misuse or other concerns, there are more extensive risk reduction strategies that can be employed. Behavioral observations, urine drug testing, pill counts, and monitoring of refill requests can be incorporated into monitoring parameters to ensure compliance with the prescribed regimen and abstinence from other non-prescribed substances. Additionally, West Virginia Code § 60A-9-5a [2021] requires practitioners to perform drug monitoring via the West Virginia Controlled Substance Monitoring Program upon initially prescribing any Schedule II controlled substance and at least annually thereafter should the practitioner continue to treat the patient with controlled substances. A practitioner may elect to check the West Virginia Controlled Substances Monitoring Program (CSMP) more frequently than annually to ensure that patients are not receiving multiple prescriptions of controlled substances from more than one practitioner and to monitor the frequency of refills. See the Risk Reduction Strategies section for more detailed information regarding risk reduction strategies when prescription stimulants are being utilized in the management of ADHD, especially in patients with a higher risk for misuse or addiction.

In May of 2023, the FDA mandated revisions to the Boxed Warning and other sections of the prescribing information for prescription stimulants. The aim was to ensure uniformity across this category of medications and address ongoing concerns related to their misuse, addiction, and overdose. Previously, the prescribing information for certain prescription stimulants lacked updated warnings regarding the dangers associated with misuse. In particular, it failed to highlight that the majority of individuals who misuse prescription stimulants obtain them from family members or peers. To rectify this lack of warning, the FDA introduced information stating that patients should never share

prescription stimulants with others. The Boxed Warning describes the risks of misuse, addiction, and overdose across all medications in this class. Additionally, healthcare professionals are advised to closely monitor patients for signs and symptoms of misuse and addiction. To aid clinicians in better educating patients/caregivers about these risks, the prescribing information includes information on these dangers in various sections, such as Warnings and Precautions, Drug Abuse and Dependence, Overdosage, and Patient Counseling. It also required updating existing Medication Guides (ADHD Stimulant Safety Alert, 2023).

In light of the FDA's revised Boxed Warning, strict adherence to the recommended management of prescription stimulants becomes paramount. CHADD advises that medications be stored in a secure manner, out of reach and in locations not easily accessible or searched by others, suggesting the use of a locked container as an additional precaution (CHADD, 2020b). Furthermore, the FDA highlights the critical need for proper disposal of unused or expired stimulants, recommending that they be promptly taken to an authorized drug take-back site or program to avert potential misuse and environmental damage.

In the absence of nearby drug take-back options, and when no specific disposal instructions are provided in the medication guide or package insert, the FDA provides a series of steps to safely dispose of medications:

1. Combine the medication (ensuring tablets or capsules remain intact) with a substance that deters consumption, such as used coffee grounds, dirt, or cat litter, to dissuade children, pets, and others from unintended ingestion.
2. Place this mixture into a secure container, such as a sealable plastic bag, to prevent leakage or access.
3. Dispose of the sealed container with your household waste.
4. Before discarding or recycling any empty medication bottles or packaging, ensure that personal information on the prescription label is thoroughly removed or obscured to maintain privacy.

Healthcare professionals must convey the prevention and risks of sharing prescription stimulants, as such actions can facilitate the development of substance use disorders in others, highlighting the severity of this issue (FDA, 2023). These measures are essential to reduce the potential for misuse and diversion, ensuring that those with ADHD

continue to benefit from their treatment safely and responsibly.

It has been the experience of the panel that parents/family/caregivers often associate the use of prescription stimulants with the risk of addiction and/or the use of prescription opioids due to the similar DEA classification. This association can cause reluctance to accept treatment, resulting in delays in treatment, undertreatment, or lack of treatment for ADHD, each of which presents potential harm to the patient. It is important to educate patients and their parents/family/caregivers that prescription stimulants used to treat ADHD are controlled substances but are not opioids. Not only does their mechanism of action and indication for use completely differ, so does their adverse event profile (i.e., opioids can cause respiratory depression leading to death). While stimulants, mainly illicit, have been involved in overdose deaths, the safety and efficacy of prescription stimulant use for ADHD is evidence-based and peer-reviewed, which differs greatly from the use of opioids in the management of pain. In the late 1990s, there was a period of time when the use of opioid prescriptions to treat chronic, non-malignant pain was encouraged by opioid manufacturers. An increase in dosage and frequency was seen, without peer-reviewed literature to support it (HHS, 2021). This increased prescribing without appropriate evidence, coupled with the addiction potential of opioids had devastating consequences, leading to the widespread and deadly misuse of prescription and non-prescription opioids. It is crucial to differentiate this historical context of opioid prescribing from evidence-based use of prescription stimulants in the treatment of ADHD. The safety and efficacy of prescription stimulants for treatment of ADHD have been extensively studied and supported by scientific evidence. In fact, in every major clinical treatment guideline, stimulants are first-line pharmacological treatment for ADHD in most age groups. A recent multimodal treatment study indicates no association between stimulant treatment for childhood ADHD and subsequent use rates of substances (including alcohol, marijuana, and cigarettes) later in life (Molina et al., 2023).

-Types of Stimulants

-Methylphenidate

(FDA-approved age range: 6 years of age and older*)

*Please note that there are various FDA-approved products containing methylphenidate and its derivatives. See Appendix 2.6: Attention-Deficit/Hyperactivity Disorder (ADHD) Medications for product-specific FDA-

approved age ranges.

Mechanism of Action: Methylphenidate increases dopamine and norepinephrine by inhibiting dopamine and norepinephrine transporters. By blocking these presynaptic transporters from reuptake of the neurotransmitters, methylphenidate increases the availability of dopamine and norepinephrine in the synaptic space (Verghese & Abdijadid, 2023).

Methylphenidate is the most widely used first-line treatment for ADHD, with an effect size of 1.0 indicating a strong relationship between use of the medication and positive effect on ADHD symptom management (Wolraich et al., 2019). Depending on the timing and duration of target symptoms, a product with a dosage form and release mechanism should be selected to minimize ADHD symptoms when needed throughout the day, with minimal side effects. For dosage form, recommended dosages, and duration of action for both long- and short-acting methylphenidate products, Appendix 2.6: Attention-Deficit/Hyperactivity Disorder (ADHD) Medications can be used as a reference. Of note, not all methylphenidate products have a 1:1 dosing conversion, and there are specific recommendations in the product labeling for transitioning from one product to another.

Preschool-Aged Children (4-6 years): There are currently no FDA-approved methylphenidate products for treatment of ADHD in children less than 6 years of age, but according to the AAP *Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents (2019),* methylphenidate could be considered for treatment in this age group. The preschool-aged patient's severity of symptoms, level of dysfunction, and prior behavioral treatment failures should be thoroughly assessed before initiating treatment with a stimulant. Methylphenidate can be initiated in this age group if significant improvement is not achieved with behavioral interventions and if moderate-to-severe continued disturbance persists in the child's functioning. It can also be considered for patients where behavioral treatments are unavailable and the benefits of treatment of ADHD exceed the potential risks of untreated ADHD. Additionally in this age group, metabolism of methylphenidate is thought to be slower; therefore, lower doses should be utilized during initiation and when dose increases occur, they should be in smaller increments (Wolraich et al., 2019).

-Amphetamines

(FDA-approved age range: IR – 3 years of age and older; ER – 6 years of age and older*)

*Please note that there are various FDA-approved products containing amphetamine salts and their derivatives. See Appendix 2.6: Attention- Deficit/Hyperactivity Disorder (ADHD) Medications for product-specific FDA- approved age ranges.

Mechanism of Action: Amphetamines also affect the levels of synaptic dopamine and norepinephrine, but via a different method. Amphetamines promote the release of dopamine and norepinephrine from their storage sites in the presynaptic terminal (Drug Facts and Comparisons online, 2019a).

Amphetamines also have an effect size of 1.0 and have various formulations available to ensure optimal duration of action (Wolraich et al., 2019). There are various FDA-approved salt forms, isomers, and prodrugs available of amphetamine products, along with multiple dosage form options to allow for manipulation of the pharmacokinetics for targeted symptom control. The differences in both salt forms and isomers can change the relative potency of the medication, so careful evaluation and selection of dosages should occur prior to initiating or rotating prescription stimulants. There is some evidence that amphetamines may have some increased risk of adverse events versus methylphenidate. In a cohort study, there was a higher association with new use of amphetamines for psychosis than with new use of methylphenidate (Moran et al., 2019). Furthermore, in a study examining the cardiovascular effects of prescription stimulants in children, amphetamines were associated with risk of increased systolic blood pressure, diastolic blood pressure, and heart rate, whereas methylphenidate was only associated with increased systolic blood pressure (Hennissen et al., 2017). However, in another meta-analysis, there was no correlation with ADHD medications and sudden death/arrhythmia, stroke, myocardial infarction, and all-cause death (Liu et al., 2018). As with the methylphenidate products, appropriate monitoring of adverse events, efficacy, and potential for misuse should be ongoing to allow for safe use.

Preschool-Aged Children: While there are several amphetamine products that have received FDA-approval for use in preschool-aged children, the AAP's *Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents (2019)* recommends off-label use of methylphenidate over amphetamines when considering medication treatment due to the available literature and less stringent requirements for approval in this age group at the time of FDA review

(Wolraich et al., 2019).

Norepinephrine Reuptake Inhibitors

Mechanism of Action: **Atomoxetine** and **viloxazine** are selective norepinephrine reuptake inhibitors that indirectly increase the concentration of norepinephrine in the synapse (Drug Facts and Comparisons online, 2021b, 2021c).

-Atomoxetine

(FDA-approved age range: 6 years of age and older)

Atomoxetine is an option for patients, both children and adults, in whom stimulants are not effective, not appropriate, intolerable, or are contraindicated. Unlike prescription stimulants, atomoxetine is not a controlled substance. This agent can be considered for patients with anxiety, tics, insomnia, or SUD, where use of stimulants may not be appropriate (Drug Facts and Comparisons online, 2021b). While atomoxetine, with an effect size of 0.7, has not been shown to be more effective than stimulants for the treatment of ADHD symptoms, multiple studies have shown atomoxetine to be more effective than placebo (Wolraich et al., 2019). Unlike psychostimulants, this medication can take time to see benefit, as the maximum treatment response may not be achieved until six to eight weeks after initiation (CADDRA, 2020). This medication can be administered daily or the dosage can be split and taken twice daily to provide up to 24 hours of symptom coverage, and it has not been associated with misuse potential.

Common side effects of this medication include headache, insomnia, drowsiness, decreased appetite, and increased diastolic blood pressure. With use of this agent, there can be an increased risk of suicidal thoughts; hence, the product has an FDA boxed warning. The risk is greatest when medication is first initiated or when dosing adjustments occur, so patients and family should be counseled to monitor for associated behaviors or unusual changes in behaviors. Additionally, while it rarely occurs, patients should be monitored for liver failure by observing for evidence of jaundice or changes in urine color. If these symptoms occur, the medication should be stopped immediately, and liver function should be assessed via liver function tests (Briars & Todd, 2016). Therefore, as with prescription stimulants, atomoxetine also requires ongoing appropriate follow-up and monitoring of therapy, both for safety and efficacy.

Atomoxetine is primarily metabolized by the cytochrome P450 2D6 enzymatic pathway. Poor metabolizers through this pathway are present in a portion of the population

(~7% of Caucasians and 2% of African Americans). This poor metabolism and reduced elimination led to 5 times higher peak plasma concentrations when compared with normal metabolizers. Other drugs (fluoxetine, paroxetine, etc.) that are inhibitors of CYP2D6 can increase drug exposure. Before prescribing atomoxetine, the patient's medication record should be reviewed for major potential drug interactions. In both scenarios (poor metabolizer and use of interacting drugs), drug dosage adjustment is likely to be required to prevent adverse events associated with increased drug levels in the body (Camber Pharmaceuticals Inc., 2021). See APPENDIX 2.9: Attention-Deficit/ Hyperactivity Disorder (ADHD) Pharmacotherapy – Drug Interactions for additional drug interaction information.

Viloxazine

(FDA-approved age range: 6 years of age and older)

Viloxazine was approved by the FDA in 2021 for the treatment of ADHD in pediatric patients 6 to 17 years of age; in 2022, it was approved for use in adults with ADHD. The drug was first approved in the 1970s in the United Kingdom and several other European countries for the treatment of depression in adults. It is a nonstimulant, non-controlled medication found to be effective for treatment of ADHD symptoms in children aged 6 years of age and older when compared with placebo. Viloxazine has a similar mechanism of action to atomoxetine, so a comparable side effect profile includes increased diastolic blood pressure, increased heart rate, drowsiness, and headache. This agent will not have an immediate effect and will take several weeks to produce a response (Yu et al., 2020). Due to the class warning of suicidal thoughts and behaviors, parents/families/caregivers should be advised to monitor for associated behaviors, such as agitation, anxiety, and impulsivity and notify their healthcare clinician if they occur (Drug Facts and Comparisons online, 2021c). This medication can be an option when a norepinephrine reuptake inhibitor is appropriate and, due to the use of other medications or poor CYP2D6 metabolism, may be an option over atomoxetine. Additionally, viloxazine capsules can be opened and their contents sprinkled on pudding or applesauce, which may make it preferable to atomoxetine in certain clinical situations. However, viloxazine may act as a reversible CYP1A2 inhibitor, which may prolong the duration of action of 1A2 substrates, such as caffeine. Due to the product being new to market during the drafting of this publication, a generic is unavailable, so patient costs may make this option undesirable or unobtainable.

Alpha-2 Agonists

-Clonidine and Guanfacine ER

(FDA-approved age range: 6-17 years of age*)

*While not FDA-approved, there is literature available to support the use of ER clonidine and guanfacine in adults with ADHD.

Mechanism of Action: The exact mechanism of action for the alpha-2 agonists is unknown in the context of ADHD treatment. It is theorized that these agents mimic the effects of norepinephrine at the alpha-2 adrenoreceptors in the prefrontal cortex. The two FDA-approved, ER alpha-2 agonists for the treatment of ADHD in children and adolescents are clonidine and guanfacine. Clonidine is active at the alpha2A, alpha2B and alpha2C adrenoreceptors, and guanfacine is selective for the alpha2A adrenoreceptor.

Prior to the FDA's approval of the extended-release version of both agents for ADHD in children, immediate-release versions were utilized but were poorly tolerated due to their side effect profile and putting the patient at an increased risk for rebound hypertension with abrupt discontinuation. ER guanfacine and clonidine are FDA-approved for ages 6 to 17 years of age for the treatment of ADHD. It is important to note that these medications can be used alone or as monotherapy, depending on the specific needs and response of the patient. Patients are less likely to experience an initial drop in blood pressure with the ER formulation, and due to the ER properties, they are generally better tolerated. Overall side effects may include somnolence, dry mouth, irritability, bradycardia, hypotension, and abdominal pain. ER alpha-2 agonists can be considered for patients who have contraindications to or failed treatment with psychostimulants and/or a norepinephrine reuptake inhibitor. For patients who start treatment with either clonidine or guanfacine, a maximum response may not be observed for 2 to 4 weeks.

Preschool-Aged Children: The AAP's *Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents (2019)* does not suggest use of clonidine or guanfacine for treatment of ADHD in preschool-aged children. However, the *Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder (2020)* does advise that clonidine or guanfacine can be considered for treatment in patients 3 to 6

years of age with ADHD with target symptoms of severe impulsivity, aggression, oppositional behavior, and/or irritability, but there is limited evidence at this time for its use (Barbaresi et al., 2020). Therefore, as previously mentioned, it is vital to adequately assess and diagnose ADHD in addition to any other coexisting conditions to ensure appropriate selection of a treatment modality, especially in preschool-aged children.

Off-Label Pharmacological Treatments

The following medications may be used in practice to treat ADHD but do not have an FDA-approved indication for the treatment of ADHD. The use of these agents may be appropriate for certain patients, such as those with coexisting conditions. However, off-label medications have less documented safety and efficacy data for use in the context of the treatment of ADHD and should only be used at the careful discretion of the clinician. In most cases, prescribing off-label medications for the treatment of ADHD should not be done by clinicians without specialized training, rather it should be reserved for specialists to whom the patient should be referred.

-Bupropion

Mechanism of Action: Bupropion is a weak inhibitor of neuronal uptake of dopamine and norepinephrine. It does not inhibit monoamine oxidase or the reuptake of serotonin (Drug Facts and Comparisons online, 2021d).

Bupropion is not FDA-approved for treatment of ADHD, but it has been shown to be superior to placebo to reduce symptoms of ADHD in a meta-analysis of 133 clinical trials involving children, adolescents, and adults with ADHD (Cortese et al., 2018). It is not recommended as a first-line treatment option for symptoms of ADHD, but the FDA-approved indications for adults include major depressive disorder, seasonal affective disorder, and smoking cessation. The drug's place in therapy for the treatment of ADHD in adults would be after failures of first-line agents or as an add-on therapy. Due to its other FDA-approved indications, use of bupropion may be beneficial for those patients with a diagnosis of ADHD who have additional coexisting conditions, such as tobacco use or SUD (Daughton & Kratochvil, 2009). Use of this agent in children and adolescents for the treatment of ADHD should be reserved until previously mentioned medications, with more evidence to support their use, have been trialed, and an evaluation by a specialist is complete.

Side effects of this agent can include tachycardia, weight loss, nausea, and vomiting. The medication has several warnings for use, such as suicidal ideation and behavior, dose-dependent seizures, and potential for precipitating mania in patients with bipolar disorder

(Drug Facts and Comparisons online, 2021d). Patient and caregiver education should include counseling to review potential adverse events, monitoring of symptoms, and when to seek additional medical advice. As with the other medications, bupropion requires regular monitoring for side effects and efficacy.

-Modafinil

Mechanism of Action: The exact modafinil mechanism of action is unclear, but it has been shown to block dopamine transporters and increase dopamine in the brain.

Modafinil also has shown benefit for treatment of ADHD symptoms in children by both clinicians and teachers, but it was not found to be efficacious for improvement of ADHD symptoms in adults when compared with placebo (Biederman, et al., 2008; Cortese, et al., 2018). Due to the drug's effect on dopamine in the brain, it does have potential for misuse, and modafinil is a DEA Schedule IV controlled substance and should be avoided in patients who are not candidates for stimulant therapy. FDA approval for the treatment of ADHD was not granted due to the potential for rare, serious, and life-threatening rashes, such as Stevens-Johnson syndrome. Therefore, this medication is not considered first- or second-line pharmacological treatment and should be used with extreme caution in adults only. Patients and caregivers should be counseled on the potential for the rare, but serious, adverse skin reaction and potential for misuse (Daughton & Kratochvil, 2009). In a randomized, placebo-controlled study, insomnia was the only adverse effect noted to be significantly increased with use of modafinil (Biederman, et al., 2006). However, ongoing monitoring for side effects and efficacy should regularly occur to ensure ongoing need for use as is required with all ADHD medications, especially of controlled substances like modafinil.

-Amantadine

Mechanism of Action: Amantadine has dopaminergic effects due to dopamine uptake inhibition in addition to being an N-methyl-D-aspartate (NMDA) receptor antagonist (Donfrancesco et al., 2007).

Amantadine has demonstrated efficacy in the treatment of ADHD symptoms and shown tolerability in children as young as 1 year of age when used as an antiviral medication. However, it is not FDA-approved for the treatment of ADHD. While reduction of ADHD symptoms may be less than with use of stimulants, amantadine has been shown to improve symptoms of irritability, impulsiveness, hyperactivity, aggression, and

oppositional behavior in children (Donfrancesco et al., 2007). In a small study comparing the effects of amantadine to methylphenidate in children with ADHD, similar reports of side effects were observed, with the exception of decreased appetite and restlessness, which were both less pronounced with amantadine (Mohammadi et al., 2010). While efficacy was not proven in the study, reduction in ADHD symptoms was not significantly different in the amantadine group versus the methylphenidate group.

Amantadine can be used as a nonstimulant option for those with ADHD who fail stimulants and other first- and second-line agents or are unable to use stimulants. Other side effects to consider prior to initiation would be suicidal ideation, psychosis, orthostatic hypotension, and dizziness (Gold Standard Inc., 2021).

-Tricyclic Antidepressants

Mechanism of Action: Tricyclic antidepressants (TCAs) increase norepinephrine and serotonin in the synapse by inhibition of presynaptic reuptake. Other effects include inhibition of histamine and acetylcholine activity.

The AACAP*'s Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder (2007)* indicate that TCAs can be used for reduction of symptoms in the treatment of ADHD, but evidence is weaker than the first-line agents. The AAP's *Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents (2019)* does not list TCAs as treatment options in their subsequent guidelines for the treatment of ADHD. Additionally, there are no TCAs approved by the FDA for the treatment of ADHD, although there is some evidence supporting their use. Due to their effect size being lower than other agents, TCAs are not used as first-line treatment, but use after failures of trials of first- and second-line agents or as an adjunctive treatment could be recommended. Desipramine is listed in the AAFP's guideline *Diagnosis and Management of Attention-Deficit/Hyperactivity Disorder in Adults (2012)*, but in a subsequent publication in 2019, no TCAs are listed as treatment recommendations for ADHD (Loskutova et al., 2019; Post & Kurlansik, 2012). If TCAs are utilized in the treatment of ADHD, concurrent behavioral therapy could also be beneficial (Pliszka, 2007). TCAs can be utilized when depression, anxiety disorders, or concerns for misuse of prescription stimulants are present. Desipramine can be beneficial for treatment of ADHD in patients with a coexisting tic disorder, but caution should be exercised due its association with sudden death (Lexi-Drugs, 2021). Desipramine, nortriptyline, and

imipramine have been utilized off-label for treatment of ADHD symptoms. Due to cardiovascular concerns, a comprehensive cardiac evaluation should be conducted prior to initiation of TCA treatment (Lexi-Drugs, 2021). Other adverse events with use of these three TCAs include weight gain, sedation, insomnia, agitation, and sexual dysfunction (San Francisco Department of Public Health, 2020).

Medication Management, Monitoring, and Follow-Up

When a patient is undergoing treatment for ADHD, appropriate monitoring and follow-up is as fundamental as the diagnosis itself. Timing of scheduled visits becomes key in the pharmacological management of this disorder and can have significant effects on the outcome of treatment. Despite monitoring recommendations, only 42.1% of children aged 6 to 12 years on a commercial Health Maintenance Organization (HMO) and 43.9% of children on Medicaid's HMO received follow-up care within 30 days of initiating a new medication for ADHD in 2020 (National Committee for Quality Assurance [NCQA], 2022). Additionally, less than half of children on a commercial HMO and only 53.5% of children on Medicaid's HMO received at least 2 follow-up visits within 9 months of initiating a drug (NCQA, 2022). Monitoring during follow-up visits should include a comprehensive review of systems, adverse effects, and efficacy of treatment. Surveillance of compliance, proper storage of medications, and the possibility of diversion is also recommended for a complete assessment. To ensure proper management, it is important for the patient to be monitored by a clinician with prescribing ability.

Upon initiation of a new medication, Johns Hopkins' "Best Practice and Measure Tips" recommends a follow-up visit within 14 to 21 days (Johns Hopkins Medicine, 2022). The AAP and AAFP recommend follow-up every 30 days until ADHD symptoms improve and then every 3 to 6 months thereafter (AAFP, 2023a; Wolraich et al., 2019). The CHADD organization recommends monitoring of the patient at least quarterly if they are stable on their regimen, and several organizations recommend scheduling 30-, 60-, and 180-day follow-up visits at the start of a new medication (CHADD, 2019; Johns Hopkins Medicine, 2022). In West Virginia, a patient should be evaluated at least every three months, since stimulant prescriptions cannot be provided for more than a total of three months' supply pursuant to West Virginia Code of State Rules, § 15-2-8. The frequency of visits can increase with the presence of coexisting conditions. At the follow-up visits, height, weight, blood pressure, and heart rate should be regularly monitored and documented. A review and documentation of functional abilities, including diurnal fluctuations, is also advisable.

Once a treatment plan inclusive of medication has been started, it is essential for effective symptom management that the dose be appropriately titrated. This process can take several months

and requires close monitoring, potentially weekly, by the clinician. For stimulants, the lowest effective dose with minimal side effects is recommended. In addition, efficacy of treatments should be regularly evaluated throughout the process to ensure use of the optimal agent or combination of agents. ADHD rating scales from the patient and other reporters may be utilized to monitor treatment response.

At each appointment, assessment of the patient's compliance to the treatment plan should be conducted. It is helpful to directly ask if the patient is taking their medication as prescribed to gain a better understanding of their clinical response. Further questions for the patient/family/caregiver should include or be constructed to determine if adverse effects of the medication are present.

Frequency and severity of side effects can be similar among different stimulants; however, a patient may be more tolerant to one stimulant over another (Adesman, 2001). In some instances, adverse effects may subside over time or with appropriate titration or tapering of the medication, and these expectations should be discussed with the patient and caregiver. In addition, height, weight, and body mass index are important to chart at each visit to track growth changes, and heart rate and blood pressure should be taken to monitor any cardiac effects.

At times, there will be less than ideal symptom control or an intolerable adverse event with medication management. At that time, the dose should be examined and potentially further titrated for efficacy or reduced to alleviate a side effect of the medication. If the patient is completely unable to tolerate a medication or there is not adequate symptom control after trials of maximum dosage, a trial of another agent is likely warranted. It is imperative to evaluate true failure of a medication versus timing of administration and intended duration of coverage when rebound symptoms appear. A simple dose adjustment or timing of administration may allow for intended symptom control. Furthermore, if failure of two different stimulants occurs, consider lack of adherence, the potential for diversion, or reevaluation of diagnosis or coexisting conditions. Assist the patient with additional management strategies and referrals where warranted.

A reiteration of the expectations of treatment goals and expected outcomes with the patient or caregiver may be required as well prior to determining that a medication has failed, especially for those medications that can take months to see the full effect. Also, making sure the patient and caregivers have clear and realistic goals for ongoing symptom management is important. A patient may deem a medication a failure, but it is known that some symptoms of ADHD cannot be managed with medication. Adequate assessment of symptom improvement, medication compliance, and medication storage (active ingredients could degrade and cause diminished response if stored improperly) should be conducted before a medication is considered a failure. For

those symptoms that may not be improved with medication, appropriate referrals for nonpharmacological treatments should be considered. Feedback from family, other professionals, teachers, or employers should be discussed. Concerns the patient or parent/family/caregiver may have should be handled at follow-up visits, and the regimen should be adjusted as needed.

Lastly, it is prudent to monitor for signs of misuse and diversion. The treatment of adolescents and adults with stimulants necessitates special attention. Despite this caution, there is no evidence that stimulant use in the context of treatment of ADHD increases the incidence of SUD. Follow-up visits allow for monitoring of adherence to the prescribed regimen to be verified through pill counts, the controlled substance monitoring program, and urine drug testing (where appropriate). Regular screenings should occur for signs of misuse or addiction, primarily for adolescents and adults. Follow-up visits are also a time to ensure the medication is being appropriately secured to prevent theft and diversion. For further information on patient risk screenings and other risk reduction strategies, please refer to the section entitled "Risk Reduction Strategies".

- Weight Management and Growth Suppression

Weight and growth management are key aspects of caring for individuals with ADHD. Specifically, managing weight is a primary concern in adults, whereas monitoring weight and growth is essential in children and adolescents. Multiple studies have shown an association between ADHD and increased rates of obesity. In addition, ADHD medications could impact weight gain and growth because of the side effect of appetite suppression. Therefore, long-term monitoring and management of weight across the lifespan and appropriate monitoring of growth in childhood and adolescence is an important aspect of caring for patients with ADHD.

A relationship between ADHD and being overweight has been evaluated in both children and adults. Boys diagnosed with ADHD in childhood were twice as likely to be obese in midlife at a 33-year follow-up than those without ADHD (Cortese et al., 2013). A subsequent study confirmed these results after following hyperactive boys to a mean age of 27 years; the study group had double the rate of obesity (40% vs. 20%) regardless of whether ADHD did or did not persist to that age (Barkley et al., 2008). It has been shown that the symptoms of ADHD are significantly associated with the risk of being overweight, and this observation was demonstrated in both children and adults (Pagoto et al., 2009; van Egmond-Frohlich et al., 2012). ADHD symptoms, in combination with deficits in executive functioning, likely lead to poor eating habits and less successful efforts at weight loss (Cortese et al., 2013). Due to this increased risk of being overweight, patients with ADHD should be closely monitored and appropriately counseled and/or referred to a specialist to ensure healthy eating habits and adequate nutrition are incorporated into

their daily lives.

