

ADHD Therapeutics: Understanding Common ADHD Medications used in Pediatrics

Introduction

Stacie Lampkin, PharmD, BCPPS, BCPA, CA



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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.

ADHD Therapeutics

Treatment Decision Making Approach

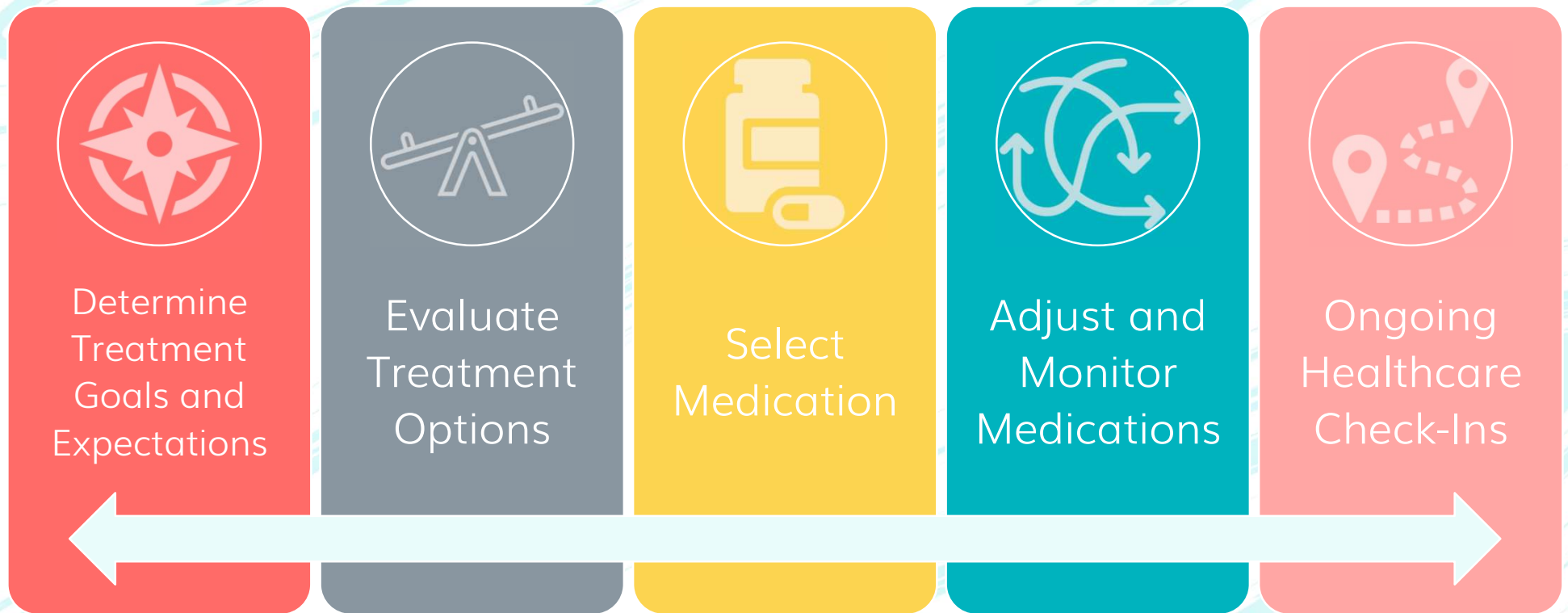


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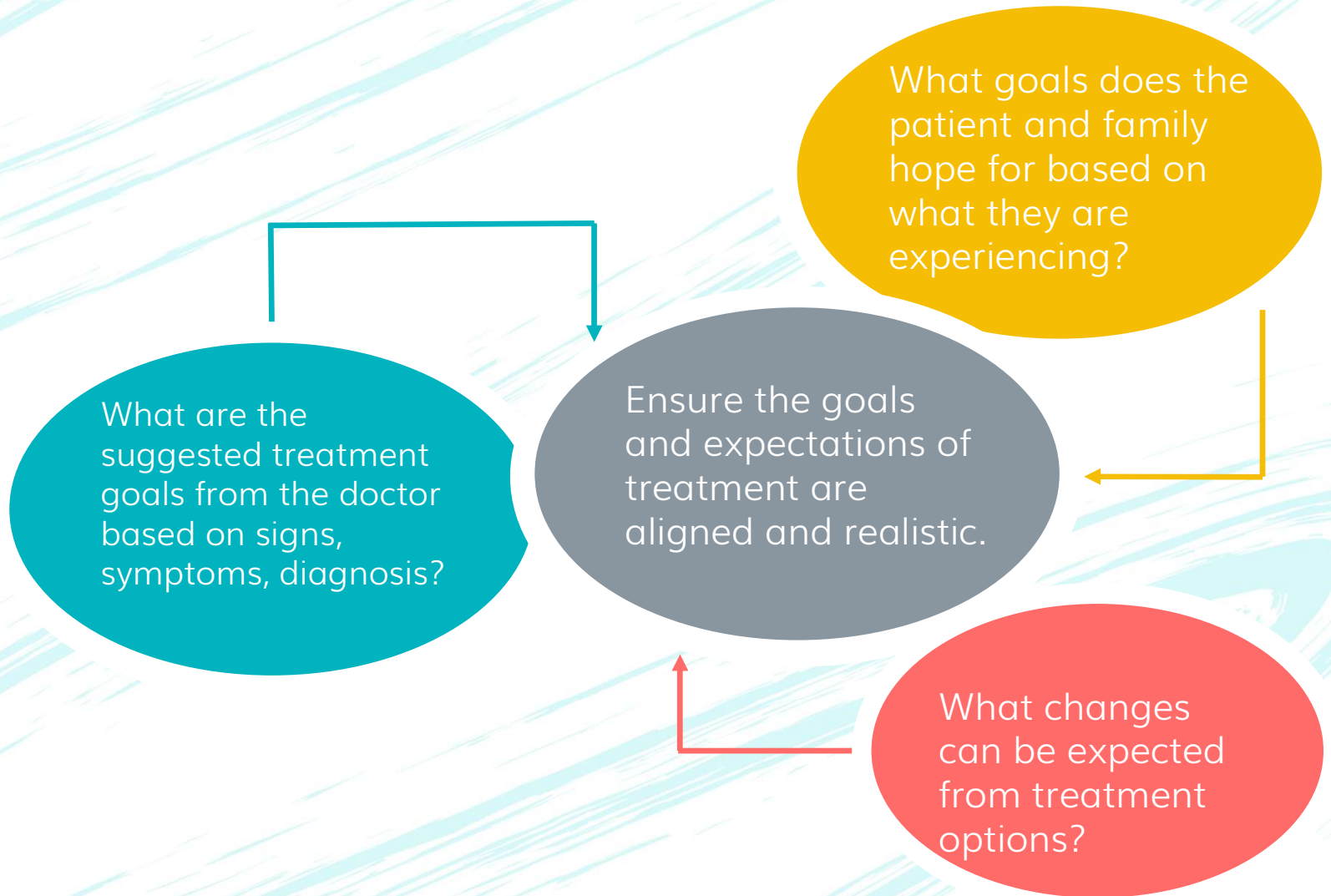
Treatment Decision Making Approach

(in collaboration with the prescriber)



