ADHD

CADDRA 2020

Updates: L Jia 2021
Slides: B Chow

Contents

1 Diagnosis of ADHD

Diagnosis of ADHD

- Chronic, often lifelong, condition
  - Impact & presentation can change over time
  - Often requires **lifelong monitoring + treatment**

- Now defined as a **neurodevelopmental disorder**
  - Usually seen in early childhood (not necessarily dx then)
  - >50% with dx in C&A continue to have **impairing sx as adults**

- Prevalence
  - C&A = **5 – 9%**
  - Adults = **3 – 5%**
  - Prevalence rates have been **stable for past 30 years**

Etiology

- Highly HERITABLE
  - Twin studies → **heritability = 76%**
  - Parents with ADHD → **>50% chance of child** with ADHD
  - Children with ADHD → **25% have parent** with ADHD
  - **30-40% risk in 1º relatives** of individuals with ADHD

- Heterogeneous disorder with complex genetics
  - Different genes linked to ADHD (DRD4, DAT)

- Other etiological factors
  - **Tobacco/alcohol use** during pregnancy
  - **Low birth weight**
  - **Psychosocial adversity**
  - Dysfunction of **fronto-striatal pathways (dorsolateral, ACC)**

Comorbidity

- Multimodal Treatment of ADHD study
  - **70%** of children with ADHD → 1+ other psychiatric disorder
  - Anxiety, depression, OCD, tic disorder, ODD

Making a Diagnosis in Primary Care

- DSM-5 Criteria
  - Inattention symptoms (6/9, if ≥17 → 5/9)
  - Hyperactive-impulsive symptoms (6/9, if ≥17 → 5/9)

  - Onset **before age 12**
  - Impairment in **2+ roles, for 6+ months**
  - Not better explained

- Specifiers
  - **Predominantly inattentive presentation**
  - **Predominantly hyperactive-impulsive presentation**
  - **Combined presentation**

Making a Diagnosis in Primary Care

A1) Inattention Sx	A2) Hyperactive-Impulsive Sx
• Not attentive to **details**	• Often **fidgets**
• Difficulty sustaining **attention**	• Often leaves **seat**
• Does not seem to **listen**	• Often **run** about
• Does not follow through on **instructions**, fails to finish work	• Often unable to play **quietly**
• Difficulty **organizing** tasks	• Often **"on the go",** driven
• **Avoids**/dislikes tasks requiring sustained mental effort	• Often **talks excessively**
• **Loses** necessary things	• Often **blurts out** answer
• Easily **distracted**	• Often has difficulty **waiting**
• **Forgetful** in daily activities	• Often **interrupts/intrudes**

Making a Diagnosis in Primary Care

- Screening tools for overall psychiatric health
  - Weiss Symptom Record (WSR)
  - Patient Health Questionnaire (PHQ-9)
  - Generalized Anxiety Disorder Item-7 (GAD-7)
  - Screen for Child Anxiety Related Disorders (SCARED)
  - Kutcher Adolescent Depression Scale (KADS)

- May need further consultation if
  - Significant medical or psychiatric comorbidities
  - Diagnostic uncertainty
  - Failure to respond to treatment algorithms
  - Patient/family reluctant to accept dx/tx

Strategies for Diagnosis of ADHD (1)

- **Clinical interview + evaluation** = mainstay of diagnosis
  - **Direct behavioral observation** (in classroom) highly recommended

- <u>Neuropsychological + psychoeducational evaluations</u>
  - Frequently recommended, esp if diagnostic uncertainty
    - **Wide Range Assessment of Memory & Learning**
    - **California Verbal Learning Test**
    - **Wisconsin Card Sort Test**
  - Tests of executive function → LOW ecological validity

  - **Should NOT be required to:**
    - Qualify for services, determine ADHD severity, quantify impact of ADHD, measure "real world" cognitive/academic impairment

Strategies for Diagnosis of ADHD (2)

- Computerized cognitive assessments
  - Conners' Continuous Performance Test, Test of Variables of Attention, Gordon Diagnostic System
  - Specifically designed to assess **attention + response inhibition**
    - But overlaps with controls

- Neuroimaging
  - NO direct clinical application currently

- EEG
  - NOT validated diagnostic tool → **NOT recommended**
  - Differences between children with ADHD (vs adolescents/adults)
    - Incr theta (absolute + relative)
    - Decr alpha/beta (absolute + relative)

Red Flags for ADHD

- **Organizational skill problems**
  - Difficulty managing routines, household, finances, self-regulation
- **Erratic work/academic performance**
  - Need to reduce course load, difficultly completing assignments
- **Anger control problems, family/marital problems**
  - Low self-esteem, chronic underachievement
  - Addictions (substance, behavioral)
- **Frequent accidents (recklessness or inattention)**
  - Problems with driving
- **Direct relative with ADHD**

Step 1: Initial Information Gathering (1)

- Reasons for Assessment or Referral
  - Someone close to individual recognized ADHD sx
  - Individual recognized ADHD sx
  - Relative dx with ADHD → individual now aware
  - Functional difficulties
  - Sx attributed to another psych dx (but may be ADHD)
  - Infrequently malingering

- Practice point
  - Review individual strengths
  - Establish rapport
  - End each interview with statement about successful coping skills
  - Affirm family's efforts to succeed
  - Self-referral neither guarantees nor eliminates dx of ADHD

Step 1: Initial Information Gathering (2)

- Presenting Complaint & Documentation Initiation
  - Review concerns + expectations
  - Psychometric evaluations → track progress
  - Review relevant documentation (report cards, assignments)
    - Good school performance does NOT rule out ADHD

- Practice point
  - Communication with school is crucial
  - Assessment of children is limited without classroom reports
  - In adults → observer reports from family/partner

Step 2: Medical Review

- Objectives
  - Collect documentation from past records
  - Score + review completed forms **(CADDRA toolkit)**
  - **Physical exam, medical history**
  - **Relevant clinical tests** → rule out medical causes + risk factors
  - Discuss possible **complications + outcomes** of having ADHD
  - Ensure **no medical contraindications** to medications for ADHD tx

Step 3: ADHD-Specific Interview

- Objectives
  - Complete childhood developmental history
    - If adult → may need collateral from parent or family member
  - Perinatal history
  - Developmental milestones
  - Temperament
  - Sx of ADHD prior to age 12
  - Any life events of emotional concern in childhood
  - Medical hx
  - Functional impact of sx

- Order tests if necessary
  - Specialty referral
  - Psychoed ax (if suspected learning disability, cognitive challenges)

Step 4: Feedback & Tx Recommendations

- Feedback of the diagnosis
- Dispelling myths
- Feedback of treatment plan
  - Psychosocial + pharmacological
- Implementation of treatment
  - **Multimodal + individualized**
- Follow-up
  - **Chronic disease management model**
  - Regular monitoring (growth chart, vitals, rating scales, SE)

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 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.

DIAGNOSIS AND TREATMENT FOR ADOLESCENTS

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QUESTIONNAIRES FOR TEACHERS

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- **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]

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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**

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2 Differential Diagnosis & Comorbid Disorders

Prevalence of Comorbidities (1)

- Comorbidity exists in MAJORITY of cases
  - **50-90%** have 1+ comorbidity
  - **50%** have 2+ comorbidities
  - Often need **concomitant treatment or prioritization**

- Explanation of comorbidities
  - One disorder is **precursor** to the other
  - One disorder is **risk factor** for the other
  - Disorders have **shared risk factors**
  - Common **underlying symptomatic basis** for behaviors

Prevalence of Comorbidities (2)

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	+	+	++

Impact of Comorbidities

- Can contribute to **FAILURE of ADHD diagnosis**
  - In children & adults

- **POORER outcome** (vs children with ADHD alone)
  - Greater social, emotional, psychological difficulties

- <u>Most common comorbidities CONSISTENT</u>
  - Across various studies (incl MTA)
  - ODD, learning disorders, anxiety disorders, SUDs

Disorder-Based Differentiation

- Can have **overlap** with other disorders
- Common medical conditions with overlap
  - Hearing/vision impairment
  - Thyroid dysfunction
  - Hypoglycemia
  - Severe anemia
  - Lead poisoning
  - Sleep disorders
  - Fetal Alcohol Spectrum Disorder (FASD)
  - Neurofibromatosis
- Medications with psychomotor SE
  - Mood stabilizers (cognitive dulling)
  - Decongestants, β-agonists (psychomotor agitation)

Disorder-Based Differentiation

- Most individuals with ADHD do NOT need labs
  - May be needed to rule out pathology
  - PSG, EEG, brain imaging

- Psychological testing
  - Suspected LD or cognitive deficits

- Adverse psychological factors
  - Disruptive family
  - Abuse/neglect
  - Attachment issues

ADHD, Comorbidity & Development

- Most common comorbidities depends on:
  - Presentation, developmental stage

Early childhood	• MOST COMMON = **ODD, Language, Anxiety d/o** • Many have a specific learning disorders • ADHD 2-3x more common if developmental or intellectual disability, borderline IQ
Mid-school-aged	• **Anxiety & tic disorders** become more common
Early adolescence	• **Mood disorder & SUD** become more observable
Adulthood	• **Anxiety, mood disorders, SUD** commonly seen

Oppositional Defiant Disorder (1)

- **Behavioral problems** → very COMMON comorbid sx
  - Oppositionality, aggression, delinquency

- <u>If comorbid ODD</u> → **sig impairment, more referrals**
  - Differentiate normal adolescent self-assertion (vs ODD)
  - May mistake **ADHD impulsivity/irritability** for ODD willfulness
  - ODD may continue into adult for some

- <u>ODD symptoms</u>
  - 3 clusters → **mood-related, provocative, vindictive**
  - **Provocative-vindictive sx LESS COMMON** (vs ADHD irritability)
    - Conceptualized as reaction to insecurity/low self-esteem
    - May be reaction to dysfunctional environment

Oppositional Defiant Disorder (2)

Table 2.2 ODD differentiation

Overlapping sx with ADHD	*ODD distinct characteristics*
• Loses temper • Angry, resentful • Touchy, easily annoyed • Argumentative	• Refuses to comply with rules • Deliberately annoys others • Blames others for mistakes • Spiteful, vindictive
CD distinct characteristics	***ODD vs CD***
• Violating basic rights of others • Aggression, lying • Stealing, truancy • ODD may be precursor in 50%	• Negative, hostile • Defiant, disobedient • Esp towards authority • BOTH can be prepubertal

Oppositional Defiant Disorder (3)

- Treatment of ODD + ADHD → multimodal approach

  - **1) Optimize pharmacotherapy of ADHD**
    - May stabilize reactive-irritable sx

  - **2) Augment with psychosocial tx**
    - Parent Management Training (PMT)
    - Cognitive Behavioral Therapy (CBT)
    - Collaborative & Proactive Solutions (CPS)

Oppositional Defiant Disorder (4)

- Key points for ODD + ADHD
  - Some may respond to **stimulants or non-stimulants** (atomoxetine, guanfacine XR)
  - Many cases likely require **augmentation**
    - Psychosocial treatment
    - Off-label medication (AAPs)
    - May require specialized care referral
  - **Effective tx** → may reduce risk of more severe conditions later
    - Conduct disorder, SUD, depression

Conduct Disorder/Aggression (1)

- Comorbid CD + ADHD → severe, persistent condition
  - Often **preceded by ODD**
  - If **pre-pubertal onset of CD (age <10)**
    - WORSE prognosis (vs adolescent-limited CD)
  - Poorer outcome than either ADHD or CD alone

