

Depression and Anxiety in Pediatric Primary Care



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NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Objective

- Understand assessment and treatment for pediatric depression
- Understand assessment and treatment for pediatric anxiety disorders
- Review off-label treatments for depression and anxiety

PART I: Depression

- Epidemiology
- Clinical features / Diagnosis
 - Assessment
 - Comorbidities
- Prevention
- Treatment
 - Therapy
 - Medications

Epidemiology

- Prevalence
 - 12-17yo in US (n>45,000) in 2010 and 2011 = 1 year prevalence of major depression was 8%
 - Another study was 11%
- Sex Ratio
 - Pre-puberty: 60% higher in boys > girls
 - Post-puberty: 2:1 ratio for girls : boys

Perou R, Bitsko RH, Blumberg SJ, et al. Mental health surveillance among children--United States, 2005-2011. MMWR Suppl 2013; 62:1.

Avenevoli S, Swendsen J, He JP, et al. Major depression in the national comorbidity survey-adolescent supplement: prevalence, correlates, and treatment. J Am Acad Child Adolesc Psychiatry 2015; 54:37. Douglas J, Scott J. A systematic review of gender-specific rates of unipolar and bipolar disorders in community studies of pre-pubertal children. Bipolar Disord 2014; 16:5.

Risk Factors

- Low birth weight
- FMHx depression and anxiety in first degree relative
- Family dysfunction or caregiver-child conflict
- Hx abuse, neglect
- Psychosocial stressors
- Gender dysphoria / LGBTQ+
- Negative style of interpreting events and coping with stress
- Hx Anxiety disorder, SUD, LD, ADHD, ODD

Clinical Features



- SIG E CAPS + M = 5 or more symptoms during the same 2-week period and represent a change from previous functioning:
 - Sleep
 - Interest*
 - Guilt
 - Energy
 - Concentration
 - Appetite
 - Psychomotor
 - Suicidal thoughts
 - Mood*

Clinical Features cont.

- At least 1 of the 5 symptoms must be
- Mood
 - Depressed mood
 - Irritable = “grouchy”, “annoyed”, argumentative, negative
 - Can still have mood reactivity
 - Can lead adolescent to seek experience to temporarily lift their mood (thrill-seeking, promiscuity, drug use, etc)
- Interest
 - Anhedonia = loss of interest or pleasure in previously pleasurable activities
 - “boring”, “stupid”, loss of interest in friends, decreased libido

Clinical Features cont.

- Sleep disturbance
- Guilt
 - Marked by inadequacy, inferiority, failure, and worthlessness
 - May not directly acknowledge these negative self-perception
 - Excessive self-critical
- Energy
 - Anergia = lack of energy
 - May present as exhausted or unmotivated
 - Parents may
 - Complain about child's lack of motivation
 - Concerned about general medical illness

Clinical Features cont.

- Concentration
 - Problem with attention, memory, processing information
 - May manifest as indecisive or procrastination
- Appetite change
- Psychomotor agitation / retardation
 - Only if noticeable to others vs. subjective feelings *
 - Retardation = talk slowly / less
 - Agitation = pacing, inability to sit still

Clinical Features cont.

- Suicidal thoughts
 - Recurrent thoughts of death
 - Preoccupation with music/literature with morbid themes
 - May contribute to pervasive hopeless -> view suicide as only option to escape
 - Functional impairment
 - School functioning
 - Interpersonal dysfunction with family or peers
 - Social withdrawal
 - Disturbance in daily activities and responsibilities
 - Seeking reassurance excessively
 - Change from baseline
-

Severity

- Mild = 5 symptoms
- Moderate = 6 or 7 symptoms
- Severe = 8 or 9 symptoms

Assessment

- Psychiatric and general medical history
- Mental status and physical exam
- Labs
 - CBC
 - Chemistries
 - Thyroid studies
 - Urine toxicology – if there's substance use concerns
- Collateral from parents

Lee ES, Findling RL. Principles of psychopharmacology. In: Dulcan's Textbook of Child and Adolescent Psychiatry, Third Edition, Dulcan MK (Ed), American Psychiatric Association Publishing, Washington, DC 2022. p.677.

