Level 2 Psychopharmacology and Tougher Situations: What to do When First-Line Treatment Has Failed

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Speakers

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Level 2 Psychopharmacology and Tougher Situations: What to do When First-Line Treatment Has Failed

- At the end of this session, learners will be able to…
  - Identify when to use Illinois DocAssist, a free statewide psychiatric access program for primary care providers who need help caring for the mental health needs of children and perinatal women.
  - Describe steps to take when first line psychotropic medications do not adequately treat a patient's mental health condition: ADHD, Mood Disorders, Anxiety, Disruptive Behavior Disorders, Trauma.
  - Describe treatment planning steps when a child is discharged to pediatric practice from a psychiatric hospital/partial hospitalization program/intensive outpatient program.
  - Recognize precautions and unique scenarios with use of antipsychotics in young children

A free statewide teleconsultation program for pediatric and perinatal health care and school clinicians

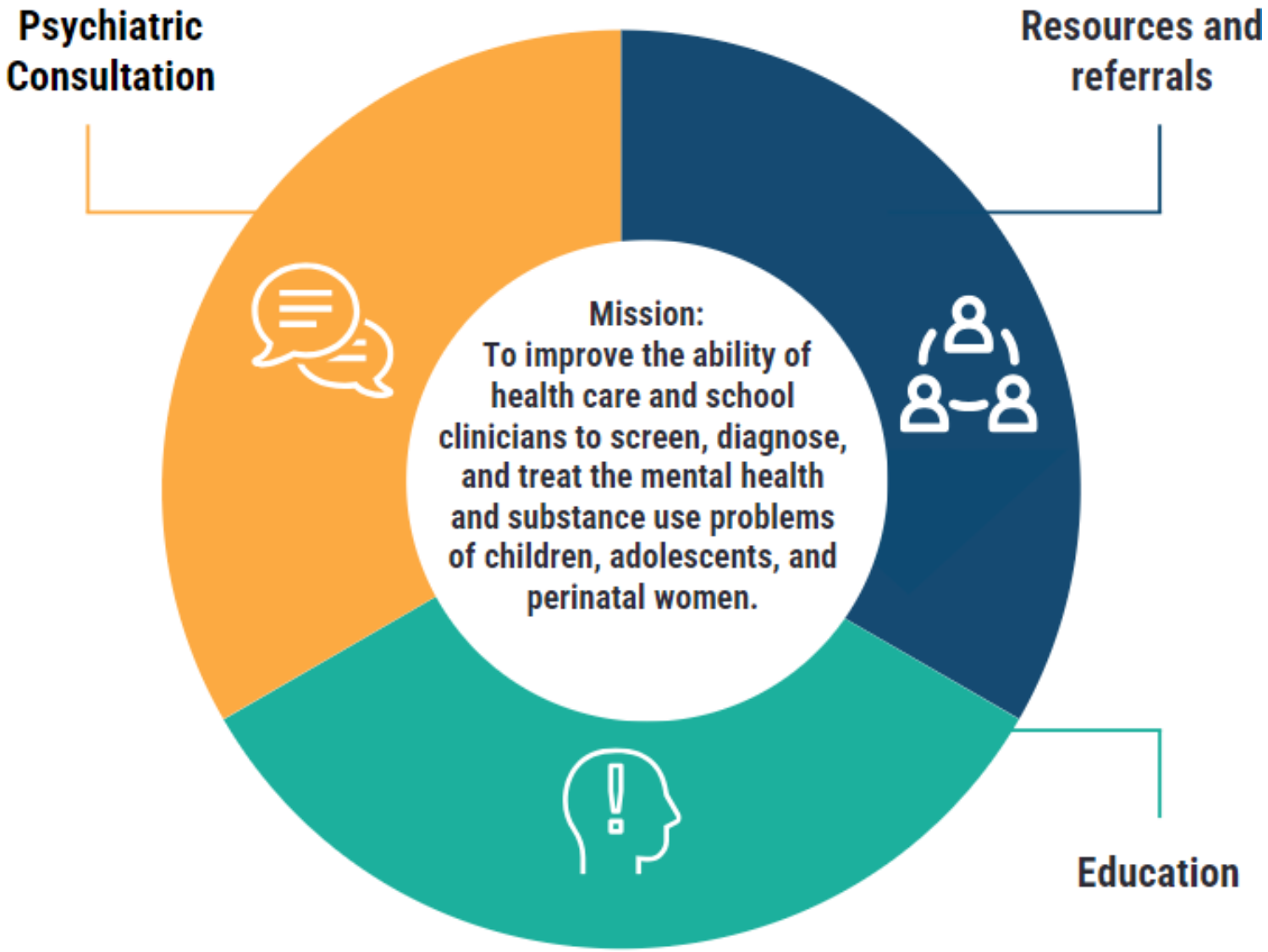
Diane Misch, MD

Rhapsody Mason, LCSW

ILLINOIS DocAssist

Established 2008

Illinois DocAssist Services



E-newsletter sign-up

ILLINOIS DocAssist

Four Steps to Consulting with Illinois DocAssist

1

Contact Illinois DocAssist

866-986-2778

illinoisdocassist.uic.edu

Monday-Friday
9:00 am to 5:00 pm

2

Triage with Intake Staff

Illinois DocAssist trained staff will obtain basic information on provider demographics and the nature of the consult for ease of call back and to match you with the appropriate consultant. DocAssist does not obtain protected health information.

3

Talk to a Consultant

Illinois DocAssist board certified child and adolescent psychiatrists will provide evidence based information to answer your child, adolescent and perinatal mental health questions. All consultations are free of charge to Illinois healthcare providers.

4

Establish Treatment Plan and Follow-up

Illinois DocAssist will help with creating a plan to care for your patient including screening tools, medication management and follow up.

All requestors are responded to within 1 business day and usually **speak with a consultant within 30 minutes**

ILLINOIS DocAssist

Referral Assistance

Vetted referrals for:

- Therapy
- Psychiatrists
- Other type of referral resources

About 3 referrals per referral request

- Insurance
- Languages
- Services
- Wait times

ILLINOIS DocAssist

Continuing Education

- **Pediatric and Perinatal Education**
  - Workshops
  - Presentations
  - Case Consultation Rounds
  - Webinars
  - Open Office Hours
- **Educational Format**
  - In person
  - Virtual
- **Other Educational Sources**
  - DocAssist Website
  - DocAssist Facebook, Twitter, You Tube, Monthly E-Newsletters