While the risk of being overweight is a concern for patients with ADHD due to the symptomology, conversely, weight loss and reduced growth can also present due to appetite suppression when stimulant medications are prescribed. Research indicates that such medications can impact weight, with treated children and adolescents showing approximately 1.6 times the odds of being underweight after adjusting for key demographic and health factors. It is essential for healthcare providers to monitor growth regularly and to be cognizant of potential appetite suppression in these patients (Waring & Lapane, 2008). Patients with ADHD are less likely to adhere to a traditional breakfast, lunch, and dinner schedule and more likely to eat more frequently throughout the day. In this cohort of ADHD patients, a link was observed to dietary choices of lesser nutritional quality, specifically exhibited in the reduced intake of fruits and vegetables and an increased preference for sugary beverages. (Ptacek et al., 2014).

Given these dietary challenges, it may be necessary in patient-specific cases to refer a patient to a dietitian to address these concerns. Dietitians provide education about foods rich in nutrient content and advise against choosing satiating "empty calories" (Phillips, 2014). Along with providing education, they can also collaborate with patients, families, and caregivers to develop tailored eating plans. These plans incorporate balanced meals and scheduled eating times, helping alleviate erratic eating patterns and ensuring patients meet their dietary requirements.

For an accurate assessment of growth and nutritional status in patients with ADHD, it is recommended to consistently document height and weight on growth charts and medical records. A dietitian or the patient/family/caregiver can maintain this record, ensuring that it informs dietary recommendations and adjustments during consultations. Patients can be educated on healthy eating habits since patients with ADHD are at risk of becoming overweight.

If weight loss or reduced growth is a concern due to treatment with stimulant medications, additional education can be provided to ensure adequate nutritional status when treated. Some strategies to promote healthy growth include ensuring that breakfast is provided before the morning dose of stimulant medication, which is crucial, and this meal should encompass as many food groups as possible to provide a balanced nutrient intake. Furthermore, a dietitian should consult with the patient's healthcare provider to determine whether a drug holiday is safe and appropriate for the patient. This time could allow the patient to regain appetite and increase caloric intake on those days, supporting healthier growth patterns (Phillips, 2014).

Planned Drug Holidays

A drug holiday is defined as a period of time when a patient has stopped medication with

the intent of restarting it at a later date. The holiday could be short term, such as a weekend, or long term, such as a summer break. Drug holidays are utilized for patients who only require pharmacological control at certain times, for instance, on days with school or work. A comprehensive study found that drug holidays are commonly attempted for approximately 25% to 70% of patients with ADHD and most frequently are trialed on a school holiday (Ibrahim & Donyai, 2018). While a hiatus from medication use has been associated with potential growth benefits, increased physician intervention, re-sensitization opportunities, and less adverse events, drug lapses have been shown to cause withdrawal symptoms, poor adherence upon restarting, diversion potential, and apprehension among patients and parents/family/caregivers (Ibrahim & Donyai, 2014; Martins et al., 2004; National Guideline Centre, 2018). In children, it can also result in greater family stress from ADHD-related behaviors. Therefore, the use of a drug holiday is not recommended as standard care and should be a clinical decision based on individual patient-specific factors only when the clinician has reason to believe it would be beneficial. Individualized decision making between the clinician and patient and/or parent/family/caregiver is pivotal when deciding if implementation of a drug holiday is appropriate and warrants the potential risks associated with stopping and restarting a medication.

Drug holidays also require clinicians to further monitor their patients using medications for ADHD for efficacy, safety, and adverse events. The clinician can assess the continued need for pharmacological intervention and adjust or discontinue therapy when applicable (Lohr et al., 2021). For patients who have developed tolerance to a medication, drug holidays may allow for a mechanistic re-sensitization of neurons to regain efficacy upon re-initiation of the agent (Yanofski, 2011). ADHD symptoms and adverse events have shown clinical improvement when a drug holiday is implemented, but the quality of data for this evidence is low (National Guideline Centre, 2018). Insomnia and appetite suppression were significantly decreased during weekend holidays in male children using methylphenidate. In this study, it was hypothesized that a return of ADHD symptoms would occur on weekends, but no significant increase in symptoms was observed (Martins et al., 2004). Patients on ADHD medications should take in the same number of calories as those not on stimulant medications. If a patient is losing weight or is not gaining weight appropriately, clinicians should re-evaluate the dose and class of medication being prescribed.

Drug holidays from ADHD medications should not be trialed without consideration of the potential risks. Most children with ADHD who discontinue their medications will see an early re- emergence of ADHD symptoms, potentially impacting self-worth, self-esteem, compliance, and on-task-related factors during drug holidays, such as weekends and summers (Lohr et al., 2021). Methylphenidate, the agent of choice for young children, has a short half -life

(2-3 hours), increasing the chances of withdrawal symptoms during a planned drug holiday. Symptoms of withdrawal can range in severity and include dysphoric mood, fatigue, vivid or unpleasant dreams, insomnia, hypersomnia, psychomotor agitation or retardation, and increased appetite (American Psychiatric Association, 2000). With regard to symptom control, parents/family/caregivers can be apprehensive about removing drug therapy for any period, particularly when their regimen is stable. Parents/families/caregivers have voiced concerns over home behavior and the return of baseline ADHD symptoms as barriers to implementation of drug holidays (Ibrahim & Donyai, 2014).

Adherence and medication availability for diversion are potential concerns when considering appropriateness of drug holidays. Patients placed on a drug holiday are more likely to be non-adherent when therapy is reinitiated (National Guideline Centre, 2018). Additionally, in typical practice, most clinicians prescribe 30-day supplies of ADHD medication, so if a drug holiday is trialed without alerting the pharmacy, the patient will have a surplus of medication. This surplus could increase the potential for nonmedical use and/or diversion, where the patient or family member may try to share or sell the unused supply.

If a prescriber, after careful clinical consideration, decides to implement a drug holiday, one potential benefit is the possibility of improved growth outcomes. As previously described, prescription stimulants are used first-line for pharmacological management of ADHD in most age groups and have been associated with growth retardation, mostly in the youth population (Greenhill et al., 1984). A 2017 study of 579 children aged seven to 10 years of age found that those who continued with medication therapy had a 2.36- to 2.55-centimeter reduction from their expected adult height at follow-up, and when compared with their peers, they were found to be an average of 1.29 centimeters shorter (Swanson et al., 2017). Implementing a drug holiday and limiting stimulant exposure may reduce these negative effects on growth. Height and weight changes in children taking stimulants have also been reported to decrease with long-term use. Children taking drug holidays saw a rebound in weight but not height, suggesting that longer holidays are needed to impact height (Waxmonsky et al., 2020). Additionally, children are less likely to suffer growth suppression with longer drug holiday periods rather than short periods (Ibrahim & Donyai, 2014; Martins et al., 2004). Ultimately, the decision to implement a drug holiday should be a very patient-specific decision between the patient and/or parents/family/caregivers and the clinician. Evidence for routine use of drug holidays is lacking, so utilization of a drug holiday is not standard care. A risk-benefit assessment for each patient is necessary to determine the potential tolerability and applicability of a drug-free period if the patient's circumstances warrant this consideration. If a drug holiday is trialed, patients should be

closely monitored, and re-initiation of medications should occur if significant functional impairment occurs. In cases where the patient functions well in the trial drug holiday, permanent medication discontinuation can be considered.

Intentional Discontinuation of Pharmacologic Therapy

The decision to discontinue pharmacological ADHD treatment agents is one that requires careful, individualized consideration by the clinician and patient. Removal of pharmacological agents should be done under the supervision of the clinician in a controlled manner and closely monitored. Most agents that treat ADHD should be tapered to avoid abrupt discontinuation causing withdrawal symptoms. Although discontinuation of medications is not a viable option for many patients, clinicians may feel it is appropriate to attempt a medication-free trial in cases where the patient has been well controlled or symptom free for an extended period without dose adjustments, the original diagnosis of ADHD is in question, or there are changes in the patient's current medical history.

In 2021, the *Frontiers in Psychiatry Journal* published a review and analysis of 35 articles (including randomized controlled trials, case studies, clinical guidelines, and literature reviews) on the intentional discontinuation of psychostimulants used to treat ADHD. It was found that while most patients experienced rapid re-emergence of ADHD symptoms following stimulant discontinuation, a subset of the population, approximately 30%, did not experience re- emergence of symptoms. The data suggested older youth (average age, 13.8) were less likely to have symptom recurrence than younger youth. Of note, the majority of patients in these studies were predominately male (Lohr et al., 2021). As discussed in the "Planned Drug Holidays" section, if a thorough review of the patient's current symptomology warrants a pharmacological discontinuation, the clinical decision to discontinue medication can be trialed based on individualized, patient-specific factors. Most sources recommend attempting the trial when a significant effect would not be observed in either academic or vocational efforts.

Genetic Testing

Pharmacogenomic tests are available, including such products as GeneSight, BiogeniQ, ClarityX, Invitae, and Traitwell PGX, among others, to assist with the treatment of patients with ADHD and many other conditions. These tests use algorithms to identify gene variations, which can alter drug metabolism, tolerance, and response, through a simple lab blood draw or an at- home buccal swab. Individualized drug and dosing recommendations for some psychotropic medications are generated based on a patient's genetic makeup. While theoretically useful, there is currently not enough data to conclude that this testing results in better patient outcomes in terms of symptom

improvement or decreased adverse drug effects. Therefore, it is not recommended to use pharmacogenomic testing in the pharmacological management of ADHD.

While it is not recommended to regularly perform pharmacogenetic testing before prescribing pharmacotherapy for ADHD, clinicians may choose to use pharmacogenomic tests to guide clinical decision making after repeated medication failures (Krull & Chan, 2021). Candidates for testing may include those patients who are treatment-experienced with multiple medication failures and are having trouble finding regimens that offer sufficient efficacy or tolerability. The clinician can utilize testing results to make an informed decision regarding an individualized treatment regimen selection in treatment resistant patients; however, the results can require careful interpretation. Clinicians should not utilize results to solely dictate medication selection. Assessing the patient's perceived medication response, tolerability, drug interactions, adherence, medication cost, and kidney and liver function should still be primary determining factors in medication selection.

Many pharmacogenomic tests have not obtained FDA approval and are seldom covered by third-party payers, resulting in additional fees for patients. Some insurance plans may cover this testing, but it is more likely that the patient will have significant out-of-pocket costs. Even for those with third party payer coverage, costs can be estimated to be anywhere between $0 to $330, and coverage can be subject to prior authorization and other payer restrictions (Pyzocha, 2021).

Overall, pharmacogenetic testing in the realm of psychiatry has not proven to be cost-effective. Careful monitoring of efficacy and side effects of medication trials tend to provide more information and successes than selection of a medication simply based on heredity without considering other environmental factors (Rosenblat et al., 2017; Zubenko et al., 2018). Therefore, as mentioned, pharmacogenetic testing before prescribing medication for ADHD is not recommended, and its use after multiple medication failures may be limited by third-party payers.

Prescription Stimulant Misuse

As the prevalence rates of ADHD increase, the number of stimulant prescriptions observed over the last decade has also grown (Piper et al., 2018). While prescription stimulants prescribed by a clinician for legitimate medical use have profound benefits in the context of treatment of ADHD when used appropriately, there is also the potential for misuse and addiction. Prescription misuse includes using medication without a prescription, using a medication other than as prescribed (e.g., greater amounts, more often, or longer than prescribed), using medication in any

way other than directed by the prescriber, or using the medication for recreational purposes or without therapeutic intent.

In 2019, it was reported that 7.5% of youth (12-17 years) used a prescription stimulant in the last year, and in the same age group, 23.4% of those who had utilized any prescription stimulant in the last year reported misuse. For young adults (18-25 years), it was reported that 12.8% had utilized a prescription stimulant in the last year, and among those, 45.2% reportedly misused a prescription stimulant in the last year. Further, rates of use in young adults have increased, and more in this age group are engaging in prescription stimulant misuse than prescribed medical use (Safer, 2015). The increasing prevalence of prescription stimulant misuse has created a major public health concern due to the addictive potential and increased risk of adverse events, especially with misuse via non-oral routes of administration, such as intravenous or intranasal misuse (SAMHSA, 2021).

To compound the issue, a college-based study found that those who misused stimulants were 2.7 times more likely to develop a SUD when compared with controls, more specifically, 4.7 times more likely to develop a combined alcohol and drug use disorder (Wilens et al., 2016). It is important to note that while those with untreated ADHD are more likely to develop a SUD, treatment with prescription stimulants for ADHD when used as prescribed does not increase the risk of later substance use disorders (Humphreys et al., 2013). In fact, it has been shown that when stimulants are initiated as early pharmacological treatment of ADHD and used for longer durations, the risk of developing a SUD is lower (McCabe et al., 2016).

Misuse of prescription stimulants is not always to get “high” or “party,” as with other misused substances. Frequently, misuse has been associated with a desire for increased productivity and improving alertness or concentration (Wilens & Kaminski, 2019). Misuse often occurs for the purposes of increasing academic performance, staying awake, and maintaining concentration or focus (Drazdowski et al., 2020; Schepis et al., 2020). However, non-medical use of prescription stimulants to increase academic performance in those without an ADHD diagnosis is a misconception and not supported by the literature (Arria & DuPont, 2010). On the contrary, for those appropriately diagnosed with ADHD, use of prescription stimulants as prescribed by a healthcare professional has been shown to reduce the negative impact of ADHD on school performance.

Prescription stimulant misuse is also a concern among prescribers. When examining the

perceptions of prescribers, 84% believed stimulant misuse is a problem, and 59% suspected one or more of their patients were diverting their stimulant medication (Colaneri et al., 2016; Loskutova et al., 2020). As a result, 44% of prescribers have counseled patients often or very often on the legal consequences of diverting medication, while 46% have counseled patients on stimulant misuse (Colaneri et al., 2016). Therefore, the comprehensive, ongoing management of ADHD should include appropriate prevention measures when prescription stimulants are utilized as part of the treatment plan for all patients but especially when prescription stimulant misuse is suspected. Such strategies include patient risk screenings, urine drug testing, use of the prescription drug monitoring program established by West Virginia law, patient provider agreements, pill counts, and more, which are further described in the next section.

Risk Reduction Strategies

Risk Screenings

While there are currently no screening tools to specifically identify prescription stimulant misuse, there are various assessments that can be used to assess risk of substance misuse and behavioral health for both adolescents and adults. With regard to older children and adolescents, the AAP recommends universal screening for substance use in pediatric primary care settings of patients aged 12 to 17 years of age. There are various screens used to detect potential for misuse of various substances and full assessments to administer following a positive screening. These are summarized in APPENDIX 3.3: Screening Tools for Substance Use: Adolescents, APPENDIX 3.4: Screening Tools for Substance Use: Adults, and APPENDIX 3.2: National Institute on Drug Abuse (NIDA) Screening Tools Chart. Literature shows that young adults tend to misuse prescription stimulants at the highest rates, so this ongoing screening should continue through adulthood. In adult patients with ADHD, it is also recommended to utilize the Screenings Brief Interventions Referral Treatment (SBIRT) model in patients with ADHD and SUD, and the AAFP recommends specific measures to be completed based on ongoing patient risk in all adult patients with ADHD (AAFP, 2019; Huang et al., 2020). Use of these ongoing risk screenings will assist the clinician in determining if the patient is at low or high risk for misuse and developing a treatment plan that is most appropriate for the patient based on that risk. Clinicians should familiarize themselves with the various screening and assessment tools to ensure appropriate scoring is completed.

Depending on age and risk factors identified in the screening/assessment for misuse, patients can be evaluated to see if they are candidates for use of prescription stimulants in the

treatment of ADHD. A patient with a high risk for substance misuse may not be a candidate, and confirmed active substance misuse would render the patient unsuitable to be a candidate for use of controlled prescription medications. If use of a controlled substance is warranted, these screening tools should be utilized in the ongoing monitoring of risk of misuse. If substance use or potential for substance use is identified as a result of these screenings and assessments, further steps should be taken to help reduce and prevent adverse effects of substance use, including but not limited to treatment and/or referral to a SUD treatment center. See APPENDIX 3.3: Screening Tools for Substance Use: Adolescents, APPENDIX 3.4: Screening Tools for Substance Use: Adults, and APPENDIX 3.2: National Institute on Drug Abuse (NIDA) Screening Tools Chart for more information.

Drug Testing (Urine/Blood)
(see APPENDIX 3.5: Urine Drug Screening & Testing)

Drug screening/testing is another important mechanism that can be utilized to monitor adherence to the prescribed pharmacotherapy and detect the use of other substances that may put the patient at an increased risk of an adverse event or overdose occurring. In this section, urine drug testing will be the specific focus due to it being the most used method of drug testing. It is reasonable for clinicians to administer urine drug tests to adult patients being considered for prescription stimulant treatment of ADHD. New patients should have a urine drug test conducted when starting therapy with a controlled substance to ensure they are not taking any unreported prescription or illicit substances. Urine drug testing results should be evaluated prior to when treatment decisions are made so that clinicians can make an informed treatment decision. Ongoing drug testing can be repeated as often as the clinician feels is necessary to ensure no concomitant illicit drug use during treatment as well as to verify compliance with the prescribed medication(s) (Huang et al., 2020). In many cases, urine drug testing and urine drug screening are covered by insurance plans, particularly when they are deemed medically necessary for monitoring compliance or managing substance misuse.

In the context of ADHD management in adults, it is recommended that a baseline urine drug test be completed in addition to random tests (at least yearly) during stimulant treatment to monitor compliance, detect use of illicit substances, and monitor for possible diversion (Huang et al., 2020). The AAFP recommends consideration of periodic random urine drug testing to verify patient compliance to the agreed-upon treatment plan for all adult patients with ADHD (Post & Kurlansik, 2012). For patients exhibiting “red flag behaviors,” such as missing appointments and

requesting early refills, urine drug testing should be performed. It is imperative that clinicians conducting urine drug testing on adults be educated regarding the interpretation of testing results to be able to appropriately adjust treatment plans and refer for more specialized evaluation if substance use is suspected.

With regards to drug testing in children and adolescents, further evidence-based studies are needed to guide best practices. However, pediatricians and family care clinicians should be prepared to deter, detect, and reduce the illicit use of drugs by children and adolescents, and urine drug testing is a tool to do such. As with clinicians of adult patients, clinicians of adolescents and children should be appropriately trained in interpreting the results, and abnormal results should be clinically evaluated as part of the treatment process (Levy et al., 2014). The AAP does not endorse the use of at-home testing kits due to the potential for parental misinterpretation of results, lack of evidence indicating that routine testing reduces drug use, and potential strain on the parent/child relationship. Parents/families/caregivers should be counseled that if substance use is suspected, professional evaluation should be considered (Levy et al., 2014).

When preparing to conduct a urine drug test, it is imperative to know the difference between drug screening and a drug test and when it is appropriate to utilize each. Drug screening can result in false-positive or negative results that can only be verified via more specific testing. Therefore, clinical treatment decisions should not be made solely on urine drug screening results, and confirmatory results should follow to verify any abnormal results (Webster, 2013). The following table summarizes the difference between drug screening and a drug test, which can aid clinicians to determine which is appropriate.

Drug Screening Versus Drug Testing (Webster, 2013)	
Urine Drug Screening (UDS)	**Urine Drug Testing (UDT)**
Immunoassay screen (i.e., cup)	Gas Chromatography-Mass Spectrometry (GC-MS) or Liquid Chromatography-Mass Spectrometry (LC-MS/MS)
In-office, point-of-care, or lab-based	Laboratory, highly specific and sensitive
Results within minutes	Results in hours or days
Detects a few legal and illicit medications by structural class	Measures concentrations of all medications, illicit substances, and metabolites
Guidance for preliminary treatment decisions	Definitive identification and analysis
Cross-reactivity common: more false positives	False-positive results are rare
Higher cutoff levels: more false negatives	False-negative results are rare
Less expensive	More expensive

Prescription Drug Monitoring Programs
(see APPENDIX 3.6: Prescription Drug Monitoring Program (PDMP))

Prescription drug monitoring programs (PDMP) are available in nearly all states to provide a tracking mechanism for controlled substances. The electronic database allows for clinicians, pharmacists, and state agencies to readily track prescribing trends of controlled substances and drugs of concern. The AAP states that this tool can be utilized as a means of identifying and preventing diversion activities, and the AAFP recommends use of this tool as a risk reduction strategy in all adult patients, regardless of their risk level (AAFP, 2019; Wolraich et al., 2019). Regular use by clinicians allows for enhanced patient monitoring to prevent misuse and diversion of controlled substances. Patient records can be reviewed to ensure that they are not receiving any unreported controlled substances from other clinicians, and pharmacists can utilize the tool to verify that the patient is not receiving multiple controlled substance prescriptions from multiple pharmacies or prescribers.

In order to ensure that timely and accurate information is available, all clinicians or pharmacies who dispense Schedule II, III, IV, and V controlled substances or opioid antagonists to residents of West Virginia must provide information to the West Virginia Board of Pharmacy within 24 hours of dispensing per West Virginia Code of State Rules § 15-8-4. All licensed prescribers in West Virginia must check the PDMP at the initiation of each Schedule-II controlled substance, as well as for any opioid or benzodiazepine, and at least annually thereafter if the prescriber continues to treat a patient with a controlled substance. Although the West Virginia PDMP must be checked at least annually by a prescriber treating a patient with controlled substance, the patient's PDMP records should be reviewed as frequently as the clinician feels is appropriate, even as often as with each prescription provided or when early refills are requested.

Patient and Provider Agreements
(see APPENDIX 3.7: Patient & Provider Agreements)

A patient-provider agreement is a written document signed by the healthcare clinician and patient (or caretaker) outlining the roles and responsibilities of both parties regarding treatment. The overall purpose of the agreement is to promote responsible medication use by the patient, clarify understanding of the risks and benefits of the medication(s), provide consent for urine drug screens and pill counts as deemed necessary by the clinician, and serve as an agreement for regular follow-ups with the clinician. Also known as a controlled substance agreement, this document serves as both an educational tool and a safety measure.

When starting therapy with a controlled substance, the patient and/or family should be informed of the risks (dependence, adverse events, etc.) and benefits of the proposed treatment plan, inclusive of a prescription stimulant. Safe storage and disposal of the medication should be

reviewed. Counseling regarding the consequences of diversion and/or misuse, that ongoing monitoring of refill requests will be performed, and that prescription drug monitoring programs will be reviewed regularly should be part of the discussion between the clinician and patient/caregiver. The use of patient-provider agreements has been implemented by clinicians to reduce diversion when prescription stimulants are prescribed. Use of these agreements ensures patients and their parents/families/caregivers are educated and advised of the expectations associated with the initiation of treatment with a controlled substance and establishes a mutual commitment from all parties to work toward reaching treatment goals. It also alerts patients and caregivers to those situations constituting a viable reason for a clinician to discontinue the prescription of controlled substances should the benefits of ongoing treatment no longer outweigh the associated risks.

The decision to initiate treatment with a controlled substance, such as prescription stimulants, should be a shared decision-making process between the healthcare clinician and the patient/parent/family/caregiver. The Substance Abuse and Mental Health Services Administration (SAMHSA) recommends obtaining signed agreements from patients or their caregivers as an approach to prevent stimulant misuse (SAMHSA, 2021). Also, the AAFP recommends that clinicians consider using patient and provider agreements to prevent misuse and diversion of prescription stimulants for adults with ADHD (Post & Kurlansik, 2012). These contracts, or agreements, should be in place prior to initiating treatment with prescription stimulants and updated every two to three years (Huang et al., 2020).

Pregnancy and ADHD Medications

The CDC reports that one in 100 women take ADHD medication while pregnant; this number more than doubled from 1998-2011. The existing safety data on use of pharmacological agents to treat ADHD during pregnancy is limited, but use of ADHD medications during pregnancy may be related to birth defects such as gastroschisis, omphalocele, and transverse limb deficiency (Anderson et al., 2018). Pregnant women are often excluded from trials examining the effects of these agents; therefore, more data is needed regarding the safety of the developing fetus to confirm the associated risks. There are certain patient-specific scenarios where the clinician may feel treatment with an ADHD medication is appropriate during pregnancy, despite the fetal risks. In these cases, close monitoring of mother and fetus is necessary.

Stimulant medications have demonstrated negative effects during fetal development in animal studies (CHADD, 2022c). Animal models using rats and zebrafish have suggested prenatal exposure to amphetamines is associated with changes in dopaminergic transmission and receptor

expression in regions of the brain and post-pubertal decreased motor activity (Freeman, 2014). Fetal malformation and death were observed in mice following parenteral administration of amphetamine doses of 50 mg/kg/day or greater (Noven Therapeutics LLC, 2022). There are also several studies in rodents that have noted long-term neurochemical and behavioral alterations, including learning and memory deficits, altered locomotor activity, and changes in sexual function with prenatal or early post-natal exposure to amphetamines at doses similar to those used clinically (Noven Therapeutics LLC, 2022). It is hypothesized that vasoconstriction of the placental blood vessels caused by amphetamines increases the risk for fetal growth restriction (Cohen et al., 2017).

To date, there have been no adequate studies to gauge safety and tolerability of ADHD medications during pregnancy in humans at doses utilized in the management of ADHD. The available literature in humans typically examines the effects of illicit stimulants in the context of SUD rather than ADHD treatment, so doses, or exposure amounts, used in studies are generally well beyond what would be expected in the treatment of ADHD. However, smaller, underpowered studies have been published examining the effects of prescription stimulant doses on developing fetuses. A cohort study suggested methylphenidate use in the first trimester was associated with a small increase in the risk of cardiac malformations, 12.7 of 1000 infants not exposed (95% CI, 12.6-12.9) versus 18.8 of 1000 infants exposed (95% CI, 13.8-25.6) to methylphenidate, yet amphetamine exposure in the context of prescription stimulant use was not shown to be correlated with a risk of cardiac malformation (Huybrechts et al., 2018). Amphetamine and cocaine misuse in pregnancy have been associated with low birth weight, prematurity, and an increase in maternal and fetal morbidity (Milanovic, 2010). Similarly, in a study to control weight gain, decreased infant birth weight was noted in pregnant women who continued to take dextroamphetamine after the 28th week of gestation (Naeye, 1983). A study with 38 participants showed methylphenidate misuse in pregnancy was associated with premature birth, growth retardation, and neonatal withdrawal symptoms, but the results were confounded by nicotine and alcohol use (Milanovic, 2010).

In the context of all medications to treat ADHD, not just prescription stimulants, fetal risk cannot be ruled out when using atomoxetine during pregnancy, as there is insufficient human data. In animal studies, a decrease in live fetuses, an increase in early resorptions, and increase in atypical origin of carotid artery and absent subclavian artery, and maternal toxicity were observed in rabbits when they received up to 100 mg/kg/day by gavage. In male and female rats given 50 mg/kg/day, two or 10 weeks prior to mating, decreases in pup weight and pup survival were observed. There were no adverse fetal effects observed when pregnant rats were treated with doses

up to 150 mg/kg/day by gavage (Eli Lilly and Company, 2009). Fertility effects were seen in rats administered various doses, including slight delays in vaginal patency (all doses), preputial separation (10 and 50 mg/kg), slight decrease in epididymal weight and sperm count (10 and 50 mg/kg), and slight decrease in corpora lutea (50 mg/kg) (Eli Lilly and Company, 2009).

For guanfacine, the available evidence is inconclusive to inadequate to determine fetal risk in pregnancy. Based on the last decades of data used in pregnancy, there has been no documented drug-associated risks of major birth defects, miscarriage, or adverse maternal or fetal outcomes. However, the use of guanfacine in pregnancy during this period has been infrequent (Shire LLC, 2019). Studies in rats have shown that guanfacine crosses the placenta; however, administration of guanfacine to rats and rabbits at 4 and 2.7 times, respectively, the maximum recommended human dose of 0.12 mg/kg/day did not result in evidence of harm to the fetus (Shire LLC, 2019). Doses of 13.5 times the maximum recommended human dose in rats and rabbits were associated with maternal toxicity and reduced fetal survival (Shire LLC, 2019).

Clonidine is known to cross the placenta in pregnant patients (Buchanan et al., 2009). Data over several decades has not determined a clear association between clonidine and the risk for major birth defects, miscarriage, and adverse maternal or fetal outcomes (Shionogi Pharma Inc., 2010). However, in pregnant female rats administered as little as one-third the maximum recommended human dose from two months prior to mating and throughout gestation, increased resorption was observed. Prenatal exposure to clonidine has resulted in neonatal transitory hypertension during the first three days of life and hyperactivity and sleep disturbances in older children (Bunjes et al., 1993; Huisjes et al., 1986).

Pregnancy should, at the very least, trigger the clinician to have a thoughtful evaluation and discussion with the patient of informed consent around the risks and benefits of treating or not treating ADHD based on their individual history. In severe cases of ADHD, the benefits of using pharmacological agents during pregnancy may outweigh the risks. If treatment is deemed necessary, with the benefits of treatment outweighing the risk, the clinician should also make an effort to re-evaluate the dose of medication so that the lowest needed dose of medicine to improve functioning is considered. While data focusing on stimulants is lacking, similar findings have been shown with other psychotropics. Changing medications or introducing new ones may introduce additional and unknown challenges, rather it may be more beneficial to maintain patients on the lowest effective dose that has proven efficacy for maintaining their health and functioning. The risk of untreated or undertreated ADHD should not be ignored. Positive outcomes associated with the pharmacological management of ADHD during pregnancy are related to driving safety, decreased obesity, increased self-esteem, social functioning, and academic performance. Open

discussion between the clinician and patient is key to determining the best course of therapy for all patients, including those who are pregnant or planning to become pregnant.