- Risk factors for **poor prognosis & antisocial PD**
  - Limited pro-social emotions (callous, no remorse/guilt/empathy)
  - Unconcerned about performance
  - Shallow/deficient affect

Conduct Disorder/Aggression (2)

Table 2.3 CD differentiation	
Overlapping sx with ADHD	***CD distinct characteristics***
• Impulsively starts fights as reaction to provocation	• **Instigates** fights, may use weapons
• May be rough with animals or people, d/t lack of self-control	• Takes **pleasure in cruelty** to animals or people
• Forgets curfew	• **Disobeys** curfew, runs away to engage in preferred activities, without regard to consequences
• Sets fire without considering consequences	• Sets fire with **vengeance**
• Steals impulsively	• Steals with **planning**
• Lies impulsively to avoid consequences	• **Lies to manipulate** others & obtain gain
• Breaks things accidently or impulsively	• **Vandalizes**

Conduct Disorder/Aggression (3)

- Treatment → more benefit from multimodal approach

  - **Pharmacotherapy for ADHD + CD + aggression**
    - **Stimulants & non-stimulants useful**
    - Usually more effective in reducing ADHD + impulsive aggression
    - Use meds to treat **most severe underlying disorder**
      - In complex situations → target specific sx
    - Some meds may augment irritability + aggression
    - **Off-label mood stabilizers, AAPs**

  - **Individual + family interventions often required**

Conduct Disorder/Aggression (4)

- Key points for ADHD + CD
  - Essential characteristic of CD → violation of rights/social norms
  - **Psychosocial tx often needed to improve outcomes**
    - Parenting, problem-solving skills training
    - Family/individual therapy
  - **Pharmacological tx**
    - May required ADHD med + med targeting aggression

Antisocial PD (1)

- Many people with ASPD have hx of ADHD
  - (but most people with ADHD do NOT develop ASPD)

- Many ASPD sx → **impulsive component**
  - But targeting ADHD sx may NOT resolve ASPD sx
    - Often crystalized in personality
    - May facilitate structured intervention for ASPD

Antisocial PD (2)

Table 2.4 ASPD differentiation	
Overlapping sx with ADHD	***ASPD distinct characteristics***
• May enter conflict with law d/t impulsive behavior	• Fails to conform to **social norms**, acts that are **grounds for arrest**
• Lying impulsively to avoid consequences	• **Deceitful** (repeated lying, aliases, conning for gain)
• Fails to plan, impulsive	• Repeated failure to sustain work behavior or financial **obligations**
• Can be irritable & have interpersonal conflict	• Can be irritable + aggressive, with **repeated fights**
• May put self/others at risk d/t impulsivity & lack of forethought	• **Reckless disregard**, lack of care for safety of self/others, lacks remorse

Antisocial PD (3)

- Both disorder must be treated SEPARATELY
  - Some pts with ASPD may have **drug-seeking behavior or SUD**
    - Consider potential misuse of stimulants
  - Non-stimulant meds may be option for ADHD sx

Antisocial PD (4)

- Key points
  - ADHD is a **treatable risk factor** for ASPD
  - Both conditions require **specific + separate interventions**
  - May help to improve impulsive behaviors first

Borderline PD (1)

- Prevalence of BPD in ADHD = **34%** (vs 5% in gen pop)
  - Most common shared sx = **IMPULSIVITY**

Table 2.5 BPD differentiation

Overlapping sx with ADHD	*BPD distinct characteristics*
• Pattern of relationship challenges/impairments	• **Intense relationships**, with "black & white" reactions, underlying **fear of abandonment**
• Impulsivity + risky behavior	• Rapid changes in **self-identity & self-image**
• Mood swings	• Periods of **stress-related paranoia**, dissociation
• Inappropriate & intense anger	• **Suicidal threats, self-harm** • Ongoing feelings of emptiness

Borderline PD (2)

- NO established optimal treatment for ADHD + BPD
  - NO evidence that improvement in ADHD leads to resolution of BPD

- Treatment strategies for BPD
  - Aim to control impulsive behaviors (often with meds)
  - **Dialectical Behavior Therapy (DBT)**
    - Emotional dysregulation
    - Distress tolerance

- Core impulsivity → risk of **medication misuse**
  - Do not necessarily deny pts with BPD effective ADHD tx

Borderline PD (2)

- Key points

  - **DBT effective for BPD**
    - Should be used in combination with meds if comorbid ADHD

  - Main goals
    - **Stabilizing impulsive behaviors**
    - **Optimizing emotional regulation**

Addictions

- ADHD features → at risk for addictions
  - Need for rapid feedback
  - Desire for immediate reward
  - High adrenaline risk-seeking behaviors

- May be substance or behavioral addictions

- Principles of management
  - Specific intervention for addictive behavior
  - Specific treatment for ADHD
  - Ideally **concurrently**

Substance Use Disorders (1)

- Pts with ADHD → **2x risk** for substance abuse/dependence
  - ?accompanying poor self-esteem + impulsivity

- Adults with SUD → 25% have ADHD
- Adolescents with SUD → 50% have ADHD

- If comorbid **bipolar disorder or CD** → GREATEST risk

- **Marijuana** → MOST COMMONLY abused agents in ADHD

- Substance use problems → incr severity of ADHD sx
  - Can also **mimic ADHD** (attention, behavior, self-control)

Substance Use Disorders (2)

- Treatment
  - Specific interventions for each disorder, **CONCURRENTLY**
    - Treatment of ADHD → may reduce cravings for substances
  - Early stimulant treatment **REDUCES OR DELAYS** onset of SUD
    - Protective effect may be lost in adulthood

  - If SUD is severe → consider sequential treatment
    - Immediate stabilization of the addictions
    - May require residential or inpatient treatment
    - Day treatment can be more cost-effective

  - Careful monitoring of psychostimulants
    - Medical interactions
    - Risk of misuse & abuse

Substance Use Disorders (3)

- Cannabis
  - May report subjective calming, improvement of other sx
  - NO evidence as effective tx for ADHD
  - No evidence that it improves attention or productivity
  - In fact → **may impair cognition, exacerbate motivation issues**

- Methylphenidate → **LOWER abuse potential**
  - Slower dissociation from site of action
  - Slower uptake into striatum
  - Slower binding/dissociation with DAT (vs cocaine)
  - Oral administration → **decr likability of a substance**
  - Parenteral usage → **NOT assoc with euphoria**

Substance Use Disorders (4)

- Misuse & diversion
  - **Comorbid SUD or CD** → HIGHEST risk for diversion/misuse
    - Also more likely to BOTH divert + misuse stimulant meds
  - Extended release preparation → LESS potential for parental use
  - Non-stimulants (atomoxetine, guanfacine XR) → NO abuse potential

- Key points
  - ADHD + SUD → need concurrent + independent treatment
  - Oral psychostimulants → less abuse liability (vs illicit stimulants)
  - Non-stimulants, long-acting psychostimulants → less abuse liability (vs immediate-release preparations)

Anxiety Disorders (1)

- Comorbid anxiety in ADHD
  - **33% of children**
  - **50% of adults**
  - Often develop anxiety due to chronic difficulties related to ADHD
    - (repeated forgetting → worrying, checking)

Anxiety Disorders (2)

Table 2.6 Anxiety differentiation	
ADHD distinct characteristics	***Anxiety distinct characteristics***
• Inattentive sx, independent of emotional state	• Inattentive sx when anxious
• Fidgetiness, independent of emotional state	• Fidgetiness while anxious
• **Social disinhibition**	• **Social inhibition**
• Initial insomnia, because of difficulty "turning off thoughts"	• Initial insomnia, because of **ruminations/anxiety sx**
• **NO subjective physical sx**	• **Physical sx** (pounding heart, nausea, SOB, tremulousness)
• Transient + realistic worries, related to prior & actual functional impairment	• Persistent cognitive sx of intense fear ± worry, focused on unrealistic specific situations or thoughts

Anxiety Disorders (3)

- Treatment
  - Treat the MOST impairing condition first
  - Psychostimulant tx may incr anxiety (esp at initiation, dose Δ)
    - Use **slower titration schedule**
  - If anxiety TOO intense → reduce or withdraw ADHD med
    - Treat anxiety until stable, then initiate ADHD meds

- Can use ANY of the ADHD stimulants with comorbid anxiety
  - **Atomoxetine** → beneficial
  - **Guanfacine XR** → well tolerated

Anxiety Disorders (3)

- Key points
  - ADHD-assoc impairments → can **induce anxiety sx**
    - (different than a specific anxiety disorder)
  - Often coexist → treatment MOST impairing condition first
  - Can use **stimulants or non-stimulants** for ADHD
  - For may patients prone to anxiety
    - May need to initiate psychostimulants at slower place
    - Monitor for carefully

Major Depressive Disorder (1)

- May have overlapping sx
  - Inattention, STM problems, irritability, impulsivity
  - Difficult sleeping, concentrating
  - Restlessness, fidgeting
  - (lifelong vs recent drop)

- Symptoms
  - If primary ADHD → dealing with failure, attacks to self-esteem
    - Often start at young age → can become demoralized/depressed
  - Lack of motivation → may mimic anhedonia
  - Difficulty going to sleep, restlessness → may mimic insomnia
  - ADHD can have dysregulated mood (dysphoria, irritability)
  - **NOT typical for ADHD alone to be assoc with entrenched, depressed affect or anhedonia**

Major Depressive Disorder (2)

Table 2.7 Depression differentiation	
Overlapping with ADHD	***Depression distinct characteristics***
• Loss of motivation, demoralization	• Feeling sad or hopeless
• Problems concentration	• Feeling tired or “slowed down”
• Being restless or irritable	• Changes in **eating, sleeping, neurovegetative sx**
	• Thoughts of death or **suicide**
	• **Episodic** (ADHD is continuous)

Major Depressive Disorder (3)

- Treatment
  - Treat MOST disabling condition first
  - Antidepressants with **catecholamine activity (**e.g. bupropion)
    - May be useful to treat MDD + ADD
  - Often need **combination of antidepressant + psychostimulants**
    - SSRIs + stimulants → SAFE
    - Risk of drug interactions
      - **Atomoxetine, amphetamines** (2D6 → fluoxetine, paroxetine)
  - If severe depression or risk of self-harm → specialized referral

Major Depressive Disorder (4)

- Key points
  - If mild depression → consider treating ADHD first
  - If severe depression or suicidal risk → treat depression first
  - Concurrent treatment often required
    - Combo antidepressants + ADHD meds commonly used

Bipolar Disorder (1)

- Many overlapping sx → can be challenging dx

Table 2.8 Bipolar Disorder Differentiation	
ADHD distinct characteristics	***Bipolar distinct characteristics***
• Initial insomnia, sleep disorders	• **Decreased need** for sleep
• Chronic restlessness	• **Excessive 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**

Bipolar Disorder (2)

- Manage + stabilize BIPOLAR symptoms first
  - Often requires mood stabilizers ± atypical antipsychotics

- Small **risk of SWITCH** to mania with **PSYCHOSTIMULANTS**
  - Prioritize treatment of BIPOLAR
    - Reduce or stop stimulants
  - Once mood stabilized → can cautiously restart stimulants

Bipolar Disorder (3)

- Key points
  - Aim to **stabilize bipolar disorder** first → then treat ADHD
  - **Stimulants** → **safe + effective** in bipolar (once sx stabilized)

Disruptive Mood Dysregulation Disorder (1)

