Canadian ADHD Practice Guidelines

Fourth Edition

CADDRA Information

Current contact details for the Canadian ADHD Resource Alliance (CADDRA) and information on ordering copies of the Canadian ADHD Practice Guidelines are available on the CADDRA website: www.caddra.ca

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French Edition

This document is available in French under the title: Lignes directrices canadiennes pour le TDAH, quatrième édition.

Feedback

Reader suggestions can be provided through our website (www.caddra.ca) or by emailing info@caddra.ca.

Please Note:

The CADDRA website (www.caddra.ca) will always have the latest version of the Guidelines available free to download and print.

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Canadian ADHD Practice Guidelines

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PREFACE

CANADIAN ADHD PRACTICE GUIDELINES INTRODUCTION

The purpose of the Canadian ADHD Practice Guidelines is to improve the quality of care and health care outcomes for all individuals with Attention Deficit Hyperactivity Disorder (ADHD) in Canada.

The Guidelines:

- Cover the lifespan of the disorder.
- Are based on published evidence.
- Involve expert consensus when there is a lack of evidence.
- Offer practical clinical advice.
- Provide assessment, treatment and follow-up questionnaires.
- Include templates for requesting accommodations.
- Recommend optimizing care on an individual basis.
- Assist healthcare providers to empower their patients to make informed choices in a collaborative process of care.
- Contain information specific to the Canadian healthcare system.

The Guidelines are targeted at health care professionals but may also be of use to additional stakeholders (policy makers, funding bodies, educators) and individuals with ADHD and their families. The tools included in the Guidelines were selected based on their validity, reliability and accessibility. These Guidelines were developed to provide information and user-friendly tools to support Canadian health care professionals diagnose and treat ADHD across the lifespan. These Guidelines are not intended to replicate or replace the many excellent textbooks on ADHD.

The evolution of the 4th Edition

The Canadian ADHD Practice Guidelines are produced and funded by the Canadian ADHD Resource Alliance (CADDRA), a national, independent, not-for-profit association whose members are drawn from family practice, pediatrics, psychiatry (child, adolescent and adult), psychology and other health professions.

The Guidelines have been in constant review for over ten years

The fourth edition of the Canadian ADHD Practice Guidelines evolved from earlier editions published in 2006, 2008, and 2011. A multidisciplinary team that included ADHD specialists, pediatricians, psychiatrists, psychologists, family physicians, pharmacists, nurses, educators and community stakeholders from across Canada and from the US contributed to its writing and review.

Disclosures and Funding

Conflicts of interest were recorded for all individuals that were a part of the process and are included in the Guidelines. As it is the case since the 1st edition of the Canadian ADHD Guidelines, all authors have donated their time and shared their expertise without receiving any financial contribution. The final draft of the 4th edition was independently reviewed by a range of relevant stakeholders (e.g. adult psychiatrist, child and adolescent psychiatrist, psychologist, patient advocate/nurse, family physician). The Guidelines development process was fully funded by CADDRA and occurred without external financial grants.

Endorsements

These Guidelines are endorsed by the Centre for ADHD Awareness, Canada (CADDAC).

CADDRA GUIDELINES – CORE PRINCIPLES

These Guiding Principles were developed and approved by the CADDRA Board.

Principles for Assessment and Diagnosis

1. The clinician has to be fully licensed and adequately trained in order to ensure Diagnostic and Statistical Manual 5 (DSM-5) diagnostic criteria for ADHD are fully met [1].
2. The assessment needs to reflect an understanding of multi-systemic issues that may confound or complicate the ADHD diagnosis (e.g. the educational/vocational, psychosocial, psychiatric and medical interfaces).
3. Symptoms and functional impairment need to be assessed. Using valid, reliable and sensitive instruments helps to evaluate frequency, severity, and outcome.
4. Regular documentation of symptoms and functional impairment, if possible at each visit, helps to track progress and monitor outcome.
5. Establishing collaborative treatment goals with the patient (and their family when appropriate) ensures that outcomes are patient-centred.
6. The results of the assessment need to be communicated to the patient and their family with clarity and compassion.

Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder	**DSM-IV**	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
AERS	Adverse Event Reporting System	**DSM-5**	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
AMP	Amphetamines	**GXR**	Guanfacine XR
ASD	Autism Spectrum Disorder	**MDD**	Major Depressive Disorder
ASPD	Antisocial Personality Disorder	**MRR**	Mortality Rate Ratio
ASRS	Adult ADHD Self Report Scale	**MPH**	Methylphenidate
ATX	Atomoxetine Hydrochloride	**NF**	Neurofeedback
BD	Bipolar Disorder	**OCD**	Obsessive Compulsive Disorder
BPD	Borderline Personality Disorder	**ODD**	Oppositional Defiant Disorder
CADDRA	Canadian ADHD Resource Alliance	**RCT**	Randomized Clinical Trials
CADDAC	Centre for ADHD Awareness, Canada	**S-ADHD**	Secondary Attention Deficit Hyperactivity Disorder
CBT	Cognitive Behavioural Therapy	**SNAP-IV**	Swanson, Nolan and Pelham Teacher and Parent Rating Scale
CD	Conduct Disorder	**SLD**	Specific Learning Disorder
CHADD	Children and Adults with ADHD	**SUD**	Substance Use Disorder
DCD	Developmental Coordination Disorder	**TS**	Tourette's Syndrome
DEX	Dextro-amphetamine	**WFIRS-P**	Weiss Functional Impairment Scale – Parent Report
DMDD	Disruptive Mood Dysregulation Disorder	**WFIRS-S**	Weiss Functional Impairment Scale – Self-Report
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition	**WSR-II**	Weiss Symptom Record II

CHAPTER 1: DIAGNOSIS OF ADHD

Attention Deficit Hyperactivity Disorder (ADHD) is typically a chronic, often lifelong, condition. The impact and presentation of ADHD can change over time [2] and often requires lifelong monitoring and treatment [3]. Clinicians who follow individual patients and their families should be knowledgeable about how ADHD presents and causes functional impairment across the lifespan.

Although the term Attention Deficit Disorder was first introduced in 1980 in the Diagnostic and Statistical Manual of Mental Disorders – 3rd Edition (DSM-III) [4], symptoms of inattention, hyperactivity and impulsivity have been described in children over the last 200 years [5]. A historical perspective reveals that Melchior Adam Weikard is credited with first describing a disorder similar to ADHD in 1775 [6], followed by Sir Alexander Crichton's description in 1798 [5]; Heinrich Hoffman M.D. created the character of "Fidgety Phil", used as a popular allegory for children with ADHD, in 1844 [5]; and Dr. George Frederic Still described a condition remarkably similar to ADHD in the English medical journal the Lancet in 1902 [5]. In 1937, psychiatrist Charles Bradley administered Benzedrine sulfate, an amphetamine, to "problem" children at a home in Providence, Rhode Island to alleviate headaches; but noticed an unexpected behavioural effect: improved school performance, social interactions, and emotional responses [7].

The Diagnostic and Statistical Manual of Mental Disorders, 2nd edition (DSM-II) described the disorder "hyperkinetic reaction of childhood (or adolescence)" in 1968 [8].

ADHD is now defined as a neurodevelopmental disorder. Characterization of ADHD has evolved through several revisions over the years, the most recent one being in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) in 2013 [1]. ADHD is usually seen in early childhood, but not necessarily diagnosed at that time. It is thought to be a lifelong disorder. More than 50% of individuals diagnosed in childhood and adolescence continue to have significant and impairing symptoms in adult life [9, 10].

The general prevalence of ADHD is estimated at between 5-9% for children and adolescents and 3-5% for adults [11, 12]. The disorder is not confined to the USA or Canada but is prevalent worldwide [13].

There is a common public misconception, reinforced by much of the media, that ADHD is over-diagnosed. However, a recent meta-analysis confirmed stable rates of the prevalence of ADHD in the past 30 years [14].

The etiology of ADHD remains under investigation. ADHD is highly heritable [15]. Parents with ADHD have a better than 50% chance of having a child with ADHD, and about 25% of children with ADHD have parents who meet the formal diagnostic criteria for ADHD [16]. Twin studies have placed the heritability of ADHD at 76% [17] with the risk of ADHD in first-degree relatives of diagnosed individuals being somewhere between 30 to 40% [18]. This includes children of adults with ADHD, their siblings or their parents.

The genetics of ADHD are complex [19]. Many different genes have been identified as linked to ADHD (DRD4, DAT) but as ADHD is a heterogeneous disorder it is most likely related to complex genetic etiologies [17].

The ongoing genome wide studies are likely to shed light on this issue in the future [20, 21]. Other etiological factors have been linked to ADHD, tobacco/alcohol use during pregnancy. Low birth weight and psychosocial adversity should be considered as possible contributors to ADHD symptomatology in an individual [22]. Neuronal networks associated with ADHD have been reviewed in neuroimaging studies and the dysfunction of fronto-striatal pathways (dorsolateral and anterior cingulate) are often targeted as a possible underlying neural mechanism [23]. A landmark study on ADHD, the Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA) study [24], found that 70% of school aged children with ADHD have at least one other psychiatric disorder such as anxiety, Oppositional Defiant Disorder, Obsessive Compulsive Disorder, Tic Disorder or depression.

Making a Diagnosis in Primary Care

ADHD patients can be managed in a primary care setting [25]. The tasks of diagnosis according to DSM-5 are to ensure:

- Current symptoms present sufficiently (see below).
- Age of onset of these symptoms is by age 12.
- Impairment in two or more roles due to these symptoms is present for the last six months or more.
- Lack of alternate explanation for the symptoms or impairment, including a broad range of alternate medical (including mental health) and circumstantial conditions.

However, the following situations may require further consultation:

- Medical (physical) or psychiatric comorbidities are present and contributing significant morbidity or diagnostic uncertainty (refer to chapter 2).
- Failure to respond to recommended treatment algorithms (chapter 5).
- Patient/family reluctance to accept diagnosis and/or treatment.

Note: **Overall psychiatric health should always be considered** and a risk assessment done at the onset.

There are several tools available to assist in the diagnosis of mental health problems. Examples of these general screeners are the Weiss Symptom Record (WSR)[26], the Patient Health Questionnaire (PHQ-9)[27] and the Generalized Anxiety Disorder Item-7 (GAD-7)[28] as well as the Screen for Child Anxiety Related Disorders (SCARED)[29] and Kutcher Adolescent Depression Scale (KADS)[30]. As always, therapeutic decisions should be based on a thorough evaluation of the patient with the most prominent or critical issues addressed first. This chapter provides information on how to systematically assess patients with features consistent with ADHD.

Table 1.1 Diagnostic and Statistical Manual 5 (DSM-5) Criteria of ADHD Symptoms

	Criteria A1 Inattention Symptoms	Criteria A2 Hyperactive-Impulsive Symptoms
1.	Often fails to give close attention to details or makes careless mistakes in school work	Often fidgets with hands or feet or squirms in seat
2.	Often has difficulty sustaining attention in tasks or play activities	Often leaves seat in classroom when remaining seated is expected
3.	Often does not seem to listen when spoken to directly	Often runs about or climbs excessively in situations where it is inappropriate
4.	Often does not follow through on instructions and fails to finish school work	Often has difficulty playing or engaging in leisure activities quietly
5.	Often has difficulty organizing tasks and activities	Often is "on the go" or often acts as if "driven by a motor"
6.	Often avoids, dislikes, or reluctantly engages in tasks requiring sustained mental effort	Often talks excessively
7.	Often loses things necessary for activities (e.g. school assignments, pencils, or books)	Often blurts out answers to questions before the questions have been completed
8.	Often is distracted by extraneous stimuli	Often has difficulty awaiting turn
9.	Often is forgetful in daily activities	Often interrupts or intrudes on others (e.g. butts into conversations/games)

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Table 1.2 Diagnostic and Statistical Manual (DSM-5) Presentations

INATTENTIVE PRESENTATION

6 of 9* symptoms are required from

Criteria A1

HYPERACTIVE-IMPULSIVE PRESENTATION

6 of 9* symptoms are required from

Criteria A2

COMBINED PRESENTATION

6 out of 9* symptoms are required from

Criteria A1

+

6 out of 9* symptoms are required from
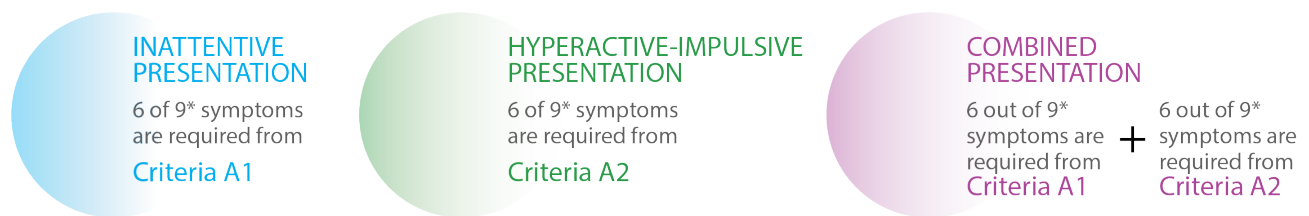
Criteria A2

Other Specified ADHD / Unspecified ADHD: Symptoms causing impairment but full criteria for ADHD are not met.
*Total number of symptoms are less in adults (17+): 5 of 9 instead of 6 of 9

Chapter One of the Canadian ADHD Practice Guidelines and the CADDRA ADHD Assessment Toolkit have been designed to give frontline workers a convenient yet comprehensive step-by-step approach to the assessment and diagnosis of ADHD throughout the lifespan. The forms, assessment tools, and handouts referred to in the diagnostic algorithms are free to download from www.caddra.ca and to print and duplicate for your personal or practice use.

Rating scales and questionnaires can be used as an efficient way to obtain information from the patient and collateral sources, but are not sufficient for a diagnosis as other conditions may screen positive on ADHD rating scales (e.g. overlapping symptoms of depression or anxiety or the presence of medical conditions like sleep apnea or anemia). A careful and thorough assessment reduces the risk of a false diagnosis of ADHD [31]. These instruments, however, are effective screening tools and can be employed to document change over time and track treatment effects.

Update on strategies for the diagnosis of ADHD

Establishing a diagnosis is an essential step in identifying pathology and developing a personalized treatment plan. Thus, clinicians are interested in keeping abreast of advances in diagnostic strategies. To address this need, a review spanning the past 10 years (2006-2016) of the literature diagnosis of ADHD was conducted. Only reviews, meta-analyses and randomized controlled trials were selected.

At this time, there is no evidence that any strategies beyond those described in the CADDRA Guidelines and recommended in the toolkit, (namely the clinical interview in combination with rating scales), offer substantial benefit in the diagnosis of ADHD. The clinical interview and evaluation continues to be the mainstay of diagnosis of ADHD.

Although rating scales alone cannot be used to diagnose ADHD because of issues such as the variability of interpretation of questions by respondent, their use to enrich the process of evaluation is widely recommended [32].

Direct behavioural observation (i.e. observing the child in the classroom) is recommended by most sources [32, 33], and has been complemented by standardized coding systems. It is associated with a high cost and may be possible where health professionals are part of school personnel [32], but is generally limited to research settings.

While, neuropsychological and psychoeducational evaluations are frequently recommended, these are most useful in situations of diagnostic uncertainty [34] and should be interpreted in the context of a broader clinical evaluation given issues of sensitivity and specificity. Certain neuropsychological tests (Wide Range Assessment of Memory and Learning, California Verbal Learning Test, Wisconsin Card Sorting Test) have been recommended as being particularly appropriate measures in ADHD [32]. However, neuropsychological tests of executive function have low ecological validity. Not all individuals with ADHD, although functionally impaired by their ADHD, show impairment levels in test data alone on standardized testing [35-37].

Furthermore, testing results should not be required to demonstrate below "average" functioning for a disability to be recognized and for the student to qualify for services and accommodations. Neuropsychological or psychoeducational testing should not be used to determine the severity of ADHD or quantify the impact of ADHD on cognitive or academic functioning as they do not accurately measure the nature of "real world" cognitive or academic impairments that characterize ADHD.

Computerized cognitive assessments (e.g. Conners' Continuous Performance Test, Test of Variables of Attention, Gordon Diagnostic System) have also been developed that specifically assess attention and response inhibition [32] but are associated with a degree of overlap between individuals with ADHD and controls [38]. Neuroimaging has identified structural alterations and dysfunctions in ADHD in population and research studies, but has no direct clinical application at this time [39].

Electroencephalography has been the focus of many publications [40]. Children with ADHD may have an increase in absolute and relative theta and decreases in absolute and relative alpha and beta [40, 41]. This continues to distinguish adolescents and adults with ADHD [40, 41]. Having said this, EEG testing Is not a validated diagnostic tool for ADHD and CADDRA does not endorse its usage for this purpose.

Red Flags for ADHD
[3, 42-44]

- Organizational skill problems (time management difficulties, missed appointments, frequent late and unfinished projects).
- Erratic work/academic performance.
- Anger control problems.
- Family/marital problems.
- Difficulty in maintaining organized household routines, sleeping patterns and other self-regulating activities.
- Difficulty managing finances.
- Addictions such as substance use, compulsive shopping, sexual addiction, overeating, compulsive exercise, video gaming or gambling.
- Frequent accidents either through recklessness or inattention.
- Problems with driving (speeding tickets, serious accidents, license revoked).
- Having a direct relative who has ADHD.
- Having to reduce their course load, or having difficulty completing assignments in school.
- Low self-esteem or chronic under-achievement.

STEP 1: INITIAL INFORMATION GATHERING

Reasons for Assessment or Referral

Individuals may come to you, or are referred, for a wide variety of reasons:

- Someone close to the individual (e.g. a relative, teacher, employer, colleague or friend) has learned about ADHD and recognizes these traits in the person.
- The individual (typically an adolescent or an adult) has learned about ADHD and recognizes the relevant symptoms.
- A relative has already been diagnosed with ADHD and this diagnosis triggers an awareness of ADHD within the individual (e.g. a child is diagnosed and one or both parents think they may also have ADHD).
- There are functional difficulties that the individual presents with (such as behavioural or attention problems, academic issues, difficulty with paperwork, time management, driving, smoking or marital problems) and the clinician postulates ADHD as a possible explanation.
- Symptoms are attributed to another psychiatric diagnosis (mania, depression, anxiety, substance use disorder) but in fact could be related to ADHD.

Some clinicians may be wary of an individual self-referring with a possible ADHD diagnosis. They may suspect that the person is looking for drugs, accommodations or an explanation/excuse for other problems. Clinical experience indicates this is an infrequent occurrence.

> **Practice Point**
>
> - Review the individual's strengths and NOT just their areas of relative weakness.
> - Establish a rapport with the individual and their family that makes future contacts easier and can aid intervention planning.
> - Ensure that each interview ends with a statement about the coping skills that the individual and/or family have successfully used to work with difficult circumstances.
> - Outline and affirm the importance and value of the individual and their family's efforts to succeed.
> - Remember that self-referral neither guarantees nor eliminates a diagnosis of ADHD.

Presenting Complaint and Documentation Initiation

Review with the individual and their family any concerns, the reason(s) for referral and the individual's/family's hopes for the assessment. Psychometric evaluations included in the CADDRA toolkit are designed to track the person's progress and assist with efficient and structured clinician charting. **The diagnosis of ADHD cannot be done through the CADDRA toolkit alone but in conjunction with a diagnostic interview and attention to medical history, psychosocial elements and clinical presentation.**

SUGGESTED ACTION - AT THE END OF STEP 1

- Give the individual the relevant inventories necessary for the next visit (see appropriate 'Diagnosis and Treatment Flowchart' for the age group).
- Ask the individual and/or family to provide any relevant prior documentation (e.g. school report cards, previous assessments, etc.). Good school performance does not necessarily rule out ADHD. Individuals with ADHD may not accurately recall symptoms [45]. Therefore, collateral information may assist in diagnosis.

The CADDRA Toolkit provides several forms (all available in the public domain), see flowcharts. An ADHD assessment should always include a general mental health screening (to consider comorbidities and differential diagnoses). In addition to a diagnostic interview, the CADDRA Toolkit contains optional assessment tools such as the CADDRA ADHD Assessment Form and the Weiss Symptom Record II (WSR II). The step-by-step flowcharts in this chapter apply after general mental health screening has been completed and ADHD is suspected. All the tools documented in this flowchart are free to download and use. Other assessment tools can be used in place of those proposed below.

Practice Point

Communicating with the child or adolescent's school is crucial to collect information and implement appropriate measures. If parents object to involving the school, the physician should let the parent(s) know that without an understanding of whether there are ADHD-related difficulties in the classroom they will only be able to provide a limited assessment. In adults, collateral information provided by observer reports, such as from family members or partners, are important assessment tools.

Inconsistent reports (i.e. disagreement between parents, teachers, and partners) may require further exploration to help better understand any discrepancy and may require referral.

STEP 2: MEDICAL REVIEW

Objectives:

- Collect the documentation from past records when available.
- Score and review completed forms from Step 1.
- Complete the physical examination (or document that a physical examination was completed by a colleague) and review medical history to ensure that there are no other medical causes that could mimic or modulate ADHD symptoms.
- Discuss the possible complications / outcomes of having ADHD (e.g. accidents, poor sleep, nutrition, and substance abuse).
- Ensure that there are no medical contraindications to the use of medications for treating ADHD (see chapter 5).

SUGGESTED ACTION - AT THE END OF STEP 2

- Order any relevant clinical tests based on the physical findings to rule out medical causes and risk factors.

STEP 3: ADHD-SPECIFIC INTERVIEW

Objectives:

A complete childhood developmental history is an important part of a comprehensive assessment. Because accurate recollection of childhood symptoms and developmental history is difficult to obtain in adults, it is suggested to obtain, when possible, the point of view of a parent or a close family member who knows the individual's early history. The CADDRA ADHD Assessment Form offers an optional ADHD interview format and is available in the CADDRA eToolkit. The Diva 2.0 Diagnostic Interview for ADHD in Adults is another tool that can be downloaded at www.divacenter.eu in various languages [46].

In order to do a complete review, explore:

- Perinatal history (birth weight, complications, maternal alcohol and tobacco usage during pregnancy).
- Developmental milestones.
- Medical history (i.e. illnesses, concussions, seizures etc.)
- Impact of symptoms on learning, socialization and independent functioning.
- Temperament.
- Symptoms of ADHD prior to the age of 12.
- Presence of any life events that were of emotional concern in childhood (e.g., abuse, bullying, divorce, loss, deaths, attachment issues).
- Content review of the completed forms with the individual and their family.

Practice Point

- Review the person's strengths uncovered in the previous steps.

- Do not rely on ADHD symptoms observed during the interview as obvious symptoms of motor hyperactivity, impulsivity and inattention may not present in a one-to-one new situation. If observed during the clinical interview, this often suggests that the symptoms are more severe.

- Remember that a diagnosis of ADHD is made on symptoms and impairments reported rather than only on direct physician observation.

- Question not only the nature of the impairment and symptoms but the triggers that allow them to become apparent.

- Separate out symptoms caused by psychosocial stressors. This can be very difficult, particularly when the patient has suffered significant loss or trauma. It's important to differentiate any acute onset symptoms that may have been caused by recent stressors, such as loss or trauma, from the more chronic neurobiological symptoms of ADHD.

SUGGESTED ACTION - AT THE END OF STEP 3

- Order any tests if necessary. If indicated, make referrals for further specialty assessments such as psychology, occupational therapy, speech language pathology, psychiatry or other medical specialists.
- A psychoeducational assessment may be requested if a learning disability or other cognitive challenges are suspected.
- Continue to emphasize the need to learn about ADHD and ensure that individuals and their families are aware of relevant websites for more information, such as:

  - CADDAC www.caddac.ca (Canada)
  - CHADD www.chadd.org (USA)

STEP 4: FEEDBACK & TREATMENT RECOMMENDATIONS

Feedback of the Diagnosis (if not previously done)

- Review all completed rating scales to determine if they meet criteria for ADHD.
- Review the developmental history, identifying impairments that are often associated with ADHD.
- For children/adolescents, review the CADDRA Teacher Assessment Form.
- Review all other available documentation, such as report cards and prior assessments.
- Give feedback related to the interview and collateral sources.
- Based on the findings above, present the diagnosis and any other concerns that might be relevant.

Dispelling Myths

Many individuals and their families come into an assessment for ADHD with false information or beliefs. Some examples are:

- They are just lazy and looking for an excuse.
- I don't want my child to take medication that could change their personality.
- I am not the one with the problem, my spouse/employer/parent/teacher/school system is the problem.
- I had it as a child but it went away.
- I don't have all of the clinical symptoms.
- ADHD is just a fad.
- Plus, many more…

Feedback of the Treatment Plan

- Address the feelings, questions and reactions to the ADHD diagnosis of the person with ADHD and their family.
- Explain the impact of the diagnosis in social/school/vocational settings. Documentation of the official diagnosis may be critical to receive various school interventions, benefits (e.g. special funding) and accommodations.
- Review the areas of impairment, trying to narrow down the primary symptoms that are troubling the patient.
- Provide further education about ADHD (e.g. the CADDRA Information handout).
- Discuss psychosocial treatments (Chapter 4) and pharmacological treatment options (Chapter 5).

Implementation of Treatment

- Treatment is often multimodal and should be individualized.
- Refer to chapters 4 and 5 for specific treatment guidelines.

Follow-up

Regular and frequent follow-up is important until ADHD is stabilized. Once stabilized, active individualized monitoring based on a chronic disease management model should occur. Frequency of follow-up is dependent on patient characteristics such as medical complications, compliance, response to treatment, social supports and lifestyle factors.

The CADDRA Clinician ADHD Baseline/Follow-up and CADDRA Patient ADHD Medication forms can help streamline these visits.

> **Practice Point**
>
> Regular monitoring includes completion of a growth chart for children plus rating scales, collection of vital signs, and side effects profiles whatever the age of the patient.

1.3 Diagnosis and Treatment – Children

DIAGNOSIS AND TREATMENT FOR CHILDREN

An ADHD assessment includes a general mental health screening (to consider comorbidities and differential diagnoses). In addition to a diagnostic interview, CADDRA recommends tools such as the **WSR II**. This eToolkit contains an optional guided assessment tool, the **CADDRA ADHD Assessment Form**.

The step-by-step flowchart below applies after general mental health screening has been completed and ADHD is suspected. All the tools documented in this flowchart are free to download and use. Other assessment tools (e.g. Vanderbilt, Conners, Strengths and Difficulties Questionnaire - SDQ, Wender Utah Rating Scale) can be used in place of those proposed below. Further information on these steps can be found in Chapter 1, Canadian ADHD Practice Guidelines, 4th Edition.

ADHD SUSPECTED

STEP 1 - INITIAL INFORMATION GATHERING

QUESTIONNAIRES FOR PARENTS/CAREGIVERS

► **SNAP-IV**

Consider also using a functional impairment scale (e.g. **WFIRS·P** - Weiss Functional Impairment Rating Scale Parent)

QUESTIONNAIRES FOR TEACHERS

► **SNAP-IV**

► **CADDRA TEACHER ASSESSMENT FORM**

STEP 2 - MEDICAL REVIEW

EXCLUDE ANY MEDICAL CAUSES THAT CAN MIMIC OR AGGRAVATE ADHD SIGNS OR SYMPTOMS

REVIEW NUTRITION AND LIFESTYLE HABITS: Sleep, exercise, screen time, high-risk activities, substance use, sexual activity (if applicable), accidents

EVALUATE POTENTIAL CONTRAINDICATIONS TO ADHD MEDICATIONS

STEP 3 - ADHD SPECIFIC INTERVIEW

DISCUSS PATIENT'S STRENGTHS AND OBSERVE PATIENT DURING INTERVIEW

REVIEW DEVELOPMENTAL HISTORY AND OBTAIN COLLATERAL INFORMATION FROM PARENTS/CAREGIVERS

REVIEW THE QUESTIONNAIRES USED IN ASSESSMENT

CONSIDER CONTRIBUTIONS OF OTHER PSYCHIATRIC, PSYCHOSOCIAL FACTORS OR LEARNING DISORDERS TO THE PRESENTING SYMPTOMS

Consider specialist referral if necessary.

STEP 4 - FEEDBACK AND TREATMENT RECOMMENDATIONS

EDUCATION ON ADHD
(Continuing process)

Provide information and resources, including:

► **CADDRA ADHD Information Handout**

Links to useful websites:
- **CADDAC** (Canada: www.caddac.ca)
- **PANDA** (Quebec: www.associationpanda.qc.ca)
- **CHADD** (USA: www.chadd.org)

FEEDBACK ON DIAGNOSIS

Feedback to patient and family on ADHD symptoms & impairments

TREATMENT OPTIONS

Discuss and initiate treatment + adaptation measures (school/work accommodations, daily strategies)

► **EDUCATIONAL ACCOMMODATION LETTER TEMPLAT**E

NON-PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Psychosocial Chart**

PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Medication Chart**

FOLLOW-UP VISITS
- ADHD is a chronic disorder that needs longterm, regular follow-up, whether or not medication is prescribed.
- Follow-up will be more frequent when adjusting medications and during life transitions.
- Document changes over time with the rating scales that are most significant for the patient (e.g. **SNAP-IV**, **WFIRS·P**).

Other forms to track changes:

► **CADDRA PATIENT ADHD MEDICATION FORM**

► **CADDRA CLINICIAN ADHD BASELINE/FOLLOW-UP FORM**

The **CADDRA PATIENT TRANSITION FORM** can be used when a patient is transferring to new healthcare professionals, including child and adolescent patients to adult services.

1.4 Diagnosis and Treatment – Adolescents

DIAGNOSIS AND TREATMENT FOR ADOLESCENTS

An ADHD assessment includes a general mental health screening (to consider comorbidities and differential diagnoses). In addition to a diagnostic interview, CADDRA recommends tools such as the **WSR II**. This eToolkit contains an optional guided assessment tool, the **CADDRA ADHD Assessment Form**.