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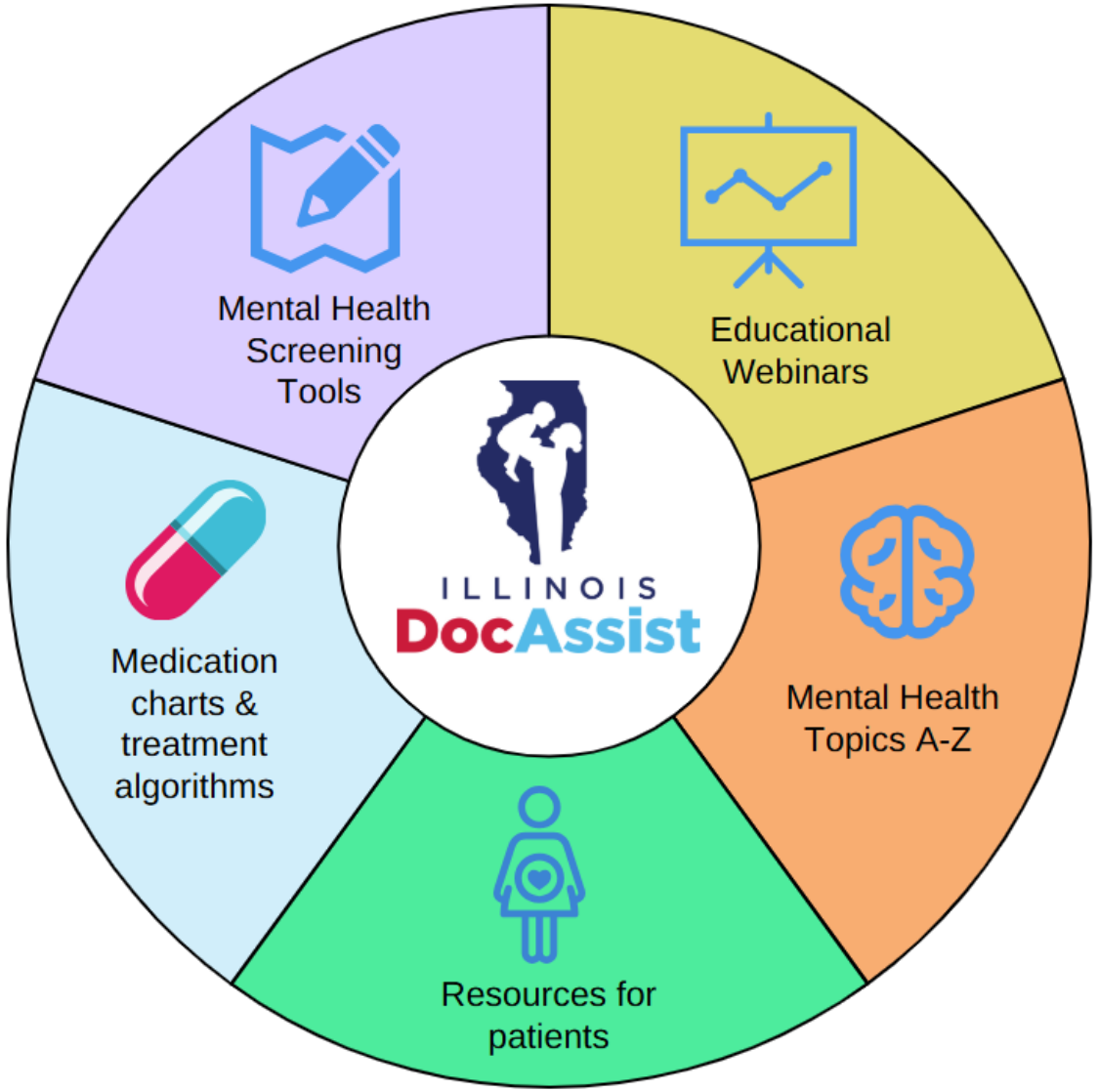
Digital Tools and Resources



Bookmark illinoisdocassist.uic.edu for quick access

ILLINOIS DocAssist

Virtual Open Office Hours for Clinical Pearls, Conversations, and Consultation

- A short presentation focused on a pediatric MH topic
- Discuss your specific questions and cases with a Child and Adolescent Psychiatrist and Psychiatric Social Worker.
- New dates and topics are continuously being added

Learn more and register

illinoisdocassist.uic.edu/news-stories/open-office-hours

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DocAssist Common Q&A

Can I refer my patients directly to Illinois DocAssist?

No; Illinois DocAssist is a problem-based consultation and training service to healthcare providers.

Who can use the services?

Health care and school-based clinicians involved in the care and treatment of children, adolescents and perinatal women.

Do the consultation services cost me anything?

No; All services are free of charge

What is the response time for DocAssist consultations?

You can either schedule a consultation for a future date or time or initiate a consultation real time. A staff member will answer the phone live when you call and connect you with a consultant usually within 30 minutes and always within a business day.

Do you collect Protected Health Information (PHI)

We do not ask callers to provide us with any PHI except in the case of a child who is a ward of the state.

Who will provide the consultation services?

Experts in the care and treatment of children, adolescents, and perinatal women with psychiatric and substance use disorders.

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Interview with an Illinois DocAssist Champion

Sandra Yockey, MD

Assistant professor of clinical pediatrics SIU School of Medicine
Pediatric Primary Care
Decatur, IL

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Thank You!

For clinical tips and program updates, sign up for our e-newsletter…

Consultation Line: 866-986-2778

Hours: 9am-5pm Monday through Friday

Email: docassistil@uic.edu

Website: illinoisdocassist.uic.edu

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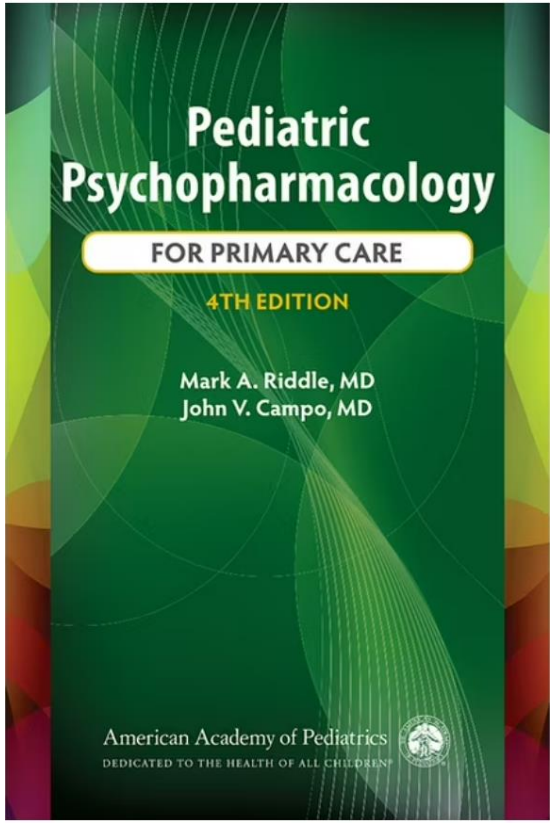
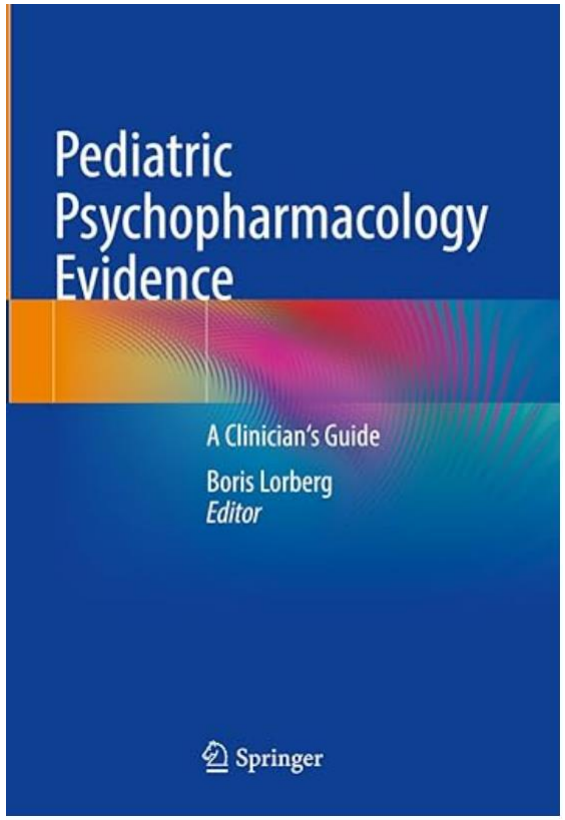
1st Line Pediatric Psychopharmacology

- Guidelines from AAP or AACAP practice parameters and algorithms
- Medication or medication class with evidence- base re: efficacy and safety for use in specific diagnoses or transdiagnostic target symptoms
- FDA approvals often for adults, extrapolated to youth
- Many medications may not be FDA approved
- Off label use may be supported by widespread and enduring clinical experience
- AAP promotes a conceptual framework for prescribing psychotropic medications according to Groups 1, 2 and 3 (Riddle et al)
- Other evidence-based classification of agents are based on the GRADE system (Lorberg et al)