- DSM5 criteria
  - Severe, recurrent, disproportional **temper outbursts**
  - Between temper outbursts **mood is irritable/dysphoric**

  - 3+ times per week
  - 2+ different settings
  - 1+ year
  - Must be diagnosed between age 6 – 18

- Considered presentation of childhood depression
  - Dx created to address potential of overdiagnosis of bipolar
  - High comorbidity with bipolar, depression, ODD, ADHD

Disruptive Mood Dysregulation Disorder (2)

Table 2.9 DMDD Differentiation	
Overlapping with ADHD	***DMDD distinct features***
• Irritable mood episodes (explosive outbursts)	• **Inter-episode dysphoria**
• Psychomotor agitation	• **Minor triggers** with extreme rage attacks
• Chronic course	
• Young age of onset	

Disruptive Mood Dysregulation Disorder (3)

- Treatment
  - Needs **combination of medication + psychosocial interventions**
    - Many meds effective for ADHD → effective for DMDD

- Key point
  - DMDD is a new diagnosis → research underway

OCD (1)

- Prevalence
  - Lifetime prevalence in gen pop = **1 – 3%**
    - If OCD + ADHD → incr risk of Tic Disorders, Tourette Syndrome

- ADHD pts → often have **behavioral problems** (checking)
  - Consider whether secondary to ADHD or from OCD

- Treatment
  - Simultaneous treatment → no worsening of OCD sx with stimulants

OCD (2)

- Key points
  - **Psychostimulants do NOT usually lead to exacerbation of OCD**
  - Presence of OCD does not change treatment approach of either

Tourette Syndrome (TS) & Tic Disorders (1)

- ADHD highly comorbid with tics + TS (50-90%)
  - Pure TS = 50%
  - TS + ADHD = 22%
  - TS + OCD = 22%
  - TS + ADHD + OCD = 6.5%
  - Commonality = **emotional lability** + behavioral problems

  - Presence of OCD → more impairing than ADHD
    - Increases rates of other comorbidities

  - Tics generally LESS impairing than ADHD

Tourette Syndrome (TS) & Tic Disorders (2)

- Treatment
  - TS → education about tics, monitoring, tx, school intervention
  - ADHD + Tic Disorder
    - **Stimulants SAFE** → monitor for worsening tics
    - **Alpha2-adrenergic agonists** (clonidine, guanfacine XR)
      - "shown promise" in tx of tics, esp if also ADHD
  - If stimulants exacerbate tics → may use **atomoxetine**
    - Rarely worsens tics
  - Population studies → stimulants do NOT raise the **risk** of tics
    - Exacerbation may be coincidental, due to wax/wane of tics

- Non-pharmacological treatments for Tic Disorders
  - **Habit Reversal Therapy**
  - **Comprehensive Behavior Intervention for Tics (CBIT)**
  - Considered FIRST-LINE if available

Tourette Syndrome (TS) & Tic Disorders (3s)

- Key points
  - Tics + TS → HIGHLY comorbid with ADHD
    - **NOT contraindication to using stimulants in ADHD**
      - But requires careful monitoring
  - Stimulants do NOT typically raise risk of tics
    - May rarely do so for some

Eating Disorders (1)

- Bulimia nervosa, anorexia nervosa-purging type
  - **MORE prevalent if ADHD**
    - Females with ADHD → 3.6x more likely to have ED
  - ADHD among ED = **11.4%**
  - Pts with anorexia may seek stimulant meds for **weight loss**

- Weight issues in ADHD
  - **Impulsive behaviors** → may lead to binge eating
    - Greater impulsivity if comorbid eating disorder (vs just ADHD)
  - Obesity is risk factor for **sleep apnea** (can mimic/worsen ADHD)
  - Unclear relationship with Binge Eating Disorder

Eating Disorders (2)

- Key points
  - Treatment of ADHD → could contribute to **behavioural control** in context of binge eating
  - Growing literature on ADHD as risk factor for obesity

Autism Spectrum Disorder (1)

- ASD previously was exclusion criterion for ADHD
  - Suggested among ASD pts → **30-70% meet ADHD**

Table 2.9 DMDD Differentiation

	ADHD distinct features	***ASD distinct features***
Age of dx	• 6-7 years and older	• As early as 2-3 years
Language	• NO delay or echolalia	• Delayed, echolalia
Eye contact	• Less eye contact because eyes frequently shift focus	• Avoids eye contact
Social interests	• More social in play	• Less social in play
Friendships	• Ostracized for impulsive behavior, inattentive to others' states of mind, drawn to impulsive peers	• Not interested in peers, "parallel play" mainly, difficulty in understanding others' state of mind
Motor	• Hyperactivity • "always on the go"	• Rhythmic, stereotyped movements

Autism Spectrum Disorder (2)

- Treatment
  - **Treatment of ADHD in ASD** → EFFECTIVE, improves functioning
    - May be MORE sensitive to side effects
      - Irritability, hyper-focus, stereotypies (vs no ASD)
      - Start low, titrate cautiously
  - **Methylphenidate** → 50% response rate (vs 70-80% without ASD)
  - **Risperidone, aripiprazole** → efficacy in controlling hyperactivity
    - Less favorable side effect profile (vs psychostimulants)
  - **Atomoxetine** → positive results, well-tolerated
    - Hyperactivity, impulsivity, **inattention**
    - **Limited** clinical & functional improvement
  - **Guanfacine XR** → effective for hyperactivity

Autism Spectrum Disorder (3)

- Key points
  - Screen for ADHD or ASD in either population
  - Treatment of ADHD in ASD → **very effective, helps functioning**
    - May have **lower effect sizes**
    - May have higher risks of side effects

Specific Learning Disorder (1)

- Comorbidity **31-45%** (depends how SLD is diagnosed)
  - SLD not necessarily synonymous with "learning disability"

- Academic difficulties in ADHD without SLD
  - Difficulties listening, reading comprehension, written expression
  - Following instructions, listening in classroom, staying on task

- Executive function difficulties in ADHD
  - Initiation, organization, planning
  - Self-directed activity, multistep tasks

Specific Learning Disorder (1)

- Diagnostic Assessment
  - Screen for academic skill deficits in ADHD, and ADHD sx in students with SLD
  - Assess academic function across subject areas
  - Evaluate if interventions for ADHD improve academic function

- Adults
  - ADHD can occur along with reading, math, writing difficulties
    - Evaluate whether previous problems in school
    - Determine if pt inattentive only in area of learning deficit

Specific Learning Disorder (3)

- Management
  - SLD → intensive, direct instruction, modifications, accommodations
  - Comprehensive intervention services
    - Require empirically supported treatment strategies

Intellectual Giftedness (1)

- High IQ → does NOT preclude ADHD
  - May help coping with ADHD sx
  - Clinically relevant impairment may not develop until later
  - Treatment critical at any age

- May misdiagnose ADHD or miss diagnosis
  - Intellectually gifted with high energy, over-excitability in school
  - Intellectually gifted meeting full ADHD criteria, but can concentrate for long periods of time
  - Important to document intellectual giftedness

Intellectual Giftedness (2)

- Symptoms
  - **Overlapping sx if reacting to inappropriate curriculum**
    - Restlessness, inattention, impulsivity, high activity, daydreaming
  - May show **similar cognitive, social, psychiatric, behavioral features**
    - (vs ADHD with average IQ)
  - Need thorough medical, developmental, educational history
    - Also comprehensive clinical + psychological evaluation

Psychological Trauma

- PTSD sx → hyperarousal, hypervigilance, dissociation
  - Can confound ADHD assessment
  - ADHD may place children at greater risk to psychological trauma
  - Hx of trauma does NOT preclude dx of ADHD

Developmental Coordination Disorder

- Prevalence → **1.7%** (7-8 year old)

- Assess
  - Gait, throwing/catching ball, balancing on one foot
  - Fine motor tasks (writing, scissors, drawing)

  - Balance, dyslexia, poor handwriting → may be cerebellar or DCD

Epilepsy

- May have higher rates of ADHD sx (20-50%)
  - Higher rates of epilepsy among ADHD (vs no ADHD), more severe

- Anticonvulsant SE → can **impair attention/learning**
  - Choose one with LESS potential for behavioral/cognitive SE

- **NO evidence** that psychostimulants worsen seizures if stable epilepsy (severity or frequency)
  - Consider potential metabolic drug interactions

Brain Injury

- ADHD → **incr risk of physical injuries** (due to ADHD sx)
  - C&A with ADHD → **3x likelihood** for mod-severe brain injury

- Secondary ADHD (acquired)
  - Lesions in **right putamen, thalamus, orbital frontal gyrus**
  - C&A with mod-severe brain injury → 20-48% chance of S-ADHD
  - Same approach as ADHD (but less evidence)
    - May be **MORE sensitive** to meds (start at lower doses)

  - **Concussions** → could mimic or exacerbate ADHD sx

  - **Non-traumatic acquired brain injury**
    - Fetal alcohol syndrome, stroke, treatment with neurotoxic meds
    - May respond to standard ADHD tx

Sleep (1)

- Sleep sx common in ADHD (>50%) → esp **insomnia**
  - More restless sleep than peers
  - NO consistent differences in sleep variables (duration, architecture)
  - May be differences in circadian rhythms

- Stimulants → can affect sleep, **shorter night sleep**

- Insufficient sleep
  - Affects attention, emotional/behavioral regulation, cognitive function, academic performance
  - **Sleep restriction** → negative impact with or without ADHD
  - **Sleep apnea** → can mimic/exacerbate ADHD sx

Sleep (2)

- Treatment
  - Little evidence for pharmacological tx of sleep problems in ADHD
    - Melatonin may be effective
  - More evidence for **behavioral sleep interventions** → FIRST-LINE
- Key points
  - Differential dx
  - Sleep disturbances → common
  - Treating sleep problems → can help ADHD
  - Stimulant meds → can affect falling asleep

Incontinence

- Strongly assoc with ADHD
  - Nocturnal enuresis
  - Daytime urinary incontinence
  - Fecal incontinence

- Enuresis
  - Boys 4.5%, Girls 2.5% → rates decrease with age
  - Children with ADHD → **2-3x MORE likely to have enuresis**
  - Children nocturnal enuresis → MORE likely to have ADHD

- Treatment
  - Investigate + manage separately
  - Successful tx of ADHD with stimulants → may help resolution

SUMMARY

- Sleep
  - Behavioural interventions first line, melatonin may help
  - Stimulant meds → can affect falling asleep

- Incontinence
  - Investigate + manage separately
  - Successful tx of ADHD with stimulants → may help resolution