The step-by-step flowchart below applies after general mental health screening has been completed and ADHD is suspected. All the tools documented in this flowchart are free to download and use. Other assessment tools (e.g. Vanderbilt, Conners, Strengths and Difficulties Questionnaire - SDQ, Wender Utah Rating Scale) can be used in place of those proposed below. Further information on these steps can be found in Chapter 1, Canadian ADHD Practice Guidelines, 4th Edition.

ADHD SUSPECTED

STEP 1 - INITIAL INFORMATION GATHERING

QUESTIONNAIRES FOR PARENTS/CAREGIVERS

► **SNAP-IV**

Consider also using a functional impairment scale (e.g.**WFIRS-P**) [Weiss Functional Impairment Rating Scale Parent]

QUESTIONNAIRES FOR TEACHERS

► **SNAP-IV**

► **CADDRA TEACHER ASSESSMENT FORM**

SELF-ASSESSMENT (when appropriate)

► **ASRS** - Adult ADHD Self-Report Scale

Consider also using a functional impairment scale e.g. **WFIRS·S** [Weiss Functional Impairment Rating Scale - Self]

STEP 2 - MEDICAL REVIEW

EXCLUDE ANY MEDICAL CAUSES THAT CAN MIMIC OR AGGRAVATE ADHD SIGNS OR SYMPTOMS

REVIEW NUTRITION AND LIFESTYLE HABITS: Sleep, exercise, screen time, high-risk activities, substance use, sexual activity (if applicable), accidents

EVALUATE POTENTIAL CONTRAINDICATIONS TO ADHD MEDICATIONS

STEP 3 - ADHD SPECIFIC INTERVIEW

DISCUSS PATIENT'S STRENGTHS AND OBSERVE PATIENT DURING INTERVIEW

REVIEW DEVELOPMENTAL HISTORY AND OBTAIN COLLATERAL INFORMATION FROM PARENTS/CAREGIVERS

REVIEW THE QUESTIONNAIRES USED IN ASSESSMENT

CONSIDER CONTRIBUTIONS OF OTHER PSYCHIATRIC, PSYCHOSOCIAL FACTORS OR LEARNING DISORDERS TO THE PRESENTING SYMPTOMS
Consider specialist referral if necessary.

STEP 4 - FEEDBACK AND TREATMENT RECOMMENDATIONS

EDUCATION ON ADHD
(Continuing process)

Provide information and resources, including:

► **CADDRA ADHD Information Handout**

Links to useful websites:
● **CADDAC** (Canada: www.caddac.ca)
● **PANDA** (Quebec: www.associationpanda.qc.ca)
● **CHADD** (USA: www.chadd.org)

FEEDBACK ON DIAGNOSIS

Feedback to patient and family on ADHD symptoms & impairments

TREATMENT OPTIONS

Discuss and initiate treatment + adaptation measures (school/work accommodations, daily strategies)

► **EDUCATIONAL ACCOMMODATION LETTER TEMPLATE**

► **EMPLOYMENT ACCOMMODATION LETTER TEMPLATE**

NON-PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Psychosocial Chart**

PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Medication Chart**

FOLLOW-UP VISITS
● ADHD is a chronic disorder that needs longterm, regular follow-up, whether or not medication is prescribed.
● Follow-up will be more frequent when adjusting medications and during life transitions.
● Document changes over time with the rating scales that are most significant for the patient (e.g. **SNAP-IV**, **WFIRS·P**).

Other forms to track changes:
► **CADDRA PATIENT ADHD MEDICATION FORM**

► **CADDRA CLINICIAN ADHD BASELINE/FOLLOW-UP FORM**

The **CADDRA PATIENT TRANSITION FORM** can be used when a patient is transferring to new healthcare professionals, including child and adolescent patients to adult services. The **JEROME DRIVING QUESTIONNAIRE** can be used to assess driving.
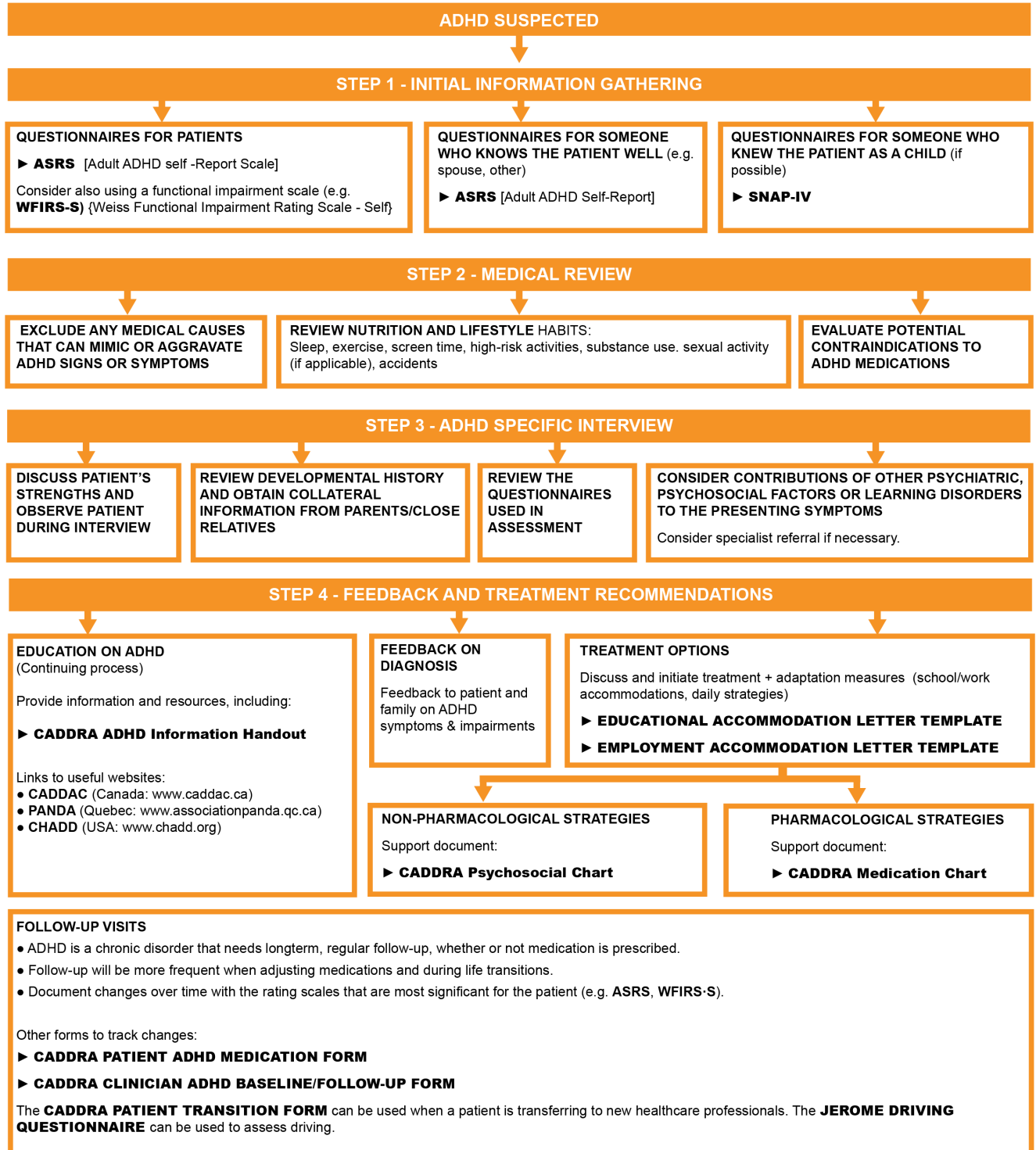
1.5 Diagnosis and Treatment – Adults

DIAGNOSIS AND TREATMENT FOR ADULTS

An ADHD assessment includes a general mental health screening (to consider comorbidities and differential diagnoses). In addition to a diagnostic interview, CADDRA recommends tools such as the **WSR II**. This eToolkit contains an optional guided assessment tool, the **CADDRA ADHD Assessment Form**.

The step-by-step flowchart below applies after general mental health screening has been completed and ADHD is suspected. All the tools documented in this flowchart are free to download and use. Other assessment tools (e.g. Vanderbilt, Conners , Strengths and Difficulties Questionnaire - SDQ, Wender Utah Rating Scale) can be used in place of those proposed below. Further information on these steps can be found in Chapter 1, Canadian ADHD Practice Guidelines, 4th Edition .

ADHD SUSPECTED

STEP 1 - INITIAL INFORMATION GATHERING

QUESTIONNAIRES FOR PATIENTS

► **ASRS** [Adult ADHD self -Report Scale]

Consider also using a functional impairment scale (e.g. **WFIRS-S)** {Weiss Functional Impairment Rating Scale - Self}

QUESTIONNAIRES FOR SOMEONE WHO KNOWS THE PATIENT WELL (e.g. spouse, other)

► **ASRS** [Adult ADHD Self-Report]

QUESTIONNAIRES FOR SOMEONE WHO KNEW THE PATIENT AS A CHILD (if possible)

► **SNAP-IV**

STEP 2 - MEDICAL REVIEW

EXCLUDE ANY MEDICAL CAUSES THAT CAN MIMIC OR AGGRAVATE ADHD SIGNS OR SYMPTOMS

REVIEW NUTRITION AND LIFESTYLE HABITS:
Sleep, exercise, screen time, high-risk activities, substance use. sexual activity (if applicable), accidents

EVALUATE POTENTIAL CONTRAINDICATIONS TO ADHD MEDICATIONS

STEP 3 - ADHD SPECIFIC INTERVIEW

DISCUSS PATIENT'S STRENGTHS AND OBSERVE PATIENT DURING INTERVIEW

REVIEW DEVELOPMENTAL HISTORY AND OBTAIN COLLATERAL INFORMATION FROM PARENTS/CLOSE RELATIVES

REVIEW THE QUESTIONNAIRES USED IN ASSESSMENT

CONSIDER CONTRIBUTIONS OF OTHER PSYCHIATRIC, PSYCHOSOCIAL FACTORS OR LEARNING DISORDERS TO THE PRESENTING SYMPTOMS

Consider specialist referral if necessary.

STEP 4 - FEEDBACK AND TREATMENT RECOMMENDATIONS

EDUCATION ON ADHD
(Continuing process)

Provide information and resources, including:

► **CADDRA ADHD Information Handout**

Links to useful websites:
● **CADDAC** (Canada: www.caddac.ca)
● **PANDA** (Quebec: www.associationpanda.qc.ca)
● **CHADD** (USA: www.chadd.org)

FEEDBACK ON DIAGNOSIS

Feedback to patient and family on ADHD symptoms & impairments

TREATMENT OPTIONS

Discuss and initiate treatment + adaptation measures (school/work accommodations, daily strategies)

► **EDUCATIONAL ACCOMMODATION LETTER TEMPLATE**

► **EMPLOYMENT ACCOMMODATION LETTER TEMPLATE**

NON-PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Psychosocial Chart**

PHARMACOLOGICAL STRATEGIES

Support document:

► **CADDRA Medication Chart**

FOLLOW-UP VISITS
● ADHD is a chronic disorder that needs longterm, regular follow-up, whether or not medication is prescribed.
● Follow-up will be more frequent when adjusting medications and during life transitions.
● Document changes over time with the rating scales that are most significant for the patient (e.g. **ASRS**, **WFIRS·S**).

Other forms to track changes:

► **CADDRA PATIENT ADHD MEDICATION FORM**

► **CADDRA CLINICIAN ADHD BASELINE/FOLLOW-UP FORM**

The **CADDRA PATIENT TRANSITION FORM** can be used when a patient is transferring to new healthcare professionals. The **JEROME DRIVING QUESTIONNAIRE** can be used to assess driving.

CHAPTER 2: DIFFERENTIAL DIAGNOSIS AND COMORBID DISORDERS

PREVALENCE OF COMORBIDITIES

When making an ADHD diagnosis, it is very important to note that, in the majority of cases, ADHD does not exist in isolation [47]. An evaluation for ADHD requires screening for possible comorbid disorders and consideration of biological, social, and psychological factors. Consideration of a second opinion or referral to an ADHD specialist should be made if the patient has a clinical history that is complex or if you are contemplating pharmacological treatment beyond those recommended in these Guidelines [48].

Most individuals with ADHD have co-occurring conditions that may complicate the clinical presentation. Often these comorbid disorders need to be dealt with concomitantly [49]. In some circumstances, as described later in this chapter, one may need to prioritize which condition to treat first.

From the Literature:

- 50-90% of children with ADHD have at least one comorbid condition [47].
- Approximately half of all children with ADHD have at least two comorbidities [47].
- 85% of adults with ADHD meet criteria for a comorbid condition [50, 51].

The literature offers multiple potential explanations for the existence of comorbidities and/or overlapping symptoms between ADHD and other disorders [52].

The main explanations are [53, 54]:

- One disorder is a precursor to another;
- One disorder is a risk factor for developmental of the other;
- The disorders share the same related risk factors; or
- There is a common underlying symptomatic basis for one or more of the behaviours in common.

Table 2.1 Prevalence of Comorbidities

Psychiatric comorbidities prevalence: **+** 1-10%   **++** 11-30%   **+++** >31%   **?** controversial/unknown

	CHILD (6-12)	ADOLESCENT (13-17)	ADULTS (18+)
ANXIETY	++	++	+++
DEPRESSION	+	++	+++
LEARNING DISABILITIES	+++	+++	+++
OPPOSITIONAL DEFIANT DISORDER	+++	++	+
CONDUCT DISORDER	++	++	++ (Antisocial PD)
BIPOLAR	+ (?)	+	++
SUBSTANCE USE	+	++	+++
AUTISM SPECTRUM DISORDER	++	++	++ (?)
TIC DISORDERS	++	++	+
DMDD	?	?	?
BORDERLINE PERSONALITY DISORDER		?	+++
OBSESSIVE COMPULSIVE DISORDER	+	+	++

Comorbidity can contribute to the failure to diagnose ADHD in adults and children [47]. In addition, follow-up studies of children with ADHD and comorbidity show that these children have a poorer outcome than children with ADHD alone, as evidenced by significantly greater social, emotional and psychological difficulties [55]. The most common comorbidities identified in the Multimodal Treatment Study of ADHD [56] and in other comorbidity studies [57-59] have been remarkably consistent (e.g. Oppositional Defiant Disorder, Learning Disorders, Anxiety Disorders, Substance Use Disorders).

Disorder-based Differentiation

Differential diagnosis is the process of differentiating between two or more conditions that share similar signs or symptoms while comorbid disorders are disorders that occur together with ADHD (either causally-related or independent and occur concurrent with ADHD). A careful assessment of other possible diagnoses should be undertaken at the time of evaluation. **As ADHD does not have a symptom that is *pathognomonic* for the condition, there can be numerous overlaps with other disorders.**

A thorough history and full functional review accompanied by a physical examination may highlight underlying physical conditions. While most individuals with ADHD do not need laboratory investigations as part of their diagnostic assessment, in certain instances, a laboratory work up or specific tests are needed to eliminate a suspected pathology.

Some special medical investigations may be required, such as polysomnography [60], electroencephalogram [61], or brain imaging [62, 63]. Psychological testing may be required to address a suspected learning disability [64] or other cognitive challenges. The clinical evaluation of a child with ADHD includes an evaluation of potentially adverse psychosocial factors such as a disruptive family environment [65], child abuse or neglect [66, 67] and attachment issues [68]. These may complicate the presentation of ADHD.

Common medical conditions that may have overlapping symptoms with ADHD:

- Hearing or vision Impairment
- Thyroid dysfunction
- Hypoglycemia
- Severe anemia
- Lead poisoning
- Sleep disorders
- Fetal Alcohol Spectrum Disorder (FASD)
- Neurofibromatosis

Medications that may have psychomotor side effects:

- Medication with cognitive dulling side effect (e.g. mood stabilizers).
- Medication with psychomotor activation (e.g. decongestants, beta-agonist like asthma medication).

Common Comorbidities

In this chapter, we will briefly describe key comorbidities that can present alongside ADHD and the auxiliary treatments that they require.

ADHD, Comorbidity & Development

- ADHD in its different presentations (combined, inattentive or hyperactive-impulsive), and the most common comorbid disorders, change over time and by developmental stage [69].
- The most common comorbid disorders in early childhood are oppositional defiant disorder (ODD) [24, 70], language disorders [71], and anxiety disorders [72].
- Many children with ADHD have a Specific Learning Disorder [73].
- ADHD may be two to three times more common in children with developmental disabilities or borderline IQ and intellectual disabilities [74].
- In the mid-school-age years, symptoms of anxiety or tic disorders become more common [75].
- Mood disorders and substance use disorders tend to be more observable by early adolescence compared to childhood [76-78].
- In adulthood, anxiety, major mood disorders (depression or bipolar disorder) [34] and substance use disorders are commonly seen with ADHD [79-81].

OPPOSITIONAL DEFIANT DISORDER

Behavioural problems (including oppositionality, aggression and delinquency) are among the most common comorbid presentations in children with ADHD [82]. The presence of comorbid Oppositional Defiant Disorder (ODD) with ADHD is likely to generate substantial impairment and is expected to result in increased referrals for treatment [83]. ODD rarely presents as an isolated diagnosis. Distinguishing between normal adolescent self-assertion and ODD may not always be easy. The impulsivity and irritability associated with ADHD is sometimes mistaken for the willfulness of ODD. In some individuals, ODD may continue into adulthood [84].

Symptoms

DSM-5 symptom classification of ODD helps distinguish between the reactive-irritable symptoms that overlap with ADHD manifestations and the provocative-vindictive symptoms [85]. The provocative-vindictive symptoms are less common and are often conceptualized as a reaction to insecurity or low self-esteem and may reflect reaction to a dysfunctional environment. The anxiety/depressive symptoms are associated with the irritable symptom construct of the DSM-5 [86].

DSM-5 provides three symptom clusters (mood related, provocative or vindictive). It is useful to examine each symptom in the light of its overlapping characteristics with ADHD.

Table 2.2 Oppositional Defiant Disorder Differentiation

OVERLAPPING SYMPTOMS WITH ADHD	ODD DISTINCT CHARACTERISTICS
Loses temper	Refuses to comply with rules
Angry, resentful	Deliberately annoys others
Touchy, easily annoyed	Blames others for their own mistakes
Argumentative	Spiteful, vindictive

[87]

Treatment

Treatment of comorbid ODD with ADHD should be multimodal [1]. In patients with comorbid ODD with ADHD, it is advisable that the first step is optimization of pharmacotherapy of ADHD, which may stabilize the reactive-irritable symptoms [88]. This should be followed by augmentation with psychosocial treatment, including Parent Management Training (PMT), Cognitive-Behavioral Therapy (CBT) or Collaborative and Proactive Solutions (CPS) [89]. It is important to distinguish ODD from conduct disorder (CD). Children with ODD have recurring negativistic, defiant, hostile and disobedient behaviour, especially toward authority figures, whereas those with CD repeatedly violate the basic rights of others or age-appropriate societal norms, as defined by a pattern of repeated aggression, lying, stealing, and truancy [90]. The onset of both disorders can be prepubertal, thus making early identification, diagnosis, and treatment crucial. In one study, ODD was found to be a precursor to conduct disorder in approximately 50% of the cases [91].

Key Points

- Some patients with ADHD and ODD may respond adequately to stimulant or non-stimulant (atomoxetine, guanfacine XR) medications [92, 93]. Since many cases are likely to require augmentation with either psychosocial treatment and/or off-label use of another medication (for example; atypical antipsychotics) [94, 95], referral to specialized care may be required in complex cases.
- Effective treatment may reduce the risk of more severe conditions in adolescent and adult years, such as CD, substance use disorder and depression [96].

CONDUCT DISORDER/AGGRESSION

Conduct Disorder (CD) comorbid with ADHD is a severe, persistent condition that is frequently preceded by ODD [84, 97, 98]. When CD has pre-pubertal onset (before the age of 10 years old), the prognosis is considered worse than for the group of children that have adolescent-limited CD [78]. DSM-5 also emphasizes that limited pro-social emotions (lack of remorse or guilt; callousness and lack of empathy); being unconcerned about performance; and shallow or deficient affect are poor prognostic indicators and increase the risk for the development of antisocial personality disorders in adulthood [84]. Furthermore, co-occurrence of ADHD and CD is often a precursor of nicotine use disorder, substance use disorder, anxiety, and depression [78, 99].

Research shows that ADHD and CD represent two complex and distinct entities that can be associated [100]. Children with either of these conditions in isolation present with different core symptoms and perform differently on objective measures of ADHD symptoms than those with ADHD + CD [101, 102]. Children with ADHD + CD show the poorest outcome within each individual group [103, 104].

Symptoms

The following table serves to help clinicians identify behavioural symptoms that may be seen in ADHD and may respond to specific treatments for ADHD. CD specific symptoms may require a multi-systemic approach and may also need to involve the legal system.

Table 2.3 Conduct Disorder Differentiation

OVERLAPPING SYMPTOMS WITH ADHD	CD DISTINCT CHARACTERISTICS
Impulsively starts fights as a reaction to provocation	Instigates fights and may use weapons
May be rough with animals/people due to lack of self-control	Takes pleasure in cruelty to animals and/or people
Forgets curfew	Disobeys curfew and runs away to engage in preferred activities without regard to consequences
Sets fire without considering consequences	Sets fires with vengeance
Steals impulsively	Steals with confrontation (planned)
Lies impulsively to avoid consequences	Lies to manipulate others and obtain gain
Breaks things accidently or impulsively	Vandalizes

Treatment

Pharmacotherapy for patients with a combination of ADHD, CD and aggression using both stimulant and non-stimulant medications has been found to be useful [105, 106]. Although medications are usually effective in reducing the symptoms of ADHD and impulsive aggression [56, 107], these patients typically receive more benefit from multimodal treatment [99].

Medications should initially be used to treat the most severe underlying disorder, but in some complex situations targeting specific symptoms could be appropriate. For example, patients with CD may show aggression before and during the course of treatment, making it imperative to document their aggressive behaviours before the introduction of medication and to make these behaviours an explicit target of therapeutic strategies. Clinicians should assess pharmacological treatment tolerability as some medications may augment irritability and aggression [108].

Conduct problems may be reduced by the most widely used evidence-based treatments for ADHD (e.g. stimulant and non-stimulant medication and psychosocial treatment) [107, 109]. However, treatment of the ADHD may not be sufficient to resolve all symptoms. Optimization of medication as part of a multimodal treatment approach indicated that psychosocial treatments including individual and family interventions are often required [110]. Specialists in this area might use mood stabilizers or an atypical anti-psychotic (both are off-label). Other treatments (besides optimizing ADHD medication and psychosocial treatments) are controversial and referral to a specialist is recommended [111, 112].

Key Points

- The essential characteristic of CD is repetitive and persistent behavior manifested by violation of others' fundamental rights or violation of social rules/norms.
- Psychosocial treatment, such as parenting and problem-solving skills training, and family and/or individual therapy, is often needed to improve patient outcomes.
- Pharmacological treatment of comorbid ADHD and CD may require combination of an ADHD medication and a medication that targets aggression.
- CD with ADHD represents a complex diagnostic entity that may require specialized interventions.

ANTISOCIAL PERSONALITY DISORDER

Antisocial Personality Disorder (ASPD) is diagnosed when a pattern of antisocial behaviour has occurred since age 15, CD is therefore a precursor to ASPD. Many people with ASPD have a history of ADHD but most people with ADHD do not develop ASPD [113].

Symptoms

Many of the ASPD symptoms have an impulsive component. It is therefore clinically indicated to carefully assess for ADHD in patients with ASPD. However, targeting and treating ADHD symptoms may not resolve ASPD symptoms as they are crystalized in the personality but may facilitate a structured intervention for the ASPD.

Table 2.4 Antisocial Personality Disorder Differentiation

OVERLAPPING SYMPTOMS WITH ADHD	ASPD DISTINCT CHARACTERISTICS
May enter into conflict with the law due to impulsive behaviour (e.g. speeding)	Fails to conform to social norms with respect to lawful behaviours as indicated by repeatedly performing acts that are grounds for arrest
Lying impulsively to avoid consequences	Deceitful, as indicated by repeated lying, use of aliases, or conning others for personal profit or pleasure
Is impulsive or fails to plan	Repeated failure to sustain consistent work behavior or honour financial obligations
Can be irritable and have interpersonal conflict (losing control)	Can be Irritability and aggressiveness, as indicated by repeated physical fights (taking control)
May put self and others at risk due to impulsivity and lack of forethought	Reckless disregard and lack of care for safety of self or others; lacks remorse (indifferent to or rationalizing having hurt, mistreated or stolen from another)

Both disorders must be treated separately using the efficacious treatments for each specific condition. Since some patients with ASPD may exhibit drug seeking behavior (for secondary gain) or concurrent substance use disorders [114], clinicians may be sometimes reluctant to consider psychostimulant treatments for these patients even if the ADHD is significant. Non-stimulant medications have not been systematically investigated in these patients but offer a treatment option for some underlying ADHD-related symptoms.

Key Points

- ADHD is a treatable risk factor for ASPD.
- Both conditions require specific interventions and education may help to improve impulsive behaviours but ASPD traits need to be addressed separately.
- ASPD with ADHD represents a complex diagnostic entity and may require specialized interventions.

BORDERLINE PERSONALITY DISORDER

According to the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) [115], the lifetime prevalence of Borderline Personality Disorder (BPD) was reported to be 33.69% in those with ADHD versus 5.17% in the general population, suggesting an association between the two disorders. The most common symptom between ADHD and BPD is impulsivity [116, 117].

Symptoms

BPD and ADHD have shared and overlapping symptoms. The following table assists the clinician in distinguishing symptoms that are more specific to BPD from those that may overlap with ADHD.

Table 2.5 Borderline Personality Disorder Differentiation

OVERLAPPING OF BPD SYMPTOMS WITH ADHD	BPD DISTINCT CHARACTERISTICS
Pattern of relationship challenges/impairments	Has intense relationships with often 'black and white' reactions and underlying intense fear of abandonment
Impulsivity and risky behavior (e.g. gambling, reckless driving, unsafe sex, spending sprees, binge-eating or drug abuse)	Rapid changes in self-identity and self-image
Mood swings	Periods of stress-related paranoia and loss of contact with reality
Inappropriate and intense anger	Suicidal threats, behaviours or self-injury
	Ongoing feelings of emptiness

Treatment

There are no studies establishing the optimal treatment for individuals with ADHD and BPD. The available literature suggests treating the two entities as separate phenomena [118]. In addition, there is no current evidence to propose that an improvement in ADHD leads to a resolution of BPD, signifying that the personality features require specific treatments [119]. However, most treatment strategies of BPD aim to control impulsive behaviours (often with medication), emotion dysregulation and distress tolerance [120]. Currently, Dialectical Behavioral Therapy (DBT) is the most commonly recognized treatment for BPD [121]. While all patients with core impulsivity are at risk of medication misuse, physicians must use their judgment and not necessarily deny patients with BPD effective treatments for ADHD.

Key Points

- BPD with ADHD represents a complex diagnostic entity that requires specific mode of interventions.
- Psychosocial interventions like DBT have been shown to be effective for BPD and should be used in combination with psychopharmacology in the presence of ADHD.
- Stabilizing impulsive behaviours and optimizing emotional regulations should be the main goals of the combined psychosocial and pharmacological interventions.
- BPD with ADHD represents a complex diagnostic entity may require specialized interventions.

ADDICTIONS

In some individuals with ADHD, the need for rapid feedback, the desire for immediate reward and the high adrenaline risk-seeking behaviours may render them vulnerable to addictions. These addictions may be to shopping, sex, pornography, internet and gambling, in addition to possible substance use disorders [122-124]. The principles in the management of addictions and ADHD should rely on a specific intervention for the addictive behaviour and a specific treatment for ADHD, ideally concurrently [125].

SUBSTANCE USE DISORDER

Compared to typically developing individuals, people with ADHD have a two-fold risk for substance abuse and dependence [126, 127]. The literature suggests that one-quarter of adults with SUD [128] and one-half of adolescents with Substance Use Disorder (SUD) have ADHD [129]. Several studies suggest a higher rate of SUD in adults with ADHD than in the general population, and ADHD itself is a risk factor for SUD [130, 131]. Among ADHD patients with a comorbid behavior disorder, those with either comorbid CD or Bipolar Disorder have the greatest likelihood of developing SUD [114, 132-135].

Individuals with ADHD are at significant risk of using substances (e.g. nicotine, cocaine and cannabis) and of starting use earlier than the general population [134]. Moreover, the accompanying poor self-esteem and impulsivity associated with ADHD may be conducive to the development of SUD.

Marijuana continues to be the most commonly abused agent in individuals with ADHD [136]. Abuse can include alcoholism, smoking and other drugs [126]. Furthermore, substance use problems may increase the severity of ADHD symptoms. On the other hand, it is also true that patients with these substance use problems may present with attention, behaviour and self-control symptoms that can mimic ADHD. A referral to a specialist may be required before establishing an ADHD diagnosis when a patient is actively using illicit substances.

Treatment

The best approach to treatment sequencing in individuals with ADHD and comorbid substance use disorder is concurrent intervention with specific interventions for each disorder [125]. Some researchers suggest that ADHD and SUD-related craving share neurobiological similarities, and that treatment of ADHD may reduce craving for substances and subsequently reduce the risk for relapse to substance use [137]. An aggregate of the literature seems to suggest that early stimulant treatment reduces or delays the onset of SUDs and perhaps cigarette smoking into adolescence; however, the protective effect may be lost in adulthood [138].

The treatment needs of individuals with ADHD and SUD need to be considered simultaneously; however, if SUD is severe, sequential treatment may be considered with immediate attention paid to the stabilization of the addiction. Depending on the severity and duration of the SUD, individuals may require residential or inpatient treatment. Day treatment can be a more cost-effective option if patients are ready and motivated for change [139, 140]. Depending on the type of substance being used, prescribing psychostimulants in the presence of active substance abuse requires careful monitoring for medical interactions and should take into account the potential risk of misuse and abuse [97, 129, 133-135, 141, 142].

