PMHI-CHCO

First Edition

PSYCHOTROPIC HANDBOOK

Psychiatric Pharmacy Team

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Attention-Deficit/Hyperactivity Disorder (ADHD)

Overview

- ADHD is a neurodevelopmental disorder that is characterized by age-inappropriate and impairing levels of inattention, hyperactivity, impulsivity or a combination. It affects approximately 10% of children in the United States, where males are twice as likely to be diagnosed in childhood.
- DSM-5-TR diagnosis based on persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development for at least 6 months.
- Common comorbidities: Oppositional defiant disorder, conduct disorder, mood dysregulation disorder, specific learning disorder, anxiety disorders and MDD, ASD

Pharmacological treatment options:

- First line: stimulants (methylphenidates > amphetamines): 65-85% of individuals achieve therapeutic response with stimulant use
    - Methylphenidates: better tolerability than amphetamines
        - Proposed MOA: Allosteric inhibition of DAT/NET; inhibits monoamine oxidase
        - Metabolism: De-esterified to ritalinic acid (via CES-1_
        - Typical dosing: 0.3-2 mg/kg/day
    - Amphetamines:
        - Proposed MOA: Competitive inhibitor of DAT/NET; Competitive inhibitor of VMAT2 at high doses; inhibits monoamine oxidase
        - Metabolism: Substrate of CYP2D6
        - Typical dosing: 0.3-1 mg/kg/day
            - Amphetamines are 2x more potent than methylphenidate
- Alternatives: alpha-2 agonists, atomoxetine, viloxazine, bupropion

Patient monitoring parameters for stimulants:

- Baseline: Assessment using a targeted cardiac history of the child and family, and physical exam of child with an ECG and/or pediatric cardiology consult when indicated
- Baseline and ongoing: height, weight, heart rate, blood pressure
- Pharmacogenetic considerations: CYP2D6 interactions with amphetamines, atomoxetine

Methylphenidates (C-II)	
Short Acting Onset: 20-60 minutes Duration: 3-5 hours Frequency: BID-TID	• Ritalin • Methylin chew, oral suspension • Focalin (dexmethylphenidate)*
Intermediate Acting Onset: 1 hour Duration: 3-8 hours Frequency: Daily-BID	• Metadate ER, Methylin ER, Ritalin SR
Long Acting Onset: 1 hour Duration: 8-12 hours Frequency: Daily ^onset ~8-10 hours after administration	• Concerta (20IR/40ER/40ER; OROS, osmotic release oral system) • Daytrana (Transdermal, controlled release) • Metadate CD (30IR/70ER) • Ritalin LA (50IR/50ER; SODAS, spheroidal oral drug absorption system) • Aptensio XR (40IR/60ER) • Quillichew (30IR/70ER) • Quillivant (20IR/80ER) • Focalin XR (dexmethylphenidate)* • Cotempla XR (25IR/75ER) • **Jornay PM (delayed release, extended release); administered QPM^**
Longer Acting Onset: 1 hour Duration: 12-16 hours	• **Azstarys (30IR dexmethylphenidate; 70 serdexmethylphenidate prodrug)**

*Dexmethylphenidate (*d*-MPH) 2x more potent than methylphenidate

Unless otherwise noted, MPH formulations are all racemic formulations (1:1 *d*-MPH to *l*-MPH)

CD: controlled dose; IR: immediate release; ER/XR: extended release; SR: sustained release

Amphetamines (C-II)	
Short Acting Onset: 20-60 minutes Duration: 6 hours Frequency: BID-TID	• Adderall IR (mixed salts) • Dexedrine, DextroStat, Procentra (solution), Zenzedi • Evekeo tablets, ODT (1:1 *d* to *l* amphetamine sulfate base)
Intermediate Acting Onset: 60-90 minutes Duration: 6-8 hours Frequency: Daily-BID	• Dexedrine spansule (dextroamphetamine, sustained release capsule = spansule)
Long Acting Onset: 1 hour Duration: 8-12 hours Frequency: Daily	• Adderall XR (50IR/50ER) • Vyvanse (lisdexamfetamine), Vyvanse chewable • **Dyanavel XR (3:1 *d* to *l* amphetamine sulfate suspension)** • Adzenys XR-ODT (50IR/50ER) • *Adzenys ER (1.25mg/mL oral suspension; 50IR/50ER) → discontinued* • **Xelstrym (Dextroamphetamine) patch**
Longer Acting Onset: 1 hour Duration: 12-16 hours Frequency: Daily	• **Mydayis (triple bead formulation; pH dependent technology)** • *Adhansia XR (20IR/80ER) → discontinued*

**Amphetamines: 2x more potent than methylphenidates

IR: immediate release; ER/XR: extended release; SR: sustained release; ODT: orally disintegrating tablet

Unless otherwise noted, MAS formulations are all racemic formulations (3:1 *d*-AMP to l-AMP)

Common Side Effects	Management Strategies to Consider
Decreased appetite	• High caloric meals when stimulant effects are low (i.e. breakfast, bedtime) • Consider stimulant holidays or cyproheptadine if appropriate • If concerns for disordered eating, discontinue the stimulant
Nausea, stomach upset	• Give stimulant on full stomach
Headache (20%)	• Divide dose; give with food
Insomnia (10-15%)	• Evaluate if related to stimulant or to undermanaged ADHD symptoms
Irritability/jitteriness	• Consider comorbid condition; reduce the dose

Rare Side Effects	Management Strategies to Consider
Transient motor tics	• Reduce dosage; consider alternative therapy
Dysphoria/irritability	• Reduce dosage; reassess diagnosis; consider alternative therapy
Hallucinations	• Discontinue stimulant; reassess diagnosis
Priapism	• Hold stimulant and obtain urgent medical attention
Hypertension, pulse fluctuations	• Reduce dosage; consider alternative therapy

Other Side Effects	Considerations
CV risk	• ECG not required prior to initiation of stimulant, but would be reasonable to consider if high CV risk
Peripheral vasculopathy, including Raynaud's phenomenon	• Obtain medical assistance if severe digital changes observed; consider dose reduction or alternative therapy
Serotonin Syndrome	• Theoretical; monitor for symptoms (e.g. mental status changes, autonomic instability, neuromuscular abnormalities, including hyperreflexia, myoclonus
Seizures	• Stimulants lower seizure threshold, but have demonstrated safety and efficacy in youth with well-controlled seizure disorders; evidence supports methylphenidate use over amphetamines and apha-2 agonists
Decreased growth velocity (long-term)	• Variable evidence, but may be related to poor nutrition, lack of appetite, inhibitor effect of increased DA on growth hormones

Non-stimulant Treatment Options:

Product	MOA	Place in therapy	Considerations
Atomoxetine (Straterra)	Selective NE reuptake inhibitor	Consider in individuals with active substance use or severe side effects with stimulants	• BBW: Suicidal ideation • Metabolism: substrate of 2D6 • Common side effects: N/V, decreased appetite, headache, dizziness, sedation, insomnia • Rare side effects: severe liver injury, priapism
Viloxazine (Qelbree)	Selective NE reuptake inhibitor	Consider in individuals with active substance use or severe side effects with stimulants	• BBW: Suicidal ideation • Metabolism: substrate of 2D6 • Common side effects: N/V, headache, dizziness, sedation, insomnia, increased BP/HR, decreased appetite, dry mouth
Clonidine (Catapres, Kapvay, Onyda XR)	Non-selective alpha-2a-c agonist; increases blood flow and functional connectivity in the prefrontal cortex	Monotherapy or adjunct to stimulants	• Common side effects: sedation, dizziness, constipation, dry mouth, bradycardia, hypotension • Rebound hypertension if abruptly discontinued
Guanfacine (Tenex, Intuniv)	Selective alpha-2a agonist; increases blood flow and functional connectivity in the prefrontal cortex	Monotherapy or adjunct to stimulants	• Has the same common side effects as with clonidine, but has a lower risk of sedation and dizziness (given receptor selectivity) • Rebound hypertension if abruptly discontinued
Bupropion (Wellbutrin)	Weak inhibitor of neuronal uptake of NE and DA (metabolite inhibits NE reuptake)	Third line option when stimulants are ineffective, poorly tolerated, or when individual may benefit from antidepressant effect	• Common side effects: nausea, insomnia, tics; dose-related risk of seizures • Contraindications: seizure disorder, eating disorder, concurrent use of MAOI • Metabolism: CYP2D6, potent inhibitor
Omega-3 fatty acids	Anti-inflammatory action via inhibition of free radical generation and oxidant stress; shown to regulate neurotransmitter and immune functions via modulation of lipid rafts signaling platforms on the cell membrane	Most widely studied alternative treatment for ADHD in combination with pharmacological treatment, targeting hyperactivity and impulsivity in combination	• EPA content significantly correlates with efficacy, where largest effective size at ~560 mg EPA

NE = norepinephrine; DA = dopamine.

ANTIDEPRESSANTS

What can antidepressants be used for?

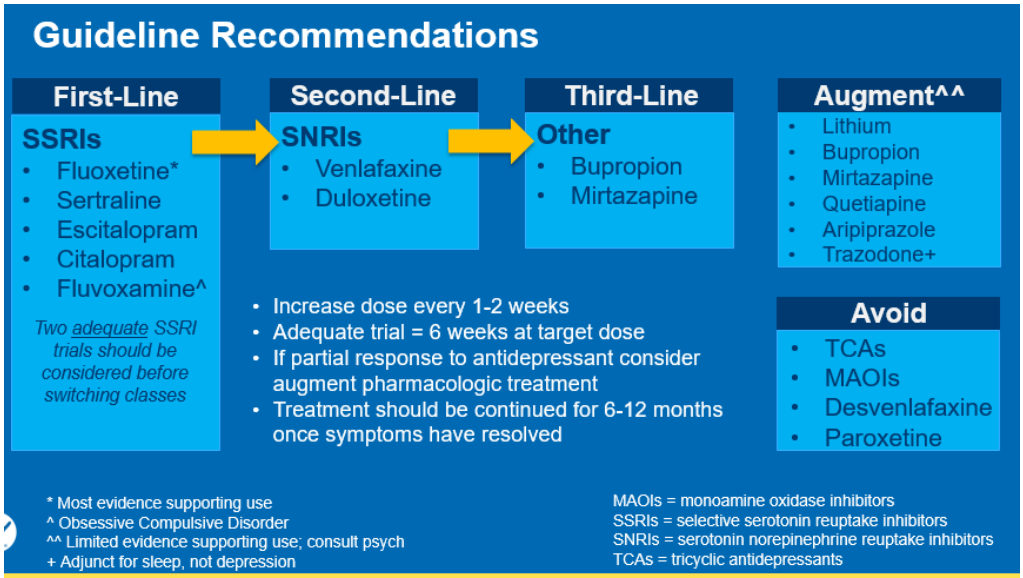
- Depression, feelings of guilt, lack of interest or pleasure from things you used to enjoy
- Fear in social situations
- Thoughts of hurting yourself or of suicide
- Low energy, motivation
- Feeling nervous, anxious or apprehensive
- Sad, irritable mood
- Difficulty thinking, concentrating, focusing
- Obsessive thoughts, compulsive behaviors
- Intrusive thoughts, hypervigilance

How quickly do antidepressants work?

- Week 1-2: improvement in physical symptoms (e.g., eating, sleep, energy)
- Week 3-4: improvement in energy, motivation, interest in doing fun activities
- Week 5-6: improvement in overall mood

Clinical pearls

- Depression, anxiety, posttraumatic stress disorder, obsessive compulsive disorder: SSRIs are typically considered first line in pediatric patients (e.g., fluoxetine, sertraline, escitalopram, citalopram)
    - Consider two adequate trials of SSRIs (4-6 weeks) at max tolerated dose, then consider SNRI
    - Psychosocial interventions considered first line children < 8 years
    - Slow dose adjustments can minimize risk for behavioral activation, irritability
    - Anxiety/compulsive-based/trauma-based: start at half the typical starting dose (given risk to transiently worsen anxiety)
    - Autism spectrum disorder/intellectual disability: risk for worsened irritability with serotonergic antidepressants (use lower doses!); better evidence for tolerability in adolescents with comorbid anxiety/depression
    - Tricyclic antidepressants: controlled trials have not demonstrated benefit for depression; some evidence for OCD/enuresis
    - SNRIs: considered second line to SSRIs; venlafaxine good evidence in PTSD
- Medical comorbidities to consider:
    - Migraine prophylaxis: venlafaxine, mirtazapine
    - Neuropathic pain/musculoskeletal pain: venlafaxine, duloxetine
    - Chronic cyclic vomiting: mirtazapine
    - Seizure disorder: avoid bupropion, TCAs; SSRIs generally safe (fluoxetine and fluvoxamine high risk for drug interactions)



Recommendations based on summary of AACAP/GLAD-PC Guidelines, TADS, TORDIA, and review articles.