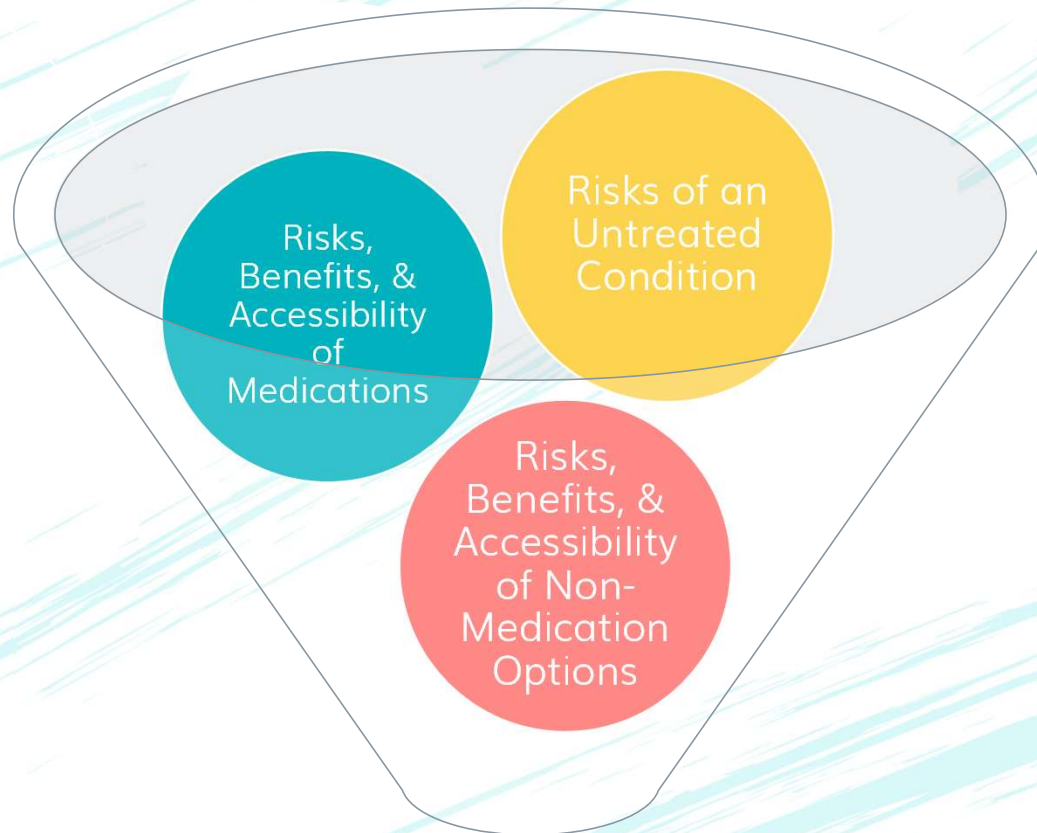


Determine Treatment Goals and Expectations





Evaluate Treatment Options



Decision



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



Adjust and Monitor Medications

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What is the health care team monitoring?

- Efficacy
- Safety

What is the patient and family monitoring?

- Efficacy
- Safety



Adjust and Monitor Medications

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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

If goals are NOT being met

Continue medication

Taper off medication

Switch medication

Add medication

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.

ADHD Therapeutics

Review of ADHD



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DSM-V* Diagnostic Criteria

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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Providers use scales to help determine the diagnosis of ADHD

Patient advocates can help the family navigate these scales and any other forms

Scales are needed from the family and the school



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Signs and symptoms

Inattention Symptoms

- 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)

