# Integrated Health Topic: Anxiety in Pediatrics

Jason Schweitzer, MD Transforming Mental Health Leading the way for children to live their best lives

### Introduction

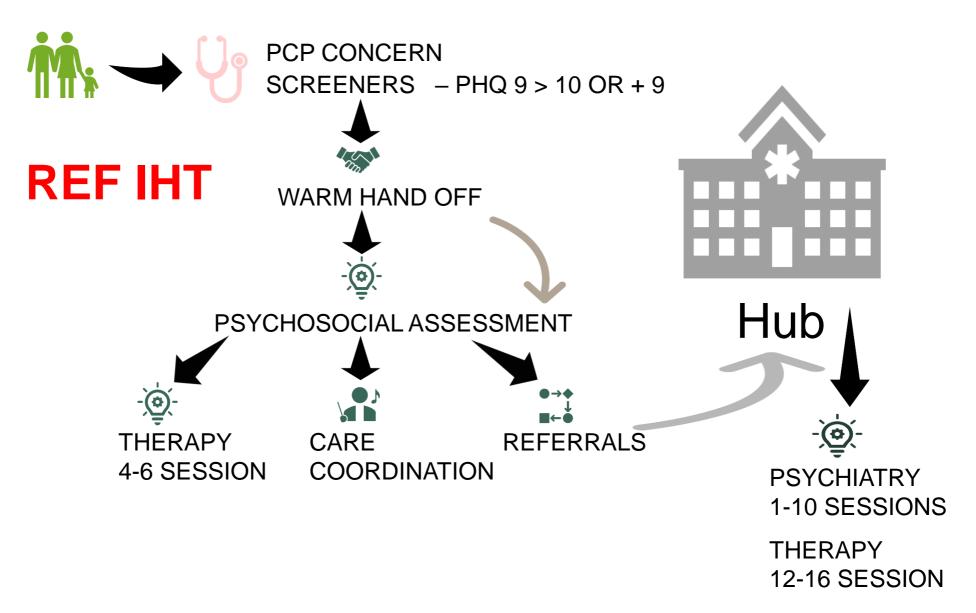
### No disclosures







## MHI Flow



- Infants
  - Loud Noises
  - Dropped
  - Startle Reflex



- 9 Months
  - Stranger Anxiety
- Toddlers
  - Monsters, Darkness



- Early School age
  - Physical wellbeing, injuries
  - Natural Disasters, storms
  - Spiders, Darkness



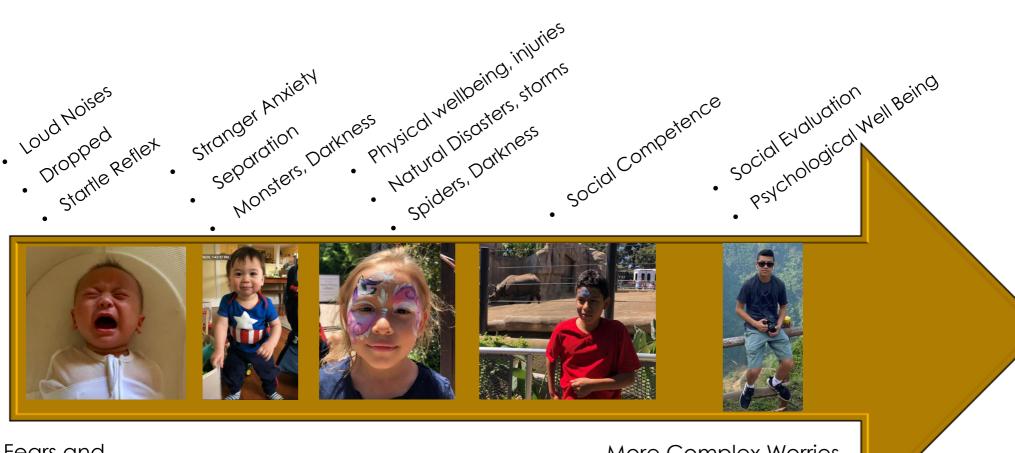
- Early Adolescence
  - Social Competence





- Social Evaluation
- Psychological Well Being





More Complex Worries Context Specific Fears

Fears and Worries

# What is Anxiety?

- Worry Cognitions Apprehension, thoughts about how things could or will go wrong
  - Gets more complex over time
- Fear Perceived imminent or likely threat, more immediate
  - Diminishes over time
- Somatic Symptoms