Although patients commonly report subjective calming with cannabis and other improved symptoms (increased appetite, better sleep), there is no evidence that cannabis is an effective treatment for ADHD or that it improves attention and productivity. In fact, there is evidence that cannabis can impair cognition and exacerbate motivation issues [143].

Methylphenidate does not have the same abuse liability as cocaine due to slower dissociation from the site of action, slower uptake into the striatum, and slower binding and dissociation with the dopamine transporter protein relative to cocaine [144]. However, it is important to remember that the route of administration may alter the abuse liability of a substance. The oral administration of psychostimulants has been shown to decrease the likability of a substance while parenteral usage (IV, snorted) has been shown to be associated with euphoria [144]. Individuals with ADHD and either SUD or CD are at highest risk for diversion and misuse and are more likely to both misuse and divert their stimulant medication [145]. Both immediate-release and, to a lesser degree, extended-release preparations of stimulant medications can be diverted or misused, with extended release preparations having less potential for parenteral usage [55, 145]. Non-stimulants such as atomoxetine and guanfacine XR do not have abuse potential.

Key Points

- In most cases, ADHD and SUD need to be treated concurrently and independently when comorbid.
- Psychostimulants taken orally do not have the same abuse liability as illicit stimulants (e.g. cocaine) due to slower dissociation from the site of action, slower uptake into the striatum, and slower binding and dissociation with the dopamine transporter protein.
- Non-stimulant and long-acting psychostimulants have less abuse potential than immediate-release preparations of psychostimulants.

ANXIETY DISORDERS

As many as a third of children and half of adults with ADHD have comorbid anxiety [146]. Individuals with ADHD often develop symptoms of anxiety due to chronic difficulties related to their ADHD symptoms. For instance, the experience of repeatedly forgetting may lead to realistic worries that one will forget. Compensatory checking may mistakenly be interpreted as evidence of a primary anxiety disorder.

Symptoms

The table of specific versus commonly seen symptoms may help clinicians distinguish ADHD from anxiety disorders.

Table 2.6 Anxiety Disorder Differentiation

ADHD DISTINCT CHARACTERISTICS	ANXIETY DISTINCT CHARACTERISTICS
Inattentive symptoms independent of emotional state	Inattentive symptoms when anxious
Fidgetiness independent of emotional state	Fidgetiness while anxious
Social disinhibition	Social inhibition
Initial insomnia because of a difficulty to 'turn their thoughts off'	Initial insomnia because of ruminations or other anxiety symptoms
No subjective physical symptoms	Physical symptoms such as pounding heart, nausea, difficulty breathing, tremulousness
Transient and realistic worries related to prior and actual functional impairment (e.g. performance anxiety)	Persistent cognitive symptoms of intense fear and/or worry focused on unrealistic specific situations or thoughts

Treatment

If ADHD exists with anxiety, a general rule of thumb is to treat the most impairing condition first [147]. Psychostimulant treatment may increase anxiety especially during treatment initiation, or when increasing dosages of medication [148]. A slower than usual titration schedule may be preferred in these cases. If the anxiety becomes too intense, then the ADHD medication should be reduced or withdrawn and the anxiety should be treated until the symptoms are stabilized and only then should the ADHD medications be started.
Any of the ADHD stimulants can be successfully used when anxiety is comorbid with ADHD [107]. A randomized control pediatric study showed that the non-stimulant atomoxetine can be beneficial in patients with co-occurring ADHD and anxiety disorders [149]. Guanfacine XR was found to be well tolerated in pediatric subjects with anxiety disorder [150].

Key Points

- ADHD-associated impairments can induce anxiety symptoms that are different from a specific anxiety disorder.
- Anxiety disorders and ADHD often coexist and the most impairing condition should be treated first.
- Stimulants and non-stimulants can be used for ADHD in the context of anxiety.
- Titration of psychostimulants may need to be initiated at a slower pace and monitored more carefully with patients prone to anxiety.

MAJOR DEPRESSIVE DISORDER

There is considerable overlap between the clinical presentations of Major Depressive Disorder (MDD) and ADHD. MDD patients (without ADHD) may have depressive episodes presenting with inattention, short-term memory problems, irritability, impulsivity, difficulty sleeping, trouble concentrating, restlessness and being fidgety [141]. A critical point to explore is the "since when" question, as a reported recent drop in mood is qualitatively different from the lifelong demoralization that may be seen in ADHD [151].

Symptoms

Patients with primary ADHD often have to deal with failure and attacks to their self-esteem, frequently at a very young age, and may become demoralized and depressed as a result. In this case, they may present with both disorders. However, patients with ADHD may look like they have a mood disorder when they do not. Lack of motivation may mimic anhedonia and chronic difficulty going to sleep and restless sleep may mimic insomnia secondary to MDD. Patients with ADHD commonly have dysregulated mood (dysphoria, irritability), but it is not typical for ADHD in the absence of a mood disorder to be associated with entrenched, depressed affect or anhedonia.

Table 2.7 Major Depressive Disorder Differentiation

OVERLAPPING SYMPTOMS WITH ADHD	DEPRESSION DISTINCT CHARACTERISTICS
Loss of motivation, demoralization	Feeling sad or hopeless
Problems concentrating	Feeling tired or "slowed down"
Being restless or irritable	Changes in eating and/or sleeping, neuro vegetative symptoms
	Thoughts of death or suicide
	Episodic (while ADHD has a continuous course since childhood)

Treatment

When a patient with ADHD also suffers from MDD, treatment of the most disabling condition should be undertaken first. It is important to note that if the depressive episode is part of a Bipolar Disorder, the treatment algorithm should follow that of Bipolar Disorder (see section on Bipolar Disorder). In some patients, antidepressants with catecholaminergic activity, such as bupropion, can be useful to treat both MDD and ADHD. Typically, the combination of an antidepressant (e.g SSRIs) with psychostimulants may be necessary to achieve remission. SSRIs are considered safe to use in combination with stimulants. However, drug interactions involving the CYP450/2D6, e.g. involving fluoxetine, paroxetine, when combined with the amphetamine class or atomoxetine, require caution and monitoring.

If the MDD continues to be impairing or worsens, referral or specialized care in depression is recommended. In severe depression, and in subjects at risk of self-harm, intervention for depression and specialized referral must be carried out as a priority.

Key Points

- If a patient presents with mild depression and ADHD, then treatment of ADHD may be considered first.
- In cases of depression or severe suicidal risk, treatment for depression must be the priority.
- Concurrent treatment of ADHD and major depression is often required and concomitant use of antidepressants and ADHD medications are commonly used.

BIPOLAR DISORDER

The diagnosis of Bipolar Disorder (BD) in the context of ADHD is challenging. Many symptoms of BD overlap with ADHD symptoms. The definitive epidemiological relationship between both disorders remains controversial. The following table may guide clinicians in differential diagnosis. However, if Bipolar Disorder is suspected, a referral to specialized care should be considered.

Symptoms

Table 2.8 Bipolar Disorder Differentiation

ADHD DISTINCT CHARACTERISTICS	BIPOLAR DISORDER DISTINCT CHARACTERISTICS
Initial insomnia, sleep disorders	Decreased need for sleep
Chronic restlessness	Episodes of speediness, increased rate of speech
Impulsive sexual encounters	Hypersexuality
Chronic course	Episodic course
Chronic distractibility and/or impulsivity	Episode-related distractibility and/or impulsivity
	Feeling "high", or an overly happy mood
	Grandiosity

Treatment

Treatment of comorbid ADHD and BD should usually start with managing and stabilizing the BD symptoms first [152]. The management of ADHD with BD is usually more complicated than managing ADHD alone and often requires the use of mood stabilizers and/or atypical antipsychotics [119]. There is a small risk of switching from euthymia or depression to mania when a bipolar patient is prescribed stimulant medication [153]. If this occurs, the stimulant should be adjusted (reduced) or discontinued, and treatment of BD should be prioritized. Once the patient's mood is stabilized, stimulant medication may cautiously be re-instituted (start low and go slow) [141, 154].

Key Points

- The co-occurrence of BD and ADHD may be difficult to diagnose and manage. A referral to a specialist should be considered.
- Treatments should be aimed at stabilizing the Bipolar Disorder first and then treating ADHD.
- Stimulants have been shown to be safe and effective in patients with BP once their symptoms have been stabilized.

DISRUPTIVE MOOD DYSREGULATION DISORDER

The diagnostic criteria for Disruptive Mood Dysregulation Disorder (DMDD) includes severe recurrent disproportional temper outbursts (verbal and/or physical) occurring three or more times a week in at least two different settings for 12 months or more [1]. Diagnoses are generally made between the ages of 6 and 10 and cannot first be made before the age of six years or after the age of 18 years [1]. Between temper outbursts, the mood of the patient with DMDD appears to be irritable/dysphoric [155].

DMDD is currently considered a presentation of childhood depression and this diagnosis was created to address concerns about the potential for the over diagnosis of, and treatment for, bipolar disorder in children [1]. A study of some 3,258 participants aged 3 to 17 [156] showed a prevalence rate for bipolar disorder of 0.8% to 3.3% with the highest rate in preschoolers. DMDD was also found to be very comorbid (62% to 92%). The highest rates of comorbidity occurred with depressive disorder (odds ratio 9.9 to 23.5) and ODD (52.9% to 100%). Rate of co-occurrence with ADHD had odds ratios which ranged from 2.9 to 12.

Table 2.9 Disruptive Mood Dysregulation Disorder (DMDD) Differentiation

OVERLAPPING SYMPTOMS WITH ADHD	DMDD DISTINCT FEATURES
Irritable mood episodes (explosive outburst)	Inter-episode dysphoria
Psychomotor agitation	Minor triggers with extreme rage attacks
Chronic course	
Young age of onset	

Treatment

A combination of medications and psychosocial interventions is needed to treat ADHD + DMDD. Many of the medications effective for treating ADHD have been shown to be effective for DMDD [157].

Key Point

- DMDD is a new DSM-5 diagnosis. Research regarding its treatment and relationship to ADHD is underway.

OBSESSIVE-COMPULSIVE DISORDER

The lifetime prevalence of Obsessive Compulsive Disorder (OCD) in the general population is 1-3% [158]. Reported rates of ADHD-OCD co-occurrence are highly inconsistent in the literature [159]. If OCD and ADHD present together, there is an increased risk of Tic Disorders and Tourette Syndrome also being present [160]. ADHD patients often develop behavioural patterns, like repetitive checking of tasks, as coping strategies to compensate for the symptoms of ADHD. Whether these behaviours are secondary to ADHD or are indicative of OCD needs to be considered.

Treatment

Treatment of OCD and ADHD should be carried out simultaneously. While there are no controlled studies, a 2014 review [161] reported no evidence showing a worsening of OCD symptoms with the concurrent use of psychostimulant medications.

Key Points

- Psychostimulants do not usually lead to an exacerbation of OCD symptoms [161].
- The presence of OCD comorbidity does not change the treatment approach to either disorder.

TOURETTE SYNDROME AND TIC DISORDERS

ADHD is highly comorbid with tics and Tourette Syndrome (TS) (50-90%) [162], so patients with tics should be screened for ADHD. In a 2014 study, four clusters of individuals were identified: pure TS (49.8%), TS + ADHD (22.2%), TS + OCD (21.5%) and TS + ADHD + OCD (6.5%) [162]. A commonality to all groups was emotional liability. All groups had significant behavioral problems compared to normal controls. The presence of OCD is considered to be more impairing than the presence of ADHD and is more likely to increase the rate of other co-morbidities [162], though there are no current long-term studies on treatment outcome for these four groups. When tics co-occur with ADHD, the tics themselves are generally less impairing than ADHD [163-166].

Treatment

Recent research studies suggest that treatment interventions for TS include education about tics and related disorders, clinical monitoring, pharmacological and/or psychological treatments, and school interventions for children and adolescents [167]. Stimulant medication is a safe and effective treatment for ADHD + Tic Disorder but requires careful monitoring of potential tic worsening [168]; the alpha-2-adrenergic agonists, clonidine and guanfacine XR, have shown promise in the treatment of tics, particularly in combination with ADHD [169]. In patients where stimulants may cause tic exacerbation, atomoxetine may be also considered as an option as it will rarely cause worsening of symptoms [170]. Recent studies indicate that on a population level stimulants do not seem to raise the risk of tics, and that the exacerbation of tics when stimulants are started is often coincidental, having to do with the waxing and waning nature of tics [163, 171].

Non-pharmacological treatments for Tic Disorder include Habit Reversal Therapy and Comprehensive Behaviour Intervention for Tics (CBIT) [172, 173] and may be considered as first-line treatments when available.

Key Points

- Tics and TS are highly comorbid with ADHD.
- The presence of tics or TS is not a contraindication to use of stimulants in ADHD but careful monitoring is required.
- Stimulants do not typically raise the risk of tics but may rarely do so in some individuals.

EATING DISORDERS

Bulimia nervosa is more prevalent in patients with ADHD versus patients without ADHD [174]. ADHD is more prevalent in anorexia nervosa purging type [175]. Females with ADHD are 3.6 times more likely to meet the diagnosis of eating disorders compared to females without ADHD [176]. The prevalence rate of ADHD in eating disorders is 11.4% [177]. This would suggest that females with ADHD in particular should be screened for an eating disorder, and vice versa. Clinicians should be alert as patients with anorexia that may not have ADHD may seek stimulant medication (feigning symptoms of ADHD) for the purpose of weight loss. Obesity has also been reported among patients with ADHD, especially in the adult population [178, 179].

One of the proposed mechanisms underlying weight issues in patients with ADHD could be the impulsive behaviours leading to binge eating [180]. Impulsivity is greater in individuals with comorbid eating disorders than in individuals with ADHD alone [181]. It is important to recognize that obesity is a risk factor for sleep apnea [182], a condition that may mimic or aggravate ADHD symptoms. Therefore, the longitudinal course of symptoms is of crucial importance before making a diagnosis of ADHD in obese patients with sleep apnea. [183]. Binge Eating Disorder (BED) is a newly recognized disorder in DSM-5 and its relationship with ADHD is currently unclear.

- The diagnosis and treatment of ADHD in the presence of anorexia nervosa can be complicated.
- Treatment of ADHD could contribute to behavioral control in the context of binge eating.
- A growing body of literature points to ADHD as a risk for obesity.

AUTISM SPECTRUM DISORDER

Until the publication of the DSM-5, Autism Spectrum Disorder (ASD) was an exclusionary criterion in making the diagnosis of ADHD, and the two diagnoses could not be made concurrently. Because of this, the relationship of ADHD and ASD remains unclear and is currently being researched. Prior research has suggested as many as 30 to 70% of patients with ASD may meet criteria for ADHD [184-189]. Many individuals with ADHD also show high level of social deficits and ASD type symptoms [190-194].

Symptoms

Table 2.10 Comparison of ADHD and Autism Spectrum Disorder (ASD) Distinct Features

	ADHD Distinct Characteristics	**ASD Distinct Characteristics**
Age of Diagnosis	Usually 6-7 years old and older	Can be as early as 2-3 years old
Language	Not delayed No echolalia	Delayed Echolalia
Eye Contact	Less eye contact as eyes frequently shift focus	Avoids eye contact
Social Interests	More social in play	Less social in play
Friendships	Ostracized for impulsive behaviour, inattentive to other's states of mind, drawn to impulsive peers	Not interested in peers, 'parallel play' predominant, difficulty in understanding other's state of mind
Motor	Hyperactivity, "always on the go"	Rhythmic, stereotyped movements

Treatment

Treatment of ADHD in patients with ASD is effective and significantly improves functioning. There have been only a small number of Randomized Controlled Trials (RCTs) that have looked at treatment of ADHD symptoms in subjects with comorbid ASD but these have shown promising results [195, 196].

RCTs with methylphenidate in comorbid samples have shown a response rate of 50% (versus 70-80% response rate for psychostimulants in ADHD without comorbid ASD) [197, 198]. Additionally, patients with ADHD and ASD may be more sensitive to side effects such as irritability, hyper focus, and stereotypies than those without ASD [199]. Clinical experience indicates that medications should be started at low doses and titrated more cautiously than usual in this population [199].

Both risperidone and aripiprazole (off-label use) have shown efficacy in controlling hyperactivity in this population, but generally have a less favorable side effect profile (metabolic changes, weight gain) than psychostimulants [200, 201].

One RCT of atomoxetine in individuals with ADHD and ASD showed positive results in improving hyperactivity, impulsivity and inattention and was generally well tolerated; however, overall improvement in clinical and functional improvement was limited [202]. Extended release guanfacine has recently been found to be effective for reducing hyperactivity in children with ASD [203].

- ADHD patients should be screened for ASD and vice-versa.
- Treatment of ADHD in patients with ASD can be very effective and help overall functioning.
- Treatment of comorbid ADHD and ASD with standard ADHD medication is often effective but may have lower effect sizes and higher risks of side effects.

SPECIFIC LEARNING DISORDER

Symptoms

Children/adolescents with ADHD frequently fall below their typically developing peers in their scores on standardized achievement tests. Teachers and parents often express concerns about a child's level of productivity and may label this child/adolescent as "lazy" or "unmotivated". There are several trajectories that can culminate in underachievement. One of the possibilities is that the individual has both ADHD and a Specific Learning Disorder (SLD). Indeed, research indicates that the comorbidity of ADHD and SLD is as high as 45% [64]. It is important to note that the comorbidity range suggested to be between 31% and 45% can vary greatly depending on how SLD is diagnosed [204].

Even without comorbid SLD, people with ADHD may still have a great deal of difficulty academically in terms of listening and reading comprehension and written expression (as well as with performance deficits such as following instructions, listening in the classroom, or staying on task) [205-210]. Additionally, individuals with ADHD often have executive function difficulties in the areas of initiation, organization, planning, self-directed activity, and ability to complete multistep tasks [211].The degree of difficulty individuals experience varies, with some individuals greatly impaired and their academic achievement subsequently falling well below their abilities. Learning disorders and executive function deficits are also developmental. That is, they may become more overt as cognitive demands in school increase [211]. **Note**: SLD is a clinical diagnosis that is not necessarily synonymous with 'learning disabilities' as identified within the education system: that is, not all children with learning disabilities/difficulties identified by the school system would meet a DSM-5 clinical diagnosis of SLD. By contrast, those with a DSM-5 diagnosis of SLD would be expected to meet the educational definition [212].

Diagnostic Assessment

In terms of assessment, practitioners should always:

a) Screen for academic skills deficits among students with ADHD and for ADHD symptoms among students with SLD.
b) Assess academic functioning across subject areas (e.g., reading, math, writing) when evaluating students with ADHD.
c) Carefully evaluate whether interventions for ADHD enhance academic functioning.

Given the relatively high comorbidity rate between ADHD and SLD, students who are evaluated for one of these disorders should always be screened for possible symptoms of the other disorder. The CADDRA Teacher Assessment Forms screens for academic performance problems in addition to ADHD. If the screening suggests the possibility of an SLD, then a letter should be sent to the school, with the parent's approval, to notify them and suggest that the school may wish to consult with support staff and/or the board psychology practitioners for further investigation and school programming.

In adults, as in children, ADHD can occur along with specific problems in reading, math or with written expression [213]. Assessing whether these difficulties have caused previous problems in school and continue to cause residual difficulty can usually identify these. The childhood history should reveal previous concerns of ADHD. It is additionally important to determine if the patient is inattentive only in the area in which learning deficits present a challenge.

Management

Learning disabilities require intensive, direct instruction, and modifications/accommodations [64]. Comprehensive intervention services for students with comorbid ADHD and SLD will require empirically supported treatment strategies that address both disorders and that are implemented across school and home settings. Although some school boards across Canada do not currently recognize ADHD as qualifying a student as a 'special needs student', this perspective is changing. Clinicians wishing to advocate for accommodations for their ADHD patient may wish to use the CADDRA Educational Accommodation Template.

SPECIAL PRESENTATIONS

Intellectual Giftedness

Research has shown that having a high IQ does not preclude the possibility that one might have ADHD [214, 215]. However, the co-occurrence of ADHD and intellectual giftedness remains controversial and under-investigated. Most previous discussions in the literature have been based largely on anecdotal comments, opinions and small clinical samples. Moreover, DSM-5 does not mention ADHD in the context of intellectual giftedness [1].

Misdiagnosis of ADHD in the context of intellectual giftedness can occur in two ways: intellectually gifted individuals with high energy and over-excitability in school contexts (particularly in those with little academic stimulation) may be misdiagnosed as having ADHD; alternatively, intellectually gifted individuals who meet full diagnostic criteria for ADHD but who can concentrate for long periods of time, may not be diagnosed with ADHD [216]. Moreover, intellectually gifted individuals with ADHD may also meet criteria for SLD and other comorbidities [217]. Thus, it is important for practitioners to recognize that intellectual giftedness in individuals with ADHD should be documented.

A high IQ may help individuals with ADHD cope with symptoms, and, therefore, in some cases clinically relevant impairment among gifted IQ children may not develop until later in elementary school or even in high school [214]. However, although ADHD may not be diagnosed until later it is not any less impairing. Diagnosis and treatment is critical at any age.

Symptoms

There are overlapping symptoms shared by individuals with high IQs and individuals with ADHD which may make differential diagnosis challenging. Frequently, bright children are referred to psychologists or pediatricians because they exhibit certain behaviors commonly associated with a diagnosis of ADHD (e.g., restlessness, inattention, impulsivity, high activity level, day-dreaming). A child may be diagnosed with ADHD when in fact the child is gifted and reacting to an inappropriate curriculum [218]. The process of completing a differential diagnosis requires specific questions to clarify what is shared and what is unique to either ADHD or giftedness or whether the child is twice exceptional.

In general, intellectually gifted individuals with ADHD show a similar pattern of cognitive, social, psychiatric, and behavioral characteristics as those with ADHD in the context of average IQ [214, 217]. However, the individual's strengths and difficulties may interact so that one presentation obscures the other [219].

Practitioners will need to undertake a thorough medical, developmental and educational history, as well as a comprehensive clinical and psychological evaluation, to ascertain an individual's behavior in different contexts and situations. The National Commission on Twice Exceptional Students concludes that the 'identification of twice-exceptional learners requires comprehensive assessment in both the areas of giftedness and disabilities [220]. When possible, the assessment and identification should be conducted by professionals from both disciplines (i.e., ADHD, giftedness) and ideally by those with knowledge and experience with individuals with twice-exceptionality.

Psychological Trauma

The interaction between psychological trauma and ADHD can be complex. Post-trauma symptoms of hyperarousal, hypervigilance, and dissociation can confound ADHD assessment. Although there is conflicting evidence, a history of psychological trauma may increase the risk of being diagnosed with ADHD [221, 222].

Various explanatory hypotheses are being explored in the literature to explain the interaction between trauma-related symptoms and ADHD symptoms [223]. First, ADHD may place children at greater risk for exposure to psychological trauma [224]. Conversely, Post Traumatic Stress Disorder (PTSD) symptoms may mimic symptoms of ADHD [225]. Additionally, some initial animal research suggests the individual response to trauma (i.e. externalizing vs. internalizing) may be influenced by genetic predispositions [226]. Under this latter hypothesis, trauma exposure merely exacerbates a prepotent genetic propensity towards having ADHD.

Although increased care should be taken to ensure the effects of historic trauma are considered during the assessment process, a history of trauma exposure does not automatically preclude the diagnosis of ADHD in an individual who otherwise meets DSM criteria for ADHD. Further, in the absence of research evidence to the contrary, clinicians are encouraged to follow the normal ADHD treatment protocols described elsewhere in these guidelines.

Clinicians are advised to:

a) screen for history of psychological trauma and where indicated, ensure appropriate trauma-informed support and interventions are mobilized; and
b) assess for ADHD based on DSM criteria, and treat in accordance with these guidelines.

Developmental Coordination Disorder

The prevalence rate of Developmental Coordination Disorder (DCD) in the general population is 1.7% in 7-8 year olds [227]. There is no reported prevalence of the co-occurrence of ADHD + DCD, in large part because DCD is often still unrecognized. Clinicians are urged to do simple assessments of balance as part of the routine workup of ADHD including: observations of gait, throwing and catching a ball, balancing on one foot (first identifying dominance) and fine motor tasks such as writing, use of scissors or drawing [228].

Balance problems, dyslexia, and poor handwriting in comorbid patients may be related to cerebellar dysfunction and may be associated with DCD [229, 230]. Occupational therapy assessment is warranted to provide recommendations [231]. Having the person learn keyboarding can often be beneficial. Relevant software programs (e.g. voice recognition) can also help to overcome problems.

Epilepsy

Studies have suggested a higher incidence of symptoms of ADHD in children with epilepsy (20% to 50% of patients) than in the general population [232]. There is a strong trend towards a higher incidence of epilepsy among children with ADHD than among children without ADHD [233] and epilepsy in children with ADHD appears to be more severe than in those without ADHD [233]. Anti-epileptic medications side effects, which can impair attention and learning, may be confused with ADHD symptoms. Therefore, improving seizure control with anti-epileptic medications that have less potential for behavioural or cognitive side effects should be a priority. In those patients with a formal diagnosis of ADHD in the presence of epilepsy, a pharmacological intervention as part of a biopsychosocial approach to treatment could be considered. No strong evidence exists that psychostimulants increase the severity or frequency of seizures in patients with stable epilepsy [234, 235].

- When choosing an anti-epileptic medication, one that has less potential for behavioural or cognitive side effects should be preferred in the context of comorbid ADHD.
- Use of psychostimulants could be appropriate in patients with epilepsy provided seizures are well controlled by antiepileptic medications.
- Consideration needs to be given to metabolic drug interaction between ADHD medications and anti-epileptics.

Brain Injury

Individuals with ADHD of all ages are at risk for physical injuries because they are impulsive, hyperactive and/or inattentive. Children and teenagers with ADHD are three times more likely to experience a moderate or severe brain injury than their peers without ADHD [236, 237]. Any injury to the brain, particularly to the frontal lobes, can produce a syndrome known as Secondary ADHD (S-ADHD) [238], also referred to as acquired ADHD. Recent literature has shown that the brain correlates of S-ADHD include the lesions in right putamen, thalamus and orbital frontal gyrus [238].

Children and adolescents with a moderate or severe brain injury have between a 20 to 48% chance of developing S-ADHD [236, 237]. S-ADHD can be treated using the same principles and medication as ADHD, but the research literature supporting this treatment is not as extensive or compelling as it is for ADHD.

Given that concussion and brain injuries are relatively common, and symptoms of persistent impairment could mimic or exacerbate the symptoms of ADHD, it is recommended that all patients being assessed for ADHD should be questioned as to whether they have ever suffered a concussion or brain injury. The literature on the association between ADHD and non-traumatic acquired brain injuries such as fetal alcohol syndrome, stroke or treatment with neuro-toxic medications is less clear, but many of these types of patients who develop ADHD symptoms may respond to standard treatments [239]. Patients with brain injury may be more sensitive to medication and thus starting off at lower doses during medication titration trials is recommended [240].

Key Points

- Assessment for ADHD includes inquiring if the person has suffered a concussion or brain injury.
- Patients with S-ADHD due to traumatic brain injury can be treated with same approaches and medication as regular ADHD although lower starting doses may be considered.

Sleep

Sleep problems, particularly the symptoms of insomnia (i.e., difficulties falling asleep and staying asleep, and early morning awakenings), are very commonly reported by individuals with ADHD. In fact, at least 50% of children and adults with ADHD report significant sleep problems [241]. While there is a high rate of reported sleep problems in individuals with ADHD, there have been inconsistent findings when objective measures of sleep, such as actigraphy and polysomnography, have been used in research [242]. Across studies examining sleep in children with ADHD, the main finding is that individuals with ADHD have more restless sleep than their peers, which can lead to fragmented sleep. There have been no consistent differences found in terms of sleep variables such as sleep duration [243] or sleep architecture (i.e., differences in the amount of REM sleep or NREM sleep) in individuals with ADHD [244]. There is consistent evidence that stimulant medications used to treat ADHD symptoms could make falling asleep more difficult, which can potentially result in shorter night sleep [245]. Shorter and/or fragmented sleep can result in problems with daytime functioning. There is also growing evidence that there may be some differences in circadian rhythms, which could make individuals with ADHD more vulnerable to delayed-phase sleep disorder and other types of sleep problems [246].

Research has clearly shown that insufficient sleep in children and adults can result in difficulties with attention, emotional and behavioural regulation, cognitive functioning (e.g., memory), and academic performance [247-249]. It would be logical to assume that individuals with ADHD may be even more affected by insufficient sleep given their existing vulnerabilities in

these areas. However, very little research has been conducted to determine if this is the case, but in the few existing studies, there is some evidence for this assumption. For example, in one study, sleep restriction negatively impacted both typically developing children and children with ADHD, but only the ADHD group moved into the clinical range on an attention task [250].

While there is a need for more research to better understand the relationship between sleep and ADHD [251], it is clear that we need to be attentive to sleep problems when conducting assessments and/or developing treatment plans for individuals with ADHD. First, we need to think of differentials in our diagnostic formulations. For example, sleep apnea can mimic or aggravate ADHD symptoms [252, 253]. Also, given that medications used to treat ADHD can impact sleep, it is important for sleep to be monitored when an individual is taking these medications. It is also likely that sleep problems could exacerbate ADHD symptoms, and therefore, sleep problems should be addressed in the treatment plan.

Treatment

While there is little evidence for pharmacological treatment of sleep problems in individuals with ADHD [254], there is a growing body of literature that demonstrates that behavioural sleep interventions can be effective for children with ADHD, even when taking stimulant medication [255]. Many individuals with ADHD take melatonin to help with their sleep problems, and the very small body of research has demonstrated that this may be an effective intervention [256, 257]. However, given that there is limited research, and the fact that behavioural interventions have been shown to be effective, it is recommended that the first line of treatment is behavioural interventions for sleep problems in individuals with ADHD. For a comprehensive overview of assessment and management of sleep problems in individuals with ADHD please see [258] or [259].