Hyperactivity and Impulsivity Symptoms

- 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

Signs and symptoms

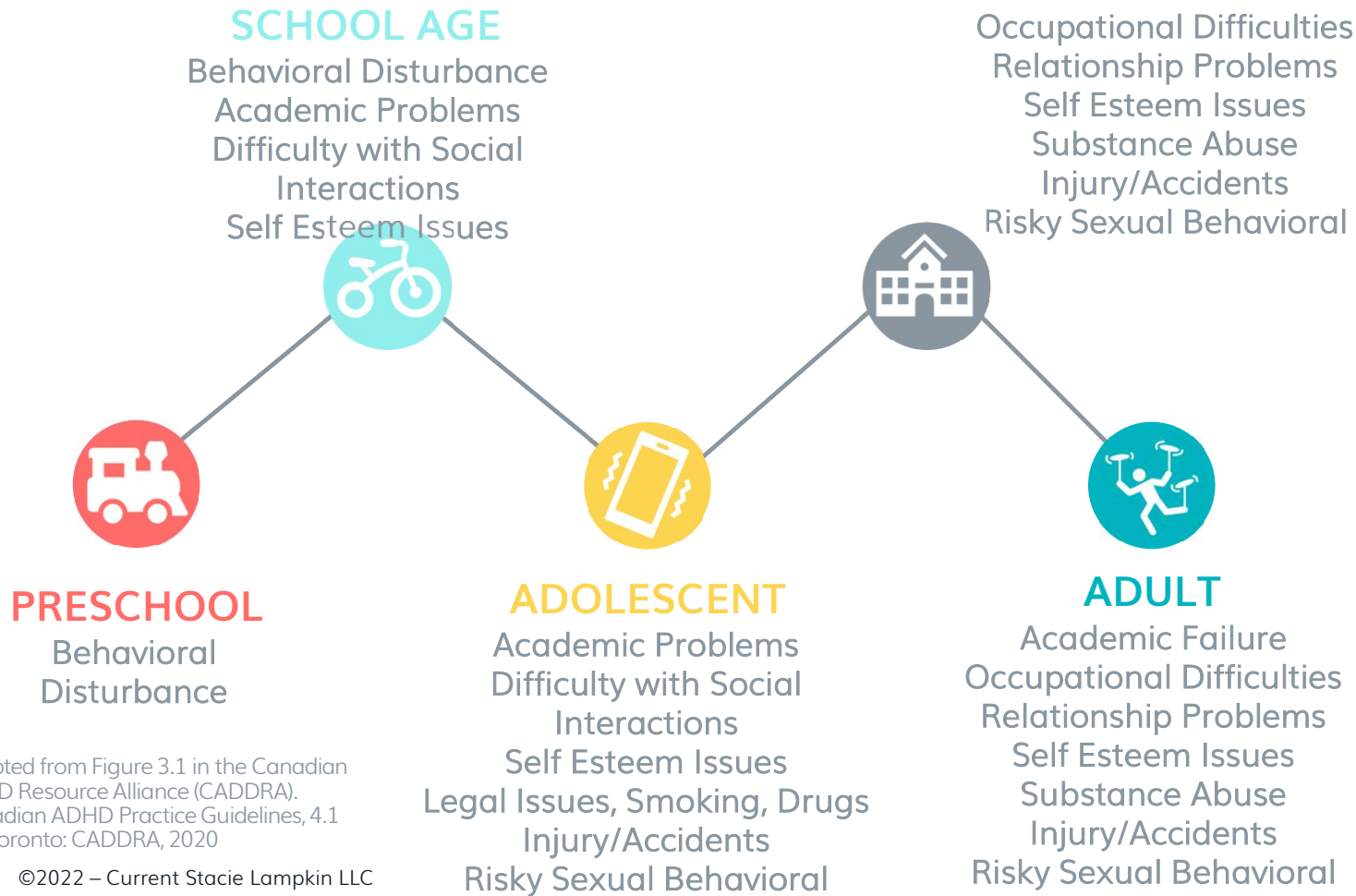
Predominantly
inattentive

Predominantly
hyperactive/
impulsive

Combined
presentation

Need 6 of 9 symptoms in either category or combined.

Functional Impairment



Adapted from Figure 3.1 in the Canadian ADHD Resource Alliance (CADDRA). Canadian ADHD Practice Guidelines, 4.1 ed. Toronto: CADDRA, 2020

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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

Primary goal

Secondary goals

Medication goals



The most important goals are the goals of the patient and family.



pro tip

Primary goal

- Improve signs and symptoms associated with ADHD

Secondary goals

- Improve relationships with family, peers, teachers
- Decrease disruptive behavior
- Improve functional impairments
- Increase independence in activities

Medication goals

- Maximize benefit and minimize medication adverse effects

Medication goals

- Medication goals need to align with what a medication is expected to do.
 - Clarify family and patient expectations about the role of ADHD medication.
- Medications should help improve a child's symptoms of ADHD.
- Medications do not fix "behavior".

