Practical Pearls in Managing Pediatric Anxiety

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No disclosures

- I will be discussing off-label medication use in this lecture.

Learning Objectives

- Identify presentations of anxiety in the pediatric population
- Create a treatment plan for a medication naïve patient with anxiety.
- Create a treatment plan for a refractory anxiety patient
- Demonstrate comfort in discussing off label use of medications in anxiety and the “black box warning”
- Evaluate patients with Autism Spectrum Disorder and anxiety
- Identify treatment options for anxiety in patients with Autism Spectrum Disorder

Anxiety is common, yet treatable!

- Anxiety is the most common psychiatric disorder with onset in childhood (6-20%)- NIH Data
- Lifetime prevalence 20-30 %, with increased anxiety during the COVID 19 Pandemic
  - If left untreated, can persist into adulthood
  - Depression, Substance abuse, Job Difficulty and Suicidal Behavior
- Anxiety is genetic + environmental
  - Twin studies + heritability
  - Not personal failing

What is normal vs. pathologic anxiety?

Normal Anxiety	**Pathological Anxiety**
Predictable triggers	Triggers are normal developmental triggers
Proportionate reaction	Disproportionate Reaction
Can occur anytime in a person's lifespan	***Predictable Age of Onset*** ***6-12 years (Separation/GAD/Social)*** ***Adolescence (Panic)***
Children exposed to severe stressors	Symptom patterns are similar/highly stereotyped

Age of Onset of Pediatric Mental Health Disorders

Toddler/Preschool (0-3 Years)	Early School Age (4-7 years)	School Age-prepuberty (6-12 years)	Adolescents (13-16 years)	Late Teen/Young Adult
ASD	ADHD	Anxiety	Depression	Bipolar/Psychosis Panic Disorder

Anxiety Disorders DSM 5

- **Separation Anxiety Disorder**
- **Generalized Anxiety Disorder**
- **Social Anxiety Disorder (Social Phobia)**
- Panic Disorder
- Agoraphobia
- Specific Phobia
- Selective Mutism
- *Obsessive compulsive disorder*
- *Acute Stress Disorder*
- *Post- Traumatic Stress Disorder*

Common Chief Complaints in Anxiety

- “Stressed out, Dread, Worry, Fear, Shy, Home sickness”
- Physical symptoms
  - Headache, stomachache, chest pain, SOB
- Struggling with peer relationships
- Eating concerns- over and under eating
- School performance- inattention/concentration
- Explosive outbursts
- Sleep disturbances- sleep onset and night time awakenings
- ***Excessive need for reassurance***
- Avoidance of kid appropriate activities- school, party refusal

Evaluation of Anxiety Patients

- **Multi Informant Approach-** parents/caregivers/teachers/school staff
- Common to have **varying reports** from child/caregiver
  - Parents unaware/accommodating for years, parents overstate/their own mental health at play
  - Child may be embarrassed or want to please
- **Interview**- face to face or virtual with the child and caregiver/parent
  - Symptoms, frequency, duration, specific thoughts/triggers
  - Assessing function and severity to help make diagnosis
  - Explore trauma/neglect/abuse
  - Developmental history, medical history, family psychiatric history, social history (HEADSS)

Rating Scales are Reliable in Anxiety!

- **SCARED**
  - Child/Caregiver Self Report-41 questions available for free in 10+ languages.
  - Ages 8-18
  - Subscales related to different anxiety disorders
  - Screening/monitoring symptoms overtime- Scale of 0-1-2.
  - If they have any amount of the symptom- answer 1 (sometimes) (0- never/rare, 2- very true/often)

- **GAD7**
  - Free/7 questions. Not pediatric focused.
  - Good for monitoring- focuses on function/good for follow up

- **Pediatric Symptom Checklist (PSC)**
  - Age 4-11, Free
  - Externalizing/Internalizing/Attention

Cannot be used alone to diagnose an anxiety disorder

Differential Diagnosis- other psychiatric Disorders

- ADHD
- Depression
- Bipolar Disorder
- Autism Spectrum Disorder
- Learning Disorder
- OCD/PTSD/Acute Stress

Differential Diagnosis- other considerations

- Bullying
- Abuse
- Adjustment Disorder
- Migraine, IBD, Asthma, Thyroid Disease
- Substance use
- Drug Side Effects
  - Asthma Meds, steroids, antipsychotics, antiseizure, antihistamines, cold medications

Separation Anxiety Disorder

- Excessive fear anticipating or actual separation from those to whom the child is attached.
- 3+ of the following symptoms
  - Recurrent distress
  - Worry about losing their attachment figure
  - Worry about getting lost/accident/kidnapped
  - **Refusal to go out/leave home**
  - **Fear of being alone even at home**
  - Sleep away from home or without attachment figure
  - Nightmares about separation
  - Physical symptoms when separation occurs/anticipated
- Persisting 4 weeks in children/adolescents. 6+ months in adults
- Consider ASD in the differential- excessive resistance to change

Generalized Anxiety Disorder

- Unable to cope with **uncertainty**. Living with **dread/worry** more days than not- 6+ months
- 1-3 symptoms
  - Restlessness/keyed
  - Easily fatigued
  - Difficulty concentrating/mind going blank
  - Irritability
  - Muscle tension
  - Sleep disturbance
- **High performing-** don't break rules, perfectionist, leads to burn out

Social Anxiety Disorder

- Hard time engaging with **less familiar peers and adults.**
  - Does have age-appropriate relationships with familiar people
- Fear or anxiety around social situations that are observed by others
  - Conversations, watched while eating or drinking, talking in front of class
- Humiliating or **embarrassing**- worried about rejection or offending others
- Crying/**tantrums**/freezing/clinging/shrinking/failing to speak
- **Adolescence- peak time of struggle.**

Panic Disorder

- Presents more commonly in **later adolescent years**
- **Worry about additional panic attacks/avoidance behaviors**
- Associated symptoms- **peaks in minutes**
  - Palpitations/increased heart rate
  - Sweating/Trembling/shaking
  - SOB/Choking
  - Nausea/GI Distress
  - Chills/heat
  - Numbness/tingling
  - Derealization or depersonalization
  - Fear of losing control
  - Fear of dying

Agoraphobia

- Marked fear/anxiety about:
  - Using public transportation (planes)
  - Being in open spaces (parking lots, bridges)
  - Being in enclosed places (shops, theater)
  - Standing in line, being in a crowd
  - Being outside of the home alone
- Avoiding spaces/situations for fear of having a panic attack and not being able to escape
- **Commonly diagnosed with Panic disorder**

Specific Phobia

- **School Age years**
- Animal (spiders, insects, dogs)
- Natural environment (heights, storms, water)
- Blood injection injury (needles)
- Situational (planes, elevators)
- **70% have another anxiety disorder**