Assessment: r/o mania

- Rule out mania
 - Overlap with ADHD, personality disorder traits, etc.
- Parental report more effective than youth or teacher reports
- Young Mania Rating Scale, parent version
- Daily mood log/dairies

Hypo/Mania symptoms

- Abnormally elevated mood
- ↑ Energy
- Grandiosity
- Decreased need for sleep
- More talkative
- Flight of ideas
- ↑ Goal-directed activities
- Impairment in social/occupational functioning

Screening

- AAP: Universal screening for depression and suicide risk annually from 12yo to 21yo
- USPSTF: screening depression for 12-18yo (Grade B)
 - Grade I for < 12yo
- Targeted screening for 10yo and older for people with
 - Personal or family hx of mood disorders, suicidality
 - Significant psychosocial stressors (hx trauma/abuse/neglect, family crises)
 - In foster care or have been adopted
 - Frequent somatic complaints



Ades AE. Evaluating screening tests and screening programmes. Arch Dis Child 1990; 65:792.
US Preventive Services Task Force, Mangione CM, Barry MJ, et al. Screening for Depression and Suicide Risk in Children and Adolescents: US Preventive Services Task Force Recommendation Statement. JAMA 2022; 328:1534.

Screening



- Limited evidence to guide the choice of depression screening tool
- Use tool that works best for each practice / organization

Zuckerbrot RA, Cheung A, Jensen PS, et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice Preparation, Identification, Assessment, and Initial Management. Pediatrics 2018; 141.

Screening: PHQ-2

- Patient Health Questionnaire-2 (PHQ-2)
 - Validated for adolescents
 - Score of ≥ 3 should undergo additional assessment
- In primary care sample of 499 adolescents, PHQ ≥ 3 had
 - Sensitivity 74%
 - Specificity 75%

Over the last 2 weeks , how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	☐ 0	☐ +1	☐ +2	☐ +3
2. Feeling down, depressed or hopeless	☐ 0	☐ +1	☐ +2	☐ +3

Screening: Others

- PHQ-9 modified for teens
 - Available in Spanish, Albanian, Arabic, Bengali, Chinese, French, Haitian Creole, Hindi, Korean, Polish, Russian, and Urdu
- Kutcher Adolescent Depression Scale (6 items)
- Columbia Depression Scale (22 items)
- Systemic review of above
 - Sensitivities: 70-90%
 - Specificities: 40-90%

Zuckerbrot RA, Cheung A, Jensen PS, et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice Preparation, Identification, Assessment, and Initial Management. *Pediatrics* 2018; 141.

Zuckerbrot RA, Cheung A, Jensen PS, et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): Part I. Practice Preparation, Identification, Assessment, and Initial Management. Supplemental information. Available at: <https://pediatrics.aappublications.org/content/141/3/e20174081/tab-supplemental> (Accessed on January 27, 2023).

Comorbidities



- Psychiatric comorbidities is the rule rather than expectation for pediatric depression
 - Nationally representative survey of adolescents in US found more than 60% of individuals with major depression had at least 1 comorbid psych disorder
- Anxiety disorders
- ADHD
- Disruptive behavior disorders (ODD and conduct disorder)
- Substance use disorders

Prevention

- Targeted prevention (subsyndromal depressive symptoms, or family history of depression)
 - Weak evidence, 2 meta-analysis (n>3900 and n> 400)
 - But may make sense if there is suicidal ideations/behaviors, functional impairment, comorbid psych disorders, or requests for treatment
- Universal prevention
 - Not recommended
 - No evidence, meta-analysis of 10 randomized trials (n>2000)

Hetrick SE, Cox GR, Witt KG, et al. Cognitive behavioural therapy (CBT), third-wave CBT and interpersonal therapy (IPT) based interventions for preventing depression in children and adolescents. Cochrane Database Syst Rev 2016; :CD003380.