Resources- 2024 publications





AAP Group 1

FDA approval for ADHD, Anxiety Disorders and Major Depressive Disorder

generally safe and PCPs should have competency using all of these

- **ADHD- Stimulants**-methylphenidate, amphetamine

  Alpha agonists-guanfacine ,clonidine

  NRIs-atomoxetine(Straterra), viloxazine (Quelbree)

- **Anxiety**- **SSRIs**-fluoxetine(Prozac), fluvoxamine(Luvox), sertraline(Zoloft)

  SNRI-duloxetine (Cymbalta)

- **Depression-SSRIs**-fluoxetine(Prozac), escitalopram (Lexapro)

AAP Group 2

FDA Approval for other diagnosis (psychosis, mania, autism)

- higher side effect profile with more need for monitoring
- most likely will be started by another prescriber, but PCP will need to monitor efficacy and tolerability
- PCP may start with consultation after CAP or other specialists
- **Antipsychotics-** aripiprazole(Abilfy), asenapine(Saphris), lurasidone(Latuda), olanzapine(Zyprexa), quetiapine,(Seroquel) risperidone(Risperdal), paliperidone(Invega)
- **Mood stabilizer-**lithium

AAP Group 3

No FDA Approval for use in children yet commonly seen in practice :

- **Bupropion (Wellbutrin**)– seizure risk, avoid in bulimia, anorexia nervosa. use to augment in MDD
- **Citalopram(Celexa)-** prolonged QTC risk, use escitalopram
- **Venlafaxine(Effexor)-** more adverse effects than SSRIs
- **Mirtazapine(Remeron**)- sedation and weight gain, sleep aid very low doses, not for MDD/anxiety
- **Ziprasidone(Geodon)-** monitor QTC
- **Divalproex sodium(Depakote**)- Risperidone or lithium better for mood stabilization, PCOS and NTD risk
- **Buspirone(Buspar)-** inferior to SSRI, perhaps as bridge or augmentation
- **Lorazepam(Ativan**)- short term use only, as a bridge or prn
- **Trazodone(Desyrel)-** short term for sleep, priapism risk, limit to low dose, not for depression

GRADE system

Grading of Recommendations Assessment Development and Evaluations

- developed in the early 2000s
- Seen in Up To Date, Cochrane, WHO publications
- identifies both the strength of each recommendation and the quality of the evidence on which the recommendation rests
- **Recommendations** are either for or against the specific treatment
- **Grade 1: strong or Grade 2- weak**
- Factors: risk vs benefits cost; resource /use , patient values / preferences
- **Evidence quality : A (high) , B(moderate) C (low) D (very low)**

Factors re: Efficacy and Safety

- Understand that FDA approval has a business and legal intention for creating patents to sell and market a medication nationally
- Many drug companies do NOT invest the money to conduct pediatric trials and /or seek FDA approvals as historically off label use in children common
- RCTs exist and provide evidence base HOWEVER the populations studied rarely have psychiatric or medical co-morbidity nor racial/ethnic minority diversity. Few studies involving youth with ASD, IDD.

Safety can be determined by

- FDA approval
- At least 10 years on the market with very rare adverse events being detected
- Minimal overdose harm
- Absence of any clinically significant boxed warnings
- Absence of other known or potentially harmful long- term effects

When first line treatments fail…

1- Are you prescribing properly?

- Understand how the prescribed medication work
- Understand key pharmacokinetic and pharmacodynamic principles
- Make adjustment to ensure optimal dosing of a given agent, noting and managing any intolerability that interferes
- Are side effects affecting clinical presentation

2-Did you diagnose properly?

- Are there medical or psychiatric co-morbidities?

3. Is patient adherent?

4. Are evidence- based **psychotherapies/behavioral interventions** in treatment plan?

5. **Are psychosocial stressors, family or individual dynamics/ beliefs affecting response?**

Medication Response and Tolerability

- **Pharmacokinetics** -how the body affects a medication
- **Pharmacodynamics** -the way in which the medication affects the body
- Absorption and distribution affect the rate of a drug's onset of action
- Metabolism and excretion determine the rate of termination of action
- Duration of a drug's action is affected by all the above factors.
- Understand these terms –"peak "concentration, $T_{max,}$ half-life, volume of distribution, bioavailability, therapeutic index
- Children are not little adults-GI transit time, excretion, metabolism, volume of distribution varies with age
- **Start low, go slow, but go all the way to the maximal optimal dose (most efficacy with least side effects)**

When stimulants fail in ADHD

- Vital to understand the difference in formulations and delivery systems
- 41% of patients will respond to both stimulant classes
- 44% of patients will respond better to either Methylphenidates or Amphetamines
- Adderall twice as potent as Ritalin, but equivalent to Focalin dose
- Many online tools for determining equivalent doses.
- Vast majority of youth will respond to stimulants -80%
- Some youth may be “rapid metabolizers” which means duration of action will be shorter than expected
- Side effects and tolerance may vary as per stimulant class and age
- ADHD management over time requires dose and formulation adjustments

Stimulant Pharmacokinetic Basics

Methylphenidate:

- Typical onset of action 30-45 minutes, delay in absorption with high fat food
- Mean duration IR is 3-4 hours, ER up to 12 hours
- Tmax in plasma range 1.5- 2 hours
- Variations of CES1 gene (carboxylesterase 1) impacts hydrolysis, altered kinetics with competing agents

Amphetamine:

- Typical onset of action 30-45 minutes, delay in absorption with high fat food
- Mean duration IR is 4-6 hours, 8-12 for ER, 16 for Mydayis (triple bead)
- Tmax of 3-4 hours.

Why is formulation important?

- “Formulation” effects bioavailability as mechanisms of drug delivery dictate onset of action, duration of effects, consistency of plasma levels, elimination, etc
- Which active metabolites are delivered, mixtures if IR vs CR vs DR
- “Long acting “-less abuse, misuse, diversion potentials, more adherence (vs IR), individualization of treatment
- Long -acting tries to mimic bid, tid IR duration of action
- Many IR and ER formulations, due to pulse release, can wear off precipitously and cause a “crash”
- Some formulations have a “prolonged release” (CR vs DR)
- Chewing or crushing some IR/ SR pills alters the pharmacokinetics of the medications

Long-Acting Formulations

- **Sprinkle caps -**mixture of IR and delayed release beads with differential coatings that dissolve during GI transit (under gastric PH, etc) OR the same bead but multilayer coatings that dissolve to release med in GI tract. Drug embedded in various polymer matrices that dissolve to release under variable conditions .
- **SODAS** (spheroidal oral drug absorption system), **Diffucaps**, **Triple bead** (Mydayis), **Delexis** DR/ER(Jornay);
- **OROS** tripartite osmotic controlled release system (Concerta)- generics try to recreate it
- **Liquid suspensions and ODT** use microparticles with differential dissolution patterns (like beads),
- **Transdermal**(Daytrana)

Case Example

7 year old male with ADHD diagnosed 2 months ago. He weighs 58 lbs.

Stared 2.5 mg bid, increased 5 mg/week , now on MPH 10 mg IR tablet tid

Currently headaches, poor daytime appetite and initial insomnia for the past 2 weeks

Mother and teacher see no response

- Is this an adequate medication trial?
- Maximal dose or maximum tolerated dose?
- Need to reassess diagnosis? Co-morbidity?
- Try alternate medication?

Case Example Follow Up

Alternative class of stimulant started. Patient returns after 2 months

Doing well on Adderall 15 mg XR.

Mom notes irritability in afternoons which subsides by dinner at 6 pm.

Patient plays afterschool sports and has been getting into more conflicts with peers.

What are the possible reasons for these problems?

- Rebound? Hunger? Social Context?
- Will increasing Adderall XR to 20 mg daily help?
- What should you do next?

Case example: One Year Later

Now 8 year old male with ADHD has done well on Adderall XR 15 mg and Adderall IR 5 mg at 3 pm. He was seen in late summer prior to school and has grown.