Selective Mutism

- Early form of social anxiety, **predictor of social anxiety disorder**
- Only speak in safe home settings- not at school
- Interferes with education
- Lasts at least one month (not the first month of school)

Treatment- Multimodal

- Education of parents and child about the anxiety disorder
  - Avoidance is reinforcing
- School Involvement
- Psychotherapy
- Pharmacotherapy
- Combination of the above
- Treatment planning should consider the severity and impairment of the anxiety disorder

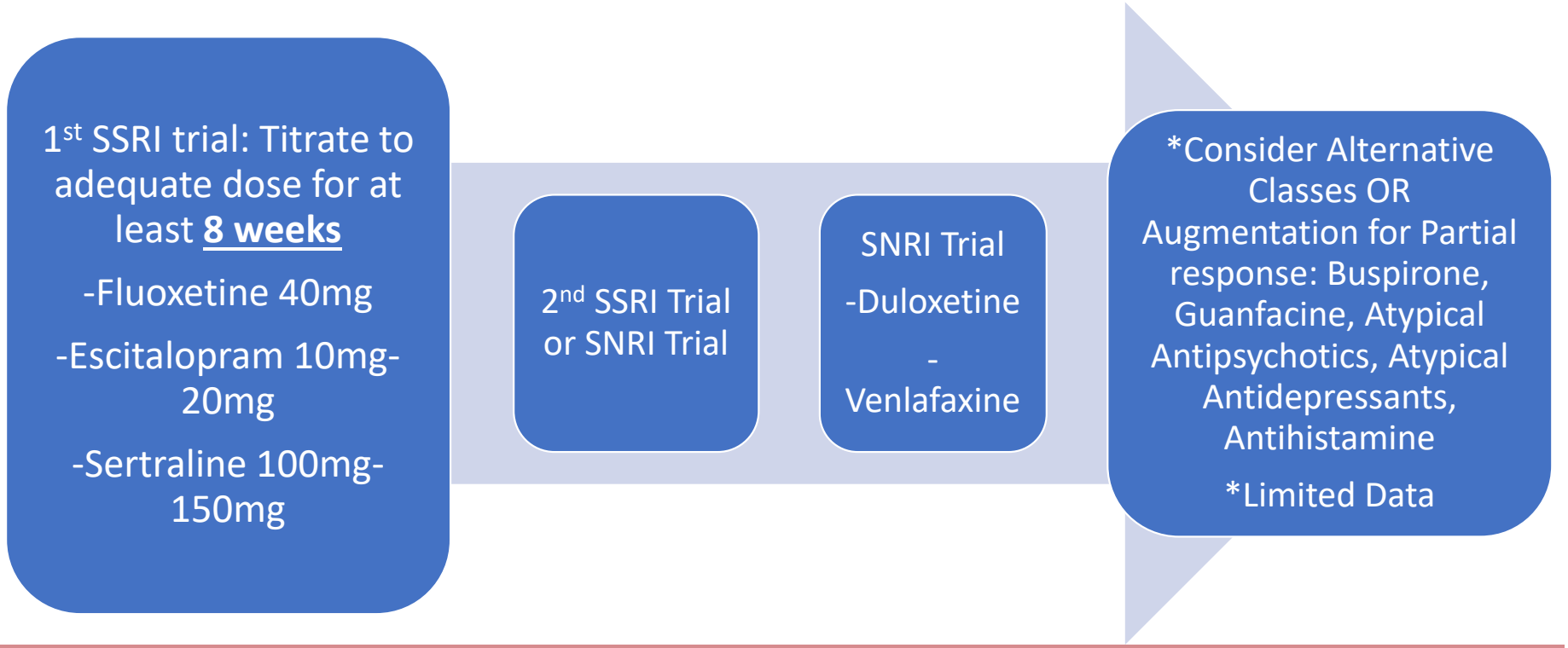
Psychotherapy

- **<u>Mild to Moderate Anxiety</u>**
  - ***Cognitive Behavioral Therapy (CBT)- evidence based, current standard for GAD, Separation Anxiety, Social anxiety, <u>Specific Phobia-</u> age 7+***
    - Exposure therapy, Identify and Change negative thoughts. Parent involvement for younger kids. Psychoeducation
    - Role of avoidance in maintaining anxiety
  - Social Effectiveness therapy for children (SET-C)- Social Anxiety
    - Exposure therapy and Social skills training
  - Acceptance and Commitment therapy (ACT)- GAD, Sep and Social Anxiety
    - More psychological flexibility-Observe negative thoughts, accept them to move forward
  - Parent-child interaction therapy (PCIT)- separation Anxiety
    - Reinforce desired behaviors, extinguish unwanted behaviors
  - Play Therapy

Pharmacotherapy- when do you start meds?

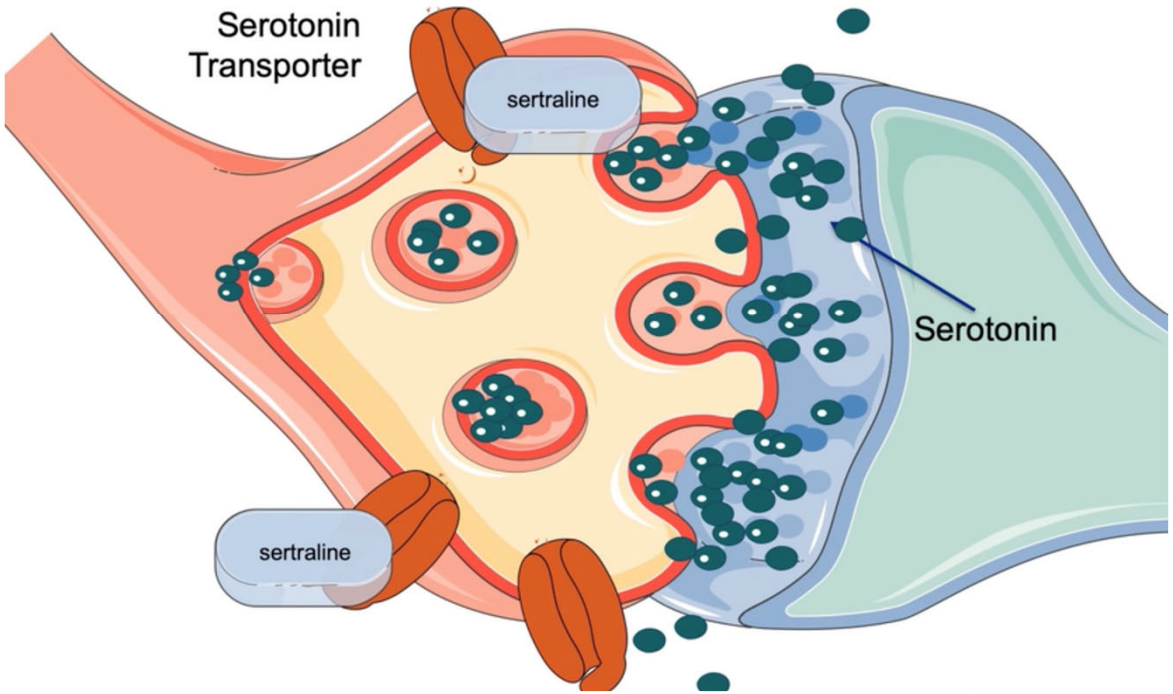
- Need for acute symptom reduction in **moderate/severe anxiety**
- Partial response to psychotherapy
- **Impairment makes psychotherapy participation difficult**

Pharmacologic Treatment Algorithm for Moderate/Severe Anxiety



Evidence based data for improved outcomes with **combination treatment (Meds- SSRIs + Therapy/CBT)**

How do Selective Serotonin Reuptake Inhibitors (SSRIs) work?



