


ADHD Therapeutics: Understanding Common ADHD Medications used in Pediatrics

Introduction

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Review	Review Attention Deficit Hyperactivity Disorder (ADHD) and provide an overview of guideline-based treatment options.
Simplify	Simplify pharmacotherapeutic properties of common ADHD medications used in pediatrics, including stimulants, selective norepinephrine reuptake inhibitors, and alpha-adrenergic agonists.
Break down	Break down common misconceptions associated with ADHD medications.
Examine	Examine key roles for patient advocates who are supporting kids and adolescents taking ADHD medications.

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ADHD Therapeutics

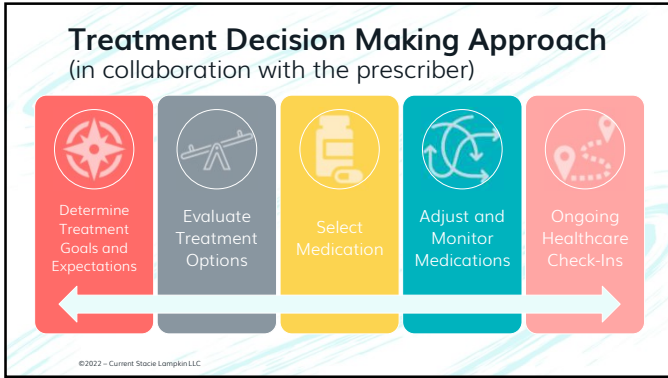
Treatment Decision Making Approach



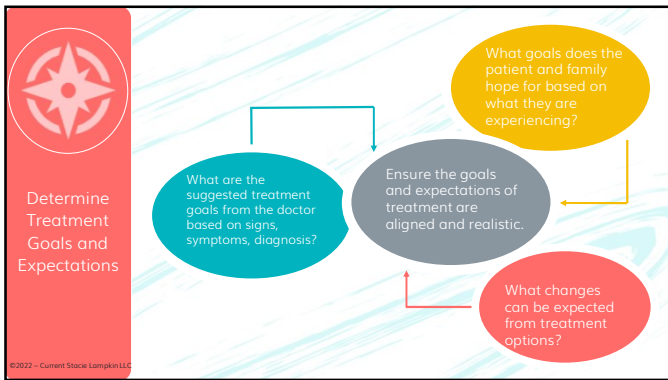
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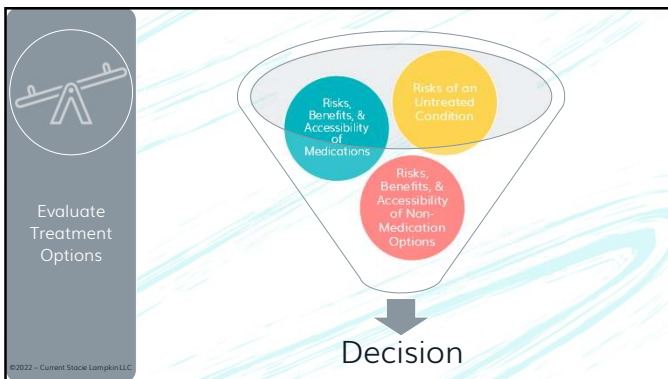
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Select Medication

Compare and contrast medications

- Efficacy
- Tolerability
- Affordability
- Accessibility
- Dosage Forms
- Onset and Duration of Action
- FDA-approved labeling
- Interactions

Consider individual patient-related factors

- Age and weight
- Pharmacogenomics
- Concurrent health concerns and diagnoses
- Signs and symptoms associated with health concern
- Family and patient's attitudes and beliefs

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Adjust and Monitor Medications

What is the health care team monitoring?

- Efficacy
- Safety

What is the patient and family monitoring?

- Efficacy
- Safety

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Adjust and Monitor Medications

Everyone responds differently to medications.

General Rule: Start low

Adjust to therapeutic dose based on efficacy and tolerability.

Titrate (increase) doses

Confirm patient is taking medication as prescribed.

- If goals are being met
 - Continue medication
 - Taper off medication
- If goals are NOT being met
 - Switch medication
 - Add medication

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What's the point?