# Cognitions of Anxiety

- High frequency and salience of negative predictions
- Catastrophizing thought style
- All or Nothing Thinking
- Mental Filter
- Often co-morbid with depression

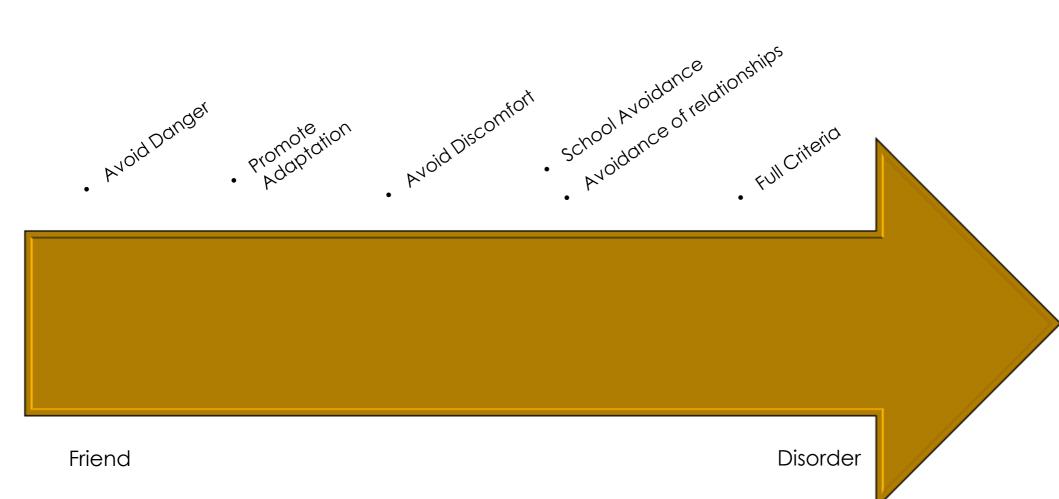
# Symptoms of Anxiety

- Hand wringing, stomach/GI upset, headaches
- Panic Attacks
  - Abrupt occurrence of
    - Palpitations, trembling, sweating, cp, n/v, dizziness, chills, heat sensations, parasthesias, derealization / depersonalization, fear of dying or "going crazy"
- Sympathetic symptoms
- Somatic symptoms

# Child and Adolescent Understanding Anxiety

- Problematic or Disorder
  - Symptoms
  - Distress
  - Dysfunction
  - Inflexibility
  - Avoidance
  - Eventually Anxiety in the absence of stimulus

# Anxiety Friend or Foe?



# Developmental Anxiety



More Complex Worries Context Specific Fears

Fears and Worries

# 2016 National Survey of Children's Health

- Anxiety Becomes more prevalent in Teen years
- 7.1% from 3-17 Years of Age
  - 3 5 yo : 1.3 %
  - 5 11 yo: 6.6 %
  - 12 17 yo: 10.5 %

Table I. Prevalence of currently diagnosed depression, anxiety, and behavioral/conduct problems among children aged 3-17 years, by sociodemographic and health characteristics, NSCH 2016

# Approach to Anxiety

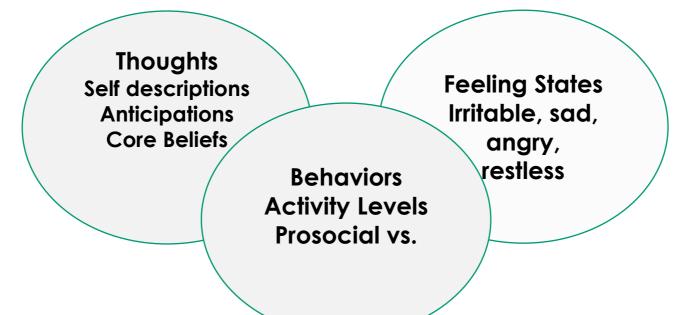
- Normalize
  - "Anxiety is a good thing, we all have it, and need it"
  - Fight or fight examples (snake, car accident)
  - Sometimes this reaction gets too strong, and people forget to turn it off. Sometimes they can't turn it off
- Does the pattern match age expected anxiety syndromes?
- Give a SCARED: 8 17 Years old
- http://www.midss.org/content/screen-child-anxiety-related-disorders-scared