- Anxiety related to serotonin dysfunction
- Increases levels of serotonin in the synapse almost immediately
- Downregulation of post synaptic serotonin receptors over time (weeks) causes the neuron to release more serotonin

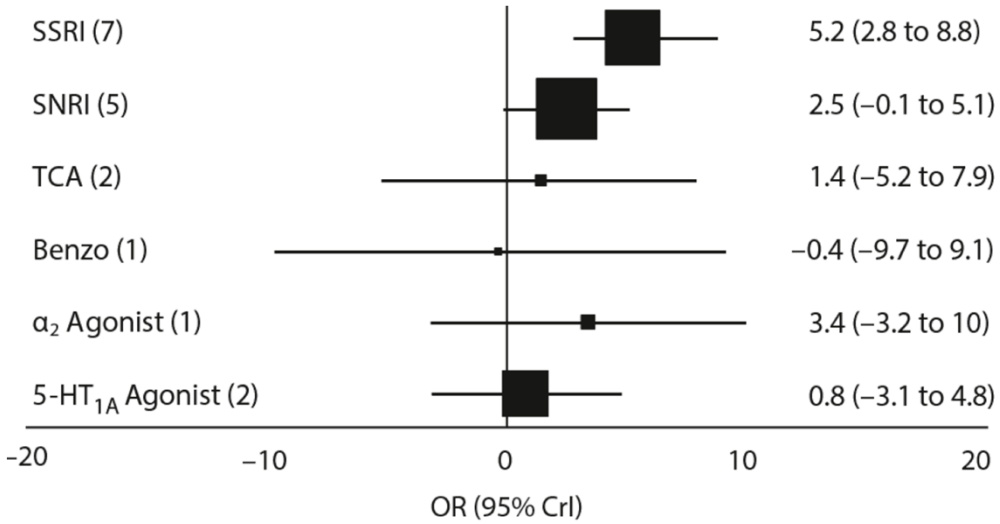
FDA approved antianxiety medications for kids- VERY FEW

Class	Medication	Age (years)							
		6	7	8	9	10	11	12	13-17
SSRI	Citalopram	NONE							
	Escitalopram	NONE							MDD
	Fluoxetine		OCD						
		NONE		MDD					
	Fluvoxamine			OCD					
	Paroxetine	NONE							
	Sertraline	OCD							
	Vilazodone	NONE							
	Vortioxetine	NONE							
SNRI	Duloxetine		GAD						
	Desvenlafaxine	NONE							
	Venlafaxine	NONE							
Atypical Antidepressant	Bupropion	NONE							
	Mirtazapine	NONE							
	Trazodone	NONE							
TCA	Clomipramine					OCD			

Treatment- SSRIs- Off Label Use for Pediatric Anxiety

- Duloxetine (SNRI) is the only FDA approved medication for GAD > 7 years
- **SSRIs are Off label for Pediatric Anxiety**
  - Proven to be safe and effective in the evidence-based data
  - Standard of care by AAP, AACAP, APA
  - 80% of medications are not approved by the FDA for use in children
- **START WITH AN SSRI**

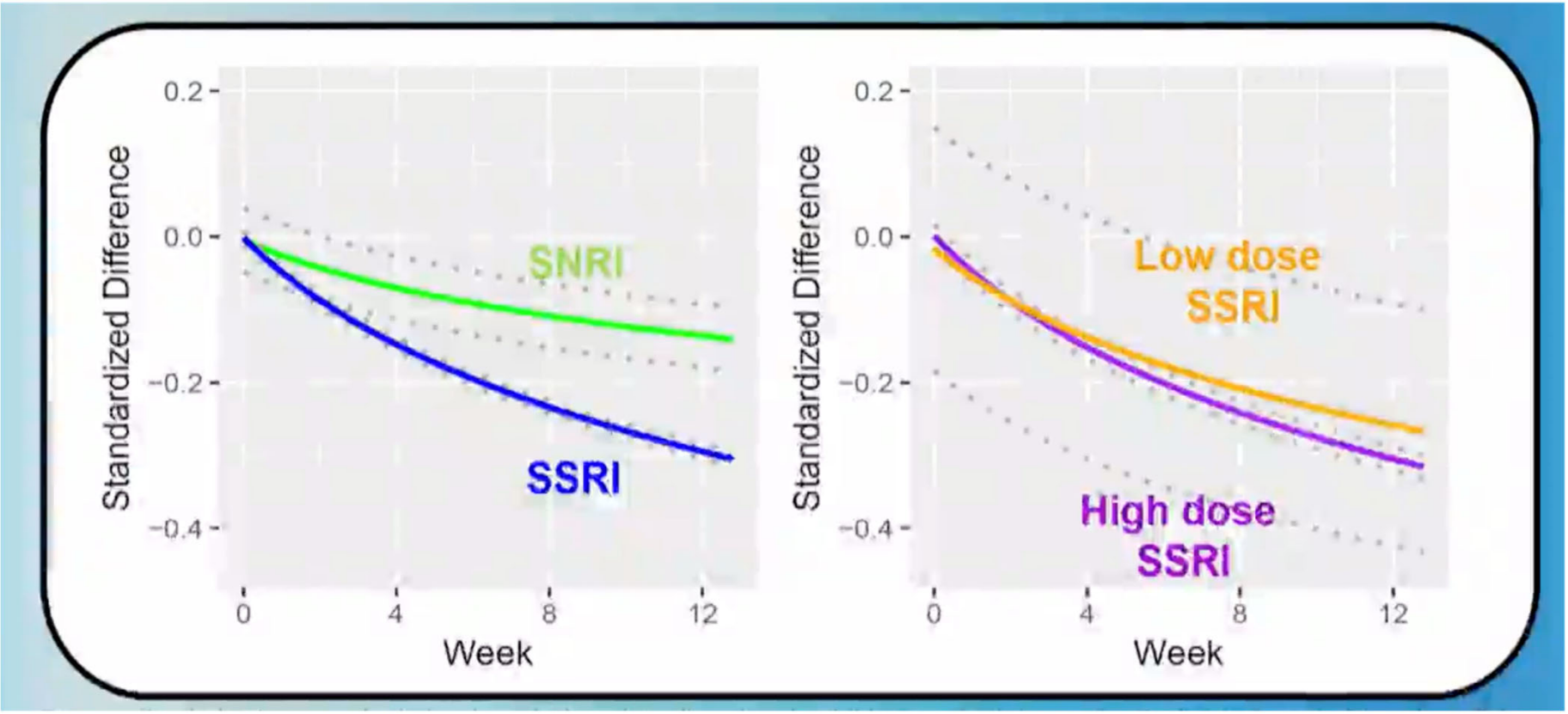
Comparing Medication Classes in Pediatric Anxiety