Ongoing Healthcare Check-Ins

1 Monitor current therapy including efficacy and safety

2 Evaluate need for continuation of treatment

★ Frequency of follow-up is determined by medication and diagnosis.

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ADHD Therapeutics
Review of ADHD

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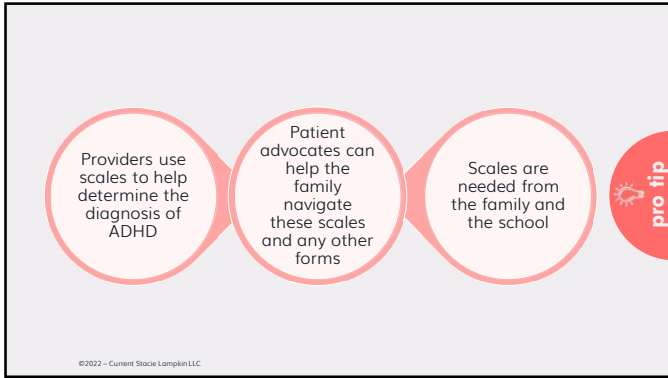
DSM-V* Diagnostic Criteria

pro tip

1. Signs and symptoms of inattention, hyperactivity, and impulsivity
2. Symptoms must interfere with functioning
3. Symptoms are present in 2 or more settings (home, school, work)
4. Alternative cause must be ruled out
5. Several symptoms were present before age 12 years old

*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
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Signs and symptoms

Inattention Symptoms	Hyperactivity and Impulsivity Symptoms
<ul style="list-style-type: none"> • Failure to provide close attention to detail, careless mistakes • Difficulty maintaining attention in play, school, or home activities • Seems not to listen, even when directly addressed • Fails to follow through (eg, homework, chores, etc) • Difficulty organizing tasks, activities, and belongings • Avoids tasks that require consistent mental effort • Loses objects required for tasks or activities (eg, school books, sports equipment, etc) • Easily distracted by irrelevant stimuli • Forgetfulness in routine activities (eg, homework, chores, etc) 	<ul style="list-style-type: none"> • Excessive fidgetiness (eg, tapping the hands or feet, squirming in seat) • Difficulty remaining seated when sitting is required (eg, at school, work, etc) • Feelings of restlessness (in adolescents) or inappropriate running around or climbing in younger children • Difficulty playing quietly • Difficult to keep up with, seeming to always be "on the go" • Excessive talking • Difficulty waiting turns • Blurting out answers too quickly • Interruption or intrusion of others

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Signs and symptoms

Predominantly inattentive

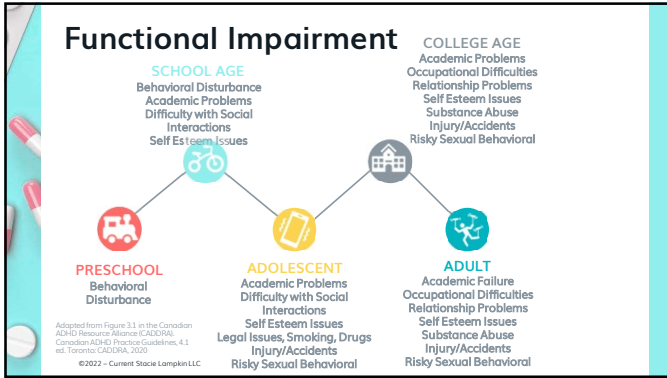
Predominantly hyperactive/impulsive

Combined presentation

Need 6 of 9 symptoms in either category or combined.

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ADHD can be diagnosed and managed in the primary care setting.

Referral might be needed for:

- Diagnostic uncertainty when comorbidities are present
- Common treatment options not working
- Patient and/or family requiring more dedicated time and support to understanding the diagnosis and/or treatment