Selective Serotonin Reuptake Inhibitors - Inhibit presynaptic serotonin (5-HT) reuptake

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Citalopram (Celexa)	MDD	• Age 6-11: 10 mg/day • Age ≥ 12: 20 mg/day	• 40 mg daily • 20 mg daily (hepatic impairment, > 60 years old, CYP2C19 PMs)	Tablet Oral solution (10mg/5mL)	• Dose-dependent QTc prolongation; ECG at baseline should be considered in the presence of other risk factors.
Escitalopram (Lexapro)	MDD (≥ 12 years) GAD	• Age 6-11: 5 mg/day • Age ≥ 12: 10 mg/day	• Age 6-11: 20 mg/day • Age ≥ 12: 30 mg/day	Tablet Oral solution (5mg/mL)	• More potent S enantiomer of citalopram • Least likely to have drug interactions • 10 mg = 30 mg citalopram
Fluoxetine (Prozac)	MDD (8-18 years) OCD (7-17 years) PMDD Bulimia Nervosa Panic Disorder	• 6-11: 5-10 mg/day • ≥ 12: 10 mg/day	• 60 mg/day	Tablet Capsule Oral solution (20mg/5mL) Weekly tablet (90 mg)	• Most well studied antidepressant in youth • Potent CYP2D6 inhibitor; caution with drug interactions • Long half-life (parent – 3 days; active metabolite – 10 days)
Sertraline (Zoloft)	OCD (6-17 years) MDD Panic Disorder PTSD PMDD Social Phobia	• 6-12: 12.5-25 mg/day • ≥ 13: 25-50 mg/day	• 200 mg/day	Tablet Oral concentrate (20 mg/mL)	• Highest risk for GI upset among SSRIs • Food increases bioavailability by ~ 40% • Oral concentrate contains alcohol; dropper (latex)
Fluvoxamine (Luvox)	OCD (8-17 years)	• ≥ 8: 25 mg/day	• 8-11 years: 200mg/day • 12-17 years: 300 mg/day • Doses > 50 mg should be divided	Tablet (IR, CR)	• Highest risk for drug interactions • Increases effect of caffeine (CYP1A2 inhibition) • No active metabolite, serotonin withdrawal likely if discontinued abruptly
Paroxetine (Paxil)	GAD MDD OCD Panic Disorder PTSD, PMDD, social phobia	• ≥ 12: 25 mg/day	• 50 mg/day	Capsule Tablet (IR, CR) Oral solution (10mg/5mL)	• Generally not recommended in pediatric patients; poor tolerability (particularly < 12 years), increased risk for hostility and agitation in youth. May be considered if severe anxiety • No active metabolite, serotonin withdrawal likely if abruptly discontinued • Anticholinergic side effects, significant sexual dysfunction • Potent CYP2D6 inhibitor
Vilazodone (Viibryd)	MDD	• No pediatric recommendations	• No pediatric recommendations	Tablet	• Inhibits reuptake of serotonin; also high affinity to 5-HT1A receptors (partial agonist)

Serotonin Norepinephrine Reuptake Inhibitors - Inhibit presynaptic serotonin (5-HT) and norepinephrine (NE) reuptake

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Venlafaxine (Effexor)	GAD MDD Panic Disorder Social Phobia	• 7-17: 37.5 mg/day	• 7-11: 150 mg/day • 12-17: 225 mg	IR/XR tablet XR capsule	• Noradrenergic effect at higher doses (≥150 mg) • Effective for migraine prevention (adult data)
Desvenlafaxine (Pristiq)	MDD	• 12-17: 50 mg/day	• 50 mg daily	ER tablet	• Evidence does not support use in youth • Active metabolite (O-desvenlafaxine) of venlafaxine; metabolized primarily via CYP3A4 • Little added benefit (efficacy) > 50 mg daily; increased risk for ADRs
Duloxetine (Cymbalta)	GAD (7-17 years) Neuropathy Fibromyalgia Musculoskeletal pain	• 7-17: 30 mg/day	• 120 mg daily	DR capsule	• Measure liver function at baseline/throughout (warning for hepatotoxicity)
Levomilnacipran (Fetzima)	MDD	• No pediatric recommendations	• No pediatric recommendations	ER capsule	• More active enantiomer of milnacipran; potent norepinephrine and serotonin reuptake inhibitor

Tricyclic Antidepressants - Inhibit presynaptic reuptake of serotonin (5-HT) and norepinephrine (NE); tertiary amines have greater affinity for 5-HT reuptake inhibition, secondary amines have greater affinity for NE reuptake inhibition.

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Amitriptyline (Elavil) *Tertiary amine*	MDD (≥ 12 years)	• Not recommended	• Not recommended	Tablet	• Other uses: migraine/tension HA prevention, fibromyalgia, neuropathic pain, IBS (adult data)
Imipramine (Tofranil) *Tertiary amine*	Enuresis (≥ 6 years)	• 10-25 mg QHS	• < 12: 2.5 mg/kg/day or 50 mg/day • > 12: 75 mg/day	Capsule Tablet	• Non-pharmacologic methods preferred for enuresis management; pharmacologic agents should be discussed after formal workup, failure of behavioral interventions
Clomipramine (Anafranil) *Tertiary amine*	OCD (≥ 10 years)	• 25 mg daily	• 3 mg/kg/day or 200 mg/day (whichever is less)	Capsule	• During titration, consider splitting dose given risk for sedation, orthostasis. Once titrated, may give as a single dose at bedtime

					• Evidence to support use for pediatric OCD
Doxepin (Silenor) *Tertiary amine*	GAD MDD Insomnia	• Silenor: 3-6 mg QHS • Doxepin: 25 mg QHS	• Silenor: 6 mg QHS • Doxepin: 50 mg QHS	Capsule Tablet (Silenor) Oral concentrate (10mg/mL)	• Dosing recommendations for insomnia only • Use caution when considering for insomnia (little evidence in pediatrics)
Nortriptyline (Pamelor) *Secondary amine*	MDD	• Not recommended	• Not recommended	Capsule Oral solution (10mg/5mL)	• Other uses: neuropathic pain, chronic pain, enuresis
Other important clinical pearls/considerations:	• Lack of evidence to support use for pediatric depression/anxiety • High risk for lethality in overdose (cardiotoxicity); higher risk for worsening suicidal thoughts/behaviors • ECG should be obtained at baseline and throughout treatment; Avoid use if high risk for QT prolongation, presence of cardiovascular disease, or family history of sudden death • Avoid in seizure disorders given high risk of lowering seizure threshold • Common ADRs: sedation, anticholinergic effects, cardiovascular effects (orthostasis, tachycardia), sexual dysfunction, weight gain				

Monoamine Oxidase Inhibitors - Irreversibly inhibit monoamine oxidase (MAO); MAO-A preferentially metabolizes 5-HT and NE; MAO-B preferentially metabolizes trace amines. Both metabolize dopamine (DA) and tyramine.

Name	**MOA**	**Clinical Pearls**
Selegiline (Emsam) Phenelzine (Nardil) Isocarboxazid (Marplan)	MAO-A/B inhibitor • *Selegiline – more selective MAO-B inhibition at low doses (6 mg/24 hours)*	• Lack of evidence to support use for pediatric depression/anxiety • Dietary restrictions (tyramine rich foods) given risk for hypertensive crisis • Risk for serotonin syndrome: At least 2 weeks should elapse after stopping an MAOI before starting therapy with another serotonergic agent; If fluoxetine, 5 weeks should elapse given long half-life of active metabolite • Must consider other medications that have MAOi properties (e.g., linezolid) • Avoid use with concurrent sympathomimetics or serotonergic agents • Discontinue 10 days before elective surgery, given concerns with concurrent use with general anesthesia
Tranylcypromine (Parnate)	MAO-A/B inhibitor • Other: Increase 5-HT, DA, NE release into the synapse; Inhibits DA, NE reuptake.	

