

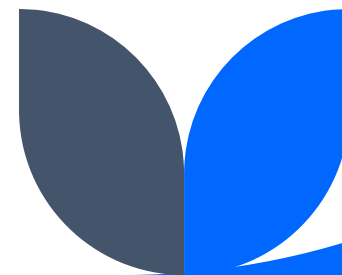
Mood Disorders in Children and Adolescents

Rebeca Sandoval, LSCSW, RPT-S



Agenda

- Introduction
- Assessment of Mood Disorders- DSM 5-TR criteria
- Differences between the mood disorders and how does this present with children and adolescents
- Summary of current findings in literature regarding mood disorder diagnosis in children and adolescents
- Case reviews
- Common approaches for treatment of mood disorders in children and adolescents-treatment planning
- Common challenges in diagnosing mood disorders in children and adolescents



Introduction

Rebeca Sandoval, LSCSW, RPT-S

- KU School of Social Welfare
- Private practice and agency experience
- Areas of specialty

DSM-5-TR CHANGES from DSM-5

Some of the diagnostic criteria were updated in DSM-5-TR to capture the experiences and symptoms of children more precisely. In addition, DSM-5-TR, like DSM-5, emphasized that like any medical issue, no child should ever be diagnosed without a careful, comprehensive evaluation, and no medication should be prescribed without equal vigilance.

Parents play an integral role in this process, as many of the DSM criteria require that symptoms be observed by them or other individuals who interact regularly with the child.

More Precise Criteria Existing criteria have been updated in DSM-5-TR to provide more precise descriptions and reflect the scientific advances and clinical experience of the last decade.

-<https://www.psychiatry.org/getmedia/178f173b-f4a1-433b-aef3-7b2fb513436b/APA-DSM5TR-DiagnosesforChildren.pdf>

Autism Spectrum Disorder: Criterion A phrase “as manifested by the following” was revised to read “as manifested by all of the following” to improve its clarity. The revision by the work group was made to maintain a high diagnostic threshold by requiring “all of the following,” and not “any of the following” criteria, as could be mistakenly implied by the previous wording of the criterion.

Disruptive Mood Dysregulation Disorder: The text in the “Development and Course” section describing the age range at which disruptive mood dysregulation disorder can be diagnosed and for which validity is established was updated to “6–18 years,” as noted in criterion G.

Posttraumatic Stress Disorder: For children 6 years and younger, the note that “witnessing does not include events that are witnessed only in electronic media, television, movies, or pictures” in Criterion A.2 was removed for its redundancy, given that criterion A.2 already indicates that the events occurring to others must be witnessed in person.

Prolonged Grief Disorder Prolonged Grief Disorder: is a new disorder in DSM-5-TR. Specific language was added to the criteria to define the difference between children and adolescents versus adults. The intent of that is to reflect current scientific evidence and highlight the different reactions children or adolescents might have in such situations.



Two broad types of Mood Disorders

Involves only depressive symptoms

Involves manic symptoms (bipolar disorders)

DSM-5 depressive disorders:

Major depressive disorder

Persistent depressive disorder

Premenstrual dysphoric disorder

Disruptive mood dysregulation disorder

DSM-5 Bipolar Disorders:

Bipolar I disorder

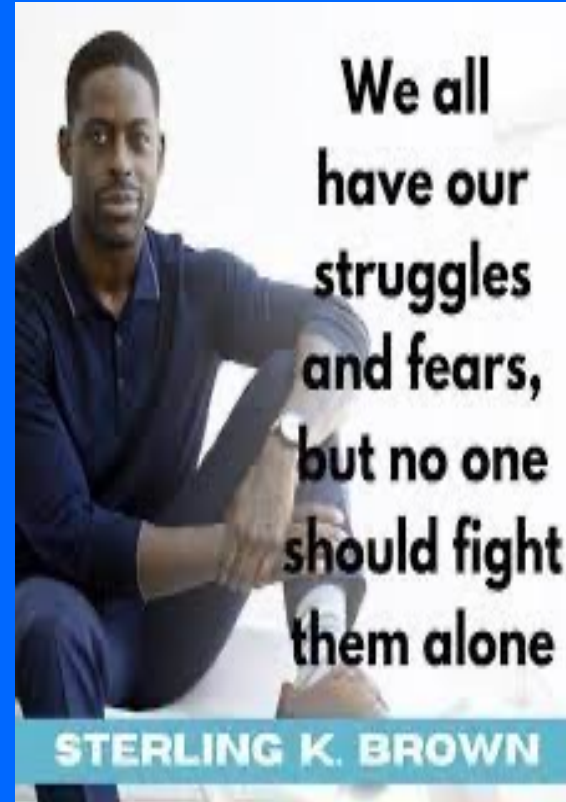
Bipolar II disorder

Cyclothymic disorder

Overview of the DSM-5-TR Mood Disorders

Major depressive disorder	<ul style="list-style-type: none">• Five or more depressive symptoms, including sad mood or loss of pleasure, for 2 weeks
Persistent depressive disorder	<ul style="list-style-type: none">• Low mood and at least two other symptoms of depression at least half of the time for 2 years. In children and adolescents: mood can be irritable, and duration must be at least 1 year.
Premenstrual dysphoric disorder	<ul style="list-style-type: none">• Mood symptoms in the week before menses with at least 5 symptoms present
Disruptive mood dysregulation disorder	<ul style="list-style-type: none">• Severe recurrent temper outbursts and persistent negative mood for at least 1 year beginning before age 10
Bipolar I disorder	<ul style="list-style-type: none">• At least one lifetime manic episode
Bipolar II disorder	<ul style="list-style-type: none">• At least one lifetime hypomanic episode and one major depressive episode
Cyclothymic disorder	<ul style="list-style-type: none">• Recurrent mood changes from high to low for at least 2 years, without hypomanic or depressive episodes. At least 1 year for children and adolescents.

Depressive Disorders



Depressive Disorders

The Diagnostic and Statistical Manual of Mental Disorders, fifth edition, text revision (DSM-5-TR) categorizes depressive disorders into the following categories:

- major depressive disorder (MDD)
- persistent depressive disorder
- disruptive mood dysregulation disorder
- premenstrual dysphoric disorder
- substance/medication-induced depressive disorder
- depressive disorder due to another medical condition
- other specified depressive disorder
- unspecified depressive disorder



Major Depressive Disorder

Sad mood OR loss of interest or pleasure (anhedonia)

Symptoms are present nearly every day, most of the day, for at least 2 weeks (in children and adolescents, can be irritable mood)

Symptoms are distinct and more severe than a normative response to significant loss

PLUS four of the following symptoms:

- Sleeping too much or too little
- Psychomotor retardation or agitation
- Poor appetite and weight loss, or increased appetite and weight gain (in children and adolescents, consider failure to make expected weight gain)
- Loss of energy
- Feelings of worthlessness or excessive guilt
- Difficulty concentrating, thinking, or making decisions
- Recurrent thoughts of death or suicide



MDD diagnostic information

Episodic

Symptoms tend to dissipate over time

Recurrent

Once depression occurs, future episodes likely

Average number of episodes is 4

Subclinical depression (some children will have subclinical depression co-occurring: ADHD or Generalized Anxiety Disorder)

Sadness plus 3 other symptoms for 10 days

Significant impairments in functioning even though full diagnostic criteria are not met



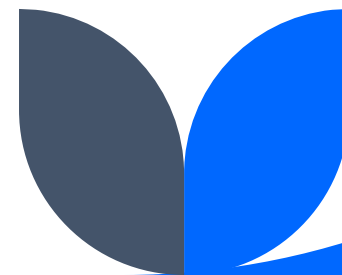
Statistical data regarding MDD in children and adolescents

- At any given time, up to 15 percent of children and adolescents have some symptoms of depression.
- Five percent of those nine to 17 years of age meet the criteria for major depressive disorder, and 3 percent of adolescents have dysthymic disorder.
- The incidence of depressive disorders markedly increases after puberty.
- By 14 years of age, depressive disorders are more than twice as common in girls as in boys, possibly because of differences in coping styles or hormonal changes during puberty.
- Adolescent depressive disorders often have a chronic, waxing-and-waning course, and there is a two- to fourfold risk of depression persisting into adulthood.
- Depression impacts growth and development, school performance, and peer or family relationships, and it can be fatal. Major depressive disorder is a leading cause of youth suicidal behavior and suicide.