Lactation and ADHD

The ability to breastfeed is another area of concern for clinicians of women with ADHD. Low levels of stimulants have been shown to be present in breast milk at normal doses. Larger doses of stimulants consumed when lactating have been associated with decreased milk production (Drugs and Lactation Database [LactMed®]., 2006). The American College of Obstetrics and Gynecology (ACOG) states that amphetamines inhibit prolactin release, which can result in a reduced supply of breast milk (ACOG, 2011). This effect is more significant at higher doses and more common with amphetamine and dextroamphetamine. Unfortunately, neurological development of exposed infants has not been studied (Drugs and Lactation Database [LactMed®], 2006). Below is a quick reference guide of common stimulants and non- stimulants used for ADHD therapy during lactation.

Amphetamine:

- Large doses may result in decreased milk production.
- One study showed a positive correlation between time after birth and lower amphetamine levels after feeding.
- A few studies showed no impact on breastfed infants.
- Breastfeeding is generally discouraged in populations with stimulant use disorder.

Dextroamphetamine/Lisdexamfetamine:

- Large doses may result in decreased milk production.
- Breastfed infants were anticipated to have 5% of the maternal dose.
- Of the few infants studied, all showed normal progress and development at two years of age.

Methylphenidate:

- Limited evidence shows very low and undetectable levels in infant serum and breast milk.
- Limited information to confirm or deny effects on prolactin/breast milk production.

- All infants reviewed met normal development measures and growth milestones.

Atomoxetine:

- No published information is currently available.
- Reports from manufacturer Eli Lilly share that there were two infants who slept longer than typical infants, but no serious adverse events occurred.
- Lack of information suggests using an alternative agent if possible.

Guanfacine:

- No published information is currently available.
- Decreasing serum prolactin levels were seen for up to seven years of continuous use in men and non-nursing women; however, this may not impact breastfeeding ability.
- Lack of information suggests using an alternative agent if possible.

Clonidine:

- Recommended to use alternative agents due to infant serum levels reaching 50% that of maternal levels.
- Some studies showed no adverse effects on breast-fed infants, while one case reported drowsiness/hypotonia/seizures that resolved after discontinuation.
- Some reported cases of galactorrhea that were resolved with drug discontinuation.

Additional Information Related to the Treatment of ADHD: Complementary and Integrative Medicine

Complementary and integrative medicine (CIM) refers to the use of non-mainstream approaches in tandem with conventional medical approaches (National Institutes of Health [NIH], 2016). Many patients and parents/family/caregivers explore CIM for a variety of conditions, and ADHD is no exception. Clinicians must be prepared to advise and counsel patients and parents/family/caregivers about safe, effective, age-appropriate, and evidence- informed therapies, including both mainstream treatments and CIM. There are many reasons patients and parents/family/caregivers seek these treatments, some of which include trying to improve overall health and quality of life, avoiding potential side effects of medications, complementing more traditional therapies, and trying to do everything possible to treat the symptoms. Some patients and

parents/families/caregivers may be hesitant to discuss these complementary treatments with clinicians for a variety of reasons. It is important for clinicians to discuss these treatments with patients and their parents/family/caregivers to enhance the therapeutic alliance and understand their values and attitude toward treatment. It is also important for the treating clinician to have accurate knowledge of what CIM treatments patients are using so that they may counsel about potential adverse effects or interactions with medications.

The AAP clinical report "Pediatric Integrative Medicine" offers a framework to use with patients and parents/families/caregivers to discuss CIM treatments (McClafferty et al., 2017). A summary with slight adaptation is provided below.

- Ask about their experience with CIM. Disclosure may improve if the clinician offers examples (e.g., special diets, vitamins, supplements) to help jog their memory. If the patient/family/caregiver indicates that they have used non-medical treatments to help attention or behavior, ask what they have tried and how useful it was. If not, ask whether they have considered complementary treatments and which ones.
- Be respectful of the patient's/family's/caregiver's perspectives, values, and cultural beliefs. Having the conversation as part of a shared decision-making process will ensure that the clinician and the patient/family/caregiver are allies in the ADHD treatment plan. This also aids in understanding what the patient's/family's/caregiver's goals are for ADHD treatment.
- Consider other medications/supplements/herbals the patient may be taking and clarify ingredients in each. Identify any drug interactions that may be present.
- Monitor the response to the treatment. Clinicians must establish the measurable outcomes of the treatment, including what the target symptoms are and what improvements are realistic in a specific timeframe. In addition, subsequent monitoring for any interaction effects with supplements or other medications should be considered.
- Reevaluate a treatment if there is no response or if there is harm.

When educating patients/families/caregivers about CIM treatments, the clinician should encourage patients/families/caregivers to discuss their CIM research and questions, including what they have read on the Internet or elsewhere or learned from others. The clinician can help families differentiate between actual scientific evidence, scientific-sounding marketing, or anecdotal evidence. As with any treatment, the clinician should discuss potential risks and benefits for CIM therapies. The patient/family/caregiver should consider potential tradeoffs to trying a CIM therapy

before an evidenced-based behavioral intervention or medication, such as effect on grades or testing, financial considerations if treatment is not covered by insurance, or potential time lost from other therapies.

The clinician should be familiar with common CIM therapies, particularly those that are available in the local area. The National Center for Complementary and Integrative Health (NCCIH) website (http://www.nccih.nih.gov) is a valuable resource for patients and clinicians. It includes fact sheets on topics such as finding and evaluating online resources, safe use of complementary health products and practices, and using dietary supplements, including specific herbs and botanicals, wisely. Among the evidence-based resources available for healthcare clinicians and others involved in the care of patients with ADHD are continuing education video lectures, results of NCCIH research, literature reviews from PubMed, and evidence reports from the Agency for Healthcare Research and Quality (AHRQ). MedlinePlus also maintains a list of herbs and supplements with links to available information on safety, effectiveness, and interactions with medications and other supplements (https://medlineplus.gov/druginfo/herb_All.html).

When discussing specific CIM therapies with patients/families/caregivers, clinicians should consider the safety and effectiveness of the proposed treatment. This balance of potential risks and benefits provides a framework for making treatment recommendations. If a CIM treatment is known to be safe and effective, it should be recommended. If a CIM treatment is considered safe but it is either not effective or the effectiveness has not been established, that treatment could be tolerated with a discussion of what the desired outcomes are and a timeframe to assess those outcomes; if there is no response after a reasonable trial or if there is harm, the treatment should be stopped. For treatments that are not safe but are known to be effective, the clinician should discourage their use or consider using them with close monitoring after discussing the balance of potential risks and benefits with the patient/family/caregiver. CIM treatments that are not safe and not effective should be discouraged.

See the figure below and the following discussion of some CIM treatments that have been proposed for ADHD.

CIM Treatment Evaluation

		Is the therapy effective?	
		Yes	**No**
Is the therapy safe?	**Yes**	Recommend	Tolerate
	No	Monitor closely or discourage	Discourage

Kemper K, Cohen M. 2004. Ethics meet complementary and alternative medicine: new light on old principles.

Contemporary Pediatrics. 21:65.

Biochemical (dietary supplements, vitamins, minerals, herbal remedies)

-Cannabidiol Products

Cannabidiol (CBD) is an active ingredient in cannabis that is derived from the hemp plant or by synthetic means. CBD should not contain tetrahydrocannabinol (THC), the psychoactive ingredient in marijuana that causes a high, since a hemp plant contains less than 0.3% of THC by definition (Small & Marcus, 2003). However, the FDA issued a report in 2020 detailing the testing of various forms of CBD products and reported significant inconsistencies regarding proper labeling of THC content. Of the 82 products sampled, only 56 reported the amount of CBD on the label, and 6 products contained less than 80% of the CBD amount indicated. Furthermore, 54 products contained THC (U.S. Food and Drug Administration [FDA], 2020).

Use of CBD products is widespread. All fifty states have laws legalizing CBD use, with varying restrictions. Cannabidiol is available in many forms, such as oil, extract, capsules, vapor, and is infused in many beauty products and foods. In recent years, cannabidiol products have gained popularity for treatment of various conditions, ranging from pain and seizures to anxiety and insomnia. In America, 26% of people used CBD products, and 40% of Americans aged 18 to 29 years of age have tried them (SingleCare Team, 2020).

Furthermore, clinicians report use among their patients with ADHD despite the lack of evidence to support efficacy. A review of the evidence in 2020 found insufficient research to support the recommendation of CBD products in the management of ADHD in

both children and adults due to lack of randomized control trials (Ayyash et al., 2020). Another recent literature review, focusing on cannabis as a whole, including THC, found the evidence to be limited as the studies had small sample sizes and lacked objective measurements for cannabis exposure's effect on ADHD symptoms. This review also did not recommend use in patients with ADHD (Francisco et al., 2023). With scarce literature available, CBD products are not recommended for the management of ADHD at the time of this publication, and clinicians should counsel patients/family/caregivers regarding the use of CBD and possible contamination with THC.

-Omega 3/6 Supplementation

Children or adolescents with ADHD who are deficient in certain nutrients are hypothesized to have worse symptoms. Consuming omega-3 and omega-6 fatty acids is considered essential because the body does not produce these fatty acids on its own. They are necessary for the structure and functionality of neuronal membranes and play a role in the production of prostaglandins and eicosanoids. Children with ADHD have been shown to have lower levels of these fatty acids, and an inverse relationship exists between fatty acid levels and severity of symptoms (Gillies et al., 2012).

In a meta-analysis that compared omega-3 and omega-6 fatty acid supplementation to placebo, low levels of statistically significant improvements were seen with symptoms of hyperactivity and inattention (Bloch & Qawasmi, 2011; Sonuga-Barke et al., 2013). Other studies have shown conflicting data regarding clinically significant differences. Furthermore, a lack of safety data for omega-3 and omega-6 fatty acid supplementation is a concern, but studies have shown the side effects to be fairly benign compared with other treatments. The most commonly reported adverse event is gastrointestinal upset; others include insomnia and hypertriglyceridemia (Manor et al., 2012). Studies that compared combination treatment of stimulants and fatty acids to stimulants alone did not find significant benefit associated with fatty acid supplementation (Behdani et al., 2013; Konigs & Kiliaan, 2016; Mohammadzadeh et al., 2019). Supplementation may have a role in patients with ADHD who are not responding to standard treatment, but it has not shown benefit in children responding well to traditional treatments. Supplementation is also not necessary, nor recommended, in patients consuming an adequate amount of fatty acids in their diet (Cooper et al., 2015). Additional research is needed to support the use of fatty acid supplementation in other areas.

Other Over-the-Counter Products

There are numerous over-the-counter (OTC) supplements and herbals that claim to relieve or "cure" the symptoms of ADHD. It is important to note that these products are not regulated like prescription medications and efficacy has not been evaluated in clinical trials. OTC products rely on a monograph system to be approved for use by the FDA. This monograph only ensures the active ingredients in the product have been tested for safety at the doses recommended on the label. These standards do not require the actual product to be tested for safety or efficacy.

There are currently no trials substantiating the use of these products. Therefore, many OTC medications have inactive ingredients that have never been evaluated by the FDA (The Pew Charitable Trusts, 2017). Additionally, many of these supplements have known drug interactions with medications prescribed by clinicians for treatment of ADHD, or the potential for interaction of these products with concurrent medication for treatment of ADHD has not been studied. It is necessary for clinicians to inquire about any OTC or herbal medication use prior to initiating pharmacological therapy, and patients should be counseled on the importance of not starting any of these products without speaking with their clinician. Some examples of OTC products advertised to "treat" ADHD have included Attentive, Brillia, Nootropics, Simple Spectrum, Focus Factor, Plenity, Equazen, MasterBrain, Neuriva, and Elevate.

-Saint John's Wort

Saint John's Wort is made from *Hypericum perforatum*, a yellow flowering plant. Its use dates back to the ancient Greeks for everything from kidney and lung ailments to insomnia, depression, and wound healing. Its efficacy in ADHD, however, is questionable. Saint John's Wort is thought to work as a norepinephrine reuptake inhibitor, similar to atomoxetine (Schwenk, 2008).

A clinical trial studying 54 children and adolescents with ADHD found that Saint John's Wort had no benefit over placebo with regard to improving ADHD symptoms (Schwenk, 2008). It was the first study comparing the drug in a double-blind trial for the treatment of ADHD, and Saint John's Wort failed to produce a benefit. There have been case studies that have shown possible benefit, but the results are difficult to extrapolate to the population due to sample size. In addition, Saint John's Wort has a multitude of drug interactions, such as with amphetamines, a first-line agent to treat ADHD. There are many other major drug interactions, including medications that patients with ADHD and comorbid disorders would likely take. Since there is no evidence of effectiveness in ADHD

and drug interactions could be dangerous, its use should be discouraged.

Lifestyle (nutrition, exercise/rest, mind-body therapies, biofeedback)

-Diet Modifications

There have been claims that diet modifications can improve the symptoms of ADHD. There are several variations of this intervention. One method is to eliminate foods that cause ADHD symptoms to worsen, known as ADHD elimination dieting. Another is to add nutrients that help decrease symptoms due to underlying deficiencies, known as supplementation dieting. In general, a healthy diet and lifestyle is always encouraged as a complementary approach to treatment. Diets that are extremely limiting or devoid of essential vitamins and nutrients are unsafe and not recommended. Below are a few examples of diet modifications.

Red Dye #40 Elimination

There have been many claims that removal of red dye #40 from a child's diet have "cured" or significantly improved their symptoms of ADHD, labeling the dye a "trigger food". The European Union has required warning labels on foods with artificial dyes stating they "may have an adverse effect on activity and attention". In 1973, Dr. Benjamin Feingold proposed that pediatric hyperactivity and learning problems were due to certain foods and food additives, based on his own clinical observations. He devised a diet called the "Kaiser Permanente" or "KP" diet, eliminating natural salicylates, artificial food colorings and flavors, and two preservatives. He claimed 60% to 70% of his patients improved on this diet (Arnold et al., 2012). To date, there have been no randomized, controlled trials of the KP diet demonstrating significant symptom improvement in patient with ADHD specifically attributed to the consumption or avoidance of Red Dye #40.

Sugar/Carbohydrate Elimination

Parents/families/caregivers of children with ADHD often report worsening of their symptoms after an excessive amount of food containing sugar, such as candy or soda. However, the majority of controlled studies looking at sucrose have failed to demonstrate a significant effect on ADHD symptoms. A meta- analysis of 16 reported studies concluded that sugar does not usually affect the behavior or cognitive performance of children, but a small subset of children cannot be ruled out

(Wolraich et al., 1994). Restriction of complex carbohydrates may be considered as adjunctive therapy and part of a healthy lifestyle, but there is not enough evidence to support carbohydrate elimination as primary therapy.

Gluten Elimination

Another special diet suspected to have an effect on symptoms of ADHD is eliminating gluten from the diet in the form of wheat, rye, and barley. Patients with celiac disease have an allergy to gluten and should avoid consuming it. Some patients have co-occurring ADHD and celiac disease, so these patients should avoid gluten intake. However, there has not been conclusive evidence that a relationship between gluten and ADHD exists (CHADD, 2017a). A systematic review of the literature found no association between ADHD and celiac disease and recommends against performing routine screening of celiac disease when assessing ADHD or implementing a gluten-free diet as a standard treatment (Ertürk et al., 2016).

-Neurofeedback Training

Neurofeedback uses a computer software system to measure brain activity. Patients with ADHD tend to have elevated theta (slow) brain waves and altered theta/beta wave ratios Lenartowicz & Loo, 2014). The software provides a positive feedback signal for desirable brain activities and a negative signal for undesirable activities. The signals are usually auditory or visual and are intended to "teach" self-control of brain function (Marzbani et al., 2016).

A randomized controlled trial showed neurofeedback was as effective as methylphenidate in post-treatment academic improvement and reducing inattentive and hyperactivity symptoms (Duric et al., 2012). In a meta-analysis, neurofeedback therapy was compared with cognitive training and stimulant therapy. It was found to have more durable and long-lasting treatment effects for at least six months following therapy than stimulants and cognitive training. This study suggested stimulant effects tend to decrease with time, while neurofeedback effects increased with time, without any additional interventions (Enriquez-Geppert et al., 2019). A significant disadvantage is that neurofeedback can be expensive and time-consuming (Harvard Medical School, 2022). It is worth noting that some insurances cover neurofeedback training, although coverage varies by plan and coverage provider. A meta-analysis found statistical significance in treatment effects for

non-blinded studies but not for blinded studies (Sonuga-Barke et al., 2013). Sensitivity analysis for medication effects was not possible due to most trials co- administering medication. Evidence showing the effectiveness of neurofeedback as sole therapy is lacking. While some research shows promising results, there are no uniform standards regarding training courses that are accepted by any expert associations (Enriquez-Geppert et al., 2019). To date, there have only been a few partially controlled trials. These studies also have weaknesses, including lack of control groups, confounding treatments, small sample sizes, validity of ADHD diagnosis in the study population, absence of blinding, lack of randomization, and lack of peer review (CHADD, 2017c). In addition, most of the trials are testing outcomes in a controlled environment, leaving a lot of doubt for real-world application.

-Physical Activity

Physical activity or exercise is a treatment method that is being considered in patients with ADHD. When studied in children at risk of ADHD, parent/family/caregiver- and teacher-rated symptoms were reported to be less burdensome than those using sedentary interventions. Improvements were also seen in inattentive and hyperactive symptoms, defiance, and moodiness. Peer difficulties were reported to be similar, but overall results favored the physical intervention (Hoza et al., 2015). In a systematic review, moderate-to-intense aerobic activity was proven beneficial and well-tolerated in children and adolescents with ADHD. Cognitive, behavioral, and physical symptoms were improved in most instances, and an improvement was seen in mental health and overall well-being (Ng et al., 2017). Evidence supports the use of physical activity as adjunctive treatment, but research is still inadequate to use physical activity as monotherapy (Hoza et al., 2015). As a general rule, physical activity is essential to overall wellbeing. While physical activity as monotherapy has not shown efficacy in ADHD, it is still recommended as an adjunct to therapy in all patients.

-Meditation

Four separate studies looked at children and adult patients with ADHD and the effects of meditation. Mantra meditation, relaxation training, and yoga meditation were

found to have no statistical differences in teacher rating scale or distraction tests between the meditation group versus the standard therapy group (Krisanaprakornkit et al., 2010). Another systematic review included 16 trials, eight targeting children with ADHD and eight including children and parents/families/caregivers. Most trials found a decrease in ADHD symptoms based on parent rating scales, but the findings were not statistically significant. The author also noted that two of the trials showed worsening ADHD symptoms (Evans et al., 2018b). However, a study using digital application of meditation tested the effects of treatment on children with sleep and anxiety problems related to ADHD. A significant reduction in symptoms on the Children's Sleep Habits Questionnaire and the Beck Anxiety Inventory Questionnaire were observed (Fried et al., 2021). A common use form of meditation frequently seen in ADHD treatment is mindfulness.

Mindfulness Meditation

Mindfulness is a type of meditation that focuses on patient experiences and practices different ways to orient a person's attention in a nonjudgmental and accepting way. Mindfulness has shown some efficacy in anxiety and depression and has been a consideration for reducing core symptoms and other impairments in adults with ADHD (Mitchell et al., 2013). A systematic review on nonpharmacological methods found mindfulness had some efficacy in adult patients with adult ADHD. However, sample size and limitations of the study seemed to have played a significant role (Nimmo-Smith et al., 2020). Therefore, evidence is also lacking to promote the use of this strategy as monotherapy.

-Yoga

Yoga is a practice of mind and body that uses physical manipulations, meditation, and breathing techniques to promote mental and/or physical wellbeing. Breathing exercises are thought to help one feel more in control of their brains and bodies, which would be beneficial for a patient with ADHD. There have been a few studies that found yoga to be helpful with attention symptoms and adaptive skills in preschoolers and elementary school-aged children with ADHD, but the sample sizes were small (Chou & Huang, 2017). There is not enough evidence to support yoga as a primary therapy to treat ADHD, but it may be considered as an adjunct to standard care.

Biomechanical (massage and bodywork, chiropractic and osteopathic adjustments)

-Chiropractic Interventions

It has been suggested that spinal misalignments put excessive pressure on nerves in the spinal column, leading to energy flow disruption and consequently functional conditions like ADHD. Following re-alignment of the spine, this energy is able to flow freely, opening the communication between brain and body and improving symptoms of ADHD (Scott, 2020). This area of chiropractic is referred to as chiropractic biophysics, a growing area of certification for chiropractors. While a few studies have shown a correlation between chiropractic manipulation and a decrease in ADHD symptoms, all have acknowledged the need for further research (CHADD, 2017d). A review of the literature in 2010 found a lack of high-quality evidence for chiropractic care in pediatric and adolescents with ADHD, and more quality research is needed (Karpouzis et al., 2010).

Bioenergetic (acupuncture, homeopathy)

-Acupuncture

Acupuncture is an ancient Chinese medicine practice that involves the insertion of very thin needles through the skin at strategic places on the body. It is described as a method to balance the flow of energy or life force, known as chi. Western clinicians use acupuncture to stimulate nerves, muscles, and connective tissue (Mayo Clinic, 2022). A systematic review on acupuncture for ADHD in children and adolescents found that not a single study met inclusion criteria for the review. There was no evidence based on randomized or quasi-randomized controlled trials (Li et al., 2011). Likewise, a systematic review in adult patients with ADHD found evidence to be highly limited, with a high risk of bias (Chen et al., 2021). More evidence is needed to evaluate acupuncture for safety and efficacy in the treatment of ADHD.

Summary

West Virginia, the Mountain State, is wild and wonderful. Its beautiful, rolling hills and outdoor culture make it a remarkable place to live and visit. However, these are the same qualities that have added to the disparity of healthcare in West Virginia. These rural attributes lead to overall limited access to appropriate healthcare, a shortage of healthcare professionals (including mental health professionals), and higher poverty rates.

ADHD has extensive pathophysiology, giving rise to symptoms that are often lifelong, and its prevalence in West Virginia is higher than the national average. Patients with ADHD

frequently require a myriad of medical services across a multidisciplinary sector that is not always readily available in most areas of the state. When left untreated, ADHD can cause significant morbidity. The appropriate diagnosis requires careful consideration of the patient's past neurodevelopmental, medical, and family history; environmental considerations (e.g., ACEs, lead exposure); and thorough evaluation of current and past symptomology. Increased prevalence of comorbid conditions in this population can further complicate both accurate diagnosis and treatment. Behavioral interventions, pharmacological treatment, and/or the combination of both are the mainstay of treatment and can be offered through telehealth services where appropriate in certain situations. Ongoing monitoring of treatment in these patients can be challenging in this state, but continuous, lifelong care, which includes monitoring of treatment, is also critical.

The intention of this guideline is to provide a foundation for the management of this condition, ultimately helping to close the gap in care for West Virginians with ADHD and comorbid concerns. The information and resources contained within are aimed to provide a comprehensive resource for clinicians and other individuals involved in the care of patients with ADHD in West Virginia. Through careful collaboration, together, we can improve the outcomes for this population of West Virginians and enhance the lives of those affected by this disorder, directly or indirectly.

Glossary of Terms

Accommodations
Changes made to the learning environment in order to address the special needs of children with learning differences.

Addiction
A chronic, relapsing brain disorder characterized by compulsive seeking and use of a substance despite adverse consequences.

ADHD
Abbreviation for attention-deficit/hyperactivity disorder, characterized by symptoms of inattention, hyperactivity, and/or impulsivity.

Adverse Child Experiences (ACEs)
Potential traumatic events experienced or observed that occur before a child reaches the age of 18. Includes emotional, physical, and sexual abuse; neglect and household challenges of parental separation; lack of resources and adequate healthcare; poverty; substance misuse; incarceration; violence; and mental illness.

Adverse Drug Reactions (ADR)
Unintended, potentially harmful events attributed to the use of medicines.

Agent
A pharmaceutical product.

Americans with Disability Act (ADA)
A federal law that protects people with disabilities from discrimination in their employment, public business, and government.

Amphetamine
A type of medication sometimes used in the treatment of ADHD that has a stimulant effect on the central nervous system.

Antecedent Techniques
This technique involves the teacher or adult attempting to manipulate the student's antecedents, or stimulus conditions, that favor desired behaviors.

Behavioral Health Services
Refers to a wide range of services related to the treatment of mental health conditions. Some examples include counseling for various reasons (e.g., marriage/relationship counseling, family counseling), addiction disorder services, preventative care, and more.

Behavioral Peer interventions
Strategies designed to encourage appropriate peer interactions. In the intervention, one or more peers are guided by an adult's direct assistance, external cues, and reinforcement to remain on-task and demonstrate positive behavior.

Behavioral Therapy/Modification
A type of treatment that involves the use of reinforcement and/or punishments to encourage positive behaviors and life skills while reducing problematic behaviors. For adults, it often involves improving time and organizational skills and adopting effective methods to manage procrastination. For children, this often involves caregivers learning strategies to elicit positive child behavior and reduce/manage challenging behaviors.

Best Practices
Treatment consensus based on recent, relevant methods, interventions, procedures, or techniques that is based on high-quality evidence and literature for a certain disease that is widely used by healthcare professionals. Also called the standard of care.

Causational Data
Statistical measurements indicating that one event is the result of the occurrence of another event.

Catecholamine
A biogenic amine that includes the neurotransmitters dopamine, norepinephrine, and epinephrine.

Classroom Behavioral Management
Techniques used by teachers in the school setting to elicit positive student behavior and decrease disruptive behavior.

Clinical Trial/Study
A type of research designed to test an intervention, treatment, or new approach in a population of patients.

Clinician
A medical provider having direct contact with and responsibility for a certain area of care related to the patient.

Cognitive Behavioral Therapy (CBT)
Form of psychotherapy focusing on improving wellbeing by addressing underlying thoughts, beliefs, and behaviors that negatively impact functioning.

Cognitive Function
Varied and complex brain activities (or cognitive functions), such as attention, memory, processing speed, and executive functions (i.e., reasoning, planning, problem-solving, and multitasking).

Combined Behavior Management Intervention
The combination of nonpharmacological behavioral approaches involving both home (i.e., behavioral parent management training) and school (i.e., behavior classroom management) techniques. Implementation across settings fosters consistency for children and adolescents.

Combined Presentation ADHD
A subtype of ADHD characterized by a combination of inattention and hyperactivity/impulsivity.

Complex ADHD
ADHD co-occurring with one or more learning, neurodevelopmental, or psychiatric disorders. Approximately 60% of children diagnosed with ADHD fit into the complex category.

Complementary and Integrative Medicine (CIM)
A wide array of healthcare practices not currently considered to be part of mainstream medicine.

Comprehensive Assessment
Evaluation process that allows for the assessment of a student's or adult's overall understanding of a curriculum or skill.

Comorbid/Coexisting Condition
The existence of more than one disease/condition/ailment within an individual at the same time.

Consequent Techniques
This technique manipulates the consequences of an action, instead of the environment, to encourage positive behaviors and discourage negative behaviors.

Correlational Data
Statistical measurements that describe the size and direction of a relationship between two or more variables but do not establish a cause and effect between them.

Counselor
Professionals who treat cognitive, behavioral, and emotional aspects of mental health and substance use conditions.

Dependence
A condition when the body requires a specific dose of a substance in order to prevent withdrawal symptoms from occurring.

Dopamine
A neurotransmitter with several important roles in the body, including internal reward.

Drug Holiday
A planned period of time when prescribed medication therapy is temporarily discontinued by the prescriber for medical or evaluation purposes.

Diagnostic and Statistical Manual of Mental Health Disorders, Fifth Edition (DSM-5)
Published in 2013 and updated as a text revision in 2022, the DSM-5 is the current standard classification of mental disorders used by mental health professionals in the United States.

Effectiveness
Measurement of the degree to which a treatment or intervention has a beneficial effect in "real-world" conditions.

Efficacy
Measurement of the degree to which a treatment or intervention produces the expected benefit under ideal clinical conditions.

Etiology
The cause or origin of disease.

Executive Function
A range of mental activities that allow individuals to set goals, organize ideas, get things done, and achieve goals.

Family Physician
A doctor who has received at least 3 years of specialty training beyond medical school in a broad discipline of primary care.

Formal Assessment
Gathering information using standardized and evidenced-informed published tests to make instructional decisions.

Foster Care
A temporary living situation for children whose parents cannot take care of them and whose need for care has come to the attention of a child welfare agency. While in foster care, children may live with relatives, a foster family, or in group facilities.