Treatment: General Guideline



- Based on severity of depression
- Mild = therapy only
- Moderate = therapy AND medication
- Severe = therapy AND medication

Treatment: Therapy

- Most of the time, referring to
 - Cognitive behavioral therapy
 - Interpersonal therapy for adolescents
 - No compelling data that one is superior to the other
- General principle
 - Individualized care = identify specific cognitive, behavioral, emotional, interpersonal, and family problems that are maintaining symptoms
 - Incorporate care givers in therapy
 - Include psychoeducation regarding relapse prevention
- Unclear if benefit of therapy varies by age
 - Meta-analysis found psychotherapy was less effective for children (≤ 12 yo) vs. adolescents

Treatment: Therapy

- No absolute contraindication
- Not effective for those with low motivation
- High drop out rate
 - Randomized trial (n = 406 adolescents with unipolar depression), drop out rate 42%
- Fair evidence
 - Network meta-analysis of 52 randomized trial of psychotherapies (approximately 3800 children and adolescents with depression). Duration of treatment 4-16 weeks.
 - Improvement post-treatment: clinical effect moderate to large

Medication: Black box warning

- Black box warning on all antidepressants
 - Increase in suicidal thoughts and behaviors (suicidality)
- Mixed results: randomized trials, observational studies, and population based studies
- Unintended effect = decreased prescribing / increased suicide
 - General practitioner Dx depression and Rx antidepressants less since label
 - US CDC: 2003 (1737) -> 2004 (1985), first increase in more than 10 yrs
 - Netherlands: ↑ suicide 49% (2003-2005), ↓ SSRI prescription 22%
 - Canada: ↑ suicide 25%, ↓ SSRI prescription 14%

Antidepressants



- Benefits of antidepressant under ordinary clinical circumstances outweigh the potential risk of suicidal ideation and behavior
- The adverse effects of untreated depression include the risk of suicide

Bridge JA, Iyengar S, Salary CB, et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. JAMA 2007; 297:1683.

Medication: General Guideline

- SSRI first line
- Starting dose approximately $\frac{1}{2}$ the usual adult dose
- After 1 week, dose titration
- Titration every 2-4 weeks thereafter, depending on response/tolerability
- Connect with patient/family **weekly** for first 4 weeks upon initiation or switching medication *
- Frequency follow up: 1-3 months
- Response: takes 4-6 weeks at therapeutic dose
- Taper: decrease by 25-50% weekly

Medication: First line

- SSRI first line

Agent	Initial dose	Maintenance daily dose range
Fluoxetine (Prozac)	children = 5mg	10 to 80mg
	adolescent = 10mg	
Sertraline (Zoloft)	children = 12.5mg	50 to 200mg
	adolescent = 25mg	
Escitalopram (Lexapro)	5mg	10-20mg
Fluvoxamine (Luvox)	children = 25mg	50 to 300mg
	adolescent = 50mg	
Don't use Paxil (DC syndrome)		
If using Celexa, consider Lexapr (active enantiomer)		

Medication: Next Step

- After 2 failed SSRI, consider SNRI

Agent	Initial dose	Maintenance daily dose range
Venlafaine ER	37.5mg	75 to 225mg
Effexor XR		
Duloxetine	30mg	30 to 60mg
Cymbalta		can to up to 120mg

Treatment: Medication SE

- Worsening depressive symptoms
- Activation
- Irritability
- Akathisia (intense subjective feeling of restlessness and inability to sit still)
- GI (nausea/vomiting)
- Appetite/weight (inc/dec)

Tx: SSRI DC syndrome

- discontinuation symptoms (can last 1-2 weeks)
- flu-like symptoms (lethargy, HA, achy, sweating)
- insomnia (with vivid dream, nightmares)
- nausea
- imbalance (dizziness, lightheaded, vertigo)
- sensory disturbance (burning, tingling, shock-like sensation)
- hyperarousal (irritability, anxiety, agitation)

Tx: Serotonin Syndrome

- Potentially life-threatening
- Tachycardia
- Hypertension
- Hyperthermia
- Tremor
- Hyperreflexia
- Ankle Clonus
- Flushed skin / diaphoresis
- Increased bowel movements / diarrhea
- Dilated pupils / ocular clonus

Tx: Serotonin Syndrome

- Amphetamines / Methylphenidate
- Cocaine
- MDMA
- Tramadol
- Dextromethorphan
- TCA (amitriptyline for headaches)
- Ondansetron
- Trazodone
- Mirtazapine
- Buspirone
- Lithium

Tx: Atypical Antidepressants



- Bupropion (Wellbutrin)
 - MOA: Dopamine Norepinephrine Reuptake Inhibitor
 - SR = 100mg qAM -> BID. Max 200mg BID
 - XL = 150mg qAM -> dose increase. Max 450mg
- Can be helpful for ADHD and nicotine cessation (Zyban)
- Contraindication = seizures
 - History of seizures
 - Active eating disorder
 - Severe head injury