- Largest meta analysis of psychopharmacology for pediatric anxiety
- Double blind RCTs
- Treatment Response
- SSRIs are far superior!
- TCAs and Benzos do not work
- Alpha-2 agonists helped in 1 study

Dobson ET, Bloch MH, Strawn JR. Efficacy and tolerability of pharmacotherapy for pediatric anxiety disorders: a network meta-analysis. J Clin Psychiatry. 2019;80(1):17r12064.

SSRIs vs SNRIs

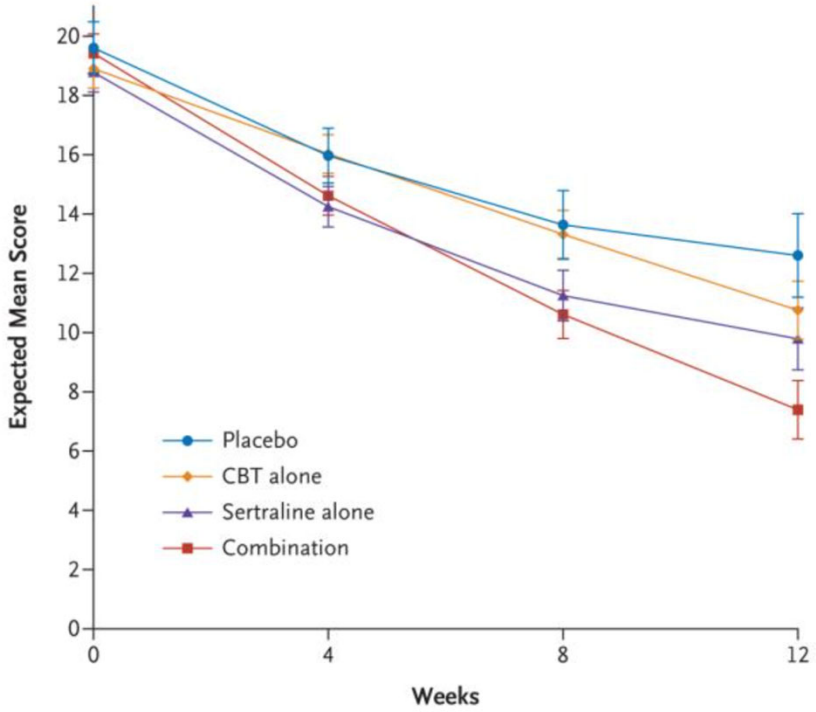


Strawn et al: Pharmacologic treatment of anxiety disorders in children and adolescents. Pediatric Anxiety Disorders. Ed: Kristensen H, Villabo M, and Compton SN. Elsevier, New York, NY pp 360-385. 2018

- ***Don't use an SNRI first- produce less improvement more slowly compared to SSRIs***
- ***Always use an SSRI first!***
- ***High Dose gets kids better quicker, but then over time there is no difference.***

Combination Treatment- SSRIs + CBT

- CAMS (Child and Adolescent Multimodal Study)
- Largest RCT to date of childhood anxiety disorders
- Combination treatment was more effective than either monotherapy
- ***Sertraline- mean dose 140mg/day***
- ***Max benefit at 24 weeks***



Walkup Et al. N Engl J Med. 2008 Dec 25; 359(26): 2753–2766.Cognitive Behavioral Therapy, Sertraline or a Combination in Childhood Anxiety

Talking to parents about SSRIs

- Emphasize medical model
  - Genes + Environmental component, not personal failing
- Not addictive- can be stopped safely anytime.
- Start low, go slow, close monitoring, frequent visits
  - Consider family history of bipolar, concern for ASD/ADHD (low/slower)
- Expected Response time
  - Goal to get to target dose by week 4-8, stay at target dose for at least 8 weeks
  - Can see improvement in 2-4 weeks but need to wait at least 8-12 weeks for full response
  - Max peak benefit at 24 weeks
- How long will SSRI treatment last?
  - 6-12 months based on adult data extrapolation
  - Will reassess and consider a trial off medications
  - No evidence showing long term negative effects of SSRIs

SSRI/SNRI Titration Schedule for Pediatric Anxiety

Medication	Starting Dose	Increments (weekly)	Target Dose Range by week 4-8, Stay for 8 weeks	Maximum Dose
Sertraline	12.5mg-25mg qAM	12.5mg - 25mg	100-150mg	200mg (300mg)
Escitalopram	2.5mg-5mg qAM	5mg	10-20mg	20mg (30mg)
Fluoxetine	5-10mg qAM	10-20mg	20-40mg	60mg (80mg)
Citalopram	10mg qAM	10mg	30-40mg	40mg
Fluvoxamine	25-50mg QHS	50mg (move to BID)	100-150mg	300mg
Paroxetine/CR	10mg QHS (12.5mg CR)	10mg (12.5mg CR)	40-50 (12.5-37.5 CR)	50mg (60mg)
Duloxetine	30mg qAM	30mg	60-120mg	120mg
Venlafaxine	75mg/day (divided BID) XR (once daily)	37.5-75mg	75-225mg	225mg (375mg)

- Initiate Med: Titrate weekly to target dose by week 4 (or slower: based on patient, family dynamics and scheduling options)
- Month 1: weekly visits
- Month 2: biweekly
- Month 3: every 4-8 weeks

Side effects of SSRIs

- **For all SSRIs, you see side effects before you see benefits!**
  - Anticipatory guidance
  - Anxiety patients are more sensitive/aware of changes in their body
  - Most common side effects start early and go away within 2 weeks
- **GI most common: Nausea, loose stools**
- Insomnia/Fatigue
  - **Peak blood levels 4-6 hours after taking medication. Change dosing time.**
- Headache, tremor

SSRI Side Effects

- **Activation-** more common with SSRIs >SNRIs > placebo
  - Early in treatment or with a dose change- most likely related to serum level of SSRI
  - Insomnia, restless, distractible, silly, irritable, agitated
  - More common in younger kids
- **Treatment approach for SSRI associated activation:**
  - Rule out medical condition
  - Wait a few days if not too impairing
  - Decrease SSRI dose (wait for activation to improve/resolve). Restart and titrate more slowly
  - Switch Medications/Stop Medication:
    - Fluoxetine (CYP2D6)  Sertraline/Escitalopram (CYP2C19)

SSRI Side Effects

- Induction of **mania** is < 2 %, no statistical difference vs placebo
  - Don't fear mania
  - Explosive outbursts can be part of anxiety
  - Elation, grandiosity, racing thoughts, decreased need for sleep, hypersexuality
  - Symptoms occur later in treatment and continue once SSRI is stopped.