Other

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Bupropion (Wellbutrin)	MDD Smoking Cessation SAD	• ≥ 6: 3mg/kg/day or 150 mg/day (whichever is smaller)	• IR: 300 mg/day (Max of 100 mg/single dose) • SR: 400 mg/day (Max of 200 mg/single dose) • XL: 450 mg/day	IR tablet SR tablet XL tablet	• Inhibits presynaptic reuptake of dopamine and norepinephrine • Lowers seizure threshold (IR greatest risk) • Potent CYP2D6 inhibitor • May be helpful in adolescents with ADHD • Weight neutral • Lack of sexual dysfunction, GI upset • Contraindications: seizure disorder, treatment with other bupropion containing products, current or prior diagnosis of BN/AN, abrupt discontinuation of alcohol or benzodiazepines, concurrent MAOI use, allergy
Mirtazapine (Remeron)	MDD	• 7.5 mg/day	• 45 mg/day	Tablet ODT	• Presynaptic alpha-2 antagonist; 5-HT3 antagonist (may be helpful for N/V); 5-HT2 antagonist (no sexual dysfunction) • Risk for increasing triglycerides, appetite, weight • Lower doses = more sedating • May be useful in chronic/cyclic vomiting • Migraine prevention (adult data)
Trazodone (Desyrel)	MDD	• 12.5-25 mg/day	• 150 mg QHS	Tablet	• Inhibits serotonin reuptake; 5-HT2A antagonism, alpha-1 antagonism • Antidepressant doses not tolerated; used primarily for sleep onset • Priapism (not dose related); counsel all male patients
Vortioxetine (Trintellix)	MDD	• No pediatric recommendations	• No pediatric recommendations	Tablet	• Inhibits serotonin reuptake; 5-HT1A agonist, 5-HT3 antagonist

Side Effect	
Most sedating	Trazodone > mirtazapine > fluvoxamine > paroxetine
Most activating	Bupropion > fluoxetine
Most weight gain	Mirtazapine ≥ TCA > MAOI > paroxetine > other SSRIs; Least: bupropion
Most GI upset	SNRIs > all SSRIs
Least potential for sexual dysfunction	No 5HT effect: bupropion Post-synaptic 5-HT2 blockade: mirtazapine, trazodone
Cardiovascular risk	TCAs (arrhythmias), MAOIs (hypertensive crisis)

Common Side Effects	Management Strategies to Consider
GI upset	• Give with food • Slow titration
Headache	• Usually disappears with time (first 1-2 weeks) • Recommend acetaminophen as needed
Anxiety, restlessness	• Start at low doses • Titrate slowly
Insomnia	• Dose in the morning • Consider switch to more sedating agent or add on trazodone
Sexual dysfunction	• Add bupropion or change to mirtazapine
Dry mouth	• Usually disappears with time • Recommend Biotene products, sugar-free gum
Increased HR/BP (SNRIs, Bupropion)	• Reduce dose • Consider alternative (SSRI)

Rare Side Effects	Management Strategies to Consider
Extrapyramidal side effects (EPSE)	• Decrease dose • Switch to alternative antidepressant
SIADH	• Monitor closely in those taking diuretics • Discontinue SSRI
GI bleed	• Monitor closely if taking anticoagulant, chronic NSAIDs, etc. • Discontinue SSRI/SNRI, consider mirtazapine or bupropion
Reduced bone mineral density	• Monitor closely in females, those taking chronic antipsychotics or mood stabilizers, steroids, etc • Consider vitamin D/calcium
QTc prolongation	• Monitor closely in patients on other QTc prolonging medications, with electrolyte abnormalities, significant cardiac history • Baseline ECG should be performed for all TCAs, with dose increase

MOOD STABILIZERS

What can these medications be used for? *[1]Bipolar mania [2]Bipolar depression*

- Rapid, pressured speech, Flight of ideas, racing thoughts[1]
- Reduced need for sleep[1]
- Mood swings, feeling on top of the world[1]
- Poor judgment, significant impulsivity[1]
- Aggression, irritability, anger[1,2]
- Suicidal thoughts[2] Depressed mood[2]

How quickly do they work? *(average, depends on setting)*

- Week 1: reduced agitation, hostility, aggression, improved sleep
- Week 2-4: more organized thinking, reduced fluctuations in mood
- Week 6-8: improved mood, less delusions

General clinical pearls

- In general, a 6-8 week trial of a mood stabilizer is recommended
- General dosing approaches:
    - Weight based pediatric dosing information is available for most mood stabilizers
    - Therapeutic Drug Monitoring should be used to guide dosing decisions for lithium and divalproex derivatives. While serum concentrations of many mood stabilizers can be drawn, there is little that we know about their impact on efficacy.
- Black box warning:
    - Carbamazepine: serious dermatological reactions (presence of HLA- B*1502 allele), aplastic anemia, and agranulocytosis
    - Lamotrigine: life-threatening rash including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS)
    - Lithium: toxicity above therapeutic serum levels
    - Valproate: hepatotoxicity, teratogenicity, pancreatitis, mitochondrial disease (POLG)
- Mood stabilizers can be used for a variety of conditions.
    - Migraine prophylaxis: divalproex derivatives, topiramate
    - Seizure disorders: divalproex derivatives, lamotrigine, carbamazepine, oxcarbazepine

Pharmacotherapy recommendations

	Acute Mania	Acute Depression	Maintenance
First-Line	Lithium, risperidone, aripiprazole, asenapine, quetiapine	Lurasidone	Lithium, aripiprazole
Second-Line	Olanzapine, ziprasidone, quetiapine (adjunct)	Lithium	VPA
Third-Line	VPA	Lamotrigine	Asenapine, risperidone, ziprasidone, quetiapine
Not Recommended	Carbamazepine, oxcarbazepine		

Mood Stabilizers

Name Generic (Brand)	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Lithium Lithobid® Eskalith® CR Duralith®	• Bipolar mania (≥ 7 years)	Children: Lesser of 15-20 mg/kg/day or 150 mg BID Adolescents: Lesser of 15-20 mg/kg/day or 300 mg BID	Children: 900-1800 mg/day Max dose based upon 12-hour post dose serum level Adolescents: 1800 mg/day Max dose based upon 12-hour post dose serum level	• Tablet • Capsule • Oral syrup (8mEq/5mL) • SR tablet • CR tablet • XR capsule	• First line for acute mania, relapse prevention, suicide protection • 100% renal elimination • Narrow therapeutic index, therapeutic drug monitoring is required • Adverse effects include weight gain, GI upset, renal toxicity, QTC prolongation • Symptoms of toxicity may include slurred speech, ataxia, persistent N/V/D, CNS depression, coarse hand tremor, arrhythmia, seizure • Excessive sodium intake, excessive caffeine intake: increase lithium clearance • Renal impairment, hyponatremia, dehydration: significant reduction in lithium clearance • Monitoring: Scr, BUN, electrolytes (baseline, 3 months, yearly), thyroid function (baseline, every 6 months), CBC (baseline, yearly)