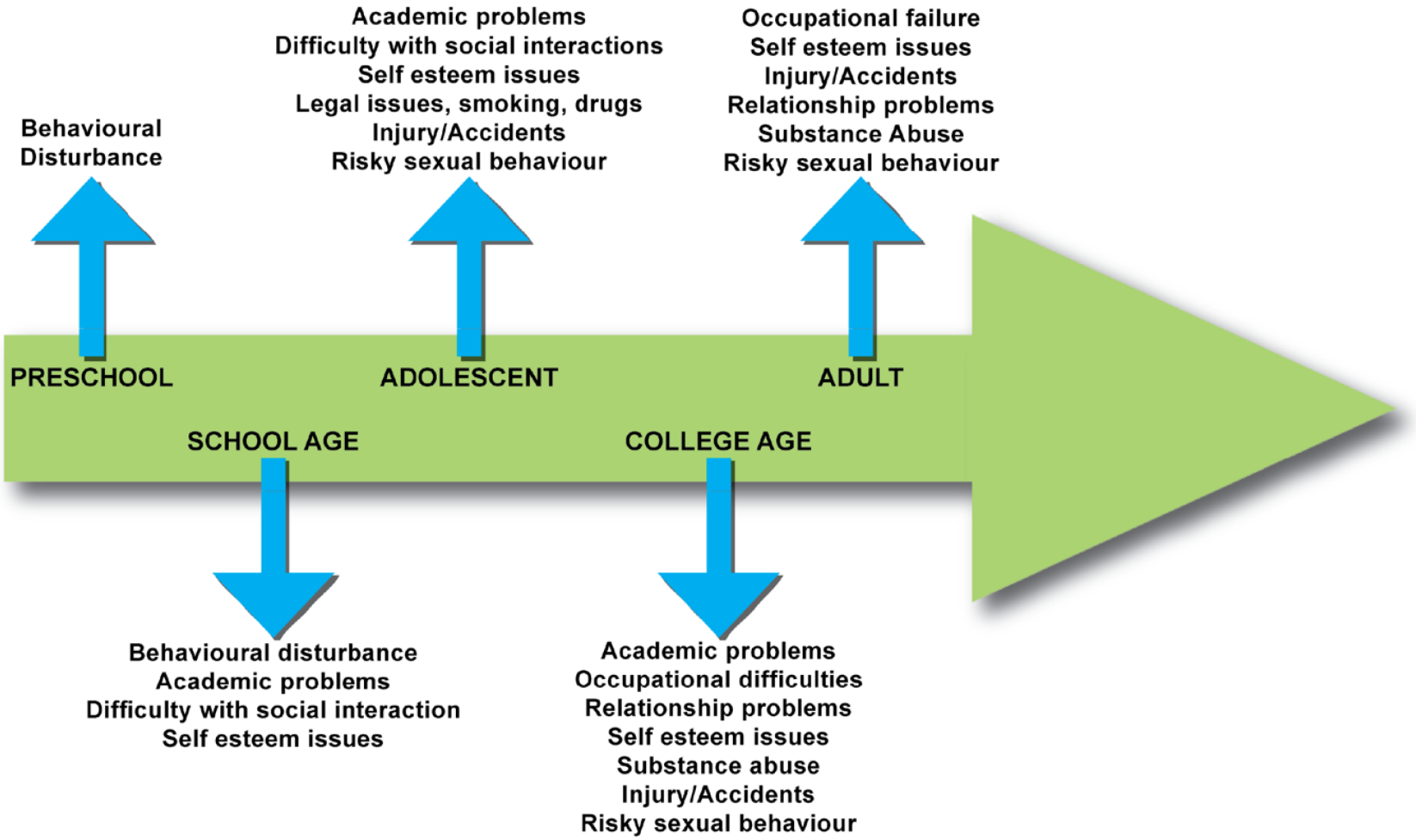
SUMMARY of TX

- ODD: **Multimodal** approach – 1) ADHD tx (reduce reactive/irritable sx), 2) Augment (PMT, CBT, CPS, AAPs)
- CD: **Multimodal** - Psychosocial (Parenting, problem-solving skills training, family/individual therapy) **AND** Pharmacological tx (for ADHD and aggression)
- ASPD: Both require specific + separate interventions; ADHD = treatable risk factor for ASPD
  - Consider non-stimulant meds if potential for stim misuse
- BPD: Goal = stabilize impulsivity and emotional regulation; **NO** evidence that improved ADHD → BPD resolution
- Substance u/d: Need concurrent **AND** independent tx; less abuse wITH PO/long-acting/MPH, or non-stimulanrt
  - Tx of ADHD may reduce substance cravings, and early ADHD treatment may reduce/delay SUD onset
- Anxiety: Often coexist, tx most impairing condition first; consider stimulants, atomoxetine, guanfacine
  - Stimulants may increase anxiety → slower titration
- MDD: Concurrent tx often needed; mild MDE → tx ADHD; severe MDE/SI → tx MDE
  - Atomoxetine and amphetamines metabolized by CYP2D6
- Bipolar: Stabilize BD first → tx ADHD (small risk of switch w/ stimulants)
- DMDD: Combo of meds + psychosocial; ADHD meds **effective** for DMDD
- OCD: Tx both; stimulants do NOT exacerbate OCD
- Tics/TS: Stimulants do NOT typically raise risk of tics (rarely for some)
  - 1st– HRT, CBIT; **stimulants** (**NOT** C/I, monitor); clonidine/guanfacine show promise; if tics exacerbated use atomoxetine
- Eating disorders: Tx of ADHD may help w/ **behavioural control** in context of binge eating
- ASD: Treatment of ADHD **effective**, helps functioning, more side effects
  - MPH, risperidone/aripiprazole (hyperactivity), atomoxetine (hyperactivity and inattention), guanfacine (hyperactivity)
- SLD: Comprehensive intervention services - intensive, direct instruction, modifications, accommodations
- Sleep: Behavioural interventions first line, **melatonin** may help; stimulants can affect falling asleep
- Incontinence: Investigate + manage separately; successful tx of ADHD with stimulants → may help resolution

3 Special Considerations Across the Lifespan

Developmental Impact of ADHD

Figure 3.1 Developmental Impact of ADHD



Preschool Children

- Of children age 3-5 → **2-8% have ADHD**

- Hyperactivity in preschoolers:
  - **Is highly heritable**
  - Tends to be temporally and situationally **stable**
  - Can be influenced by different factors:
    - Intellectual impairment, expressive language issues
    - Response to child abuse, neglect, conflictual environments

- **Non-pharmacological tx** = FIRST-LINE for preschool ADHD

School-Aged Children

- Of school-aged children → **3-9% have ADHD (avg ~7%)**
  - When MOST individuals are diagnosed with ADHD
  - Boys → 3x more likely to be identified
  - Girls → consistently **under-identified + under-diagnosed**
    - LOWER levels of disruptive symptoms

- Multimodal approach – aim to minimize functional impairment

- May have associated problems
  - Learning difficulties, low self-esteem
  - Manage in addition to ADHD sx

Adolescents (1)

- Among adolescents → **6-12% with ADHD**
  - Of children with ADHD → **50-80% maintain** sig sx into adolescence
  - **Males** → 3x more likely to be dx
    - Gender dx discrepancy lessens over time, nearing adulthood

- Obtain hx of risk factors (collateral necessary)
  - Reckless driving, smoking, drug use, sexual activity
  - Family/interpersonal conflicts, illegal activities, bullying

- Difficulties in school usually continue and get worse
  - Inattention, lack of focus, impulsivity, forgetfulness
  - Risk-taking can increase
  - Sig negative outcomes if untreated

Adolescents (2)

- Adherence to tx → can be very poor in adolescence
  - 48-90% of adolescents stop taking meds
  - Once-daily dosing improves adherences
  - Psychoeducation, motivational interviewing may help

College/University Students

- Among post-secondary students → **2-12%;** *possible histories:*
  - A) Students prev diagnosed + treated → wanting to adapt tx
  - B) Students who have stopped their medication + want to restart
  - C) Never dx before, but now facing difficulties coping
  - Lifetime prevalence of **non-prescribed stimulant use = 5-43%**

- Careful assessment necessary → *sx may be exaggerated*
  - *Reasons*: enhance performance, sell/use, weight loss
  - May require multiple visits, and includes a review of:
    - Parental reports of childhood sx, school report cards, current collateral
  - Screen for SUD and CD (associated with diversion, misuse)
  - Consider advocating for accommodations and additional services

Adults

- Among adults → **4.4%**; *many un-dx and un-tx, may present because:*
  - A) They are parents of children recently assessed for ADHD
  - B) Individuals who have learned about ADHD + related to sx
  - C) No sig sx prior to adulthood (may be due to prev supports)
  - D) Prev ADHD, seeking re-assessment

- Most have comorbid mental health condition (85%)
  - May receive tx for other disorders (i.e. antidepressants, mood stabilizers, anxiolytics) **without** adequate sx response

Older Adults

- Among older adults → **3%**
  - **Un**diagnosed ADHD can lead to lifelong impairments
  - May result in **incorrect assumption** that those with ADHD are undergoing neurogenerative process
  - May be difficult to dx due to depression/cognitive impairments

- Neuropsychological testing may help to make the dx

- Use FIRST-LINE meds for ADHD (but limited data in age >65)
  - May improve functional outcomes, including those with dementia

Impact/Functional Disability (1)

- 33-year follow-up study
  - Greater risk of POOR long-term outcomes in almost every aspect of life (vs those without ADHD)
  - Depends on supports, coping strategies, cognitive capacity, insight

- Individual effects
  - Low self-esteem, negative beliefs of self
  - "Imposter complex" (difficulty taking credit for success)

- Family effects
  - Parental stress, parental emotional/mental health problems
  - Sibling conflict, disruption to family cohesion/family time
  - Having child with ADHD → increased risk substance use, depression, and anxiety in parents
  - *Highly heritable* – family members should be screen or assessed if appropriate
    - Untreated ADHD may explain higher rate of separation

Impact/Functional Disability (2)

- Parents with ADHD
  - Parental psychopathology → can impact child
  - Important to treat parent at same time as child
    - **"All in the family"** approach

- School
  - If untreated → more likely to **be expelled or be truant**
  - May have lower grades, may disrupt others' education
  - May impact future economic status

- Occupation
  - **Higher absenteeism, lower productivity** at work
  - More likely to **impulsively quit, change jobs, be fired**

Impact/Functional Disability (3)

- Healthcare & Society
  - ADHD → higher medical costs
  - **MORE likely to have MVA (2-4x)**

  - Children with ADHD → **MORE injuries**
    - Multiple body regions, head injuries, severe injuries

Accidents/Risks – Childhood (1)

- **2x greater risk** for ALL types of accidental injuries
  - Including severe injuries, repeated injuries
  - Further increase risk if comorbid ODD or aggression

- Among children admitted for accidental injuries
  - 3x MORE likely to have ADHD (vs admitted for other reasons)
  - Further associated factors
    - Inattention, impulsivity, risk-taking behaviors
    - Motor incoordination
    - Comorbidity with ODD/CD, anxiety, depression
    - Parental characteristics (decr parental monitoring)
  - Medications can **DECREASE injuries**

Accidents/Risks – Childhood (2)

- Practice point
  - Discuss with parents:
    - Provide physical safety
    - Assure adequate supervision, reinforce positive risk management
    - Encourage physical activity
    - Balance between overprotection and safety
    - Calm, structured, positive approach to child rearing
    - Allow for more acceptable response to limit setting
    - Aim for parent to retain enjoyable relationship with their child
      - Encourage self-esteem

Accidents/Risks – Adolescence

- Higher risk of negative outcomes from risky behavior
- <u>If untreated</u>
  - Accidents, **driving accidents**
  - School failure, dropout, family conflict/fighting
- <u>Sexual activity</u>
  - Incr risk of **early sexual activity**, more sexual partners, STDs
  - Incr risk of **teen pregnancies**
- <u>Substance use</u>
  - Incr risk of **earlier use,** more severe difficulties
  - Comorbidity of ADHD + SUD commonly starts in adolescence
  - Ask about caffeine/energy drinks

Accidents/Risks – Adulthood

- Problematic risky behaviors continue to impact individuals into adulthood
  - Adjusted mortality rate ratio → higher in ADHD
    - MRR 1.86 if dx < 6 yrs old
    - MRR 4.25 if dx > 18 yrs old
  - **Increased suicide mortality**