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.

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

Psychosocial Treatment Efficacy

Most Efficacious

Behavioral therapy in combination with stimulant therapy



Medication alone



Least Efficacious

Behavioral therapy alone

Overview of Medications based on Guideline Recommendations

Risks,
Benefits, &
Accessibility
of
Medications

First-line (if using medication)

- Stimulants
(Response rate of 70 to 90%)
 - methylphenidate
 - amphetamines

Alternatives

- Selective Norepinephrine Reuptake Inhibitors
 - atomoxetine
 - viloxazine

Adjuncts

- Alpha-adrenergic Agonists
 - clonidine
 - guanfacine



Ongoing Healthcare Check-Ins

When starting a medication (Initial)

- Monitor every 1 to 4 weeks
 - Efficacy of treatment
 - Tolerability of treatment

While taking a medication (Maintenance)

- Monitor every 3 months

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 (dextroamphetamines)
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, Quillivant 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)
Jornay PM	



What is a stimulant?

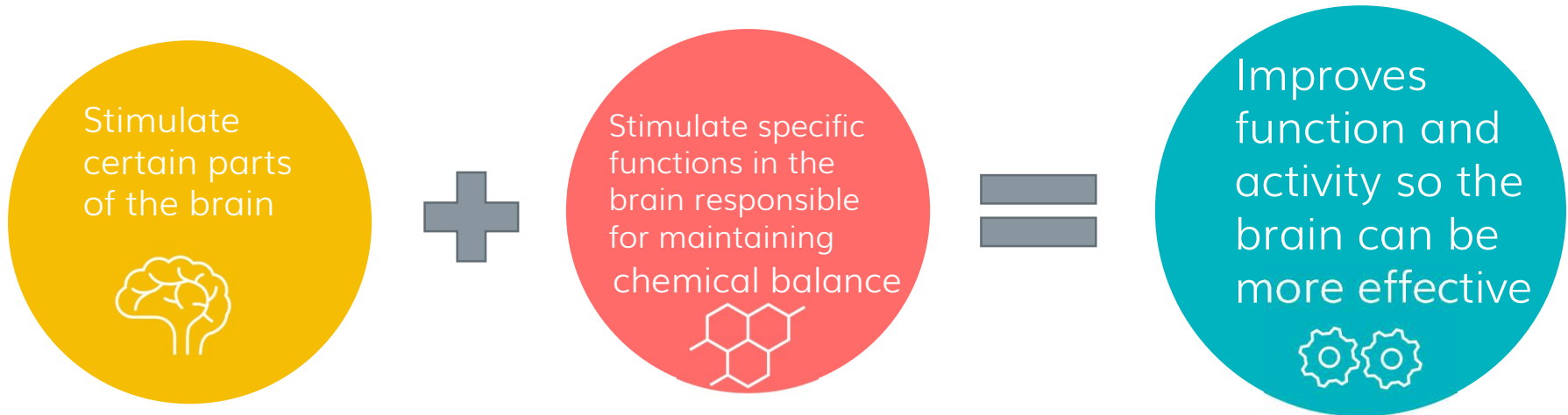
Definition per the Drug Enforcement Administration (DEA)

"Stimulants speed up the body's systems."