Mom anticipates a need for more medication because of additional homework and afterschool activities. He is increased to Adderall XR 20 mg in am and Adderall IR 10 mg at 3 pm. On this dose, he is eating well but often has trouble settling down to sleep.

What can be done?

- Majority of people with ADHD have sleep issues
- Falling asleep requires ability to ignore distractions so stimulants can help but sometimes hurt!
- Bedtime Medications: Melatonin (1-10mg), Clonidine (0.1-0.3mg)
- Sleep Routines
- Dim lights, devices off, climate control, sound machine, eye masks, relaxation, warm bath, warm milk/protein rich snack, bedtime ritual

Case Example: Four Years Later

Now 12 year old male patient is in junior high school and doing well. Patient no longer wants to take medication at school because of fear of being "stigmatized."

He is having some impairments in the afternoon**.**

Parents work.

Thoughts?

- Start Vyvanse(d-Amphetamine bound to lysine which is cleaved in body)
- This occurs in bloodstream, so GI tract is not affected
- Metabolized like other AMPs
- Onset 1.5-2 hours, **lasts 12-14 hours**
- Best for older kids, delayed onset, can affect sleep more

Case Example Caveats (and others)

- Try both classes of stimulants before nonstimulant trial- response and tolerability are determined by individual genetics
- Know the duration of action for formulations to “sculpt” dose according to need – do not increase am dose for perceived “failure” in afternoon- add IR or change to longer acting delivery medication
- Identify and manage common side effects on appetite, sleep , mood
- Manage rebound if indicated
- Use objective scales (Vanderbilts) , specify exact points of the day when efficacy wanes to see if cause is related to medication vs environment . For example, a rapid metabolizer of an XR formulation may be more symptomatic at lunch time, when structure is less, prior to the second pulse of medication- adjust formulation. A youth may not eat lunch and be hungry later in day, appearing more inattentive and irritable. A youth may not be sleeping well on a longer acting agent and daytime fatigue effects functioning

When to trial Straterra or Quelbree?

History of adverse effect to stimulants

Comorbid anxiety, depression, tics or Tourette's -especially if stimulants worsen symptoms

Require 24-hour symptom relief

Severe stimulant rebound

Personal or family history of substance abuse

Concern about insomnia or appetite suppression

Any newly diagnosed patient for whom you determine the treatment to be appropriate

- those youth with cardiac contraindications, medical condition where weight stability required BUT educate families about first line use with stimulants and collaborate to generate a good treatment plan
- Note than combination treatment with stimulant is safe practice

Indications for α-2 Agonists

- Useful for residual hyperactivity & impulsivity, insomnia, treatment emergent tics, & aggression
- Can be used to augment stimulant if side effects preclude full optimization
- Note that in some youth, guanfacine in pm can disrupt sleep and cause more daytime symptoms of “ADHD” due to fatigue and sleep deprivation
- Clonidine or Kapvay is often first line for stimulant induced sleep disruption

Another case

In mid October, you see a 7 year old female with recent onset of irritability, temper tantrums. Parents request medications as two older brothers that you treat have ADHD. Several known stressors include the following: 6 months ago, a sibling died from SIDS; the parents were so traumatized that they moved out of the home and into a new one in a new community. Thus, the youth is in a new setting and school. Her teacher just went on maternity leave. The new teacher is raising concerns.

You administer Vanderbilts to the new teacher and parents . Symptoms of inattention, impulsivity and hyperactivity are endorsed. The parents are very concerned about their child falling behind in school. You observe the parents to be very anxious and overwhelmed in the care of the other older siblings who are “acting out” .

You start Metadate CD and give a titration schedule to parents. You see them two months later. They report patient is more attentive in the morning part of class and is progressing well in reading. She is still “moody” at home which parents attribute to conflicts with brothers. She is also having more trouble falling asleep but shares a room with 10 year old brother who is often on his tablet in bed, playing games. You note she has lost 3 lbs.

Case continued

Given the weight loss, you suggest trialing Focalin which may have less effect on appetite and sleep. You instruct parents to use Melatonin if sleeps issues persist.

The parents seem to have their hands full. You do not schedule a follow up.

The family returns in January voicing concerns. They report that child did ok in school on the Focalin XR but irritability with defiant explosions have worsened. Sleep and appetite are disrupted but mother forces protein shakes each night. They stopped the Focalin over break but did not see much change. Child was very isolative with cousins during a holiday trip and seemed to complain about being bored. She told a cousin that she sees herself as “stupid” and “ugly”. The child found a photo of the deceased infant sibling in her grandmother’s home. The parents felt unable to talk about the death and told child to put the photo back.

The parents think child should try an alternative medication for her ADHD. They are adamant the stimulant isn’t working.

Case Discussion

Last October, this child likely had the beginnings of a depressive episode, exhibiting behavioral variants seen in younger children. The history also highlighted risk factors. She may have also had anxiety as the pregnant teacher may have evoked trauma reactions. She has developed more symptoms including poor appetite, sleep disruption, social withdrawal, anhedonia, poor self esteem. Note that more “focus” on a stimulant, seen in school, does not confirm an ADHD diagnosis.

An age-appropriate screening tool for depression can be used and direct questions about self harm, passive and active suicidal ideations should be asked.

The PCP may wish to examine their own countertransference and the family dynamics. The PCP knows the family and may have wanted to offer a “quick fix” , to avoid further “burden”, to avoid talking about painful issues, etc.

PCP should inquire if the family has had bereavement counseling.

Parents can ask for resources at school.

Close monitoring should occur with follow up and mental health referral as this child may develop a high risk for suicide.

PCP can start a SSRI if this is indicated but not resume a stimulant at this time.

Reasons ADHD Medications “Fail”

Failure to optimize stimulant dose in timely manner which can result in ongoing functional impairment and risks for co-morbidity(anxiety, depression, ODD)

Efficacy on a known dose can be determined immediately due to short onset and duration of action. Tolerance to a given dose can develop in a few days-eg appetite, sleep

Increase dose weekly, allowing time for side effects to subside ,until ADHD scales note response below threshold

Target dosing can be mg/kg but stop at lower dosing if ADHD scales indicate

Common target: 2mg/kg MPH, 1-1.5 mg/kg AMP/d-MPH but slow metabolizers or mild cases, inattentive type can do well on lower dose. Note maximum dose recommendations but if use more if needed and tolerated.

Note that Concerta mimics tid but “loses” some -18 mg equals 5 mg tid

No need to “taper”- medication eliminated by next day

Reasons ADHD Medications "Fail"

When stimulants offer partial response and/or optimization is limited by significant side effects at higher dosing. Can lower dose on weekends, holidays BUT do not stop- this will increase the side effects when medication resumed due to renewed intolerance.

Can offer Periactin for appetite, use nutritional supplements, extra snacks, etc

Can switch to or augment with nonstimulant

Can maintain stimulant when introducing Straterra, then stop when Straterra is optimized. Straterra has a latency of response so full effect on a given dose seen 4-8 weeks out. Start 0.5 mg/kg, target 1.0-1.4 mg/kg, max 1.8 mg/kg

Straterra can be in divided dosing for younger kids if too sedating, but one can shift given agent to q24 hr pm. For GI upset, give after meal.

Note that alpha agonists are third line monotherapy-not as effective for inattention, good for hyperactivity, impulsivity, aggression, hyperarousal states, tics. They also have latency of effects and IR should be given in divided dosing to have steady state. Do not combine IR and XR.

In summary for ADHD Failures…

- Vast majority of time , stimulants will result in effective treatment.
- PCP needs to know the pharmacokinetics of various formulations to “sculpt” dosing as indicated.
- Always trial both classes of stimulants before nonstimulants
- Straterra and Quelbree are 2nd line monotherapy agents
- Tenex, Intuniv, Clonidine , Kapvay are 3rd line monotherapy agents
- Combination Treatment is often indicated to augment a stimulant response, especially if optimal dosing is limited by tolerability
- Attempt to optimize dosing as tolerability allows. One can allow time for tolerance to develop and reattempt up titration when indicated. Follow mg/kg guidelines if needed.
- Evidence base recommends combination of parent management/ behavioral treatments and medications so add therapy when medication alone is not working.