Key Points

- Differential diagnosis needs to be considered in diagnostic formulations (e.g., sleep apnea can mimic ADHD symptoms).
- Sleep disturbances are common in ADHD and treatment of sleep problems can help ADHD.
- Stimulant medications used to treat ADHD symptoms can make falling asleep more difficult, which can potentially result in shorter night sleep.

Incontinence

ADHD and incontinence (nocturnal enuresis, daytime urinary incontinence, and fecal incontinence) are strongly associated with each other. Children with ADHD are two to three times more likely to have enuresis than those without ADHD [260]. In typically developing samples, the rate of enuresis is 4.45% in boys and 2.5% in girls, with prevalence rates decreasing with age. The trend is similar for fecal incontinence [260] and daytime urinary incontinence [261]. Likewise, children with nocturnal enuresis are more likely to have ADHD than those without incontinence [262].

Treatment

In most cases, ADHD and issues of incontinence need to be investigated and managed separately. However, recent studies have found that successful treatment of ADHD with stimulant medication can result in resolution of incontinence in some children [263, 264]. Enuresis treatment must begin with the correction of any underlying medical cause. Daytime enuresis may be improved with medication. Nighttime enuresis often requires individualized management. In a double-blind study, atomoxetine has been associated with a significant increase in dry nights in children with nocturnal enuresis [265].

CHAPTER 3: SPECIAL CONSIDERATIONS ACROSS THE LIFESPAN

ADHD is a persistent disorder, with functional impairment and treatment needs varying through the lifespan for many. It is important for clinicians to be aware of these differences to better serve individuals with ADHD. Below is a summary of the functional impairments commonly seen across different age groups for individuals with ADHD.

Figure 3.1 Developmental Impact of ADHD
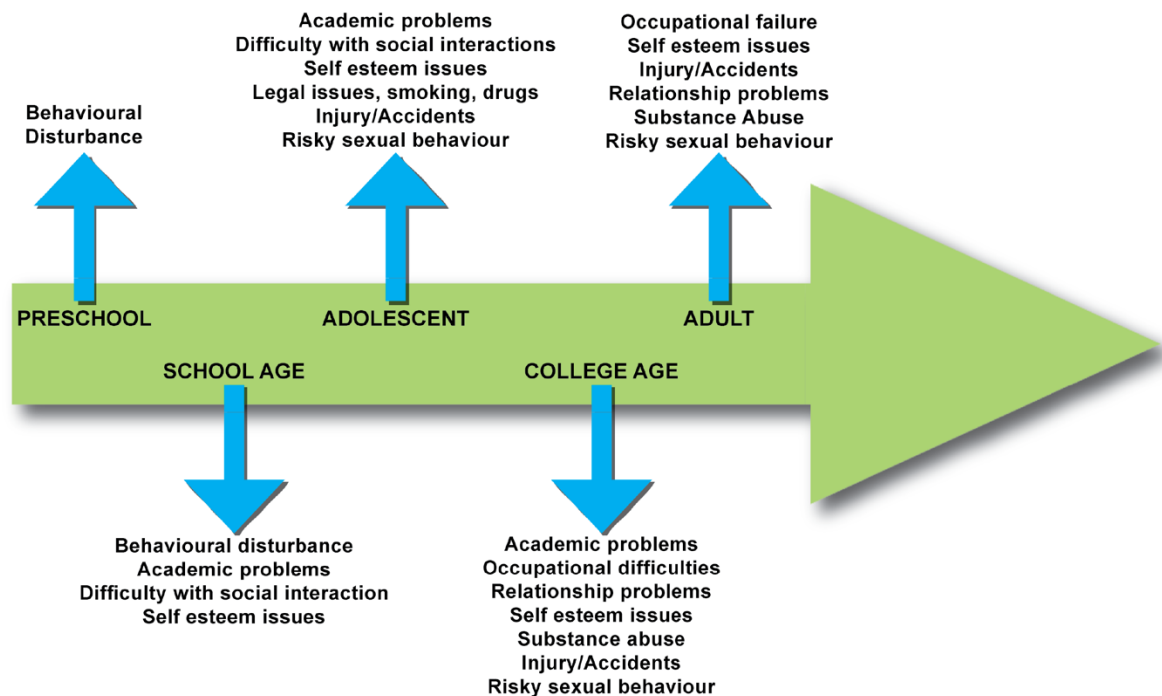
OVERVIEW

Preschool children

Hyperactivity in preschoolers tends to be temporally and situationally stable [266] and is highly heritable [267]. However, clinicians should remember that inattention and hyperactivity in preschoolers can be influenced by a number of factors. These can include intellectual impairment, expressive language issues, and their response to child abuse and neglect as well as conflictual environments [268].

Epidemiological data indicates that approximately 2-7.9% of children from three to five years of age have ADHD [269]. The American Academy of Pediatrics has suggested that ADHD can be diagnosed in children as early as age four [270]. Non-pharmacological approaches should be the first-line treatment for preschool children [72, 271].

School-aged children

ADHD is one of the most common psychiatric disorders diagnosed in children. Prevalence rates range from 3 to 9% of school-age children [11, 272]. A recent meta-analysis determined that the prevalence rate for children and adolescents was 7.25% [273].

Research indicates that girls may be consistently under-identified and under-diagnosed [31]. Commonly seen differences between boys and girls with ADHD exist during this period [274-277]:

- Boys may be three times more likely to be identified; girls are consistently under-identified and under-diagnosed.
- Girls with ADHD have lower levels of disruptive symptoms than boys with ADHD.

Childhood is usually the time where ADHD is diagnosed for most individuals. Challenges may occur in all areas of the child's life including at school, at home and during social activities. Interventions are aimed at minimizing the functional impairment that can occur and are part of what is known as a **multimodal approach to treating ADHD.**

There can be associated problems with ADHD, such as learning difficulties or low self-esteem, which must be managed in addition to the ADHD symptoms. The clinician must utilize the resources available in the team or in the community to provide additional supports for the child and the family. This may be through referral to other professionals such as a psychologist, occupational therapist, social worker, educational aid, resource teacher or behavioural consultant. Examples of useful accommodations for school-aged children can be found at www.caddac.ca under the Understanding ADHD, In Education tab.

Adolescents

Prevalence rates of ADHD in the adolescent population range from 6-12% [278, 279]. Between 50% and 80% of youth diagnosed with ADHD in childhood maintain significant symptoms and meet diagnostic criteria for the disorder in adolescence [87]. Males are three time more likely to be diagnosed with ADHD than females [276]. This discrepancy starts to lessen over time nearing adulthood.

As children grow into adolescents, it is important to work with both the individual and their parents together. This acknowledges the emerging autonomy of the adolescent. Clinicians should not rely exclusively on the parent as an intermediary. It is important to use language that adolescents can understand and avoid the use of excessive medical jargon. Adolescents should at some point be seen alone and during that time the clinician should develop rapport directly with the adolescent and obtain a history of risk factors such as reckless driving, smoking, drug use, sexual activity, family or interpersonal conflicts, illegal activities and issues of bullying. A review of their peer relationships helps to assess their social development and to flag any risky behaviour. Peers tend to be in trouble together.

Adolescents with ADHD are not always the best historians. They frequently do not have full insight into their condition and they may have a self-centered perception and a tendency to deflect blame onto others [280]. Gathering collateral information from key people who know the adolescent can be very helpful. Even though there can be considerable variability in ratings completed by adolescents, serial ratings (see CADDRA ADHD Assessment eToolkit) done by the same individual provide valid measures of treatment outcomes compared to pre-treatment.

Many of the symptoms seen in adolescence are like those seen during childhood but they can affect an adolescent's life in many different areas. Difficulties in school usually continue and often, because of increasing school challenges, become worse. Inattention, lack of focus, impulsivity and forgetfulness can impact assignments and grades. Even athletic and extra-curricular activities can be negatively affected. Adolescence is also a developmental period where risk-taking can increase dramatically. Clinicians need to be aware of the very significant negative outcomes that can occur when ADHD during adolescence is untreated (see Accidents/Risks in Adolescence later in this chapter).

Adherence to medication and to psychosocial interventions can be very poor in adolescence. Studies indicate 48-90% of adolescents stop taking their medications[24] [281], though the use of once-daily dosing improves adherence [282]. Psychoeducation is a very useful tool for augmenting adherence by making the adolescent a partner in treatment [283]. Knowledge of the individual's acceptance level of their diagnosis will help determine if intervention is required to address resistance. Using motivational interviewing techniques can be helpful with adolescents who will not adhere to treatment [284].

College/University Students

The prevalence of ADHD among post-secondary students is between 2-12% [285]. Young people with ADHD attending university programs may present with varying histories, such as:

- Students already diagnosed and treated in childhood may want to adapt their ADHD treatment to their studying schedule. This may be a challenge as students may require treatment coverage further into the evening or night.
- Some students may have stopped taking their medication and may want to restart their treatment as they face increasing cognitive demands of the university curriculum.
- Similarly, some individuals who may never have been diagnosed before consult for the first time while facing difficulties coping with the high cognitive demands of university classes.

Young adults presenting for the first time for a diagnosis of ADHD should be carefully assessed. Some reports in the literature suggest a subset of students may exaggerate their symptoms to obtain accommodations/benefits or to obtain medications to enhance performance, to sell or to use for recreational purposes [286]. A recent study found that some female college students endorsed having used ADHD specific stimulant outside a doctor's prescription for weight loss [287, 288].

Life-time prevalence rates of non-prescribed stimulant use in college and university students range from 5%-43% [289].

Despite a minority of misusers, students with ADHD will benefit from access to treatments and accommodations. The CADDRA Assessment eToolkit includes an educational accommodation letter template and CADDAC provides a detailed chart of appropriate accommodations linked to specific impairments in the post-secondary environment on its website (www.caddac.ca).

PRACTICE POINT

Information gathered from standardized rating scales help identify ADHD symptoms, comorbid disorders and associated impairments.
If necessary, standardized cognitive evaluation focusing on attention and other executive dysfunction may help quantify IQ, identify specific cognitive dysfunction and is particularly important to diagnose Specific Learning Disorders.

When assessing ADHD in post-secondary students, an assessment may require multiple visits and comprises a review of (when available):

- Parental/guardian reports of symptoms during childhood.
- School report cards.
- Reports from current collateral informants.

Some reports suggest misuse or diversion of stimulants is associated with SUD and CD, these conditions should be carefully screened for [290].

Additional school services and accommodations in the university setting can be very useful (e.g., separate testing environments, longer testing times, reduced homework and provision of a note taker).

Adults

Many adults go undiagnosed and untreated for ADHD. In a study published by Kessler et al., [47] the prevalence of ADHD in adults (20-64 y/o) was 4.4%.

Some adults may present to healthcare professionals seeking an assessment for ADHD with no prior diagnosis. This occurs for a variety of reasons, including:

- Parents of children who have recently been assessed for ADHD begin to wonder if they may have the same diagnosis.
- Individuals who have heard or read about ADHD in adulthood and can relate to the symptomatology.
- A subset of adults who have not experienced significant symptoms or struggles prior to adulthood. Lack of challenges prior to adulthood may be due to significant supports, structure and routines earlier in life, and/or an above average IQ [291]. With increasing responsibilities and demands and diminishing "scaffolding" in adulthood, many of these individuals begin to experience significant symptoms and associated impairment [291].

In those adults with ADHD who were initially diagnosed during childhood, a significant number of individuals treated for ADHD choose to discontinue their medication management in adolescence [281]. This may be due to medication side effects, a desire for independence, a lack of continuity of healthcare, social stigma, or "remission" [292]. However, due to the re-emergence of symptoms and associated impairment in adulthood, they may seek re-assessment of their ADHD and choose to resume treatment.

In adults, most individuals with ADHD (85%) suffer from a comorbid mental health condition [50]. Thus, many adults with undiagnosed ADHD may present to their primary care physician and/or mental health professional seeking treatment for what may appear to be a primary mood, anxiety or other mental health disorder. Others may get medical attention because of SUD, high risk behaviour consequences, but also trauma or unplanned pregnancies. It is important to know which of these individuals should be screened for possible underlying ADHD. Missing this diagnosis can result in years of trials with antidepressants, mood stabilizers and anxiolytics without adequate symptom response.

Examples of useful workplace accommodation and information for employees and employers can be found on the CADDAC website (www.caddac.ca). CADDRA has a template for requesting occupational accommodations in the eToolkit.

Older adults

Results from a large epidemiological study have demonstrated that ADHD symptoms can persist in older adulthood, with an estimated prevalence of about 3% [293].

However, there is relative paucity of data available on the aging ADHD population compared to younger age groups. Small observational studies have characterized the presence, impact, and treatment of ADHD in adults over the age of 50 years [294].

Undiagnosed ADHD in older patients can lead to lifelong functional and psychosocial impairments. In addition, the presence of comorbidities including depression and cognitive impairment can make diagnosing an older patient's ADHD complex. Furthermore, diagnosis of ADHD in older adults can be tricky because some ADHD symptoms are seen in the normal aging process, or are similar to certain symptoms of minimal cognitive impairment or dementia, thus leading to the incorrect assumption that older adults with ADHD are undergoing a neurodegenerative disease process [295].

It is therefore crucial to raise clinician awareness about ADHD in older adults. Detailed history-taking (longitudinal cognitive difficulties since childhood) and neuropsychological testing may help the clinician to make a diagnosis of ADHD [296]. In summary, diagnosis in older adults requires identification of past and current symptoms/impairments, and differential diagnosis should include other neuropsychiatric conditions.

The first-line medications for ADHD recommended in these guidelines remain the treatment of choice for older adults when their medical condition permits their use. It is important to note that very few clinical drug trials have included ADHD

subjects over age 65. However, appropriate treatment with specific medication for ADHD might improve functional outcomes for older adults with ADHD, including those with comorbid dementia [297]. An important consideration in treatment is drug interactions since older adults often take multiple medications. Medication and psychotherapy trials should be conducted in older adults to determine best treatment approaches.

IMPACT/FUNCTIONAL DISABILITY ACROSS THE LIFESPAN

ADHD can impact all aspects of an individual's life, both personally and systemically. In a 33-year follow-up study, children with ADHD were found to have a greater risk of poor long-term outcomes as adults in almost every aspect of life compared to their non-ADHD counterparts [298].

The core difficulties in executive functioning seen in many individuals with ADHD [299] cause varying degrees of functional impairment depending upon the demands made on the individual by their environment and the supports available. Variable factors include family and school or occupational resources, as well as personal responsibilities, coping strategies, cognitive capacity and insight of the individual.

Individual - Regardless of academic, personal, occupational, professional or financial success, many individuals with ADHD struggle with low self-esteem [300]. Some often describe negative beliefs or expectations of their own abilities. Some describe an "imposter complex" whereby they have trouble taking credit for their success. This may be due to lifelong inconsistent performance and a history of negative feedback for perceived failures.

Family - Due to the high heritability of ADHD [15] there is seldom only one individual with ADHD within a family unit. In addition, untreated ADHD may be a significant explanation for a higher rate of separation and divorce in these individuals [301]. Other impacts on the individual or the family can include: parental stress; parental emotional/mental health problems; sibling conflict; disruption to family cohesion; and less time available to spend on family activities [302]. In a survey of 500 individuals with ADHD compared to 501 matched controls it was found that the annual US household income losses due to ADHD were $77 Billion USD per year and up to $15,000 per household per year [303]. The literature supports the fact that ADHD runs in families [318] and where appropriate, other family members should be screened or encouraged to seek out assessment. Parents, siblings and extended family members may have ADHD and therefore have problems with organization, consistency, impulsivity and emotional liability. In addition, having a child with a disability may increase the likelihood of substance abuse, depression and anxiety in parents [319]. Parental psychopathology can have a significant impact on the parents' ability to structure, monitor and generally help their child [141, 320]. Identifying this psychopathology and referring the parents for appropriate treatment will improve the psychiatric state of the parents and their parenting ability, and thus be of great help to the child or adolescent and their family. It is important for the parent(s) to be treated at the same time as the child or adolescent. This "all in the family" approach to intervention is good for the child/adolescent as it shows that the parent can empathize with their experiences. When parents learn skills to control their own lives, it is easier to institute structure in the child's life [321-323].

School - Individuals with untreated/undertreated ADHD are more likely to be expelled or be truant, may have lower grades than expected, and also disrupt others' education [304]. This may impact the individual's future economic status.

Occupation - Adults suffering from ADHD have higher absenteeism and lower productivity in the job setting [305]. They are also more likely to impulsively quit or change jobs or be fired [306]. Specific ADHD treatment may diminish this risk (87).

Healthcare and Society - A population-based, historical cohort study followed 4,880 individuals from 1987 to 1995 and compared the nine-year median medical cost per person: ADHD medical costs were US$4,306, whereas non-ADHD medical costs were US$1,944 (p<0.01) [307]. Individuals with ADHD have a 33% increased rate of emergency room visits [307] and may be more vulnerable to motor vehicle accidents with some studies suggesting a rate that is two to four times as high [42]. Children with ADHD may be more likely to sustain injuries to multiple body regions, head injuries, and to be severely injured [308]. The increased rate of accidents in individuals with untreated/undertreated ADHD has economic impacts on the healthcare system, as well as economic and social effects within the family (reduced income, missing education) [309].

ACCIDENTS/RISKS

Accidents/risk in childhood

ADHD in children has been linked to a two times greater risk for accidental injuries of all types, for more severe injuries, as well as for repeated injuries [310]. Comorbidity of ODD/aggression with ADHD in children is thought to exacerbate these risks [87].

Children admitted to hospitals due to accidental injuries are three times more likely to have ADHD (approx. 30%) than are children admitted for other reasons. Factors that have been associated with these elevated risks are inattention, impulsivity and risk-taking behaviours, motor incoordination, comorbidity with ODD/CD, anxiety, and depression, and parental characteristics such as reduced parental monitoring of the child's activities. Medication can decrease injuries [87].

PRACTICE POINT

Promote safety in the home and outside, especially for the hyperactive impulsive child. To reduce risks, children with ADHD may need supervision of activities, such as walking to school, that peers may not require.

Points to discuss with parents:

- Provide physical safety (e.g. safety proofing, ample outdoor places that can be safely used and supervised, opportunities for physical movement).
- Assure adequate supervision, and reinforce behaviours where the child shows risk management (e.g. wearing a helmet/protective gear, asking permission, wanting advice, following rules, reading instructions, showing good judgment).
- Children with ADHD benefit from physical activity and may find opportunities for success in play or sport.
- Balance must be struck between providing safe environments and overprotection.
- It is also important to create a calm, structured, positive approach to child rearing to not only optimize appropriate developmental progression, but also allow for a more acceptable response to limit setting.
- **Above all, it is crucial that parents retain an enjoyable relationship with their child that encourages their self-esteem**. Doing things that the child excels at or enjoys is very important. Parenting should include not only structure and guidance, but fun. The school must create a similar environment.

Accidents/risk in adolescence

Adolescence is a developmental period when a significant percentage of individuals start to engage in activities that have associated risk [311]. Adolescents who have ADHD are at higher risk than the general population for experiencing the negative outcomes of risky behaviours [312]. Impulsivity, in particular, can negatively impact an adolescent's executive functioning. There is much evidence that untreated ADHD can lead to higher rates of accidents, school failure and dropout, driving accidents and family conflict/fighting [313].

Sexual activity starts for some during adolescence. Both male and female adolescents who have ADHD are at increased risk for early sexual activity, sexual transmitted diseases and more sexual partners [314]. Females with ADHD are at risk of higher rates of teenage pregnancy compared to adolescents without ADHD [314, 315]. Information should be provided about risky sexual activities and use of birth control methods should be encouraged where appropriate.

Adolescence is frequently the time where experimentation with alcohol and drugs begins. Adolescents with ADHD have higher risk than the general population to start using earlier and to develop more severe difficulties with substances [131]. Comorbidity of ADHD and SUD commonly starts in adolescence [316].

Abstinence from illicit drug use is ideal, though a harm reduction approach may be a useful option. Another group of substances that should be asked about are beverages containing excessive caffeine, including for example "energy drinks".

Accidents/risk in adulthood

Many of the risky behaviours that are problematic in childhood and adolescence continue to impact individuals with ADHD into adulthood. In a recent study, the adjusted mortality rate ratio (MRR) was greater for individuals diagnosed with ADHD, and increased with delay in diagnosis. The adjusted MRR was 1.86 when diagnosis occurred before six years of age and increased to 4.25 when diagnosis was delayed to 18 years or older [317]. The cause-specific mortality for suicide was significantly higher among ADHD cases (SMR, 4.83). This study concluded that childhood ADHD is a chronic health problem, with significant risk for mortality, persistence of ADHD, and long-term morbidity in adulthood.

Richards et al. [42] assessed negative driving outcomes in individuals with ADHD, reporting more driving anger and aggression expressed using vehicles as well as less adaptive and constructive anger expression compared to peers without ADHD. College student adult drivers with ADHD rated themselves as angrier, riskier, and more unsafe behind the wheel, and reported more struggles with concentration and vehicular control [318].

DRIVING

ADHD symptoms can negatively impact the ability to drive safely for both adolescents and adults [319]. Not all patients with ADHD who drive have significant driving problems. However, the epidemiological data suggest that
ADHD drivers as a whole have an increased risk [329, 330]. It is important that all adolescents with ADHD have driver training and that their driving risks be minimized (e.g. curfews, staying off major highways, absolutely no drugs or alcohol while driving). Driving assessments can be done and an example of such is the Jerome Driving Questionnaire (JDQ), which is provided in the CADDRA Assessment eToolkit).

Clinical studies indicate that young drivers with untreated or sub-optimally treated ADHD have between two to four times as many motor vehicle collisions and moving violations than a comparable non-ADHD population [320]. These driving problems are seen independent of comorbidity. The problem profile commonly includes speeding, distractibility and driving anger or road rage. The presence of ADHD and comorbid substance use disorders magnifies driving risk [321, 322].

Neurodevelopmental immaturities in executive functioning (resulting in problems with attention, impulse control and emotional regulation) combined with a lack of driving experience can lead to problem driving styles in young people in general [323]. On-road data demonstrates the benefits of long term use of stimulant medication in reducing MVCs in older adults [324].

Simulator and on-road observation studies suggest that methylphenidate, dexamphetamine and atomoxetine improve driving behaviours in ADHD populations [325, 326]. At the time of writing (March 2017) there are no current studies evaluating other agents for treating ADHD. Clinicians should monitor individual response to medications, both for improvement as well as worsening of driving abilities. For example, agents like guanfacine or clonidine may be sedative initially and worsen driving in the initial titration period. In addition, some medications may not last up until late evening or adherence with the use of an "as needed" short-acting stimulant medication is particularly poor in the evening, which is the time of maximum driving risk for young drivers.

Restrictions on cell phone use, nighttime and weekend driving and on use of a manual transmission may all have an impact on improving driving performance. Psychosocial and legislative measures may prove to be a more effective preventative public health measure in the long run [327, 328].

EVALUATION OF DRIVING RISK AND DOCUMENTATION

Discussion with young drivers and their families should include information on functional impairment and driving risks [87]. Problems with speeding, following too close, road rage, inattention and distractibility when driving should be reviewed. When developing a therapeutic alliance with a family, it may be useful to encourage contracts between young drivers and their families where adherence with medications and other issues such as good school performance are exchanged for access to a motor vehicle.

Documentation of discussions regarding driving safety, along with the use of an assessment of driving style and behaviour, would demonstrate that the clinician is exercising due diligence for their ADHD patients around driving safety issues. The Canadian Medical Association (CMA) Guidelines on Fitness to Operate a Motor vehicle continue to remind physicians that if ADHD drivers have a demonstrated problem with driving and are non-compliant with treatment recommendations, doctors have a duty to report their concerns to the Provincial Ministries of Transportation [329]. Reporting in Alberta, Quebec and Nova Scotia is discretionary [329]. The latest CMA guidelines continue to recommend the same reporting requirements and have an updated reference list on ADHD and driving.

CHAPTER 4: PSYCHOSOCIAL TREATMENT OF ADHD

Until recently, symptom control was the main priority in the assessment and treatment of ADHD [330]. In recent years, the clinical focus has shifted towards functional impairments and outcomes, with improvement of overall life quality as the main goal [330, 331]. ADHD can impact many aspects of an individual's daily life such as social and emotional functioning, academic/work-related success, relationships, marriage, family life and even physical health [332]. This is true for individuals with ADHD across the lifespan. Generally considered to be a chronic lifetime disorder, ADHD requires a **comprehensive, collaborative and multimodal treatment approach** [333] tailored to meet the unique needs of the person with ADHD.

Research studies and clinical experience show that a multimodal approach (incorporating psychosocial interventions together with medication) improves not just core ADHD symptoms but the overall quality of life by improving the resultant functioning impairments [330, 331, 334]. Medications are an important aspect of treatment and assist the facilitation of changes in these areas by improving focus, self-regulation and decreasing impulsivity/hyperactivity and thus allowing the individual to use psychosocial strategies more effectively [335, 336].

Psychosocial treatment is the treatment approach preferred by many individuals over medications and is recommended as a **first line for preschoolers** by the American Academy of Pediatrics and the Choosing Wisely Canada campaign (choosingwiselycanada.org). Psychosocial interventions play a particularly crucial role during key life transitions, for instance in the move from adolescence to adulthood [291, 337-339]. It is important to incorporate a patient-centered approach to ADHD treatment, by considering individual/family treatment preferences [340-342]. Psychological interventions for ADHD include a range of cognitive and behavioural approaches, including cognitive behavioural therapy for ADHD, behavioural interventions, parent training, cognitive training and social skills training.

Although front-line clinicians may see time constraints and perceived lack of expertise as barriers to implementation of psychosocial treatments [343], these individuals are in fact ideally placed to assess and provide treatment for ADHD beyond traditional pharmacological approaches. Primary care practitioners are in the unique position of being able to diagnose, treat and follow individuals with ADHD across the lifespan [344]. They can provide or support some of these interventions in a timely manner either on their own (with community resource supports) or in co-ordination with other medical specialists, health-care providers and professionals from the educational system.

A solid therapeutic alliance is best achieved by spending time listening to a patient's concerns and understanding their perspective and goals. CADDRA wishes to highlight this principal as being the core foundation for all effective treatment approaches.

PSYCHOEDUCATION

The overall purpose of psychoeducation is to educate and empower patients and their families by providing information on ADHD (e.g., impact on daily functioning, treatment options, strategies for optimizing functioning).

PRACTICE POINT

CADDRA Guide to ADHD Psychoeducation can be downloaded from the CADDRA website from the Resources section. This guide provides a quick overview of the components of psychoeducation along with a summary of strategies and interventions that can be recommended to individuals with ADHD and their families.

Key Elements of Psychoeducation

Discover

Find out what the patient and family already know, or think they know, about ADHD [345]. This may help guide your approach to diagnosis and treatment.

Demystify

Take the time to discuss some of the societal myths commonly associated with ADHD. For example, the following myths are adapted from the "Take Ten Series" from the CanLearn Society, Calgary.

Table 4.1 ADHD Myths and Facts

MYTHS	FACTS
ADHD is not a real condition	ADHD is a neurobiological condition that can cause inattention, hyperactivity and/or impulsivity, along with several related difficulties, inappropriate for an individual's age.
ADHD is over-diagnosed	A US 2014 national survey found that healthcare practitioners are carefully diagnosing children. The vast majority (9 out of 10) of the 2,976 children diagnosed with ADHD had been diagnosed by practitioners using best practice guidelines [346]. Possible explanations for increased diagnosis of ADHD include improved healthcare practitioner and parental awareness; more screenings by pediatricians and other primary care givers; decreased stigma about ADHD; availability of better treatment options, and more cases arising from suspected environmental causes such prenatal exposure to toxins or high blood lead levels [347].
All children with ADHD have disruptive behavioural problems	Approximately 50 percent of children with ADHD demonstrate significant problems with disruptive behaviour [348, 349].
ADHD results from ineffective teaching and/or poor parenting	ADHD is primarily biological and genetic in its origins. Environmental factors such as teaching and parenting quality, however, can minimize or intensify the difficulties experienced by an individual with ADHD [16].
Children with ADHD can never pay attention or complete their work	Inconsistency is a pervasive characteristic of ADHD. Sometimes, and under some circumstances, individuals with ADHD can focus and concentrate, while at other times they experience extreme difficulty. They are, for example, often able to hyper focus on stimulating activities, like video games, or creative activities such as Lego or drawing.

All children with ADHD are hyperactive	A person with ADHD may not necessarily demonstrate hyperactivity. In fact, some individuals with ADHD may appear to lack energy and seem quiet and reserved.
ADHD only occurs in boys	Boys are four to nine times more likely to be diagnosed [277]; however, the disorder occurs in both boys and girls. Girls are more prone to inattentive type ADHD [276], which is marked by disorganized and unfocused behaviour rather than the disruptive, impulsive conduct typically seen in boys. Girls with ADHD tend to have higher rates of overall distress, anxiety and depression compared to boys with ADHD [275].
Food allergies, refined sugar, food additives and poor diet cause ADHD	The actual correlation between ADHD and diet has not been proven [350]. Good nutrition and general health are always important. An unhealthy lifestyle, including poor diet, can influence attention and functioning [351].
Medication alone can manage ADHD	While there is no cure for ADHD, medication can have positive effects on symptoms of inattention, impulsivity and hyperactivity. A "multi-modal" or comprehensive approach is most beneficial and includes appropriate diagnosis, improve personal and family understanding of the disorder, behavioural interventions and educational supports.
Individuals with ADHD are lazy or lack willpower	Everyone finds it easier to focus on a topic or activity that catches their attention. Many people with ADHD have some domains of activity (such as sports, music, video games, art, mechanical activities and areas of work) in which they can focus very well. As a result, their inability to focus in other areas is often misunderstood.
There is a test that can diagnose for ADHD	ADHD is a clinical diagnosis that should be arrived at through a comprehensive evaluation of the history and presentation. This is true of many other medical conditions (e.g. migraine).
Everyone has ADHD because everybody is inattentive sometimes, especially these days.	The core symptoms of ADHD can occur in everyone occasionally (e.g. forgetting items). People with ADHD, however, have significantly greater numbers of these symptoms (meeting a threshold of at least 6/9 symptoms for children, 5/9 for adults (17+)) occurring frequently and they experience more significant difficulties and impairment from them (e.g. job loss, academic underachievement).