- **Serotonin syndrome**-confusion, delirium, rapid heart rate, restlessness, muscle rigidity, sweating/shivering, tremor, dilated pupils
  - Risk very low with SSRI monotherapy (more common with TCAs, MAOIs). Occurs within 24 hours.
  - Adolescents using illicit drugs (MDMA/ecstasy), supplements (St. John's Wort)

- **Suicidality?**

Black Box Warning

- October 2004: Black Box warning on all antidepressants for suicidality in adolescents and children, up to age 24
  - 24 Trials examined, containing 4400 children and adolescents
  - 9 Antidepressants included
  - **No completed suicides in these trials**
  - More youth on a med spontaneously reported suicidality vs. youth on placebo (4/100 vs. 2/100). Treat 100-140 children to see 1 child report increased suicidality
    - **Only reported suicidal thoughts and behaviors: None of these studies had any completed suicides!**
    - **Based on spontaneous reports, no systematic suicide risk assessment**

Black Box Warning Discussion/Suicidality

- **Further studies found no increased risk when SI was systemically assessed using structured rating scales**

- Population studies show higher rates of antidepressant rx are associated with lower rates of attempted and completed teen suicide

- Treatment Emergent suicidality differs among specific medications- not across medication classes
  - Higher rates of SI with starting at high doses (always start low)
  - Paroxetine- most suicidality
  - **Sertraline- least suicidality. Lower rates of suicidality compared to placebo**
  - Benzodiazepine treatment- more SI compared to placebo

Black Box Warning Discussion/Suicidality

- **No scientific consensus exists on whether these medications are truly associated with an increased risk of new-onset suicidal ideation**
- **Benefits of SSRIs much greater than the risks for suicidality.**
- **Recommend frequent monitoring of children for suicidal thoughts when these medications are started.**
- **Create partnership with the family**

How to pick your first line SSRI?

- Your personal preference
- Family's preference, family's experiences
- Family's dose response/history
- Compliance Issues
- Liquid/Capsule/Tablet
- Insurance coverage

Sertraline

- **Best studied in Pediatric Anxiety, most evidence based**
- Comes in liquid and pills
- Start at 12.5mg-25mg, FDA max is 200mg
- Increase by 12.5mg or 25mg- weekly
- Goal of 100-150 mg/day by week 8
- Can go up to 300mg (OCD or refractory anxiety)
- Only FDA approved for OCD

Fluoxetine

- **Longest half life**
- Great for patients with medication compliance issues
- Pill/Liquid
- **Lots of pediatric data, SSRI that has been on the market the longest**
- First FDA approved SSRI for kids- depression and OCD
- Start at 10mg, target dose 20-40mg.
- Will go up to 80mg for refractory anxiety or OCD
- Less discontinuation symptoms
- More drug drug interactions (CYP2D6 inhibitor-antiseizure/ migraine/ anticoagulants)
- Possibly more activation side effects

Escitalopram

- Start at 5mg. Target dose 10-20mg
- Easy dose titrations
- **FDA approved for adolescents with depression**
- NIH and industry funded double blind RCT show improvement in children/adolescents with GAD compared to placebo.
- Will go up to 30mg for refractory anxiety or OCD
- More sedation- move to bedtime if needed
- Tablet or liquid

Paroxetine

- **Highest treatment emergent suicidality of the SSRIs**
- More withdrawal symptoms due to very short half life
- Tablet or Liquid
- Start at 10mg, target dose 10-50mg

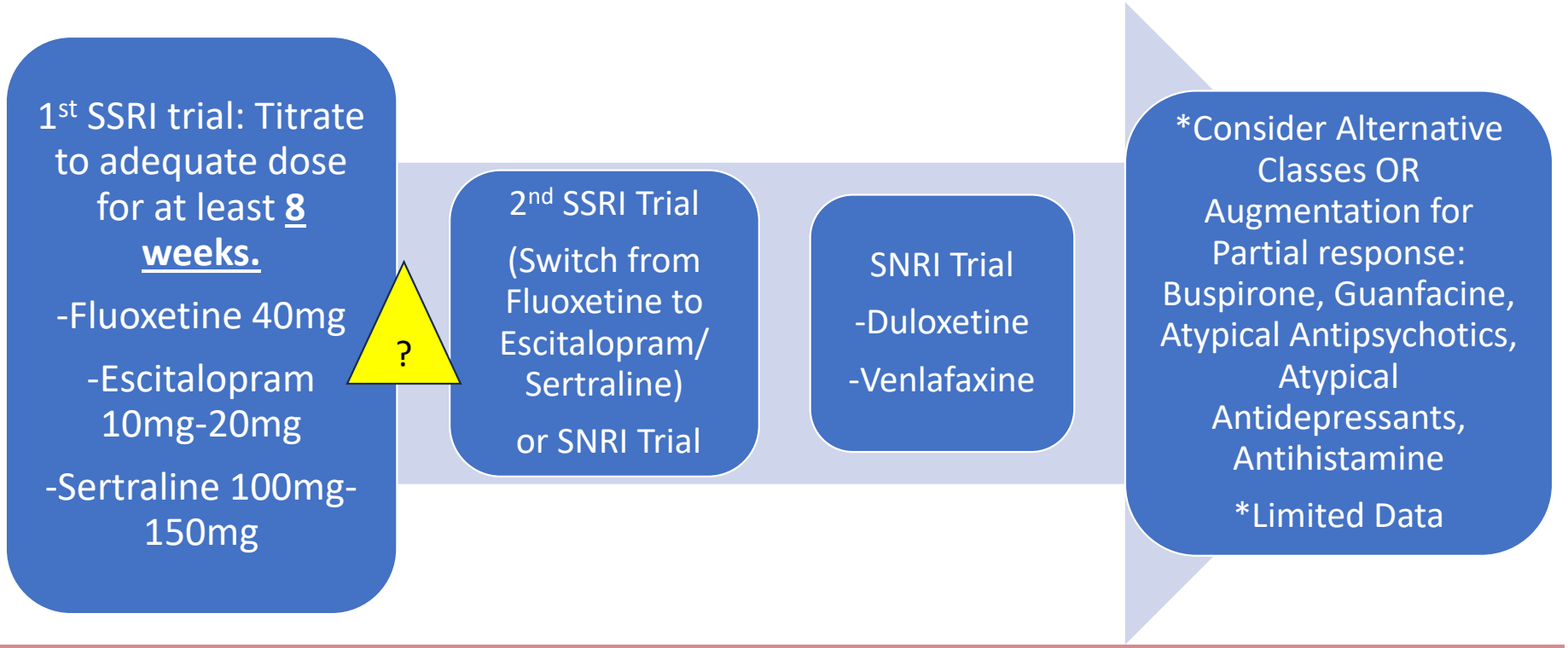
Citalopram

- No pediatric anxiety studies
- Weight gain side effect when compared to fluoxetine and sertraline
- Tablet and liquid