Medications with Poor Evidence Base for ADHD treatment

- Modafanil
- Wellbutrin
- Amantadine
- Buspirone
- Armodafanil
- Tricyclic antidepressants
- Venlafaxine

Treatment Definitions: Anxiety / Depression

Response Significant reduction or no symptoms for at least 2 weeks

Recovery Minimal to no symptoms for at least 2 weeks and no more than 2 months

Remission Absence of significant symptoms for at least two months

Relapse An episode during the period of remission

Recurrence A new episode, emergence of symptoms during period of recovery

Acute Treatment Phase –achieve response and full symptom remission

Continuation Treatment Phase -consolidate response and avoid relapses

Maintenance Treatment Phase- avoid recurrences/new episodes

1st Line Treatment-Anxiety /Moderate MDD

Cognitive Behavioral Therapy (**CBT**) is an evidence base psychotherapy for both depression and anxiety

Interpersonal Psychotherapy (**IPT**) is an additional evidence base therapy for depression in teens

Both modalities involve a therapist who meets with youth on a consistent basis over several months

Treatment is based on techniques well established by research

Skills acquired will help to reduce risk of recurrence and future functional impairment

Unlike ADHD, anxiety and depression are characterized by “episodes” that “remit” so therapy and medication use is to be time limited

Medication-Moderate to Severe MDD

Selective Serotonin Reuptake Inhibitors (SSRIs) are the first line of treatment for depression

Fluoxetine(Prozac)*

Escitalopram(Lexapro)*

Citalopram(Celexa)**

Sertraline(Zoloft)

*Most evidence for use in children and adolescents

** trial Lexapro instead due to QTC risk

Medication-Moderate to Severe Anxiety

Selective Serotonin Reuptake Inhibitors (SSRIs)

Fluoxetine(Prozac)

Escitalopram(Lexapro)

Fluvoxamine(Luvox)

Sertraline(Zoloft)

Selective Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

Duloxetine (Cymbalta) –GAD

Tricyclic Antidepressant

Clomipramine(Anafranil)- OCD

Choosing Antidepressant Medications

Prozac or Lexapro as first line for MDD + Zoloft, Luvox, Cymbalta in Anxiety D/O
Can consider family member medication responses
Address pharmacogenetic testing if raised by family
Do not obtain testing to make drug choices
Possible role to explain intolerance/inefficacy

AACAP (Facts for Families):

Pharmacogenetic testing CAN tell your doctor:

How quickly your child's body might process a medication

How effectively your child's body might process a medication

Pharmacogenetic testing CANNOT tell your doctor:

Which medication will work most effectively for your child

Whether or not a medication will cause side effects

What side effect a medication might cause for your child

If there are Side Effects….

Adverse effects tend to come before symptom improvement

- Can be transient
- Associated with dose changes

Educate families on SAFETY and EFFICACY

- Allows for tolerance of mild adverse effects for a full medication trial
- Build therapeutic alliance

Decrease to lowest tolerated dose

- If resolved, wait a week and re-increase at a smaller interval
- If continues, switch medication

Encourage families to contact you with concerns before stopping medication

- Not all side effects necessitate discontinuation

For Serious Side Effect

- Consult psychiatrist or send to ER

Common Side Effects and Management

Side effect	Management
GI upset	Usually self-resolves symptomatic care
Headache	Usually self resolves symptomatic care
Diaphoresis	Usually mild and tolerable
Sedation	Administer at bedtime
Sexual dysfunction	Consider medication change
Weight gain	Counsel on healthy diet
Sleep disruption	Administer in the morning

Pediatric Behavioral Activation Syndrome

Worsening of clinical presentation with one or more: irritability, akathisia, disinhibition, manic appearing, self harm

- Typically, NOT mania or bipolar disorder, even with a strong family history
- No change in mood
- Susceptibility decreases with age

Manage by lowering dose and resuming slower titration, switching to another agent, discontinuation

Akathisia(subjective feeling of restlessness with inability to sit still)-beta blocker

Bipolar switching- MOOD changes to anxious, manic/hypomanic. Occurs later in course of treatment, less common, may persist after discontinuation of SSRI

Recognize Serotonin Syndrome

Avoid polypharmacy to reduce risk, commonly seen in SSRI overdose.

The common clinical triad is

MSE changes (agitated delirium) +ANS Hyperactivity +Neuromuscular excitation

- Fever over 41 C, ANS instability
- Vital sign changes- hypertension, tachycardia, tachypnea
- Neuromuscular excitation with myoclonus, tremor, hyperreflexia.
- Other signs include mydriasis, diaphoresis, sialorrhea

Toxicology should be consulted for a PICU admission to provide supportive care, lowering of fever, addressing ANS instability. Cyproheptadine is used in severe cases.

Medication Management Steps

Start low, go slow (but not too slow)

Monitor

- First follow up in one week (phone or in person)
- Monthly until remission

Treat to REMISSION not RESPONSE

- Prevents relapse
- Monitor using symptom measures
- Remission would be subthreshold symptoms on screening forms

Partial Improvement in 6-8 Weeks

Add medication to mild depression with no improvement with only supportive therapy

If medication trial already started, increase to maximum dosage

- **“Adequate” SSRI trial means at least 8 weeks with last 4 weeks on 40 mg Prozac equivalent (20 mg equivalent if intolerant at higher dose)**
- Add therapy if not already started
- Provider further education- adherence essential to attain therapeutic plasma levels. Marijuana use can increase side effects with Lexapro/Zoloft and should be stopped during trial
- Review safety plan
- Continue to monitor

No Improvement in 6-8 Weeks

Reassess initial diagnosis and treatment plan (substance use? bipolar symptoms?)

- Adherence? New family dynamics? Stressors?
- Maximize dose(if maximized and no improvement, switch medication)
- Ensure participation in CBT/IPT-A

If No or Minimal Improvement With Second Agent

Continue to assess for other “treatment interfering” causes:

- Poor medication adherence
- Comorbidities
- Ongoing psychosocial stresses/abuse

No Response on Adequate Dose/ Duration

1.Try another SSRI

60% of teens with MDD/Anxiety responded to a second SSRI

2.Try an SNRI medication:

Duloxetine(Cymbalta)

Venlafaxine/Desvenlafaxine(Effexor, Pristiq)

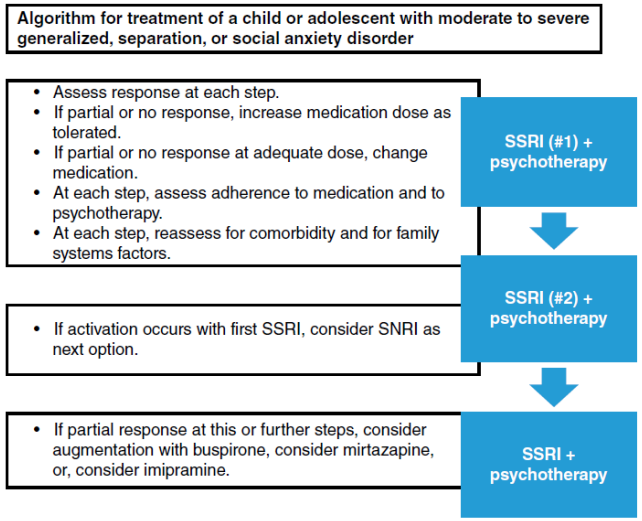
3.If partial response in MDD, unable to increase dose(at maximum or side effects):

Augment with Lithium, Wellbutrin, low dose Abilify

4.Other agents used but not recommended in MDD/Anxiety

Remeron, Trazodone

Anxiety Algorithm Review



Step 1 - SSRI
Step 2 - different SSRI
Step 3 - different antidepressant class (SNRI) : Venlafaxine, Desvenlafaxine, Duloxetine
Step 4- augmentation with Buspar