Genetic Testing
A medical test that can clarify the risk for developing certain genetic conditions; determine the chances of passing on a genetic disorder; or identify mutations in an individual's genes, chromosomes, or proteins that might indicate the presence or absence of specific genetic conditions.

Hyperactivity
A condition characterized by constant movement and excessive fidgeting and/or talking that is considered inappropriate for the age of the patient and situation.

IEP (Individualized Education Plan)
A plan, as put forth by the IDEA Act, for eligible students with learning disabilities that outlines educational or behavioral goals and a plan and guide on how to achieve them.

Illicit Drug Use
The use of illegal drugs or the use of prescription or over-the-counter drugs for purposes other than those for which they are intended, or in excessive amounts.

Impulsivity
A condition characterized by hastily making important decisions or acting without thought of consequences.

Insomnia
Inability to fall or stay asleep, or difficulty sleeping.

In Utero
Within the womb, before birth.

Mental Health Disorder
Disorder characterized by a clinically significant disturbance in an individual's cognition, emotional regulation, or behavior.

Mental Health Providers Professionals that diagnose and/or treat mental health conditions.

Methylphenidate
A type of medication sometimes used to treat ADHD related to amphetamines that has a stimulant effect on the central nervous system.

Modifications
Changes made to the grade-specific curriculum, or "what" is learned, to address the special needs of children with learning differences.

Multidisciplinary Care
A care team consisting of healthcare professionals from different disciplines of the medical and mental health fields that come together to address the needs of the patient.

Neonatal Abstinence Syndrome (NAS)
A group of conditions caused when a baby experiences withdrawal from exposure to certain drugs they were exposed to in the womb before birth.

Non-Traditional Households
Households where the primary caregivers are not the biological parents.

Nonstimulant Medication
A medication sometimes used in the treatment of ADHD that does not have a stimulant effect on the central nervous system. An example is atomoxetine.

Norepinephrine
A neurotransmitter that has several important roles in the body, including sleep-wake cycle, alertness, arousal, and attention. Usually, activity is considered reduced in patients with ADHD.

Off-Label Drug Use
The practice of prescribing currently available medication for an indication (disease or symptom) for which it has not received FDA approval. Off-label drug use is not the same as experimental or research use. Once a drug is FDA-approved for a specific indication, legally it can be used for any indication. Off-label drug use is common; it accounts for 10 to 20 percent of all prescriptions written.

Organizational Skills Training Technique that focuses on teaching children and adolescents to better organize home and school materials. Skills taught within the training include, but are not limited to, time management, organization/folder systems, list creation, and self-reinforcement.

Parent Management Training
A treatment approach where parents use antecedents, behaviors, and consequences to change child and adolescent behavior at home, school, and other settings.

Pathophysiology
The functional bodily changes that accompany a particular syndrome or disease.

Pharmacological
The science of drug composition, uses, and effects.

Predominantly Hyperactive-Impulsive Presentation
A subtype of ADHD characterized primarily by hyperactive and/or impulsive behaviors at inappropriate times that is inappropriate for the age of the patient. Inattentive symptoms may still be present.

Predominantly Inattentive Presentation
A subtype of ADHD characterized primarily by inattentiveness that is inappropriate for the age of the patient. Some signs of hyperactivity and/or impulsivity may be present.

Prefrontal Cortex
The outer, front part of the frontal lobe of the brain that plays a vital role in controlling attention, behavior, judgment, and emotion.

Prescription Drug Monitoring Program (PDMP)
A web-based system that optimizes the collection, analysis, and reporting of information on the prescribing, dispensing, and use of controlled substances.

Prevalence
The proportion of a population who have a particular attribute at a specified point in time or over a specified period of time.

Provider/Medical Provider
A licensed professional who provides healthcare services.

Psychological Counseling/Emotional Therapy
Intervention strategies designed to assist individuals in processing and either overcoming or adapting to emotional and behavioral struggles that result from individual, social, familial, romantic, and/or occupational challenges.

Psychologist
A master's or doctoral level health professional trained in the study of behavior, emotions, and functioning and trained in psychological therapy, consultation, and testing.

Psychotherapy
A variety of treatment techniques used by trained mental health providers to help a patient identify and change troubling emotions, thoughts, and behaviors.

Section 504
As part of the Rehabilitation Act of 1973, prohibits discrimination against individuals with disabilities.

Serotonin
A chemical neurotransmitter that plays a key role in a host of bodily functions, including mood and sleep.

Schedule II Controlled Substance
Medications that can be legally prescribed and have a high potential for "abuse," which may lead to dependence.

Social Skills Training
A series of strategies designed to encourage appropriate social responding among children and adolescents. Skills include, but are not limited to, making appropriate eye contact, initiating conversations, discussing shared interests and employing other conversational skills, turn taking, and respecting personal space.

Social Worker
A professional, many with a master's or doctoral level degree, who assesses the well-being of clients and assists them in obtaining services to meet their physical and mental health needs.

Socioeconomic Status
A measure combining a person's economic and social position in relation to others, based on income, education, and occupation.

Specialist
A highly skilled healthcare professional whose practice concentrates primarily on a particular subject or activity.

Stimulants
The most commonly prescribed type of medication for ADHD that stimulates the central nervous system, increasing production and activity of the neurotransmitters dopamine and norepinephrine.

Time Blindness
The inability to accurately perceive the passing of time or estimate the time needed to complete a task.

Titration
Describes the process of finding the right dose of medication by making small increases or decreases over time as appropriate for the patient.

Tolerance
A person's diminished response to a drug, which occurs after repeated use and the body adapts to the continued presence of the drug.

Urine Drug Screening (UDS)
Collection of patient's urine to analyze for the presence of certain illegal drugs and prescription medication.

Urine Drug Testing (UDT)
A comprehensive diagnostic method that involves analyzing a urine sample to detect, identify, and quantify specific drugs or their metabolites, providing detailed information about the type and concentration of substances present.

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Table of Contents for Appendices

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text** Reprinted with permission from the Diagnostic and Statistical Manual of Mental Disorders: DSM-5-TR, p. 68-70	**DSM-5-TR Updated Wording/Added Text**
Diagnostic Codes	Combined Presentation: 314.01 (F90.2) Predominantly Inattentive: 314.00 (F90.0) Predominantly Hyperactive/Impulsive: 314.01 (F90.1)	Combined Presentation: F90.2 Predominantly Inattentive: F90.0 Predominantly Hyperactive/Impulsive: F90.1
Diagnostic Features	Lack of persistence	Failing to follow through on instructions or finishing work or chores
		ADHD cannot be diagnosed in the absence of any symptoms prior to age 12. When symptoms of what appear to be ADHD first occur after age 13, they are more likely to be explained by another mental disorder or to represent the cognitive effects of substance use.
Associated Features Supporting Diagnosis	*Mild* delays in language, motor, or social development are not specific to ADHD but often co-occur.	Delays in language, motor, or social development are not specific to ADHD but often co-occur.
	Associated features may include low frustration tolerance, irritability, or mood lability.	Emotional dysregulation or emotional impulsivity commonly occurs in children and adults with ADHD. Individuals with ADHD self-report and are described by others as being quick to anger, easily frustrated, and overactive emotionally.
	Inattentive behavior is associated with various underlying cognitive processes, and individuals with ADHD may exhibit cognitive problems on tests of attention, executive function, or memory.	Individuals with ADHD may exhibit neurocognitive deficits in a variety of areas, including working memory, set shifting, reaction time variability, response inhibition, vigilance, and planning/organization.
	By early adulthood, ADHD is associated with an increased risk of suicide attempt, primarily when comorbid with mood, conduct, or substance use disorder. No biological marker is diagnostic for ADHD. As a group, compared with peers, children with ADHD display increased slow wave electroencephalogram, reduced total brain volume on magnetic resonance imaging, and possibly a delay in posterior to anterior cortical maturation, but these findings are not diagnostic. In the uncommon cases where there is a known genetic cause (e.g., fragile X syndrome, 22q11 deletion syndrome), the ADHD presentation should still be diagnosed.	Although ADHD is not associated with specific physical features, rates of minor physical anomalies (e.g., hypertelorism, highly arched palate, low-set ears) may be elevated. Subtle motor delays and other neurological soft signs may occur. (Note that marked co-occurring clumsiness and motor delays should be coded separately [e.g., developmental coordination disorder].) Children with neurodevelopmental disorders with a known cause (e.g., fragile X syndrome, 22q11 deletion syndrome) may often also have symptoms of inattention and impulsivity/hyperactivity; they should receive an ADHD diagnosis if their symptoms meet the full criteria for the disorder.

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text**	**DSM-5-TR Updated Wording/Added Text**
Prevalence	Population surveys suggest that ADHD occurs in most cultures in about 5% of children and about 2.5% of adults.	Population surveys suggest that ADHD occurs worldwide in about 7.2% of children; however, cross-national prevalence ranges widely, from 0.1% to 10.2% of children and adolescents. Prevalence is higher in special populations such as foster children or correctional settings. In a cross-national meta-analysis, ADHD occurred in 2.5% of adults.
Environmental	Very low birth weight (less than 1,500 grams) conveys a two- to three-fold risk for ADHD, but most children with low birth weight do not develop ADHD. Although ADHD is correlated with smoking during pregnancy, some of this association reflects common genetic risk.	Very low birth weight and degree of prematurity convey a greater risk for ADHD; *the more extreme the low weight, the greater the risk. Prenatal exposure to smoking is associated with ADHD even after controlling for parental psychiatric history and socioeconomic status.*
	There may be a history of child abuse, neglect, multiple foster placements, neurotoxin exposure (e.g., lead), infections (e.g., encephalitis), or alcohol exposure in utero. Exposure to environmental toxicants has been correlated with subsequent ADHD, but it is not known whether these associations are causal.	Neurotoxin exposure (e.g., lead), infections (e.g., encephalitis), and alcohol exposure in utero have been correlated with subsequent ADHD, but it is not known whether these associations are causal.
Genetic and Physiological	ADHD is elevated in the first-degree biological relatives of individuals with ADHD. The heritability of ADHD is substantial. While specific genes have been correlated with ADHD, they are neither necessary nor sufficient causal factors.	The heritability of ADHD is approximately 74%. Large-scale genome-wide association studies (GWAS) have identified a number of loci enriched in evolutionarily constrained genomic regions and loss-of-function genes as well as around brain-expressed regulatory regions. There is no single gene for ADHD.
	ADHD is not associated with specific physical features, although rates of minor physical anomalies (e.g., hypertelorism, highly arched palate, low-set ears) may be relatively elevated. Subtle motor delays and other neurological soft signs may occur. (Note that marked co-occurring clumsiness and motor delays should be coded separately [e.g., developmental coordination disorder].)	ADHD is elevated in individuals with idiopathic epilepsy.

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text**	**DSM-5-TR Updated Wording/Added Text**
Culture-Related Diagnostic Features	Differences in ADHD prevalence rates across regions appear attributable mainly to different diagnostic and methodological practices. However, there also may be cultural variation in attitudes toward or interpretations of children's behaviors.	Differences in ADHD prevalence across regions appear attributable mainly to different diagnostic procedures and methodological practices, including using different diagnostic interviews and differences in whether functional impairment was required and, if so, how it was defined. Prevalence is also affected by cultural variation in attitudes toward behavioral norms and expectations of children and youth in different social contexts, as well as cultural differences in interpretations of children's behaviors by parents and teachers, including differences by gender.
	Caucasian populations. Informant symptom ratings may be influenced by cultural group of the child and the informant, suggesting that culturally appropriate practices are relevant in assessing ADHD.	White populations. Under detection may result from mislabeling of ADHD symptoms as oppositional or disruptive in socially oppressed ethnic or racialized groups because of explicit or implicit clinician bias, leading to overdiagnosis of disruptive disorders. Higher prevalence in non-Latinx White youth may also be influenced by greater parental demand for diagnosis of behaviors seen as ADHD-related. Informant symptom ratings may be influenced by the cultural background of the child and the informant, suggesting that culturally competent diagnostic practices are relevant in assessing ADHD.
Gender-Related Diagnostic Issues	Gender-Related Diagnostic Issues	Sex- and Gender Related Diagnostic Issues
Sex- and Gender Related Diagnostic Issues		Sex differences in ADHD symptom severity may be due to differing genetic and cognitive liabilities between sexes.

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text**	**DSM-5-TR Updated Wording/Added Text**
Added "Diagnostic Markers"		No biological marker is diagnostic for ADHD. Although ADHD has been associated with elevated power of slow waves (4–7 Hz "theta") as well as decreased power of fast waves (14–30 Hz "beta"), a later review found no differences in theta or beta power in either children or adults with ADHD relative to control subjects. Although some neuroimaging studies have shown differences in children with ADHD compared with control subjects, meta- analysis of all neuroimaging studies do not show differences between individuals with ADHD and control subjects. This likely is due to differences in diagnostic criteria, sample size, task used, and technical aspects of the neuroimaging technique. Until these issues are resolved, no form of neuroimaging can be used for diagnosis of ADHD.
Added "Association with Suicidal Thoughts or Behavior"		ADHD is a risk factor for suicidal ideation and behavior in children. Similarly, in adulthood, ADHD is associated with an increased risk of suicide attempt, when comorbid with mood, conduct, or substance use disorders, even after controlling for comorbidity. Suicidal thoughts are also more common in ADHD populations than in non- ADHD control subjects. ADHD predicted persistence of suicidal thoughts in U.S. Army soldiers.
Functional Consequences of Attention- Deficit/ Hyperactivity Disorder	Social rejection removed from association	
		Elevated likelihood of hypertension among individuals with ADHD
		Individuals with ADHD have lower self- esteem relative to peers without ADHD.
Specific Learning Disorder	However, inattention in individuals with a specific learning disorder who do not have ADHD is not impairing outside of academic work. (removed)	
Anxiety Disorders	ADHD shares symptoms of inattention with anxiety disorders. Individuals with ADHD are inattentive because of their attraction to external stimuli, new activities, or preoccupation with enjoyable activities	ADHD shares symptoms of inattention with anxiety disorders. Individuals with ADHD are inattentive because of their *preferential engagement with novel and stimulating activities or preoccupation with enjoyable activities.*

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text**	**DSM-5-TR Updated Wording/Added Text**
Posttraumatic Stress Disorder (added)		Concentration difficulties associated with posttraumatic stress disorder (PTSD) may be misdiagnosed in children as ADHD. Children younger than 6 years often manifest PTSD in nonspecific symptoms such as restlessness, irritability, inattention, and poor concentration, which can mimic ADHD. Parents may also minimize their children's trauma-related symptoms, and teachers and other caregivers are often unaware of the child's exposure to traumatic events. A comprehensive assessment of past exposure to traumatic events can rule out PTSD.
Bipolar Disorder	Individuals with bipolar disorder may have increased activity, poor concentration, and increased impulsivity, but these features are episodic, *occurring several days at a time*	Individuals with bipolar disorder may have increased activity, poor concentration, and increased impulsivity, but these features are episodic, *unlike ADHD, in which the symptoms are persistent.*
	Children with ADHD may show significant changes in mood within the same day; such lability is distinct from a manic episode, which must last 4 or more days to be a clinical indicator of bipolar disorder, even in children.	Children with ADHD may show significant changes in mood within the same day; such lability is distinct from a manic or hypomanic episode, which must last 4 or more days to be a clinical indicator of bipolar disorder, even in children.
Neurocognitive Disorders	Early major neurocognitive disorder (dementia) and/or mild neurocognitive disorder are not known to be associated with ADHD but may present with similar clinical features. These conditions are distinguished from ADHD by their late onset.	While impairment in complex attention may be one of the affected cognitive domains in a neurocognitive disorder, it must represent a decline from a previous level of performance to justify a diagnosis of major or mild neurocognitive disorder. Moreover, major or mild neurocognitive disorder typically has its onset in adulthood. In contrast, the inattention in ADHD must have been present prior to age 12 and does not represent a decline from previous functioning.

DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022		
Sub-Section of Criteria	**DSM-5 Wording/Removed Text**	**DSM-5-TR Updated Wording/Added Text**
Comorbidity	In clinical settings, comorbid disorders are frequent in individuals whose symptoms meet criteria for ADHD.	Although ADHD is more common in males, females with ADHD have higher rates of a number of comorbid disorders, particularly oppositional defiant disorder, autism spectrum disorder, and personality and substance use disorders.
	Speci ic learning disorder commonly co-occurs with ADHD. Intermittent explosive disorder occurs in a minority of adults with ADHD, but at rates above population levels.	
	Other disorders that may co-occur with ADHD include obsessive-compulsive disorder, tic disorders, and autism spectrum disorder.	ADHD may co-occur in variable symptom profiles with other neurodevelopmental disorders, including specific learning disorder, autism spectrum disorder, intellectual developmental disorder, language disorders, developmental coordination disorder, and tic disorders.
		Comorbid sleep disorders in ADHD are associated with daytime impairments in cognition (e.g., inattention). Many individuals with ADHD report daytime sleepiness that may meet criteria for hypersomnolence disorder. One quarter to one-half of individuals with ADHD report sleep difficulties; studies have shown an association of ADHD with insomnia, circadian rhythm sleep-wake disorder, sleep- disordered breathing, and restless legs syndrome. Individuals with ADHD have been found to have elevated rates of a number of medical conditions, particularly allergy and autoimmune disorders, as well as epilepsy

References for Appendix 1.1: DSM-5 to DSM-5-TR Modifications to Attention-Deficit/Hyperactivity Disorder (ADHD) Chapter [APA], 2022

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Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments					
Achenbach System of Empirically Based Assessment (ASEBA)©: Child Behavior Checklist (CBCL)© Caregiver-Teacher Report Form(C-TRF)© Teacher's Report (TRF) Form© Youth Self-Report (YSR)©	• Parent • Teacher • Self-report	Teacher and Parent Scales: Preschool 1.5 to 5 years of age Child: 6 to 18 years of age Adult: 18 to 59 years of age Self-Report: Preschool: 1.5 to 5 years of age Child: 6 to 18 years of age Adult: 18 to 59 years	10 to 20 minutes	**Preschool** • Emotionally reactive • Anxious/depressed • Somatic complaints • Withdrawn • Attention problems • Aggressive behavior • Sleep problems (CBCL/1½-5 years of age only) **Child** • Anxious/depressed • Withdrawn/depressed • Somatic complaints • Social problems • Thought problems • Attention problems • Rule breaking behavior • Aggressive behavior **Adult and Older Adult** • See section below	CBCL/C-TRF/Spanish CBCL 1½-5 years of age for purchase CBCL/1½-5 years of age-C C-TRF/1½-5 years of age-C CBCL/TRF/6-18 years of age to purchase YSR/11-18 years of age for purchase CBCL/6-18 years of age-Copy TRF/6-18 years of age-Copy YSR/11-18 years of age-Copy
Barkley Functional Impairment Scale – Children and Adolescents (BFIS-CA)©	• Parent	6 to 17 years of age	5 to 7 minutes	• Impairment in 15 different domains of major life activities	BFIS-CA for purchase

Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments (Continued)					
Behavior Assessment System for Children Third Edition (BASC-3)© Teacher Ratings Scale (TRS)© Parent Rating Scale (PRS)© Self-Report of Personality Form (SRP)©	• Parent • Teacher • Self-report	Teacher and Parent Scales: Preschool: 2 to 5 years of age Child: 6 to 11 years of age Adolescent: 12 to 21 years of age Self-Report: SRP-I: 6 to 7 years of age Child: 8 to 11 years of age Adolescent: 12 to 21 years of age College: 18 to 25 years of age	10 to 20 minutes	**Teacher Rating Scale and Parent Rating Scale** • Adaptive skills • Behavioral symptoms index • Externalizing problems • Internalizing problems • School problems (TRS child and adolescent only) **Self-Report of Personality Form (child, adolescent and college)** • Emotional symptoms • Inattention/hyperactivity • Internalizing problems • Personal adjustment • School problems (child and adolescent only)	Behavior Assessment System for Children Third Edition for purchase
Child and Adolescent Functional Assessment Scale (CAFAS)©	• Parent • Self-report	5 to 19 years of age	10 minutes	• Emotional symptoms • Behavioral problems • Psychiatric symptoms • Substance use problems	CAFAS for purchase

Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments (Continued)					
Conners 4™ Conners 4th Edition (Full-length form)	• Parent • Teacher • Self-report	6 to 18 years of age 8 to 18 years of age (self-report)	12-15 minutes	**Content Scales** • Inattention/executive dysfunction • Impulsivity • Emotional dysregulation • Depressed mood • Anxious thoughts **Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and DSM-5-TR Symptom Scales** • Attention-Deficit/Hyperactivity Disorder (ADHD) inattentive symptoms • ADHD hyperactive/impulsive symptoms • Total ADHD symptoms	Conners 4™ Conners 4th Edition for purchase
Conners 4™ Conners 4th Edition (Short forms)	• Parent • Teacher • Self-report	6 to 18 years of age 8 to 18 years of age (self-report)	5-7 minutes	**Content Scales** • Inattention/executive dysfunction • Hyperactivity • Impulsivity • Emotional dysregulation • Depressed mood • Anxious thoughts **DSM-IV and DSM-5-TR symptom scales** • ADHD inattentive symptoms • ADHD hyperactive/impulsive symptoms • Total ADHD symptoms • Oppositional Defiant Disorder symptoms • Conduct Disorder symptoms **Impairment and Functional Outcomes Scales** • Schoolwork • Peer interactions • Family life (parent and self-report only)	Conners 4™ Conners 4th Edition for purchase

Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments (Continued)					
Pediatric Symptom Checklist (PSC)©*	• Parent • Self-report	4 to 16 years of age Youth: 11 to 18 years of age or older (self-report)	5 to 10 minutes	• Cognitive problems • Emotional problems • Behavioral problems	PSC- Online Parent Youth Report(Y-PSC)- Online Youth SR PSC- Form Youth Report(Y-PSC) SR Form Pediatric Symptom Checklist-17 (PSC-17) Short Form Youth Pediatric Symptom Checklist -17 (Y-PSC-17) SR Short Form
Narrowband Assessments					
Academic Performance Rating Scale (APRS)	• Teacher	6 to 12 years of age	10 to 15 minutes	• Assesses ability to perform in school related subject areas	APRS (assessment is provided in Appendix A of the journal article)
ADHD Rating Scale-5 for Children and Adolescents (ADHD-RS-5)©	• Parent • Teacher	5 to 17 years of age	5 minutes	ADHD • Frequency of symptoms • Severity of symptoms • Functional impairment	ADHD-RS-V for purchase
Attention-Deficit Disorder Evaluation Scale-Fifth Edition (ADDES-5)©	• Parent • Teacher	5 to 17 years of age	20 minutes	ADHD	ADDES-5 for purchase ADDES-5 SAMPLE

Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Narrowband Assessments (Continued)					
Brown Attention-Deficit Disorder Scales©	• Parent • Teacher • Self-report	Teacher and Parent Scales: Preschool: 3 to 7 years of age School-age: 8 to 12 years of age Adolescent: 12 to 18 years of age Adult: 18 to 59 years of age Self-Report: School age: 8 to 12 years Adolescent: 12 to 18 years of age Adult: 18 to 59 years of age	10 to 20 minutes	• Organizing, prioritizing and activating to work • Focusing, sustaining and shifting attention to tasks • Regulating alertness, sustaining effort and processing speed • Managing frustration and modulating emotions • Utilizing working memory and accessing recall • Monitoring and self-regulating action	Brown Attention-Deficit Disorder Scales for purchase
Conners 4™ Conners 4th Edition-ADHD Index	• Parent • Teacher • Self-report	6 to 18 years of age 8 to 18 years of age (self-report)	5 minutes	• 10 items that best differentiate youth with ADHD from youth in the general population.	Conners 4™ Conners 4th Edition for purchase
Impairment Rating Scale*	• Parent • Teacher	All ages	10 to 15 minutes	• Assesses functioning across domains	IRS
NICHQ Vanderbilt Assessment Scales©*	• Parent • Teacher	6 to 12 years of age	10 to 20 minutes	• Symptoms of ADHD (DSM-IV criteria) • Oppositional Defiant Disorder • Conduct Disorder • Anxiety • Depression	NICHQ Vanderbilt Assessment Scales

Assessments for Children					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Narrowband Assessments (Continued)					
Strengths and Difficulties Questionnaire (SDQ)©*	• Parent • Teacher • Self-report	3 to 16 years of age	5 to 10 minutes	• Emotional symptoms • Conduct problems • Hyperactivity/inattention • Peer relationship problems • Prosocial behavior	SDQ
Swanson, Kotkin, Agler, M-Flynn, & Pelham (SKAMP) Rating Scale*	• Teacher	7 to 12 years of age	5 minutes	• Assesses functional impairment related to ADHD	SKAMP (scale available within journal article)
Swanson, Nolan, and Pelham Teacher and Parent Rating Scale (SNAP-IV)*	• Parent • Teacher	6 to 18 years of age	10 minutes	• ADHD • Oppositional Defiant Disorder	SNAP-IV
Structured Interviews					
Children's Interview for Psychiatric Syndromes (ChIPS and P-ChIPS)©	• Clinician	6 to 18 years of age	40 minutes	• 20 DSM-IV Axis I Disorders	ChIPS and P-CHIPS

Diagnostic Interview Schedule for Children-IV (DISC-IV)©	• Clinician
	• Community
		Parent of children 6 to 17 years of age
		Youth 9 to 17 years of age
			Clinician:
			90 to 120 minutes
			Community: 70 minutes
				• 34 common psychiatric diagnoses
				  • Anxiety disorders
				  • Mood disorders
				  • Disruptive disorders
				  • Alcohol/substance use disorders
				  • Miscellaneous disorders
					DISC-IV Interviewer Manual

Mini International Neuropsychiatric Interview for Children and Adolescents (MINI KID)©	• Clinician	6 to 17 years of age	15 minutes	• 30 most common and clinically relevant disorders or disorder subtypes in pediatrics mental health	MINI KID for purchase

Assessments for Children					
Interview (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Semi-Structured Interviews					
Child and Adolescent Psychiatric Assessment (CAPA)© Preschool Age Psychiatric Assessment (PAPA)©	• Clinician	CAPA: 9 to 17 years of age PAPA: 3 to 6 years of age	<70 minutes	• Disruptive behavior disorders • Mood disorders • Anxiety disorders • Eating disorders • Sleep disorders • Elimination disorders • Substance use/abuse/dependence • Tic disorders • Others	CAPA PAPA
Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Aged Children Present and Lifetime (K-SADS-PL)©*	• Clinician	6 to 18 years of age	60 to 120 minutes	• Mood disorders • Anxiety disorders • ADHD • Oppositional Defiant Disorder • Conduct Disorder • Substance use disorders • Psychotic disorders	K-SADS-PL DSM-5

Assessments for Adults					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments					
Achenbach System of Empirically Based Assessment (ASEBA)©: Adult Behavior Checklist (ABCL)© Adult Self-Report (ASR)© Older Adult Behavior Checklist (OABCL)© Older Adult Self-Report (OASR)©	• Self-report • Friend; spouse/partner	Adults: 18 to 59 years of age Older adults: 60 to 90 years of age	10 to 20 minutes	**ABCL/OBCL** • Personal strengths **ASR/OASR** • Adaptive functioning • Empiric based syndromes • Substance use • Internalizing problems • Externalizing problems • Total problems	ABCL/ASR for purchase ABCL-C ASR-C OABCL/OASR for purchase OABCL-C OASR-C
Minnesota Multiphasic Personality Inventory (MMPI-3)©	• Self-report	18 years of age and older	25 to 35 minutes (computer) 35 to 50 minutes (paper and pencil)	**Symptoms:** • Depression • Anxiety • Anger • Stress • Psychotic symptoms • Sleep disturbances • Eating disturbances • Suicidal ideation • Hypochondriasis **Conditions:** • Anxiety disorders • Eating disorders • Mood disorders • Personality disorders • Post-traumatic stress disorder • Psychotic disorders • Somatoform disorders • Substance use disorders	MMPI-3 for purchase

Assessments for Adults					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Broadband Assessments					
Personality Assessment Inventory (PAI)™	• Self-report	18 years of age and older	50 to 60 minutes	• Alcohol misuse • Anger • Antisocial features • Anxiety • Bipolar features • Borderline features • Depression • Drug use/misuse • Narcissism • Negative impression management • Paranoia • Positive impression management • Psychoticism • Schizophrenia • Social introversion • Somatic complaints	PAI for purchase
Narrowband Assessments					
Adult ADHD Self-Report Scale Symptom Checklist (ASRS-DSM-5)©*	• Self-report	18 years of age and older	5 minutes	• Assess Attention Deficit/Hyperactivity Disorder (ADHD) symptoms	ASRS-DSM5
Barkley Adult ADHD Rating Scale – IV (BAARS-IV)	• Self-report • Other- report • (e.g., spouse, parent, and sibling)	Score sheet differs for ages 18 to 39 years of age 40 to 59 years of age 60 to 89 years of age	5 to 7 minutes 3 to 5 minutes (quick)	• ADHD Symptoms	BAARS-IV for purchase