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pro tip

Primary goal

Secondary goals

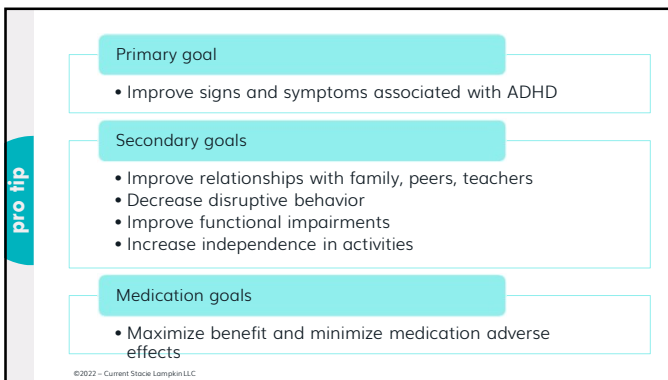
Medication goals

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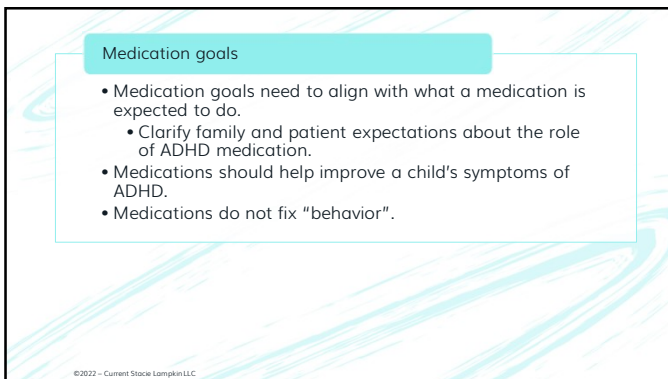
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Common ADHD Medications

Overview of Treatment Options



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Psychosocial Treatment

Numerous cognitive and behavioral approaches can be used to support kids, adolescents, and adults with ADHD




- ⇒ Cognitive behavioral therapy
- ⇒ Behavioral interventions
- ⇒ Parent training
- ⇒ Cognitive training
- ⇒ Social skills training

Due to misconceptions some families may be resistant to psychosocial treatments.

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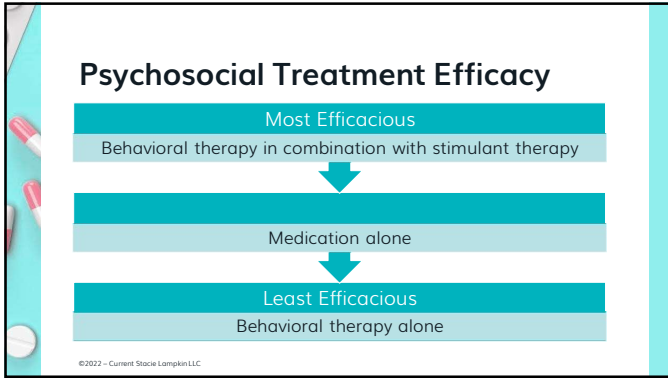
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Psychosocial Treatment Notes

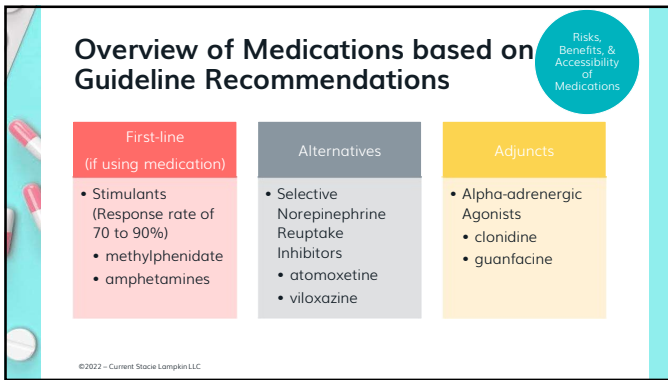
-  Guidelines recommend psychosocial treatment before medications in preschoolers
-  Psychosocial treatment requires involvement from parents, teachers and any other caregivers
-  Psychosocial treatment may not be available and may be difficult to access

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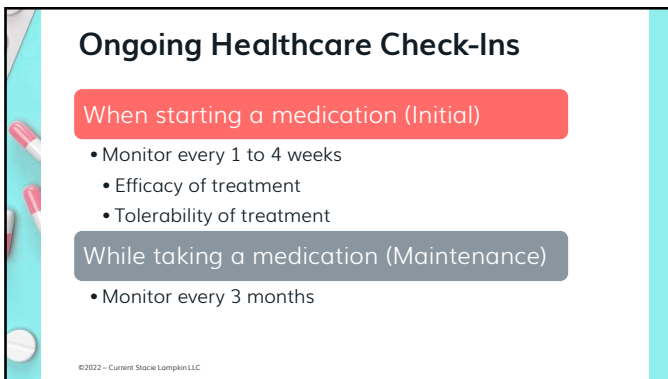
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Common ADHD Medications