# Approach to Anxiety

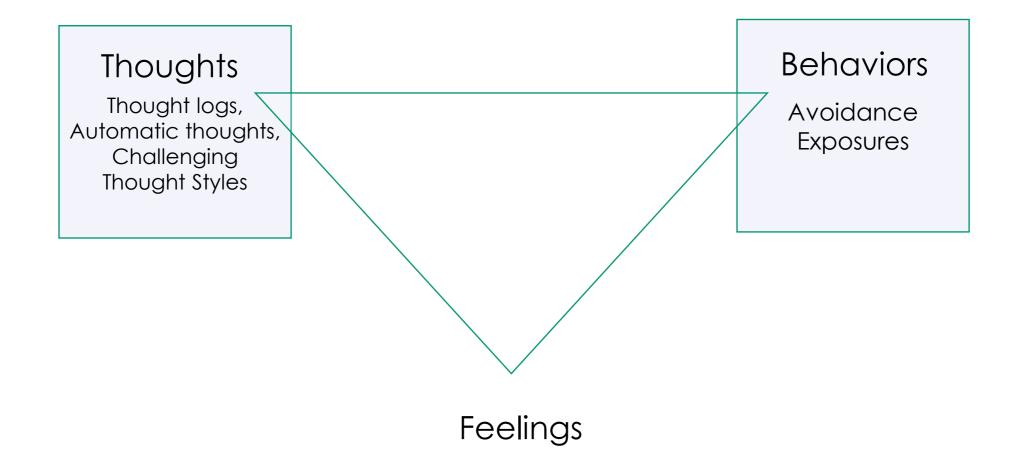
- Connect family with resources
- Therapy is first line
  - CBT
    - Anxiety scales followed by exposures targeting avoidance
- SSRIs Can be helpful
  - Medication without therapy is not first-line

### Treatment

- Therapy
- Medication
- Combination therapy has best data
  - CBT for Anxiety



### Treatment



- Social Anxiety Disorder
  - Fear about social settings with PEERS (not just adults), out of proportion to context
  - Concern with scrutiny of others
  - CBT
  - SSRI > SNRI
  - Multiple RCTs



- First Line: Big Three
  - Fluoxetine
  - Escitalopram
  - Sertraline
- Return in 1-4 weeks to see if tolerating, ask about SI.
  - Follow-up meetings can be brief
    - The pay off comes in the form of improved compliance, placebo response and better titration
- Up-titrate
  - Week 8 good response or maximal dose



- Second Line: A different of the big Three
  - Fluoxetine
  - Escitalopram
  - Sertraline

### SSRIs for Anxiety

#### General

Headache, Gi Upset, SI Rare activation or mania/Hypo Mania

Black Box Warning

Cross placenta and breast milk but Generally Safe

#### Fluoxetine

Start at 5 -10 mg 40 - 60 mg MAX Can be more activating Withdrawal is usually well tolerated

Most interactions

#### Escitalopram

Start 5 – 10 mg Max is 20 mg Can be more sedating, /

orthostasis

**Fewest Interactions** 

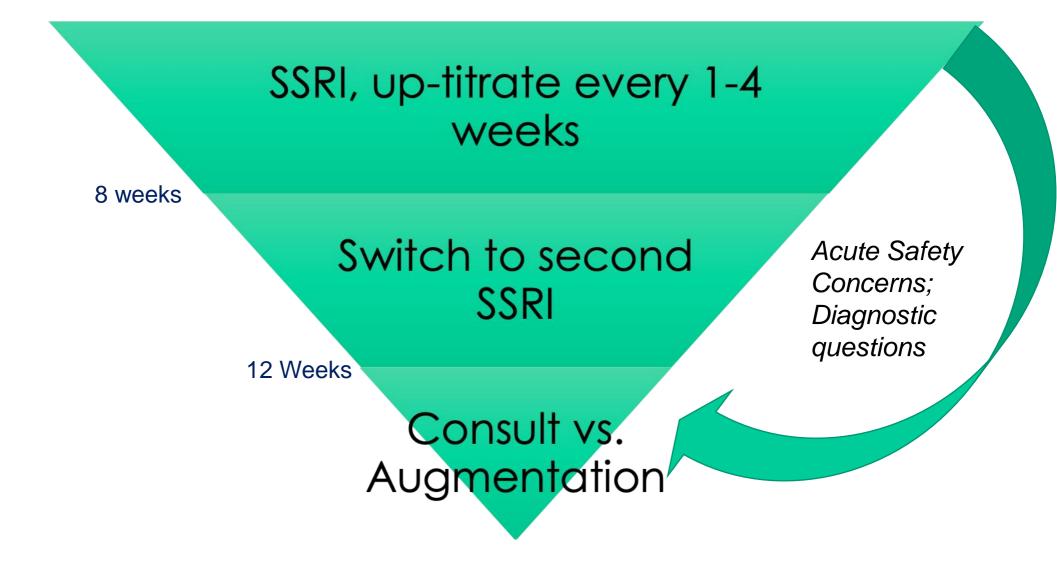
When stopping taper over 1-2 weeks, or slower