Fluvoxamine

- **Very short half life**
- Needs to be dosed BID
- Start at 25-50mg daily, then move to BID >50mg (Target dose 100-150mg)
- Tablet only
- **FDA approved for Pediatric OCD**
- Can be helpful for OCD tendencies- skin picking, nail biting

Pharmacologic Treatment Algorithm for Moderate/Severe Anxiety



Combination treatment (Meds- SSRIs + Therapy/CBT) is the most effective treatment!
-MAKE SURE YOUR PATIENT IS IN THERAPY.

Cross Titration between SSRIs

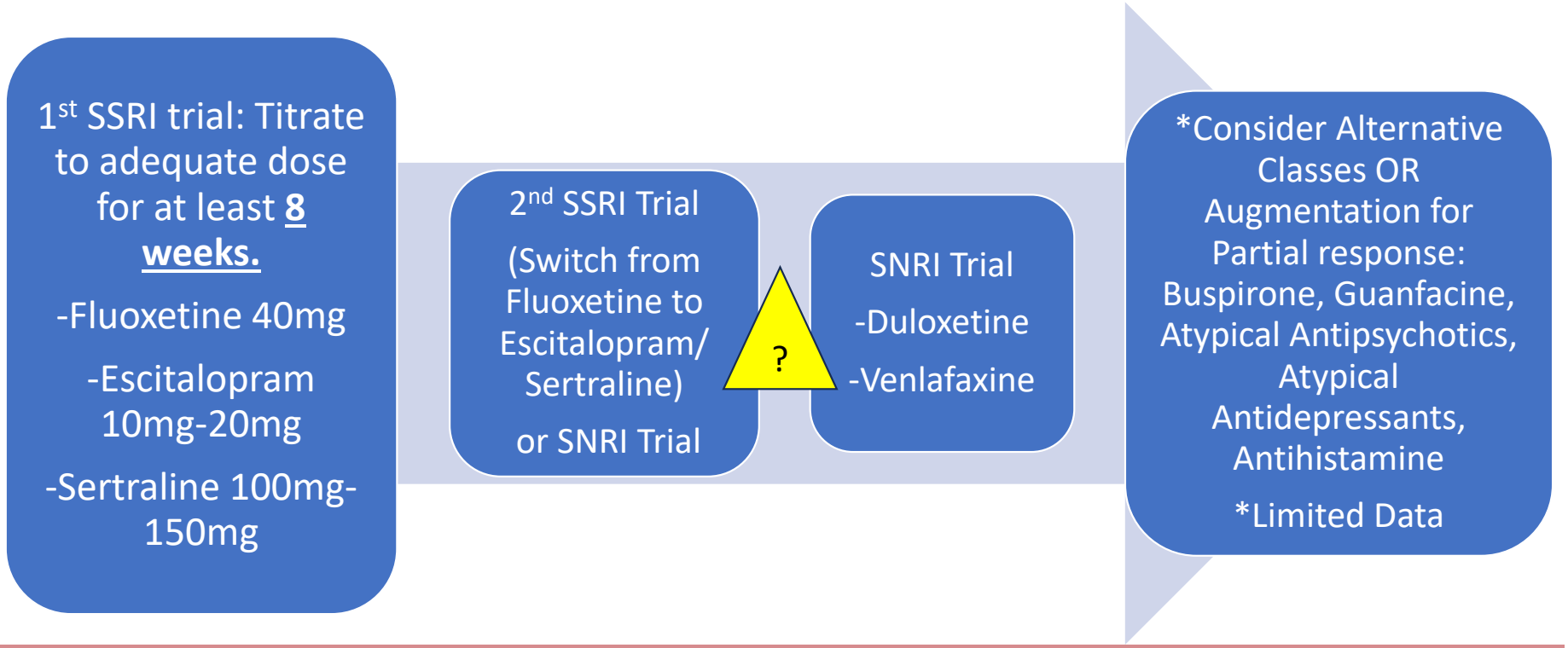
- **Risk/Benefit Talk with patient to make the titration schedule.**
- Fast Cross Titration
  - Quicker anxiety improvement, but possible more side effects
- Slow Cross Titration
  - Slower anxiety improvement, but likely less side effects
- Dosage forms- liquid/tablet or capsule
- Fluoxetine- consider stopping at once, and starting new med in 4-7 days

SSRI Dose Equivalents

Fluoxetine (mg/day)	Sertraline (mg/day)	Escitalopram (mg/day)
5-10	12.5-25	2.5
20	50	5
30	75	7.5
40	100	10
50	150	15
60	200	20
70	250	25
80	300	30

Rule of 3 for Cross Titration:
Week 1: Cut Med 1 by 25-30%, Start Med 2 at 25-30% of target dose
Week 2: Cut Med 1 by another 30%, Increase Med 2 by another 30%
Week 3: STOP Med 1, Increase Med 2 by another 25-30%, ideally at or close to target dose
Week 4: Increase Med 2 to target dose. Stay on this dose for 6-8 week trial