Stimulants



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Stimulant Products List

Methylphenidates	Amphetamines
<ul style="list-style-type: none"> Ritalin, Methylin Focalin (dexmethylphenidate) 	<ul style="list-style-type: none"> Adderall (amphetamine/dextroamphetamine) Dexedrine, Zenzedi, Procentra (dextroamphetamine)
Ritalin SR, Metadate ER	<ul style="list-style-type: none"> Evekeo (amphetamine salt) Dexedrine (dextroamphetamine)
Daytrana	Vyvanse (lisdexamfetamine)
<ul style="list-style-type: none"> Metadate CD, Ritalin LA, Concerta, Apetensio XR, Quilivant XR, Quilichew ER, Adhansia, Contempla Focalin XR (dexmethylphenidate) Azstaryz (serdexmethylphenidate and dexmethylphenidate) 	<ul style="list-style-type: none"> Adderall XR, Mydayis (amphetamine/dextroamphetamine) Adzenyz XR, Dynavel (amphetamine salt)
Jornay PM	

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What is a stimulant?

Definition per the Drug Enforcement Administration (DEA)

"Stimulants speed up the body's systems."

Stimulants include prescription medications and illicit drugs.

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What is a stimulant?

Why give a stimulant to a child who is already hyperactive?

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What is a stimulant?

chemical balance

Certain neurotransmitters in the brain seem to be reduced in the presynaptic nerve terminals in people with ADHD

Dopamine	Norepinephrine
<ul style="list-style-type: none"> Involved with the reward system Responsible for regulating learning, motivation, goal setting, and memory 	<ul style="list-style-type: none"> Responsible for alertness and attention

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What is a stimulant?

Mechanism of Action of Stimulants

Methylphenidates	Amphetamines
<ul style="list-style-type: none"> Appears to stimulate the cerebral cortex and subcortical structures Blocks the reuptake of norepinephrine and dopamine into presynaptic neurons 	<ul style="list-style-type: none"> Appears to stimulate the cerebral cortex and subcortical structures Promote dopamine and norepinephrine from their storage sites in the presynaptic nerve terminals

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What is a stimulant?

Both methylphenidates and amphetamines "increase" norepinephrine and dopamine BUT the how is different.

Therefore, people often respond differently to a methylphenidate product versus an amphetamine product.

Leads to wide variation from person to person in:

- Response/efficacy, tolerability, and duration of action

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What to expect when starting a stimulant?

Stimulants are controlled substances (CII)

- Additional laws and regulations impact prescribing and dispensing

Most stimulants have FDA-approved labeling for ≥ 6 years old

- Amphetamine IR products are approved for ≥ 3 years old.
- Some newer formulations are approved for ≥ 13 years old.

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What to expect when starting a stimulant?

Medication should be started at the recommended starting dose for that product

Increased dosing will likely be needed to get optimal benefit

Doses can be increased every week	Logistically dosing is often adjusted monthly
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What to expect when starting a stimulant?

Some therapeutic benefits should be seen within a few days

Benefit will only occur when the medication is in a person's body

Based on the duration of action the specific medication

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Products list

	Methylphenidates	Amphetamines
Short Acting (-4-6 hours)	<ul style="list-style-type: none"> Ritalin, Methylin Focalin (dexmethylphenidate) 	<ul style="list-style-type: none"> Adderall (amphetamine/dextroamphetamine) Dexedrine, Zenzedi, Procentra (dextroamphetamines)
Intermediate Acting (-6-8 hours)	Ritalin SR, Metadate ER	<ul style="list-style-type: none"> Evekeo (amphetamine salt) Dexedrine (dextroamphetamine)
Long Acting (-10 hours)	Daytrana	Vyvanse (lisdexamfetamine)
Long Acting with Rapid Onsets (-8-12 hours)	<ul style="list-style-type: none"> Metadate CD, Ritalin LA, Concerta, Apetensio XR, Quilivant XR, Quillichew ER, Adhansia, Contempla Focalin XR (dexmethylphenidate) Azstaryz (serdexmethylphenidate and dexmethylphenidate) 	<ul style="list-style-type: none"> Adderall XR, Mydayis (amphetamine/dextroamphetamine) Adzenyz XR, Dynavel (amphetamine salt)
Long Acting with Delayed Onset	Jornay PM	