Assessments for Adults					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Narrowband Assessments (Continued)					
Barkley Deficits in Executive Functioning Scale (BDEFS for Adults)©	• Self-report • Other- report • (e.g., spouse, parent, and sibling)	Score sheet differs for ages 18 to 34 years of age 35 to 49 years of age 50 to 64 years of age 65 to 81 years of age	Long form: 15 to 20 minutes Short form: 4 to 5 minutes	Dimensions of Adult Executive Functioning in Daily Life Capacities Involved in: • Time management • Organization and problem solving • Self-restraint • Self-motivation • Self-regulation of emotions • Adult ADHD risk index (long form)	BDEFS for Adults for purchase
Barkley Functional Impairment Scale (BFIS for Adults)©	• Self-report • Other- report • (e.g., spouse, parent, and sibling)	Score sheet differs for ages 18 to 39 years of age 40 to 59 years of age 60 to 89 years of age	Long form: 5 to 7 minutes Quick screen: 3 to 5 minutes	• Assesses psychosocial impairment in 15 domains of major life activities	BFIS for Adults for purchase
Brown Adult Attention-Deficit Disorder Scales	• Self-report	18 years of age and older	10 to 20 minutes	• Organizing, prioritizing and activating to work • Focusing, sustaining and shifting attention to tasks • Regulating alertness, sustaining effort and processing speed • Managing frustration and modulating emotions • Utilizing working memory and accessing recall	Brown Attention-Deficit Disorder Scales for purchase
Conners' Adult ADHD Rating Scales (CAARS)©	• Self-report • Observer report forms	18 to 80 years of age	10 to 20 minutes	• Inattention/memory problems • Hyperactivity/restlessness • Impulsivity/emotional lability • Problems with self-concept	CAARS for purchase

Assessments for Adults					
Assessment (*free of charge)	**Completed by:**	**Age Range (years of age)**	**Time to Complete (minutes)**	**Symptoms/Conditions Assessed**	**Link (click to access)**
Narrowband Assessments (Continued)					
Copeland Symptom Checklist for Adult ADHD*	• Self-report	18 years of age and older	10 to 15 minutes	• Cognitive symptoms • Emotional symptoms • Social symptoms	Copeland Symptom Checklist
Structured Interview					
Conners Adult ADHD Diagnostic Interview for DSM-IV™ (CAADID™)	Part I • Clinician • Self-report Part II • Clinician	18 years of age and older	2 parts: 90 minutes for each	• ADHD	CAADID™ for purchase
Mini International Neuropsychiatric Interview (MINI) (Adult Version)©	• Clinician	18 years of age and older	15 minutes	• 17 Most common disorders in mental health	MINI
Semi-Structured Interviews					
The Young Adult Psychiatric Assessment (YAPA)©	• Clinician	18 years of age and older	<70 minutes	• Full range of common psychiatric disorders • Focus on diagnoses, living situations, relationships, and areas of functioning relevant to this age group	YAPA

The Diagnostic Interview for ADHD in Adults (DIVA-5)©	• Clinician	18 years of age and older	60 to 90 minutes	• ADHD Symptoms
				  • Chronicity
				  • Impairments
					DIVA-5 for purchase

References for Appendix 1.2: Assessments for Children & Appendix 1.3: Assessments for Adults

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Screening/Assessment Tools for Attention-Deficit/Hyperactivity Disorder (ADHD) and Related Conditions			
Condition	**Test Name**	**Measure Details**	**Cost and Access**
ADHD	Vanderbilt Assessment Scales©	Ages 6 to 12 years of age Forms: Parent and teacher Estimated Time: 10 to 20 minutes Description: Brief scale to assess ADHD symptoms of inattention and hyperactivity along with conduct disorder, oppositional defiant disorder, anxiety, depression, and academic performance	Free - can be downloaded at Vanderbilt Rating Scales
ADHD	Swanson, Nolan, and Pelham Teacher and Parent Rating Scale (SNAP- IV)	Ages: 6 to 12 years of age Forms: Parent and teacher Estimated Time: 15 minutes Description: Assessment (DSM-IV criteria) for ADHD that also includes oppositional defiant disorder and conduct disorder	Free - can be downloaded at SNAP-IV
For additional ADHD rating scales and interviews, SEE APPENDIX 1.2 & 1.3			
Anxiety	Screen for Child Anxiety Related Disorders (SCARED)	Ages: 8 to 18 years of age Forms: Parent and child (self-report) Estimated Time: 10 minutes Description: Screening tool for overall anxiety and five specific anxiety types of panic/somatic, generalized anxiety, separation anxiety, social phobia, and school phobia	Free - can be downloaded at SCARED Parent and Child Forms
Anxiety	Generalized Anxiety Disorder-7 (GAD-7)	Ages: 11 years of age and older Forms: Self-report Estimated Time: Less than 5 minutes Description: Screening tool to evaluate the presence and severity of generalized anxiety disorder	Free - can be downloaded at GAD-7
Anxiety and Depression	Revised Children's Anxiety and Depression Scale (and Subscales) (RCADS)	Ages: 8 to 18 years of age Forms: Parent and child (self-report) Estimated Time: 5 to 10 minutes Description: Questionnaire that includes subscales for separation anxiety disorder, social phobia, generalized anxiety disorder, panic disorder, obsessive compulsive disorder, and major depressive disorder	Free - can be downloaded at RCADS

Screening/Assessment Tools for Attention-Deficit/Hyperactivity Disorder (ADHD) and Related Conditions			
Condition	**Test Name**	**Measure Details**	**Cost and Access**
Depression	Patient Health Questionnaire-9 (PHQ-9)©	Ages: 12 years of age and older Forms: Self-report Estimated Time: 5 minutes Description: Questionnaire that assesses depression symptoms	Free - can be downloaded at PHQ-9
Depression	Center for Epidemiological Studies Depression Scale for Children (CES-DC)	Ages: 6 to 17 years of age Forms: Child (self-report) Estimated Time: 5 minutes Description: Scale used to assess depressive symptoms	Free - can be downloaded at CES-DC CES-DC Scoring
Bipolar Disorder (Mania or Mixed)	The Mood Disorder Questionnaire	Ages: 11 years of age and older Forms: Self-report Estimated Time: 5 to 10 minutes Description: Screening tool for bipolar disorder that assesses symptoms of mania	Free - can be downloaded at The Mood Disorder Questionnaire
Bipolar Disorder (Mania or Mixed)	General Behavior Inventory (GBI)	Ages: 18 years of age and older Forms: Self-report Estimated Time: 15 minutes Description: Self-report used to identify presence and severity of depressive and manic/hypomanic symptoms, including cyclothymia	Free - can be downloaded at GBI
Autism	Modified Checklist for Autism in Toddlers, Revised, with Follow-up (M-CHAT-R/F)©	Ages: 16 to 30 months of age Forms: Parent Estimated Time: 5 minutes Description: Two-stage parent-report screening tool to assess risk for Autism Spectrum Disorder	Free for clinical, research and educational purposes - can be downloaded at M-CHAT-R/F
Autism	Autism Spectrum Screening Questionnaire (ASSQ)	Ages: 6 to 17 years of age Forms: Parent or teacher Estimated Time: 10 minutes Description: Screening instrument for autistic disorders in high-functioning children, including Asperger's disorder	Free - can be downloaded at ASSQ

Screening/Assessment Tools for Attention-Deficit/Hyperactivity Disorder (ADHD) and Related Conditions			
Condition	**Test Name**	**Measure Details**	**Cost and Access**
Trauma	Post-Traumatic Stress Disorder Checklist Civilian Version (PCL-C)	Ages: 18 years of age and older Forms: Self-report Estimated Time: 5 to 10 minutes Description: Screening tool to assess for Post-Traumatic Stress Disorder (PTSD) and monitor symptom changes during and after treatment	Free - can be downloaded at PCL-C
Trauma	Clinician- Administered PTSD Scale for *DSM-5*- Child/ Adolescent Version (CAPS- CA-5)	Ages: 7 to 17 years of age Forms: Clinician-administered Estimated Time: 45 minutes Description: Scale used to assess for 30 DSM-5 PTSD symptoms	Forms can be requested at CAPS-CA-5
Learning Disorder(s)	Wechsler Intelligence Scale for Children Fifth Edition (WISC-V)©	Ages: 6 to 16 years of age Forms: Administered test Estimated Time: 60 minutes Description: Intelligence test that measures a child's intellectual ability and cognitive domains that impact performance	Can be purchased from WISC-V
Learning Disorder(s)	Wechsler Individual Achievement Test Fourth Edition (WVIAT-4)©	Ages: 4 to 50 years of age Forms: Administered test Estimated Time: Varies by grade level and number of subtests administered Description: Analyses of academic achievement to support diagnoses of specific learning disabilities	Can be purchased from WIAT-4
Oppositional Defiant Disorder	Vanderbilt Assessment Scales©	Ages: 6 to 12 years Forms: Parent and teacher Estimated Time: 10 to 20 minutes Description: Brief scale to assess ADHD symptoms of inattention and hyperactivity along with conduct disorder, oppositional defiant disorder, anxiety, depression, and academic performance	Free - can be downloaded at Vanderbilt
Oppositional Defiant Disorder	Swanson, Nolan, and Pelham-IV SNAP-IV	Ages: 6 to 12 years Forms: Parent and teacher Estimated Time: 15 minutes Description: Assessment (DSM-IV criteria) for ADHD which also includes oppositional defiant disorder and conduct disorder	Free - can be downloaded at SNAP-IV

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Overlapping Symptoms With Attention-Deficit/Hyperactivity Disorder (ADHD)

Much of the symptomatology of Attention-Deficit/Hyperactivity Disorder (ADHD) is suggestive of executive dysfunction and loss of inhibitory control. Similar symptoms can be present across a host of psychiatric and neurologic conditions and, unfortunately, no single ADHD symptom is diagnostic. As there is no singular definitive symptom or test for ADHD, clinicians should consider ADHD a diagnosis of exclusion. In this way, the clinician evaluating for ADHD must at least consider and rule-out common conditions that would alternatively explain their patient's presentation. Further complicating the diagnostic picture is the fact that many of the conditions described below commonly co-occur with ADHD, sometimes referred to as "complex ADHD" (APA, 2022). Cases of diagnostic uncertainty should be referred to a pediatric or mental health subspecialist for more comprehensive assessment (Barbaresi et al., 2022).

When evaluating a child for suspected ADHD and considering the differential diagnosis, it is helpful to remember the following guidelines (Wolraich et al., 2019):

- At least some of the symptoms of ADHD must be present prior to the age of 12 years. For many children, onset of symptoms will be much younger. Onset of symptoms after the age of 12 cannot be diagnosed as ADHD.
- ADHD symptoms occur in more than one setting (e.g., school, home, church, recreation). Symptoms that only occur at home, for example, are not consistent with an ADHD diagnosis. It is therefore often necessary to obtain collateral information from other sources (after obtaining and documenting consent), such as teachers or other caregivers.
- ADHD symptoms are inconsistent with developmental level and therefore symptoms are noticeably more pronounced than their peers. This is another reason collateral information, particularly from school, is usually necessary.
- Symptoms that occur exclusively during periods of substance use/misuse/withdrawal cannot be diagnosed as ADHD.

The following symptom overlap chart is provided as a quick reference to aid clinicians in the differential diagnosis of ADHD. Note that the chart is not comprehensive but includes many of the conditions whose presentation can be confused with ADHD. Also note that it is possible for ADHD to co-occur with any of the diagnoses listed on the following page.

Overlapping Inattentive Symptoms with ADHD

Inattentive Symptoms	ADHD	GAD	MDD	BP	ASD	TSD	LD	ODD	ID
Frequently overlooks details or making careless mistakes	X	X	X	X	X	X	X		X
Often has difficulty maintaining focus on one task or play activity	X	X		X		X	X		X
Often appears not to be listening when spoken to, including when there is no obvious distraction	X	X	X	X	X	X		X	X
Frequently does not finish following instructions, failing to complete tasks	X		X	X	X	X	X	X	X
Often struggles to organize tasks and activities, to meet deadlines, and to keep belongings in order	X		X	X	X	X			X
Is frequently reluctant to engage in tasks that require sustained attention	X								
Frequently loses items, including those required for tasks	X			X					X
Is frequently easily distracted by irrelevant things, including thoughts in adults and teenagers	X			X	X	X			
Often forgets daily activities, or is forgetful while completing them	X		X	X					X

KEY

ABBREVIATION	DISORDER
ADHD	Attention-Deficit/Hyperactivity Disorder
GAD	Anxiety Disorders
MDD	Depressive Disorders (Unipolar or Bipolar)
BP	Bipolar Disorder (Mania or Hypomania)
ASD	Autism Spectrum Disorder
TSD	Trauma-and-Stressor-Related Disorders
LD	Learning Disorders
ODD	Oppositional Defiant Disorder
ID	Intellectual Disability
SUD	Substance Use Disorders
SD	Sleep Disorders

Overlapping Hyperactive-Impulsive Symptoms With ADHD

Hyperactive-Impulsive Symptoms	Diagnosis								
	ADHD	GAD	MDD	BP	ASD	TSD	LD	ODD	ID
Is often fidgeting or squirming in seat	X	X		X		X			
Frequently has trouble sitting still during dinner, homework, at work, etc.	X	X		X					
Frequently runs around in inappropriate situations: In adults and teenagers, this may be present as restlessness.	X	X		X					
Often cannot quietly engage in leisure activities or play	X			X					
Frequently seems to be in constant motion, or uncomfortable when not in motion	X	X		X					
Often talks too much	X			X		X			
Often answers a question before it is finished, or finishes people's sentences	X				X				
Often struggles to wait his or her turn, including waiting in lines	X			X	X			X	
Frequently interrupts or intrudes, including into others' conversations or activities, or by using people's things without asking.	X			X	X			X	

KEY

ABBREVIATION	DISORDER
ADHD	Attention-Deficit/Hyperactivity Disorder
GAD	Anxiety Disorders
MDD	Depressive Disorders (Unipolar or Bipolar)
BP	Bipolar Disorder (Mania or Hypomania)
ASD	Autism Spectrum Disorder
TSD	Trauma-and-Stressor-Related Disorders
LD	Learning Disorders
ODD	Oppositional Defiant Disorder
ID	Intellectual Disability
SUD	Substance Use Disorders
SD	Sleep Disorders

Differentiating ADHD From Other Diagnoses	
Diagnosis	**Distinguishing Factors**
Anxiety	One of the core symptoms of many anxiety disorders is difficulty concentrating or maintaining attention. Individuals with anxiety are inattentive because their focus is turned inward by worry or rumination. In contrast, those with ADHD struggle with inattention and distractibility because their attention is drawn outward by novel stimuli or excessively held by pleasurable activities. Additionally, individuals with anxiety often engage in restless behaviors that can mimic hyperactivity.
Depressive Disorders (Unipolar or Bipolar)	Individuals with depressed mood frequently experience poor concentration. However, the symptoms of depression are episodic, rather than continuous and diminished concentration will occur alongside other depressive symptomatology such as changes in sleep patterns, appetite, feelings of guilt, and anhedonia. The symptoms of ADHD, on the other hand, are not episodic and are present at some level most or all the time.
Bipolar Disorders (Mania or Hypomania)	Increased energy, poor concentration, distractibility, and impulsivity are core symptoms of manic or hypomanic mood states. However, elevated mood states occur as discrete episodes that are a change from the patient's baseline behavior. In contrast, those with ADHD display symptoms on a more continuous basis. Further, those with mania or hypomania will display other symptoms consistent with their mood disorder, such as grandiosity, decreased need for sleep, racing thoughts, or risk-taking behavior out of the norm from their baseline.
Autism Spectrum Disorder	Those with Autism Spectrum Disorder (ASD) display symptomatology that involves impairment in social skills, communication, restricted interests, and repetitive behaviors. There can be broad differences in symptom severity within this group. In addition, some children with ASD have intellectual and/or language impairments as well. Many of their symptoms can look like those seen in ADHD. Communication or social skill deficits can be mistaken for inattentiveness to conversation or instructions. A strong desire to preferentially engage with restricted interests can be misinterpreted as lack of attention or distractibility. Stereotyped behaviors can be misunderstood as hyperactive behavior.
Trauma- and Stressor-related Disorders	Individuals with trauma-related disorders often struggle with attentiveness and sustained concentration. This can be due to recurrent and intrusive memories, dissociative states that negatively impact awareness of situations or surroundings, or diminished interest in activities. Trauma-related symptoms, by definition, have an onset following a traumatic event and are often triggered or worsened following exposure to reminders of the event. In contrast, ADHD symptoms may worsen under certain situations but are mostly non-contextual.
Learning Disorders	Children with specific learning disorders are often inattentive when engaged in learning activities related to their area of disability. However, they do not show attention deficits with other tasks, and they are not more hyperactive or impulsive than their peers. In contrast, by definition, children with ADHD struggle with symptoms across more than one setting. ADHD is commonly comorbid with learning disorders.
Oppositional Defiant Disorder	Those with Oppositional Defiant Disorder (ODD) display argumentativeness and defiance toward adult authority figures solely out of a desire to resist conforming to rules or demands. The child with ADHD, on the other hand, is more likely to resist requests related to academic or mentally demanding tasks. Alternatively, failure to follow through with tasks in ADHD can be secondary to forgetfulness, distractibility, or impulsivity. Annoying others is common to both conditions, but for those with ODD, this behavior is typically deliberate, while for those with ADHD, the annoyance may be more of an unintended consequence of their symptoms. ADHD and ODD commonly co-occur.
Intellectual Disability	Individuals with intellectual disability can struggle with attention if placed in academic settings that are not commensurate with their intellectual level. Outside of these settings, however, their ability to focus will be on par with their mental age. Those with ADHD will struggle with attentional tasks across multiple settings to include non-academic situations.

Differentiating ADHD From Other Diagnoses	
Diagnosis	**Distinguishing Factors**
Other Conditions	
Substance Use Disorders	Many substances, either prescription or illegal, can cause similar symptoms to ADHD, either during intoxication or withdrawal states. For example, alcohol intoxication can cause inattentive and impulsive behavior while intoxication with stimulants, such as cocaine or methamphetamine, can lead to hyperactivity and impulsivity. A comprehensive list of substances and their effects is well beyond the scope of this document. If substance use is infrequent then hyperactive, impulsive, and inattentive symptoms should mostly be confined to periods of use or withdrawal. However, differentiating ADHD from substance use can be challenging if use is very frequent. A clear history of onset of ADHD symptoms prior to the onset of drug use or during sustained periods of sobriety is key.
Sleep Disorders	Sleep disorders such as insomnia, sleep-disordered breathing, circadian rhythm sleep disorders, narcolepsy, and others can lead to insufficient sleep or sleep fragmentation. This can result in disturbances of mood, behavior, and attention that can resemble many of the symptoms of ADHD. Attentional and behavioral symptoms that chronologically begin after onset of the sleep disorder are unlikely to be related to ADHD. ADHD and sleep disorders often co-occur, sometimes as a consequence of stimulant therapy or due to poor bedtime routines seen with many children who have ADHD.

References for Appendix 1.5: Overlapping Symptoms With ADHD

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Attention-Deficit/Hyperactivity Disorder (ADHD) Diagnostic Process

New or existing patient presenting with attention or behavioral symptoms; ADHD considered as possible diagnosis

- Identify relevant symptoms and the timeline of development.
- Obtain and review any relevant reports/documentation such as:
  - Previous evaluations or ADHD rating scales
  - Prior interventions
  - Relevant school documentation, collateral reports, observations, medical records, or employment history

Screening for evidence consistent with ADHD based on DSM-5-TR and within scope of practice

- 6 or more DSM-5-TR listed symptoms of either inattention and/or hyperactivity/impulsivity present in children 16 years or younger (in 2 or more settings)
  - Documentation of ADHD symptoms prior to 12 years of age
  - Symptoms presenting for >6 months
  - Symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning
- 5 or more DSM-5-TR listed symptoms of either inattention and/or hyperactivity/impulsivity present in ado-lescents and adults 17 years or older (in 2 or more settings)
  - ADHD symptoms prior to 12 years of age
  - Symptoms presenting for >6 months
  - Symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning

Positive Screening and within scope of practice?

No

- Refer for specialized evaluation
- Explain the evaluation process to the caregiver/patient and address any questions

Yes

Explain the evaluation process to the caregiver/patient and address any questions

Conduct:

- Narrowband and/or broadband assessments to include multiple informants in multiple settings
- A thorough physical examination to rule out any medical causes of symptoms/behavior
- Interview regarding social situations and family history
- Additional mental health evaluations, interviews, or assessments for possible alternative diagnoses and/or coexisting conditions which may present overlapping symptoms with ADHD (SEE OVERLAPPING SYMPTOMS WITH ADHD for further details):
  - Developmental disorder
  - Learning disability
  - Past medical history
  - Trauma disorder
  - Anxiety disorder
  - Medical illness
  - Sleep disorder
  - Other potential conditions with overlapping symptoms

Negative Screening

If not consistent with ADHD: attempt to identify any other possible causes of presenting behaviors and treat accordingly. If not within scope of practice, specialist referral/consultation may be warranted.

No

Confirmed diagnosis of ADHD?

Yes

- Educate caregivers/patients about nonpharmacologic treatment strategies and initiate where appropriate
- Evaluate if the patient is a candidate for pharmacological treatment. (See ADHD PHARMACOLOGICAL TREATMENT RECOMMENDATIONS)
- Ensure treatment of coexisting conditions.
- Refer to specialist, if needed, for more complex cases with increased severity of symptoms.

Attention-Deficit/Hyperactivity Disorder (ADHD) Treatment Recommendations

Preschool-aged children: <6 years*

A. Primary Care Clinicians (PCC) should prescribe evidence-based behavioral parent management training (BPMT) and/or classroom interventions.

B. In patients greater than 4 years of age, methylphenidate may be considered if there is not significant improvement with behavioral interventions and there is continued moderate to severe disturbance.

C. In areas in which evidence-based treatments are not available, the clinician needs to weigh the risk of starting medication before the age of 6 years against the harm of delaying treatment.

**Of note, the AAP advises to avoid a diagnosis of ADHD prior to the age of 4 years.*

School-aged children: 6 years to 12th birthday

A. PCC should prescribe U.S. Food and Drug Administration (FDA)-approved medication for ADHD along with BPMT and/or behavioral classroom interventions.

B. Educational interventions and instructional supports are a necessary part of the treatment plan.

Adolescents: 12 years to 18th birthday

A. PCC should prescribe FDA-approved medication for ADHD.

B. PCC is encouraged to prescribe evidence-based training interventions and/or behavioral interventions.

C. Educational interventions and instructional supports are a necessary part of the treatment plan.

Adults: 18 years and older

A. FDA-approved stimulant (for those determined to be candidates for use of prescription stimulants) or atomoxetine are considered first-line treatments for ADHD after coexisting mental health and substance use disorders are treated.

   i. Consider long-acting stimulants for all patients who are candidates for stimulants due to lower misuse and diversion potential.

   ii. Consider a non-stimulant (atomoxetine, bupropion, clonidine/guanfacine) with recent substance use or history of substance use disorder.

B. Without sufficient symptom improvement, consider adjusting the dose or trying alternative medications (TCAs, modafinil, etc.).

C. CBT has been shown to be helpful as adjunctive treatment with medication.

D. To monitor for misuse or diversion of stimulants, clinicians should consider using a patient and provider agreement and other risk reduction strategies at their discretion.

Nonpharmacological Treatments

	Preschool-aged Children *(<6 Years)*	School-aged Children *(6 years to 12th birthday)*	Adolescents *(12 years to 18th birthday)*	Adults *(18 years and older)*
First-Line	• Behavioral Classroom Management • Behavioral Parent Management Training • Combined Behavior Management Interventions	• Behavioral Classroom Management • Behavioral Parent Management Training • Behavioral Peer Intervention • Combined Behavior Management Interventions • Organization Training	• Organization Training	• Not Applicable (N/A)
Second-Line	• Combined Training Interventions (extensive practice)	• Combined Training Interventions (extensive practice)	• Combined Training Interventions (extensive practice)	• Cognitive Behavioral Therapy (group or individual)
Third-Line	• N/A	• N/A	• Behavioral Parent Management Training	• Psychological Counseling/Emotional Therapy • Use of technological aids
Limited Evidence	• Combined Training Interventions (limited practice)	• Cognitive Behavioral Training • Combined Training Interventions (limited practice) • Modified Behavioral Parent Training	• Combined Training Interventions (limited practice)	• Organizational Training
Lacking Evidence	• Social Skills Training	• Social Skills Training	• N/A	• N/A

Level of Evidence Key

First Line: Statistically significantly superior to control group or equivalent to an already well established treatment

Second Line: At least two experiments showing superiority to control group

Third Line: At least one experiment showing superiority to control group

Limited Evidence: Not yet tested in a randomized controlled trial

Lacking Evidence: Tested and found to be inferior to control group or experimental studies suggest treatment produces no beneficial effect

Examples Of Common Recommendations for School Accommodations and Interventions *(Recommendations and interventions are not listed in any particular order and are often implemented in combination and tailored to the needs of the individual student.)*	
Accommodation	**Description**
Behavioral	
Behavior Chart-Individualized	Establish individualized target behaviors and couple with specific goals and consequences that are shared with the child. Can be combined with a token/incentive program. An example would be keeping an index card on student's desk with goals or a colored reward/privilege system.
Breaks	Providing a student with additional brief breaks. This may include sharpening pencils, getting a drink of water, or running an errand for the teacher.
Classroom Rules/Structure	Rules tailored to developmental level that contain expectations for student behavior of the class as a whole. This should be clearly posted in the classroom and reviewed daily.
Classroom Incentives	Whole-class program, which rewards the class for overall good behavior.
Individual Incentives	Individual programs, such as behavior charts, that reward students on an individual level for good behavior.
Daily Report Cards	A report sent home to the parent/guardian at the end of each day with a quantitative rating of targeted student behavior(s). Frequency can be adjusted as goals are reached.
Train Self-Awareness	Student records own work productivity on a chart so they can see their own progress and rates themselves on behavior for the day. The teacher uses "cue" words or non-verbal signals that alert student to self-direct back to task.
Instructional	
Computer-Assisted Instruction	Uses computer game-like format to convey material and assess knowledge as a supplement, not replacement, to face-to-face instruction.
Interest Incorporation	Adding an element of interest to each assignment using multi-sensory modes. Using visual instructions as well as verbal. Song and movement may aid memorization.
Modifying Academic Assignments and Expectations	Assigning academic work to match student's ability, varying presentation styles, shortening assignments or breaking assignments into small chunks, and providing task related choices.
Peer Tutoring/Assistance	Instructional strategy involving two students working together academically, with one student providing assistance, instruction, and feedback to the other. Peer(s) may share notes with ADHD student.
Read Aloud	An option for the student to receive examinations and assignments in an oral format as opposed to written only.
Seating Considerations/Teacher Proximity	Placing student close to instruction zone for frequent check-ins/reinforcement. Also, seating students next to a role model student, away from distractions in the environment. Seating should be single and spaced apart if room allows.
Strategic Teacher Attention	The practice of purposely using attention to help students stay on task and redirect when off task. Frequent, positive feedback is given when student stays on task and follows directions.
Test Accommodations	Teacher gives the option to receive the exam orally. Also, giving the student the option of taking the test in a private room or behind a privacy board.
Time/Scheduling Change	Allow students more time to complete assignments and exams. Teach material requiring more attentiveness in the morning hours. Evidence of effectiveness in increasing correct answers but not always improvements in behavior.

Organizational	
Assignment Notebook	Prepare an assignment notebook for student to help student keep track of work.
Organizational Training	Teaches student time management, planning skills, and ways to keep materials organized to optimize learning and reduce distractions. Allowing a second set of textbooks for home use or providing already high-lighted books. Color coded binders help students keep track of materials and work.

References for Appendix 2.3: Examples of Common Recommendations for School Accommodations and Interventions

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Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacological Treatment Recommendations

Treatment Recommendations for a Patient with a Confirmed Diagnosis of ADHD AND Level of Impairment to Warrant Pharmacological Management

Preschool-aged children 4 years to 6th birthday	School-aged children 6 years to 12th birthday	Adolescents 12 years to 18th birthday	Adults 18 years and older
First-line treatment: Evidence-based behavioral interventions and classroom behavioral interventions **Second-line:** May prescribe methylphenidate if no significant improvement and moderate-to-severe continued disturbance	Treat with pharmacologic therapy AND *evidence-based behavioral interventions and/or classroom behavioral interventions	Treat with pharmacologic therapy and may consider *evidence-based behavioral interventions and/or classroom behavioral interventions	Treat with pharmacologic therapy and cognitive behavioral therapy/ psychosocial treatment

*For further information regarding evidence-based behavioral interventions please see Appendix 2.2 “Nonpharmacologic Treatments”

Guidance for Initial Pharmacological Management of ADHD

Stimulant therapy is usually considered first-line in patients 6 years of age and older, unless the patient is not a suitable candidate. Methylphenidate and amphetamine options tend to have similar effectiveness, but amphetamines may be associated with more side effects. Patient-specific factors should be evaluated to determine if the patient is a candidate for use of a stimulant medication.