Tx: Atypical Antidepressants

- Mirtazapine (Remeron)
 - MOA: presynaptic alpha 2 antagonist = increase NE/5HT release
 - Dosing: 7.5mg qHS. Max 45mg qHS
- Side effect
 - Anticholinergic effects
 - Appetite/weight increase
 - Sedation

Tx: Med (Measurement)

- Patient Health Questionnaire – Nine Item (PHQ-9): Modified for Teens = most widely used for adolescents
- Mood and Feelings Questionnaire = validated for both children and adolescents
 - Separate forms for patient and caregiver
 - Short version (13 items) = lacks question about SI
 - Long version (33 items)
- Quick Inventory of Depressive Symptomatology, Adolescent Version
 - Self-reported, 17-item

Any questions so far?



PART II: ANXIETY

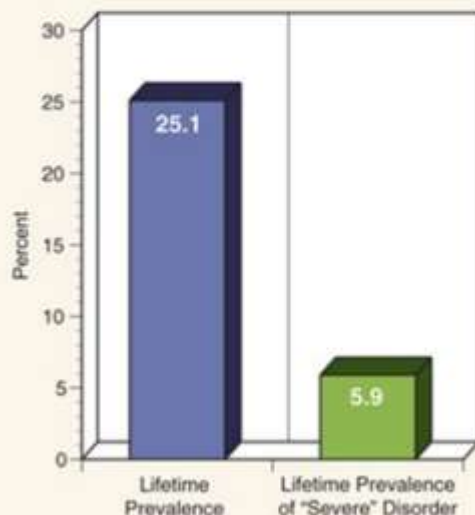
- Epidemiology
- Diagnoses
- Comorbidities
- Assessment
 - comorbidities
- Treatment

Prevalence



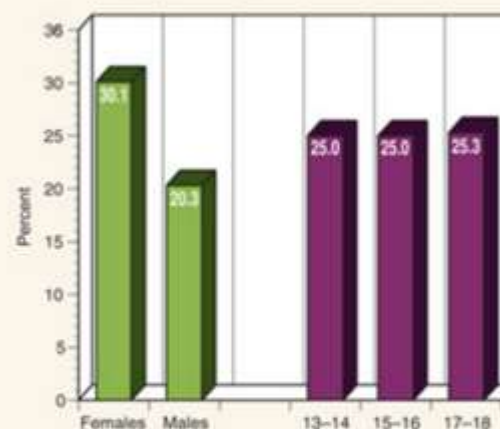
Lifetime Prevalence of 13 to 18 year olds

- **Lifetime Prevalence:** 25.1% of 13 to 18 year olds
- **Lifetime Prevalence of "Severe" Disorder:** 5.9% of 13 to 18 year olds have "severe" anxiety disorder



Demographics (for lifetime prevalence)

- **Sex:** Statistically different
- **Age:** Not statistically different



- **Race:** Statistically significant differences were found between non-Hispanic whites and other races

*Merikangas KR, He J, Burstein M, Swanson SA, Avenevoli S, Cui L, Benjet C, Georgiades K, Swendsen J. *Lifetime prevalence of mental disorders in U.S. Adolescents*. Under review.

Genetic Factors

- Twin studies show familial aggregation among various anxiety disorder
- Heritability around 30% but some studies show as high as 50-60%
- Genetic contribution largest with early onset cases (childhood onset)

-Eley TC, Gregory AM. Behavioral genetics: Anxiety disorders in children and adolescents., Guilford Press, New York 2004.

-Trzaskowski M, Eley TC, Davis OS, et al. First genome-wide association study on anxiety-related behaviours in childhood. PLoS One 2013; 8:e58676.

Developmental Factor

- Behaviorally inhibited toddlers = greater risk for developing clinical anxiety disorders in childhood
 - Behaviorally inhibited = apprehensive, hesitant, distressed with novelty => likely to avoid novel stimuli

Perez-Edgar K, Child Adolesc Psychiatr Clin N Am. 2005 Oct;14(4):681-706, viii.