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Products list

Long-acting with rapid onsets (preferred)	Short-acting
<ul style="list-style-type: none"> Duration ranges from 8 to 12 hours depending on product and person Some newer products are even longer Must give in the morning Don't give too late if morning dose was missed Prevents the need for a dose in school or work Maintains more steady symptom control 	<ul style="list-style-type: none"> Duration ranges from 4 to 6 hours depending on product and person Often given in the morning and at noon May be added on in the afternoon if need medication coverage into the evening May be required when more flexibility is needed due to side effects on a long-acting medication

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But there are still so many options...

Next consider:

- What is affordable?
- What will the child or adolescent take?
- What has already been trialed?

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Which specific product is best is yet to be determined.

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Key Points

1. If started on **an amphetamine** product and it isn't meeting goals after titrating dose and taking for 3 months switch to **a methylphenidate** product.
2. If trialed two stimulants switch to another stimulant product or a non-stimulant or re-evaluate diagnosis.

⇒ If experiencing side effects, make adjustments based on specific side effects.

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What are common side effects that require monitoring?

```
graph TD; A[Decreased Appetite] --> B[Concerning when results in decrease in growth]; B --> C[Monitor height and weight];
```

Decreased Appetite

Concerning when results in decrease in growth

Monitor height and weight

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What are common side effects that require monitoring?

```
graph TD; A[Sleep Disturbance] --> B[Important to note any sleep disturbances before starting medication]; B --> C[Confirm medication is not given too late in the day];
```

Sleep Disturbance

Important to note any sleep disturbances before starting medication

Confirm medication is not given too late in the day

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What are common side effects that require monitoring?

```
graph TD; A[Moodiness and Irritability] --> B[If experience during the time medications should be having an effect,]; A --> C[If experienced when medications are wearing off,]; B --> D[Could be too high of a dose]; C --> E[Could be rebound symptoms];
```

Moodiness and Irritability

If experience during the time medications should be having an effect,

Could be too high of a dose

If experienced when medications are wearing off,

Could be rebound symptoms

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What are common side effects that require monitoring?

```
graph TD; A[Increased blood pressure] --> B[Monitored by the doctor]
```

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What about warnings, precautions, and contraindications?

Hypersensitivity or allergy to the products • Treatment with MAOI and for up to 14 days after discontinuation • Glaucoma (narrow angle) • Untreated hyperthyroidism • Seizure disorders • Tic disorders • Moderate to severe hypertension • Cardiovascular disease • History of bipolar or mania or psychosis • Abuse Potential • Anxiety • Renal impairment • Pregnancy and Lactation • Peripheral vasculopathy including Raynaud's Phenomenon • Priapism

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Cardiovascular Events

Controversy surrounding the cardiovascular safety of stimulants exists

- ⇒ Increased dopamine and norepinephrine can increase heart rate and blood pressure
- ⇒ Routine ECG screening or cardiologist clearance is not recommended unless patients have a preexisting cardiac disease or a family history sudden cardiac death

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Abuse Potential

- ⇒ Research has shown that stimulant use in kids and adolescents with a diagnosis of ADHD has no effect on future substance misuse.
 - ⇒ Untreated ADHD has a risk of substance misuse and stimulants have not been shown to increase this.
- ⇒ Diversion of stimulants to people without a diagnosis of ADHD is a concern.
- ⇒ If a person concurrently has a substance-use disorder, both require treatment.

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Common ADHD Medications

Selective Norepinephrine Reuptake Inhibitors



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What is an SNRI?

- Non-stimulant
- Two products
 - Atomoxetine
 - Viloxazine
- Impact norepinephrine only
 - Selectively inhibits the reuptake of norepinephrine
- FDA-approved labeling in ≥6 years old

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What is an SNRI?