The Most Common Symptoms of MDD in Children and Adolescents

- Feeling or appearing depressed, sad, tearful, or irritable (excessive crankiness)
- Not enjoying things as much as they used to
- Spending less time with friends or in after school activities (saying no to friends more)
- Sleeping more or less than usual (sleep disturbances)
- Feeling tired or having less energy (can appear unmotivated)
- Somatic complaints (stomach pain, head hurts) Kids don't feel good, so they are trying to make sense of the "pain."
- Feeling like everything is their fault or they are not good at anything ("I'm not good at that. I always mess up. I'm so stupid.")
- Having more trouble concentrating (not completing assignments or doing poorly)
- Caring less about school or not doing as well in school (missing a lot of school/ skipping classes)
- Having thoughts of suicide or wanting to die



Persistent Depressive Disorder

Depressed mood for at least 2 years; 1 year for children/adolescents

PLUS 2 other symptoms:

- Poor appetite or overeating
- Sleeping too much or too little
- Poor self-esteem
- Trouble concentrating or making decisions
- Feelings of hopelessness

Symptoms are present for more than 2 months at a time

Bipolar disorder symptoms are not present



Premenstrual dysphoric disorder

In most menstrual cycles during the past year, at least five of the following symptoms were present in the final week before menses and improved within a few days of menses onset:

- Affective lability
- Irritability
- Depressed mood, hopelessness, or self-deprecating thoughts
- Anxiety
- Diminished interest in usual activities
- Difficulty concentrating
- Lack of energy
- Changes in appetite, overeating, or food craving
- Sleeping too much or too little
- Subjective sense of being overwhelmed or out of control
- Physical symptoms such as breast tenderness or swelling, joint or muscle pain, or bloating

Consider referral to a medical provider to check physical needs/concerns



Disruptive mood dysregulation disorder

Severe recurrent temper outbursts, including verbal or behavioral expressions of temper that are out of proportion in intensity or duration to the provocation.

- Temper outbursts are inconsistent with developmental level.
- The temper outbursts tend to occur at least three times per week.
- Negative mood between temper outbursts most days.

These symptoms have been present for at least 12 months and do not clear for more than 3 months at a time.

Temper outbursts and negative mood are present in at least two settings (at home, at school, or with peers) and are severe in at least one setting.

Age 6 or older (or equivalent developmental level). Onset before age 10.

There has never been a distinct period lasting more than 1 day during which elevated mood and at least three other manic symptoms were present.

The behaviors do not occur exclusively during major depressive disorder and are not better accounted for by another mental disorder.



Disruptive mood dysregulation disorder

- The diagnosis of DMDD cannot coexist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder, though it can coexist with others, including major depressive disorder, attention-deficit/hyperactivity disorder, conduct disorder, and substance use disorders.
- Individuals whose symptoms meet criteria for both disruptive mood dysregulation disorder and oppositional defiant disorder should only be given the diagnosis of disruptive mood dysregulation disorder.
- If an individual has ever experienced a manic or hypomanic episode, the diagnosis of disruptive mood dysregulation disorder should not be assigned (as this indicates a diagnosis of bipolar disorder).
- The epidemiology of DMDD is not well understood as it is a new diagnosis; it is estimated to have a prevalence between 2 to 5%.
- Individuals presenting to clinical attention are most commonly male.
- There are currently no current validated scales for DMDD.



Bipolar Disorders

Bipolar disorder it's a challenge, but it can set you up to be able to do almost anything else in your life.

CARRIE FISHER



HealthyPlace.com

Bipolar Disorders

Three forms:

Bipolar I, Bipolar II, and Cyclothymic disorder

Mania defining feature of each

Differentiated by severity and duration of mania

Usually involve episodes of depression alternating with mania

Depressive episode required for Bipolar II, but not Bipolar I

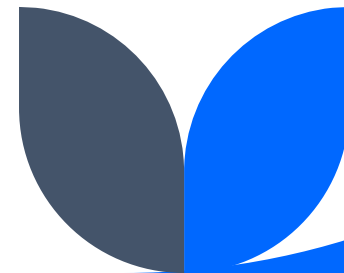
Mania

State of intense elation or irritability

Hypomania (hypo = “under”; hyper = “above”)

Symptoms of mania but less intense

Does not involve significant impairment, mania does



DSM-5-TR Criteria for Bipolar Disorders

Bipolar I

At least one episode of mania

Bipolar II

At least one major depressive episode with at least one episode of hypomania

Cyclothymic disorder (Cyclothymia)