- Driving
  - More driving **anger/aggression**
  - Less adaptive/constructive anger expression
  - College drivers → **angrier, riskier, more unsafe**
    - Worse concentration, vehicular control

Accidents/Risks – Driving (1)

- ADHD drivers as a whole → **increased** risk
  - Adolescents: suggest driver training and minimize risks
    - Curfews, staying off major highways, no drugs/alcohol
  - Driving assessment tool - **Jerome Driving Questionnaire (JDQ)**
  - If sub-optimally treated ADHD → **2-4x MVAs + moving violations**
    - Due to speeding, distractibility, driving anger, road rage
    - Risk magnified by comorbid substance use

- ADHD medications
  - Methylphenidate, dexamphetamine, atomoxetine → **improve** driving behaviours in ADHD populations
  - Guanfacine, clonidine → may be sedating, worsen driving abilities initially
  - Meds may not be effective in late evening → consider PRN short-acting stimulant

Accidents/Risks – Driving (2)

- Helpful restrictions
  - Cell phone use
  - Nighttime driving
  - Weekend driving
  - Use of manual transmission

- Evaluation of Risk + Documentation
  - CMA Guidelines on Fitness to Operate a Motor Vehicle
  - **If ADHD drivers have demonstrated a problem with driving** and are **non-compliant** with treatment recommendations
    - → MDs have a **duty to report** concerns to Provincial Ministry of Transportation
    - *Discretionary in Alb, Qb, NS*

4 Psychosocial Treatment of ADHD

Treatment Approach

- **Comprehensive**, **collaborative** and **multimodal**
  - Improves overall quality of life (+ core ADHD sx)
  - Medications may allow individual to use psychosocial strategies more effectively

- Psychosocial treatment may be preferred by some
  - **FIRST-LINE for preschoolers**
  - Particularly crucial role during **key life transitions**
    - I.e. adolescence to adulthood
  - Psychological interventions include:
    - CBT for ADHD
    - Behavioral interventions
    - Parent training
    - Cognitive training
    - Social skills training

Psychoeducation

- Overall purpose = **educate + empower patients**
- **Key elements:**
  - *Discover* – what pt and family already know
  - *Demystify* – i.e. ADHD is a neurobiological condition, boys are more likely to be dx but girls have higher rates of distress/anxiety/depression, NO proven correlation between ADHD and diet
  - Instill *hope* – about evidence-based tx
  - *Educate* – nature of ADHD, sx, emotional dysregulation, and tx
  - *Empathize*
  - *Encourage, guide & motivate* – identify strengths and talents
  - Be culturally & gender *sensitive*
  - *Promote a balanced lifestyle* – self-care is a priority, anxiety helps core sx of ADHD, promote sleep hygiene/nutrition/relaxation
- Give online resources, local community resources, book lists

Psychosocial Interventions – at **HOME**

Instructional Interventions at home

- Poor sustained attention, difficulty following multistep direction
- Needs **clear & direct communication**

- Get person to repeat instructions before proceeding
- Gentle approach before giving instructions

Behavioral Interventions at home

- Higher rates of emotional dysregulation, can cause interpersonal conflicts
- Prefer **immediate, small rewards**

- Positive, calm approach
- De-escalate conflicts calmly
- Teach “stop and think”
- “Catch them being good”
- Set clear attainable goals/limits
- Use positive incentives & natural consequences
- Use empathy statements
- Adults should model self-regulation
- Encourage balanced lifestyle
- Schedule family + partner time
- Limit choices to 2 or 3 options
- Meaningful rewards, timed in close proximity to desired behavior

Psychosocial Interventions – at **HOME**

Environmental Interventions at Home	
• Difficulties with transition times, homework times, daily routines • **External scaffolding** → establish daily expectations, structure, success	
• Implement structure + routines • Parents → united, consistent fair • Help with prioritizing • Post visual reminders • Use timers/app for deadlines	• Use labeled, colored folders • Suitable work areas • Chunking tasks • Plan frequent movement breaks • Allow for background noise/music

Psychosocial Interventions – at **SCHOOL**

Instructional Interventions at School

- Often have difficulty with "language" in classroom
- May have difficulty following instructions, interpreting pragmatic language

- Give **clear & precise directions**
- Get student's attention first
- Check **student's understanding**
- Use **direct requests** ("when-then")

Behavioral Interventions at School

- More responsive to **consistent, immediate reinforcement**
- Use behavior modification, identify goals, target behaviors, boost self-esteem
- Collaborate with student + family → meaningful incentives

- Immediate + frequent feedback
- More positive feedback (vs negative)
- Specific feedback
- Visual cues for transitions, tasks
- Chunking tasks
- Reduce amount of work
- Clear expectations + structure
- "Walking passes"

Psychosocial Interventions – at **SCHOOL**

Environmental Interventions at School	
• May require changes in environment, decrease distractors • More opportunities for **monitoring + interaction**	
• Seat away from distractions • Proximity to teacher • Quiet place for calming down/working	• Seat beside "more attentive" buddy • More change, introduce novelty

Academic Interventions at School	
• May have **co-morbid learning needs** in addition to distractibility	
• Actively engage student, by providing work at appropriate academic level • Allow for extended time • Allow for quiet room	• Allow for ear plugs, headphones • Provide scribes, note-taker, assistive technology • Assign work as necessary, monitor

Psychosocial Interventions – at **SCHOOL**

Executive Function Interventions at School	
• Struggles with **organization, time management**, prioritization, task completion	
• Tutor, academic coach • Structured classroom • Routine • Assignment + organization notebook	• Organize night before school • Monitor + prompt tasks • Teach time management • Use graphic organizer for projects

Post-Secondary Interventions	
• May have challenges with executive function, anxiety, depression • Easily overwhelmed if supports not in place	
• Accessibility/Disability Centres • Extended time for work, tests • Organizational apps, tech • Concept mapping • Identify strengths, problems, goals	• Preferential seating in lectures • Scribe, note-taker • Advanced copies of lecture notes • Video taped lectures • Access prompt sheets, memory aids

Psychosocial Interventions – **Workplace**

Workplace Interventions	
• Often prefer to NOT discloses ADHD → **fear of stigma**	
• Accommodation needs, supports • Regular + frequent meetings with manager → collaborative approach • Set goals, prioritize, review progress • Time management techniques	• Declutter • Work friendly environment • Productivity websites • ADHD coach

Manualized Interventions - Summary

- **Parent Management Training Models** (pre-school children)
  - 1) Reinforce + behaviour
  - 2) Ignore low-level provocative behaviours
  - 3) Provide clear, consistent, safe responses to unacceptable behaviours
- **Social Skills Training** – teach children to:
  - Perceive/interpret social cues
  - Problem-solve in social interactions
  - Reinforce appropriate skill display in group
- **Cognitive Behavioral Therapy** – focus on time management and organization skills
  - CBT + meds > CBT alone
- **Mindfulness Training**
  - Involves meditation
  - Associated with structural brain changes (amygdala, increased hippocampal grey matter)
  - Useful tool for parents

Parent Management Training Models

- For PRESCHOOL-aged children
  - Parent-child interaction therapy (PCIT)
  - Incredible Years series
  - New Forest Program
  - Triple P (Positive Parenting Program)
  - Helping the Noncompliant Child

  - All EFFECTIVE in **decr ADHD sx, disruptive behaviors disorders**
    - Parents actively involved, with or without child

  - **1) Reinforce positive behaviors**
  - **2) Ignore low-level provocative behaviors**
  - **3) Provide clear, consistent, safe responses to unacceptable behavior**

Social Skills Training

- Spectrum of impairment in social skills
  - Impulsivity may detract from ability to make friends
  - Consider possible ASD
  - **Good friendships** → can be **protective factor** (vs neg outcomes)

- Social Skills Training (SST)
  - Teach how to perceive & interpret subtle social cues
  - Problem-solve in social interactions
  - Reinforce appropriate skill display in group setting
  - Traditional SST → may have difficulty generalizing
    - Changing peer bias towards ADHD
    - Cochrane review → **NO sig tx effects of SST on behavior/sx**
  - Other SST → parents/teacher as friendship coaches (?promise)

Cognitive Behavioral Therapy

- CBT specifically targeting ADHD
  - **Time management, organizational skills**

- EFFECTIVE for **adults with ADHD**
  - Functional effect on brain, similar to stimulant meds
    - **Fronto-parietal network, cerebellum**
  - **Combo CBT + meds** → greater improvement than CBT alone

- MIXED results for **C&A with ADHD**
  - Adolescents with **ADHD + anx/dep** → benefit MORE (vs ODD)
  - **Group CBT effective** in reducing ADHD sx in adolescents

Mindfulness Training

- Cognitive-based therapy → often incl **mindful meditation**
  - Incr **mindful attention** to one's own thoughts + actions
    - Focus on present, inhibit distracting thoughts/stimuli
  - Related to structural changes in **amygdala**
  - Incr grey matter volume in **hippocampus**
- REDUCES → **hyperactivity, impulsivity, inattention**
- INCREASES → **self-directedness, self-regulation**
- Improvements → **maintained over time**
  - Mood, anxiety, social behavior

5 Pharmacological Treatment of ADHD

First-Line Treatments

- **LONG-acting psychostimulants** = FIRST-LINE
  - Augments **compliance, sx coverage, tx response**
    - Less need for multiple dosages
  - Less risk for **diversion, rebound sx** (vs immediate release)
  - Often **better tolerability**

- Methylphenidate vs amphetamines
  - Similar efficacy, similar tolerability profiles (at population level)
  - Individual response/tolerability may vary

- ***Recommendation*** **= adequate trial of BOTH classes** of long-acting psychostimulants (before trial of second-line)

Second-Line Treatments

- **SECOND-LINE**
  - **Atomoxetine** = SECOND-LINE
  - **Guanfacine XR** = SECOND-LINE
  - **Shorter-acting psychostimulants** = SECOND-LINE

- If suboptimal response, SE or no access to FIRST-LINE

- Non-stimulants
  - Can be used in **COMBINATION** with FIRST-LINE
    - Augmentation for suboptimal first-line treatment
  - Can be used if **stimulants contraindicated**
    - High risk of stimulant misuse

Third-Line Treatments

- **THIRD-LINE**
  - **Bupropion**
  - **Clonidine**
  - **Imipramine**
  - **Modafinil**
  - **Atypical antipsychotics**
  - **Exceeding recommended maximum dosages**