When to Obtain a Lithium Level

- 3 to 5 days after initiation or a dose change
- If symptoms of toxicity are present (e.g., slurred speech, ataxia, persistent N/V/D, CNS depression, coarse hand tremor, arrhythmia, seizure)
- Every 3-6 months once stable (outpatient)
- Level should be drawn 12 hours post dose for **all formulations**

Lithium Level Interpretation

- Has steady state been reached? → 5 days of lithium therapy
- Was the level drawn appropriately? →12 hours post dose; at least 8 hours
- Is the level within therapeutic range?
  - Acute mania = 0.8-1.5 mEq/L
  - Maintenance = 0.6-1.2 mEq/L
  - Toxicity: > 1.5 mEq/L; Remember that **toxicity can occur at any level**, monitor closely for signs and symptoms of toxicity.
  - Note: therapeutic lithium goals may vary based on indication, medical/psychiatric comorbidities, and tolerability. Please use clinical judgment when establishing patient goal.

Dose Adjustment Considerations

- **For acute management, serum levels should be obtained on day 2-3 to facilitate quicker optimization of lithium therapy**
- Because lithium follows a first order linear pharmacokinetic model, we can easily predict what the level would be at steady state
- Important drug interactions: NSAIDS, ACE/ARBs, diuretics

Days of Li therapy	**% steady state reached**	**Calculation to predict lithium level at steady state (Css)**
Day 1	50% SS	$\frac{\text{Lithium Level}}{\text{\% SS Reached}} = \frac{\text{Lithium Css}}{100\%}$
Day 2	75% SS	
Day 3	87.5% SS	
Day 4	94.5% SS	
Day 5	97% SS	
******At steady state, expect that each 300 mg of lithium will increase serum level by 0.15-0.35 mEq/L******		

Name Generic (Brand)	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Divalproex derivatives/ valproate Valproate Depacon® Depakene® Depakote® Stavzor®	• Seizure disorders (≥10 years)	Children ≥ 6 years: 10-15 mg/kg/day	Maximum dose based upon serum level: 50-125 µg/mL, or 60 mg/kg/day	• DR enteric coated tablet • DR sprinkle capsules • ER tablet • Capsule • Oral syrup (250mg/5mL) • IV solution (100mg/mL)	• First line for bipolar mania, though must consider risks in adolescent females • Particularly beneficial in treating mania that occurs with mixed features • BBW: hepatotoxicity, mitochondrial disease [screen for polymerase γ (POLG) gene mutation], pancreatitis, teratogenicity • Adverse effects include weight gain, polycystic ovary syndrome (PCOS), GI upset, and rash • Less favored in adolescent females due to high teratogenic potential and increased risk for PCOS • ER tablets are not bioequivalent to delayed release → If converting from delayed release to extended release, increase the total daily dose by 20% • Monitoring: LFTs, CBC with platelets (baseline, 1-2 weeks after each dose increase, every 3 months for first year, yearly), serum ammonia, serum VPA level

Timing of Serum Drug Concentration Sampling

- Optimal timing of sampling dependent on formulation prescribed
  - Immediate release, oral syrup: 8 hours post dose
  - Delayed release: 12 hours post dose
  - Extended release: 24 hours post dose

Valproate Level Interpretation

- Is the level within therapeutic range?
  - Acute mania = 80-125 mcg/mL
  - Maintenance = 50-125 mcg/mL

Name Generic (Brand)	FDA Approved Indication(s)	Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Lamotrigine Lamictal® Lamictal® XR	• Adjunct for seizure disorders (> 2 years)	Lamotrigine monotherapy Age 6-11 years: 4.5-7.5 mg/kg/day Age ≥12 years: 225-375 mg/day Lamotrigine VPA Age 6-11 years: 1-3 mg/kg/day Age ≥12 years: 100-200 mg/day Lamotrigine inducer Age 6-11 years: 1-5 mg/kg/day Age ≥12 years: 300-500 mg/day	Lamotrigine monotherapy Age 10-12 years: 6 mg/kg/day or 200 mg/day Age 13-17 years: 300 mg/day Lamotrigine VPA Age 10-12 years: 3 mg/kg/day or 100 mg/day Age 13-17 years: 150 mg/day Lamotrigine inducer Age 10-12 years: 12 mg/kg/day or 300 mg/day Age 13-17 years: 400 mg/day	• Tablet • Chewable tablet • ODT • XR tablet	• To decrease risk of rash, must be titrated up slowly, increasing the dose every 2 weeks, will take 2 months to achieve a therapeutic dose and a therapeutic response • If 2-3 missed days of continuous therapy with lamotrigine, treatment must be restarted with a low dose and titrated up • Adverse effects: Headache, nausea, dry mouth, itching, rash • BBW: Serious skin rash including Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) • **Decrease lamotrigine dose by 50% if administered with valproate** • Significant increased serum lamotrigine levels with: valproate, oral contraceptives • Significant decreased serum lamotrigine levels with: carbamazepine, oxcarbazepine, phenytoin, phenobarbital, primidone

ANTIPSYCHOTICS (THOUGHT ORGANIZERS)

What can these medications be used for?

- Poor concentration, rapid, racing thoughts
- Paranoia, fearful feelings, suspiciousness
- Depressed mood, low energy, lack of motivation
- Fluctuations in mood, agitation, aggression, irritability
- Hallucinations (hearing voices, seeing things that aren't there)
- Delusions (fixed, false beliefs)

How quickly do they work?

- Week 1: reduced agitation, hostility, aggression
- Week 2-4: reduced paranoia, hallucinations, bizarre behaviors, more organized thinking
- Week 6-12: improved mood, motivation, less delusions
- 3-6 months: improved cognitive symptoms

What makes an antipsychotics typical vs atypical?

Typical antipsychotics primarily antagonize post-synaptic D_2 receptors. Atypical antipsychotics antagonize both post-synaptic D_2 and 5-HT_2 receptors. The serotonergic effect of atypical antipsychotics results in reduced risk for extrapyramidal side effects (EPS), but more risk for metabolic effects. Additionally, atypical antipsychotics are thought to have improved efficacy for treating negative (mood) symptoms compared to typical antipsychotics due to 5-HT_2 antagonism.