#### Sertraline

Start 12.5 – 25 mg

Target 125 -150 mg or remission When stopping, taper

# Stepped Treatment



# SSRI : Adverse Effects

- Headache, Glupset
- Black Box Warning: Suicide Events
- Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders

## Medications: SSRIS

- Rates of suicide events vary .7% 4%
- FDA and TADS study show no completed suicides
- <u>https://www.uptodate.com/contents/effect-of-antidepressants-on-suicide-risk-in-children-and-adolescents</u>
- For Families:
  - Communication about safety
  - Monitoring

### Fluoxetine

- Fluoxetine 10 to 40 mg po daily (TADS Study; Cochrane Review)
- FDA Approved for Depression
- Adolescents: Start at 10 mg, within 1-4 weeks increase to 20 mg, true target is remission
- School Age: Start lower 5; Use Liquid; go Slow

### Fluoxetine

- Long Half-life! (2-3 days parent, 2 week metabolite)
  - Good: no withdrawal
  - Bad: 5 week washout for MAOi
- Can be activating
  - Less often can be sedating
- CYP inhibition (2D6  $\rightarrow$  Codeine, B blockers; 3A4  $\rightarrow$  some benzos, Statins)

# SSRI : General Approach

- Lowest effective dose, target remission
- Symptomatic and tolerating? Increase
- Effect can take 3-5 Weeks per dose change
- Monitor weekly or bimonthly
  - Suicidal ideation
  - Mania or hypomania (SLEEP, personality change, etc.)



- At baseline: IF clinical exam is concerning for biological underpinnings or any association with eating disorder
  - CBC, TSH, CMP, B12, Vit D.
- Follow-up Labs if symptoms of electrolyte abnormality

# SSRI: Other Cautions

- Use with other serotonergic medications can cause
  Serotonin Syndrome
- Risk Category C, present in breast milk
- Rare adverse effects can be serious: Suicidal Ideation (Black Box), Bleeding, Electrolyte abnormalities
- Likely safe with OCPS, more studies needed (Berry-Bibee et al, 2016)

# SSRI: Other Considerations

- Higher doses tend to be helpful for more anxiety
- Co-treatment with stimulants is usually safe
  - There are studies that show increase hypomania risk with this combination

# Resource List

- SmartCare for Families : 858-956-5900
- SmartCare for Providers : 858-880-6405
- Psychologytoday.com
- County Sevices
  - <u>https://www.optumsandiego.com/content/dam/sandiego/documents/socdirectory/SBC\_DBH-SUDRS\_Provider\_Directory\_English.pdf</u>

### References

Ghandour, R. M., Sherman, L. J., Vladutiu, C. J., Ali, M. M., ... Blumberg, S. J. (2018). Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *The Journal of Pediatrics*, *206*, 256–267.e3. https://doi.org/10.1016/j.jpeds.2018.09.021

Ipser JC., Dj, S., Hawkridge, S., & Hoppe, L. (2010). Pharmacotherapy for anxiety disorders in children and adolescents (Review), (3). doi:10.1002/14651858.CD005170.pub2.www.cochranelibrary.com

Treating and Preventing Adolescent Mental Health Disorders: What We Know and What We Don't Know: A Research Agenda for Improving the Mental Health of Our Youth. Edited by Dwight L. Evans, Edna B. Foa, Raquel E. Gur, Herbert Hendin, Charles P. O'Brien, Martin E.P. Seligman, and B. Timothy Walsh. 818 pp. New York, Oxford University Press, 2005