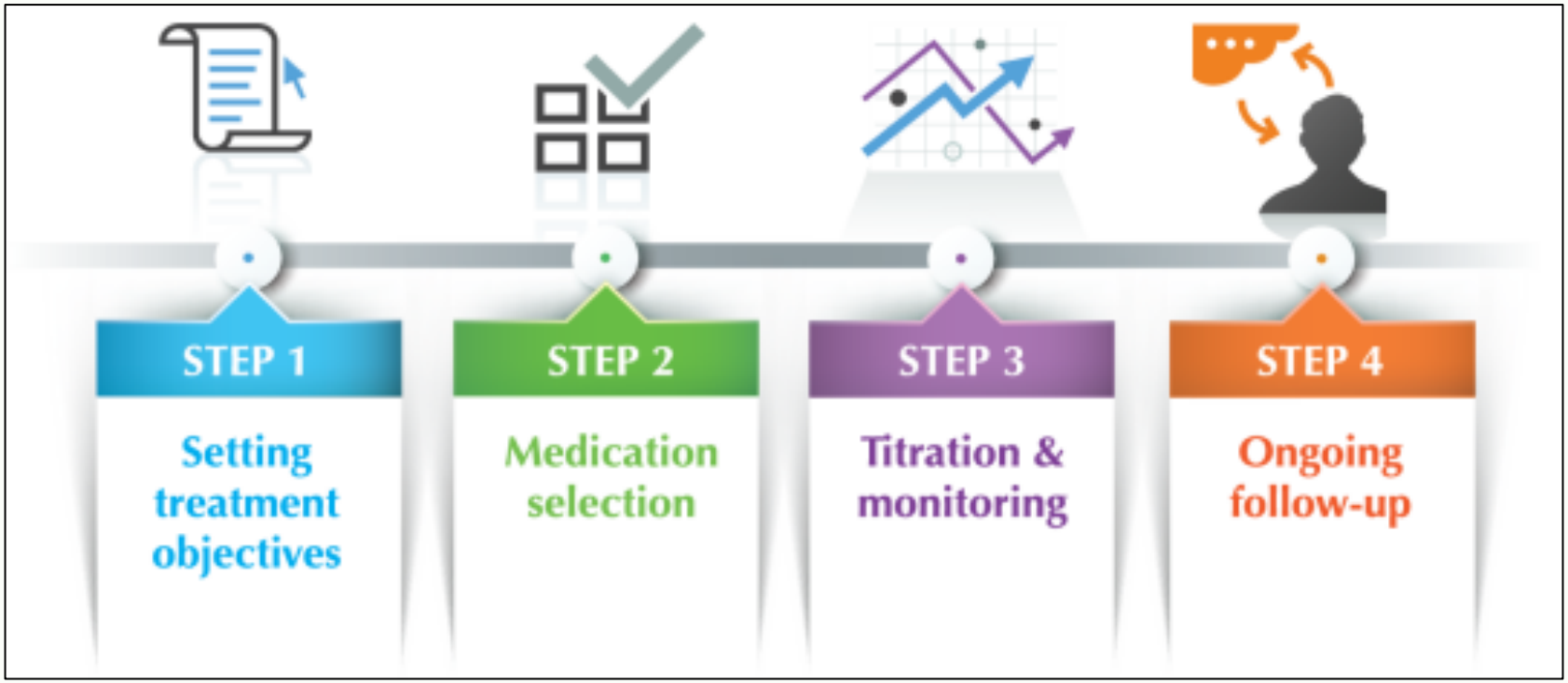
- Generally reserved for **treatment-resistant cases**
  - Off-label use, may have higher risks/SE/lower efficacy

- Atypical antipsychotics
  - Often used for comorbidities, used in combination with other meds

Summary Recommendations for Pharmacological Treatment of ADHD			
	Medication	*Mechanism*	*Dosing (Children)*
FIRST LINE	**Vyvanse (lisdexamfetamine)**	Long-acting amphetamine	20-60 mg
	Adderall XR (mixed amphetamine)	Long-acting amphetamine	5-30 mg
	Biphentin (multilayer beads)	Long-acting methylphenidate	10-60 mg
	Concerta (OROS)	Long-acting methylphenidate	18-72 mg
	Foquest	Long-acting methylphenidate	25-100 mg
SECOND LINE	Atomoxetine	NRI	10-100 mg
	Guanfacine XR	α2A-agonist (selective)	1-4 mg
	Dexedrine (dextroamphetamine)	Short-acting amphetamine	5-20 mg total
	Ritalin	Short-acting methylphenidate	10-60 mg total
THIRD LINE	Bupropion	NDRI	
	Clonidine	α2A-agonist (non-selective)	
	Imipramine, Desipramine	TCA	
	Modafinil	Stimulant	
	Atypical antipsychotics	Atypical antipsychotic	
	Exceed maximum dose	Psychostimulants	

Stepped Approach to Prescribing

- **1) Setting treatment objectives**
- **2) Medication selection**
- **3) Titration & monitoring**
- **4) Ongoing follow-up**



Step 1 – Setting Treatment Objectives

- ADHD diagnosis in collaboration with pt + collateral

- **Identify treatment targets** → ADHD sx, functional issues
  - May be in multiple domains (home, school, work)
  - "SMART" goals
    - Specific, measurable, attainable, relevant, timely

Step 2 – Medication Selection

- Informed consent
  - Clinical indications, goals of treatment
  - Dosing strategies, degree of efficacy, side effects, adherence issues

Table 5.2 Factors to Consider for ADHD Medication Selection

Patient-Related Factors	*Medication-Related Factors*
• Age & individual variation • Duration of effect required (timing of symptoms) • Comorbidities • Patient, family, physician attitudes	• Active ingredient, mode of action • Delivery system, onset/duration • Drug interactions • Canadian clinical indications • Affordability, accessibility • Combination for adjunct effects • Risk of abuse, misuse, diversion • Generic formulations

Medication Selection: Patient Factors

- Age & individual variation
  - **NO specific clinical profile**

  - **NO age-specific match criteria** → can be used across lifespan
  - **NO maximum age** → if health + CV status appropriate for tx
  - **Women of childbearing age** → unknown effects on fetus, breastfeeding
  - **Weight** → does NOT predict optimal dosing

  - **Difficulty swallowing pills** → teach techniques, sprinkle, liquids
  - **Adherence to treatment** → once daily dosing
  - **Predicted compliance** → psychoeducation, support, follow-up
    - If compliance issues, caution with medications that CANNOT be stopped suddenly (α2-agonists)

Medication Selection: Patient Factors

- Duration of Effect Required by Timing of Symptoms
  - **WHEN to administer & HOW LONG effect needed**
    - Consider level of insight (esp adolescents)
    - Duration usually needs to extend **beyond school/work settings**
    - May need **day-to-day variation**
    - Consider **driving risk**
  - For some pts → duration of effect shorter than expected

Medication Selection: Patient Factors

- Psychiatric comorbidities
  - **Treat MOST IMPAIRING disorder first**
    - Esp psychosis, bipolar, severe mood disorder, SUD
    - Suicidality, violence
    - Consider dx certainty, pt preference, likelihood of response
  - Common for mood/anxiety distress secondary to ADHD
    - **Effective ADHD tx can reduce sx**
    - Often COMPATIBLE with anxiety disorders
  - Select meds with **LESS cognitive impairment** (may worsen ADHD sx)
  - Consider potential **drug-drug interactions, side effects**

ADHD Medication Precautions

- Weight & Height
  - Initial + ongoing measurement in C&A
  - Refer to percentile charts

- Pre-existing tics or sleep problems
  - Can be positively or negatively affected by ADHD meds

- Cardiovascular issues
  - Can affect **blood pressure, heart rate**
    - Initial measurement, follow-up
  - Work-up before initiation if
    - Unexplained hx of **light-headedness, SOB, cardiac sx**
    - Family hx of **suspected cardiac sudden death**

Cardiovascular Risks of Psychostimulants

- Psychostimulants generally SAFE + well-tolerated
  - Controversy over potential risk of **arrhythmias**
  - Small incr in systemic adrenergic activity (BP, HR)
    - Rarely clinically important
  - 2006 → 27 cases of sudden death in children, warnings added
    - Since 2006, studies suggest NO DIFFERENCE vs gen pop
    - **"should NOT be used if structural cardiac abnormalities"**
      - LV dysfunction, scarring, hypertrophy, valvular disease
      - Get cardiology consultation → weigh risks/benefits
  - **Routine ECG monitoring** → **NOT RECOMMENDED**
    - Unless identifiable risk factors for cardiac disease
      - Abn physical exam, personal hx, family hx

Cardiovascular Risks of Psychostimulants

- Long QT syndrome
  - Stimulants + beta-blockers → **no adverse outcomes** (one study)
  - Suggest consultation

- Structural or hereditary heart disease
  - May be related via **common syndrome** (e.g. VCFS)
  - Pts with **congenital heart disease** → increase prevalence of ADHD
  - Some pts may have greater BP/HR effects from stimulants

- Adults with HTN or CAD
  - Caution is advised → closer monitoring of BP/HR

Precautions for ALL ADHD Medications

Precautions for ALL ADHD Medications		
Contraindications	***Precautions***	***Monitoring***
• Known allergy or hypersensitivity	• Cardiac disease • Bipolar disorder • Psychosis • Pregnancy, lactation	• Height/wt (children) • Sleep, appetite • Anxiety, mood d/o • SUD • Manic/psychotic sx • Suicidality • Aggression, irritability • Mood swings

Precautions for Psychostimulants

Precautions for Psychostimulants		
Contraindications	***Precautions***	***Monitoring***
• Tx with **MAOI** & up to 14 days after d/c • Hx **mania/psychosis** • Mod-severe **HTN** • Symptomatic **CVD** • **Pheochromocytoma** • Untx **hyperthyroidism** • **Glaucoma** (narrow)	• Anxiety • Hx substance abuse • Tic disorders • Epilepsy • Renal impairment • Periph vasculopathy (incl Raynaud's)	• BP, HR incr • Priapism • Growth retardation • Periph vasculopathy

Precautions for Atomoxetine

Precautions for Atomoxetine		
Contraindications	***Precautions***	***Monitoring***
• Tx with **MAOI** & up to 14 days after d/c • Mod-severe **HTN** • Symptomatic **CVD** • **Severe CVD** • Adv **arteriosclerosis** • **Pheochromocytoma** • Untx **hyperthyroidism** • **Glaucoma (narrow)**	• Poor CYP2D6 metabolizers • Asthma • Periph vasculopathy (incl Raynaud's)	• Liver injury sx • Urinary retention • Priapism • Growth retardation • Periph vasculopathy

Precautions for Alpha-2 Agonists

Precautions for α2-agonists (guanfacine, clonidine)		
Contraindications	***Precautions***	***Monitoring***
• Inability to ensure **regular daily dosage** (risk of rebound HTN)	• Hepatic impairment • Kidney impairment	• Sedation, somnolence • BP (hypotension risk) • Bradycardia • Syncope • Rebound incr BP/HR • QTc interval (if other contributing risks)

Patient, Family & Physician Attitudes

- Psychological Biases, Misunderstandings
  - Misinformation about SE, stigma, guilt
  - Common reasons for non-adherence
    - Lack of **physician awareness/understanding**
    - **Pt reluctance** to explain discomfort
  - Consider whether negative sx due to **medication WEARING OFF**

- Previous experiences with ADHD meds
  - Family hx of pos/neg response (but no evidence of prediction)
  - Perception of med efficacy/tolerability
  - Any non-prescribed trials

Medication Selection: Medication Factors

- Active ingredient, mode of action
- Delivery system, onset/duration
- Drug interactions
- Canadian clinical indications
- Affordability, accessibility

- Combination for adjunct effects
- Risk of abuse, misuse, diversion
- Generic formulations

Drug Interactions – Amphetamines

Drug Interactions – Amphetamines			
Drug Class	***Molecule***	***Interaction***	***Intervention***
Acidifying agents	• Fruit juices • Ascorbic acid	• May ↓ **AMP** levels	• Monitor response to AMP
Alkalinizing agents	• Sodium bicarb	• May ↑ **AMP** levels	• Monitor response • Consider alternatives
Analgesics	• Opioids	• May ↑ analgesia	• Monitor analgesia • May need less opioid
Antibiotics	• **Linezolid**	• May ↑ HTN	• **AVOID combination**
Antidepressants	• **MAOI, RIMA**	• ↑ NE • Risk of **hypertensive crisis**	• **AMP (within 14 d) CONTRAINDICATED**
	• SSRI, SNRI	• May ↑ SE of SSRI • Serotonin syndrome risk	• Monitor for serotonin syndrome
	• TCA	• May ↑ stimulatory + CV effects of AMP	• Monitor effects + CV response to AMP
Antihypertensives	• α2-agonists • β-blockers	• May ↓ hypotensive effect	• Monitor BP + HR
Antipsychotics	• CPZ • Fluphenazine	• **May ↓ effect of AMP**	• Monitor response to AMP
Decongestants	• Ephedrine	• May ↑ HTN + HR effects of decongestant	• Monitor BP + HR