General Clinical pearls

- Start low and go slow, given increased risk for specific side effects in pediatric patients; always target the lowest effective dose
- Alternative formulations may be available if a kiddo cannot swallow tablets
- Young age and male gender are risk factors for acute dystonic reactions; use caution with high-potency D_2 blockers in young boys

Atypical Antipsychotics

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Clozapine (Clozaril)	• Treatment resistant schizophrenia • Suicidal behavior in schizophrenia and schizoaffective disorder	Age 8-11 years: 6.25-12.5mg/day Age ≥12 years: 6.25-25mg/day	Age 8-11 years: 150-300mg/day Age ≥12 years: 600mg/day	Tablet ODT (FazaClo)* Oral suspension (Versacloz, 50mg/mL)*	• Most effective antipsychotic • Prescribers, patients, pharmacy must be enrolled in REMS (severe neutropenia; not dose dependent) • Obtain CRP/troponin weekly for the first month of treatment to screen for myocarditis • If miss > 48 hours, must re-titrate given risk for dose dependent risks for seizure, respiratory depression, sedation, orthostasis, bradycardia • Potent anticholinergic effects; important to monitor for constipation • Drooling may occur given direct stimulation of the salivary gland at M_4 receptors • Serum clozapine levels can be measured (350-600 ng/mL) to optimize efficacy/safety • BBW: severe neutropenia, seizures (highest risk among atypicals; dose dependent), myocarditis (monitor CRP and troponin for first 8-weeks, time-dependent), cardiovascular and respiratory effects (consider ECG at baseline)
Olanzapine (Zyprexa)	• Manic or mixed episodes associated with bipolar I, and bipolar I maintenance (age 13-17 years) • Schizophrenia (age 13-17 years) • Acute agitation associated with schizophrenia or bipolar I	Age 4-5 years: 1.25mg/day Age 6-12 years: 2.5mg/day Age ≥13 years: 2.5-5mg/day	Age 4-6 years: 12.5mg/day Age 6-17 years: 20mg/day	Tablet ODT (Zyprexa Zydis) Rapid acting IM LAI (Relprevv)*	• High risk for weight gain and metabolic syndrome (should be considered 2nd or 3rd line in pediatrics), sedation, anticholinergic • Relprevv – must be enrolled in REMS program given risk for PDSS • Coadministration of rapid acting IM olanzapine and parenteral benzodiazepines must be separated by at least 2 hours given risk for significant respiratory suppression

Risperidone (Risperdal)	• Schizophrenia (age 13-17 years) • Acute manic or mixed episodes associated with bipolar I (age 10-17 years) • Irritability associated with ASD (age 5-17 years)	Age 4-5 years: <20kg: 0.25mg/day >20kg: 0.5mg/day Age ≥6 years: 0.5mg/day	Age 4-11 years: 3mg/day Age ≥12 years: 6mg/day	Tablet ODT (Risperdal M-tab) Oral solution (1mg/mL) LAI (Risperdal Consta, Rykindo, Risvan)* SQ LAI (Uzedy)*	• Consider starting with BID dosing (to minimize risk for orthostasis) • High risk for hyperprolactinemia • Highest risk for EPS among atypicals • Substrate of CYP2D6
Paliperidone (Invega)	• Schizophrenia and schizoaffective disorder (age 12-17 years)	Age ≥12 years: 3mg/day	Age ≥12 years: <51kg: 6mg/day ≥51kg: 12mg/day	XR tablet* LAI (Invega Sustenna, Invega Trinza*, Invega Hafyera*)	• Active 9-OH metabolite of risperidone • High risk for hyperprolactinemia • Cannot cut tablets
Quetiapine (Seroquel)	• Bipolar disorder (age 10-17 years) • Schizophrenia (age 13-17 years) • MDD	Age 5-9 years: 12.5-25mg/day Age 10-17 years: 50mg/day	Age 5-9 years: 400mg/day Age 10-17 years: 800mg/day	IR tablet XR tablet*	• High risk of sedation, anticholinergic effects; alpha-1 blockade (orthostasis) • BBW: increased risk for SI • Short half-life (IR ~6 hours; XR ~ 7 hours); peaks (IR ~1 hour; XR ~6 hours) • Different doses have different pharmacologic profiles (25-50 mg antihistamine; 200-400 mg antidepressant; 500-800 mg antipsychotic)
Aripiprazole (Abilify)	• Bipolar I (age 10-17 years) • Schizophrenia (age 13-17 years) • Irritability associated with ASD (age 6-17 years) • Tourette syndrome, tic disorder (age ≥6 years) • MDD adjunct • Acute agitation	Age ≥4 years: 2mg/day	Age 4-11 years: 15mg/day Age ≥12 years: 30mg/day	Tablet ODT* Oral solution (1mg/mL) LAI (Abilify Maintena, Aristada*, Abilify Initio*) Abilify Mycite*: drug-device product to track adherence	• Partial D_2 agonist (reduces prolactin) • BID dosing may help reduce risk for N/V in youth (who reach a higher peak) • BBW: increased risk of SI • Akathisia
Ziprasidone (Geodon)	• Bipolar I: manic or mixed episodes, maintenance as adjunct to lithium or valproate	Bipolar: 20mg/day Tourette's: 5mg/day	Bipolar: ≤45kg: 80mg/day >45kg: 160mg/day	Capsule Rapid acting IM (mesylate, 20mg/mL)	• Take with food for increased absorption • BID dosing with ≥500 calorie meal • Higher risk for QTc prolongation • Obtain ECG at baseline

	• Schizophrenia • Acute agitation in schizophrenia		Tourette's: 40mg/day		
Asenapine (Saphris)	• Acute treatment of bipolar (age 10-17 years) • Schizophrenia	Age ≥10 years: 2.5mg BID	Age ≥10 years: 10mg BID	Sublingual tablet*	• Wait 10 minutes after administration before eating or drinking • CYP2D6 substrate • Decreased bioavailability if swallowed (35% vs <2%) or if taken with food
Lurasidone (Latuda)	• Bipolar depression • Schizophrenia (age 13 to 17 years)	Age ≥10 years: 20mg/day	Age 13-17 years: 40-80 mg/day	Tablet*	• Weak CYP3A4 inhibitor, substrate of CYP3A4 • BBW: increased risk of SI • Take with food to optimize absorption • Take BID to avoid GI upset
Brexpiprazole (Rexulti)	• MDD • Schizophrenia	No peds dosing	No peds dosing	Tablet*	• Partial D_2 and $5HT_{1A}$ agonist; $5\text{-}HT_{2A}$ antagonist • BBW: increased risk of SI • Primary substrate CYP2D6 • Monitor for compulsive behaviors/pathological gambling
Cariprazine (Vraylar)	• Schizophrenia • Bipolar I	No peds dosing	No peds dosing	Capsule*	• Partial D_3 and D_2 agonist; $5\text{-}HT2_{a\text{-}b}$ antagonist, H1 antagonist; minimal alpha-1 • Two major active metabolites desmethyl cariprazine (DCA; steady state week 1-2) and didesmethyl cariprazine (DDCAR; steady stated week 4-8) • Primary CYP3A4 substrate • Adverse reactions may appear several weeks after initiation, given accumulation of metabolites with time

BBW = Black Box Warning, REMS = Risk Evaluation Mitigation Strategy, PDSS = Post-injection Delirium/Sedation Syndrome, LAI = Long Acting Injectable, ASD = Autism Spectrum Disorder, MDD = Major Depressive Disorder

*Not available on CHCO formulary

Class adverse effects: weight gain, metabolic syndrome (e.g., type 2 diabetes, hypertriglyceridemia)