Pharmacologic Treatment Algorithm for Moderate/Severe Anxiety



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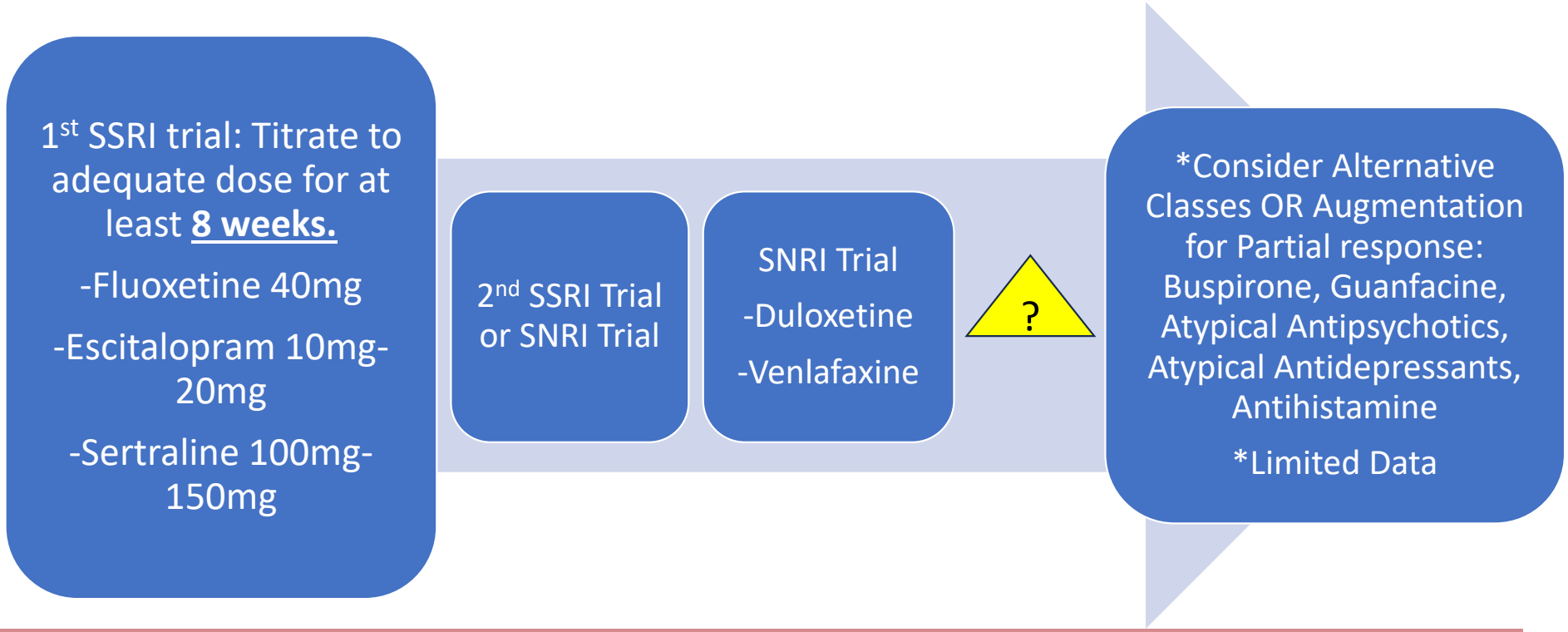
SNRIs: Duloxetine

- If failed 2 adequate trials of SSRIs, try an SNRI
- **The only FDA approved medication for Generalized Anxiety Disorder!**
- Age 7+
- Capsules and Sprinkle Capsules that can be opened.
- Monitor Blood pressure (HTN)
- Start at 30mg/day, increase weekly or every 2 weeks.
- Target dose 60mg-120mg

SNRI: Venlafaxine

- If failed 2 SSRIs, try an SNRI
- **Very short half life (3-13 hours)**
- Tablets/Capsules
- Start at 50-75mg/day- in divided doses
- XR formulation- dosed once/day
- **High rates of discontinuation symptoms**
  - **Slower taper off**
- Brain Zaps/fogs when starting and stopping
- Monitor blood pressure (HTN)

Pharmacologic Treatment Algorithm for Moderate/Severe Anxiety



Combination treatment (Meds- SSRIs + Therapy/CBT) is the most effective treatment!
-MAKE SURE YOUR PATIENT IS IN THERAPY.

If failed both SSRIs and SNRIs…

- Is therapy in place? Adequate?
  - Is the family engaged, both parents? Family work is critical
- Did it really fail?
  - Assess adherence, 3+ missed doses can drop blood level to almost 0
  - Check with guardian, get collateral info
  - Repeat SCARED/GAD/compare screens with the family
- Think back to differential- are you treating the primary diagnosis?
- Consider alternative medication options

Buspirone

- 5-HT1A/5-HT2 receptor agonist, mild blocking on dopamine D2 receptor, no effect on GABA (Benzo) receptors
  - **FDA approved for adult anxiety**
  - **Adjunct** for sexual side effects of SSRIs, SSRI intolerability
- 2 RCTS looking at **pediatric GAD-** underpowered to show effect size, high placebo response rate
- Well tolerated, side effect: lightheadedness
- **Start at 5mg-7.5mg BID, Max: 15mg—60mg day (divided BID)**
- Very short half life: 2-4 hours
- **Limited evidence in Autism Spectrum Disorder**

Guanfacine XR

- Alpha-2 adrenergic agonist (FDA Approved for ADHD)
- Study looked at Anxiety in 6-17 year olds WITHOUT ADHD
- Safe and well tolerated
- **Dose range from 1mg- titrated weekly up to 6mg**
  - **> 50 kg (3-6mg)**
  - < 50 kg (0.06-0.12mg/kg). (Typical 25kg/60lb =3mg)
- Compared to placebo- had **improved CGI-I scores-** clinician rated scale but not on SCARED or PARs scores
- **Adjunct for a dysregulated child or ASD**

Clonidine

- Alpha- 2 agonist
- Pill and Patch
- No evidence in pediatric anxiety
- **Potential use in Anxiety/Insomnia and ADHD,** including daytime doses.
  - 0.05mg-0.2mg QHS, increase dose weekly
  - Max Dose 0.4mg qday divided TID/QID
  - **Half life is 3 hours- possible night-time awakening**
- Can build a tolerance, needing higher doses
- Monitor BP- hypotension and rebound hypertension
- **Extended-Release formulation**
  - Start at 0.1mg QHS, increase dose weekly. Max dose 0.4mg divided BID

N-Acetyl Cysteine

- Natural supplement- Glutamate modulating/antioxidant
- Compulsive behaviors (skin picking, hair pulling, some ritualistic behaviors)
- **Irritability (Autism)**
- 600mg/day for 3 days then increase to 600mg BID. If after 2 weeks, there is some response, can move to 600mg TID
- Open trials for **Pediatric OCD**

Atypical Antipsychotics/Dopamine Blockers

- No evidence in pediatric anxiety
- **Low dose as augmentation strategy for aggression/self injury or refractory anxiety**
  - Aripiprazole (1-5mg)
  - Risperidone (0.25mg-0.5mg starting dose)
  - Quetiapine (12.5-25mg)
  - Olanzapine (2.5mg-5mg)
- Side effect: weight gain, metabolic syndrome
- Consider baseline fasting glucose, lipids, TSH

Autism Spectrum Disorder

- Core Features of Autism
  - Impaired social interaction and communication
  - Repetitive behavior/restricted interests
- No medications to target core symptoms
- **All medication in ASD target specific behavioral problems**
  - Aggression/Irritability/Self injury
  - Hyperactivity
  - **Anxiety**
  - Sleep

Autism Spectrum Disorder and Anxiety

- Diagnostic Dilemma
  - **ASD ONLY: experiences challenges in life due to their deficit**
  - **ANXIETY ONLY**: severe, early onset behavioral inhibition or social anxiety
    - Fail to development language (don't talk due to the anxiety)
    - Fail to development social skills due to fear of interaction (due to the anxiety)
    - **+ Presence of interpersonal reciprocity – NOT ASD**
  - **ASD + ANXIETY: and a core symptom of anxiety (Sep, Social or GAD)**

