

BIPOLAR DISORDERS IN CHILDREN AND ADOLESCENTS

2019 edition

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Starry Night, Vincent van Gogh, 1889.
Museum of Modern Art, New York City

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It is now widely accepted that bipolar disorder (BD) occurs in children and adolescents and the controversy has shifted from a debate about whether it can be diagnosed in youth to how it is diagnosed, how it can be distinguished from other more common childhood psychiatric disorders, and how it can be treated and prevented (Diler, 2007; Goldstein et al, 2017). BD severely affects the normal development and psychosocial functioning of the child and is associated with increased risk for suicide, psychosis and substance abuse, as well as for behavioral, academic, social, and legal problems (Diler et al, 2019).

Despite concerns about over-diagnosing BD, this disorder is still undiagnosed in many children.

BD-I is classified under mood disorders and characterized in its classic form by cyclic changes between mania and major depressive episodes. Other subtypes of BD include episodes of major depression with hypomania (BD-II), multiple episodes of hypomania with depressed mood but without clear episodes of major depression (cyclothymia), and subthreshold (i.e., shorter) episodes of mania or hypomania with or without depression (other specified bipolar and related disorders, BD-OS). There are subtle diagnostic differences between the International Classification for Diseases-11 (ICD-11) and the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), but in parallel with the majority of reports in youth, unless otherwise specified, the DSM criteria will be used in this chapter (APA, 2000; 2013). For the purposes of this chapter the word “youth” denotes children and adolescents. The aim of this chapter is to review the diagnosis and subtypes, epidemiology, age of onset and course, etiology and risk factors, clinical presentation, differential diagnosis, and treatment of BD in children and adolescents.

DIAGNOSIS AND SUBTYPES

It is important to use a common language between professionals (and with patients and families) when describing, reporting, and monitoring mood changes in youth. DSM-5 defines several subtypes of BD:

- Bipolar-I (BD-I)
- Bipolar-II (BD-II)
- Cyclothymic disorder
- Otherwise specified/unspecified bipolar and related disorder (BD-OS)
- Medication/substance induced BD, and
- BD due to another medical condition.

Except for cyclothymia, the diagnostic criteria are the same for adults and children (APA, 2013). DSM-5 introduced some changes to BD, classified under the heading of “bipolar and related disorders” (APA, 2013):

- In order to enhance the accuracy and facilitate earlier detection in clinical settings, the primary criteria for manic and hypomanic episodes now include an emphasis on the presence of *changes in activity and energy*, not just mood. In other words, in DSM-5, a manic episode diagnosis cannot be made without a change in activity or energy level, in addition to elated/irritable mood.
- The “mixed episode” diagnosis of DSM-IV was eliminated and a new specifier (“with mixed features”) has been added that can be applied to episodes of mania or hypomania when depressive features (e.g., three

or more depressive symptoms) are present. It can also be applied to episodes of depression when features of mania/hypomania are also present. In contrast, ICD-11 keeps the “mixed episode” diagnosis and defines it as “either a mixture or very rapid alternation between prominent manic and depressive symptoms *on most days during a period of at least 2 weeks*” (WHO, 2018).

- A new specifier for “anxious distress” is now defined in DSM-5 to identify patients with anxiety symptoms during the mood episode that are not part of the bipolar and other anxiety disorders diagnostic criteria.
- Instead of the “BD-not otherwise specified” (BD-NOS) diagnosis in DSM-IV, “other specified” and “unspecified” bipolar and related disorders categories were introduced in DSM-5 for patients that present with mania/hypomania but who do not meet full BD-I or BD-II criteria. “Other specified” is used when the reason for not meeting the full BD-I/II criteria can be explained (e.g., not meeting the duration criteria—less than 7 days), and “unspecified” is used when no explanation is provided (e.g., in the emergency room setting when limited information can be gathered). Similar to DSM-5, ICD-11 included “other specified and unspecified” bipolar or related disorder categories (WHO, 2018).