Contraindications

- Known sensitivity
- Serious cardiac conditions
- Hyperthyroidism
- Glaucoma
- Patients who have used an MAOI, linezolid, or methylene blue within the last 14 days
- History of substance misuse
- Agitated state (use caution in patients with bipolar disorder/mania, as stimulants have the potential to induce mania)

Precautions

- Patients with suicidal ideation or major depression
- Mild hypertension or tachycardia
- Significant hepatic or renal impairment
- History of seizure disorders
- Eating disorders
- Cerebrovascular disease
- Pregnancy/ breastfeeding
- Geriatric patients

Caregiver/patient/family preference regarding use of a stimulant versus a non-stimulant medication should be discussed and considered. When starting adolescents and adults on stimulant medications clinicians should obtain the patient’s consent to treat and assess for symptoms of substance use and monitor prescription refill requests for signs of misuse or diversion. Consider the patient’s insurance coverage and formulary requirements when selecting an agent. Starting a stimulant:

- Long-acting formulations are recommended
- Children and adolescents starting stimulants should be initiated at the starting dose and then gradually titrated weekly to the dose that optimally controls symptoms with minimal adverse effects
- Adults starting stimulants should start at the lowest possible dose and titrate slowly. Before switching to another agent, titrate to the maximum dose if no side effects are present.

If the patient is **not** a candidate for stimulant therapy and/or caregiver/patient/family preference is to avoid stimulant therapy, common non-stimulant treatment includes atomoxetine, viloxazine, guanfacine and clonidine. Consider and educate the patient on the duration of time to maximum response of the chosen agent. The time for maximum response tends to be within a few weeks for stimulants whereas clonidine and guanfacine can take about 2 to 4 weeks and viloxazine and atomoxetine may take up to 6 to 8 weeks. Once pharmacological and/or non-pharmacological treatment is initiated continue to closely monitor all patients receiving pharmacological therapy.

See “ADHD Monitoring and Follow Up” for specific recommendations.

Attention-Deficit/Hyperactivity Disorder (ADHD) Monitoring and Follow-up

Maintenance follow-up visits should occur at least every 3 to 6 months

Review of Systems

- Special attention given to blood pressure, heart rate, height, and weight
- Comparison with patient's baseline
- Comorbid concerns

Medication Management

- Adverse effects
- Efficacy/symptom control (use of ADHD rating scales)
- Dosage adjustments (titration vs. dose reduction)
- Adherence (timing of refill request)
- Risk Reduction Strategies (prescription stimulants in patients who require additional monitoring)
  - Prescription Drug Monitoring Program
  - Urine drug testing
  - Ongoing risk screening

Nonpharmacological Management

- Appropriate referrals and coordination of care
- Adherence to nonpharmacological treatments
- School or workplace accommodations

Overall Review of Treatment Plan

- Symptom management assessment (ADHD assessment scales)
- Referrals to additional specialists where indicated
- Parental/caregiver/family member concerns addressed
- Scheduling of follow-up visits

Attention-Deficit/Hyperactivity Disorder (ADHD) Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Methylphenidate (MPH) - Immediate-Release					
Methylin 5 mg/5 mL 10 mg/5 mL **U.S. Food and Drug Administration (FDA) approved age:** Age 6 years and older	**Initial:** 5 mg twice daily (BID) (6 years to 17 years) 10 mg BID to three times daily (TID) (18 years and older) **Titration:** 5 to 10 mg weekly	FDA: 60 mg	3 to 5 hours	• Take 30 to 45 minutes before meal • Grape-flavored	• Immediate-release solution • Bioequivalent to MPH tablets
Methylin 2.5 mg, 5 mg, 10 mg **FDA approved age:** Age 6 years and older	**Initial:** 5 mg BID (6 years to 17 years) 10 mg BID to TID (18 years and older) **Titration:** 5 to 10 mg weekly	FDA: 60 mg	3 to 5 hours	• Take chewable tablet with at least 8 oz of fluid at least 30 to 45 minutes before a meal • Grape-flavored	• Immediate-release tablets • Chewable • Bioequivalent to MPH tablets
Ritalin 5 mg, 10 mg, 20 mg **FDA approved age:** Age 6 years and older	**Initial:** 5 mg BID (6 years to 17 years) 10 mg BID to TID (18 years and older) **Titration:** 5 to 10 mg weekly	FDA: 60 mg	3 to 5 hours	• Take 30 to 45 minutes before meal	• Immediate-release
MPH - Long-Acting					
Adhansia XR 25 mg, 35 mg, 45 mg, 55 mg, 70 mg, 85 mg **FDA approved age:** Age 6 years and older	**Initial:** 25 mg once a day in the morning (QAM) **Titration:** 10 to 15 mg after at least 5 days	FDA: (85 mg (children and adolescents) 100 mg (adults)	12 hours	• May open capsule and sprinkle on applesauce, then should be taken immediately without chewing	Capsules contain multi-layered beads: • Immediate-release layer that contains approximately 40% of the MPH dose • Controlled-release layer that contains approximately 80% of the MPH dose
Aptensio XR 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg **FDA approved age:** Age 6 years and older	**Initial:** 10 mg QAM **Titration:** 10 mg	FDA: 60 mg	12 hours	• May open capsule and sprinkle on applesauce, then should be taken immediately without chewing	Capsules contain multi layered beads: • Immediate-release layer that contains approximately 40% of the MPH dose • Controlled-release layer that contains approximately 60% of the MPH dose

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
MPH - Long-Acting (Continued)					
Concerta 18 mg, 27 mg, 36 mg, 54 mg **Relexxii** 72 mg **FDA approved age:** Age 6 years and older	**Initial:** 18 mg QAM (6 years to 17 years) 18 to 36 mg QAM (18 years and older) **Titration:** 18 mg	FDA: 54 mg (children) 72 mg (adolescents and adults)	12 hours	• Must be taken with fluid; swallow whole • Empty tablet shell may be seen in stool • A 72-mg dose is often more cost-effective when prescribed as two 36 mg tablets per dose	Osmotic delivery system surrounded by a semipermeable membrane with an immediate-release drug overcoat 22% of total MPH available for immediate-release in drug coating
Cotempla XR-ODT 8.6 mg, 17.3 mg, 25.9 mg **FDA approved age:** Age 6 years to 17 years	**Initial:** 17.3 mg QAM **Titration:** Weekly increments of 8.6 to 17.3 mg	FDA: 51.8 mg	12 hours	• Allow to disintegrate on tongue without chewing or crushing • Grape-flavored	Comprises two types of MPH: • 25% immediate-release MPH • 75% extended-release MPH
Daytrana 10 mg/9 hours 15 mg/9 hours 20 mg/9 hours 30 mg/9 hours **FDA approved age:** Age 6 years to 17 years	**Initial:** 10 mg/9 hours **Titration:** Increase to next available patch strength if tolerated/response not achieved	FDA: 30 mg/9 hours	12 hours (with 9 hours patch wear)	• Do not cut patch • Apply at the same time each day two hours before effect is needed and wear for nine hours; effect persists three hours after removal • Apply to a clean, dry area of the hip, then hold in place for 30 seconds. Change application site daily • Do not expose application site to external heat sources (e.g., heating pads) • After removal, used patch should be folded so that it adheres to itself and flushed down the toilet or disposed of in a secure lidded container	Transdermal delivery system with 3 layers: • Protective film removed prior to application • Matrix delivery system with MPH embedded into the adhesive for controlled-release • Outside backing

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
MPH - Long-Acting (Continued)					
Jornay PM 20 mg, 40 mg, 60 mg, 80 mg, 100 mg **FDA approved age:** Age 6 years and older	**Initial:** 20 mg in the evening The first dose should be administered at 8pm. Then adjust timing of administration between 6:30pm and 9:30pm to optimize the tolerability and efficacy the next morning and throughout the day. **Titration:** 20 mg	FDA: 100 mg	Peak concentration occurs 14 hours after dose with gradual decline throughout the rest of the day	• Can be taken whole or opened to sprinkle contents onto applesauce, then taken immediately without chewing • If an evening dose is missed, dose should not be administered the following morning	Capsules contain beads with 2 functional film coatings: • Outer delayed-release coating that delays the initial release of MPH • Inner extended-release coating controls release throughout the day due to the slow absorption in the colon No more than 5% of drug is available within first 10 hours after dosing
Metadate CD 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg **FDA approved age:** Age 6 years and older	**Initial:** 20 mg QAM **Titration:** 10 to 20 mg weekly	FDA: 60 mg	8 hours	• Take before breakfast • May open and sprinkle over applesauce and take without chewing, followed by a drink of water • Capsules or contents cannot be chewed or crushed • Avoid alcohol due to effects to the drug release properties	Capsule contains: • 30% immediate-release beads • 70% extended-release beads
Metadate ER 10 mg and 20 mg **FDA approved age:** Age 6 years and older	**Initial:** Replace immediate-release tablets when the 8-hour dosage corresponds to extended-release tablet size. **Titration:** 10 mg every 3 to 7 days	FDA: 60 mg	8 hours	• Take 30 to 45 minutes before a meal • Swallow whole and never crush or chew	Extended-release tablets
QuilliChew ER 20 mg, 30 mg, 40 mg **FDA approved age:** Age 6 years and older	**Initial:** 20 mg QAM **Titration:** 10, 15, 20 mg weekly	FDA: 60 mg	8 hours	• May be cut in half (20- and 30-mg tablets are scored). • Cherry-flavored	Tablets contain: • 30% immediate-release MPH • 70% extended-release MPH Drug is released from sodium polystyrene sulfonate particles via ion exchange.

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
MPH - Long-Acting (Continued)					
Quillivant XR 25 mg/5 mL **FDA approved age:** Age 6 years and older	**Initial:** 20 mg QAM **Titration:** 10 to 20 mg weekly	FDA: 60 mg	12 hours	• Must be reconstituted by pharmacist • Shake vigorously for at least 10 seconds prior to dose • Bottle sizes are 60, 120, 150, and 180 mL • Banana-flavored • Stable at room temperature for up to 4 months after reconstitution • Avoid alcohol	Oral solution contains: • 20% immediate-release • MPH 80% extended-release MPH
Ritalin LA 10 mg, 20 mg, 30 mg, 40 mg **FDA approved age:** Age 6 years to 12 years	**Initial:** 20 mg QAM **Titration:** 10 mg weekly	FDA: 60 mg	6 to 9 hours	• May open and sprinkle over cool applesauce and take immediately, then followed with a drink of water • Patients should avoid alcohol while taking this medication	Capsules contain: • 50% immediate-release beads • 50% enteric-coated, delayed-release beads
Dexmethylphenidate - Immediate-Release					
Focalin 2.5 mg, 5 mg, 10 mg **FDA approved age:** Age 6 years and older	**Initial:** 2.5 mg BID **Titration:** 2.5 to 5 mg weekly	FDA: 20 mg	3 to 5 hours	• Take at least 4 hours apart without regard to meals • D-threo enantiomer of racemic methylphenidate • If converting from MPH, use half of total daily dose	Immediate-release tablets
Dexmethylphenidate - Long-Acting					
Focalin XR 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg **FDA approved age:** Age 6 years and older	**Initial:** 5 mg QAM (6 years to 17 years) 10 mg QAM (18 years and older) **Titration:** 5 mg weekly (6 years to 17 years) 10 mg weekly (18 years and older)	FDA:30 mg (6 years to 17years) 40 mg (18 years and older)	8 to 12 hours	• May open and sprinkle over applesauce, then take immediately without chewing	Capsules contain: • 50% immediate-release beads • 50% enteric-coated, delayed-release beads

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Dexmethylphenidate - Long-Acting					
Azstarys 26.1 mg/5.2 mg 39.2 mg/7.8 mg 52.3 mg/ 10.4 mg **FDA approved age:** Age 6 years and older	**Initial:** 6 to 12 years: 39.2/7.8 mg QAM **Titration:** After 1 week, increase to 52.3/10.4 mg or decrease to 26.1/5.2 mg based on response and tolerability **Initial:** 13 years and older: 39.2/7.8 mg QAM **Titration:** Increase to 52.3/10.4 mg after 1 week	FDA: 52.3 mg/10.4 mg	10 to 13 hours	• May open capsule and sprinkle on applesauce or into 2 oz. (50 mL) of water and then take immediately • Commercially available doses of this medication roughly correspond to 20, 30, or 40 mg of dexmethylphenidate hydrochloride	Capsules contain fixed molar ratios: • 30% dexmethylphenidate (immediate-release) • 70% serdexmethylphenidate (prodrug) converted to dexmethylphenidate slowly over several hours

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Mixed Amphetamine Salts - Immediate-release					
Adderall 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30mg **FDA approved age:** Age 3 years and older	**Initial:** 3 years to 5 years: 2.5 mg daily 6 years and older: 5 mg daily or BID **Titration:** 3 years to 5 years: 2.5 mg weekly 6 years and older: 5 mg weekly	FDA: 40 mg	6 hours (dose-dependent)	• Can be dosed daily to TID, 4 to 6 hours apart	• Immediate-release tablets • Combination of all 4 amphetamine salts in equal parts by weight
Mixed Amphetamine Salts - Immediate-release					

Adderall XR
5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg
FDA approved age: Age 6 years and older
	Initial: 10 mg QAM (6 years to 17 years)
	20 mg QAM
	(18 years and older)
	Titration: 5 to 10 mg weekly
	(6 years to 12 years)
	20 mg weekly
	(13 years and older)
		FDA: 30 mg (6 years to 12 years)
		20 mg (13 years and older)
			10 to 12 hours	• May open and sprinkle over applesauce and taken immediately without chewing
				• Patients taking divided doses of immediate-release mixed amphetamine salts,(for example, twice daily), may be switched to mixed amphetamine salts, extended-release at the same total daily dose taken once daily
					• Capsules contain:
					  • 50% immediate-release beads
					  • 50% delayed-release beads
					Combination of all 4 amphetamine salts in equal parts by weight

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**

Mydayis
12.5 mg, 25 mg, 37.5 mg, 50 mg
FDA approved age: Age 13 years and older
	Initial: 12.5 mg QAM upon awakening (13 years to 17 years)
	12.5 to 25 mg QAM upon awakening (18 years to 55 years)
	Titration: 12.5 mg weekly
		FDA: 25 mg (13 years to 17years)
		50 mg (18 years to 55 years)
			16 hours	• May open and sprinkle over applesauce and take immediately without chewing
				• Due to potential for insomnia (up to 16-hour duration), ensure administration upon awakening in the morning
				• If dose is missed, do not administer later in the day
					• Capsules contain 3 types of beads:
					  • Immediate-release beads
					  • Delayed-release beads release at pH 5.5
					  • Delayed-release beads release at pH 7.0
					• Labeling states that 37.5 mg capsule provides similar blood concentrations to 25 mg extended-release capsule followed by 12.5 mg immediate-release tablet taken eight hours later.

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Dextroamphetamine - Immediate-release					
ProCentra 5 mg/5 mL **FDA approved age:** Age 3 years to 16 years	**Initial:** 2.5 mg daily (3 years to 5 years) 5 mg daily to BID (6 years to 16 years) **Titration:** 2.5 mg weekly (3 years to 5 years) 5 mg weekly (6 years to 16 years)	FDA: 40 mg, rarely higher	4 to 6 hours	• Bubble gum-flavored • If dividing doses, separate by 4 to 6 hours	• Immediate-release solution
Zenzedi 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg **FDA approved age:** Age 3 years to 16 years	**Initial:** 2.5 mg daily (3 years to 5 years) 5 mg daily to BID (6 years to 16 years) **Titration:** 2.5 mg weekly (3 years to 5 years) 5 mg weekly	FDA: 40 mg, rarely higher	4 to 6 hours		• Immediate-release tablet
Dextroamphetamine - Long-Acting					
Dexedrine Spansule 5 mg, 10 mg, 15 mg **FDA approved age:** Age 6 years to 16 years	**Initial:** 5 mg once daily (QD) to BID **Titration:** 5 mg weekly	FDA: 40 mg, rarely higher	6 to 8 hours		• Spansule contains an initial dose released promptly, and the remaining medication is released gradually over prolonged period

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Xelstrym 4.5 mg/9 hours, 9 mg/9 hours, 13.5 mg/9 hours, 18 mg/9 hours **FDA approved age:** Age 6 years and older	**Initial:** 4.5 mg/ 9 hours (6 years to 17 years) 9 mg/9 hours (adults) **Titration:** 4.5 mg weekly (6 years to 17 years)	FDA: 18 mg/9 hours	9 hours	• Apply system 2 hours before an effect is needed and remove within 9 hours • Apply system to clean, dry, intact skin to any of the following application sites: hip, upper arm, chest, upper back, or flank • Select a new application site each time a new system is applied • Wash hands if adhesive side of transdermal system is touched • Upon removal, fold transdermal system so that the adhesive side of the system adheres to itself and placed in a lidded container. System should not be flushed down the toilet • Do not expose application site to external heat sources (e.g., heating pads)	Translucent transdermal delivery system with three layers. • The first layer is an oversized protective silicone-coated, polyester release liner that is removed and discarded before applying. • A second acrylic adhesive matrix containing dextroamphetamine. • A third polyester and polyurethane laminate film layer (backing).

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Amphetamine - Immediate-Release					
Desoxyn 5 mg **FDA approved age:** Age 6 years and older	**Initial:** 5 mg daily to BID **Titration:** 5 mg weekly	FDA: 25 mg	4 to 5 hours	• Insulin requirements in diabetes mellitus may be altered with use • Teratogenic	• Immediate-release tablets (methamphetamine)
Evekeo 5 mg, 10 mg **FDA approved age:** Age 3 years to 17 years	**Initial:** 2.5 mg daily (3 years to 5 years) 5 mg daily to BID (6 years to 17 years) **Titration:** 2.5 mg weekly (3 years to 5 years) 5 mg weekly (6 years to 17 years)	FDA: 40 mg, rarely higher	At least 9.25 hours	• Give dose on awakening and additional doses (1 to 2) at intervals of 4 to 6 hours	• Immediate-release tablets in a 1:1 ratio of dextroamphetamine/levoamphetamine
Evekeo ODT 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg **FDA approved age:** Age 3 years to 17 years	**Initial:** 2.5 mg daily (3 years to 5 years) 5 mg daily to BID (6 years to 17 years) **Titration:** 2.5 mg weekly (3 years to 5 years) 5 mg weekly (6 years to 17 years)	FDA: 40 mg, rarely higher	10 hours	• Tablet should be placed on tongue and allowed to disintegrate, do not crush or chew	• Orally disintegrating tablet in a 1:1 ratio of dextroamphetamine/levoamphetamine
Amphetamine - Long-Acting					

Adzenys XR-ODT
3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, 18.8 mg
FDA approved age: Age 6 years and older
	Initial: 6.3 mg QAM (6 years to 17 years)
	12.5 mg once daily (QD) (18 years and older)
	Titration: 3.1 to 6.3 mg weekly (6 years to 17 years)
		FDA: 18.8 mg (6 years to 12 years)
		12.5 mg (13 years and older)
			13 hours	• Tablet should be placed on tongue and allowed to disintegrate, do not crush or chew
				• Orange-flavored
				• Product is dosed as amphetamine base and is not interchangeable with other amphetamine salts on a milligram-per-milligram basis
					• Orally disintegrating tablet in a 3:1 ratio of dextroamphetamine/levoamphetamine
					• Tablets contain:
					  • 50% immediate-release
					  • 50% delayed-release

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**

Dyanavel XR
2.5 mg/mL
FDA approved age:
Age 6 years and older
	Initial: 2.5 to 5 mg QAM
	Titration: 2.5 to 10 mg every 4 to 7 days
		FDA: 20 mg	13 hours	• Do not mix with food/liquid
				• Bubble gum-flavored
				• Store at room temperature
				• Shake vigorously before dosing and administration
				• Onset in as little as 1 hour
				• Product is dosed as amphetamine base and is not interchangeable with other amphetamine salts on a milligram-per-milligram basis
					• Extended-release suspension
					• Each 1 mL contains:
					  • 2 mg of amphetamine (in a 3.2 to 1 ratio of dextroamphetamine to levoamphetamine complexed with sodium polystyrene sulfonate)
					  • 0.5 mg amphetamine (present as 0.3 mg of amphetamine aspartate and 0.5 mg of dextroamphetamine sulfate)

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**

Dyanavel XR
5 mg, 10 mg, 15 mg, 20 mg
FDA approved age: Age 6 years and older
	Initial: 2.5 to 5 mg QAM
	Titration: 2.5 to 10 mg every 4 to 7 days
		FDA: 20 mg	13 hours	• May be chewed or swallowed whole
				• 5 mg tablets are scored for easy splitting
				• Bubble gum-flavored
				• Onset of action in as little as 1 hour
				• Product is dosed as amphetamine base and is not interchangeable with other amphetamine salts on a milligram-per-milligram basis
					• Extended-release tablets contain immediate-release and extended-release components:
					  • 80% amphetamine (present as 3.2 to 1 ratio of dextroamphetamine to levoamphetamine complexed with sodium polystyrene sulfonate)
					  • 20% amphetamine (present as 0.7:1 ratio amphetamine aspartate to dextroamphetamine sulfate)

Lisdexamfetamine - Long-Acting					
Vyvanse 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg **FDA approved age:** Age 6 years and older	**Initial:** 30 mg QAM **Titration:** 10 to 20 mg weekly	FDA: 70 mg	10 to 12 hours (up to 14 hours adults)	• May open capsule and add to yogurt, or orange juice. Must completely disperse by mixing prior to consuming mixture. Take immediately after mixing	• Capsule • Lisdexamfetamine dimesylate: prodrug of dextroamphetamine • Labeling states that product is activated primarily by red blood cells

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Vyvanse 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg **FDA approved age:** Age 6 years and older	**Initial:** 30 mg QAM **Titration:** 10 to 20 mg weekly	FDA: 70 mg	10 to 12 hours (up to 14 hours adults)	• Must be chewed thoroughly before swallowing • Strawberry-flavored	• Chewable tablet • Lisdexamfetamine dimesylate: prodrug of dextroamphetamine • Labeling states that product is activated primarily by red blood cells
Non-Stimulants - Alpha$_2$ Agonists					
Kapvay 0.1 mg **FDA approved age:** Age 6 years to 17 years	**Initial:** 0.1 mg at bedtime **Titration:** 0.1 mg weekly	FDA: 0.4 mg/day	10 to 12 hours	• Can be added in to a psychostimulant (dose adjustment of stimulant can occur) • Do not crush, split, break, or chew • Daily doses above 0.1 mg should be divided into twice-daily dosing, with either an equal or higher dosage being given at bedtime • When discontinuing, taper the dose in decrements of no more than 0.1 mg every 3 to 7 days to avoid rebound hypertension	• Extended-release clonidine tablets

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Intuniv 1 mg, 2 mg, 3 mg, 4 mg **FDA approved age:** Age 6 years to 17 years	**Initial:** 1 mg/day QAM or once a day in the evening (QPM) **Titration:** No more than 1 mg/week to a target dose of 0.05-0.12 mg/kg/day based on clinical response and tolerability	FDA: 4 mg (6 years to 12 years) 7 mg (13 years to 17 years)	8 to 12 hours	• Do not crush/break/chew • Do not take with high-fat meal • Immediate-release and extended-release formulations are not interchangeable on a mg to mg basis • When discontinuing, taper the dose in decrements of no more than 1 mg every 3 to 7 days to avoid rebound hypertension	• Extended-release guanfacine tablets
Non-Stimulants - Norepinephrine Reuptake Inhibitors					
Strattera 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg **FDA approved age:** Age 6 years and older	<70kg: 0.5 mg/kg/day QAM for 3 days, then can be increased to 1.2mg/kg ≥70kg: 40 mg/day for 3 days, then 80 mg/day	FDA: <70kg: 1.4 mg/kg ≥70kg: 100 mg	24 hours	• Do not crush, chew, or open capsule (contents of capsule are ocular irritants) • CYP2D6 substrate • Associated with hepatotoxicity • Boxed Warning: may increase suicidal ideation in children and adolescents • Effect may take up to 2 to 8 weeks • Can be administered either as a single daily dose in the morning or as evenly divided doses in the morning and late afternoon/early evening. Some pharmacy plans may limit to one capsule per day	• Atomoxetine immediate-release capsules

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Qelbree 100 mg, 150 mg, 200 mg **FDA approved age:** Age 6 years to 17 years	**Initial:** 100 mg daily (6 years to 11 years) 200 mg daily (12 years to 17 years) **Titration:** 100 mg weekly (6 years to 11 years) 200 mg weekly (12 years to 17 years)	FDA: 400 mg	24 hours	• May be sprinkled over applesauce and consumed without chewing within 2 hours • CYP1A2 inhibitor; increases area under the curve (AUC) of caffeine per labeling	• Extended-release viloxazine capsules
Off-Label Medications					
Wellbutrin 75 mg, 100 mg **FDA approved age:** Off label	**Initial:** Less than 3 mg/kg or 150 mg/day	Off-label: Less than 6 mg/kg or 300 mg/day (no single dose >150 mg)			• Immediate-release bupropion tablet
Wellbutrin SR 150 mg **FDA approved age:** Off label	**Initial:** Less than 3 mg/kg or 150 mg/day Typically dosed BID	Off-label: Less than 6 mg/kg or 300 mg/day (no single dose >150 mg)		• Mimics bupropion TID	• Sustained-release bupropion tablets
Wellbutrin XL 150 mg, 300 mg **FDA approved age:** Off label	**Initial:** Less than 3 mg/kg or 150 mg/day Typically dosed daily	Off-label: Less than 6 mg/kg or 300 mg/day (no single dose >150 mg)		• Mimics bupropion TID • Mimics bupropion sustained-release BID dosing • Empty tablet shell may be seen in stool	• Extended-release bupropion tablets
Catapres 0.1 mg, 0.2 mg, 0.3 mg **FDA approved age:** Off label	**Initial:** ≤45 kg: 0.05 mg at bedtime 45 kg: 1 mg at bedtime	Off-label: 2 mg (27 to 40.5 kg) 3 mg (40.5 to 45 kg) 4 mg (> 45kg)		• Immediate-release and extended-release formulations are not interchangeable on a mg to mg basis	• Immediate-release clonidine tablets

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Catapres-TTS 0.1 mg/24 hours, 0.2 mg/24 hours, 0.3 mg/24 hours **FDA approved age:** Off label	**Initial:** ≤45 kg: 0.05 mg at bedtime 45 kg: 1 mg at bedtime	Off-label: 2 mg (27 to 40.5 kg) 3 mg (40.5 to 45 kg) 4 mg (> 45kg)	Patches to be worn for 7 days	• 2 to 3 days for results	• Transdermal film containing clonidine
Provigil 100 mg, 200 mg **FDA approved age:** Off label	**Initial:** 100 mg to 200 mg daily **Titration:** May increase from 100 mg to 200 mg as tolerated on day 3	Off-label: Maximum dosages ranged from 200 mg to >500 mg (in divided doses) in clinical trials		• Not approved by FDA for ADHD due to possibility for dermatologic effects (severe) • Dosages of 300 mg or more were typically studied in patients weighing more than 30 kg	• Immediate-release modafinil tablets
Off-Label Medications (Continued)					
Amantadine hydrochloride 100 mg **FDA approved age:** Off label for ADHD	**Initial:** 50 mg/day in divided doses 1 to 3 times daily (morning, noon, and 4 PM) **Titration:** 50 mg at 4 to 7 day intervals	Off-label: <30 kg: 100 mg/day ≥30 kg: 150 mg/day			• Immediate-release tablets
Tofranil 10 mg, 25 mg, and 50 mg **Tofranil PM** 75 mg, 100 mg, 125 mg and 150 mg **FDA approved age:** 6 years and older	**Initial:** 1 mg/kg/day in 1 to 3 divided doses (children 6 years to 17 years)	Manufacturer's labeling warns against use of doses > 2.5 mg/kg/day in pediatric patients. Studies have shown use of up to 4 mg/kg or 200 mg *Monitor for ECG changes			• Tofranil immediate-release imipramine tablets • Tofranil PM sustained-release imipramine capsules