Treatment for Anxiety in ASD

- **Significant comorbidity: 22-85% of patients with ASD have anxiety**
- Very poor measures/screening of anxiety in ASD population
  - ADI-R/ADOS + SCARED
  - Age of onset of symptoms –ASD symptoms earlier (possible undx until anxiety presents later on)
- Very few studies-no controlled trials
- Recommendation- follow pediatric anxiety guidelines: **SSRIs first**
  - More likely to experience activation/agitation-may consider an **SNRI first line or shorter half life SSRI (sertraline)**

Treatment for Anxiety in ASD

- **Consider Alpha 2 agonists as 1st or 2nd line options**
  - Guanfacine XR (1-4mg), Clonidine, Clonidine XR
  - Short acting can sometimes be better than long acting
  - Long acting can be dosed BID
- **Buspirone 15-45mg/day- divided BID**- low risk, some limited evidence of benefit in Autism.
- **N-Acetyl Cysteine**- irritability, simple repetitive behaviors
- **Atypical Antipsychotics/Dopamine Blockers (aripiprazole and risperidone)** for aggression/self injury

Treatment Guidelines in ASD

- Start low and go slow
- Higher rates of side effects/limitation in patient communication/monitoring challenging
- Response may be unpredictable
- One change at a time
- One medication at a time
- Collaborate with others treating the patient- Therapists, teachers, parents
- Reduce dosing regularly to establish ongoing benefit

Benzodiazepines

- Binds GABA Receptors- GABA is an inhibitory neurotransmitter/CNS Depressant- Alprazolam, Clonazepam, Diazepam
- Subject to misuse, addiction, diversion
  - Class IV controlled substances
- **Limited data-no efficacy in controlled pediatric anxiety trials**
- **Limited role- single low dose benzo for procedures- intranasal midazolam for suture anxiety**
- Significant adverse events- increased treatment emergent suicidality

Hydroxyzine

- Antihistamine and works at 5HT2a (serotonin) receptors
- Minimal data to support its use
- 25-50mg QHS for sleep
- 50mg-100mg daily in 3-4 divided doses
- Short half life: 7 hours
- **Often used as a PRN/Short term Bridge**
  - PRNs are form of avoidance
  - Teach skills on pill-based coping
  - Goes against the psychotherapy principles

Atomoxetine

- SNRI
- Clinical trials focused on **anxiety and ADHD**. Had to have both diagnoses.
  - Is it treating the ADHD or the anxiety? Appears to work on both!
- **FDA approved for ADHD (non stimulant)**
  - < 70kg : Start with 0.5mg/kg/day- increase to 1.2mg/kg qday or BID. Max Dose: 1.4mg/kg/day or 100mg
  - >70kg. Start with 40mg. Increase to 80mg (qday or BID). Max Dose: 100mg
- Time to effect: 4 weeks
- **Not first line for either ADHD or Anxiety**

Trazodone- Atypical Antidepressant

- Antihistaminic properties at low doses (sedation)
- Serotonergic activity at higher doses (anxiolytic)
- **Minimal data in pediatric anxiety**
- Often used as a **sleep adjunct** to the SSRI
- FDA approved for adult depression
- 25-50mg starting dose QHS, 100mg -300mg per day

Propranolol

- Nonselective Beta Blocker
- Can help with somatic symptoms of anxiety
- **Can be considered in performance anxiety**
- 10-20mg daily
- Short half life: 4-6 hours
- Monitor blood pressure
- Consider baseline EKG- rule out sinus bradycardia or heart block

Mirtazapine- Atypical Antidepressant

- Antagonist of Presynaptic NE receptor -> releases NE and 5HT, blocks post synaptic 5HT receptors
- Limited data in pediatrics for anxiety
- Possible adjunct for **sleep (sedating) and increasing appetite (weight gain)**
- Start at 7.5mg-15mg daily. Max 45mg daily
- **Study of with Anxiety/ASD- showed no improvement vs placebo**

Tricyclic Antidepressants (TCAs)

- Serotonin and Norepinephrine Reuptake Inhibitors
- **Clomipramine- FDA approved for OCD 10+**
- Highest risk for serotonin syndrome at high doses
- Low doses can be used as an adjunct with an SSRI (sleep, OCD)

THC/Cannabis Considerations

- CBD and THC- metabolized through several P450 liver enzymes — increases blood levels of escitalopram and sertraline
  - **More variations in SSRI levels**
  - **More side effects**
  - Takes longer to reach steady state

- THC is pro-psychotic and can increase anxiety

Melatonin

- **Insomnia**
- CBT-for insomnia
- 1-6mg immediate release
- 5-10mg extended release

Take home points

- Anxiety disorders are very common, yet highly treatable
- Use standardized screening tools
- Treatment- Most effective is combination treatment: CBT+ SSRIs
- The benefits of SSRIs outweigh the risks
- Pick the right SSRI or SNRI for you and your patient
- Refractory Anxiety Medication options
  - Limited Data with other medications- consider Guanfacine, Buspirone
- Patients with Autism Spectrum Disorder have a high rate of anxiety.
  - Higher Side Effects with SSRIs, Consider SNRIs or alpha 2 agonists (Guanfacine)

Thank you!

Questions?

Stopping SSRIs when in Remission

- During a period of some stress (to be able to identify any resurgence of anxiety) but lower stress
- 25-50% taper of dose weekly or monthly
  - Consider the patient's initial side effects, duration of treatment and half life of SSRI
  - Fluoxetine- long half life may not need a taper
  - Paroxetine- short half life- will need a taper
- **Discontinuation syndrome- anxiety patients are more prone- so go slow**
  - Flu like illness, insomnia, sensory disturbances
- **Close follow up for at least 3 month (watch for resurgence of symptoms)**

OCD

- Preoccupation with recurrent, intrusive thoughts, images, urges
  - Dirt, germs
- Accompanied by compulsive and repetitive behaviors or rituals to reduce the distress
  - Ordering and arranging, checking
- Impairing, time consuming > 1 hour/day
- Prepubertal age around 10 years old. Male dominance
- Comorbid with Tic Disorder and ADHD
- Children have poor insight. Parents may be unaware

OCD Treatment

- POTS Study- RCT. Combined treatment with sertraline/CBT to both SER alone and CBT alone
  - COMBO > CBT > SERTRALINE
- CBT first for mild/moderate disease
- Trial at least 2 SSRIs for 8-10 weeks
- Third line: clomipramine (TCA) FDA improved > age 10. start at 25-50mg. Target dose is 100-250mg
- Consider higher/maximum tolerated doses of SSRIs in OCD
- Fluoxetine common first medication tried

PTSD/Acute Stress Disorder

- Avoidance, intrusions, hypervigilance, emotion/regulatory problems associated with an index traumatic event (s)
- Therapy Therapy Therapy!!
- May consider an alpha agonist like clonidine for sleep issues