Cognitive Factors

- Threat bias in cognitive processing of information
- difficulty distinguishing between contexts/cues signal safety and those that represent threat
 - Difficulty to learn to ignore these associations when they are no longer applicable

Parenting Style

- Shape anxiety-driven behaviors
- Anxious, overprotective, overly critical parenting
 - Insensitive to child's expressive, exploratory, and independent behaviors
 - Reinforce and maintain anxious and avoidance behaviors

General Presentation

- Avoidance – school, parties, camp, sleep over, talking to safe adults
- Somatic symptoms – HA, dizziness, chest pain, dyspnea, stomachache, etc.
- Sleep problems – early/middle
- Excessive need for reassurance – bedtime, storm, school time, or general
- Poor school performance – inattention, incomplete tasks
- Explosiveness and oppositional behavior – irritability*
- Eating problems
- Suicidal thoughts – in the absence of depression

Generalized Anxiety Disorder

- Anxiety is hard to control
- Occurring more days than not, at least 6 months
- 3+ additional symptoms for adolescents
- only 1 required for children
- Additional symptoms
 - Restlessness
 - Fatigue
 - Poor concentration
 - Irritability
 - Muscle tension
 - Sleep disruptions

Social Anxiety Disorder

- Key Feature: Fear/anxiety about being judged
 - Fear that he/she will act in an embarrassing manner (negatively evaluated)
 - Performance only subtype
- Median age at onset: 13yo

Separation Anxiety Disorder

- 1st anxiety to present
 - Most common anxiety disorder in < 12 years old
 - Duration: > 4 weeks (in children/adolescents)
- Key feature: Excessive distress when separated from home or primary attachment figures
 - Can occur in anticipation of separation
 - Worry about harm to self or attachment figure
 - Avoidance: School refusal, No sleepovers/camp

Specific Phobia



- Object/situation: Provokes immediate, intense fear or anxiety
- Behavior: Avoidance or endured but with intense fear
- Fear/anxiety is out of proportion to actual danger posed

Animal (spiders, insects, dogs, etc)

Natural environment (heights, storms, water, etc)

Blood-injection-injury (needles, IV, etc)

Situational (airplane, elevators, etc)

Other (costumed character, etc)

Panic Disorder

Key feature: Recurrent, unexpected panic attacks

+

Anticipatory anxiety and/or Maladaptive change in behavior

+/- Agoraphobia: Cannot escape or will not be able to get help should a panic attack occur

- * Public transportation
- * Open spaces
- * Enclosed spaces
- * Standing in line or being in a crowd
- * Being outside of the home alone

Panic Attacks

- Abrupt and Peaks within minutes
- Symptoms: 4 or more
 - Cardiac: chest pain, palpitations, sweating
 - Respiratory: dyspnea, smothering sensation
 - GI: nausea, abdominal distress
 - Neuro: Trembling, chills/hot flashes, dizziness, paresthesias, derealization, depersonalization
 - Other: Fear of losing control/going “crazy”, Fear of dying

Comorbidities



- Second anxiety disorder
- ADHD
- ODD
- Depression
- Learning disabilities

Screening

- USPSTF recommends screening all children 8 and above for anxiety (Grade B)
 - Grade I for those younger than 8

<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/screening-anxiety-children-adolescents>