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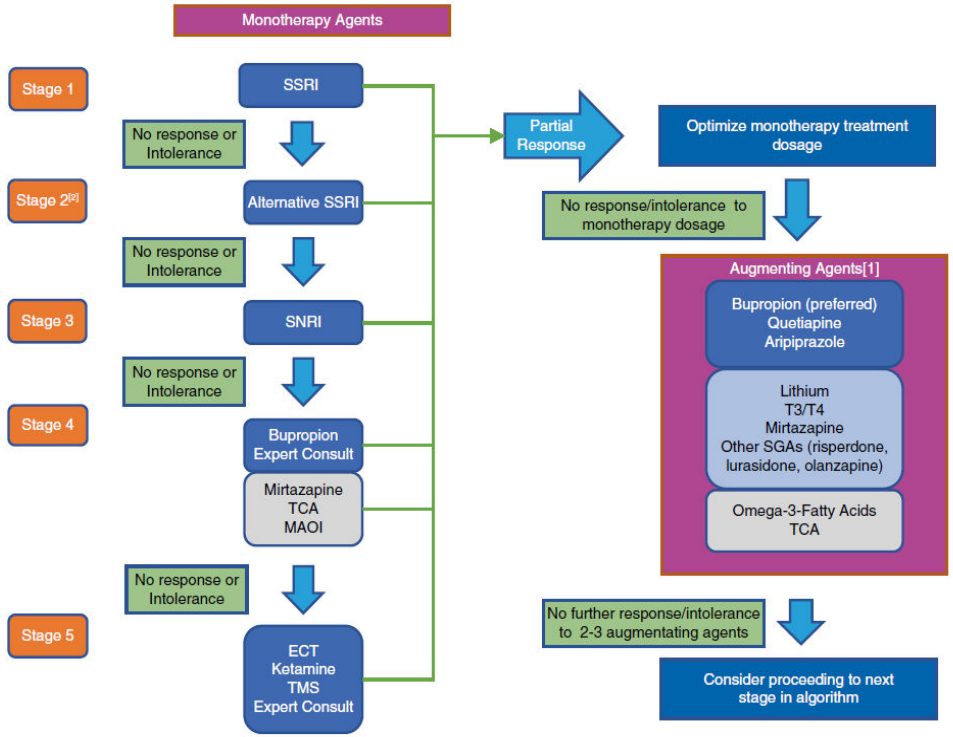
Depression Algorithm Review



Step 1 - SSRI
Step 2 - different SSRI
Step 2A - augment for partial response with Lithium, Wellbutrin, Abilify
Step 3 - different antidepressant class (SNRI) : Venlafaxine, Desvenlafaxine, Duloxetine
Step 4 – combine antidepressants – SSRI + Wellbutrin
Step 5 - combine mood stabilizer (Lithium, Lamotrigine, Abilify)
Step 6-7 - MAOIs used in past , consider ECT, ? Ketamine

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Medications for Anxiety by GRADE

Grade A

Prozac, Luvox, Zoloft ,Cymbalta ,Effexor, Paxil (not used)

Grade B

Lexapro, Buspar , Intuniv and Imipramine

Grade C

Klonapin, Straterra ,Remeron

Grade D

Antihistamines ,Benzodiazepines ,Propranolol ,Pristiq

Dose Equivalents for Full Trials

SSRI	
Fluoxetine	40 mg
Escitalopram	20 mg
Citalopram	40 mg
Sertraline	100 mg
SNRI	
Duloxetine	60 mg
Venlafaxine	150 mg
Atypical agents	
Bupropion	300 mg
Mirtazapine	30 mg

Switching Techniques: Recommended

Conservative switch:

1st drug is gradually reduced and stopped, drug free washout interval of five half lives, 2nd drug started at its initial dose.

Most appropriate for general practice -low risk of drug interactions, discontinuation symptoms may occur

Moderate switch:

1st drug gradually reduced and stopped, drug free washout interval 2-4 days, 2nd drug started at lower dose.

Still low risk of drug interactions, discontinuation symptoms may occur

Switching Techniques: Not Recommended

Direct switch:

1st drug is stopped, 2nd drug started next day at the usual therapeutic dose.

Drug interaction risk is high, discontinuation symptoms likely.

Appropriate for one short half life SSRI to another

Cross taper:

1st drug gradually reduced and stopped as 2nd drug introduced at low dose, taking both simultaneously

Once 1st drug stopped , increase 2nd drug

Should be done in a hospital setting

Discontinuation Syndrome

Can be seen in 1 in 5 patients tapering off SSRI

- **FINISH:**
- Flu-like symptoms
- Insomnia
- Nausea
- Imbalance
- Sensory disturbances
- Hyperarousal (anxiety/agitation)

Slow the taper if intolerable

Sleep Disruption Contributing to "failures" in treatment

Common in patients with depression and anxiety
Ensure teen is not using marijuana or having withdrawal

Importance of Sleep routines

- Dim lights, climate control, sound machine, eyemasks
- Relaxation techniques and rituals
- Remove devices and other electronics from the bedroom
- CBT-I and several apps effective(Calm, Breath2Relax, Belly Bio)

Bedtime Medications:

- Melatonin 1-10 mg (consider XR)
- Clonidine 0.1-0.3mg (consider XR)

Challenge off sleep aid once SSRI optimized and anxiety/depression remits

Case example

A 14 year old started on an oral contraceptive at which time her PHQ-9 is 3. She returns 6 months later with onset of mood changes. Initially she felt sad, would sleep excessively, and isolate herself. In the past month, her depressed mood is daily. She has trouble concentrating, and she is very worried about school performance. Her PHQ-9 is 15 and she denies suicidality.

This case illustrates that many teen and young adult females may develop depression after initiation of oral contraceptives. The OCP should be stopped and antidepressant started if needed. Always notice if there is a temporal association of mood changes and use of hormonal contraceptives. Be mindful using OCPs for acne, can offer copper IUD for birth control.

Case example Follow up

Oral contraceptive is changed and fluoxetine 5 mg qhs is started. The girl returns one week later, distraught and panicky. She complains of feeling “wired” all the time and exhausted from poor sleep.

She changed fluoxetine administration time to early morning and noted feeling restless and jittery by midmorning each day.

Screening reveals no mania or suicidality, but patient remains depressed with onset of panic attacks. Family is scared and she does not wish to miss school.

What is the next step?

What side-effect do you think this is?

What is the cause?

What are some follow-up questions to ask the patient?

Do you stop fluoxetine or lower the dose?

Do you treat the side-effect?

Do you switch to a different antidepressant?

Is the second medication trial a first line SSRI or second line SNRI like Effexor?

What switching strategy do you use?

Case Example

You explain to the parent and patient that she has activation/ akathisia which will subside with discontinuation of fluoxetine.

After a washout of a week, you prescribe Lexapro at a low dose with slow titration. You also prescribe a limited amount of Ativan 0.5 mg prn for Panic.

In several follow ups, patient reports tolerating medication q am and her depression remits. She used Ativan twice.

What to do with more Complex Cases

PCPs often inherit patients started on a complicated medication regimen and are expected to manage symptoms and renew psychotropic prescriptions for youth discharged from acute inpatient, RTC or PHP stays.

Recognize that youth are acutely hospitalized for behavioral concerns that imminently endanger themselves or others. Acute psychiatric stabilization mandates rapid resolution of suicidal, self harm, aggressive behaviors with administration of one or more psychotropic medications targeting acute symptoms and based on preliminary underlying diagnoses. In time, symptom evolution and response to medications may result in clarification and revision of diagnoses and thus interventions.

Psychotropic medications often have a latency of response, eg weeks or months, that will not be fully appreciated during an acute 1-2 week acute psychiatric admission. Titration to optimal dosing and monitoring for adverse effects will fall upon the primary care provider until a psychiatrist is secured.