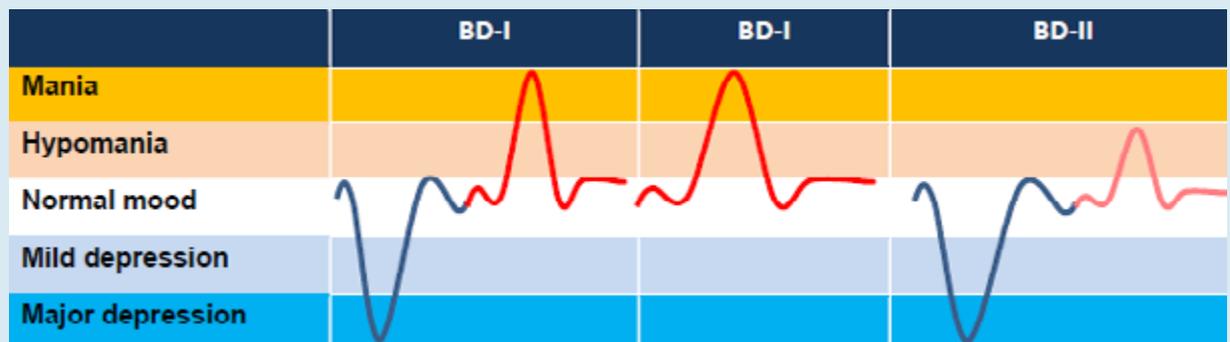
Bipolar Disorder I

- BD-I requires the presence or history of an episode of mania with or without a major depressive episode.
- To make a BD-I diagnosis both, *symptom criteria*—elation plus 3, or irritability plus 4 manic symptoms, one of which should be increased activity/energy level—and *duration criteria*, should be met in addition to “significant functional impairment or psychosis” during mania. To meet the duration criteria, mania should last at least 7 consecutive days or require an inpatient admission anytime during the episode.
- In DSM-5, a manic episode is described as a *distinct period* of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy level *lasting at least 7 consecutive days* and present most of the day, nearly every day. Other symptoms of mania are:
 - Inflated self-esteem or grandiosity
 - Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
 - More talkative than usual or pressure to keep talking
 - Flight of ideas or subjective experience that thoughts are racing
 - Distractibility (e.g., attention too easily drawn to unimportant or irrelevant external stimuli), as reported or observed
 - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
 - Excessive involvement in activities that have a high potential for

BD in young people is an episodic illness with subsyndromal and syndromal episodes mainly with depressive and mixed symptoms and rapid mood changes.



[Click on the picture to access the transcripts of an interview with David Axelson MD about issues related to the rate of BD diagnosis in youth.](#)

Figure E.2.1 Mood episodes in bipolar disorder-I and bipolar disorder-II

BD: bipolar disorder

painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

- In ICD-11, a manic episode is described as an *extreme mood state lasting at least one week* unless shortened by a treatment intervention, characterized by euphoria, irritability, or expansiveness, and by increased activity or a subjective experience of increased energy, accompanied by other characteristic symptoms such as rapid or pressured speech, flight of ideas, increased self-esteem or grandiosity, decreased need for sleep, distractibility, impulsive or reckless behavior, and rapid changes among different mood states (i.e., mood lability) (WHO, 2018).

Bipolar Disorder II

- BD-II is characterized in DSM-5 by *at least one major depressive episode and at least one hypomanic episode* (hypomania should last *at least 4 consecutive days*).
- In ICD-11, the *4-day duration criterium is not specified*; instead, a hypomanic episode is described as a persistent mood state characterized by euphoria, irritability, or expansiveness, and excessive psychomotor activation or increased energy, accompanied by other characteristic symptoms such as grandiosity, decreased need for sleep, pressured speech, flight of ideas, distractibility, and impulsive or reckless behavior lasting *several days* (WHO, 2018).
- Both DSM-5 and ICD-11 agree that hypomanic symptoms represent a change from the individual's typical behavior but are not severe enough to cause marked impairment in functioning.

Cyclothymic Disorder

Is characterized by numerous hypomanic episodes together with numerous periods of depressive mood or loss of interest or pleasure that do not meet all the criteria for BD or for a major depressive episode lasting at least one year—versus 2 years in adults (Van Meter et al, 2013).

Hypomania

Hypomania is a milder form of a manic episode. The patient should have distinct change from baseline functioning but not have marked functional impairment. Sometimes patients actually like being hypomanic because they are able to do more things such as working on more projects.