ADHD Medications					
Product *(by brand name)*	**Initial and Titration Dose**	**Max Daily Dose**	**Duration of Action**	**Clinical Pearls**	**Delivery System**
Pamelor 10 mg, 25 mg, 50 mg and 75 mg **Nortriptyline oral** solution 10 mg/5mL **FDA approved age:** Off label	**Initial:** 0.5 mg/kg/day (children and adolescents) 10 mg BID (adults) **Titration:** Weekly by 0.5 mg/kg/day (children) Increase in 25 mg increments until therapeutic range is reached (3 to 4 week trial at each dose)	Off-label: Lesser of 2 mg/kg or 100 mg (children and adolescents) 50 to 150 ng/mL (adult)- Monitor plasma levels when doses above 100 mg daily are administered			• Immediate-release nortriptyline capsules
Off-Label Medications (Continued)					
Norpramin 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, and 150 mg **FDA approved age:** 6 years and older Off label for ADHD	**Initial:** 1.5 mg/kg/day divided twice daily (children and adolescents) **Titration:** Weekly up to a target dose of 3.5 mg/kg/day in 2 divided doses by week 3 (children and adolescents)			• Because of reports of sudden death in children, desipramine should not be used first-line or when other TCAs are an option	• Immediate-release desipramine tablets

References for Appendix 2.6: ADHD Medications

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Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management		
Class	**Side Effects**	**Monitoring/Management**
Stimulants • Methylphenidate • Dexmethylphenidate • Dextroamphetamine • Amphetamine • Dextroamphetamine/amphetamine • Lisdexamfetamine • Methamphetamine	• Appetite suppression (potentially increased for amphetamines) • Nausea/vomiting • Headache • Dizziness	• Administer with food • Monitor height and weight every 6 months • Use shorter-acting agent
	• Growth suppression in children	• Monitor height and weight at follow-up appointments • If at any point, patients who are not growing or gaining weight as expected may have to have their therapy interrupted
	• Cardiovascular risk	• Prior to initiating stimulant, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical examination to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as electrocardiogram (ECG) and echocardiogram • Promptly conduct cardiac evaluation in patients who develop exertional chest pain, unexplained syncope, or any other symptoms of cardiac disease during stimulant treatment • Baseline heart rate and blood pressure measurements • Blood pressure and heart rate monitored at follow-up appointments
	• Misuse and dependence	• Assess the risk of misuse prior to prescribing • Monitor for signs of misuse and dependence while on therapy
	• Irritability	• Decrease dose • Consider discontinuation of medications with evaluation for comorbidities
	• Sleep disturbances	• Late evening and nighttime doses should be avoided (unless drug is indicated to take in the evening) • Avoidance of nighttime stimuli • Use short-acting agents or change to atomoxetine • Consider addition of melatonin
	• Tic disorder	• Monitor for worsening of tics exacerbated by medication • Consider switching to non-stimulant therapy if conditions worsen
	• Hallucination and other psychotic symptoms	• Assess and evaluate for coexisting conditions prior to initiating therapy • Consider changing therapy if new psychiatric symptoms occur with initiation of treatment
	• Priapism	• May occur during or after discontinuation of therapy • If condition presents, medical treatment should be initiated immediately
	• Leukoderma • (Daytrana only)	• Discontinue patch if loss of skin pigmentation is reported

Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management		
Class	**Side Effects**	**Monitoring/Management**
Selective Norepinephrine Reuptake Inhibitors • Atomoxetine • Viloxazine	• Appetite suppression • Nausea/vomiting • Abdominal pain	• Titrate via recommended starting doses when new treatment is initiated • May give with food • Atomoxetine only- divide daily dosage into twice daily (BID) to help decrease side effects
	• Tachycardia • Hypertension	• Prior to initiating treatment, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical exam to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as ECG and echocardiogram • Promptly conduct cardiac evaluation in patients who develop exertional chest pain, unexplained syncope, or any other symptoms of cardiac disease during stimulant treatment • Baseline heart rate and blood pressure measurements • Blood pressure and heart rate monitored at follow-up appointments
	• Growth suppression in children	• Monitor height and weight at follow-up appointments • If at any point, patients who are not growing or gaining weight as expected may have to have their therapy interrupted
	• Psychotic or manic symptoms	• Treatment is emergent • Consider discontinuation of treatment if symptoms occur
	• Somnolence • Fatigue	• Administer dose at bedtime
	• Suicidal thoughts or behaviors • (Boxed Warning)	• Before therapy, evaluate for existing psychiatric conditions • Advise families and caregivers of the need for close observation and communication with the prescriber • Therapy change should be considered if new symptoms arise after drug is started
	• Priapism • (atomoxetine only)	• May occur during or after discontinuation of therapy • If condition presents, medical treatment should be initiated immediately
	• Urinary retention • (atomoxetine only)	• Use with caution when there is a history of urinary retention or bladder outlet obstruction
	• Hepatitis • (atomoxetine only- Boxed Warning)	• Rarely, associated • Monitor liver enzymes (upon signs/symptoms of liver dysfunction and for several weeks after discontinuation for liver dysfunction)

Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management		
Class	**Side Effects**	**Monitoring/Management**
Selective Alpha-2 Agonists • Clonidine • Guanfacine	• Somnolence • Fatigue • Dizziness	• Administer dose at bedtime
	• Hypotension • Bradycardia	• Prior to initiating stimulant, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical exam to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as ECG and echocardiogram • Promptly conduct cardiac evaluation in patients who develop exertional chest pain, unexplained syncope, or any other symptoms of cardiac disease during stimulant treatment • Baseline heart rate and blood pressure measurements • Blood pressure and heart rate monitored at follow-up appointments
	• Rebound hypertension (abrupt discontinuation)	• Medications should be tapered rather than suddenly discontinued
Off-Label Medications		
Bupropion	• Suicidal thoughts or behaviors • (Boxed Warning)	• Before therapy, evaluate for existing psychiatric conditions • Advise families and caregivers of the need for close observation and communication with the prescriber • Therapy change should be considered if new symptoms arise after drug is started
	• Seizures	• Contraindicated in patients with a history of seizures • Permanently discontinue if seizure occurs during therapy
	• Psychosis in patients with an underlying psychiatric illness.	• Symptoms may abate with dose reduction and/or withdrawal of treatment
	• Cardiovascular risk	• Prior to initiating treatment, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical exam to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as ECG and echocardiogram • Baseline heart rate and blood pressure measurements • Blood pressure and heart rate monitored at follow-up appointments
	• Abuse/misuse	• Monitor for signs of abuse and/or misuse while on therapy

Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management		
Class	**Side Effects**	**Monitoring/Management**
Off-Label Medications		
Modafinil	• Cardiovascular risk	• Prior to initiating treatment, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical exam to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as ECG and echocardiogram • Baseline heart rate and blood pressure measurements • Blood pressure and heart rate monitored at follow-up appointments
	• Psychotic or manic symptoms	• Treatment is emergent • Consider discontinuation of treatment if symptoms occur
	• Tic disorder	• Monitor for worsening of tics exacerbated by medication • Consider switching therapy if conditions worsen
	• Seizures	• Discontinue if seizure occurs during therapy
	• Psychosis	• Monitor for the occurrence of these symptoms especially at initiation and after dose increases • Use is not recommended in patients with preexisting psychotic disorders
	• Suicidal thoughts or behaviors	• Before therapy, evaluate for existing psychiatric conditions • Advise families and caregivers of the need for close observation and communication with the prescriber • Therapy change should be considered if new symptoms arise after drug is started

Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Side Effects & Monitoring/Management		
Class	**Side Effects**	**Monitoring/Management**
Off-Label Medications		
Tricyclic Antidepressants • Desipramine • Nortriptyline • Imipramine	• Cardiovascular risk	• Prior to initiating treatment, assess medical history and family history of sudden death or ventricular arrhythmia; conduct a physical exam to assess for cardiac disease; patients should receive further evaluation if findings suggest cardiac disease, such as ECG and echocardiogram • Monitor for symptoms (syncope, SOB, dizziness, palpitations, etc.) once treatment is started. Obtain ECG or refer to cardiology if present
	• Suicidal thoughts or behaviors	• Before therapy, evaluate for existing psychiatric conditions • Advise families and caregivers of the need for close observation and communication with the prescriber • Therapy change should be considered if new symptoms arise after drug is started
	• Anticholinergic (blurred vision, constipation, dry mouth)	• Monitor therapy
	• Orthostatic hypotension	• Use with caution in patients at risk or those who cannot tolerate
	• Seizures	• Use with extreme caution in patients with a history of seizures • Permanently discontinue if seizure occurs during therapy
	• Overdose	• Can be fatal in as little as 10 times the daily dose. Toxicity related to QT prolongation, anticholinergic toxicity and seizures. Avoid in patients who appear to be at high risk of intentional overdose

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Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Conversion Aid*				
Current Medication	**Current Total Daily Dose (mg/day)**	**Conversion Factor**	**New Medication**	**Total Daily Dose (mg/day)**
Amphetamine Salts				
Mixed Amphetamine Salts Immediate-Release (IR)/ Extended-Release (ER)	20 mg	1	**Mixed Amphetamine Salts IR/ER**	20 mg (may divide IR dose in 1 to 3 equally divided doses)
	20 mg	2	**Methylphenidate HCl IR/ER**	40 mg* (may divide IR dose in 1 to 3 equally divided doses)
*Alternatively, consider switching amphetamines to methylphenidate at the same dose and titrating up				
Mixed Amphetamine Salts IR/ER	20 mg	2.5	**Vyvanse** (lisdexamfetamine dimesylate)	50 mg
Mixed Amphetamine Salts IR/ER	20 mg	0.625	**Adzenys XR-ODT, Adzenys ER (amphetamine) ODT-XR tablet and ER oral suspension**	12.5 mg
Adzenys XR-ODT, **Adzenys ER** (amphetamine) **ODT-XR tablet and ER oral suspension**	12.5 mg	1.6	**Mixed Amphetamine Salts IR/ER**	20 mg (may divide IR dose in 1 to 3 equally divided doses)
Lisdexamfetamine				
Vyvanse (lisdexamfetamine dimesylate)	10 mg	~0.77	**Methylphenidate HCl IR/ER**	7.7 mg* (may divide IR dose in 1 to 3 equally divided doses)
Vyvanse (lisdexamfetamine dimesylate)	50 mg	0.4 - 0.6	**Mixed Amphetamine Salts IR/ER**	25 mg* (may divide IR dose in 1 to 3 equally divided doses)

Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Conversion Aid*				
Current Medication	**Current Total Daily Dose (mg/day)**	**Conversion Factor**	**New Medication**	**Total Daily Dose (mg/day)**
Methylphenidate and Derivatives				
Aptensio XR (methylphenidate HCl) capsule	10 mg	1	**Methylphenidate HCl IR/ER**	10 mg (may divide IR products in 1 to 3 equally divided doses)
Dexmethylphenidate HCl IR/ER	10 mg	2	**Methylphenidate HCl IR/ER**	20 mg (may divide IR products in 1 to 3 equally divided doses)
		1	**Dexmethylphenidate HCl IR/ER**	10 mg (may divide IR products in 1 to 3 equally divided doses)
Methylphenidate HCl IR	15 mg (may divide IR dose in 1 to 3 equally divided doses)	~0.67	**Daytrana** (methylphenidate transdermal) patch	10 mg/ 9 hr wear time
Daytrana (methylphenidate transdermal) patch	10 mg/ 9 hr wear time	1.5	**Methylphenidate HCl IR**	15 mg (may divide IR dose in 1 to 3 equally divided doses)
Methylphenidate HCl IR/ER	20 mg	0.5	*The conversion of methylphenidate to dextroamphetamine/amphetamine is done at approximately ½ the dose of methylphenidate. However, it may be reasonable for children who are already receiving ≥ 20 mg/day methylphenidate to convert to dextroamphetamine-amphetamine at a starting dose of 10 mg once per day and titrate based on response.	
		1.3	**Vyvanse** (lisdexamfetamine dimesylate)	26 mg* (available in 20 mg, 30 mg)
Concerta (methylphenidate osmotic release) ER tablets	18 mg	~0.56	**Daytrana** (methylphenidate transdermal) patch	10 mg/ 9 hr wear time
Daytrana (methylphenidate transdermal) patch	10 mg/ 9 hr wear time	1.8	**Concerta** (methylphenidate osmotic release) ER tablets	18 mg

The recommendation for the following medications is to start with the initial dose and titrate when switching due to pharmacokinetics and salt form differences*

Adhansia XR
Adzenys XR-ODT
(if switching to another product other than Adderall XR)
Azstarys
Dyanavel XR
Evekeo ODT
Jornay PM
Mydayis
QuilliChew ER
Quillivant XR

Chart Considerations

The ADHD Medication Conversion Aid is not an all-inclusive list of strengths and dose conversions from one medication to another medication, the chart is intended to be an aid for how to make these mathematical conversions based on available evidence from expert consensus, journal articles, product labeling, and online dose calculators.

Note that the dosing provided does not account for pharmaceutical labeling indications such as age. Please consult labeling for dose recommendations based on age.

New medication total daily doses may need to be rounded to the nearest available strength or rounded as clinically appropriate by the prescriber. Also, total daily dose may be dosed in partial tablets depending on the dose. For example, Ritalin (methylphenidate IR) is available in 5 , 10 , and 20 mg doses, a dose of 8mg after conversion can be rounded up to 10 mg or rounded down, and the patient be given 1 and ½ tablets of 5 mg resulting in a 7.5 mg dose. Clinical judgment must be utilized independently of this aid when deciding whether to round up or down when dosing or titrating a medication.

Be aware to check product labeling for medications that can or cannot be crushed/split.

This chart should not replace clinical judgment, it is only to be used as an aid. Medication doses should be based on a wide variety of factors including body weight, patient age, severity of symptoms, response to medication or previous medications, medication duration of action, concurrent medications, comorbid conditions, and patient specificity (e.g., sex, ethnicity, age etc.).

For a more detailed and accurate approach to converting between ADHD medication products and the methodology of conversion factors see “Guidance for Off-Label Conversions.”

Guidance for Off-Label Conversions

Product labeling should be given strong consideration when converting from one stimulant medication to another. However, product labeling is silent on most stimulant conversions. This may be because labeling for older products has not been updated as newer products have been approved, or because manufacturers of newer products did not offer guidance on product conversions when seeking approval with the U.S. Food and Drug Administration. Clinicians wishing to undertake a conversion should treat any conversion factors as suggestions that will need to be tailored to the patient’s clinical presentation. Patients whose behavioral symptoms are a very significant impairment may benefit from more aggressive dosing, while patients at higher risk for adverse effects (including, but not limited to, cardiac abnormalities, insomnia, or anorexia) may need to be converted with more cautious doses. This section will provide guidance on how to conceptualize off-label conversions and how to create off-label conversions on an *ad hoc* basis.

If product labeling does not suggest a conversion to the target medication, it may be appropriate to consider reversing a conversion that exists for the starting medication. For example, if a patient was taking dexmethylphenidate immediate-release 5 mg, 1 tablet twice daily and the prescriber wished to convert to methylphenidate immediate-release tablets, the labeling for methylphenidate may be silent on the conversion. However, the labeling for dexmethylphenidate tablets suggests that converting to dexmethylphenidate from methylphenidate involves dividing the methylphenidate dose by 2. Therefore, it may be clinically reasonable to multiply the dexmethylphenidate dose by 2 to reverse this process, resulting in a suggested dose of methylphenidate immediate release 10 mg, 1 tablet twice daily.

In most cases, however, off-label conversions will require patient-specific consideration of biopharmaceutic, pharmacodynamic, and pharmacokinetic factors. Biopharmaceutic factors pertain to the medication’s dosage form and formulation, including salt forms (for

example, amphetamine sulfate versus mixed amphetamine salts). Pharmacodynamic factors pertain to the way that the medication's active ingredients interact with the body and may be most relevant when converting between methylphenidate products and amphetamine products. Pharmacokinetic factors pertain to the way in which the body will absorb, activate, and metabolize the medication, and may be particularly relevant for medications with both immediate- and extended-release formulations.

Biopharmaceutic Factors

In general, the term *biopharmaceutics* refers to the study and engineering of medication dosage forms (Mobley, 2013). This includes the medication's inactive ingredients and variations in extended-release formulations. Medication salt forms must also be considered in the discussion of biopharmaceutic factors. A medication is said to be formulated as a salt if its active ingredient is bound to a counterion or other molecule. This may be done to help the medication remain stable in solid forms or to alter other biological or chemical characteristics (Paulekuhn, Dressman, & Saal, 2007). Different salt forms can be recognized by inclusion of the salt form's name after the name of the active ingredient, as with "sulfate" in "amphetamine sulfate" or "dimesylate" in "lisdexamfetamine dimesylate." A medication formulated without a salt form can be referred to as the "base" medication.

Under the assumption that salt forms do not have a significant and predictable impact on parameters such as absorption time, equivalent dosages of a medication in its base form should be equivalent. Therefore, differences in molecular weights of different salt forms can complicate conversion between stimulants. For example, labeling for methylphenidate extended-release orally disintegrating tablets (ODTs) state that the product contains methylphenidate base molecules that are bound to a polymer. Thus, methylphenidate extended-release ODT products are dosed by methylphenidate base and may appear to contain smaller dosages than the corresponding methylphenidate hydrochloride products. As a result, labeling for methylphenidate extended-release ODT states that 8.6 mg of that product contains the same amount of methylphenidate as 10 mg of the methylphenidate hydrochloride salt form; conversely, hydrochloride takes up 1.4 mg of every 10 mg of methylphenidate hydrochloride. Similarly, each molecule of amphetamine sulfate contains two amphetamine base moieties bound to a single sulfate counterion. Therefore, converting from amphetamine sulfate to amphetamine base requires factoring out the mass of the sulfate counterion, then accounting for the fact that two amphetamine groups are present in each unit of amphetamine sulfate. Arguably the most complicated salt form among the stimulants is mixed amphetamine salts (MAS), which contain equal parts by mass of dextroamphetamine saccharate, dextroamphetamine sulfate, amphetamine aspartate monohydrate, and amphetamine sulfate. However, a full consideration of MAS equivalent dosing will also require a discussion of pharmacodynamics.

Pharmacodynamic Factors

In pharmacy, *pharmacodynamics* is a blanket term that refers to the study of how medications act upon the body. This term may refer to mechanisms of action, receptor binding affinities, and other means by which a medication may exert therapeutic or adverse effects. The major pharmacodynamic distinction in stimulant medications is the distinction between amphetamine derivatives and methylphenidate derivatives. Amphetamine derivatives are believed to exert therapeutic effect by blocking reuptake of catecholamines (i.e., dopamine and norepinephrine), but may also promote catecholamine release from neurons (Stahl, 2013). Methylphenidate derivatives are believed to act primarily as catecholamine reuptake inhibitors (Stahl, 2013). Therefore, both types of agents are believed to increase dopaminergic and noradrenergic tone and therefore neurological activity in the prefrontal cortex, but amphetamine derivatives may have a "two-hit" mechanism of action, while methylphenidate products may have a "one-hit" mechanism of action.

These differing mechanisms of action complicate conversion between amphetamine derivatives and methylphenidate derivatives. Relatively few head-to-head studies exist. One study of 58 children published in 2000 comparing dosages of MAS and methylphenidate found that

final methylphenidate doses were approximately double the final doses of MAS, with a broad standard deviation in the methylphenidate group (Pliszka, Browne, Olvera, & Wynne, 2000). Labeled dosages for methylphenidate are also approximately double the labeled dosages of MAS. Thus, it may sometimes be reasonable to assume that methylphenidate dosages are roughly double the comparable dosages of MAS (Comparison of ADHD Medications (United States), 2022). However, providers should use this conversion with care and should place the conversion in the context of the severity of the patient's ADHD symptoms and the potential adverse effects that the patient may experience when switching from methylphenidate derivatives to amphetamine derivatives.

Another source of pharmacodynamic complication is the possible variability in biological activity of stereoisomers of the same compound. Many medications, including methylphenidate and amphetamine, are chiral compounds. This means that these compounds have two or more forms with the same chemical and structural formulas, but different orientations in three-dimensional space. For example, amphetamine sulfate exists as a mixture of equal parts of the dextro-isomer and levo-isomer of amphetamine sulfate. This equal mixture of stereoisomers is called a racemic mixture, and the stereoisomers are sometimes called dextroamphetamine and levoamphetamine. Similarly, "methylphenidate" exists as a mixture of dextro- and levo-isomers. Unless otherwise specified, medications are generally assumed to be racemic or equal mixtures of stereoisomers, if a chiral center is present. Thus, "amphetamine sulfate" is an even mixture of dextroamphetamine sulfate and levoamphetamine sulfate, while "dextroamphetamine sulfate" contains only the dextroamphetamine moiety.

The field of pharmacy often assumes that certain stereoisomers are relatively inert (McConathy & Owens, 2003). This assumption is illustrated by the labeled conversion between dexmethylphenidate and methylphenidate: labeling for dexmethylphenidate assumes that patients who are prescribed methylphenidate can switch to dexmethylphenidate at one-half of their methylphenidate dose. Thus, the labeling assumes that only dexmethylphenidate has a therapeutic effect in most people. In principle, omitting any other isomers may therefore reduce the risk of side effects without compromising therapeutic outcomes (McConathy & Owens, 2003).

The assumption that one stereoisomer is biologically inert may not be true or may not be completely true for every patient. For example, levoamphetamine seems to produce fewer effects in the central nervous system than dextroamphetamine but has some effect in the brain and some effects in the periphery (Berman, Kuczenski, McCracken, & London, 2008). Therapeutic and adverse effects of levoamphetamine may therefore be uncertain and may vary from patient to patient. The reasons for this potential variation in response are likely to be broad and may include pharmacogenomic factors or variations in patient expectations.

Despite the limits of these assumptions, the simplest way to convert between stimulants may be to convert the starting medication's dosage to the base equivalence of the more pharmacologically active agent—usually dextroamphetamine base or dexmethylphenidate base. If a product exists as a racemic mixture, this can usually be done by dividing the base dose in half. For example, 8.6 mg of methylphenidate base—the labeled equivalence for 10 mg of methylphenidate hydrochloride—could be roughly equivalent to 4.3 mg dexmethylphenidate base.

Since MAS includes two racemic amphetamine salts and two dextroamphetamine salts, converting to dextroamphetamine base equivalents would involve uneven divisions of dosages of each component. Labeling for MAS extended-release capsules has already performed this conversion: product labeling states that the MAS extended-release contains 3.1 units of dextroamphetamine base to 1 unit of levoamphetamine base. Labeling for this product also presents the results of this conversion in mass units: 10 mg of MAS extended-release is stated to contain a total of 6.3 mg of amphetamine base equivalence, of which 4.7 mg is dextroamphetamine base and 1.5 mg is levoamphetamine base. Thus, it may be reasonable to assume that 10 mg of MAS extended-release would be comparable to approximately 5 mg of dextroamphetamine extended-release, though this conversion would ignore the role that levoamphetamine may have in therapeutic or adverse effects.

Pharmacokinetic Factors

Pharmacokinetics is the study of how medications are absorbed, distributed, metabolized, and eliminated by the body. Thus, this field includes studies of anticipated durations of action and peak blood concentrations. Pharmacokinetics may also be relevant when discussing medications that are converted to their active form by the body after the medication is taken. Medications formulated in this way are referred to as *prodrugs* and include lisdexamfetamine and serdexmethylphenidate.

Pharmacokinetic factors are of most obvious concern when converting to or from an extended-release formulation. Different extended-release formulations of the same active ingredient will have different durations of action, and some extended-release products will release medication in multiple "phases". For example, labeling for the methylphenidate extended-release ODT indicates that the product acts over approximately 12 hours and releases its methylphenidate in two phases, with 25% being released immediately and 75% being released with a peak in concentration approximately 5 hours later. By contrast, the methylphenidate extended-release/delayed-release extended-release capsules should not release significant amounts until they have been in the body for at least 10 hours, after which time the medication is released in one phase with a maximum concentration occurring approximately 14 hours after dosing.

In principle, it should be possible to estimate the immediate-release conversion for any corresponding extended-release product, though the immediate-release doses may be scheduled for inconvenient times. For example, in the methylphenidate extended-release ODT example, 25% of the equivalent methylphenidate base dose could be given as immediate-release methylphenidate tablets, with 75% of the corresponding methylphenidate base dose being administered approximately 4 to 5 hours later. Similar conversions could be constructed as-needed by consulting the labeling for most methylphenidate extended-release products.

Special attention must be given to the stimulants that are converted to their active form by the body. According to product labeling, lisdexamfetamine is converted to dextroamphetamine base after the prodrug is absorbed into the bloodstream. Labeling for the commercially available lisdexamfetamine dimesylate product states that 20 mg of this product contains 11.6 mg of lisdexamfetamine base. Given that the prodrug is converted to dextroamphetamine on a 1:1 basis and given that the molecular weight of lisdexamfetamine base is 263.38 mg per mmol, 20 mg of lisdexamfetamine dimesylate can be expected to produce 0.0440428 mol of dextroamphetamine base under physiological conditions (National Center for Biotechnology Information, PubChem Compound Summary for CID 11597698, Lisdexamfetamine, 2023). Since each dextroamphetamine sulfate molecule contains two dextroamphetamine base moieties and has a molecular weight of 368.5 mg per mmol, this amount of dextroamphetamine base should correspond to roughly 8.12 mg of dextroamphetamine sulfate (National Center for Biotechnology Information, PubChem Compound Summary for CID 5825, Dextroamphetamine sulfate., 2023). Extending these conversions to MAS or racemic amphetamine products will necessarily involve making some assumptions about the biological activity of levoamphetamine.

The commercially-available serdexmethylphenidate/dexmethylphenidate product is a more complicated example, as the dexmethylphenidate portion of this product acts immediately, while the serdexmethylphenidate portion must be activated. However, the product labeling provides conversions to dexmethylphenidate; for example, serdexmethylphenidate/dexmethylphenidate 26.1/5.2 mg is equivalent to 20 mg dexmethylphenidate hydrochloride or 17.3 mg dexmethylphenidate base.