Common guidelines for best practice

- Always request that a parent share a discharge summary and perhaps bring in medication bottles or the name of pharmacy. Obtain a release of information in order to request records and/or to speak with the prescribing clinician at the hospital.
- Understand the rationale for use of each medication prescribed- the target symptoms, the proposed diagnoses.
- Most medications may be at starting doses and will need to be increased as per tolerability and response. Mood stabilizers (Lithium Tegretol, Depakote) may require titration to a therapeutic serum level while also checking CBC, CMP, TFTS, etc. Atypical antipsychotics may induce changes in prolactin, HA1c and other metabolic indices. Inquire about breast tenderness, galactorrhea, weight gain. Check for EPS and use AIMS.

Common guidelines for best practice

- Depakote in females of or near reproductive age is to be avoided due to risk for PCOS and NTDs. Monitor menses and hormones. If continued, ensure birth control use.
- Medications for sleep are frequently initiated in hospitals. With rare exceptions, youth should not be maintained on these medications. Safe medications for chronic use include clonidine or prazosin(for ADHD, PTSD related insomnia). Antihistamines should not be used long term. Melatonin use also merits trial tapers. Insomnia due to a mood disorder, PTSD, psychosis, substance use should subside as the underlying disorder is treated. Finally, use of Trazodone and Seroquel for sleep, despite use in hospital settings, is not best practice and should not be chronically maintained.
- Always educate youth and parents about supportive psychosocial interventions- therapy, safety plans, diet/sleep/exercise hygiene, counselling for safe sex and substance use. Always check in for compliance and address barriers through motivational interviewing. Consider changes if adverse effects are intolerable.

Case Example

A 16 year old female with history of ADHD disorder returns home after a 4 week psychiatric inpatient stay for history of aggressive impulsivity and mood lability. During this stay, she was diagnosed with Bipolar Disorder and PTSD from recent sexual assault PTA.

She had done well for years on Concerta but after sexual assault, she started to use cannabis and alcohol more regularly and exhibited significant mood instability with probable mania.

Upon discharge from the hospital, she is on lithium 300 BID , Seroquel 300 mg QHS, Trazodone 100 mg QHS , Zoloft 50 mg qam, Concerta 72 mg qam . She complains of sedation and hunger with weight gain. She is unsure if medications are helping.

How do you proceed?

Case Example

You obtain records and collateral information. It seems she did experience mania. There is a positive family history of Bipolar Disorder . She had hypomanic episodes prior to substance use despite mood instability worsening after the trauma.

Steps:

- Refer to therapy, contract regarding abstinence from substances
- Titrate lithium to a therapeutic level on 600 mg bid to address bipolar disorder
- Taper and stop Seroquel- unclear rationale for use ONLY at bedtime. Mood lability or psychosis treatment requires divided dosing to maintain steady state. Use confers unnecessary risk for sedation and weight gain, etc. It is not to be used for sleep.
- Zoloft is low dose. After titrating lithium and several months in TF-CBT to address PTSD, youth tolerates the discontinuation.
- She is unable to sustain sleep off Trazodone but a reduced dose of 25 mg qhs is effective.
- She continues the Concerta as trial off resulted in re-emergence of ADHD symptoms as per teacher and parent report.

Additional Algorithm Overviews

In managing youth with comorbidities and more complex psychiatric presentations, it is always best to consult with providers who have more experience.

Polypharmacy is to be avoided whenever possible and " deprescribing" should be done with guidance when a duration of treatment has been attained. Additionally, a youth may have become "older and wiser" and more able to handle environmental and interpersonal stressor. Environmental, family and social stressors may have subsided and trial taper off selected or all mediations is to be considered.

Nonetheless, current algorithms are presented for review

PTSD

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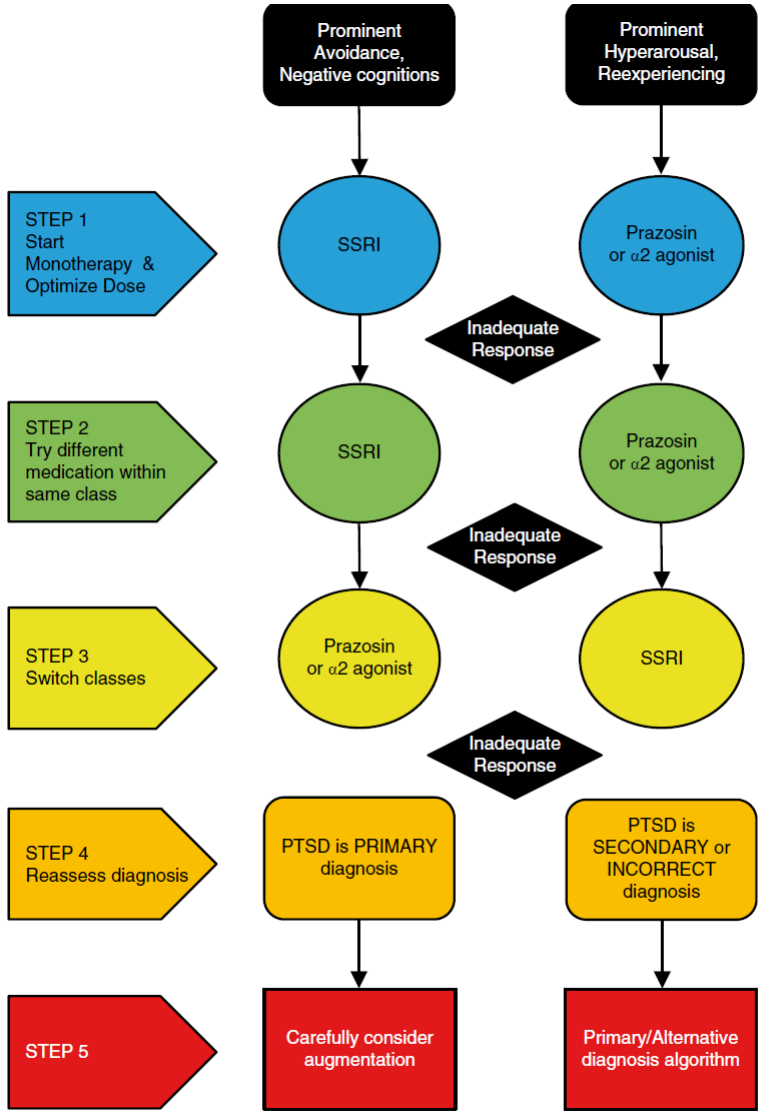