Milder, chronic form of bipolar disorder

Lasts at least 2 years in adults, 1 year in children/adolescents

Numerous periods with hypomanic and depressive symptoms

Does not meet criteria for mania or major depressive episode

Symptoms do not clear for more than 2 months at a time

Symptoms cause significant distress or impairment



DSM-5-TR Criteria for Manic and Hypomanic Episodes

Distinctly elevated or irritable mood for most of the day nearly every day

Abnormally increased activity and energy

At least three of the following are *noticeably changed from baseline* (four if mood is irritable):

- Increase in goal-directed activity or psychomotor agitation
- Unusual talkativeness; rapid speech
- Flight of ideas or subjective impression that thoughts are racing
- Decreased need for sleep
- Increased self-esteem; belief that one has special talents, powers, or abilities
- Distractibility; attention easily diverted
- Excessive involvement in activities that are likely to have undesirable consequences, such as reckless spending, sexual behavior, or driving

For a manic episode:

- Symptoms last for 1 week or require hospitalization or include psychosis
- Symptoms cause significant distress or functional impairment

For a hypomanic episode:

- Symptoms last at least 4 days
- Clear changes in functioning that are observable to others, but impairment is not marked
- No psychotic symptoms are present

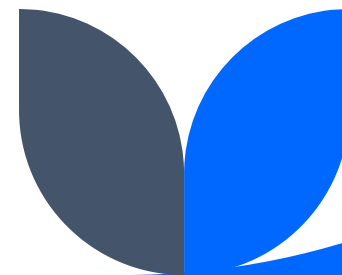


Cyclothymic Disorder

According to the DSM-5-TR, there are six diagnostic criterion, with one specifier:

1. For at least a two-year period (1 year in children and adolescents), there have been episodes of hypomanic and depressive experiences which do not meet the full DSM-5 diagnostic criteria for hypomania or major depressive disorder.
2. The above criteria had been present at least half the time during a two-year period, with not more than two months of symptom remission.
3. There is no history of diagnoses for manic, hypomanic, or a depressive episode.
4. The symptoms in criterion A are cannot be accounted for by a psychotic disorder, such as schizophrenia, schizoaffective disorder, schizophreniform disorder, or delusional disorder.
5. The symptoms cannot be accounted for by substance use or a medical condition.
6. The symptoms cause distress or significant impairment in social or occupational functioning.

A specifier the clinician can add is With anxious distress.



Epidemiology and Consequences with Bipolar Disorders

Prevalence rates lower than MDD

1% in U. S.; 0.6% worldwide for Bipolar I

0.4% – 2% for Bipolar II

4% for Cyclothymia

Average age of onset in 20s

No gender differences in rates of bipolar disorders

Women experience more depressive episodes

Severe mental illness

A third unemployed a year after hospitalization (Harrow et al., 1990)

Suicide rates high (Angst et al., 2002)



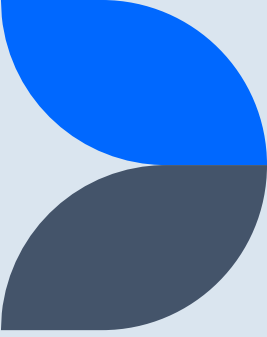


Case Reviews

Case Reviews

- Read the case and discuss it
- Give a diagnosis and the justification for the diagnosis
- What other questions do you need to ask to help clarify information???
- Discuss treatment plans and all considerations

7 year old female in 1st grade



- Referred with symptoms of aggression, disruptive behavior, social issues, and mood changes.
- Distractible, impulsive, and rage outbursts since the age of 2.
- Mom has trouble getting her to do anything, especially school work.
- Reports by adults that she negatively attention seeks.
- Behavior worse since the age of 5. Grandma died then.
- Has attention deficits, both staring and distractibility. Gets bored easily, excessive need for validation and praise. Hypersensitivity for perceived ignoring her. Demanding. Has trouble keeping friends due to mood swings.
- Milestones early. No evidence of abuse, neglect, physical illness, or psychosis.