Important monitoring: BMI, waist circumference, fasting plasma glucose, blood pressure, fasting lipid panel at baseline, then every three months, then annually (if normal); BMI, waist circumference, and blood pressure should be measured each clinic visit

Typical Antipsychotics

Name	FDA Approved Indication(s)	Typical Starting Dose	Maximum Dose	Available Dosage Forms	Clinical Pearls
Haloperidol (Haldol)	• Psychotic disorders (≥3 years) • Tourette's disorder (≥3 years) • Severe behavioral problems (≥3 years)	Age 3-12 years: 15-40kg: 0.025-0.05 mg/kg/day ≥40 kg: 1mg/day	Age 3-12 years: 0.15 mg/kg/day or 6mg/day, whichever is less Age >12 years: Acute agitation: 10mg/dose Psychosis: 15mg/day Tourette's disorder: 15mg/day	Tablet Oral concentrate (2mg/mL) Rapid acting IM, IV (lactate, 5mg/mL) Long acting IM (decanoate, 50-100mg/mL)*	• High potency D_2 blockade (highest risk for EPS) • Risk for QTc prolongation (IV > IM > PO) • Divide doses initially to minimize adverse effects
Perphenazine (Trilafon)	• Psychotic disorders (≥ 12 years)	Age >12 years: 4-16mg 2-4 times daily	Age >12 years: 64mg/day	Tablet	• Moderate potency D_2 blockade • BID-QID dosing
Pimozide (Orap)	• Tourette's disorder (≥ 12 years)	Age ≥7 years: 0.05mg/kg	Age 7-12 years: 6mg/day or 0.2 mg/kg/day, whichever is less Age ≥12 years: 10mg/day or 0.2 mg/kg/day, whichever is less	Tablet*	• Moderate potency D_2 blockade • Consider ECG prior to initiation, given risk for QTc prolongation, dysrhythmias • Consider pharmacogenomic testing prior to initiation (metabolized via CYP2D6)
Chlorpromazine (Thorazine)	• Severe behavioral problems (age 6 months – 12 years) • Manifestations of psychotic disorder (age >12 years)	Age >6 months: 0.25mg/lb Q 4-6 h PRN Adolescents: 10-25mg Q 4-6 h	Age <5 years: 40mg/day Age 5-12 years: 75 mg/day Age >12 years: 800mg/day	Tablet Rapid acting IM (25mg/mL)	• Low potency D_2 blockade (lowest risk for EPS) • Significant M1 (anticholinergic, weight gain), H1 (antihistaminic), alpha-1 (orthostasis) antagonism • Highest risk for lowering seizure threshold (after clozapine) • Poor oral bioavailability (50 mg IM = 200 mg PO)

*****Not available on CHCO formulary

Class adverse effects: Extrapyramidal symptoms (Parkinsonism, akathisia, dystonia)

Important monitoring: AIMS exam every clinic visit

Note: all antipsychotics have a BBW given increased risk of death in elderly patients with dementia-related psychosis

Adverse Effect Table

	Metabolic Syndrome	Weight Gain	QTc Prolongation	Sedation	Orthostasis	Hyperprolactinemia	EPS
Clozapine (Clozaril)	++++	++++	+	++++	+++	-	+/-
Olanzapine (Zyprexa)	++++	++++	+	++++	+++	++	+
Risperidone (Risperdal)	++	+++	+	++	+++	+++	++
Paliperidone (Invega)	++	+++	+	++	++	+++	++
Quetiapine (Seroquel)	++	+++	+	++++	++	+/-	+/-
Aripiprazole (Abilify)	+/-	+/-	+/-	+	+/-	--	+
Ziprasidone (Geodon)	+/-	+/-	+++	+	++	+	+
Asenapine (Saphris)	+	++	+	++	+++	+	+
Lurasidone (Latuda)	+/-	+/-	+/-	++	+	+/-	+
Brexpiprazole (Rexulti)	+	++	-	+/-	++	+/-	+/-
Cariprazine (Vraylar)	+/-	+	-	++	+/-	-	+++
Chlorpromazine (Thorazine)	++++	++++	+	+++	+++	+	+
Haloperidol (Haldol)	+	+	++	+	++	+++	++++
Perphenazine (Trilafon)	++	++	+	++	+	++	++
Pimozide (Orap)	++	++	+++	++	++	++	++

++++ = almost always/highest risk, +++ = often/high risk, ++ = sometimes/moderate risk, + = low risk, +/- = neutral, -- = decrease

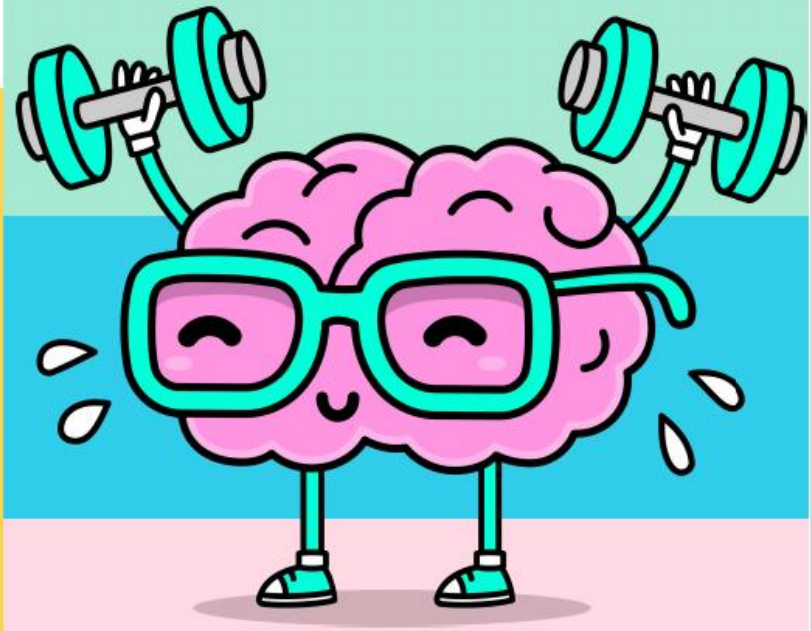
Trial	*Study Characteristics*	*Intervention*	*Results*
Treatment for adolescents with depression study (TADS) randomized controlled trial. *JAMA*. 2004.	• Randomized, controlled • N=439 adolescents with moderate-severe depression • Objective: determine efficacy of monotherapy vs combination ○ CDRS-R; CGI-I	*Randomized to:* 1) Placebo; 2) CBT; 3) Fluoxetine; or 4) CBT + fluoxetine *Duration: 12 weeks*	• Combination treatment superior to fluoxetine (p=0.02) and CBT (p=0.01) monotherapy • Fluoxetine superior to CBT alone (p=0.01) • Faster improvement/time to stabilization for combination and fluoxetine monotherapy compared to placebo (p=0.001)
The treatment of resistant depression in adolescents (TORDIA) randomized controlled trial. *JAMA*. 2008.	• Randomized, controlled • N=334 adolescents who failed to respond to initial antidepressant therapy • Objective: identify effective treatment switch strategy ○ CDRS-R; CGI-I	*Random switch to:* 1) Second SSRI; 2) Second SSRI + CBT; 3) Venlafaxine; or 4) Venlafaxine + CBT *Duration: 12 weeks*	• Combination treatment superior to medication monotherapy (54.8% vs. 40.5%, p=0.009) • No difference: second SSRI vs venlafaxine (p=0.83) • No differences in adverse effects
Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety – Child/Adolescent anxiety multimodal study (CAMS). *N Engl J Med*. 2008.	• Randomized, controlled • N=488 children with separation anxiety disorder, generalized anxiety disorder, or social phobia • Objective: compare the relative efficacy of 3 treatments with placebo ○ CGI-I; PARS	Randomized to: 1) CBT; 2) Sertraline; 3) CBT + sertraline; or 4) Placebo *Duration: 12 weeks*	• Combination treatment superior to CBT and sertraline alone (80.7% vs 59.7% and 54.9%; p<0.001) • All therapies superior to placebo (23.7%) • Less insomnia, fatigue, sedation, and restlessness in the CBT group than sertraline
Child/Adolescent anxiety multimodal extended long-term study (CAMELS). *J Am Acad Child Adolesc Psychiatry*. 2018.	• Prospective, observational • N=319 youths originally diagnosed with anxiety disorders and enrolled in CAMS study (see above) • Objective: report long-term anxiety outcomes ○ ADIS-5	Randomized to: (see above) 1) CBT; 2) Sertraline; 3) CBT + sertraline; or 4) Placebo *Duration: 4 years*	• 22% of youth were in stable remission, 30% were chronically ill, and 48% relapsed • Acute treatment responders were less likely to be chronically ill (OR 2.73; p<0.02) • Treatment type was not associated with remission status