Drug Interactions – Methylphenidate

Drug Interactions – Methylphenidate			
Drug Class	***Molecule***	***Interaction***	***Intervention***
Antibiotics	• **Linezolid**	• May ↑ hypertension	• **AVOID combination**
Anticoagulant	• Warfarin	• May ↑ warfarin levels	• ↑ INR monitoring with MPH changes
Anticonvulsants	• Phenobarbital • Phenytoin • Primidone	• May ↑ anticonvulsant levels	• Monitor anticonvulsant levels with MPH changes
Antidepressants	• **MAOI, RIMA**	• May ↑ hypertension • Risk of **hypertensive crisis**	• **MPH (within 14 d) CONTRAINDICATED**
	• SSRI, SNRI	• **May ↑ SE of SSRI**	• Monitor for serotonin syndrome
	• TCAs	• **May ↑ TCA levels + SE**	• Monitor levels + toxicity
Antihypertensives	• α2-agonists (clonidine)	• **May ↑ SE of clonidine**	• Monitor for SE
Decongestants	• Ephedrine	• May ↑ HTN + HR effects of decongestant	• Monitor BP + HR

Drug Interactions – Guanfacine XR (1)

Drug Interactions – Guanfacine XR (3A4 substrate)			
Drug Class	***Molecule***	***Interaction***	***Intervention***
Anticonvulsants	• Phenobarbital • Phenytoin	• May ↓ GXR levels (CYP3A4 induction)	• Monitor GXR effect • May need ↑ dose
	• Valproic acid	• May ↑ VPA levels	• Monitor response to VPA if GXR changed
Antidepressants	• SSRI	• May ↑ SE, psychomotor impairment of SSRI	• Monitor SSRI psychomotor imp
Antihypertensives	• **α2-agonists (clonidine)**	• **Similar mechanism to GXR**	• **Combination NOT RECOMMENDED**
	• β-blockers	• May ↑ AV-blocking effect of BB • May ↑ rebound HTN if GXR abruptly stopped	• Closely monitor BP + HR if GXR withdrawn
Antipsychotics	• **CPZ, Haldol**	• **May ↑ QTc interval**	• **Generally NOT RECOMMENDED**
CNS depressants	• Alcohol, sedatives, hypnotics, barbiturates	• May ↑ sedation + somnolence	• Monitor for additive effects • **Avoid unprescribed CNS-depressants**

Drug Interactions – Guanfacine XR (2)

Drug Interactions – Guanfacine XR (3A4 substrate)			
Drug Class	***Molecule***	***Interaction***	***Intervention***
CYP3A4 inducers	• Rifampin, etc.	• May ↓ GXR levels	• Closely monitor response to GXR
CYP3A4 inhibitors	• Fluconazole, grapefruit, etc.	• May ↑ GXR levels	• Closely monitor response to GXR
Prokinetic agents	• **Domperidone**	• **May ↑ QTc interval**	• **Generally NOT RECOMMENDED**
QTc prolonging agents	• Quinidine, quetiapine, citalopram, atomoxetine	• May ↑ QTc interval	• Consider alternatives • Closely monitor QTc

Drug Interactions – Atomoxetine

Drug Interactions – Atomoxetine (2D6 substrate)			
Drug Class	***Molecule***	***Interaction***	***Intervention***
Antiarrhythmics	• Quinidine	• May ↑ ATX levels (CYP2D6 inhibition)	• Start ATX lower • May need to ↓ ATX
Antiasthmatics	• Salbutamol	• May ↑ tachycardia effect	• Monitor BP + HR
Antibacterial	• **Linezolid**	• **May ↑ neurotoxic effect of ATX**	• **AVOID combination**
Antidepressants	• **MAOI, RIMA**	• **May ↑ neurotoxic effect of ATX**	• **Combination CONTRAINDICATED**
	• Paroxetine, bupropion	• May ↑ ATX levels (CYP2D6 inhibition)	• Start ATX lower • May need to ↓ ATX
	• **TCAs**	• May ↑ ATX levels (CYP2D6 inhibition)	• Start ATX lower • May need to ↓ ATX • **Generally NOT RECOMMENDED**
Decongestants	• Ephedrine	• May ↑ HTN + HR effect of decongestant	• Monitor BP + HR
Other CYP2D6 inhibitors	• Terbinafine, ritonavir, etc.	• May ↑ ATX levels (CYP2D6 inhibition)	• Start ATX lower • May need to ↓ ATX
QTc prolonging agents	• Quetiapine, guanfacine, etc.	• May ↑ QTc interval	• Consider alternatives • Closely monitor QTc

Affordability, Accessibility & Reimbursement

- All patient should have **access to optimum treatment**
  - Special access programs
  - Third party insurers
  - Generic formulations may not be as effective

Considerations – Combining Medications

- **Adjunct prescribing**
  - Adding ADHD with **different mechanism**
  - Short-acting ADHD agents for **uncovered portions** of day
  - Agent for concurrent **mood, sleep or anxiety disorders**

- Check **drug interaction** database!
- Consider **additive side effects**
  - E.g. sedation, sympathomimetic
  - May be contraindication or require careful monitoring

- **Only guanfacine XR** approved as adjunctive tx with psychostimulants (Health Canada)

Considerations – Abuse, Misuse, Diversion

- **Be alert to signs**
  - **Abuse** → parenteral routes to achieve a "high"
  - **Misuse** → mask fatigue, academic performance
  - **Diversion**

- Higher risk with **short-acting stimulants**
  - Pharmacokinetics + easily crushed

Considerations – Generic Formulations

- **“Bioequivalence”**
  - Max concentration (Cmax) & area-under-curve (AUC) similar
  - But **length of ascending concentration curve** (time to Cmax = Tmax) may be more related to duration of effect

- Especially for Concerta (OROS) vs generic Concerta
  - CADDRA considers generic formulation to be DIFFERENT DRUG
    - Different distribution curve
    - Different delivery system
    - Easily crushed

Key Points for a Successful Medication Trial

- Involve **patient + family**
- Identify **specific ADHD sx** that impair function
  - Define treatment goals
  - Select treatment option + clinical tools → measure change
- Start with **first-line treatment options**
  - Take time to adjust dose → balance efficacy vs side effects
  - Follow titration protocol
- **Measure response** at planned intervals
- If unsatisfactory response, **explore why**
  - Try different treatment option until sx control optimized
- **Follow-up** + re-assess efficacy + need for tx regularly

Key Points when Selecting an ADHD Medication

- Which medication is indicated in the pt's age group?
  - Health Canada approval for ADHD → first-choice
- What impairments, what time of day?
  - Take medication when most needed
- What medication does the patient prefer?
  - Pts may better respond to meds they strongly believe in
- Is a family member on ADHD medications?
  - Consider same medication if family members has positive response
  - (insufficient evidence for recommendation)
- Drug coverage?
- Trouble swallowing pills?
  - Adderall, Biphentin, Vyvanse → can be dissolved or sprinkled
- Comorbidities requiring interventions?
  - Decide which disorder to treat first

Step 3 – Titration & Monitoring (1)

- Establish schedule for visits + contact
  - Structured approach to measure treatment response
    - Patient + family report, collateral from teachers/others
    - Use specific targets + formal observational rating scales
  - **During titration phase** → regular contact recommended
    - Check physical health, vital signs, SE, family function, well-being

- Optimal treatment
  - Symptoms decreased + improvement in general functioning

- Optimal dose
  - Above which there is not further improvement
  - May be limited by SE
  - **Exceeding recommended max dose = THIRD-LINE**

Step 3 – Titration & Monitoring (2)

- Effect stabilization on particular dose
  - Stimulants → 1-3 weeks
  - Atomoxetine → 4-6 weeks
  - Full response → up to 3 months

- Some may report loss of effect with stimulants of time
  - Taking intermitted breaks MAY allow for maintenance of effect

Step 4 – Ongoing Follow-Up

- Chronic Disease Model
  - Proactive, integrated care → BEFORE long-term consequences
  - Active involvement of pts in own care
  - Multimodal treatment approaches, evidence-based
    - May attenuate high attrition rate of medication compliance
  - Provider education + resources
  - Access to specialist expertise

Managing Side Effects

- Usually mild + temporary (if appropriate dosage)
  - Usually appear when medication is started or dose changed

- Clinicians should monitor
  - Growth, sleep, nutrition, pre-existing conditions, BP, HR
  - Mood, anxiety, distress, thought patterns, behavior

- Find positive balance

Common Adverse Events

Common Adverse Events in ADHD Medications				
System	***Adverse Reaction***	***Psychostimulants***	***Atomoxetine***	***α2-Agonist***
CV	**↓ BP + HR**	-	-	**X**
	↑ BP + HR	**X**	**X**	If abrupt stop
GI + Nutrition	**Appetite suppression**	**X**	**X**	Low incidence
	Decreased weight	**X**	**X**	-
	Constipation, diarrhea	**X**	**X**	**X**
	Dry mouth	**X**	**X**	**X**
	GI upset	**X**	**X**	Upper abdo pain
Neuro	**Dizziness**	**X**	-	-
	Headache	**X**	**X**	**X**
	Somnolence	-	**X**	**X**
	Rebound effect	**X**	-	-
	Tics	**X**	Uncommon	-
Psychiatric	**Anxiety**	**X**	**X**	Low incidence
	Dysphoria, irritability	**X**	**X**	Uncommon
	Initial insomnia	**X**	**X**	Low incidence
Other	**Sexual dysfunction**	Uncommon	**X**	-
	Skin reactions	**X**	**X**	Low incidence

When to Reduce or Stop a Medication

- Provide education on how to reduce or stop
  - Adverse mood or personality changes → less likely to resolve
  - Physical discomforts (sleep, appetite) → more likely to resolve

- "Drug holiday" or dose reduction
  - During vacation periods → minimize impact on role performance
  - Consider whether taper needed to minimize withdrawal effects
  - Interrupting psychostimulants every weekend → may increase SE

- Non-stimulant medications (ATX, GXR, BUP)
  - Need to be taken **continuously** for clinical effect
  - Discontinuing α2-agonist → NEED TO BE TAPERED
    - Sig risk of **withdrawal hypertensive crisis**

How to Stop Medication

- Psychostimulants
  - Some may experience withdrawal, esp if high doses → taper
- Atomoxetine
  - Less likely to produce withdrawal
- α2-agonists (guanfacine, clonidine)
  - Should NOT be interrupted abrupted → ALWAYS TAPER
    - **By 1 mg every 3-7 days** (do not cut GXR in half)
  - Risk of hypertensive crisis

Choosing to Change to a Different Medication

- If medication benefit, but adverse effects
  - If **>mild SE or risky SE:**
    - Change to different class or medication
    - Manage underlying vulnerability
  - If **mild SE** or SE related to **delivery system:**
    - Consider same active ingredient with different pattern of release
    - Stimulants
      - Can change from one long-acting form to another
      - Spread out initial dosing during day
    - Atomoxetine
      - Daily vs BID dosing

Side Effect Management Techniques (1)