Strawn, J. R., Welge, J. A., Ph, D., Wehry, A. M., Keeshin, B., & Rynn, M. A. (2015). EFFICACY AND TOLERABILITY OF ANTIDEPRESSANTS IN PEDIATRIC ANXIETY DISORDERS : A SYSTEMATIC REVIEW AND META-ANALYSIS, *157* (November 2014), 149–157. doi:10.1002/da.22329

### References

Table I. Prevalence of currently diagnosed depression, anxiety, and behavioral/conduct problems among children aged 3-17 years, by sociodemographic and health characteristics, NSCH 2016

	Currently diagnosed with depression				Currently diagnosed with anxiety				Currently diagnosed with behavioral or conduct problems			
Characteristics	Unweighted, n	Weighted, N	Weighted, %	95% CI	Unweighted, n	Weighted, N	Weighted, %	95% CI	Unweighted, n	Weighted, N	Weighted, %	95% CI
All children (3-17 y)		1 934 000	3.2	2.9-3.5		4 355 000	7.1	6.6-7.6		4 509 000	7.4	6.9-7.9
Severity of diagnosed condition												
Mild	806	885 000	46.3	41.4-51.2	1796	1 949 000	45.2	41.5-48.9	1342	1 748 000	39.5	36.1-42.9
Moderate	716	841 000	44.0	39.1-49.0	1634	2 037 000	47.2	43.4-51.1	1445	2 110 000	47.6	44.1-51.2
Severe	135	185 000	9.7	6.6-14.0	308	326 000	7.6	6.2-9.2	335	572 000	12.9	10.6-15.7
Current depression		N/A			1280	1 402 000	32.3	29.1-35.8	673	908 000	20.3	17.7-23.2
Current anxiety	1280	1 402 000	73.8	69.4-77.8		N/A			1308	1 630 000	36.6	33.2-40.1
Current behavioral or conduct problems	673	908 000	47.2	42.3-52.2	1308	1 630 000	37.9	34.3-41.6		N/A		
Sociodemographic characteristics	0.0	000 000		12.0 02.2			01.0	01.0 11.0				
Sex												
Male	715	932 000	3.0	0.2-2.6	1783	2 164 000	6.9	6.2-7.7	2205	3 155 000	10.1	9.3-10.9
Female	957	1 002 000	3.3	0.2-2.9	1980	2 191 000	7.3	6.6-8.1	968	1 354 000	4.5	4.0-5.1
Age, y	301	1 002 000	0.0	0.2 2.0	1000	2 101 000	1.5	0.0 0.1	500	1 004 000	4.0	4.0 0.1
3-5	7	9000	*0.08	0.0-0.2	113	153 000	1.3	0.9-1.7	288	410 000	3.4	2.8-4.2
6-11	271	421 000	1.7	1.3-2.2	1115	1 624 000	6.6	5.7-7.6	1390	2 259 000	9.1	8.3-10.1
12-17	1394	1 504 000	6.1	5.5-6.8	2535	2 578 000	10.5	9.7-11.3	1495	1 840 000	7.5	6.7-8.3
	1394	1 304 000	0.1	5.5-0.0	2000	2 5/6 000	10.5	9.7-11.5	1490	1 040 000	7.5	0.7-0.3
Race/ethnicity	184	330 000	2.2	1.6-2.9	375	915 000	6.0	4.8-7.5	364	837 000	5.5	4.5-6.7
Hispanic												
Non-Hispanic white	1198	1 088 000	3.4	3.1-3.8	2908	2 713 000	8.6	8.0-9.2	2158	2 394 000	7.6	7.0-8.2
Non-Hispanic black	110	331 000	4.2	3.1-5.6	136	358 000	4.5	3.4-5.9	287	848 000	10.7	9.1-12.7
Non-Hispanic multiracial/other	180	184 000	2.9	2.3-3.6	344	368 000	5.7	4.4-7.5	364	430 000	6.7	5.3-8.5
Family structure												
Two parents, married	899	904 000	2.3	2.0-2.7	2385	2 504 000	6.4	5.8-7.0	1753	1 986 000	5.1	4.6-5.6
Two parents, unmarried	130	172 000	3.5	2.3-5.2	249	404 000	8.1	5.9-11.1	253	508 000	10.2	7.7-13.4
Single mother	404	585 000	5.9	5.0-7.0	736	946 000	9.6	8.4-11.0	674	1 177 000	12.0	10.6-13.6
Other	218	254 000	4.5	3.6-5.6	340	430 000	7.6	6.3-9.3	422	715 000	12.7	10.7-15.0
Household educational attainment												
Less than high school	53	262 000	4.6	3.0-7.0	83	419 000	7.3	5.3-10.1	111	499 000	8.7	6.5-11.6
High school, GED, or vocational training	266	422 000	3.6	2.9-4.4	467	810 000	6.9	5.7-8.3	524	988 000	8.4	7.2-9.7
More than high school	1317	1 191 000	2.9	2.6-3.2	3139	3 013 000	7.2	6.7-7.8	2438	2 840 000	6.8	6.3-7.4
Household poverty												
<100% FPL	273	625 000	4.8	3.8-6.0	463	984 000	7.6	6.3-9.0	557	1 405 000	10.8	9.4-12.4
100%-199% FPL	334	420 000	3.1	2.4-3.9	659	1 010 000	7.4	6.1-9.0	650	1 024 000	7.5	6.4-8.8
200%-399% FPL	500	453 000	2.8	2.2-3.4	1136	1 124 000	6.8	5.9-7.9	923	1 066 000	6.5	5.6-7.5
≥400% FPL	565	436 000	2.4	2.0-2.8	1505	1 237 000	6.8	6.1-7.6	1043	1 014 000	5.6	5.0-6.3
												(continued)
												(continued)