Fluoxetine treatment for obsessive compulsive disorder in children and adolescents (POTS): A placebo-controlled trial. *J Am Acad Child Adolesc Psychiatry.* 2001.	• Randomized, controlled • N=103 • Objective: assess efficacy and tolerability of fluoxetine in the acute treatment of OCD ○ CY-BOCS	Randomized to: 1) Fluoxetine; or 2) Placebo *Duration: 13 weeks*	• Fluoxetine superior to placebo (p=0.026) • Fluoxetine discontinuation for adverse events similar to placebo (p=1)
The treatment of adolescent suicide attempters study (TASA): Predictors of suicidal events in an open treatment trial. *J Am Acad Child Adolesc Psychiatry*. 2010.	• Randomized, open-label • N=124 adolescents who had made a suicide attempt within 90 days on intake • Objective: identify predictors of suicidal events and re-attempts in depressed adolescents ○ SSRS	Randomized to: 1) Psychotherapy; 2) Medication; or 3) Both *Duration: 6 months*	• Risk of suicidal events 0.19 and attempts 0.12 • Median time to event of 44 days • Higher self-rated depression, suicidal ideation, family income, greater number of previous suicide attempts, lower maximum lethality attempts, history of sexual abuse, and lower family cohesion predicted occurrence and earlier time to event
A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD (MTA). *Arch Gen Psychiatry*. 1999.	• Randomized, controlled • N=579 children with ADHD	Randomized to: 1) Medication management; 2) Intensive behavioral treatment; 3) Two combined; or 4) Standard community care *Duration: 14 months*	• Combined treatment and medication management groups superior to intensive behavioral treatment alone and community care • Combined and medication management treatments did not differ significantly
Safety and tolerability of methylphenidate in preschool children with ADHD (PATS). *J Am Acad Child Adolesc Psychiatry*. 2006.	• Randomized, controlled • N=183 preschool aged children with ADHD • Objective: report the safety and tolerability of methylphenidate (MPH)	Phases: 1) 1-week lead-in period; all patients to MPH 2) 5-week placebo-controlled, double-blind; half of patients	• 33% of parents reported moderate to severe adverse effects including emotional outbursts, difficulty falling asleep, repetitive behaviors/thoughts, appetite decrease, and irritability

	○ Clinician adverse effects recording; parent/teacher adverse effects checklist	to placebo and half to MPH 3) 5-week parallel phase; placebo and MPH switch 4) 10-months open-label maintenance: all patients to MPH *Duration: 12 months*	• Decreased appetite ($p<0.03$), trouble sleeping ($p<0.03$), and weight loss ($p<0.05$) occurred more often in methylphenidate group than placebo • During maintenance, trouble sleeping, and appetite loss persisted • 11% discontinued because of adverse effects
What does risperidone add to parent training and stimulant for severe aggression in child attention-deficit/hyperactivity disorder? (TOSCA). *J Am Acad Child Adolesc Psychiatry.* 2013.	• Randomized, controlled • N=168 children with severe aggression • Objective: evaluate the efficacy of adding risperidone to concurrent psychostimulant and parent training (PT) in behavior management ○ NCBRF; ABS; CGI-I	Randomized to: 1) PT + methylphenidate + placebo; or 2) PT + methylphenidate + risperidone *Duration: 9 weeks*	• Augmented treatment with risperidone <u>superior</u> to placebo (NCBRF, $p=0.0016$) • Difference between groups statistically significant at week 9 ($p=0.0143$; ES of 0.43) • CGI scores improved for both groups (79% for risperidone vs 70% for placebo) • Prolactin elevations and GI upset more common with risperidone • Weight gain with risperidone was minor
Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders study (TEOSS). *Am J Psychiatry*. 2008.	• Randomized, controlled • N=119 youth with early-onset schizophrenia • Objective: compare the efficacy and safety of two SGAs with a FGAs ○ CGI-I; PANSS	Randomized to: 1) Olanzapine; 2) Risperidone; or 3) Molindone *Duration: 8 weeks*	• Risperidone and olanzapine <u>not superior</u> to molindone (response rates: molindone 50%; olanzapine 34%; risperidone 46%) • Olanzapine and risperidone with significantly greater weight gain • Olanzapine with the greatest risk of weight gain, hyperlipidemia, and increases in live transaminase levels • Molindone with the highest reports of akathisia

Double-blind maintenance safety and effectiveness findings from the Treatment of Early-Onset Schizophrenia Spectrum Study (TEOSS). *J Am Acad Child Adolesc Psychiatry*. 2011.	• Prospective, observation • N=54 • Objective: examine the long-term safety and efficacy of three antipsychotics ○ CGI-I; PANSS	Randomized to: (see above) 1) Olanzapine; 2) Risperidone; or 3) Molindone *Duration: 12 months*	• Adverse effects (n=15), inadequate efficacy (n=14), or study non-adherence (n=8) most common reasons for discontinuation rates • Treatment arms did not significantly differ in symptom reduction or time to discontinuation • Akathisia more common with molindone and hyperprolactinemia more common with risperidone • No significant differences in weight gain or metabolic events between medication groups

MENTAL HEALTH *Matters*



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