8 year old boy in the 2nd grade

- Increasing episodes of explosive anger, typically in response to frustration. Home > school, several times a day.
- Formerly a good, well-liked student and is now more socially withdrawn.
- He is hyperactive, impulsive, inattentive and easily frustrated.
- He has anxiety, somatic symptoms (headaches, stomach aches, enuresis) and some sensory sensitivities.
- He reports thoughts of harming himself but no plans to do so. Reports increase when there is stress at school especially around peer issues.
- Parents are currently going through a divorce, but parents do get a long. Mom has been dating recently and patient states he is mad at her.
- There is a family history of mood disorders (maternal grandmother: bipolar, and paternal grandpa: depression and completed suicide many years before patient's birth)

15 year old female in the 10th grade

- Referred by school due to truancy and falling grades
- Formerly a good, well-liked student and is now more socially withdrawn.
- She lives with single mother and 2 sisters age 17 and 12. Mother works various shifts at a manufacturing plant. 17 year old sister recently dropped out of school.
- She self reports that she cannot stop crying and feels like all she wants to do is sleep. Reports she likes to read and ride bike but hasn't felt like doing those things for a couple of months now.
- She stated that she cannot visit biological dad anymore because he is in jail for child molestation.
- She has a 19 year old boyfriend that does take her to school sometimes and she does stay the night with him sometimes. Mom is okay with it. Occasional pot smoking with boyfriend but reports she doesn't like it.
- There is a family history of mood disorders (MDD biological mother and Bipolar disorder with biological dad)

Screening tools

Complete at intake and throughout treatment

<https://www.psychiatry.org/psychiatrists/practice/dsm/educational-resources/assessment-measures>

Depression Scale for Children (DSC)

The Center for Epidemiological Studies Depression Scale for Children (DSC) is a 20-item self-report for children and adolescents ages 6 to 17 years that screens for depression. Questions focus on feelings over the past week and the tool takes about five minutes to complete. The tool and brief instructions for scoring are available at Center for Epidemiological Studies Depression Scale for Children (CES-DC) .

Columbia Suicide Severity Rating Scale (CSSRS)

The Columbia Suicide Severity Rating Scale (CSSRS) can be used to screen children and adolescents (ages five years and older) for suicide risk. It is available in 103 languages. Completion of a 30-minute, on-line training is necessary to use the tool and provides a two-year certification. More information on the administration of the scale can be found on the [main CSSRS website](#).

Pediatric Symptom Checklist (PSC)

The Pediatric Symptom Checklist (PCS) is a self-administered, 35-item tool used to identify cognitive, emotional, and behavioral problems in children and youth ages 4-16 years of age. There are two versions: parent and child. The items on each of the checklists are parallel. The parent checklist can be administered for children as young as four years old. The youth checklist can be administered to adolescents beginning at age 11 years. The PSC is available in 16 languages. Extensive information is available at the [PSC home page](#) maintained by Massachusetts General Hospital. Extremely helpful in treatment planning.

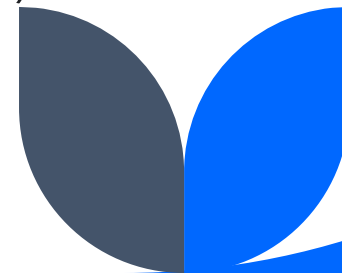


Strengths and Difficulties Questionnaire (SDQ)

The Strengths and Difficulties Questionnaire (SDQ) is a self-administered behavioral questionnaire that screens children and youth ages 3-16 years using 25 items on five scales: 1) emotional problems, 2) conduct problems, 3) hyperactivity and inattention, 4) peer relationships, and 5) prosocial behaviors. There are several versions to meet the needs of researchers, clinicians, and educators. The initial administration of the tool covers the last six months, while the follow-up version asks about the last month. As such, the SDQ can be used to assess the effectiveness of interventions. The SDQ is completed by teachers and parents. A parallel version is completed by youth ages 11-16 years. There is a modified version for preschool and early childhood teachers and parents of two- to four-year-olds. Performance is enhanced by use of multiple informants (i.e., teacher, parent, student). The SDQ has been studied extensively, has norms available from six countries, including the United States, and is available in 67 languages. Extensive information is available at [Information for Researchers and Professionals about the Strengths & Difficulties Questionnaires](#), including a description, norms, links to journal articles, tools, and scoring. Very helpful during treatment planning on interventions.

The Severity Measure for Depression—Child Age 11–17 (adapted from PHQ-9 modified for Adolescents [PHQ-A]) is a 9- item measure that assesses the severity of depressive disorders and episodes (or clinically significant symptoms of depressive disorders and episodes) in children ages 11–17.