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Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Amphetamines (AMP)		
Acidic agents (e.g., fruit juices, ascorbic acid)	May decrease amphetamine absorption, increase amphetamine excretion, decrease amphetamine plasma levels	Monitor response to therapy
Alkalizing agents Gastrointestinal (GI) (e.g., sodium bicarbonate) Urinary (e.g., acetazolamide)	May increase amphetamine absorption, decrease amphetamine excretion, increase amphetamine half-life	Alternative treatment should be considered
Antibacterial agent (linezolid)	May increase hypertensive effect of amphetamines	Combination of linezolid and amphetamines **should be avoided**
Antidepressants -monoamine oxidase inhibitor (MAOI) (e.g., phenelzine, selegiline)	May increase hypertensive effect that could lead to hypertensive crisis	Amphetamine products are **CONTRAINDICATED** during or within 14 days of MAOI therapy
Antidepressants – selective serotonin reuptake inhibitor (SSRI e.g., paroxetine) selective serotonin/norepinephrine reuptake inhibitor (SNRI, e.g. venlafaxine)	May increase adverse effects of SSRI and may increase risk of serotonin syndrome	Monitor for signs and symptoms of serotonin syndrome *Dosage may need to be reduced
Antidepressants -tricyclic (e.g., amitriptyline)	May increase stimulatory effect and cardiovascular effect of amphetamines	Monitor stimulant and cardiovascular response
Antihypertensives	May decrease hypotensive effects	Periodic evaluation of blood pressure is advisable
Antipsychotics (e.g., chlorpromazine, risperidone)	May decrease effect of amphetamines	Monitor response to AMP therapy
Decongestants (e.g., pseudoephedrine)	May increase heart rate and blood pressure	Blood pressure and heart rate should be monitored
Opioids	Amphetamines may enhance the analgesic effect of opioid agonists	Monitor therapy
Methylphenidate (MPH)		
Antibacterial agent – (linezolid)	May increase pharmacological effect of methylphenidate. Headache, GI symptoms, and hypertension may occur.	Combination of linezolid and methylphenidate **should be avoided**

Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Methylphenidate (MPH)		
Anticoagulant – (warfarin)	May increase serum concentration of warfarin	International normalized ratio (INR) should be monitored whenever MPH use is started or stopped and during dose changes. *Dosage may need to be reduced
Anticonvulsants (e.g., phenobarbital, phenytoin, primidone, fosphenytoin)	May increase serum levels of anticonvulsants	Anticonvulsant serum levels should be monitored at the start and stop of MPH use and during dose changes. *Dosage may need to be reduced
Antidepressants-MAOI (e.g., phenelzine, selegiline)	May increase hypertensive effect of MPH that could lead to hypertensive crisis	MPH products are **CONTRAINDICATED** during or within 14 days of MAOI therapy
Antidepressants*- *- selective serotonin reuptake inhibitor (SSRI), selective norepinephrine reuptake inhibitor (SNRI) (e.g., paroxetine, venlafaxine)	May increase adverse effects of SSRI and may increase risk of serotonin syndrome	Monitor for signs and symptoms of serotonin syndrome. *Dosage may need to be reduced
Antidepressants*-Tricyclic (e.g., amitriptyline)	May increase serum levels and adverse/ toxic effect of tricyclics antidepressants	Monitor serum levels and toxicity of tricyclic antidepressants. *Dosage may need to be reduced
Antihypertensives	May decrease hypotensive effects	Periodic evaluation of blood pressure is advisable
Decongestants (e.g., pseudoephedrine)	May increase heart rate May increase blood pressure	Blood pressure and heart rate should be monitored.
Antipsychotic- second generation (e.g., risperidone)	May increase risk for extrapyramidal symptoms (EPS) during dose changes of MPH or risperidone	Monitor for signs of EPS
Guanfacine (CYP3A4 substrate)		
Antihypertensives	May increase hypotensive effects	Periodic evaluation of blood pressure is advisable
Central Nervous System (CNS) depressants (e.g., alcohol, sedatives, hypnotics)	May increase sedation and somnolence	Monitor for additive CNS-depressant effects, avoid use of unprescribed CNS depressants
Strong and moderate CYP3A4 inhibitors (e.g., ketoconazole, fluconazole, and grapefruit juice)	Plasma concentrations can be significantly affected resulting in increased exposure	Consider guanfacine dose reduction
Strong and moderate CYP3A4 inducers (e.g., rifampin, efavirenz)	Plasma concentrations can be significantly affected resulting in decreased exposure	Consider guanfacine dose increase
Valproates	May increase plasma concentrations of valproic acid	Monitor response to valproic acid/ valproic acid derivatives when guanfacine is started or stopped
QTc prolonging agents (e.g., citalopram, quetiapine)	May increase QTc interval	Consider alternatives or closely monitor for evidence of QTc prolongation

Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Guanfacine (CYP3A4 substrate)		
Beta blockers, calcium channel blockers	May increase risk of sinus bradycardia and atrioventricular (AV) block. May enhance the rebound hypertensive effects of clonidine	Closely monitor heart rate during treatment with a beta blocker and clonidine Withdraw beta blockers several days before clonidine withdrawal when possible and monitor blood pressure closely
Clonidine		
Antihypertensives	May increase hypotensive effects	Periodic evaluation of blood pressure is advisable
CNS depressants (e.g., alcohol, sedatives, hypnotics)	May increase sedation and somnolence	Monitor for additive CNS-depressant effects, avoid use of unprescribed CNS depressants
Beta blockers, calcium channel blockers	May increase risk of sinus bradycardia and AV block May enhance the rebound hypertensive effects of clonidine	Closely monitor heart rate during treatment with a beta blocker and clonidine Withdraw beta blockers several days before clonidine withdrawal when possible and monitor blood pressure closely
Atomoxetine (CYP2D6 substrate)		
Antidepressants -MAOI (e.g., phenelzine, selegiline)	May increase neurotoxic effects of atomoxetine (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma)	Atomoxetine is **CONTRAINDICATED** during or within 14 days of MAOI therapy
Antihypertensives	May decrease hypotensive effects	Periodic evaluation of blood pressure is advisable
Beta-2 agonists (e.g., albuterol)	Can increases in heart rate and blood pressure	Atomoxetine should be administered with caution to patients being treated with systemic (oral or IV) albuterol or other Beta-2 agonists
Strong inhibitors of CYP2D6 (e.g., paroxetine, fluoxetine, and quinidine)	Increase atomoxetine serum concentrations	Initiate atomoxetine at a reduced dose in patients receiving a strong CYP2D6 inhibitor. Increase to usual target dose after 4 weeks if needed. Consider therapy modification
QTc prolonging agents (e.g., citalopram, quetiapine)	May increase QTc interval	Consider alternatives or closely monitor for evidence of QTc prolongation

Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Viloxazine (CYP1A2- strong inhibitor, CYP2D6- weak inhibitor, and CYP3A4-weak inhibitor)		
Antidepressants-MAOI (e.g., phenelzine, selegiline)	May increase hypertensive effect that could lead to hypertensive crisis	Viloxazine products are **CONTRAINDICATED** during or within 14 days of MAOI therapy
Antihypertensives	May decrease hypotensive effects	Periodic evaluation of blood pressure is advisable
CYP1A2 substrates- sensitive or within a narrow therapeutic range (e.g., duloxetine, tizanidine, theophylline)	Increased exposure of CYP1A2 substrates which may increase the risk of adverse events	Coadministration with viloxazine is **CONTRAINDICATED**
CYP1A2 substrates- moderate (e.g., clozapine, olanzapine, caffeine)	Increased exposure of CYP1A2 substrates which may increase the risk of adverse events	Not recommended for coadministration with viloxazine. Dose reduction may be warranted if co-administered.
CYP2D6 substrates (e.g., dextromethorphan, nortriptyline, venlafaxine)	Increases the exposure of CYP2D6 substrates when co-administered	Monitor for adverse reaction and adjust dosages of the CYP2D6 substrate as clinically indicated
CYP3A4 substrates (e.g., tacrolimus, lurasidone, buspirone)	Increases the exposure of CYP3A4 substrates when co-administered	Monitor for adverse reaction and adjust dosages of the CYP3A4 substrate as clinically indicated
Bupropion (CYP2B6- substrate, CYP2D6- inhibitor)		
Alcohol	Enhancement of the adverse/toxic effects of alcohol	Consumption of alcohol should be minimized or avoided
Antidepressants -MAOI (e.g., phenelzine, selegiline)	May increase hypertensive effect that could lead to hypertensive crisis	Bupropion products are **CONTRAINDICATED** during or within 14 days of MAOI therapy
Citalopram	Bupropion may increase the serum concentration of citalopram which may also enhance the adverse/toxic effect of citalopram	Monitor therapy and/or consider therapy modification
CYP2D6 substrates (e.g., venlafaxine, aripiprazole, paroxetine)	Can increase the exposures of drugs that are substrates of CYP2D6	Dosage decrease of the dose of CYP2D6 substrates may be necessary, particularly for drugs with a narrow therapeutic index
Dopaminergic drugs (e.g., levodopa and amantadine)	CNS toxicity (restlessness, agitation, tremor, etc.) has been reported with concurrent use of bupropion	Use caution and monitor therapy when using concurrently
Drugs that lower seizure threshold (e.g., antipsychotics, antidepressants)	Risk of seizures with bupropion which can be increased with other drugs lowering seizure threshold	Use extreme caution. Use low initial doses of bupropion and increase gradually. Do not exceed max dose.

Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Bupropion (CYP2B6- substrate, CYP2D6- inhibitor)		
Drugs that require activation by CYP2D6 (e.g., tamoxifen)	Could have reduced efficacy if concurrent use with bupropion	May require increased doses of the drug
Inhibitors of CYP2B6 (e.g., ticlopidine, clopidogrel)	Can increase bupropion exposures but decrease hydroxybupropion exposure	Dosage adjustment of bupropion may be necessary when co-administered with CYP2B6 inhibitors
Inducers of CYP2B6 (e.g., ritonavir, lopinavir, efavirenz)	Can decrease bupropion and hydroxybupropion exposure	Dosage increase of bupropion may be necessary when co-administered with inducers of CYP2B6 but should not exceed the maximum recommended dose
Amantadine (OCT2- Substrate)		
Alcohol	May increase the potential for CNS effects (dizziness, confusion, lightheadedness)	Concomitant use with alcohol is not recommended
Anticholinergic drugs	May potentiate the anticholinergic-like side effects	Dose reductions may be necessary
Live attenuated influenza vaccines	Amantadine may interfere with efficacy of live attenuated influenza vaccines.	Live vaccines are not recommended. Inactivated influenza vaccines may be used, as appropriate.
OCT2 Inhibitors	OCT2 Inhibitors may increase serum concentrations of amantadine	Monitor therapy and/or consider therapy modification
QTc prolonging agents (e.g., citalopram, quetiapine)	May increase QTc interval	Consider alternatives or closely monitor for evidence of QTc prolongation
Modafinil (CYP2C19- inhibitor, CYP3A4- moderate inducer)		
Antidepressants -MAOI (e.g., phenelzine)	Could induce severe cardiovascular reactions, such as hypertensive crisis with concurrent use	Caution should be used when concomitantly administering MAOIs and modafinil
CYP2C19 substrates (e.g., phenytoin, diazepam)	Higher systemic exposure of CYP2C19 substrate may occur	Dosage adjustments may be necessary
CYP3A4 substrates (e.g., cyclosporine, steroidal contraceptives, guanfacine)	Lower systemic exposure of CYP3A4 substrates	Dosage adjustments should be considered Alternative or concomitant methods of contraception are recommended for patients taking steroidal contraceptives (e.g., ethinyl estradiol) when treated concomitantly with modafinil and for one month after discontinuation of modafinil treatment
Warfarin	Modafinil may increase or decrease the effect of warfarin	Closely monitor INR if coadministration is necessary

Attention-Deficit/Hyperactivity Disorder (ADHD) Pharmacotherapy - Drug Interactions		
Offending Agent(s)	**Possible Interaction**	**Response**
Tricyclic Antidepressants (TCA) Desipramine (CYP1A2- minor substrate, CYP2D6- major substrate) Imipramine (CYP1A2, CYP2B6, CYP3A4 and CYP2C19- minor substrate, CYP2D6- major substrate) Nortriptyline (CYP1A2 & CYP2C19- minor substrate, CYP2D6 major substrate)		
Amphetamines	May enhance the adverse/toxic effect and cardiovascular effects of amphetamines Amphetamines may enhance the serotonergic effect of imipramine resulting in serotonin syndrome	Monitor therapy
Anticholinergics agents	May enhance the adverse/toxic effect of other anticholinergic agents	Monitor therapy/avoid combination depending on individual agent
Antipsychotic agents	May enhance the serotonergic effect resulting in serotonin syndrome	Monitor therapy
Antidepressants -MAOI (e.g., phenelzine)	Could induce severe cardiovascular reactions, such as hypertensive crisis with concurrent use	Caution should be used when concomitantly administering MAOIs and imipramine.
CYP2D6 inhibitors (e.g., fluoxetine, paroxetine)	Higher systemic exposure of TCA may occur	Monitor therapy: dosage adjustments may be necessary
Methylphenidates	May enhance the serotonergic effect resulting in serotonin syndrome	Monitor therapy
Serotonergic agents (e.g., paroxetine, venlafaxine)	May increase adverse effects of SSRI and may increase risk of serotonin syndrome	Monitor for signs and symptoms of serotonin syndrome *Dosage may need to be reduced
QTc prolonging agents (e.g., citalopram, quetiapine)	May increase QTc interval	Consider alternatives or closely monitor for evidence of QTc prolongation

Drug disclaimer:

The authors do not endorse or recommend the use of any particular drug mentioned in this publication. Before prescribing a new drug to a patient, practitioners are advised to check the product information accompanying each drug to ensure it is appropriate for a specific patient and to identify appropriate dosage, contraindications, side effects and drug-to-drug interactions.

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Risk Reduction Strategies

Risk Screenings

Prescreening Tools (adolescents and adults)

- AUDIT-C Questionnaire, NIDA Quick Screen, TAPS-1 Screening Tool, NIAAA Screening Tool

Full Assessment Tools (adolescents and adults)

- CAGE Questionnaire, ASSIST Questionnaire© MAST Screening Tool, DAST© Screening Tool, TAPS-2 Assessment, CRAFFT© Screening Tool, BSTAD Screening Tool, S2BI© Screening Tool

Drug Testing

- Urine screen/testing
- Saliva

Prescription Drug Monitoring Program (PDMP)

- All practitioners who prescribe controlled substances must register with the West Virginia Controlled Substance Monitoring Program (CSMP)
- All dispensed controlled medications must be reported to the West Virginia Board of Pharmacy CSMP each 24-hour period and documented to the patient's medical record
- Per West Virginia Code 60A-9-5a, section b: the CSMP must be checked upon initiation of controlled substance, and yearly
- Recommended: Utilize CSMP data with each new prescription and every 3 months for high-risk patients

Patient and Provider Agreements

- Risk versus benefit counseling
- Drug interaction review
- Monitoring of refill requests
- Medication storage and disposal techniques
- Drug diversion consequences
- Pill counts as needed

National Institute on Drug Abuse (NIDA) Screening Tools Chart						
	Substance		Patient Age		How Tool is Administered	
Tool	Alcohol	Drugs	Adults	Adolescents	Self-administered	Clinician-administered
Screens						
Screening to Brief Intervention (S2BI)	X	X		X	X	X
Brief Screener for Tobacco, Alcohol, and other Drugs (BSTAD)	X	X		X	X	X
Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	X	X	X		X	X
Alcohol Screening and Brief Interventions for Youth: A Practitioner's Guide (NIAAA)	X			X		X
Opioid Risk Tool – OUD (ORT-OUD) Chart		X	X		X	
Assessments						
Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	X	X	X		X	X
CRAFFT©	X	X		X	X	X
Drug Abuse Screen Test (DAST-10)© For use of this tool, please contact Dr. Harvey Skinner		X	X		X	X
Drug Abuse Screen Test (DAST-20 Adolescent version)© For use of this tool, please contact Dr. Harvey Skinner		X		X		X
Alcohol Screening and Brief Interventions For Youth: A Practitioner's Guide (NIAAA)	X			X		X

References for Appendix 3.2: NIDA Screening Tools Chart

National Institute on Drug Abuse (NIDA). (2023, January 6). *Screening and Assessment Tools Chart*. https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools

Screening Tools for Substance Use: Adolescents				
Name of screening	**Type of screening**	**Assesses**	**Scoring**	**Interpretation**
Alcohol and Illicit and Prescription Drug Use				
CRAFFT©	Full screen	Alcohol and drug consumption for patients under 18 years old	3 Prescreening and 6 yes or no questions regarding alcohol and drug use as well as social impacts of use. The same questions are asked once individually in writing and once orally by the physician	A score of 2 or more yes answers indicates increased risk
BSTAD	Full screen	Alcohol and drug consumption for patients under 18 years old	Questions assessing the frequency of alcohol and drug use over the past year	0 Days used in the last year of any drug: no reported use 1 Day used in the last year of any drug: lower risk 2+ Days (alcohol or other drugs) and/or 6+ days used (tobacco): higher risk
S2BI	Full screen	Alcohol and drug consumption for patients under 18 years old	Questions assessing the frequency of alcohol and drug use over the past year	For each drug: Never used in last year- no reported use Once or twice in past year- lower risk Monthly or more - higher risk
GAIN-SS©	Full screen	Alcohol and drug consumption as well as behavioral traits including internalizing disorder, externalizing disorder, crime/ violence screener, and a total disorder screener	Scoring is based on the recency of use/behavior. 3 Points for use/behavior in the last month, 2 points for use/behavior in the last 2-12 months, 1 point for use/behavior 1+ years ago, 0 points for never used/behaved. Number of past year symptoms are counted and used to calculate risk, while lifetime is used to monitor remission and used as a covariate	Low (0): unlikely to have a diagnosis or need services Moderate (1-2): a possible diagnosis; the client is likely to benefit from a brief assessment and outpatient intervention High: (3+ on the total screener, 3-5 on the subscreeners): high probabilities of a diagnosis, the client is likely to need more formal assessment and intervention, either directly or through referral

Screening Tools for Substance Use: Adolescents				
Name of screening	**Type of screening**	**Assesses**	**Scoring**	**Interpretation**
Illicit and Prescription Drug Use				
DAST-20©	Full screen	Drug consumption for patients under 18 years old	Questions assessing drug use and experiences related to drug use using 20 yes or no questions. One point for each yes answer and total is applied to a 5 tier severity assessment scale	Total scores determine risk level: 0: None 1-5: Low level 6-10: Intermediate 11-15: Substantial 16-20: Severe
Alcohol				
NIAAA	Prescreen	Alcohol consumption for under 18	Patient reports if they drink and amount consumed	Ages 9-11: Any drinking is highest risk Ages 11-14: Any drinking is moderate or highest risk Ages 14-18: Reference chart for risk level
Adolescent Mental Health				
PHQ-A	Prescreen	Screening for depression in adolescents	9 Questions with a score 0-3. Total number of responses are weighted for severity. Each "Not at All" response is multiplied by 0, each "Several Days" response is multiplied by 1, each "More than Half the Days" response is multiplied by 2, each "Nearly Every Day" response is multiplied by 3.	Total score: 0-4 None or minimal depressive symptoms 5-14: Mild to moderate depressive symptoms 15-19: Moderate to severe depressive symptoms 20-27: Severe depressive symptoms

References for Appendix 3.3: Screening Tools for Substance Use: Adolescents

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Screening Tools for Substance Use: Adults				
Name of screening	**Type of screening**	**Assesses**	**Scoring**	**Interpretation**
Alcohol and Drug				
TAPS	Prescreen and full screen	Assesses tobacco, alcohol, prescription medications, and other substance use over the previous 3 months	TAPS-1 contains a 4 item screen for tobacco, alcohol, illicit drugs, and non-medical use of prescription drugs. If TAPS-1 screens positive, TAPS-2 will begin	Total scores: 0: No use in past 3 months 1: Problem use 2+: Higher risk
ASSIST	Full screen	Alcohol consumption, tobacco use, and illicit substance use along with their impact on the patient's life	10 drug categories with breakdowns of usage. Scores for each answer are worth 0, 2, 3, 4, 5, 6, 7, or 8 points depending on category and answer	A score of 27+: Determines high risk 11-26: for alcohol and 4-26: All other categories determines moderate risk
GAIN-SS©	Full screen	Alcohol and drug consumption as well as behavioral traits including internalizing disorder, externalizing disorder, crime/ violence screener, and a total disorder screener	Scoring is based on the recency of use/behavior 3 Points for use/behavior in the last month, 2 points for use/behavior in the last 2-12 months, 1 point for use/ behavior 1+ years ago, 0 points for never used/behaved Past month count measures change, # past year symptoms are used to screen for current disorders, while lifetime measure is used to monitor remission and used as a covariate	Low (0): Unlikely to have a diagnosis or need services Moderate (1-2): A possible diagnosis; the client is likely to benefit from a brief assessment and outpatient intervention High: (3+ on the total screener, 3-5 on the subscreeners): High probabilities of a diagnosis, the client is likely to need more formal assessment and intervention, either directly or through referral
Alcohol				
AUDIT-C	Prescreen	Alcohol consumption	3 questions with answers that are assigned a scale 1-4	A total score of 3 or more for women is considered positive A total score of 4 or more for men is considered positive Further screening is needed for positive results
CAGE	Full screen	Alcohol consumption	4 yes or no questions worth 1 point each	2 or more positive answers indicate an alcohol problem 1 positive answer suggests further screening is needed
AUDIT	Full screen	Alcohol consumption	10 questions about alcohol use with scores from 0-4	Total scores determine risk level I-Low risk; II- Risky; III-Harmful; IV-Severe
MAST	Full screen	Alcohol consumption	Yes or no questions with each question being 1 point	Total score: 0-2: No apparent problem 3-5: Early or middle problem drinker 6+: Problem drinker

Screening Tools for Substance Use: Adults				
Name of screening	**Type of screening**	**Assesses**	**Scoring**	**Interpretation**
Illicit and Prescription Drug Use				
DAST-10©	Full screen	Illicit and prescription drug use	10 Yes or no questions about drug use with a total score of up to 10	Total scores determine risk level 0: No Problems reported 1-2:- Low level 3-5:-Moderate 6-8:- Substantial 9-10:- Severe
ORT-OUD	Prescreen	Illicit and prescription drug use	Nine yes or no questions about family and personal drug use and psychological disease	A score of 2 or lower indicates low risk for future opioid use disorder; a score of ≥ 3 indicates high risk for opioid use disorder
Pregnancy -Alcohol				
TWEAK	Full screen	Alcohol consumption in pregnant patients	5 questions ranging from 1-2 points	A score of 2 or more points indicates a risk of a drinking problem
T-ACE	Full screen	Alcohol consumption in pregnant patients	4 questions worth 0-1 points each	A score of 2 or greater indicates potential risk
Mental Health				
PHQ-9©	Prescreen	Screening for depression in adults	Nine questions each scored 0-3	Total score: 0-4 no signs present; 5-9: Mild; 10-14: Moderate; 15-19: Moderate severe 20+: Severe

References for Appendix 3.4: Screening Tools for Substance Use: Adults

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Urine Drug Screening & Testing	
Urine Drug Screens (UDS)	**Urine Drug Testing (UDT)**
Immunoassay screen	GC-MS or LC-MS/MS
In-office, point of care, or lab-based	Laboratory
Results within minutes	Results within hours or days
Detects some legal and illicit medications by structural class	Measures concentrations of all medications, illicit substances and metabolites
Guidance for preliminary treatment and decisions	Definitive identification and analysis
Cross-reactivity common	False positive results are rare
More false negatives	False negatives are rare
$	$$$

Target Drug Screen	Potential Agents Causing False Positives
Amphetamine/Methamphetamine	Amantadine, bupropion, chlorpromazine, desipramine, dextroamphetamine, ephedrine, labetalol, MDMA, VICKS levomethamphetamine inhaler, methylphenidate, phentermine, phenylephrine, promethazine, pseudoephedrine, ranitidine, selegiline, trazodone
Benzodiazepines	Oxaprozin and sertraline
Cannabinoids	Dronabinol, efavirenz, hemp, NSAIDS, proton pump inhibitors, tolmetin
Cocaine	Coca leaf, tropical cocaine anesthetics
Opioids	Dextromethorphan, diphenhydramine, poppy seeds, quinine, quinolones, rifampin, verapamil
Phencyclidine	Dextromethorphan, diphenhydramine, doxylamine, ibuprofen, ketamine, meperidine, tramadol, and venlafaxine

**The above chart is a summary of common agents and not a comprehensive list.*

Stimulant	Detection
Dextroamphetamine (Adderall, Dexedrine, Dextrostat, Xelstrym, Zenzedi)	Amphetamine
Lisdexamfetamine (Vyvanse)	Amphetamine
Methamphetamine (Desoxyn, Crystal Meth)	Amphetamine/Methamphetamine*
Benzphetamine (Didrex)	Amphetamine
Methylphenidate (Concerta, Daytrana, Metadate, Methylin, Ritalin)	Ritalinic Acid
Dexmethylphenidate (Focalin)	Ritalinic Acid
Phentermine	Phentermine

**Further confirmatory testing of d and l isomers of methamphetamine may be required to determine if results are falsely positive due to use of over-the counter products containing l-methamphetamine*

References for Appendix 3.5: Urine Drug Screening & Testing

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Prescription Drug Monitoring Program (PDMP)

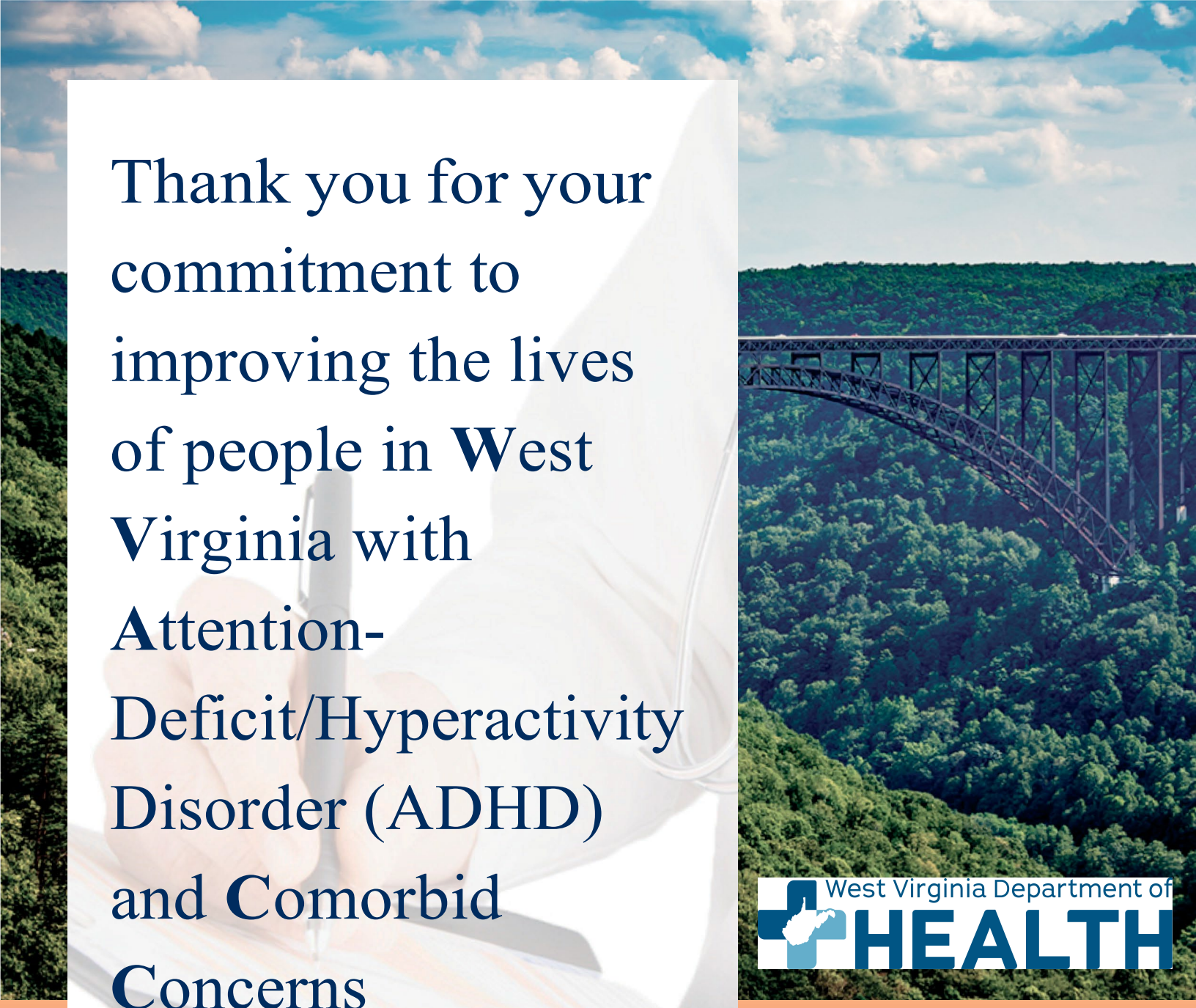
West Virginia's Controlled Substance Monitoring Program (CSMP)

- To register, assign delegate access, or log-in, visit: https://www.csappwv.com/Account/Login.aspx
- All practitioners who prescribe or dispense Schedule II, III, IV, or V controlled substances shall register with the West Virginia CSMP and maintain online, or other electronic access to the program database.
- All licensed prescribers must check the CSMP when initially prescribing a Schedule II controlled substance, any opioid, or any benzodiazepine for a patient not suffering from a terminal illness and at least annually thereafter if treatment is continued.
- "Best Practice" - Check the CSMP when a new prescription is provided, or at least every 3 months.
- All information found from the CSMP must be documented in the patient's medical record at private prescriber practices and inpatient facilities.
- All licensees who dispense Schedule II, III, IV, and V controlled substances to residents of West Virginia must provide the dispensing information to the West Virginia Board of Pharmacy each 24-hour period.
- For more information on CSMP laws: https://www.wvlegislature.gov/wvcode/code.cfm?chap=60A&art=9

Patient & Provider Agreements

Items to include at the provider's discretion

- Emphasis of treatment goal is to improve daily function while minimizing risks
- Coexisting conditions and/or alternate diagnosis such as anxiety, learning, mood, sleep disorders, etc., should be considered, identified, and adequately treated
- Behavioral treatments and other nonpharmacological treatment options should be considered and integrated into the treatment plan where appropriate
- Drug interaction review
- Adverse effects of stimulants, especially with immediate-release formulations, higher doses, and prolonged, continuous use:
  - Serious adverse effects
    - Cardiomyopathy, myocardial infarction, seizures, cerebrovascular accident
  - Common adverse effects
    - Headaches, insomnia, appetite/weight loss, mood changes, increased systolic arterial pressure
- Potential for suppressed growth with continuous use in children
- Periodic reassessment of function, risk, and psychological state
- Expectations to verify compliance
  - Controlled Substance Monitoring Program (CSMP) review
  - Pill counts
  - Urine drug screening and testing
- Discuss risks to other individuals if stimulants are shared
- Safe and secure storage of stimulants
- Medication storage and disposal
- Co-manager of medication therapy if cognitive limitations are present
- Expectations for early refills due to theft, loss, incident
- Consequences of diversion



Thank you for your commitment to improving the lives of people in **W**est **V**irginia with **A**ttention-Deficit/Hyperactivity Disorder (ADHD) and **C**omorbid Concerns

West Virginia Department of HEALTH

WV ACC Guidelines

A West Virginia Guide to Evidence-Informed Evaluation, Diagnosis, and Treatment of ADHD and Comorbid Concerns