Stimulants include prescription medications and illicit drugs.

What is a stimulant?

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



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

- Involved with the reward system
- Responsible for regulating learning, motivation, goal setting, and memory

Norepinephrine

- Responsible for alertness and attention

What is a stimulant?

Mechanism of Action of Stimulants

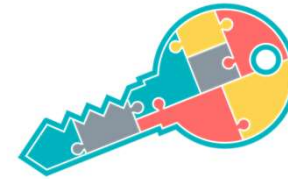
Methylphenidates

- Appears to **stimulate** the cerebral cortex and subcortical structures
- Blocks the reuptake of **norepinephrine** and **dopamine** into presynaptic neurons

Amphetamines

- Appears to **stimulate** the cerebral cortex and subcortical structures
- Promote **dopamine** and **norepinephrine** from their storage sites in the presynaptic nerve terminals

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

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.

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

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

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, Quillivant 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	



Products list

Long-acting with rapid onsets (preferred)




- 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

Short-acting

- 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

But there are still so many options...

Next consider:

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

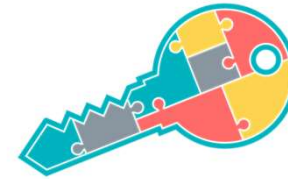


Which specific product is
best is yet to be
determined.



pro tip

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.



What are common side effects that require monitoring?

Decreased Appetite



Concerning when results in decrease in growth



Monitor height and weight

What are common side effects that require monitoring?

Sleep Disturbance

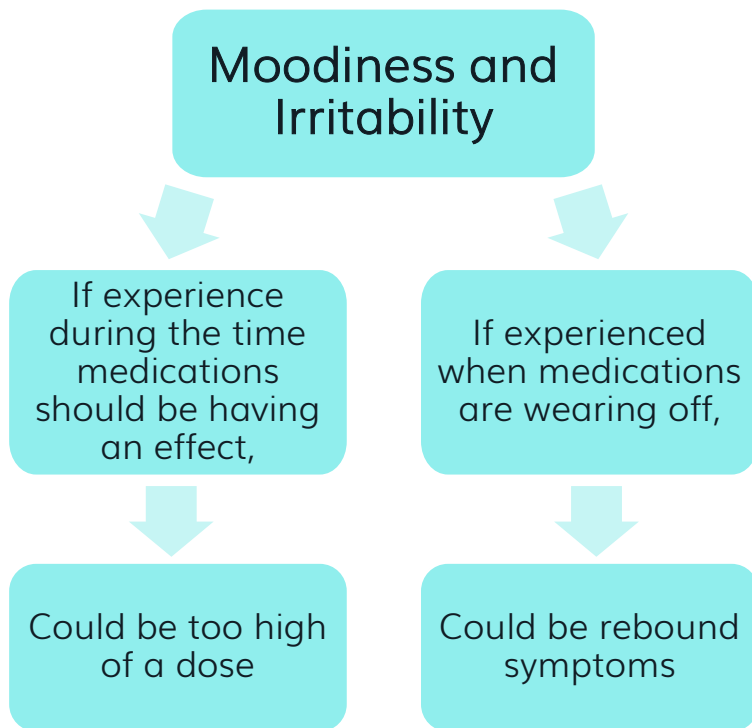


Important to note any sleep disturbances before starting medication



Confirm medication is not given too late in the day

What are common side effects that require monitoring?



What are common side effects that require monitoring?

Increased blood pressure



Monitored by the doctor

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



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

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.

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

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

What to expect when starting an SNRI?

Atomoxetine (Strattera)

- May be administered once or twice daily
- Titrate every 2 to 4 weeks to effect

Viloxazine (Qelbree)

- Administer once daily
- Titrate weekly to effect

Therapeutic benefit may not be seen for 1 to 2 months

⇒ Full effect may take effect 3 months on a particular dose

What to expect when starting an SNRI?

Atomoxetine (Strattera)

- May be administered once or twice daily
- Titrate every 2 to 4 weeks to effect



Do not crush, chew, or open capsule

Viloxazine (Qelbree)

- Administer once daily
- Titrate weekly to effect



Swallow capsules whole or open and sprinkle entire contents on teaspoonful of applesauce

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

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

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

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

What to expect when starting an Alpha-adrenergic Agonists?