Young Mania Rating Scale is a reliable valid assessment tool, clinicians use to check and track a patient's manic symptoms. It's a diagnostic questionnaire with eleven items, enumerating the core mania symptoms. There is a parent version, also.



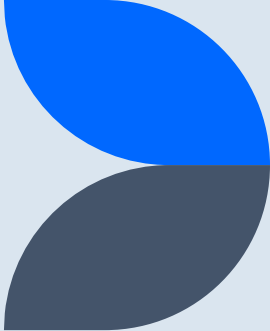
Treatment Planning Ideas

- Systematically assess for manic and depressive symptoms and episodes in all youth presenting with mood problems—incorporating assessment tools—both at **baseline and throughout course of treatment.**
- Assess for family history of bipolar disorder, inclusive of mania/hypomania symptoms, especially in first- and second-degree relatives. Have parents or caregivers involved.
- Refer to primary care provider to rule out any medical conditions.
- Look for symptoms with high specificity for bipolar disorder, especially those with an episodic nature, to distinguish the condition from disorders with overlapping symptoms.
- Consider utilizing age-appropriate interventions and treatment modalities.
- Trauma informed care approach.
- Collaborate with school and medical providers as needed.
- Make sure parents and care givers are involved in the treatment planning and throughout the course of treatment.



- Most mood disorders are treated with a combination of individual and family therapy, psychotherapy and medication. Research does indicate that combining psychotherapy with medication yields the best outcomes for individuals.
- Treatment also encourages positive interaction and reinforcement in the school setting.
- Assess for safety within the family and history of suicidal ideation/attempts/completion.
- Psychoeducation is a consistent part of the therapeutic process with individual and family members.

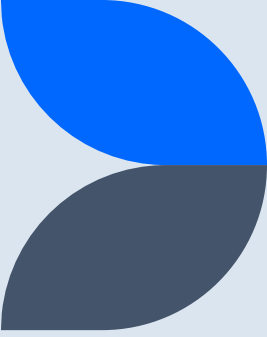




Cognitive Behavioral Therapy (CBT)- is the most widely researched form of therapy for mood disorders, including depression and bipolar disorder. With CBT, children, adolescents and young adults learn about the connections among their thoughts, feelings and behaviors. Once these connections are made, patients and therapists actively collaborate to meet specific goals, such as helping patients notice and change their unhelpful thoughts, improving their problem-solving abilities and increasing their involvement in positive activities that promote healthy choices. Treatment may also include Behavioral Activation — planned activities aimed at promoting increased mood and energy level.

Dialectical Behavior Therapy (DBT)- is recommended for adolescents and young adults who have difficulty regulating their emotions. DBT involves learning skills to tolerate distress, manage strong and upsetting emotions, decrease impulsive behaviors, including self-harm, and improve relationships with friends and family.

Mindfulness-Based Intervention, when appropriate, is used as an adjunctive treatment for mood disorders to assist in helping children and adolescents manage challenging emotions. Mindfulness means being aware and being focused on what's happening right now in this moment – without rejecting it or judging it.



Play Therapy- Usually reserved for younger children, during play therapy a therapist uses games, toys, drawings and other things that are generally fun for kids to help them recognize and discuss their emotions. Through observation of a child's play, the therapist pieces together the child's emotional life and then uses a combination of conversation and interactive play to help the child productively process his or her emotions, thoughts and behaviors.

Family therapy- is mainly concerned with helping families find positive and productive ways to communicate. Sometimes children and parents are involved in therapy sessions and sometimes therapy sessions involve only parents or only children. Therapeutic sessions can also include siblings or grandparents. The goal of family therapy is to find solutions which work for everyone involved: parents, children, siblings and any other relevant individuals.

Remember STAR...We are creating stars

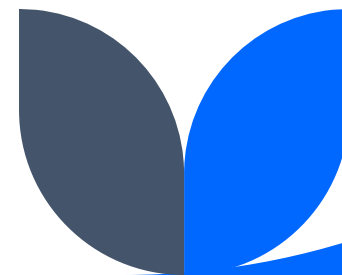


S: screen the patient using the evidence-based screeners to help you evaluate the presenting needs

T: Therapy Process is how you explain informed consent especially when it comes to working with children and adolescents. During this therapy process...I think about how I can build a relationship with all members of the family. What does everyone think progress looks like?