Instill Hope

Families will respond positively when told evidence-based treatments and interventions do exist. This in turn will promote solid therapeutic alliance and a positive outcome.

Educate

The first step is to educate individuals and families about the nature of ADHD and its symptoms. If relevant, explain the concept of emotional dysregulation. This refers to the fact that many individuals with ADHD can experience difficulty self-modulating, have hyper-reactive emotions, often referred to as "a short fuse". They can impulsively over-react verbally or physically, causing significant conflicts.

Explain the rationale behind your treatment approach (e.g. the use of pharmacological or psychosocial interventions and the risks and benefits of each). For example, ADHD medications can improve focus and decrease impulsivity/hyperactivity, allowing individuals to make better use of psychosocial strategies [335]. Provide handouts and information on relevant websites, community resources, parent training and support/social skills groups, etc.

Empathize

Acknowledge feelings of discouragement and frustration (e.g. "that must make you feel so sad, mad…"). Empathize with the challenges of living and coping with ADHD every day, of raising a child with ADHD or living with a spouse, grandparent etc. who has ADHD. Keep in mind that ADHD is a highly hereditary disorder and therefore often multigenerational [107, 352, 353].

Encourage, Guide and Motivate

Because an assessment often focuses on areas of difficulties, the process may be an overly negative experience for some. Identifying strengths during the assessment and follow-up may mitigate this and establish a solid therapeutic alliance.

Encourage individuals and families to nurture strengths and talents (e.g. encourage skills in areas such as sports, music, arts or drama). Families can showcase their children's achievements, attend their games, recitals, productions, hang their art, display trophies etc.). Existing strengths and talents can be leveraged as part of the therapeutic intervention.

Be Culturally and Gender Sensitive

Ethnic, gender and cultural issues may shape the perception and beliefs about ADHD and its treatment. For example, some cultures may have lower acceptance and higher stigma associated with ADHD. Demystifying ADHD may be especially crucial in those circumstances.

Promote a Balanced Lifestyle

Individuals with ADHD often struggle with their daily needs (e.g. sleep, meals and personal hygiene) and need assistance creating a balanced lifestyle by developing healthy habits and routines including regular exercise, consistent sleep hygiene, and eating nutritious foods. The clinician can instruct a patient to make self-care a priority.

Promote regular exercise to decrease stress and frustration, improve focus and cognitive clarity, increase endorphins, improve mood and restore a sense of well-being [354-357]. Aerobic exercise has been shown to improve core symptoms of ADHD plus anxiety, often a concurrent comorbidity [358].

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Outline consistent sleep hygiene. ADHD is often associated with delayed sleep phases [359]. Describe sleep patterns and outline consistent sleep hygiene routines.

Encourage good nutrition, meal planning, grocery lists, consistent meal times, and eating as a family. Eating pathology such as binge eating has been associated with ADHD [183, 360]. Encourage active practice of relaxation techniques such as meditation, deep breathing exercises, yoga or music. These can be helpful, although research is limited [361].

Give Online Resources / Local Community Resources / Book Lists

The CADDRA toolkit includes the CADDRA ADHD Information Handout.

Other online resources:

- The Centre for ADHD Awareness Canada (CADDAC) provides information and resources for individuals with ADHD, their families, educators and other stakeholders. www.caddac.ca
- Quebec-based physician and CADDRA member Dr. Annick Vincent provides information in both English and French through www.attentiondeficit-info.com
- PANDA is a French-language network of associations that work together to meet the needs of individuals with ADHD and their families. www.associationpanda.qc.ca
- Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD), is an American organization providing education, advocacy and support for individuals with ADHD. In addition to its website, CHADD also publishes a variety of printed materials to keep members and professionals current on research advances, medications and treatments affecting individuals with ADHD. www.chadd.com
- Alberta, Canada-based ADHD Families provides information and resources for families on ADHD. www.adhdfamilies.ca

PSYCHOSOCIAL INTERVENTIONS OVERVIEW

Understanding that ADHD is not just a school/ post-secondary/ workplace problem is crucial for optimized management and improved quality of life. Recognizing that ADHD symptoms significantly impact an individual's and family's functioning from the time they get up in the morning until they go to bed at night, every single day of the week, including weekends, is vital for a successful outcome.

What can be done at home?

Improved functioning within unstructured environments such as home life, social situations, extracurricular activities, may require the development of planning and organization skills, which are often sub-optimal in ADHD individuals in general. Individuals lacking these skills commonly feel overwhelmed, resulting in stress, frustration, anger, panic, loss of self-esteem, chaos, dysfunction and significant family /relationship conflicts [362, 363].

Promoting a structured lifestyle and home life is key to success [364]. Emphasize the importance of having a home life that is organized, predictable, consistent, calm, and focused on positive outcomes. Providing such external structure and modelling expected behaviours is essential for increasing self-esteem, improving self-control and ensuring more harmony in family life and relationships. Keep in mind that ADHD can be multi-generational, some families will experience more difficulty creating a structured environment than others will.

Table 4.2 Interventions at Home

INSTRUCTIONAL INTERVENTIONS	
Rationale	Strategies
Because of poor sustained attention and difficulty following multi-step directions, communication needs to be clear and direct.	• Get eye and/or gentle physical contact before giving one or two clear instructions. • Get the person to repeat the instructions before proceeding.

BEHAVIOURAL INTERVENTIONS	
Rationale	Strategies
Individuals with ADHD have a higher rate of emotional dysregulation (i.e. short fuse, easily frustrated) and this can cause significant family/spouse/partner/child/peer conflicts [44, 365-367]. These deficits lead to detrimental effects in several aspects of daily life [368, 369]. Individuals with ADHD prefer immediate, small rewards over a larger delayed reward [370].	• Use a positive approach and calm tone of voice. Avoid yelling and arguing. • Encourage calming techniques to de-escalate conflict. Example: Teach "stop and think" [344]. Help them put on their brakes by taking deep breaths. • Use praise, "catch them being good" (doing chores, playing nicely). • Set clear attainable goals and limits (specific homework routine, bedtime routine, chores, etc.) and tie them to earning privileges, special outings, etc.' • Use positive incentives and natural consequences; "When you...(do homework) ...then you ...(may go play)"; if...then [371]. • Use empathy statements such as "I understand" / "however" can be useful. • Recommend that adults model emotional self-regulation and encourage a balanced lifestyle (nutritious meal planning, exercise, hobbies and sleep hygiene). • Schedule family and partner time. • Keep choices limited to two or three options. • Make rewards meaningful and timed in close proximity to the desired behavior.

ENVIRONMENTAL INTERVENTIONS	
Rationale	Strategies
Transition times, homework times and daily routines are difficult for individuals with ADHD, therefore, external scaffolding is crucial to establish daily expectations and structure and promote success. [372, 373].	• Implement structure and routines. • Parents/partners must be united, consistent, firm and fair. Follow through with agreed consequences. • Help them prioritize instead of procrastinating. • Post visual reminders (rules, lists, reminders, sticky notes, calendars) in prominent locations, using different colors to accentuate/prioritize. • Use timers/apps for deadlines (routines, homework, chores, paying bills, limiting electronics).

	• Keep labeled, different coloured folders or containers in prominent locations for items (keys, electronics, household items).
	• Find work area best suitable to individual, e.g. dining room table, quiet areas.
	• Chunk tasks (divide larger tasks into smaller ones) and assign specific deadlines to each step.
	• Allow planned frequent movement breaks during prolonged tasks.
	• Allow white noise, a fan or background music during homework, work or at bedtime.

What can be done at school?

Many individuals with ADHD struggle most at school. School interventions can be either proactive or reactive. Proactive interventions (e.g., visual cues and prompts) are directed at anticipating and reducing the likelihood of the child with ADHD engaging in disruptive behaviours. Schools should provide instructional and environmental accommodations for all students with ADHD. For some students, the proactive interventions may not be sufficient and behavioural approaches will be required. These reactive interventions consequence target behaviour by reinforcing positive behaviour (e.g., token economy) and ignoring or punishing negative behaviour (e.g., timeout; response costs) [331, 334]. It is important to monitor the actual outcomes of these "reactive" interventions as they may inadvertently increase disruptive behaviour [374].

Sharing information about ADHD and its impact with the family and the school is a way to begin promoting success at school. The following strategies focus on instruction, behaviour and environment within the classroom that can enhance success.

Table 4.3 Interventions at School

INSTRUCTIONAL INTERVENTIONS	
Rationale	**Strategies**
Students with ADHD often have difficulty with the "language" in the classroom [209, 375, 376]. Students with ADHD may have difficulties following instructions (particularly if they are multi-step instructions) or interpreting pragmatic language [377].	• Give clear and precise directions. • Get the student's attention before providing instructions. • Check the student's understanding by having the student repeat instructions and provide clarification as needed. • Use direct requests – "when-then".

BEHAVIOURAL INTERVENTIONS	
Rationale	**Strategies**
Students with ADHD are more responsive to consistent, immediate reinforcement. With behavior modification, parents, teachers and children learn specific techniques that will help improve children's behavior. Approaches identify goals and target behaviors to be modified; emphasize consistency and routine; boost individual self-esteem through verbal recognition and tangible rewards; and identify incentives that are developmentally appropriate. It is critical that goals are developed through collaboration with the student and their family. Incentives need to be meaningful to the individual.	• Provide immediate and frequent feedback. • Provide students with positive feedback and encouragement more frequently than negative feedback. • Provide students with specific feedback – "thank you for putting your hand up to ask a question". • Use visual cues in the classroom or on the desk for transitions. • Use visual prompts/pictures or lists for task initiation and task completion. • Chunk and break down steps to initiate tasks. • Reduce the amount of work required to show knowledge i.e. rather than asking a child to do 10 addition questions, requiring them to do 5. • Providing clear expectations and structure in the classroom. • Allow for acceptable opportunities for movement: "walking passes".

ENVIRONMENTAL INTERVENTION	
Rationale	**Strategies**
Students with ADHD often require changes in their physical environment that will decrease the likelihood of distractors and allow for more opportunities for teacher monitoring and interaction.	• Preferential seating away from distractions. • Proximity to the teacher. • A quiet place in the classroom for calming down or working. • Being seated beside a "more attentive" buddy. • Increase change and introduce novelty.

ACADEMIC INTERVENTION	
Rationale	**Strategies**
Students with ADHD may have co-morbid learning needs (e.g., fine motor difficulties, slower processing speed, weaker working memory) in addition to problems with distractibility that require specific accommodations in the classroom.	• Actively engage the student by providing work at the appropriate academic level. • Allow extended time (1.5 x) to complete quizzes, tests and exams. • Permit student to write quizzes, tests and exams in a quiet room. • Allow ear-plugs/ head-phones to help reduce external noises during tests • Provide a scribe or note taker or access to assistive technology. • Assign homework as necessary but monitor quantity.

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EXECUTIVE FUNCTION INTERVENTIONS	
Rationale	**Strategies**
Increase in classroom demands are frequently accompanied by increased struggles with organization, time management, prioritization and task completion. Executive function deficits have a significant and negative impact on academic progress and productivity. As the student moves into later grades the most common service provided are academic accommodations (e.g., testing accommodations preferential seating, copies of class notes etc.) which are not designed to develop or improve skills but rather that the expectations are being changed to permit the student a better chance at advancement [331].	• Find a tutor or academic coach. • Seek a structured classroom. • Establish a routine. • Keep an assignment notebook. • Develop an organization notebook. • Organize what needs to be taken to school the night before. • Monitor and prompt to get started on tasks. • Teach awareness of time; time management. • Use graphic organizer for long-term projects.

POST SECONDARY INTERVENTIONS	
Rationale	**Strategies**
Students with ADHD in college and university are often very challenged by executive function deficits and other comorbidities such as anxiety and depression, which places significant demands on the student's ability to maintain consistent and efficient pace. Students are easily overwhelmed when supports are not in place which begins a cycle of frustration and failure [378].	• Encouraging students to contact the Accessibility/Disability Centres. • Allow extended time for assignments, especially if numerous assignments are all due at the same time. • Allow extended time on tests/exams. • Organizational apps to keep notes, lists, ideas and more e.g. Evernote and Simplenote, Mind Manager. • Technological support to better organize thinking, taking notes, writing, e.g. Livescribe, AudioNote, One Note, SoundNote, Audiotorium and Screen Record • Concept Mapping can be achieved on the computer by using graphic organizers (e.g., Inspiration, Writers Companion, Draft Builder). • Access to preferential seating in lectures (close to the lecturer, away from visual or auditory distractions such as cycling heating/cooling units). • Access to a scribe or note taker to take notes for those courses where it is necessary to focus on the lecture rather than switching attention between the lecture to ensure lecture notes are adequate and thorough enough to review for tests/exams.

	• Obtaining advance copies of lecture notes, overheads, etc. so that the student can focus on the lecture rather than read what's on the board, take notes, and listen all at the same time.
	• Use videotape lectures if granted permission and review them later to reinforce class work.
	• Devices such as a tablet as well as apps that help with writing such as planning (e.g., Inspiration); drafting (e.g., Dragon Dictation, iPad Dictation); and note-taking (e.g., Notability).
	• Work with accessibility/disability staff to review and chunk assignments, check details, assist with time management and due dates and review progress.
	• Access to 'prompt' sheets/memory aids with outline of steps, formulas etc.
	• Coaching to identify strengths, negotiate problems, and work on specific goals.

What can be done in the workplace?

Table 4.4 Interventions in the Workplace

WORKPLACE INTERVENTIONS	
Rationale	**Strategies**
Setting individuals up for success in the work environment is critical. Individuals with ADHD often prefer to not disclose their ADHD in the work place given the stigma attached to ADHD and the fear of being judged as incompetent [379].	• Identify accommodation needs. • Request accommodations supports (Suggest using the CADDRA Template letter and adapting to your patient's situation). • Suggest regular and frequent meetings with manager and support collaborative approach. • Set goals, learn to prioritize, review progress on a regular basis. • Identify time management techniques that work for individual, i.e. using a planner, apps). • Declutter and create work friendly environment. • Use organizational Apps (i.e. Evernote, Omnifocus, Todoist). • Explore productivity Websites (e.g. 43folders.com, zenhabits.net). • Get assistance from an ADHD Coach. • Review workplace strategies and accommodations at www.caddac.ca.

MANUALIZED INTERVENTIONS

Parent Management Training Models

For preschool-aged children, parent management training models, including parent–child interaction therapy (PCIT), the Incredible Years series, the New Forest Program, Triple P (Positive Parenting Program), and Helping the Noncompliant Child, [380] are effective in decreasing symptoms of ADHD and disruptive behaviour disorders. Parents are actively involved in all of these interventions, sometimes without the child and sometimes in parent–child interactions. According to the American Academy of Pediatrics [381], all share similar behavioral principles, most consistently engaging parents as partners to: (1) reinforce positive behaviors; (2) ignore low-level provocative behaviors; and (3) provide clear, consistent, safe responses to unacceptable behaviors.

Social Skills Training

Many children with ADHD may be socially awkward. They may wish to be more social but their impulsivity may detract from their ability to make friends [382]. Sometimes they miss social cues or misunderstand social conventions like when to ask to join in or when not to interrupt. It is important to note that there is a spectrum of impairment in social skills. Some levels of impairment may be due just to ADHD, but for others there may be sufficient impairment in social skills and related problems to warrant an evaluation for a possible Autism Spectrum Disorder (ASD) diagnosis. Making friends is an important skill set that both the school and parents can facilitate. Good friendships can be a protective factor in reducing some of the negative outcomes associated with ADHD [383].

Social Skills Training (SST) generally focuses on teaching children how to perceive and interpret subtle social cues and problem-solve in social interactions while being reinforced for appropriate skills display within a group setting [384, 385]. Traditional SST involves a group of children receiving training, and parents are informed of the skills taught each week. These traditional approaches may have difficulty with encouraging treated children's generalization of knowledge to out-of-session contexts and with changing peers' negative biases toward children with ADHD [386]. In fact, a Cochrane review of the effects of SST interventions on children's social competences, general behaviour, ADHD symptoms and performance in school showed no statistically significant treatment effects on social skills, teacher-rated behavior or on the ADHD symptoms [384]. Other SST programs involve simultaneous parent or teacher training as friendship coaches [387] and may hold promise in providing children with in vivo reminders during real-world peer interactions, and in helping to alter peers' behaviours toward children with ADHD [386].

Cognitive Behavioural Therapy

Cognitive Behavioural Therapy (CBT) focuses on the interaction between an individual's cognition, emotion and behaviour [388, 389]. In CBT specifically targeted for ADHD, such issues as time management and organizational skills are primarily addressed.

CBT is recognized as an effective psychological treatment for adults with ADHD [390, 391].   One recent study has suggested that this therapy has a functional effect on the brain of adults with ADHD (specifically, the fronto-parietal network and cerebellum). These are the same regions affected by stimulant medications often used to treat ADHD [392]. Another study found CBT treatment for ADHD was effective but CBT plus medication resulted in greater improvement than CBT alone [393].

Studies on treatment outcomes of CBT in children and adolescents with ADHD have been mixed [394]. Adolescents with ADHD and anxiety/depression appear to benefit more than those with Oppositional Defiant Disorder [395]. Group CBT, along with medication, has been associated with reducing ADHD symptoms in adolescents [396].

Mindfulness Training

Mindfulness training is a cognitive-based therapy, often including mindful meditation, designed to increase mindful attention to one's own thoughts and actions (i.e., training individuals to focus on the present and to inhibit distracting thoughts and stimuli). Neuroimaging studies have shown that mindfulness training appears related to structural changes in the amygdala and increased grey matter volume in the hippocampus [397-399]. It has been found to lessen ADHD symptoms such as hyperactivity/impulsivity and attention problems, emotional dysregulation, while increasing self-directedness and self-regulation. These and other improvements in mood, anxiety, and social behaviour have been reported in children, adolescents and adults with ADHD, with the improvements being maintained over time. Mindfulness may also be a useful tool for parents to improve their interactions with their children with ADHD [400-406].

CHAPTER 5: PHARMACOLOGICAL TREATMENT OF ADHD

INTRODUCTION

Medications are part of an integrated and multimodal treatment plan that may include educational and psychosocial interventions. As with all pharmacological treatments in medicine, risk/benefit ratios need consideration before initiating any medication. Among the factors to be considered, the high morbidity of ADHD makes it important that we also weigh the risk of not treating ADHD [407]. ADHD has been associated with decreased social, educational, vocational and self-care functioning, as well as higher rates of accidental injury [317]. The burden of untreated ADHD also includes the time and energy it requires individuals, and those that support them, to cope with ADHD-related challenges [408].

It is important to clearly identify all areas of impairment due to ADHD at the onset of treatment, and regularly re-evaluate the ongoing impact of the condition. It is also important to systematically identify other potential causes of impaired functioning in a patient. Sleep deprivation, poor nutrition, lack of routines, psychosocial issues and comorbid disorders can affect outcome and should always be considered when assessing the patient's condition and when measuring clinical response.

Medication treatment should target symptoms that cause impairment. Clinicians are invited to use the documents in the CADDRA Assessment eToolkit in order to allow efficient and regular tracking of symptoms and impairments. Those tools are free to use and can be shared between patients, families, teachers and physicians in helping to guide an informed and evidence based treatment plan. Patients and their families should be aware that such questionnaires can help measure symptom frequency and associated impairment. However, just as a thermometer records a fever but does not identify the many reasons it could be occurring, ADHD symptom scales do not tell you if ADHD is the specific reason the symptoms are occurring. Clinical judgment is important to uncover if symptoms are due to, or modulated by, another disorder, both before starting treatment, and during treatment.

As with any chronic medical condition, follow up is important if medication continues to be taken. Medication may be reduced, temporarily interrupted or completely stopped, either because ADHD symptoms have improved and the patient does not need it anymore, or because the patient experiences unacceptable side effects or a lack of response. However, in some cases, medications are stopped for non-clinical reasons such as stigma or lack of financial coverage or other lack of access to care.

MEDICATION CLASSIFICATION

For purposes of medication selection, CADDRA categorizes ADHD medications as described below. CADDRA recommends that clinicians first consider viable first-line therapy choices, then second-line therapies, and only then third-line medications may be considered. However, physician discretion and clinical judgement determines final choice as ADHD treatment needs to be individualized.

First-Line Treatments

Long-acting psychostimulants are first-line treatment agents. First-line pharmacological treatments for ADHD are medications approved by Health Canada that have the best evidence base, risk-benefit profile, effectiveness as measured by effect size, and duration of effect. Additionally, sustained-release preparations maintain privacy for patients and families in the context of the school, work and social situations. CADDRA recognizes that long-acting ADHD medications use diminishes the need for multiple dosages and therefore augments compliance, symptom coverage and treatment response [409]. In addition, compared to immediate-release psychostimulants, use of long-acting psychostimulants may diminish diversion and rebound and is often associated with better tolerability [410].

It is important to note that both classes of stimulant medication (methylphenidate and amphetamines) have similar efficacy and tolerability profiles at the population level. However, at the individual level, patients may respond to, or tolerate one class better than the other [411, 412]. CADDRA therefore recommends an adequate trial of both classes of long-acting psychostimulants before engaging in a trial of a second-line treatment.

Second-Line Treatments

Atomoxetine, Guanfacine XR and short/intermediate acting psychostimulants are second-line treatment agents. Second-line treatments are medications approved by Health Canada for the treatment of ADHD but may have lower effect sizes, sub-optimal duration of action compared to first-line treatment, or reduced tolerability and risk-benefit profile [409, 413]. They can be used for patients who experience significant side effects, have had suboptimal response with first-time medications, or do not have access to first-line medications [414]. Non-stimulants may also be used in combination with first-line agents as a potential augmentation for first-line treatment suboptimal responders [415]. Second-line non-stimulant agents also are appropriate where stimulant agents are contraindicated, such as in cases where there is high risk of stimulant misuse [133].

Third-Line Treatments

Bupropion, clonidine, imipramine and modafinil are examples of third-line treatment agents. Atypical antipsychotics are among agents used for comorbidities commonly seen with ADHD, often in combination with other agents. They are medications whose use is off-label, or have higher risks, or a higher side-effect profile or a lower efficacy profile. Third line pharmacological treatments are generally reserved for treatment-resistant cases and may require specialized care. Exceeding recommended maximum dosages by CADDRA is a third-line treatment option and may be considered after regular dosages of different options have been tried.

STEPPED APPROACH TO PRESCRIBING

STEP 1 - Setting Treatment Objectives

Figure 5.1 Stepped Approach to Prescribing

STEP 1	STEP 2	STEP 3	STEP 4
Setting treatment objectives	Medication selection	Titration & monitoring	Ongoing follow-up
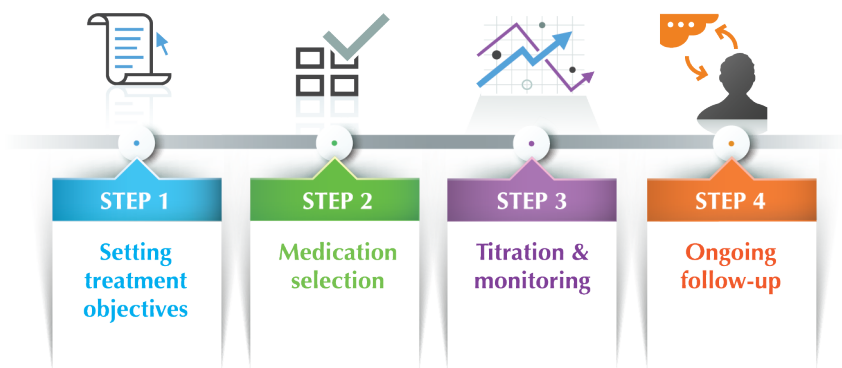
Once ADHD is diagnosed, in collaboration with the patient and collateral informants, the next step is to identify ADHD symptoms and functional challenges as treatment targets. Consider targets in multiple domains including home, school, work, etc. Good treatment objectives are Specific, Measureable, Attainable, Relevant and Timely (SMART).

STEP 2 - Medication Selection

When medication is discussed, use principles of informed consent to ensure the patient and family (where applicable) are adequately educated when addressing medication questions, particularly regarding clinical indications, reasonable goals of treatment, dosing strategies, degree of efficacy, side effects and adherence issues. Both patient related and medication related factors should be considered in the selection of a specific medication for the treatment of ADHD. These factors are outlined below.

Table 5.2 Factors to Consider for ADHD Medication Selection

Medication Selection: Patient-related factors	Medication Selection: Medication-related factors:
- Age and individual variation - Duration of effect required by timing of symptoms - Concurrent psychiatric and medical issues - Physician, family and patient attitudes	- Active ingredient /mode of action/drug interactions - Delivery system / onset of action / duration of action - Available doses - Canadian clinical indications - Affordability, accessibility and reimbursement (public/private)
	Special considerations:
	- Combining medication for adjunct effects - Potential of abuse, misuse and diversion - Generic formulations

Medication Selection: Patient-related factors

Age and individual Variation

- **There are no age-specific match criteria** – In general, ADHD medications could be used across the lifespan, although not every medication has received an "official" approval for all ages through the process required by the Therapeutic Products Directorate (TPD) of the Canadian government. Some ADHD medications (e.g. guanfancine XR), are lacking in trials and evidence in some age groups. Treatment before the age of six, if necessary, should be within the context of specialized care [270].
- **There is no maximum age to treat ADHD - if the general health and cardiovascular status** of the patient permits use of those treatments. See chapter three for special considerations in treatment in older adults with ADHD.
- **Women of childbearing age -** the effects of ADHD medications on the foetus and on the baby while breastfeeding are unknown and require careful weighing of any potential benefits and risks.
- **Children and some adult patients may experience difficulty swallowing pills -** Although this can often be improved by teaching swallowing techniques, it should also be noted that some medications can be sprinkled on soft food or diluted in liquid (See section on delivery).
- **No specific clinical profile** can predict which medication will be better.
- **Adherence to treatment** – ADHD-related forgetfulness may cause difficulty adhering to a plan that requires multiple daily doses. Once daily doses are more helpful.
- **Predicted compliance –** Medications that cannot be stopped suddenly (e.g. alpha-2 agonist class agents) should be used with caution in patients who have compliance issues. Compliance can be improved with psychoeducation, regular support and follow-up.
- Weight of the patient does not predict optimal dosage for psychostimulants.
- At this time, there is insufficient evidence that symptom profile, family history or genetic testing can help predict which medication will work best for an individual in clinical practice. While patients respond differently, all medications approved for use in ADHD by Health Canada can reduce both inattention as well as impulsive/hyperactive symptoms of ADHD.

Duration of Effect Required by Timing of Symptoms

With time, or with change in environmental supports or demands, the burden of ADHD may change. Medication use can be titrated to meet increased demands or to cover longer periods of daytime impairment. When considering duration of effect of the medication, it is important to remember that ADHD may impact all aspects of the patient's daily life, not just in the classroom or workplace. Attention and self-control are also important outside of school and work. Thus, the severity of impairment from ADHD will vary from individual to individual and between different developmental stages and ages.

The decision about **when** to administer treatment during the day and **how long** the effect of that treatment needs to last must be explored by the clinician in consultation with the patient and patient's family. This decision must be made considering the context of the individual's experience. The numerous ways ADHD symptoms can impact a person's daily life - at home, at school, at work, at play - makes it important to not only optimize treatment for core symptoms and to minimize side effects but to consider WHEN treatment is required.

In considering patient preferences regarding duration of effect it is also important to keep in mind that the level of insight regarding the functional impact of having ADHD varies from patient to patient. For example, an adolescent patient may only be concerned about the impact of ADHD on academic functioning during the day and may be unaware of its impact on their driving or evening risk taking activities.

To improve the overall quality of life for the majority of individuals, regardless of age, the duration of effect of the medication usually needs to extend beyond the classroom/work settings into the evening, weekend and holidays. Similarly, a patient may realize that the best option may be to have individualized treatment based on day-to-day variation. This may be critical for tasks such as driving, where the maximal risk period for young drivers may be during the evenings and at weekends. It is important to remember that the duration of effect for a specific medication can vary from patient to patient. Clinical experience indicates that, for some patients, the duration of effect is shorter or longer than what is stated in the product monograph.

Concurrent Psychiatric & Medical Issues

Psychiatric Comorbidities

When there is a co-occurring psychiatric disorder along with ADHD, it is generally advised that the most impairing disorder be treated first. A variety of considerations may be important in determining sequence of treatment including diagnostic certainty, patient preference, the disorder with greatest impairment, or the disorder most likely to respond to treatment. However, psychosis, severe mood disorder, substance use disorder and all types of bipolar disorders should be identified and treated prior to ADHD, as these may complicate treatment. If the patient is expressing suicidal or violent thoughts these need to be addressed as a priority.

It is common for patients to have mood and anxiety distress secondary to ADHD. Treatment strategies should take into account those issues. Often, an effective ADHD treatment may contribute to reduce mood and anxiety related to ADHD-associated impairments. Although stimulants are thought to upregulate sympathetic nervous system activity, they are often compatible with anxiety disorders. For a more detailed discussion of comorbid conditions please refer to Chapter 2.

When treating comorbid psychiatric conditions, physicians should try to select medications that impair cognition less since this may aggravate ADHD symptoms, and consider potential drug-drug interactions. Treatment of ADHD combined with comorbid psychiatric disorders often involves polypharmacotherapy, increasing the risk for pharmacological interactions and side effects.

Medical Precautions with ADHD Medications

It is important for clinicians to be aware of any medical risk the patient may have that affects suitability for an ADHD medication. Although some pre-existing conditions like tics and sleep problems may be positively affected by ADHD medications, in some cases they can be aggravated.

Weight and Height

Weight and height require initial and ongoing measurement in children and adolescents. Referencing percentile charts and growth charts is recommended.