May take 1 to 2 weeks to notice a therapeutic effect

Clonidine

Kapvay (extended release)

- Start once daily at bedtime
- Titrate every 7 days until desired response or maximum dose

Catapress (immediate release)

- Start once daily at bedtime
- Increase every 3 to 7 days to twice daily, then 3 times daily, then 4 times daily

Guanfacine

Intuniv (extended release)

- Give once daily at bedtime or in the morning
- Titrate every 7 days until desired response or maximum dose

Tenex (immediate release)

- Give once daily at bedtime
- Increase every 3 to 4 days to twice daily, then 3 times daily, then 4 times daily

What to expect when starting an Alpha-adrenergic Agonists?

Do not discontinue

- Increased heart rate and rebound hypertension
- Taper the dose down and monitor blood pressure and pulse following dosage reduction/ discontinuation

Off-label use with

- Only the ER products have FDA-approved labeling for ADHD in ≥ 6 years old

Administration

- Do not crush, break, or chew the extended-release dosage forms

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



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)

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:

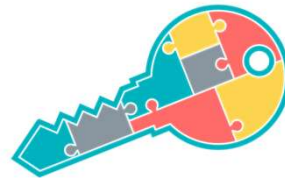
- Dose
- Age
- Indication
- Route of administration
- Contraindications

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

- Extemporaneous compounding
- Importation
- Use of chemicals

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



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

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

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



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

Key Roles for Patient Advocates

ADHD Medication at School



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Key Roles for Patient Advocates

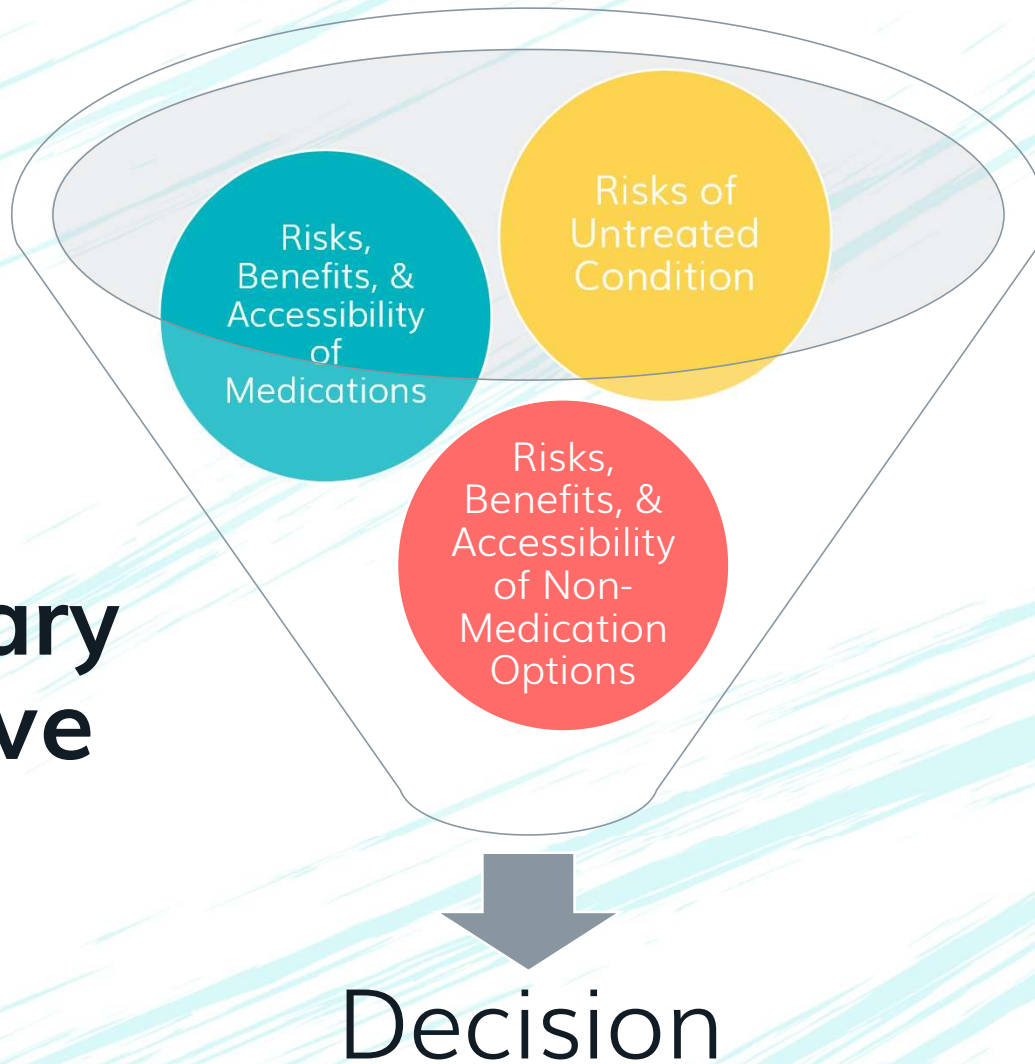
Medications and Supplements



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Complementary and Alternative Options