15.1 Pediatric PTSD Medication Treatment Algorithm

Bipolar Disorder Algorithms

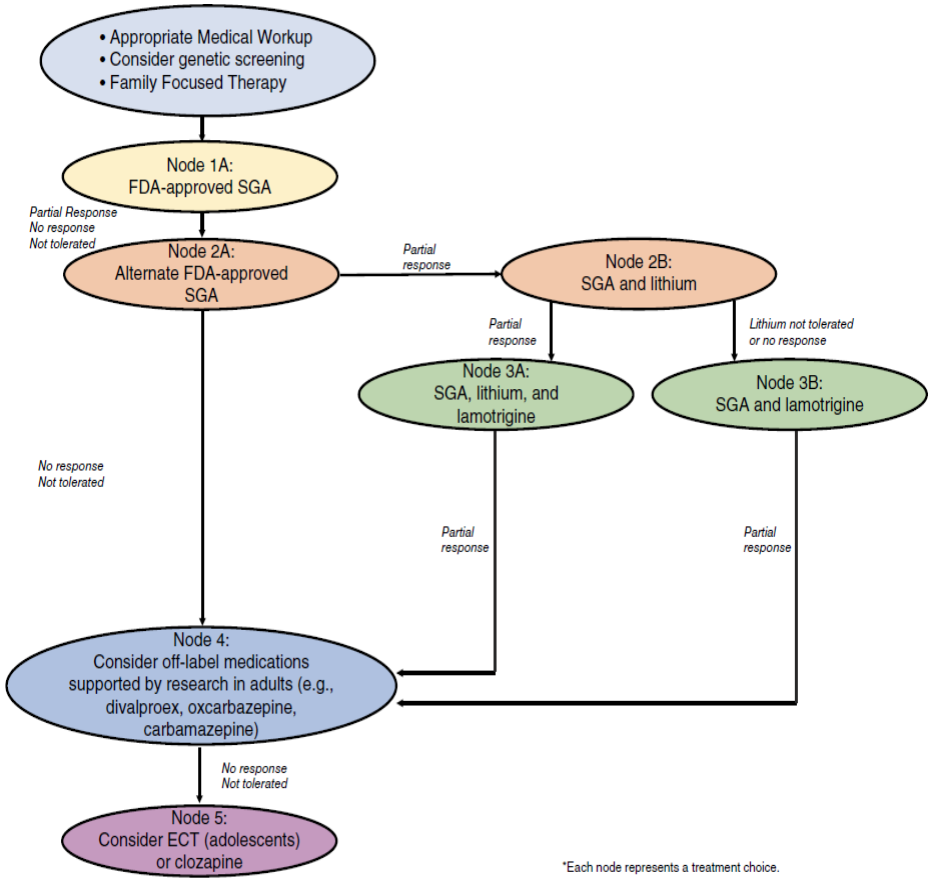
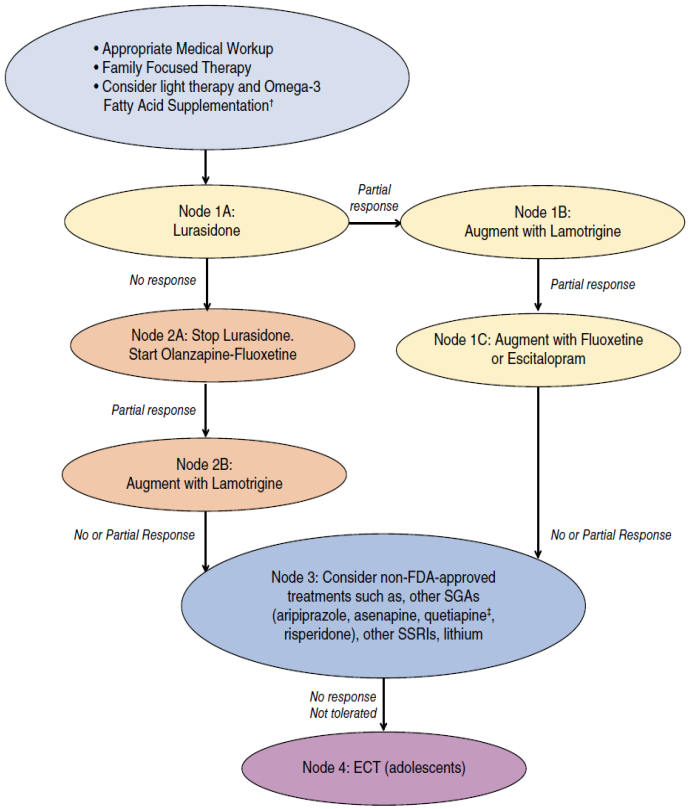


Fig. 17.2 Pediatric bipolar disorder, manic/mixed episodes with psychosis. (Adapted from Hobbs et al. [18])



†These treatments are not FDA approved.
‡Quetiapine has evidence in adults which may make it the preferred alternative treatment.

Fig. 17.3 Treatment algorithm for pediatric bipolar disorder, depressive episode. (Adapted from Hobbs et al. [18])

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ASD Pathway-Irritability/Agitation/Aggression

1. Consider alpha agonist (if impulsivity is significant)
2. Mixed receptor antagonist -eg Risperidone, Aripiprazole
3. Dopamine receptor antagonist- Haloperidol
4. N-acetylcysteine (Pharma-NAC)-for self mutilation
5. Propranolol?—is it akathisia?
6. Divalproex/lithium/carbamazepine/oxcarbazepine?- if bipolar

Medications Worth Trying in ASD

Second generation antipsychotics for irritability, but the side effect burden is high

Metformin as indicated when weight neutral agent less effective

Melatonin is safe and effective for the treatment of insomnia.

Clonidine or Kapvay for insomnia are also good choices

Straterra or Intuniv for impulsivity, hyperactivity

Methylphenidate is effective in some patients with ASD + ADHD but adverse effects likely

SSRIs may help for anxiety/depression BUT start low and go slowly. If the first medication fails, try another one. Use short half life formulations first

NAC (**N-acetylcysteine**)**-**for skin picking, self mutilation

Clinical Pearls: Co-Morbidity

Youth with established treatment for ADHD develop anxiety/depression- add SSRI

Youth with ? ADHD and ? anxiety/depression- SSRI first and reassess after remission

Youth develops psychosis, mania, extreme mood lability on ADHD medication or SSRI- stop agent, wait and then trial atypical antipsychotic or mood stabilizer as indicated . If initial symptoms persist, rechallenge with ADHD or SSRI medication after stabilization on the other agents

Youth with and ADHD and ODD- maximize ADHD treatment

Youth with Anorexia Nervosa with anxiety and depression- no SSRI until weight stable

Youth with Anorexia Nervosa-Zyprexa daily or prn, Antihistamine, Benzodiazepines prn BUT

Hydroxyzine in 50 mg doses can cause QTC prolongation(AN cardiac risk)

No Wellbutrin use in Anorexia Nervosa, Bulimia- emesis/electrolyte lowers seizure threshold

Clinical Pearls: Co-Morbidity

Youth with ASD are more sensitive to stimulants, SSRIs

Youth with IDD metabolize similarly to neurotypical youth

Depakote can cause elevated ammonia so check if MSE changes, sedation, irritability

Keppra can also cause MSE changes with more agitation

Be aware of polypharmacy risk for drug-drug interactions, delirium, toxicity

Always evaluate for substance use if response is poor- note that cannabis can interfere with metabolism of some SSRIs and cannabis withdrawal can cause anxiety(eg sleep aid)

Youth with medical issues with GI tract(G-tube, short bowel, IBS)- choose agents with best bioavailability profiles. Choose accordingly in hepatic and renal disease, adjust in dialysis.

Youth with underlying medical illnesses contributing to depression, anxiety can still benefit from SSRI if indicated- eg Lyme, autoimmune disease, IDDM, etc

High functioning ASD youth, especially female teens/young adults, may socially mask and experience “burnout” or exhibit mood lability which is NOT depression, mania-evaluate carefully

Final Topic: Psychotropics Use in Preschool Children

Medications are rarely the first line approach. Behavioral interventions and parent management training are.

- Young children have slower metabolism and experience more adverse effects
- There are relatively few studies supporting use , most all with limited effect size

ADHD Pathway

- 1st Methylphenidate Product
- 2nd Mixed Amphetamine Salts
- 3rd Alpha Agonist
- 4th Atomoxetine

Final Topic: Psychotropics Use in Preschool Children

In general, no SSRI RCTs in preschool population but use in very low dosing

Anxiety Pathway

- Consider Fluoxetine, Escitalopram or Sertraline

Depression Pathway

- Consider Fluoxetine, Escitalopram or Sertraline

DMDD or other Disruptive Behavior Disorders

- Consider Fluoxetine, Escitalopram or Sertraline
- Try to avoid atypical antipsychotics-low dose Risperdal but watch prolactin
- Alpha agonist but watch for cardiovascular effects

Final Topic: Psychotropics Use in Preschool Children

Sleep Pathway

- Melatonin first choice-0.25 mg-3 mg qhs
- Clonidine –low dose start 0.025 mg (Max Daily Dose - 0.01mg/kg/d)
- Antihistamines may have paradoxical effects, QTC changes

ASD Pathway

- Risperdal or Abilify-low dose
- Tenex or Clonidine if safety assured

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