Consider using when:

- 2-3 stimulant medications have not worked
- A patient is experiencing side effects with stimulants such as anxiety, insomnia, or worsened tics
- Symptom coverage is required throughout the entire day
- There are concerns about substance misuse with a stimulant

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What to expect when starting an SNRI?

Atomoxetine (Strattera) <ul style="list-style-type: none"> • May be administered once or twice daily • Titrate every 2 to 4 weeks to effect 	Viloxazine (Qelbree) <ul style="list-style-type: none"> • Administer once daily • Titrate weekly to effect
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Therapeutic benefit may not be seen for 1 to 2 months
 ↳ Full effect may take effect 3 months on a particular dose

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What to expect when starting an SNRI?

Atomoxetine (Strattera) <ul style="list-style-type: none"> • May be administered once or twice daily • Titrate every 2 to 4 weeks to effect <p>↓</p> <p>Do not crush, chew, or open capsule</p>	Viloxazine (Qelbree) <ul style="list-style-type: none"> • Administer once daily • Titrate weekly to effect <p>↓</p> <p>Swallow capsules whole or open and sprinkle entire contents on teaspoonful of applesauce</p>
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What are common side effects that require monitoring?

- Hypertension, tachycardia
- Decreased appetite
- Aggression, irritability
- Insomnia, somnolence
- Headache
- Dry mouth, nausea, abdominal pain
- Decreased libido

Monitor: heart rate, blood pressure, height, weight, aggression

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What about warnings, precautions, and contraindications?

Hypersensitivity or allergy to the products • Treatment with MAOI and for up to 14 days after discontinuation.

- Narrow angle glaucoma
- Current or history of pheochromocytoma
- Cardiovascular disorders
- Drug interactions
- CYP2D6 poor metabolizers (atomoxetine)
- Peripheral vasculopathy including Raynaud's Phenomenon
- Priapism
- Urinary retention
- Signs / symptoms of liver injury
- History of bipolar disorder
- Suicide ideation

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Common ADHD Medications

Alpha-adrenergic Agonists



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What is an Alpha-adrenergic Agonists?

- Non-stimulant
- Two products
 - Clonidine
 - Guanfacine
- Unknown how it works for ADHD
 - Thought to bind to the prefrontal cortex which impacts working memory and behavioral inhibition

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What is an Alpha-adrenergic Agonists?

- An adjunct option for ADHD
 - Symptom coverage into the evening
 - Patients who experience insomnia or elevated blood pressure on stimulants
- Less frequently an alternative for ADHD
 - Patients with tic disorders, substance-use disorders, anxiety, oppositional behaviors, or aggression
 - Stimulants nor SNRIs have worked

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What to expect when starting an Alpha-adrenergic Agonists?

May take 1 to 2 weeks to notice a therapeutic effect

Clonidine	Guanfacine
Kapvay (extended release) <ul style="list-style-type: none"> Start once daily at bedtime Titrate every 7 days until desired response or maximum dose 	Intuniv (extended release) <ul style="list-style-type: none"> Give once daily at bedtime or in the morning Titrate every 7 days until desired response or maximum dose
Catapress (immediate release) <ul style="list-style-type: none"> Start once daily at bedtime Increase every 3 to 7 days to twice daily, then 3 times daily, then 4 times daily 	Tenex (immediate release) <ul style="list-style-type: none"> Give once daily at bedtime Increase every 3 to 4 days to twice daily, then 3 times daily, then 4 times daily

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What to expect when starting an Alpha-adrenergic Agonists?

Do not discontinue	Off-label use with	Administration
<ul style="list-style-type: none"> Increased heart rate and rebound hypertension Taper the dose down and monitor blood pressure and pulse following dosage reduction/discontinuation 	<ul style="list-style-type: none"> Only the ER products have FDA-approved labeling for ADHD in ≥6 years old 	<ul style="list-style-type: none"> Do not crush, break, or chew the extended-release dosage forms

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What are common side effects that require monitoring?

- Sedation (clonidine is more sedating than guanfacine)
 - Sedation tolerance may occur in 2-3 weeks
- Nausea, constipation
- Dizziness, headache
- Lower blood pressure
 - Monitor blood pressure

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What about warnings, precautions, and contraindications?