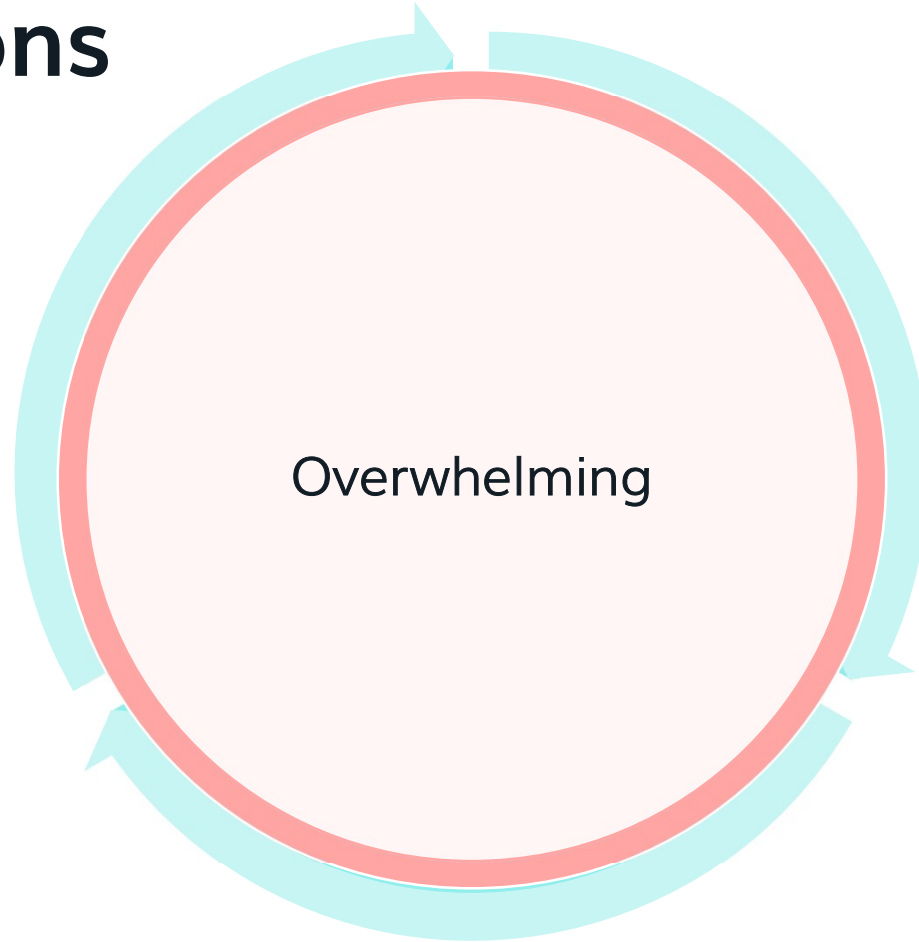
Complementary and Alternative Options

[ADHD and Complementary Health Approaches | NCCIH \(nih.gov\)](#)