# Cochrane Review

- Ipser JC, Stein DJ, Hawkridge S, Hoppe L (2009). Pharmacotherapy for anxiety disorders in children and adolescents (Review). Cochrane Review
- 22 short-term (<= 16 weeks) RCTs (2519 participants)
- 15/22 studies assessed the efficacy of the SSRIs
  - Medication and placebo response occurred in 58.1% and 31.5% of patients,
  - Number needed to treat = 4.
  - Medication was more effective than placebo in reducing overall symptom severity in OCD in a post-hoc comparison (N = 7, Weighted Mean Difference (WMD) = -4.45, 95%Cl = -5.94, -2.97, n = 765).
- Medication treatments can reduce core symptoms
- Best data is for OCD
- No clear evidence to show that any particular class of medication is more effective or better tolerated than any other.
- Routine use of benzodiazepines cannot be recommended, especially given concerns of dependency and AEs

- Separation anxiety
  - > 4 weeks and >= 3 of
    - Developmentally inappropriate fear concerning separation for attachment figures
    - Persistent worry about bad things happening to attachment figures
    - Alterations in sleep, absenteeism, nightmares, somatic symptoms
  - CBT and SSRIs

- Selective Mutism
  - > 1 month of consistent failure to speak in certain settings, that interferes with schooling, social relationships
  - Exposures, CBT
  - SSRI

- Panic Disorder
  - Recurrent panic attacks
  - Fear of inducing attacks (> 1 Month)
  - Resulting change in behavior
  - Treatment: CBT and SSRIs (at least 3 RCTS)

- Generalized Anxiety Disorder
  - >= 6 mo of worry that is difficult to control and about many things
  - >= ]
    - Restlessness, fatigue, poor concentration, irritability, muscle tension, sleep probs
  - CBT
  - SSRI, SNRI

- Specific Phobia
  - > 6 Mo → Marked fear or anxiety of a thing that is out of proportion to associated danger
  - Can be expressed by tantrums, freezing or clinging
  - Impairing
- EXPOSURES
- Data for SSRI is less convincing, but exposures work so well, that we use medication less

### Escitalopram

- Escitalopram 10 to 20 mg po daily (TADS Study; Cochrane Review)
- FDA Approved for depression
- Adolescents: Start at 5 mg, increase to 10 mg, true target is remission, increase accordingly
- School age kids go slower

### Escitalopram

- Half life is 24 32 hrs
- Discontinuation withdrawal symptoms rare, but can happen  $\rightarrow$  taper
- Few interactions

### Sertraline

- Sertraline 25 150 mg
- 130 mg is the average studied dose
- FDA Approved for OCD
- Adolescents: Start at 25 mg, increase to 50 mg, true target is remission, increase accordingly
- School age kids go slower

### Sertraline

- Half-life is 24-36 hours, can be longer
- Taper on discontinuation 50% over 3 days to week
- Some CYP inhibition