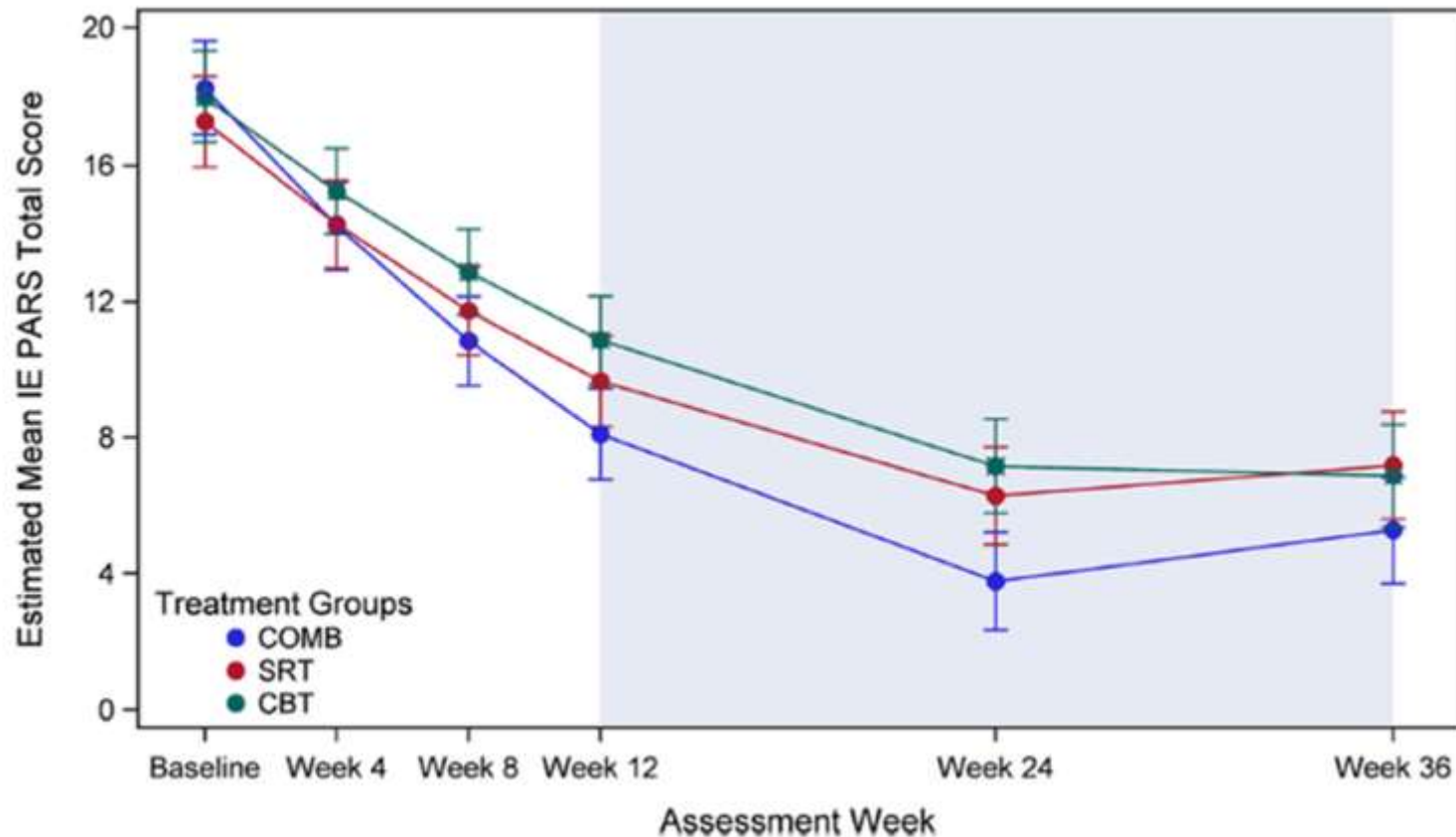
SCARED



- Screen for Child Anxiety-Related Emotional Disorders
- Why
 - Provides subscale related to different anxiety disorders
 - Shows sensitivity to treatment effects
 - Public domain
 - Has short 5-item screening form
- Sensitivity = 0.5 – 0.88
- Specificity = 0.56 – 0.98

Johnson JG, J Adolesc Health. 2002 Mar;30(3):196-204.

Treatment: Medication or therapy?