- Somatic effects
  - Peripheral nervous system effects via catecholamines
    - Physical SE sometimes improve or resolve over a few days
    - Minimize caffeine + other sympathomimetic agents
    - **SE are reversible**
  - Vulnerability + severity → may be higher in pre-existing conditions
    - Peripheral vascular disease
    - Tic disorders → may be exacerbated, sometimes improve
    - Narrow angle glaucoma
    - Urinary dysfunction

Side Effect Management Techniques (2)

- Appetite & Growth Effects
  - May prompt tx reduction or interruption (weekends, holidays)
  - Or switch to non-stimulant in children

  - **If appetite reduction:**
    - Maximize nutrition when appetite-suppression not in effect
    - ↓ portions, but ↑ snack times (mandatory snack in evening)
    - Consider nutritional supplements, meal replacements
    - Consider dose reduction, alternative agent, drug holidays if low BMI or familial short stature

Side Effect Management Techniques (3)

- Matching Coverage to Daily Patterns
  - **If insomnia** → take med earlier or use shorter-acting agent
  - **"Rebound" sx** → return of sx when untreated
    - Divide long-acting agent to increase coverage
    - Overlap with low dose short-acting stimulant

Managing Changing Medication Effects

- New adverse effects or loss of benefit
  - Broad differential if well-established response prior

  - **Brand name vs genetic**
  - **Drug breaks** → may have "rejuvenating' effect (not well-studied)
  - **"Tolerance"**
    - Energetic SE may reduce
    - But sustained attention should continue
    - If escalating dose, may be inappropriate treatment

Unsatisfactory Response to Treatment (1)

Factors to Consider Prior to Making Medication Changes (DATER)	
Dosage	• Optimized dose? Adequate duration of effect? • Side effects → dosage too low or high?
All	• Have all higher lines of treatment been attempted?
Time	• Enough time for pt response + SE resolution
Examine	• Specific tx targets? Means to measure change? • Standardized measures
Review	• Potential comorbidity, psychosocial + lifestyle issues?

Unsatisfactory Response to Treatment (2)

- **Augmentation strategies if:**
  - Non-optimal response to monotherapy
  - At least one medication from each psychostimulant class

- Second-line medications
  - **Guanfacine XR** (well-studied in age 6-17)
    - Only med with specific indication for use as adjunctive in C&A
    - Adjunctive use with stimulants or ATX in adults is off-label

- Third-line options → off-label use, specialist referral
  - **Bupropion**
  - **Clonidine**
  - **Modafinil**
  - **Imipramine**

Unsatisfactory Response to Treatment (3)

- If switching:
  - Consider switch during **long vacations or during summer**
  - Reduce periods of non-response or SE that may be impairing

- If partial or no response to treatment
  - Review diagnosis + treatment plan
  - Ensure compliance to treatment
  - Check for external factors

- If non-optimal response to one class → **try other class**
  - E.g. methylphenidate to amphetamines (or vice-versa)

Unsatisfactory Response to Treatment (3)

- Reasons for switching ADHD medication classes
  - **Peak & trough effects**
    - Change delivery mechanisms (IR vs XR)
  - **End-of-dose rebound effects**
    - Change IR for more sustained release
    - Or take additional, short-acting dose before rebound
  - **Adverse effects preventing optimization of dose**
    - Change release mechanism
    - Change molecule
    - Add adjunctive medication
  - **Drug-drug interaction**
    - If side effect, decide between reducing stimulant or other drug

ADHD Pharmacotherapy in Children (6-12)

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[5]	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		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 Alpha$_{2A}$-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	

Now also **chewable** tab form

Foquest	methylphenidate	start at 25 mg QAM	increase by 10-15mg	max 70mg

ADHD Pharmacotherapy in Adolescents (13-17)

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 Now also **chewable** tab form	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 Alpha$_{2A}$-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	

Foquest methylphenidate start at 25 mg QAM increase by 10-15mg max 70mg

ADHD Pharmacotherapy in Adults (18+)

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	5, 10, 15, 20, 25, 30 mg cap	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 Now also **chewable** tab form	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	

Foquest methylphenidate start at 25 mg QAM increase by 10-15mg max 100mg

Psychostimulants

- **Response to one class does NOT predict response to other**

- **Long-acting psychostimulants = FIRST-LINE**
  - Lower abuse potential (pro-drug, OROS, beads delivery)
- **Short-acting psychostimulants** = **SECOND-LINE**
  - Multi-dosing may reduce adherence to tx
  - Shorter duration of effect → peak/valley effect, sx coverage, SE
  - Higher potential for abuse (crushable)

  - Useful if need for shorter-duration of treatment
    - Top-up of once-daily medication
    - Only few hours of coverage needed
    - More flexibility in dose schedule

Amphetamine-Based Products

- 2 mechanisms to increase NE/DA in synaptic cleft
  - **1) Block reuptake** of NE/DA into presynaptic neuron
  - **2) Increase release** of NA/DA into extra-neuronal space

- Well-established safety + efficacy profile
- Subject to controlled substance regulation in Canada

- Amphetamine-based products
  - Mixed amphetamine sales (Adderall XR)
  - Dextroamphetamine (Dexedrine)
  - Lisdexamfetamine (Vyvanse)

Mixed Amphetamine Salts (Adderall XR)

Mixed Amphetamine Salts (Adderall XR)	
Active ingredient	• Mixed amphetamine salts • Mainly dextroamphetamine
Delivery system	• Extended release capsule • Granule delivery system (2 layers, digested)
Duration	• 12 hours
Notes	• May be opened + sprinkled without loss of efficacy • Do NOT crush or chew beads • Bioavailability affected by pH changes in GI tract

Dextroamphetamine (Dexedrine)

Dextroamphetamine (Dexedrine)	
Active ingredient	• Dextroamphetamine (DEX)
Delivery system	• Tablets: immediate • Spansules: intermediate
Duration	• Tablets: 4 hours • Spansules: 6-8 hours
Notes	• Tablets can be divided in two, but NOT crushed • Spansules should be swallowed whole

Lisdexamfetamine (Vyvanse)

Lisdexamfetamine (Vyvanse)	
Active ingredient	• Dextroamphetamine (DEX)
Delivery system	• Pro-drug → enzymatic transformation to DEX • Activation takes place in gut + blood
Duration	• 13 hours (children), 14 hours (adults)
Notes	• May be opened + diluted in water, juice, yogurt without loss of efficacy • NOT affected by transit time or pH changes in GI tract

Methylphenidate-Based Products

- 1 mechanism to increase NE/DA in synaptic cleft
  - **1) Block reuptake** of NE/DA into presynaptic neuron
    - Preferential effect on dopamine

- Well-established safety + efficacy profile
- Subject to controlled substance regulation in Canada

- Methylphenidate-based products
  - Methylphenidate immediate/sustained-release (Ritalin, Ritalin SR)
  - Methylphenidate CR (Biphentin, Foquest)
  - Methylphenidate OROS (Concerta)

Methylphenidate IR/SR (Ritalin, Ritalin SR)

Methylphenidate IR/SR (Ritalin, Ritalin SR)	
Active ingredient	• Methylphenidate (MPH)
Delivery system	• Ritalin: immediate • Ritalin SR: intermediate
Duration	• Ritalin: 3-4 hours • Ritalin SR: 5-6 hours
Notes	• Ritalin tablets can be divided in two • Ritalin SR tablets should be swallowed WHOLE • Do NOT crush tablets

Methylphenidate CR (Biphentin, Foquest)

Methylphenidate CR (Biphentin, Foquest)	
Active ingredient	• Methylphenidate (MPH)
Delivery system	• Multilayer beads, digested at different pH
Duration	• 10-12 hours (Biphentin) • 16 hours (Foquest)
Notes	• May be opened + sprinkled without loss in efficacy • Do NOT crush or chew beads

Methylphenidate OROS (Concerta)

Methylphenidate OROS (Concerta)	
Active ingredient	• Methylphenidate (MPH)
Delivery system	• OROS (22% IR outer layer, 78% from osmotically active trilayer tablet core)
Duration	• 12 hours
Notes	• MUST be swallowed WHOLE • Not affected by absence/presence of food • Bioavailability affected by transit time

Non-Stimulants

- Slower onset of action vs stimulants
  - Atomoxetine → 6-8 weeks
  - Guanfacine XR → 4 weeks

- **Gradual clinical changes**
  - NOT suitable if need rapid onset of action or “as needed” tx

- Start low + titrate slowly → **every 14 days**
  - Different SE than stimulants, not less

- Other medications (off-label)
  - Modafinil, bupropion, desipramine

Atomoxetine (Strattera)

Atomoxetine (Strattera)	
Mechanism	• Norepinephrine reuptake inhibitor
Duration	• Up to 24 hours (may provide continuous coverage)

Notes	• **SECOND-LINE treatment** (lower efficacy vs stimulants)
	  • Need 24 hour coverage
	  • Comorbid tics, anxiety that worsen with stimulants
	  • Resistance or SE to stimulants (incl sleep)
	  • Concurrent SUD (no known abuse potential)
	  • Concurrent enuresis
	• Should be swallow WHOLE (do NOT open)
	• NO special monitoring, watch for hepatic dysfunction
	• Poor metabolizers UNLIKELY to have toxic effects
	• Metabolized by **CYP2D6**
	• Dosing based on WEIGHT
	• Rare reports of ↑ **SUICIDAL IDEATION** (monitor)

Guanfacine XR (Intuniv XR)

Guanfacine XR (Intuniv XR)	
Mechanism	• Selective α2a-adrenergic receptor AGONIST
Duration	• Up to 24 hours (may provide continuous coverage)

Notes	• **SECOND-LINE treatment** (lower response rate)
	  • Requires close follow-up due to SE profile
	  • Can be first choice if stimulants not recommended
	  • Non-response or intolerance to stimulants
	  • Indication for **combo with stimulants** (age 6-17)
	  • Comorbid tic disorder or sig anxiety
	  • Comorbid oppositional behavior aggression
	• Adherence is essential (risk of **rebound hypertension**)
	• No known abuse potential
	• SE: somnolence, sedation (esp at start, dose changes)
	• May ↓ HR/BP (unlike stimulants, atomoxetine)
	• Can split dose to reduce SE
	• Should be swallowed WHOLE
	• Cutting/crushing will alter slow-release mechanism
	• Caution with: **3A4 inhibitors/inducers** (grapefruit), valproate, HR-lowering agents, QTc prolonging agents
	• NO ECG (unless positive cardiac history)
	• Avoid dehydration
	• Do **NOT** administer with high-fat meals

Pharmacogenetics

- Refers to **individual differences** in response to medication treatment due to genetic variation
  - May be useful re: titrating ADHD medication

- Use in treating ADHD
  - One RCT in adults with depression – use of pharmacogenetics can improve remission rates
  - More research needed – no data on tx of ADHD

- Current consensus: **NO** evidence to recommend pharmacogenetics for standard practice
  - Metabolist may effect tx response, however rates represent a small portion of many factors that affect tx response

6 Treatments Requiring Further Research

Treatments Requiring Further Research

- INSUFFICIENT EVIDENCE to recommend as alternative to standard treatments

Omega-3 fatty acids	• NOT RECOMMENDED to replace TAU • May be useful as adjunct
Phosphatidylserine	• Some evidence for improvement
High dose vitamins or mineral supplement	• NO robust evidence
Eliminating food colorants/additives	• NO good evidence
Neurofeedback	• Insufficient evidence for recommendation
Chiropractic care	• Insufficient evidence for recommendation