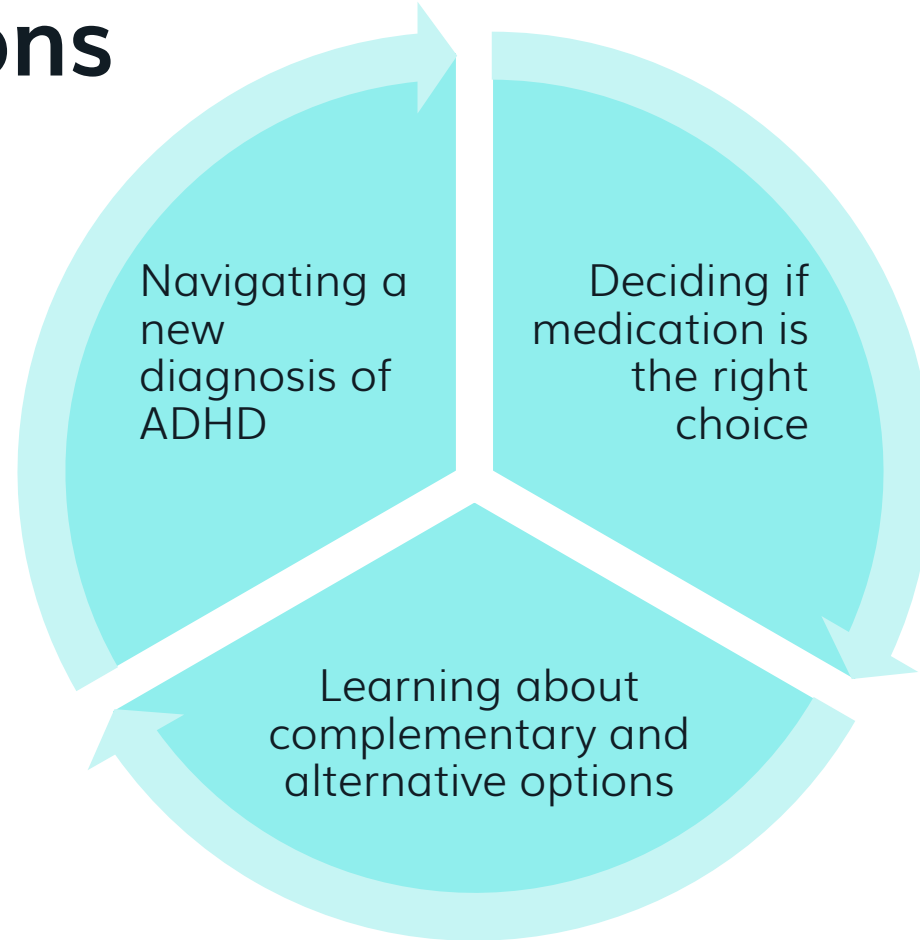
[Understanding ADHD: Complementary and Alternative Treatment of ADHD \(ucdavis.edu\)](#)

[ADHD Alternative Treatment | Understood - For learning and thinking differences](#)

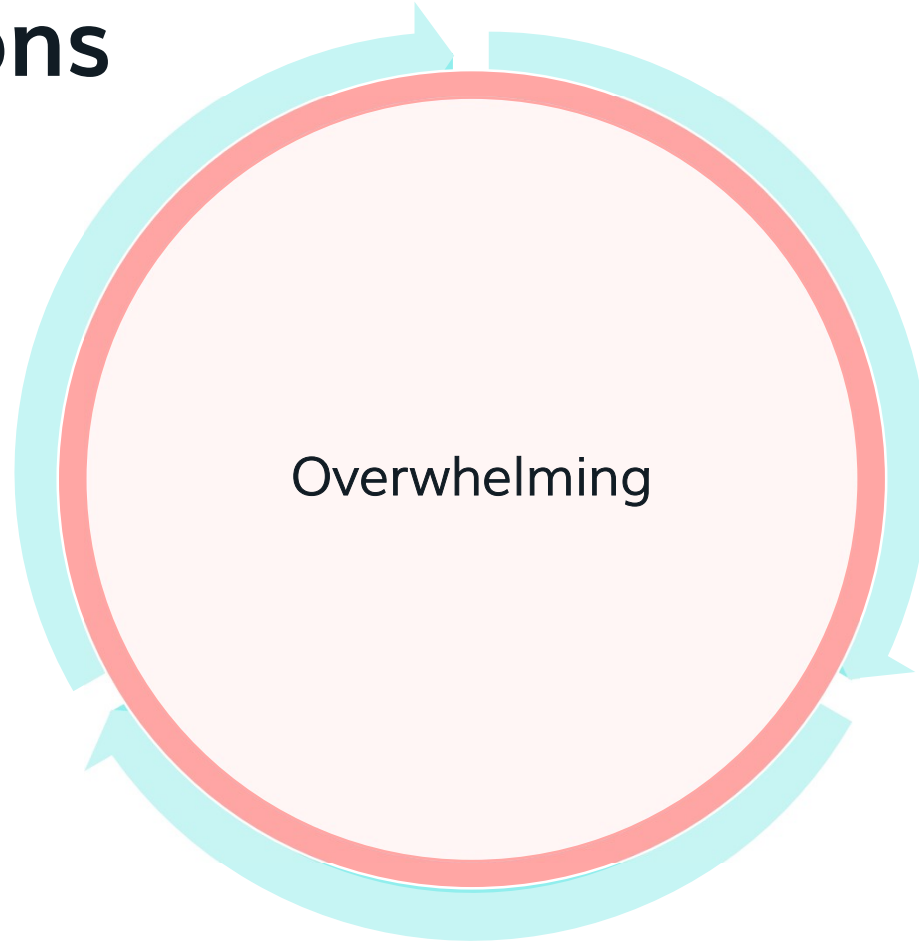
Complementary and Alternative Options



Complementary and Alternative Options



Complementary and Alternative Options



Complementary and Alternative Options



Supplements with therapeutic properties

Can confound the efficacy and tolerability of medications

May interact with medications



Do not start medications and supplements at the same time

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Thank You !! 😊

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