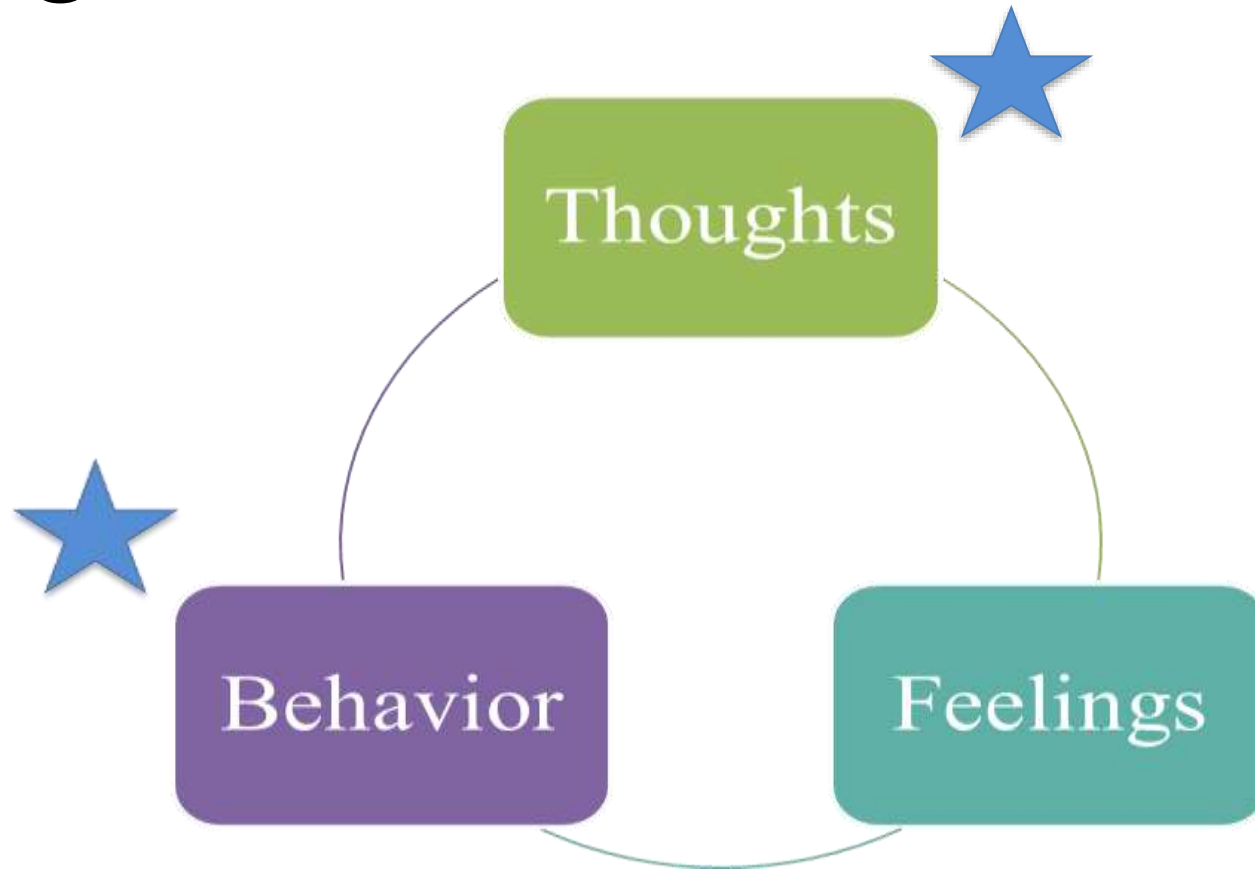
Piacentini. J Acad Child Adolesc Psychiatry. 2014.

Treatment:



- Mild SYMPTOMS = supportive care + monitor
- Mild disorder = therapy
- Moderate disorder = medication
- Severe disorder = medication + CBT

Cognitive Behavioral Therapy



CBT Components

- 1) Psychoeducation
- 2) Skill building
- 3) Cognitive Restructuring
- 4) Exposure methods
- 5) Relapse prevention

Treatment: Medication

Agent	Initial dose	Maintenance daily dose range
Fluoxetine (Prozac)	children = 5mg adolescent = 10mg	10 to 80mg
Sertraline (Zoloft)	children = 12.5mg adolescent = 25mg	50 to 200mg
Escitalopram (Lexapro)	5mg	10-20mg
Fluvoxamine (Luvox)	children = 25mg adolescent = 50mg	50 to 300mg
Don't use Paxil (DC syndrome)		
If using Celexa, consider Lexapr (active enantiomer)		

Treatment: Medication (Augmentation)

- Buspirone (Buspar) = low evidence
 - Start 5mg daily, increase by 5mg to 7.5mg-30mg BID (15 – 60mg total daily dose)
- Guanfacine (Tenex/Intuniv) = better evidence
- Avoid benzodiazepine

Connolly SD, J Am Acad Child Adolesc Psychiatry. 2007;46(2):267.
Strawn JR, J Child Adolesc Psychopharmacol. 2017;27(1):29. Epub 2017 Feb 6.

Consultation

- BH-TIPS
 - Google: NCH BH TIPS
- Physician Direct Connect
 - **(614) 355-0221** or **1 (877) 355-0221**

QUESTIONS?

THANK YOU