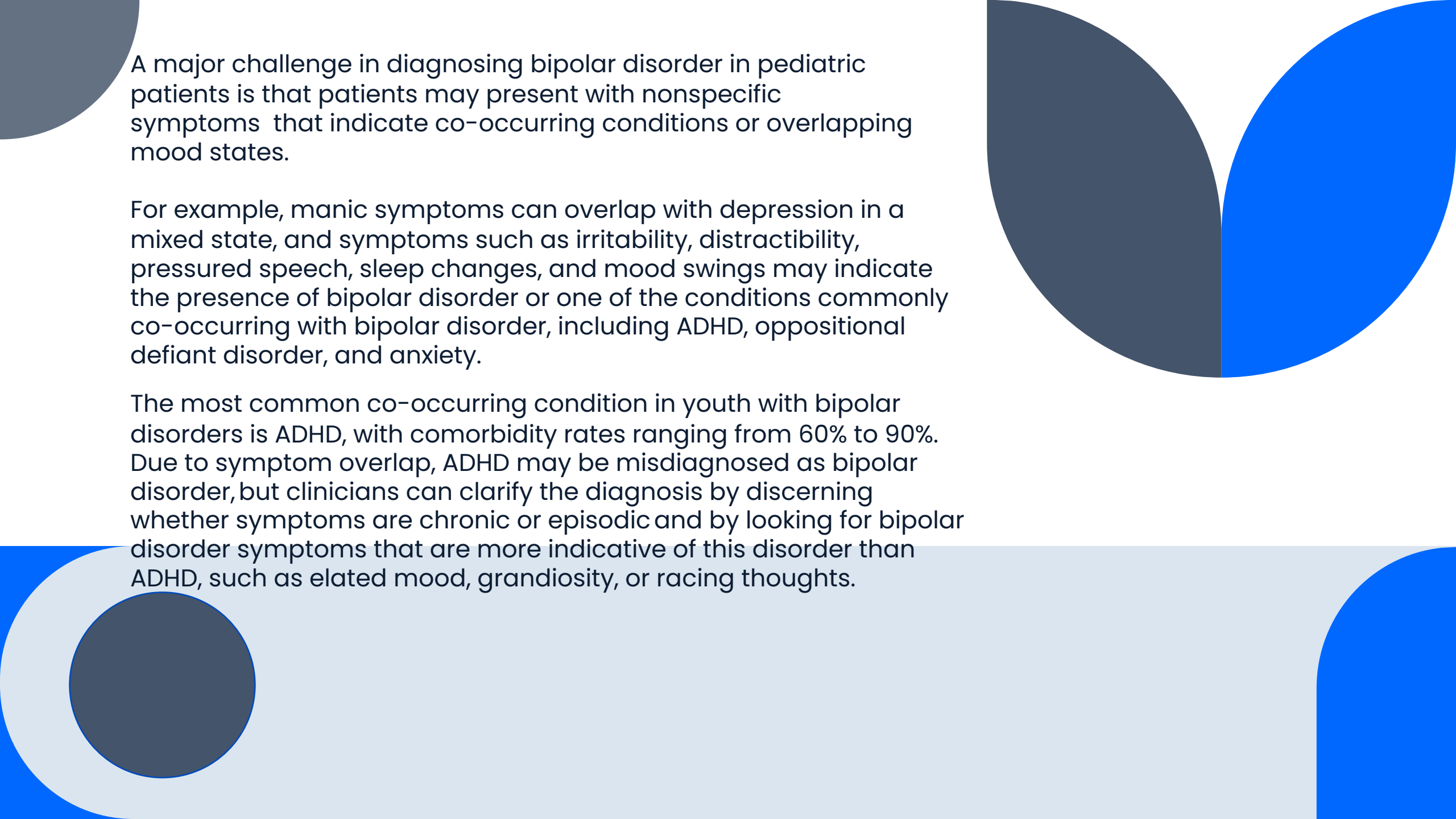
A: Ask questions. We are only as good as the information that we have so we must ask a lot of questions. Make sure we explain why we might be asking certain questions...

R: Rate the level of intensity with the patient/families help. When the “thing” happens...what’s the duration? How long does it last? When it comes to treatment planning...it is so helpful to establish a baseline.



Diagnostic Challenges when working with children and adolescents

- Overlapping Symptoms
- Symptoms of depression or mania may present differently in pediatric patients than in adults
- Children and adolescent cases can be very complex when more people/systems are involved
- Trauma history



A major challenge in diagnosing bipolar disorder in pediatric patients is that patients may present with nonspecific symptoms that indicate co-occurring conditions or overlapping mood states.