Hypersensitivity or allergy to the products • Hepatic impairment • Kidney impairment • Somnolence and sedation • Risk of hypotension • Drug interactions • Inability for parents or patients to ensure regular daily dosage (due to the risk of rebound hypertension when stopped abruptly)

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Key Roles for Patient Advocates

Medication Off-label Use, Access, and Cost



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Medications can be used Off-label

Off-label drug use is when a drug is used for an unapproved reason:

- Dose
- Age
- Indication
- Route of administration
- Contraindications

Unlicensed medicines are used when there is no commercially available formulation:


- Extemporaneous compounding
- Importation
- Use of chemicals

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Medications can be used Off-label

Guideline recommendations and FDA-approved labeling do not always align



ADHD medications will be used off-label across the lifespan

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Common Medication Access Barriers for ADHD

Stimulants are controlled substances

- Regulated by federal and state laws
- There are more restrictions and barriers than medications that are not controlled substances

Finding a medication product the kid or adolescent can take

- Make sure to communicate if a child can swallow pills
- Ask questions about how to administer the medication being prescribed

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Cost and Insurance Barriers

Doctor's offices

- Often do not know the cost of drugs or if a medication is covered by insurance

Pharmacies

- Can tell you a cash price without a prescription
- Can tell you the insurance price WITH a prescription

Insurance companies

- Can tell you if a drug is on formulary but not necessarily the price


Prior authorizations often needed for "newer" medications

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Key Roles for Patient Advocates

Navigating Concurrent Conditions and Medications



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Per the CDC

Approximately 64% of children with ADHD also have at least one other neuropsychiatric condition

- ⇒ Behavioral or conduct disorders
- ⇒ Anxiety
- ⇒ Depression
- ⇒ Autism spectrum disorder (ASD)
- ⇒ Tourette syndrome

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Medication Considerations and Concurrent Conditions

If another concurrent condition is diagnosed at the same time:

- In general, the most impairing condition is treated first
- Polypharmacy will likely be needed, but usually only one medication should be started or adjusted at a time

If a person is already being treated for a concurrent condition:


- Monitor more closely for side effects
- Ask about drug interactions

Treatment of ADHD may "unmask" another condition

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Key Roles for Patient Advocates
ADHD Medication at School



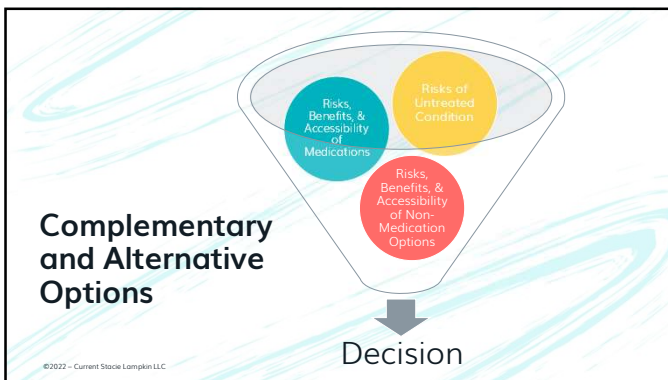
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Key Roles for Patient Advocates
Medications and Supplements

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Complementary and Alternative Options

[ADHD and Complementary Health Approaches | NCCIH \(nih.gov\)](https://www.nccih.nih.gov/)

[Understanding ADHD: Complementary and Alternative Treatment of ADHD \(ucdavis.edu\)](https://www.ucdavis.edu/)

[ADHD Alternative Treatment | Understood - For learning and thinking differences](https://www.understood.org/)

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Complementary and Alternative Options

Overwhelming

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Complementary and Alternative Options

Navigating a new diagnosis of ADHD

Deciding if medication is the right choice

Learning about complementary and alternative options

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Complementary and Alternative Options

Overwhelming

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Complementary and Alternative Options

Supplements with therapeutic properties

Can confound the efficacy and tolerability of medications May interact with medications

Do no start medications and supplements at the same time

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ADHD Therapeutics: Understanding Common ADHD Medications used in Pediatrics

Thank You !!

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