Cardiovascular Issues

ADHD medications can affect blood pressure and heart rate. Personal history of unexplained light headedness, shortness of breath, or other possible cardiac symptoms, as well as any family history of suspected cardiac sudden death should lead to workup prior to initiation of stimulant treatments. Blood pressure and heart rate should be measured initially before starting ADHD medication and during follow-up. To understand the effect of ADHD pharmacology on blood pressure or heart rate, it is important to take measurements while medication is present in the patient's system. To assess the effects of stimulants on vital signs, it may be useful to make measures before a dose is taken and compare to measures while the dose is active.

PRACTICE POINTS

- Prescribers should thoroughly weigh the risks versus benefits of treating ADHD patients.

- Psychostimulants have been broadly prescribed for more than a half-century, with considerable safety data in the general population.

- A detailed medical history is recommended to identify potential cardiovascular risks of psychostimulants.

- Routine ECG monitoring, either before drug administration or after starting therapy, is not recommended in young patients with no history of heart disease or normal physical examination.

- Blood pressure and heart rate should be measured initially before starting ADHD medication and during follow-up.

- Cardiology consultation should be considered in patients with established or suspected heart disease.

Special Section on Potential Cardiovascular Risks of Psychostimulants

Psychostimulant medications are generally safe and well tolerated in children, adolescents, and adults with ADHD. However, there has been controversy regarding the cardiovascular safety of these drugs, particularly the potential risk of arrhythmias. The direct consequence of small increases in systemic adrenergic activity lead to the expected cardiovascular effects of small increases in blood pressure and heart rate, which are statistically significant, but rarely clinically important [416-419]. However, some individuals may have much stronger sympathetic effects.

In 2006, the FDA and Health Canada raised concerns about ADHD medications after identifying 27 cases of sudden death in children from Adverse Event Reporting System (AERS) data between 1992 and 2004, and Health Canada withdrew market authorization for some medications. Following incorporation of the number of patient-years of prescribed medication into the interpretation of the AERS data and a detailed review, market authorization was reinstated, but warnings were added to ADHD medications labels.

There has been epidemiologic evidence related to ADHD medications and sudden cardiac death subsequent to the 2006 labeling that is reviewed below. **It should be noted that this labeling does not constitute a recommendation for routine ECG screening prior to initiating ADHD medication in patients without identifiable risk factors for cardiac disease from history and examination.** Population-based ECG screening is a controversial topic, with costs, benefits and feasibility that are highly dependent on the health care jurisdiction in which they are applied.

Using AERS data adjusted for drug exposure, the frequency of reported sudden death per year of ADHD therapy ranges from 0.2 to 0.5 per 100,000 patient-years [420-423], compared to a recognized baseline risk of 1.2 to 1.3 per 100,000 patient-years in the ostensibly normal paediatric population [424]. It is recognized that adverse events are usually under-reported by 75 to 90%, although true underreporting for an event as dramatic as sudden death is not known. To study such low event rates, administrative databases have been used. Using Florida Medicaid beneficiary data on patients 3 to 20 years of age over 10 years in over two million individuals, rates of cardiac death or cardiac hospitalization were similar for ADHD patients prescribed psychostimulants as compared to the general paediatric population [425]. An administrative database study of children and young adults funded by the Agency for Healthcare Research and Quality and the FDA (>2.5 million person-years including 373,667 person-years of ADHD drug use) showed no increased risk of sudden death or stroke in patients with compared to without ADHD drug prescription [426]. In a third claims records database study, neither current nor previous stimulant use was related to cardiovascular symptoms or events [427]. A study of over 440,000 adults, with over 150,000 ADHD medication users, found no evidence of an increased risk of MI, sudden cardiac death or stroke [426].

On the other hand, two studies have identified associations of ADHD medication use with sudden death. A case-control study assessed matched groups of 564 children aged 7–19 years from state mortality data over an 11-year period, comparing those who had suffered sudden unexplained death to those who had died as passengers in motor vehicle accidents. Ten (1.8 %) of the sudden unexplained death cases were treated with a stimulant at the time of their death, compared with only two (0.4 %) of the motor vehicle accident victims. However, the histories related to the sudden unexplained death cases may have been subject to a recall bias, and in the absence of autopsy information, assigning cause of death in young individuals with sudden unexplained cardiac arrest is difficult [428]. In an administrative database study of Medicaid and commercial insurers, 43,999 new adult methylphenidate users were matched to 175,955 nonusers, and had a significant hazard ratio of 1.84 for sudden death or ventricular arrhythmias. Dosage was inversely associated with risk, and this lack of an expected dose-response relationship suggested that the association might not be a causal one. In addition, ventricular arrhythmias and sudden death are not synonymous and may arise by very different mechanisms, especially in persons without structural heart disease [429].

Taken as a whole, subsequent studies support the 2006 assertion that, when adjusted for medication exposure, sudden death rates in ADHD patients do not appear to differ from the general population. The AERS data had also demonstrated that sudden deaths in patients receiving ADHD medications has similar associations to those seen in sudden death within the general population, including male and teenage preponderance, occurrence during exertion, family history of sudden death or life-threatening ventricular arrhythmias, and pathology findings of cardiomyopathy, valvular defects or coronary anomalies. Despite the similarities to sudden death victims in the general population, and the absence of any identified incremental risk, ADHD medication labelling continues to advise that they "should generally not be used in patients with known structural cardiac abnormalities". "Structural abnormalities" are in general meant to encompass LV dysfunction, scarring, hypertrophy, and significant valvular disease, although the term is not precisely defined. Such patients where identified will benefit from expert cardiac assessment. Although they may have sudden death risks above the normal population, these risks are likely unrelated to ADHD medication use. The very low absolute risk of sudden death in these patients should be considered when weighing the benefits and potential risks of therapy for a disorder with substantial morbidity such as ADHD.

Even for patients with long QT syndrome, where the risk of arrhythmias with increased sympathetic activity is established, a recent report of a small series of children with LQTS and ADHD treated with stimulants concomitant with beta blockade demonstrated no adverse outcomes over 56 patient years. The study [430] was published along with a particularly pointed editorial entitled "People with long QT syndrome who have attention deficit hyperactivity disorder deserve to be treated properly" [431]. Specialty consultation is important to address whether patients with arrhythmia contraindications can be treated with ADHD medications.

It should be noted that in a subset of patients, ADHD and structural and/or hereditary heart disease may be intrinsically related to each other based on a common syndrome (e.g. Velocardiofacial Syndrome) [432] in association with complex congenital heart disease or [146] its surgical repair [433, 434]. Patients with congenital heart disease have an increased prevalence of ADHD, and can benefit from ADHD therapies, including medication [435]. Drugs used in the treatment of ADHD do lead to a small increase in heart rate, (average 5-10 beats/min), and systolic blood pressure (average 4-6 mmHg [436]. It is uncommon, but some patients will have much higher effects from stimulant treatment. These effects can be evaluated by comparing heart rate and blood pressure before and on treatment – in the case of stimulants this can also be evaluated before a dose and after the dose the same day. In adult patients with hypertension or coronary heart disease, caution is advised and a closer monitoring of heart rate and blood pressure is recommended in these cases.

Psychiatric and Medical Precautions or Contraindications

Table 5.3 Psychiatric and Medical Contraindications and Precautions for ADHD Medications

ALL ADHD MEDICATIONS		
CONTRAINDICATIONS	**PRECAUTIONS: Pre-existing conditions in patients**	**To be monitored during treatment**
Known hypersensitivity or allergy to the products	• Cardiac disease • Bipolar disorder • Psychosis • Pregnancy and lactation	• Height and weight in children • New mood, anxiety, substance use disorder, psychotic or manic symptoms • Suicidal behaviour or ideation • Aggressive behaviour (new or worsening) • Sleep, appetite • Irritability / mood swings
SPECIFIC TO PSYCHOSTIMULANTS		
CONTRAINDICATIONS	**PRECAUTIONS: Pre-existing conditions in patients**	**To be monitored during treatment**
• Treatment with MAOI and for up to 14 days after discontinuation. • Glaucoma (narrow angle) • Untreated hyperthyroidism • Moderate to severe hypertension • Pheochromocytoma • Symptomatic cardiovascular disease • History of mania or psychosis	• History of substance abuse • Anxiety[1] • Renal impairment • Tic disorders[2] • Epilepsy • Peripheral vasculopathy including Raynaud's Phenomenon	• BP, HR (may increase) • Priapism • Growth retardation • Peripheral vasculopathy including Raynaud's Phenomenon

SPECIFIC TO ATOMOXETINE		
CONTRAINDICATIONS	**PRECAUTIONS: Pre-existing conditions in patients**	**To be monitored during treatment**
• Treatment with MAOI and for up to 14 days after discontinuation. • Narrow angle glaucoma • Uncontrolled hyperthyroidism • Pheochromocytoma • Moderate to severe hypertension • Symptomatic cardiovascular disease • Severe cardiovascular disorders • Advanced arteriosclerosis	• Asthma[3] • CYP2D6 poor metabolizers • Peripheral vasculopathy including Raynaud's Phenomenon	• Priapism and urinary retention • Signs / symptoms of liver injury • Growth retardation • Peripheral vasculopathy including Raynaud's Phenomenon

SPECIFIC TO ALPHA-2 AGONISTS i.e. guanfacine, clonidine		
CONTRAINDICATIONS	**PRECAUTIONS: Pre-existing conditions in patients**	**To be monitored during treatment**
Inability for parents or patients **to ensure regular daily dosage** (due to the risk of rebound hypertension when stopped abruptly)	• Hepatic impairment • Kidney impairment	• Somnolence and sedation • BP, risk of hypotension • Bradycardia, syncope • Elevated BP and HR upon abrupt discontinuation • QTc interval (to be monitored if underlying conditions or other medication increase the risk of prolonged QTc interval)

MAOI = monoamine oxidase inhibitors; BP = blood pressure; HR = heart rate

[1] *Psychostimulant medications are used cautiously in patients with anxiety disorders but the CADDRA ADHD Practice Guidelines Committee agrees that the benefits of psychostimulants to treat ADHD often exceeds the risk*

[2] *Psychostimulant medications are used cautiously in tic spectrum disorders but the Committee agrees that use can be indicated if there is sufficient impairment of the concurrent ADHD. In these cases, the medications for ADHD are often combined with other drugs for tics (e.g., atypical neuroleptics or alpha-2 agonists).*

[3] *Atomoxetine may be used in combination with inhaled beta2 agonists like salbutamol, but should be used with caution in patients being treated with oral or intravenous beta2 agonists*

Note: This table summarizes key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

Physician, Family and Patient Attitudes

All patients and their families need to be educated about the potential benefits and drawbacks of treatment with ADHD medications. It is important to have a comprehensive discussion regarding all treatment options. Patients may be reluctant to start a specific product or class of ADHD medication for a variety of reasons.

Psychological Biases, Misunderstandings and Side Effects

Psychological biases against the use of ADHD medications may be due to misinformation regarding side effects, stigma, or in the cases of parents, guilt about having 'caused' the problem through 'bad' parenting.

Patients may have **questions and worries about side effects**. They may be afraid that medication will cause them to "*lose their sparkle*" or their brain will become "*lazy*". A frank discussion about therapeutic and side effects may help patients make better choices. All medications may cause side effects. It should be stressed that most side effects settle after two or three weeks of continuous use and alternative options will be sought if a person feels they are impaired by a prescription.

A common reason for non-adherence is related to a lack of physician awareness or understanding of side effects, or patients' reluctance to explain their discomfort. Patients should be informed about how to determine if their medication dosage is too high. For example, they might experience feeling too "wired", too irritable or excessively focused, or experiencing restricted affect, sometimes called a "*zombie effect*".

Please note: If negative symptoms are experienced at the time when medications would be expected to be wearing off, or with sudden cessation of pharmacotherapy, it is likely that those symptoms are not from an excessively high dose but from withdrawal, where the medication is wearing off too quickly.

Previous Experience with ADHD Medication

Some patients may have past experience with ADHD medication. That experience, positive or negative, may colour their attitudes towards the suggested course of treatment. For instance, they may have suffered the disappointment that comes with over-estimation of the effectiveness of medication, especially without concurrent educational and psychosocial interventions.

A family history of prior positive response to ADHD treatment should also be considered as well as any negative experience on specific medications. Although there is no evidence indicating that a family member's response indicates a greater likelihood of patient response, it is understandable that a positive response to a specific treatment in a family member could increase positive expectations for this treatment while the contrary can occur for a negative outcome.

When a patient mentions that they have a friend or a family member on ADHD medication, clinicians can inquire about their perception of the medication efficacy and tolerability. They may also inquire if the patient themselves "tried" the medication outside a treatment regime; patients may not spontaneously provide this information unless asked.

Medication Selection: Medication-related factors

See the following section for medication-specific differences. These differences allow for matching of medication characteristics to patient needs and preferences.

5.4 Clinical Comparison of Long-Acting Medication

Brand Name	Active Ingredient	Canadian Indication	Clinical Efficacy Studies	Long-acting Technology Used	Duration of Effect[1]	(%IR/%XR) Delivery	Available Doses / Dosage Form	Sprinkle Format	Cost	Controlled Substance
PSYCHOSTIMULANTS Amphetamine based products										
Adderall XR®	Mixed Amphetamine Salts	All age groups	Yes	Two beads	~12 hours	50/50	6 / Capsules	Yes[2]	$$	Yes
Vyvanse®	Dextro-amphetamine	All age groups	Yes	Pro-drug	13-14 hours	Continuous	6 / Capsules	Dissolvable in water, orange juice or yogurt	$$	Yes
Generic[3]	Mixed Amphetamine Salts (Generic substitute for Adderall XR®)	No	Unspecified	Unspecified	Unspecified	Unspecified	6 / Capsules	Yes[2]	$	Yes
Biphentin®	Methylphenidate	All age groups	Yes	Multilayer beads	10-12 hours	40/60	8 / Capsules	Yes[2]	$+ low doses – $$ higher doses	Yes
Concerta®	Methylphenidate	All age groups	Yes	OROS®	~12 hours	22/78	4 / Tablets	No[4]	$$	Yes
Various Generics[3]	Methylphenidate	All age groups (Generic substitutes for Concerta®)	No	Unspecified	Unspecified	Unspecified	4 / Tablets	No[4]	$	Yes
Intuniv XR®	Guanfacine	6-17 y.o. patients: monotherapy / adjunct therapy to psychostimulants	Yes	Polymer matrix	Continuous	Continuous	4 / Tablets	No[4]	$$$	No
Strattera®[3]	Atomoxetine	All age groups	Yes	None	Continuous	Continuous	7 / Capsules	No[5]	$$$	No
Generic	Atomoxetine	All age groups			Continuous	Continuous			$	No

IR = immediate release; XR = extended release; = Per CADDRA Board; y.o. = years old.

[1] Clinical experience indicates that, for some patients, duration of effect is shorter or longer than what is indicated in the product monograph.

[2] Beads should not be crushed or chewed to preserve extended release feature.

[3] Clinical ADHD Practice Guidelines' committee has reported loss of control in some patients when switched from original to generic drugs. Given the unpredictability of response, long-acting generic psychostimulants are considered 2nd line agents.

[4] To be swallowed whole - Do not cut, break, crush or chew tablet to preserve extended release feature

[5] To be swallowed whole – Do not open capsule to prevent gastric irritation

Note: This table summarizes key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

Drug Interactions

AMPHETAMINE BASED PRODUCTS [1]

5.5 Drug Interactions - Amphetamines

Drug Class	Molecule(s) Implicated (or examples if many)	Interaction Description / Action to Be Taken
Acidifying agents	(e.g. Fruit juices, ascorbic acid)	May ↓ AMP absorption, ↑ AMP excretion, ↓ AMP plasma levels Monitor response to AMP therapy
Alkalinizing agents	(e.g. sodium bicarbonate)	May ↑ AMP absorption, ↓ AMP excretion, ↑ AMP half-life Consider alternatives, or monitor for AMP excessive effect
Analgesics (opioids)	(e.g. meperidine, codeine)	May ↑ analgesic effect Monitor analgesic response, lower dose of opioid may be required
Antibacterial	linezolid	May ↑ hypertensive effect of AMP ✖ Avoid combination
Antidepressants	MAOI, RIMA (e.g.phenelzine, moclobemide)	↑ noradrenaline, may lead to hypertensive crisis ✖ AMP are contraindicated during or within 14 days of MAOI/RIMA therapy
	SSRI, SNRI (e.g. paroxetine, venlafaxine)	May ↑ adverse/toxic effect of SSRI, May ↑ risk of serotonin syndrome Monitor closely for signs/symptoms of serotonin syndrome
	Tricyclics (e.g. amitriptiline)	May ↑ the stimulatory and cardiovascular effect of AMP Monitor stimulant and cardiovascular response to AMP
Antihypertensive agents	alpha$_2$ agonists, beta-blockers (e.g. clonidine, propranolol)	May ↓ hypotensive effect of antihypertensive Monitor BP and HR when starting, stopping or adjusting AMP dose
Antipsychotics	(e.g. chlorpromazine, fluphenazine)	May ↓ effect of AMP Monitor response to AMP therapy
Decongestants	(e.g. ephedrine, pseudoephedrine)	May ↑ hypertensive and tachycardic effect of decongestant Monitor BP and HR

METHYLPHENIDATE BASED PRODUCTS[2]

5.6 Drug Interactions - Methylphenidate

Drug Class	Molecule(s) Implicated (or examples if many)	Interaction Description / Action to Be Taken
Antibacterial	linezolid	May ↑ hypertensive effect of MPH ✖ Avoid combination
Anticoagulant	warfarin	May ↑ serum concentration of warfarin Increase INR monitoring when MPH is started/stopped or dose is changed
Anticonvulsants	phenobarbital, phenytoin, primidone	May ↑ serum concentration of anticonvulsants Monitor serum concentrations of anticonvulsants when MPH is started, stopped or dose is changed
Antidepressants	MAOI, RIMA (e.g. phenelzine, moclobemide)	May ↑ hypertensive effect of MPH, may lead to hypertensive crisis ✖ MPH are contraindicated during or within 14 days of MAOI/RIMA therapy
	SSRI, SNRI (e.g. paroxetine, venlafaxine)	May ↑ adverse/toxic effect of SSRI and may ↑ risk of serotonin syndrome Monitor for signs/symptoms of serotonin syndrome
	Tricyclics (e.g. amitriptiline)	May ↑ serum levels and adverse/toxic effect of tricyclics Monitor tricyclics serum levels and toxicity
Antihypertensive agents	Alpha$_2$ agonists clonidine	May ↑ adverse/toxic effect of clonidine Monitor for adverse effect of clonidine
Decongestants	(e.g. ephedrine, pseudoephedrine)	May ↑ hypertensive and tachycardic effect of decongestant Monitor BP and HR

AMP = amphetamine based products; MAOI = monoamine oxidase inhibitors; RIMA = reversible inhibitors of monoamine oxidase type A; SSRI = selective-serotonin reuptake inhibitors; SNRI = serotonin-norepinephrine reuptake inhibitors; BP = blood pressure; HR = heart rate; MPH = methylphenidate based products; INR = International Normalized Ratio

[1] Amphetamine based products include Adderall XR®, Dexedrine®, Dexedrine® Spansules® and Vyvanse®

[2] Methylphenidate based products include Biphentin®, Concerta®, Ritalin® and Ritalin® SR

✖ Avoid Combination

Note: These tables summarize key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

INTUNIV XR® (guanfacine XR) (CYP3A4 substrate)

5.7 Drug Interactions – Guanfacine XR

Drug Class	Molecule(s) Implicated (or examples if many)	Interaction Description / Action to Be Taken
Anticonvulsants	(e.g. phenobarbital, phenytoin)	May $\downarrow$ serum concentrations of GXR through CYP3A4 induction Monitor GXR effect, dose $\uparrow$ may be necessary
	valproic acid	May $\uparrow$ serum concentrations of valproic acid Monitor response to valproic acid when GXR is started / stopped
Antidepressants	SSRI (e.g. paroxetine)	May $\uparrow$ adverse/toxic effect, psychomotor impairment of SSRI Monitor psychomotor impairment of SSRI
Antihypertensive agents	Alpha$_2$ agonists clonidine	2 agents with similar mechanism of action Combination not recommended
	Beta-blockers (e.g. propranolol)	May $\uparrow$ AV-blocking effect of BB, may $\uparrow$ rebound hypertensive effect of GXR when stopped abruptly Closely monitor HR and BP particularly if GXR is withdrawn
Antipsychotics	(e.g. chlorpromazine, haloperidol)	May $\uparrow$ QTc interval Combination not generally recommended
CNS depressants	alcohol, sedatives, hypnotics, barbiturates, antipsychotics	May $\uparrow$ sedation and somnolence Monitor for additive CNS-depressant effects, avoid use of unprescribed CNS-depressants
CYP3A4 inducers or inhibitors	(e.g. rifampin, fluconazole, ritonavir, grapefruit)	Inducers may $\downarrow$ serum concentrations of GXR Inhibitors may $\uparrow$ serum concentrations of GXR Closely monitor response to GXR
Prokinetic Agent	Domperidone	May $\uparrow$ QTc interval Combination not generally recommended
QTc prolonging agents	(e.g. quinidine, quetiapine, citalopram, atomoxetine)	May $\uparrow$ QTc interval Consider alternatives, closely monitor for evidence of QTc prolongation

STRATTERA® (atomoxetine) (CYP2D6 substrate)

5.8 Drug Interactions – Atomoxetine

Drug Class	Molecule(s) Implicated (or examples if many)	Interaction Description / Action to Be Taken
Antiarrhythmics	(e.g. quinidine)	May ↑ serum concentrations of ATX through CYP2D6 inhibition Initiate ATX at a reduced dose, titrate slowly PRN. If on ATX and starting antiarrhythmic, ATX dose may need to be ↓. Monitor ATX effect.
Antiasthmatics	salbutamol oral or IV only	May ↑ tachycardic effect of salbutamol Monitor BP and HR when systemic salbutamol is used with ATX
Antibacterial	linezolid	May ↑ the neurotoxic effect of ATX ✖ Avoid combination
Antidepressants	bupropion	May ↑ serum concentrations of ATX through CYP2D6 inhibition Initiate ATX at a reduced dose, titrate slowly PRN. If on ATX and starting bupropion, ATX dose may need to be ↓. Monitor ATX effect.
	MAOI, RIMA (e.g. phenelzine, moclobemide)	May ↑ the neurotoxic effect of ATX ✖ Combination contraindicated
	SSRI (e.g. paroxetine)	May ↑ serum concentrations of ATX through CYP2D6 inhibition Initiate ATX at a reduced dose, titrate slowly PRN. If on ATX and starting SSRI, ATX dose may need to be ↓. Monitor ATX effect.
	Tricyclics (e.g. desipramine)	May ↑ serum concentrations of ATX through CYP2D6 inhibition and potentiate noradrenergic effects Combination not generally recommended
Decongestants	(e.g. ephedrine, pseudoephedrine)	May ↑ hypertensive and tachycardic effect of decongestant Monitor BP and HR
Other CYP2D6 inhibitors	(e.g. terbinafine, ritonavir, mirabegron)	May ↑ serum concentrations of ATX through CYP2D6 inhibition Initiate ATX at a reduced dose, titrate slowly PRN. If on ATX and starting CYP2D6 inhibitor, ATX dose may need to be ↓. Monitor ATX effect.
QTc prolonging agents	(e.g. quinidine, quetiapine, citalopram, guanfacine)	May ↑ QTc interval Consider alternatives, closely monitor for evidence of QTc prolongation

GXR = guanfacine XR; SSRI = selective-serotonin reuptake inhibitors; BB = beta-blockers; AV = atrioventricular; HR = heart rate; BP = blood pressure; CNS = central nervous system; ATX = atomoxetine; IV = intravenous; MAOI = monoamine oxidase inhibitors; RIMA = reversible inhibitors of monoamine oxidase type A; PRN = as needed; ✖ Avoid Combination

Note: These tables summarize key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

Affordability, Accessibility and Reimbursement (Public/Private)

All patients should have access to optimum treatment. Unfortunately, some medications are beyond the financial reach of a significant number of patients without extended health insurance. Some medications can be supported through special access programs, but entrance can be limited by the procedures required or the constricted time for which medication is supplied.

Third party insurers cover most ADHD medications; however, patients may have to rely on generic formulations that may not be as effective (refer to the section in this chapter about generics). CADDRA continues to advocate for a resolution of this problem at the government level. Clinicians need to be informed about the cost of medications and the patient's coverage or ability to afford them before deciding what to prescribe.

Most Canadians have access to reimbursement for prescription medications through private insurance plans (third-party insurance), the provincial / territorial drug benefit programs or federal programs for certain groups. Because healthcare falls within provincial and territorial jurisdiction, the funding available for ADHD medication varies considerably depending on an individual's address. An online guide to provincial reimbursement for prescription medications in Canada can be found here: http://bit.ly/PublicDrugBenefit.

Special Considerations

Combining Medications for Adjunct Effects

Common scenarios for adjunct prescribing in addition to an ADHD medication include adding an ADHD agent with a different mechanism, a short acting ADHD agent to cover uncovered portions of the day, or an agent to address concurrent mood, sleep, or anxiety disorders. The clinician should query a drug metabolic interaction database to understand how metabolism of either agent may be impacted (e.g. fluoxetine and atomoxetine) through an interaction of the cytochrome P450/2D6. Separately, clinicians should consider whether agents have additive effects that may preclude their combination or require careful monitoring – such as sedative or sympathetic effects. Special monitoring or consultation may be required to maximize the safety of unstudied combinations.

Only guanfacine XR has been approved by Health Canada for the adjunctive treatment of ADHD in combination with psychostimulants. However, other combinations are frequently used in clinical practice (e.g. atomoxetine and psychostimulants).

Potential for Abuse, Misuse and Diversion

Individuals who abuse stimulants to achieve a "high" typically administer them via parenteral routes. Others misuse psychostimulants trying to mask fatigue, believing that the non-medical use of stimulants will increase academic performance.

Short-acting formulations of stimulants have a much higher risk of misuse/ diversion than the longer-acting stimulants due to their pharmacokinetic profile and easy crushability.

All professionals involved in treating ADHD patients should be alert to the signs of abuse, diversion and misuse and consider these behaviours as significant and not benign. For more information about the signs of diversion and misuse, please see Health Canada 2006, Abuse and Diversion of Controlled Substances: A Guide for Health Professionals [437].

To be considered "bioequivalent", Health Canada only requires the maximum concentration (Cmax) and area-under-the-curve (AUC) of a generic product to be similar to the reference (brand-named) product. These are appropriate measures for most medications. However, the duration of effect may be more related to the length of the ascending concentration curve (time to maximum concentration – Tmax) than to the Cmax or AUC. For example, a generic brand for Concerta® available in Canada has a distribution curve that looks more like Ritaline SR than Concerta®, with an earlier Tmax and a shorter duration of effect than Concerta®. However, both are considered "bioequivalent" by Health Canada.

> **PRACTICE POINT**
>
> The decision to switch to a generic formulation is an individual-based decision and the CADDRA Guidelines Committee strongly advocates that the patient/family be advised of the switch, told to check for clinical changes in efficacy or tolerability and report any changes to their pharmacist and doctor.

Therefore, the CADDRA Guidelines Committee considers this generic formulation substituted for the methylphenidate OROS® tablets to be a different drug because:

- Clinical studies and experience have shown a clinical difference between the generic and the original product [438].
- The delivery system of the generic formulation differs from the original product.
- The generic tablets may be easily crushed, therefore potentially increasing the risk for abuse by snorting or intravenous use.

> **Practice Point**
>
> It is important that patients are given a realistic view of what they can expect from medication. They need to understand that each person has a different risk/benefit profile ranging from those who cannot tolerate or benefit from medication at all to those who have full remission with no side effects.
>
> While research allows us to provide patients with a great deal of information about their medication options, patients and parents must be made to understand that every person is unique. A dosage that is effective for one patient might not work for another.
>
> It is important to point out that agreeing to a "trial" of medication is not a decision to use it forever. A trial is an experiment that carries minimal if any risks that would extend beyond a very brief period of time, and can be discontinued at any point.
>
> Key points for a successful medication trial:
>
> - Involve the patient and their family
> - Identify the specific ADHD symptoms that impair function to define treatment goals,
> - Select treatment options and clinical tools to measure change
> - Start with first line treatment options and take the time to adjust doses balancing clinical efficacy and side effects
> - Follow titration protocol outlined in the medication charts by age-group
> - Measure response at planned intervals
> - If response is unsatisfactory, explore why and try a different treatment option until symptom control is optimized
> - Follow-up and re-assess efficacy and need for treatment regularly.
>
> **Note:** It is not a valid trial if patient is not adhering to doses prescribed, taking other interfering medications, or physician is not tracking changes.

Key Points When Selecting an ADHD Medication

Which medication is indicated in the patient's age group?

The first choice should be a medication that has an approved indication by Health Canada for ADHD within the specified age group. Even though some ADHD medications are not officially approved by Health Canada for a specific age group, doctors may decide to use them based on scientific evidence and expert consensus.

What impairments does the patient have and at what time(s) of the day?

Is it mainly during school or work hours, meetings, exam times, leisure times, driving periods, morning routines, etc.? Ensure the medication is taken so that it is effective when most needed for the patient's individual needs.

What medication does the patient prefer?

Has the patient ever taken any medications before or heard of something they might want to try? Patients may respond better to the medications they most strongly believe in. This also addresses the belief that patients must be educated and they should have a partnership in the treatment agenda.

Is a family member on medication for ADHD?

If yes, then consider trying the same medication first if the family member's clinical response is positive. Patients may be more inclined to try a medication that worked well in someone they know, whether it is a family member or not. The inverse is also true; patients may be more reluctant to try a medication if they know someone who experienced strong side effects with a specific product. Note: Currently, there is not sufficient evidence to recommend a routine pharmacogenetics-based approach. However, the field is involving and this approach may be helpful in situations where it is difficult to find the optimal medication for a particular patient. However, in clinical practice, family response to certain types of medication may guide in medication selection.