For example, manic symptoms can overlap with depression in a mixed state, and symptoms such as irritability, distractibility, pressured speech, sleep changes, and mood swings may indicate the presence of bipolar disorder or one of the conditions commonly co-occurring with bipolar disorder, including ADHD, oppositional defiant disorder, and anxiety.

The most common co-occurring condition in youth with bipolar disorders is ADHD, with comorbidity rates ranging from 60% to 90%. Due to symptom overlap, ADHD may be misdiagnosed as bipolar disorder, but clinicians can clarify the diagnosis by discerning whether symptoms are chronic or episodic and by looking for bipolar disorder symptoms that are more indicative of this disorder than ADHD, such as elated mood, grandiosity, or racing thoughts.

In some instances, the younger the patient, the more likely the initial episode will be depression, which may lead to the patient being misdiagnosed with major depressive disorder.

Clinical characteristics such as a family history of bipolar disorder and a younger age at onset may indicate a possible risk for bipolar rather than unipolar depression, and considering such clinical risk factors may assist clinicians in making an accurate diagnosis before mania symptoms emerge.

With any presentation of depression, clinicians should assess patients for mania or hypomania. Pediatric bipolar disorder may be difficult to detect because moodiness and irritability are common in childhood and adolescence, but symptoms of irritability, rage, mood lability, or unusual sleep habits, activity levels, or behavior should prompt a clinician to assess patients for bipolar disorder.

Diagnostic criteria for bipolar disorders are available, but clinicians must be aware that symptoms of depression or mania may present differently in pediatric patients than in adults. Frequencies of various diagnostic symptoms among youth with bipolar disorder, according to research are shown on the next slide.

SYMPTOM

PEDIATRIC BIPOLAR

ADHD

Elevated mood

Common with
element of grandiosity

Much less common

Hypersexuality

Common

Not seen

Psychotic symptoms

Common

Not seen

Irritable mood

Very prominent

Less prominent

Self-injurious/suicidal
behavior

Common

Rare

Family history

Bipolar disorder and
depression common

ADHD/ADD

Flight of ideas/racing
thoughts

Could be present

Not seen

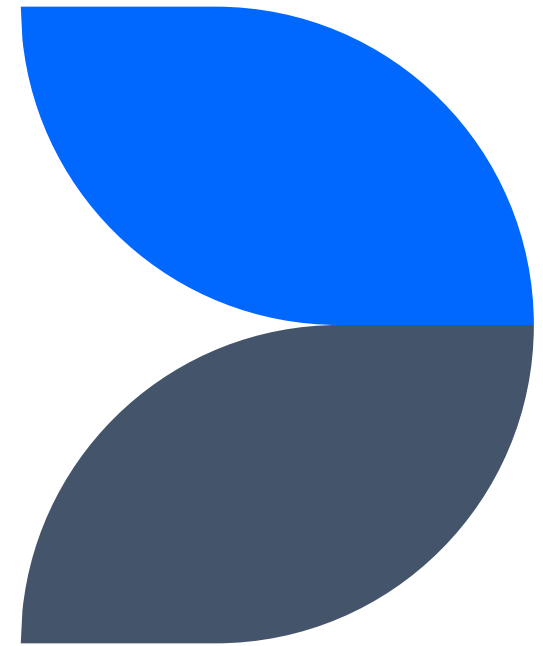
Tidbits For The Treating Clinician

- Utilize supervision to talk about difficult cases
- Refer patients as needed for testing and medication evals
- Ask more questions regarding the identified problems and remember “the team” produces possible solutions
- There is no one size fits all approach
- Take care of yourself and this is more than just go to bed early or take a nice hot bath



**Please share what
you do to manage
your own
capacity...**

Emotion Regulation...



Summary

Final thoughts

Questions?

Reference Articles and Resources

- <https://www.aafp.org/pubs/afp/issues/2019/1115/p609.pdf>
- <https://www.aafp.org/pubs/afp/issues/2007/0101/p73.pdf>
- <https://www.nimh.nih.gov/sites/default/files/documents/health/publications/disruptive-mood-dysregulation-disorder/disruptive-mood-dysregulation-disorder-the-basics.pdf>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2695748/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6345140/?report=printable>

Thank you

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