Does the patient have third party coverage or do they plan to pay for the medication?

Many of the current medications are expensive so there should be an open discussion related to government plans, third party insurance coverage, direct payment, co-payment plans and limited benefit plans. An online guide to provincial reimbursement for prescription medications in Canada can be found here: http://bit.ly/PublicDrugBenefit.

Does the patient have trouble swallowing a pill?

If yes, that could indicate the need for medications that can be dissolved or sprinkled, e.g. Adderall, Biphentin, Vyvanse. One should make an attempt to teach the individual to swallow a capsule if age appropriate and not limited by medical conditions. www.pillswallowing.com

Does the patient have comorbid disorders that require more complex interventions?

If yes, a decision will need to be made as to which disorder to treat first. If it is ADHD, then initiate the ADHD medication and see what residual symptoms are left over that require further management. Anticipation of drug-drug interaction issues should be made when choosing the medication. Complex and comorbid presentations require specialist consultation.

STEP 3 -Titration & Monitoring

Establish a schedule for visits and contact with the patient and family

It is useful to take a structured approach to measuring treatment response beyond patient and family report. For example, target treatment could be to improve the person's capacity to be able to stay on-task for X amount of time. In evaluating this, particularly in younger patients, collateral information from the teacher and others may help measure efficacy. An adolescent may target their ability to sustain attention during their less interesting and less structured tasks. An adult may use a specific target that needs to change (e.g., their level of procrastination at work).

Formal observational rating scales are available to quantify specific medication changes, particularly at school and home. The CADDRA toolkit includes questionnaires and forms (Clinician ADHD Baseline/Follow-up Form and the CADDRA Patient ADHD Medication Form) that can be used to evaluate change.

During the titration phase, regular contact with the patient reporting in either by phone, email, fax or visit is recommended. Ideally, the patient would be seen for a review of medication doses during the titration period and to check physical health, vital signs, side effects, family functioning, patient and family well-being, and coping strategy management.

Please note: The recommended starting doses and schedule for dose increases noted in the medication charts that follow are meant as a guide that should be followed in most cases. Specific exceptions may be made under clinician discretion. In addition, the CADDRA Guide to ADHD Pharmacological Treatments in Canada Chart can be found in the Resources Section on the CADDRA website (www.caddra.ca).

A general rule is to start low and go slow but continue to increase the dose until the desired goals of treatment have been reached or side effects preclude dose increases or when maximum recommended dosage is reached. **Optimal treatment** means that the symptoms have decreased and that there is improvement in general functioning. **Optimal dose** is that dose above which there is no further improvement. Sometimes side effects limit the dose titration. The threshold maximum dosage of medication in this document is consistent with the off-label standards established by the American Academy of Child and Adolescent Psychiatry [439], published clinical trials [440] and consensus-based within the CADDRA Guidelines committee. Exceeding CADDRA's recommended maximum dosage is a third-line treatment option and should be done cautiously after regular dosages of different options have been tried.

It is useful to alert the patient in advance that there may be variations in their experience of effect of ADHD medications. In general, a stimulant medication's effects are likely to be stable at a given dose after one to three weeks [93], and for atomoxetine after four to six weeks [441] and full response may not even take effect until after three months on a particular dose. Individual variation occurs, however, and should be addressed individually to achieve dose optimization. Under dosing can occur when full optimization is not adopted as a treatment goal. Some patients report loss of effect from stimulant treatments over time. In some cases, taking breaks from stimulant treatment intermittently has reportedly allowed for the maintenance of effects at lower doses. Research on this is underway [442].

STEP 4 - Ongoing Follow-up

Long-term follow-up of individuals with ADHD should follow a chronic disease model which involves [443]:

- Pro-active, integrated care that is easily navigated by the patient: it is crucial to treat ADHD proactively before long-term negative consequences occur (e.g.: school drop-out, delinquency, job loss, divorce, substances use issues, comorbidities).
- Active involvement of patients in own care and advocacy: patients should be a partner in ADHD management. Furthermore, patients may serve as role models for other patients; services such as support groups may be useful.

- Multimodal treatment approaches supported by evidence-based guidelines: medication is an important aspect of ADHD management and should be accompanied by psychosocial approaches. This integrated approach may attenuate the high attrition rate of medication compliance. Furthermore, regular encounters with mental health providers may also allow for a stronger therapeutic alliance. The frequency of visits may vary from one patient to another. Many factors may play a role: e.g. patient engagement, symptoms stability and environmental support. During the stabilization period, regular (e.g. every two to four weeks) may be required while once stabilized, less frequent visits (e.g. every three to six months) may be sufficient.
- Provider education and resources: health care providers, teachers and other stakeholders require ongoing education on the management of ADHD. Resources like CADDAC, CADDRA and other organizations are essential to meet educational needs.
- Access to specialist expertise: in complex cases, health care providers may have to refer to specialized care and access in a timely manner is an important aspect of long-term ADHD management.

MANAGING SIDE EFFECTS

Medications used to manage ADHD, like other psychopharmacologic agents, may produce a wide range of adverse effects. Usually, those side effects are mild and temporary if dosage is appropriate and medications are taken as prescribed. Most side effects appear when the medication is started or when dosages are modified. Often, they disappear over time (side effect tolerance), particularly when taken regularly.

ADHD medications are generally well tolerated overall, but one cannot predict the sensitivity of an individual person. Patients and their families should be advised that unwanted physical side effects, emotional or behaviour changes might occur while on or just after stopping psychotropic medication.

Analyzing timing of the side effects profile may help manage them. Clinicians should monitor for adverse changes in growth, sleep, nutrition, pre-existing conditions, blood pressure, heart rate, mood or anxiety distress, thought pattern, and behaviour.

The aim is to find a positive balance between clinical benefit versus adverse effects. Positive clinical outcome should not be shadowed by the inconvenience of the side effects. See chapter 2 on comorbidity for special considerations in supporting individuals with histories of comorbid mental health conditions.

Common Adverse Events

Table 5.9 ADHD Medications - Common Adverse Events

Body System	Adverse Reaction	Psychostimulants	Non-Psychostimulants	
			Atomoxetine	Alpha-2 Agonist (i.e. Guanfacine XR)
Cardiovascular system	BP and HR decrease	-	-	✓
	BP and HR increase	✓	✓	When stopped abruptly
Gastrointestinal System and Nutritional Disorders	Appetite suppression	✓	✓	Low incidence
	Constipation / Diarrhea	✓	✓	✓
	Dry mouth	✓	✓	✓
	GI upset	✓	✓	Abdominal upper pain reported
	Nausea / vomiting	✓	✓	✓
Nervous System and Psychiatric Disorders	Anxiety	✓	✓[1]	Low incidence
	Dizziness	✓	-	-
	Dysphoria / irritability	✓	✓	Uncommon

	Headache	✓	✓[1]	✓
	Initial insomnia	✓	✓[2]	Low incidence
	Somnolence	-	✓	✓
	Rebound effect	✓	-	-
	Tics	✓	Uncommon	
Other	Decrease in weight	✓	✓	-
	Sexual dysfunction	Uncommon	✓	-
	Skin reactions	✓	✓	Low incidence

BP = blood pressure; HR = heart rate; GI = gastrointestinal; LA = Long-acting preparations
[1] Clinically reported by Canadian ADHD Practice Guidelines Committee
[2] Clinically observed initial insomnia in adults reported by Canadian ADHD Practice Guidelines Committee
Note: This table summarizes key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

When to Reduce the Dose, or Stop a Medication

Medication can be reduced or interrupted for different reasons. Patients could forget to renew their prescription. Patients may be reluctant to take the medication because of side effects while others could wonder if the medication is still appropriate. Some patients observe a reduction of ADHD symptoms over time and may even report that they feel that the medication dose is now "too high". It is good clinical practice to re-evaluate if medication is still needed. Adjusting dosages up or down should occur under the supervision of the health care provider.

Safety may be improved by educating a patient how to reduce the dose or stop if they are uncomfortable. Adverse mood or personality changes induced by medication may not be as likely to resolve as physical discomforts such as sleep and appetite problems. It may be helpful to educate patients that if they are uncomfortable or if they do not feel "like themselves" they should contact their health care provider and reduce the dose or stop the medication.

If side effects require a period off medication ("drug holiday") or a reduced dose, it could be done during vacation periods, i.e. summer vacations or on long weekends, which minimize impact on critical role performance. Attention should be given to whether tapering off or on the agent is needed for an individual to have less withdrawal effects such as fatigue, or initiation effects such as sympathetic nervous symptom side effects. Clinically, it is observed that interrupting psychostimulants every weekend may in fact increase side effects.

Non-stimulant medications (e.g. atomoxetine, guanfacine XR, buproprion) need to be taken continuously for clinical effect. When discontinuing Alpha-2 agonist medications in particular, they should be tapered due to the significant danger of withdrawal effects (e.g. a hypertensive crisis for guanfacine XR and clonidine).

How to Stop Medication

Some individuals may experience withdrawal from psychostimulants agents when they are stopped, particularly if dosages are high. If individuals are at robust doses, tapering these agents may avoid withdrawal. Atomoxetine is less likely to produce this withdrawal.

Alpha-2 agonists (e.g. guanfacine XR (GXR), clonidine) should not be interrupted abruptly and should always be tapered down progressively (e.g., tapered in decrements of no more than 1mg every three to seven days) due to the risk of rapid increase in blood pressure if stopped abruptly. Clinicians should prescribe the different dosages for the diminution of GXR and advise their patients that GXR pills should not be cut in half to reduce dosing since this would disturb the delivery system and increase immediate release, thus increasing side effects and reducing the duration of clinical effect.

Choosing to Change to a Different Medication:

When a patient benefits from a medication indicated for ADHD but has adverse effects, the kind and severity of adverse effect and its timing (e.g., if it occurs at peak concentration or when the dose is reduced at the end of the effect) is useful to consider before changing to alternate treatment. As a general guide, when adverse effects are more than mild or pose risk, changing to a different class of medication or managing an underlying vulnerability is advisable. However, where mild adverse effects occur or if the side effects seem related to the delivery system, a product with a different pattern of release of the same active ingredient may resolve the discomfort. Changes in release pattern may improve side effects that occur at a specific time of day – which conceptually could be due to peaks or valleys in the serum level. With stimulants, changing from one long acting form to another, or having the patient spread out initial dosing during the day into portions can achieve this. With atomoxetine, daily versus twice daily doses may be differently tolerated.

Side Effects Management Techniques

Somatic effects:

Many medications used to treat ADHD work through the catecholaminergic system. This is thought to explain many of the peripheral nervous system effects of stimulants, atomoxetine and guanfacine XR. Clinicians should expect and monitor potential variations in heart rate and blood pressure (increasing for psychostimulants and atomoxetine while decreasing for guanfacine XR), dry mouth, headache, decreased appetite, initial insomnia vs. daily sedation, gastrointestinal upset, and other perturbations of peripheral nervous system function. Key points to understand about these effects include:

- Physical side effects sometimes improve or resolve over a several-day period at steady daily dosing.
- Minimizing caffeine and other sympathomimetic agents sometimes eliminates or reduces side effects.
- Adverse effects of medications are reversible.
- Vulnerability and severity may be higher in pre-existing conditions impacted by peripheral CNS function like peripheral vascular disease, tic disorders, narrow angle glaucoma, or urinary dysfunction.

Stabilization of many comorbid conditions will facilitate ADHD medication administration, and collaboration with other clinicians may be important to stabilize and monitor conditions that sympathetic agents may exacerbate such as hypertension or narrow angle glaucoma. Tics may be exacerbated by psychostimulants, but in some cases tics improve with treatment of ADHD. In all cases of possible symptom exacerbation, risk assessment should be personalized.

Appetite and growth effects:

Medication-related growth delay may prompt treatment reduction or interruption during some periods like weekends or holidays or a switch to a non-stimulant treatment in children, as some studies associate stimulant treatment with effects on weight and height [90, 444].

In cases of appetite reduction:

- Nutrition should be maximized during periods when appetite-suppression is not in effect (e.g. breakfast and after medication has worn off in the evening).
- Reduce portions but increase snack times, including mandatory snack time in the evening.
- Consider nutritional supplements or meal replacements.
- Consider dose reduction, change to alternate agent, or drug holidays for low body mass index or familial short stature.

Matching coverage to daily patterns

In some cases, reports of adverse experiences may reflect suboptimal onset or duration of medication coverage, prompting changes in dosing patterns or agent. For example, stimulants may induce insomnia, prompting administration of medication as early as possible in the morning or use of a shorter acting agent. "Rebound" of symptoms is reported, where

symptoms return or appear worse than when untreated. This should prompt a change in coverage or change in medication level during the period of concern. For example, in the case of a long-acting agent taken in the morning, this might be divided into two doses taken 20 to 30 minutes apart to ensure they wear off over a longer time period, or a lower dose of a short acting stimulant can be overlapped with the tail end of the long-acting stimulant.

Managing Changing Medication Effects Over time

Some patients will report onset of new adverse effects, or loss of benefit from medication over time. If the treatment is well established over months prior to such a change in response to medicine, a broad differential diagnosis of new conditions should be considered.

Points to consider:

- Some individuals report less effect from medications when switched from a brand name product to a generic formulation.
- Some clinical reports state that some individuals find that taking breaks from the stimulant medication may have a "rejuvenating" effect. This phenomenon is not well studied, but it is advisable to have patients take such breaks rather than to increase dose in a previously effective treatment.
- A pattern of escalating doses over time may reflect "tolerance" or may suggest that the specific treatment targets may not reflect what ADHD medication can do to help. It has been noted that some patients confuse the energetic, mood or pleasure side effects of a stimulant from the attention and behaviour control clinical effects. While the energetic side effect tends to be reduced over time, the improvement of sustained attention is usually still there. Escalating doses and other atypical responses to medication should prompt consideration that the treatment goals or treatment itself may be inappropriate for the individual.

UNSATISFACTORY RESPONSE TO TREATMENT

CADDRA recommends reviewing the DATER diagram prior to considering whether second and third line therapies be considered.

Table 5.10 Facts to Consider Prior to Making Medication Changes

D	**Dosage** – Has the medication been tried on a high enough dose, is the duration of effect adequate? Side effects: Is the dosage too low or too high?
A	**All** – Have all medications within the higher line(s) of treatment (when clinically indicated and reasonable) been attempted? If not, explore why.
T	**Time –** Has enough time been given to examine patient response and for side effects to resolve?
E	**Examine –** Has the patient-doctor team determined specific targets for treatment and means to measure changes? Select standardized measures to examine response and plan examination of response from many perspectives (e.g., teacher, parent, spouse and self-report).
R	**Review** – Has the diagnostic process reviewed potential comorbidity, psychosocial complications and lifestyle issues?

Generally, if the patient does not respond optimally to monotherapy with at least one medication from each of the two psychostimulant classes (methylphenidate and amphetamine), augmentation strategies may be employed.

   a. Use of second line medications such as guanfacine XR may be an option, as this has been systematically studied in 6-17 years old patients with ADHD [445].
   b. Third line options like off-label use of buproprion, clonidine, modafinil or imipramine may also be helpful, but in this case a specialist referral should be made. This is essential for ensuring optimal risk management, deciding that first and second line treatments have been optimally managed, and avoiding any contraindications.

When a switch in medication is required, if the situation allows, consider switching medication during long vacations or during the summer to avoid periods of non-response or possible side effects that may impair academic or work performance in the short-term.

If there is partial or no response to treatment, it is important to review both the diagnosis (including comorbidities) and treatment plan to ensure compliance to treatment as well as to check if there are external factors that could complicate the clinical picture. Patients' responses to medication cannot be predicted based solely on the clinical symptoms displayed. Some patients may respond preferentially to one versus the other class of medications. If response or side effects to one class of medication are not optimal, another class of ADHD medication should be tried. In particular, if a patient does not have an adequate response to one class of stimulant, a switch to the other class of stimulant should be considered (e.g. methylphenidate to amphetamines or vice-versa).

There are several reasons why one ADHD medication may be substituted for another:

   a. Peak and trough effects: change delivery mechanism, for example the immediate-release mechanism for a more sustained one.

   b. End-of-dose rebound effects: change the immediate-release mechanism for a more sustained one or take an additional, short acting dose of the same psychostimulant just before the rebound routinely occurs.

   c. Adverse effects don't allow dosage to be optimized: change the release mechanism, change the molecule, or add an adjunctive medication*.

   d. Drug-to-drug interaction following usual titration strategies. If side effects occur, decide between reducing the psychostimulant versus the non-stimulant dosage. *

 *Note: Guanfacine XR is the only medication with a specific indication as an adjunctive therapy to psychostimulants for the treatment of ADHD in children and adolescents aged 6-17 years with a sub-optimal response to psychostimulants. Long-term combination of a psychostimulant with guanfacine XR in adults – or with atomoxetine – are off-label [138].

> **Practice Point**
>
> **Best Time to Switch Medication in School-Age Children?**
>
> The summer or winter vacation may be the best time to switch medications for children. Be wary of switching meds at the beginning of a new school year with a new teacher. It is better to let the child continue on the current medication until after the first report card period, and then switch. In this way, the teacher can also provide feedback on the effect of the change.

INFORMATION ON SPECIFIC MEDICATIONS

ADHD medications are not all the same. Their content (active ingredients) and formulation can affect response for a specific person. Medical treatment for ADHD needs to be individualized.

ADHD Medication Chart

The CADDRA ADHD Medication Chart provides information on the dosage and appearance of ADHD medications and is a useful tool when discussing medication options with individuals and their families. It is available in both Canada-wide and Quebec versions on the CADDRA website. It was originally developed by the Continuing Medical Education Team at Laval University in Quebec City in collaboration with the organizational committee for the Conference on the Pharmacological Treatment of ADHD in April 2007. This team, led by Dr. Annick Vincent, continues to collaborate with CADDRA to update these charts when new medications are launched or changes in medication occur.

Practice Point

- Medication effects are based on average population studies.

- Efficacy and tolerability can vary for individuals.

- Treatment should always be individualized and reviewed over time, to better target patients' needs.

Canadian Medication Tables per Age Group

Table 5.11 –Medical Treatment for ADHD – Children (6-12 Years)

To check for generic availability, refer to Health Canada. 2015. Drug Product Database. [ONLINE] Available at: *http://webprod5.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp.* [Accessed 20 January 2016].

Brand Name	Active Ingredient	Dosage Form	Starting Dose[1]	Titration Schedule Every 7 Days		Total Maximum Daily Dose[2]	
				Product Monograph	CADDRA[3]	Product Monograph	CADDRA[3]
FIRST LINE AGENTS - Long-acting psychostimulants							
Adderall XR®[4]	amphetamine mixed salts	5, 10, 15, 20, 25, 30 mg cap	5-10 mg q.d. a.m.	→ 5-10 mg	→ 5 mg	30 mg	30 mg
Biphentin®	methylphenidate	10, 15, 20, 30, 40, 50, 60, 80 mg cap	10-20 mg q.d. a.m.	→ 10 mg	→ 5-10 mg	60 mg	60 mg
Concerta®[4]	methylphenidate	18, 27, 36, 54 mg tab	18 mg q.d. a.m.	→ 18 mg	→ 9-18 mg	54 mg	72 mg
Vyvanse®	lisdexamfetamine	10, 20, 30, 40, 50, 60, 70 mg cap	20-30 mg q.d. a.m.	By clinical discretion	→ 10 mg	60 mg	60 mg
SECOND LINE / ADJUNCTIVE AGENTS - Short-acting and intermediate-acting psychostimulants *Indications for use: a) p.r.n. for certain activities; b) to augment[6] long-acting formulations early or late in the day, or early in the evening and c) when long-acting agents are cost prohibitive*							
Dexedrine®[4]	dextro-amphetamine	5 mg tab	2.5-5 mg b.i.d.[7]	→ 2.5-5 mg	→ 2.5-5 mg	40 mg	20 mg
Dexedrine® Spansule®[8]	dextro-amphetamine	10, 15 mg cap	10 mg q.d. a.m.	→ 5 mg	→ 2.5-5 mg	40 mg	30 mg
Ritalin®[4]	methylphenidate	10, 20 mg tab (5 mg generic only)	5 mg b.i.d. to t.i.d.[6]	→ 5-10 mg	→ 5 mg	60 mg	60 mg
Ritalin® SR[9],[4]	methylphenidate	20 mg tab	20 mg q.d. a.m.	→ 20 mg		60 mg	60 mg
SECOND LINE / ADJUNCTIVE AGENTS - Long acting non-psychostimulants Selective Alpha₂A-adrenergic receptor agonist *Indications for use: Monotherapy and as an adjunctive therapy to psychostimulants*							
Intuniv XR®	guanfacine	1, 2, 3, 4 mg tab	1 mg	Increments of 1 mg every 7 to 14 days		4 mg	4 mg
SECOND LINE / ADJUNCTIVE AGENTS - Long-acting non-psychostimulants **Selective norepinephrine reuptake inhibitor** *Indications for use: Monotherapy (off-label; prescribed as an adjunctive therapy)*							
Strattera®[4]	atomoxetine	10, 18, 25, 40, 60, 80, 100 mg cap	0.5 mg/kg/day	Adjust dosage every 7-14 days; to 0.8 mg/kg/day, then 1.2 mg/kg/day		Lesser of 1.4 mg/kg/day or 60 mg/day	

p.r.n. = as needed

1 CADDRA generally recommends starting at the lowest dose available. Young children should be titrated slowly, e.g. Concerta: 18, 27, 36 and Biphentin 10, 15, 20 mg

2 Refer to the adolescent table for children > 40 Kg

3 A consensus decision has been made based on clinical use and research data. Doses per CADDRA that are over or under product monograph maximum or minimum doses should be considered off-label use

4 Generic available. The Canadian ADHD Practice Guidelines' committee reported loss of symptom control in some patients when switched from original to generic drugs. Therefore, long-acting psychostimulant generics are considered second line agents

5 Vyvanse® 70mg is an off-label dosage for ADHD treatment in Canada

6 To augment Adderall XR® or Vyvanse®, short-acting and intermediate-acting dextro-amphetamine products can be used. To augment Biphentin® or Concerta® short-acting methylphenidate products can be used

7 b.i.d. refers to qam and qnoon and t.i.d. refers to qa.m., qnoon and q4p.m.

8 Dexedrine® Spansule may last 6-8 hours

9 Ritalin® SR may help cover the noon period but clinical experience suggests an effect similar to short-acting preparations. An increased dose could be spread out to include q2pm dose with a daily maximum of 60 mg

Note: These tables summarize key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

Table 5.12 – Medical Treatment for ADHD – Adolescents (13-17 Years)

Brand Name	Active Ingredient	Dosage Form	Starting Dose[1]	Titration Schedule Every 7 Days		Total Maximum Daily Dose[2]	
				Product Monograph	CADDRA[3]	Product Monograph	CADDRA[3]
FIRST LINE AGENTS - Long-acting psychostimulants							
Adderall XR®4	amphetamine mixed salts	5, 10, 15, 20, 25, 30 mg cap	5-10 mg q.d. a.m.	→ 5-10 mg	→ 5 mg	20-30 mg	50 mg
Biphentin®	methylphenidate	10, 15, 20, 30, 40, 50, 60, 80 mg cap	10-20 mg q.d. a.m.	→ 10 mg	→ 5-10 mg	60 mg	80 mg
Concerta®4	methylphenidate	18, 27, 36, 54 mg tab	18 mg q.d. a.m.	→ 18 mg	→ 9-18 mg	54 mg	90 mg
Vyvanse®	lisdexamfetamine	10, 20, 30, 40, 50, 60, 70[5] mg cap	20-30 mg q.d. a.m.	By clinical discretion	→ 10 mg	60 mg	70 mg
SECOND LINE / ADJUNCTIVE AGENTS - Short-acting and intermediate-acting psychostimulants							
Indications for use: a) p.r.n. for certain activities; b) to augment[6] long-acting formulations early or late in the day, or early in the evening and c) when long-acting agents are cost prohibitive							
Dexedrine®4	dextro-amphetamine	5 mg tab	2.5-5 mg b.i.d.[7]	→ 5 mg	→ 2.5-5 mg	40 mg	30 mg
Dexedrine® Spansule®8	dextro-amphetamine	10, 15 mg cap	10 mg q.d. a.m.	→ 5 mg	→ 2.5-5 mg	40 mg	30 mg
Ritalin®4	methylphenidate	10, 20 mg tab (5 mg generic only)	5 mg b.i.d. to t.i.d.[7]	→ 5-10 mg	→ 5 mg	60 mg	60 mg
Ritalin® SR[9,4]	methylphenidate	20 mg tab	20 mg q.d. a.m.	→ 20 mg (add q2pm dose)		60 mg	80 mg
SECOND LINE / ADJUNCTIVE AGENTS - Long-acting non-psychostimulants Selective Alpha2A-adrenergic receptor agonist							
Indications for use: Monotherapy and as an adjunctive therapy to psychostimulants							
Intuniv XR®	guanfacine	1, 2, 3, 4 mg tab	1 mg	Increments of 1 mg every 7 to 14 days		7 mg for monotherapy and 4 mg for adjunctive therapy	
SECOND LINE / ADJUNCTIVE AGENTS - Long-acting non-psychostimulants - Selective norepinephrine reuptake inhibitor							
Indications for use: Monotherapy (off-label; prescribed as an adjunctive therapy)							
Strattera®4	atomoxetine	10, 18, 25, 40, 60, 80, 100 mg cap	0.5 mg/kg/day	Adjust dosage every 7-14 days; to 0.8 mg/kg/day, then 1.2 mg/kg/day[10]		Lesser of 1.4 mg/kg/day or 100 mg/day	

p.r.n. = as needed

[1] For adolescents > 40 kg
[2] CADDRA generally recommends starting at the lowest dose available
[3] A consensus decision has been made based on clinical use and research data. Doses per CADDRA that are over or under product monograph maximum or minimum doses should be considered off-label use
[4] Generic available. The Canadian ADHD Practice Guidelines' committee reported loss of symptom control in some patients when switched from original to generic drugs. Therefore, long-acting psychostimulant generics are considered second line agents
[5] Vyvanse® 70mg is an off label dosage for ADHD treatment in Canada
[6] To augment Adderall XR® or Vyvanse®, short-acting and intermediate-acting dextro-amphetamine products can be used. To augment Biphentin® or Concerta® short-acting methylphenidate products can be used
[7] b.i.d. refers to qam and qnoon and t.i.d. refers to qa.m., qnoon and q4p.m.
[8] Dexedrine® Spansule may last 6-8 hours
[9] Ritalin® SR may help cover the noon period but clinical experience suggests an effect similar to short-acting preparations
[10] This titration schedule applies to adolescents <70 kg. For adolescents >70 kg, use the adult titration schedule

Note: These tables summarize key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information

Table 5.13 – Medical Treatment for ADHD – Adults (18+)

Brand Name	Active Ingredient	Dosage Form	Starting Dose[1]	Titration Schedule Every 7 Days		Total Maximum Daily Dose	
				Product Monograph	CADDRA[2]	Product Monograph	CADDRA[2]
FIRST LINE AGENTS – Long-acting psychostimulants							
Adderall XR®[3]	amphetamine mixed salts cap	5, 10, 15, 20, 25, 30 mg	10 mg q.d. a.m.	→ 10 mg	→ 5 mg	20-30 mg	50 mg
Biphentin®	methylphenidate	10, 15, 20, 30, 40, 50, 60, 80 mg cap	10-20 mg q.d. a.m.	→ 10 mg	→ 5-10 mg	80 mg	80 mg
Concerta®[3]	methylphenidate	18, 27, 36, 54 mg tab	18 mg q.d. a.m.	→ 18 mg	→ 9-18 mg	72 mg	108 mg
Vyvanse®	lisdexamfetamine	10, 20, 30, 40, 50, 60, 70 mg cap	20-30 mg q.d. a.m.	By clinical discretion	→ 10 mg	60 mg	70 mg
SECOND LINE / ADJUNCTIVE AGENTS - Short-acting and intermediate-acting psychostimulants							
Indications for use: a) p.r.n. for certain activities; b) to augment[5] long-acting formulations early or late in the day, or early in the evening and c) when long-acting agents are cost prohibitive							
Dexedrine®[3]	dextro-amphetamine	5 mg tab	2.5-5 mg b.i.d.[6]	→ 5 mg	→ 2.5-5 mg	40 mg	50 mg
Dexedrine® Spansule®[7]	dextro-amphetamine	10, 15 mg cap	10 mg q.d. a.m.	→ 5 mg	→ 2.5-5 mg	40 mg	50 mg
Ritalin®[3]	methylphenidate	10, 20 mg tab (5 mg generic only)	5 mg b.i.d. to t.i.d.[6] consider q.i.d	→ 5-10 mg	→ 5 mg	60 mg	100 mg
Ritalin® SR[8,3]	methylphenidate	20 mg tab	20 mg q.d. a.m.	→ 20 mg (add q2pm dose)		60 mg	100 mg
SECOND LINE / ADJUNCTIVE AGENT - Long-acting non-psychostimulant - Selective norepinephrine reuptake inhibitor							
Indications for use: Monotherapy (off-label; prescribed as an adjunctive therapy)							
Strattera®	atomoxetine	10, 18, 25, 40, 60, 80, 100 mg cap	40 mg q.d.[4]	Adjust dosage every 7-14 days; to 60 then 80 mg/ day[9]		Lesser of 1.4 mg/kg/day or 100 mg/day	

1 CADDRA generally recommends starting at the lowest dose available

2 A consensus decision has been made based on clinical use and research data. Doses per CADDRA that are over or under product monograph maximum or minimum doses should be considered off-label use

3 Generic available. The Canadian ADHD Practice Guidelines' committee reported loss of symptom control in some patients when switched from original to generic drugs. Therefore long-acting psychostimulant generics are considered second line agents

4 Vyvanse® 70mg is an off label dosage for ADHD treatment in Canada

5 To augment Adderall XR® or Vyvanse®, short-acting and intermediate-acting dextro-amphetamine products can be used. To augment Biphentin® or Concerta® short-acting methylphenidate products can be used

6 b.i.d. refers to qam and qnoon and t.i.d. refers to qam, qnoon and q4p.m.

7 Dexedrine® Spansule may last 6-8 hours

8 Ritalin® SR may help cover the noon period but clinical experience suggests an effect similar to short-acting preparations

9 Some adults may better tolerate a lower starting dose of 25 mg

10 This Strattera® titration schedule applies to children and adolescents > 70 kg of body weight, and adults

p.r.n. = as needed

Note: These tables summarize key information and cannot be considered exhaustive. Physicians should refer to Product Monographs for complete prescribing information.

Psychostimulants

Based on their active ingredients, the psychostimulants are divided in two classes: amphetamines-based and methylphenidate-based products. Both classes are available in short, intermediary and long-acting preparations.

Long-acting psychostimulants are first line treatments for ADHD. A patient's response to one class of stimulant does not predict their response to the other class [411, 412]. Thus, failure to respond to one class of stimulant should typically lead to a trial of the other class before moving to second-line treatments.

The CADDRA Guidelines Committee recommends that short or intermediate acting psychostimulants be used as second line treatments because:

- Multi-dosing may reduce adherence to treatment [446].
- Their duration of effect is shorter than that of long-acting versions and they are therefore prone to having peak/valley effects that may reduce symptom coverage and be associated with more side effects [447].
- Their potential of abuse is higher since short acting tablets are crushable, therefore increasing the potential risk for abuse by snorting or intravenous use [448].

Short or intermediate acting psychostimulants may be useful in specific situations where there is need for a medication with shorter duration of action:

- When a top-up of the once-daily medication is required.
- When coverage is required only for a few hours in the day.
- When more flexibility in the dosing schedule is necessary.

Due to their specific delivery systems, the abuse potential of pro-drug, osmotic pump and beads delivery systems are significantly reduced in comparison to short-acting medications due to the product formulation [449, 450].

Amphetamine (AMP)-based products

Amphetamines (AMP) are thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extra neuronal space [451], thereby increasing these neurotransmitters' availability in the synaptic cleft. AMP has a well-established safety and efficacy profile for the treatment of ADHD [452, 453]. In Canada, AMP based products are subject to controlled substances regulation and are available in various delivery systems allowing short, intermediary and long-acting duration of effect.

NOTE: Mixed amphetamine salts: A focused review of sudden unexplained deaths was carried out by Health Canada in 2006 and the medication's safety has been assured [454].

Table 5.14 Amphetamine-based Products

MIXED AMPHETAMINE SALTS	
BRAND NAME	Adderall XR®
GENERIC AVAILABLE IN CANADA	Yes
HEALTH CANADA INDICATION	All patients with ADHD six years and older
ACTIVE INGREDIENT	Mixed amphetamine salts (4), predominantly dextro-amphetamine (DEX)
DELIVERY SYSTEM	Extended release capsule with granules delivery system Half of the granules have a special layer that can be digested rapidly in the acidic environment of the stomach and the other half have a different coating that needs a higher PH to be digested, allowing a later release in the gut.
IMMEDIATE-DELAYED RATIO	50/50
DURATION OF EFFECT	12 hours
DOSAGES	Available in six doses: 5, 10, 15, 20, 25 and 30 mg
CHARACTERISTICS	Capsules may be taken whole in the morning or may be opened and the entire contents sprinkled on applesauce, with no loss in efficacy (particularly important to improve adherence in patients who can't swallow pills) Beads should not be crushed or chewed Bioavailability can be affected by PH changes in the GI tract (e.g.: antacid medications)

LISDEXAMFETAMINE DIMESYLATE (LDX)	
BRAND NAME	Vyvanse®
GENERIC AVAILABLE IN CANADA	none
HEALTH CANADA INDICATION	All patients with ADHD six years and older
ACTIVE INGREDIENT	Dextro-amphetamine (DEX)
DELIVERY SYSTEM	Pro-drug The capsule content is an inactive complex, lisdexamfetamine (LDX), that needs a biological enzymatic transformation to release DEX (active drug). This activation takes place in the gut and blood system.
IMMEDIATE-DELAYED RATIO	Gradual delivery system (prodrug)
DURATION OF EFFECT	13 hours in children -14 hours in adults [455]
DOSAGES	Available in Canada in seven doses: 10, 20, 30, 40, 50, 60 and 70 mg*
PARTICULARITIES	Capsules may be taken whole in the morning or may be opened and the entire contents diluted in water, orange juice or yogurt, with no loss in efficacy (particularly important to improve adherence in patients who can't swallow pills) Bioavailability is not influenced by transit time or by PH changes in the GI tract due to the ProDrug Delivery System (e.g. antacid medications)
NOTE FROM THE CADDRA GUIDELINES COMMITTEE	NOTE: In United States, the FDA has approved dosages of LDX from 20 mg to 70 mg for the treatment of ADHD. Although the 70mg capsule is officially approved by Health Canada for Binge Eating Disorder only, CADDRA recommendS the off-label use of this dosage in adolescents and adults with ADHD when needed. Since the bioavailability of the active ingredient is not influenced by route of administration (oral, intranasal or intravenous), the abuse potential of this pro-drug delivery system is significantly reduced in comparison to short-acting medication due to the product formulation.

DEXTROAMPHETAMINE (DEX)-BASED PRODUCTS SHORT-ACTING AND INTERMEDIARY-ACTING MEDICATIONS	
BRAND NAME	Dexedrine® (tablets) and Dexedrine® Spansules®
GENERIC AVAILABLE IN CANADA	Yes
HEALTH CANADA INDICATION	All patients with ADHD six years and older
ACTIVE INGREDIENT	Dextroamphetamine (DEX)
DELIVERY SYSTEM	Tablets: immediate and Spansules: intermediate
IMMEDIATE-DELAYED RATIO	Tablets: 100-0 Spansules®: 50-50
DURATION OF EFFECT	Tablets: 4 hours Spansules®: 6-8 hours
DOSAGES	Dexedrine® tablets are available in Canada in one dose: 5mg Dexedrine® Spansules® are available in Canada in two doses: 10 and 15mg
CHARACTERISTICS	Tablets can be divided in two to adjust dosage Tablets should not be crushed Capsule should be swallowed whole

Methylphenidate (MPH)-based products

Methylphenidate hydrochloride (MPH) is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron, with a preferential effect on dopamine, thereby increasing these neurotransmitters' levels in the synaptic cleft [456]. MPH has a well-established safety and efficacy profile for the treatment of ADHD [174, 410, 457]. In Canada, MPH based products are subject to controlled substances regulation and are available in various delivery systems allowing short, intermediary and long-acting duration of effect [458].

5.15 Methylphenidate Products

METHYLPHENIDATE HYDROCHLORYDE (MPH) CONTROLLED RELEASE CAPSULE	
BRAND NAME	Biphentin®
GENERIC AVAILABLE IN CANADA	None
HEALTH CANADA INDICATION	Indicated in patients with ADHD six years and older
ACTIVE INGREDIENT	Methylphenidate hydrochloride (MPH)
DELIVERY SYSTEM	Multilayer beads All granules have an outer layer that can be digested rapidly in the acid environment of the stomach, providing an immediate release of 40% of the MPH and the rest of the granule needs a higher PH to be digested, allowing a later release of the remaining MPH (60%) in the gut
IMMEDIATE-DELAYED RATIO	40 / 60
DURATION OF EFFECT	10-12 hours
DOSAGES	Available in eight doses: 10, 15, 20, 30, 40, 50, 60 and 80 mg
CHARACTERISTICS	Capsules may be taken whole in the morning or may be opened and the entire contents sprinkled on applesauce, ice cream or yogurt, with no loss in efficacy (particularly important to improve adherence in patients who can't swallow pills) Beads should not be crushed or chewed

METHYLPHENIDATE HYDROCHLORIDE (MPH) OROS® TABLETS	
BRAND NAME	Concerta®
GENERIC AVAILABLE IN CANADA	Yes
HEALTH CANADA INDICATION	Indicated in all ADHD patients 6 years and older
ACTIVE INGREDIENT	Methylphenidate hydrochloride (MPH)
DELIVERY SYSTEM of BRAND NAME **(Generic delivery system differs)**	Oros® technology The outer layer of the tablet delivers an immediate release of 22% of the dose. The remaining 78% of MPH dose is released gradually from the osmotically active trilayer tablet core, achieving a peak plasma concentration between 6-10 hours after morning dosing, before gradually decreasing to baseline over the remainder of the 24-hour period
IMMEDIATE-DELAYED RATIO	22 / 78
DURATION OF EFFECT	~12 hours
DOSAGES	Available in four doses: 18, 27, 36, 54mg
CHARACTERISTICS	Tablets must be swallowed whole Concerta® effectiveness is not affected by absence or presence of food, including high-fat breakfast. (Concerta Product Monograph p26) Bioavailability can be affected by transit time

METHYLPHENIDATE HYDROCHLORIDE (MPH) BASED PRODUCTS – SHORT-ACTING AND INTERMEDIARY-ACTING MEDICATIONS	
BRAND NAME	Ritalin® and Ritalin SR®
GENERIC AVAILABLE IN CANADA	Yes
HEALTH CANADA INDICATION	Indicated in all ADHD patients 6 years and older
ACTIVE INGREDIENT	Methylphenidate hydrochloride (MPH)
DELIVERY SYSTEM	Ritalin : immediate and Ritalin SR: intermediate
IMMEDIATE-DELAYED RATIO	Ritalin®: 100-0 Ritalin SR®: The compound has a wax matrix which at times results in inconsistent release of medication and thus inconsistent effects
DURATION OF EFFECT	Ritalin: 3-4 hours Ritalin SR: 5-6 hours
DOSAGES	Ritalin® is available in Canada in two doses: 10 and 20mg; its generic is also available in 5mg tablets Ritalin SR ® is available in Canada in one dose: 20mg
CHARACTERISTICS	Ritalin® tablets can be divided in two to adjust dosage Ritalin SR ® tablets should be swallowed whole Tablets should not be crushed

Brand names in Canada may differ from the same product's brand name elsewhere. Other formulations of MPH and the isomer dextro-methylphenidate are available in the U.S.A. but currently not available in Canada. These are examples:

- Ritalin® LA - a once-a-day extended-release MPH formulation
- Quillivant XR ® - a once-a-day extended-release MPH liquid formulation
- Methylin® - a once-a-day extended-release MPH chewable formulation
- Daytrana® - a MPH transdermal patch
- Focalin® - a short-acting dextro-methylphenidate formulation
- Focalin XR ® - a long-acting dextro-methylphenidate formulation
- Mydayis ® - a long-acting triple-bead, mixed amphetamine salts formulation

Non-Stimulants

The onset of action of non-stimulants is often slower than stimulants and the maximum treatment effect may not be reached for six to eight weeks for atomoxetine (ATX) and four weeks for guanfacine XR (GXR) [459, 460]. The clinical changes are gradual. It would not be suitable in cases where there is a clinical need to obtain a rapid onset of action or an "as needed" treatment plan. The CADDRA Guidelines Committee recommends starting low and titrating slowly, every 14 days, depending on clinical response. If higher doses or off-label use are contemplated, a referral to an ADHD specialist should be made. If the doses exceed one pill a day, the cost of the medication increases.

5.16 Non-Stimulant Products

ATOMOXETINE HYDROCHLORIDE (ATX)	
BRAND NAME	**STRATTERA®**
GENERIC AVAILABLE IN CANADA	Yes
HEATH CANADA INDICATION	Indicated in all patients with ADHD six years and older
ACTIVE INGREDIENT	Atomoxetine (ATX)
MECHANISM OF ACTION	Noradrenaline reuptake inhibitor
DURATION OF EFFECT	Up to 24 h May provide continuous coverage including the late evening and early morning periods

NOTE FROM THE CADDRA GUIDELINES COMMITTEE	The CADDRA Guidelines Committee recommends that atomoxetine be used as a second line treatment because clinical experience and clinical studies suggest a lower efficacy rate in ADHD with non-stimulants compared to psychostimulants [413]. ATX may be may be particularly useful in ADHD patients who: • Need 24h symptom coverage • Have tics or comorbid anxiety symptoms that are worsened with stimulants • Experience resistance and/or side effects to stimulant medications, including problems with worsening of sleep • Have concurrent SUD since there is no substance abuse or diversion potential • Have comorbid enuresis [461, 462] ATX does not have the indication for combined treatment with psychostimulants. Combining ATX with psychostimulants is an off-label use and should be reserved to complex resistant ADHD cases
DOSAGES	Strattera® is available in Canada in seven doses (10, 18, 25, 40, 60, 80 and 100 mg)
CHARACTERISTICS	ATX has no known abuse potential ATX can be given once-a-day in the morning or the evening or as a morning and evening split dose which is sometimes optimal to reduce side effects (but this strategy increases costs) ATX capsules should not be opened and should be swallowed whole since the content can cause significant nausea and stomach upset in some patients The contents are an ocular irritant. If the contents get in the eye, there should be immediate eye flushing and seek medical attention if needed ATX safety profile has been established, including risk factors related to cardiovascular conduction irregularity like those of stimulant drugs Rare cases of reversible alteration in hepatic enzyme are noted. No special monitoring protocol is required (i.e. blood tests) but patients should be advised of the clinical symptoms of hepatic dysfunction. Poor metabolizers (i.e., 7% Caucasians and 2% African-Americans) are unlikely to have toxic effects given the slow titration schedule In children, the dose of ATX is calibrated to the weight of the patient. There have been rare reports of increase in suicidal ideation; one suicide attempt (overdose) was identified; no completed suicides occurred [51, 466]. Clinicians need to carefully monitor suicidal ideation, especially in the early phases of treatment, not unlike with many antidepressant medications.

GUANFACINE HYDROCHLORIDE EXTENDED-RELEASE TABLETS (GXR)

BRAND NAME	Intuniv XR®
GENERIC AVAILABLE IN CANADA	None
HEATH CANADA INDICATION	Indicated in patients with ADHD 6-17 years only as monotherapy and as adjunctive therapy to psychostimulants
ACTIVE INGREDIENT	Guanfacine hydrochloride extended-release (GXR)
MECHANISM OF ACTION	Selective alpha2a-adrenergic receptor agonist
DURATION OF EFFECT	Up to 24 h May provide continuous coverage including the late evening and early morning periods
NOTE FROM THE CADDRA GUIDELINES COMMITTEE	Considering that GXR has a lower response rate than psychostimulants and requires close follow-up due to its side effects profile [463], the CADDRA Guidelines Committee recommends it as a second line treatment. But in specific circumstances where psychostimulants are not recommended, GXR could be a first choice. In such cases, referral to an ADHD specialist may be made. Adherence to treatment is essential for GXR because of the potential risk of rebound hypertension if abruptly stopped GXR may be particularly useful for patients with ADHD who: GXR has the indication for combined treatment with psychostimulants for children with ADHD aged 6 to 17 that do not achieve optimal response on stimulants alone. The CADDRA Guidelines Committee recommends trying AMP and MPH medications before trying a combination of GXR to psychostimulants Need 24h symptom coverage Have comorbid tic spectrum disorders [464] or significant comorbid anxiety, oppositional behaviours, aggression or where atypical neuroleptics or other alpha 2 agonists might have been used Would benefit from a monotherapy when they are not responsive or have intolerable side effects to stimulant medications, including problems with worsening of sleep or pulse/blood pressure elevation No literature is available for adult ADHD, therefore all prescriptions for patients over 17 years old are off-label use and should be supervised by an ADHD specialist

DOSAGES	Intuniv XR® is available in Canada in four doses (1, 2, 3 and 4mg)
CHARACTERISTICS	GXR is not classed amongst the psychostimulants and it is not a controlled substance
	There is no known abuse potential
	The side effects profile of guanfacine is unique. Somnolence, sedation may occur, particularly at the initiation and after dose adjustments.
	Unlike stimulant drugs and atomoxetine, it may reduce pulse and blood pressure. Close monitoring of those parameters should be done while titrating up or down the dose
	Adherence to treatment is essential since GXR should not be stopped abruptly since this may significantly increase pulse and blood pressure [467]. Intuniv XR® can be given once–a-day in the morning or the evening or as a morning and evening split dose which is sometimes optimal to reduce side effects (but this strategy increases costs)
	Intuniv XR ® tablets should be swallowed whole since cutting or crushing the pill will alter the slow release mechanism therefore increasing side effects
	The side effects profile of guanfacine is unique and necessitates close follow-up. Somnolence, sedation may occur, particularly at the initiation and after dose adjustments. Unlike stimulant drugs and atomoxetine, it may reduce pulse and blood pressure. Close monitoring of those parameters should be done while titrating up or down the dose
	GXR should not be stopped abruptly since this may significantly increase pulse and blood pressure
	Use caution when administered to patients taking medications like CYP3A4/5 inhibitors (e.g. ketoconazole), CYP3A4 inducers, valproic acid, heart rate-lowering and QT prolonging drugs
	GXR should not be administered with high fat meals
	It is recommended not to use grapefruit products with this medication
	Intuniv XR® does not require any blood tests before starting treatment. As well, no ECG is required (when using as monotherapy) if there is NOT a positive cardiac history (which should be asked before initiating any medication for ADHD)
	To help maintain adequate blood pressure, patients should be advised to avoid dehydration

FREQUENTLY ASKED QUESTIONS ON ADHD MEDICATIONS

1. **Can you tell if a patient has ADHD by their response to medication?**

No. Psychotropic medications may have effects on individuals whether they have a clinical syndrome for which the agent was studied or not. As example, psychostimulants can improve attention and vigilance in patients with ADHD but also in patients with sleep apnea, diurnal hypersomnolence and depression [465].

2. **Can a medication trial be used to diagnose ADHD?**

No. A positive response does not prove that ADHD is the cause of the inattention. A negative response does not rule out ADHD as patients may respond to one ADHD medication and not another.

3. **Can you predict which ADHD medication will help based on specific symptoms?**

No. While individual patients respond differently, all medications approved for use in ADHD by Health Canada can reduce both inattention as well as impulsive/hyperactive symptoms described in the DSM definition of ADHD.

4. **Can medication choice be predicted by testing or laboratory studies?**

There is insufficient evidence to support use of brain scans or EEG, or genetic or metabolic screening to predict which agent will be most effective or best tolerated for a specific individual with ADHD.

It is appealing to think that someone could base the choice of a specific ADHD medication on the results of genetic testing. At this time, use of pharmacogenetics is not generally recommended in clinical practice. However, pharmacogenetics is emerging as a potential future source of additional information regarding possible treatment direction in treatment-resistant cases.

5. **Do non-stimulants have a lower risk of side effects compared to stimulants?**

No. Non-stimulants may have risks different from those associated with stimulants. While non-stimulants are less likely to be misused or abused than stimulants [133], non-stimulant medications used to treat ADHD may also have other potential risks such as sympathomimetic physical effects for ATX or hypotension or reduced heart rate for GXR.

6. **Should patients be started on a short acting medication before taking a long acting medication?**

No. This practice is not recommended. There may be administrative reasons for why this approach must be taken (e.g., a provincial drug formulary). However, there is no scientific data to support this practice. Clinical and side effect response to short and long acting medications may vary in an individual so experience on short and long acting agents should not be assumed to be predictive of each other. Furthermore, initiating a medication that is less effective, less tolerable, and with peak and valley effects may preclude the patient from pursuing medical treatment. In addition, the mandatory step of starting a short acting psychostimulant first increases the cost on the medical system by increasing not only the number of appointments needed to adjust the medication, but could also increase the total number of visits to the emergency room as there is evidence to suggest that patients on short-acting ADHD psychostimulants consult more often at the emergency room for physical traumas than those on long-acting stimulants [466].

7. *Can you tell if a medication is working by how the patient "feels"?*

No. Ability to self-observe is variable with age and between individuals, and this variation should be considered in the monitoring of medication effects. Also, some patients may confuse the perceived stimulating energizing effect of a stimulant (that is a side effect and will attenuate over time) from the real clinical effect of being able to better self-control attention, movements and behaviours (targeted effect, that should be stable over time).

Long-acting medication use is often associated with less peaks and valleys effects and some patients who have tried short-acting stimulants first can confuse the lack of "feeling that the medication is onboard" with lack of efficacy.

8. *Can you tell how a medication is working by patient report alone?*

Yes and no. Clinicians should be aware that studies often demonstrate discord between collateral/observer and personal reports of ADHD symptoms in some individuals [467]. Sufficient personal and, whenever possible, collateral information help to monitor symptom pattern and function before and during treatment. Using specific age-appropriate questions that the patient understands and can report on is advisable.

9. *Are there other medications used in treating ADHD?*

Other medications like modafinil, bupropion and desipramine have shown some efficacy in ADHD [441] and are considered third-line treatments for this disorder. Since their use is off-label, clinicians usually consult with an ADHD specialist when these medications are considered.

CHAPTER 6: TREATMENTS REQUIRING FURTHER RESEARCH

Individuals suffering from ADHD and their parents often request information regarding alternatives to medications indicated for ADHD. Thus, the clinician needs to be aware of the data regarding the efficacy and side-effects of these alternatives in order to respond to these requests. The aim of this section of the CADDRA guideline was to review available information on alternatives to treatments typically used for the treatment of ADHD in a systematic fashion in order to allow clinicians to respond to these queries in an informed manner.

The methodology involved a systematic literature review. Publications spanning the past 10 years were searched using the electronic databases PubMed, PsycInfo, Embase and CINAHL. This process yielded 754 research articles found on the first iteration of the search (as of June 21st, 2016). Once the selection was narrowed to include clinical trials, meta-analyses and reviews the final database included 186 articles. Of these 186 articles, research articles on omega-3 supplementation, neurofeedback and dietary means other than omega-3 fatty acids yielded the most results, with 45, 43 and 19 articles respectively. Each of these approaches are discussed separately in the following paragraphs.

Omega-3 fatty acids

Omega-3 fatty acids (OFA) have been extensively studied as an alternative to pharmacological treatment of ADHD.

Western diet is rich in omega-6 fatty acids. Arachidonic acid, an omega-6 fatty acid, is found in cell membranes and is a precursor to inflammatory molecules such as prostaglandins and thromboxane. On the other hand, omega-3 fatty acids have anti-inflammatory properties. Unlike omega-6 acids, omega-3 fatty acids cannot be synthesised by humans and must be integrated in a person's diet for adequate daily intake. It is believed that a high omega-6 to omega-3 ratio promotes neuroinflammation. Omega-6 inflammatory mediators alter the structure of cell membrane phospholipids and the proteins imbedded in it therefore altering cell membrane fluidity, ultimately hampering the effective neurotransmission of serotonin and dopamine. Adding omega-3 to diet increases its concentration in the cell membrane therefore improving transmission of neurotransmitters by diminishing neuroinflammation, especially in the frontal cortex [468]. Furthermore, some studies have found that omega-3 levels are lower in the blood of children with ADHD [468-470].

Most randomized clinical trials (RCT) included in this review conclude that the benefits of omega-3 supplementation are modest at best when compared to treatment as usual [468, 471, 472], while others state they have no effect on the cognition of either the general population or those with neurodevelopmental disorders [473, 474]. Furthermore, supplementation of children with lower levels of omega 3 did not result in a significant reduction of ADHD symptoms [469].

Based on current evidence, omega-3 supplementation is not recommended as a replacement to treatment as usual in people with significant ADHD symptoms although the literature suggests that omega 3 supplementation may possibly be a useful adjunct [475].

Nutritional Supplements

Dietary interventions as alternatives to standard treatment of ADHD can be broadly divided into two categories : those that remove a particular kind of food (elimination diets) and others that increase the intake of a particular one [476]. Research on elimination diets consists mostly of eliminating either artificial food colorants, sugar or diets that eliminate all but a few food items (''few food diets'') [476]. Interventions where a particular food was increased postulate that children with ADHD may be lacking a particular kind of nutrient. Nutrients studied were mostly amino acids, essential fatty acids, vitamins and minerals [476].

The literature review identified 13 articles on dietary interventions; these consisted largely of studies of dietary supplementation, rather than restriction. The effects of amino-acids (phosphatidylserine), broad-based preparations of micronutrients and zinc were studied in the articles reviewed. Only one article specifically studied a restrictive elimination diet.

Phosphatidylserine (PS) monotherapy, the object of 2 RCTs, is a fat soluble amino acid derivative that is mostly found in the cell membrane of organs with high metabolic activity e.g. the brain. It is considered to be one of the most important brain nutrients as it influences many neurotransmitter systems, including those involved in ADHD (dopamine and norepinephrine). One double-blind RCT assessing effectiveness of supplementation with 200 mg of PS for the treatment of ADHD found an improvement of ADHD symptoms and short-term auditory memory in children [477]. Another double blind RCT was designed to determine its safety. Three hundred milligrams of PS administered daily for 15 weeks detected no difference in safety or side effects compared to placebo [478].

Broad-based preparations of micronutrients include vitamin D, B9 (folate), B12 and essential minerals such as zinc. These vitamins and minerals are known to act as essential cofactors in the synthesis of monoaminergic neurotransmitters [476, 479]. One double-blind placebo-controlled RCT claiming to be the first to investigate the efficacy and safety of such a preparation found that micronutrient treatment induced statistically significant improvements in ADHD symptoms as well as being a safe alternative to ADHD treatment [479]. Another randomized double-blind placebo-controlled trial found that supplementary nutrition given mostly to 14 and 15 year olds might have a protective effect against worsening behaviour when assessed using the Conners' Teachers Rating Scale, but less clearly when using school discipline records [480]. Children's behaviour in the control group worsened without supplementation, yet children in the intervention group showed a reduction in problematic behaviour [480]. These trials do not allow us to determine which specific nutrient might be of particular relevance in the treatment of ADHD. Overall, the paucity of such trials shows that there is no robust evidence that high dose vitamin and minerals supplementation significantly improves ADHD symptomatology [476].

Zinc is an essential micronutrient that has a major role in synaptic transmission. It increases the affinity of methylphenidate for the dopamine transporter and inhibits dopamine uptake through binding to the dopamine transporter [481]. Few double blind RCTs have investigated the effect of Zinc in ADHD [481]. This review identified one double blind RCT which found that zinc was not more effective than placebo in either monotherapy or in combination with stimulants [482].

The rationale for restrictive elimination diets is that eliminating artificial food colourants and other additives implicated in hypersensitivity reactions will result in improving brain function [483]. One RCT found considerable improvement in ADHD symptomatology [483] during the first phase of the study; however, the control group intervention consisted of dietary instructions while the active group had a restrictive diet and only the rater was blinded. Hence the conclusions cannot be considered unbiased. Furthermore, restrictive diets are difficult to implement in children and adults [476, 483] and may not be a realistic alternative to standard treatment.

Neurofeedback

Neurofeedback (NF) consists of measuring the brain wave activity of participants in real time and rewarding them when EEG readings show brain activity that is correlated with focus, attention and problem-solving [484]. Usually, theta and beta brain waves in the right prefrontal cortex are measured. Beta waves are associated with thinking, focusing and sustained attention whereas theta waves are linked to distractibility [484]. ADHD is believed to be caused by dysfunction in the right prefrontal cortex [484]. Therefore, it is hypothesized that lowering the theta-beta ratio in this region is a means of increasing focus [484]. Slow cortical potential protocol (SCP) and theta-beta ratio (TBR) are the most frequent treatment protocols [485].

Initial non randomized placebo-controlled studies showed positive outcomes of NF are mostly specific to inattention and impulsivity with large effect sizes for inattention and impulsivity but medium effect sizes for hyperactivity [486]. It is important to note that these effect sizes were obtained in semi-active control protocols (such as a waiting-list control

group). However, under randomized placebo control conditions no study has shown significant effect sizes [487-489]. Most proximal raters to the treatment condition (e.g. parents) tend to over-estimate the effect of NF when compared to more distal, blinded raters (e.g. teachers, research staff) [490]. On the other hand, treatment effects are limited yet tend to be durable over time (when evaluated again at 6 month follow-up) [491].

Although some authors propose that NF can be an efficacious alternative to treatment-as-usual in children who cannot tolerate the side effects of medication or do not pursue pharmacological treatment for any reason [491, 492] other, more recent studies, cast doubt on the specificity and efficacy of NF as treatment of ADHD altogether [493].

Further research of NF should be conducted with more rigorous research designs and include more subjects [494]. In light of the data available at this stage, we conclude there is insufficient data to recommend NF as a standard treatment for ADHD.

Chiropractic Care

A systematic review published in a major chiropractic journal concluded that there is currently insufficient evidence to support chiropractic care for the treatment of ADHD [495].

PRACTICE POINT

Overall, this review concludes that:

- There is insufficient evidence to recommend neurofeedback, computer-assisted cognitive training [496](e.g. Cogmed), dietary restriction or dietary supplementation as alternatives to standard treatments.
- While not in themselves harmful, these interventions may be expensive, time consuming and may divert individuals affected with ADHD away from more effective treatment.

In most alternative methods studied in this review, there seems to be a proximity bias in studies such that the closer the rater is to the participant being evaluated the more favourable the effect of treatment seems to be. Parents, and sometimes teachers, tend to notice subtle changes in the child's behavior that can account for the modest effects observed.

On the other hand, most large-scale studies and those that use a double-blind design, do not confirm these subtle changes and find no significant effects attributable to these interventions.

Further, these interventions may be expensive, time consuming and may divert individuals affected with ADHD away from more effective treatment.

CONTRIBUTOR DISCLOSURES

Conflict of Interest Declarations (2 years)

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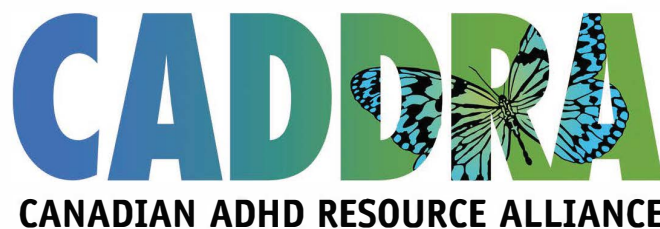
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