[Click here to view a summary of DSM diagnoses of BD based on the type of mood episode.](#)

Bipolar Disorder Otherwise Specified (BD-OS)

BD-OS is used when there are features of hypomanic or mixed episodes that do not meet diagnostic criteria for any of the more specific BD subtypes. Because criteria for BD-OS are vague, researchers have developed clearer definitions to identify other specified BD diagnosis, for example, at least 2-day long history of hypomania or at least 4 shorter (≥ 4 hours each) episodes of hypomania (one less symptom to meet the symptom criteria) (Axelson et al, 2011b).

BD-OS in youth is not a mild or “soft” BD phenotype with less impairment but may developmentally exist on a continuum with BD-I (Axelson et al, 2011b).

EPIDEMIOLOGY

The prevalence of BD-I and BD spectrum disorders in adults is around 1-2% and 3-6%, respectively, and the majority of them had the onset before the age of 20 years (Carlson & Paraki, 2016; Perlis et al, 2009). In clinical populations the prevalence of BD in youth in the US has been reported between 0.6% and 15% depending on the setting, the referral source, and the methodology to ascertain BD. Some studies, especially those in the US, have shown dramatic increases in recognition and rates of BD in youth over the past 20 years and some authors have raised the possibility of over diagnosis, whereas others highlight the possibility of neglecting the existence of this condition in childhood (Diler et al, 2019).

A meta-analysis about epidemiology of BD in youth around the world reported that the overall rate was 1.8% (95% CI, 1.1%–3.0%). The study, which included 16,222 youth between the ages of 7 and 21 years from 1985 to 2007 (Van Meter et al, 2011), suggests that:

- Prevalence of BD-I in youth is consistent with the current prevalence estimates of BD in adults
- The prevalence of BD-I in youth was not different in the US relative to other countries (e.g., the Netherlands, UK, Spain, Mexico, Ireland, and New Zealand), and
- Despite BD being diagnosed more commonly in clinical settings, the prevalence of BD in youth in the community is not increasing (Van Meter et al, 2011).

Studies suggest that it takes on average 10 years to identify and begin treatment of BD, indicating the need for timely detection and treatment of this serious illness.

Gender and Age Differences in Prevalence

Similar to adults, studies in clinical populations suggest that rates of bipolar spectrum disorders in youth are equally common in males and females (Axelson et al, 2006; Diler et al, 2019). However, BD-II and adolescent-onset BD are more prevalent in females (Birmaher et al, 2009b). A large epidemiological study in the US reported slightly higher rates of BD-I and -II in female than in male adolescents (3.3% versus 2.6%, respectively) with increasing rates of BD with older ages (Merikangas et al, 2010). The meta-analysis of international BD studies concluded that BD can have its onset in childhood, but prevalence was much higher during adolescence (Van Meter et al, 2011).

Burden of Illness

The WHO indicates that BD is the 6th leading cause of disability in the world. BD in youth is increasingly recognized as a significant public health

There was no significant difference in the mean rates of BD in youth between US and non-US studies, but US studies had a wider range of rates, especially when a broader definition of BD was used (Van Meter et al, 2011).

problem often associated with impaired family and peer relationships, poor academic performance, high rates of chronic mood symptoms, psychosis, disruptive behavior disorders, anxiety disorders, substance use disorders, medical problems (e.g., obesity, thyroid problems, diabetes), hospitalizations, and suicide attempts and completions (Diler, 2007; Diler et al, 2019). Moreover, youth with BD have higher behavioral health costs and greater utilization of medical services compared with youth with unipolar depression or non-mood disorders. Patients with undiagnosed BD may also have higher behavioral health costs than those with diagnosed BD. Given the high rates of morbidity and mortality and the chronic course of the condition, early diagnosis and treatment is critical (Birmaher & Axelson, 2005; Carlson & Pataki, 2016; Diler, 2007).

AGE OF ONSET AND COURSE

Retrospective studies in adults with BD have reported that 10%–20% had the onset before 10 years of age and up to 60% before the age of 20 (Diler, 2007; Kozloff et al, 2010; Perlis et al, 2009). BD in adults is frequently preceded by childhood disruptive behavior disorders and anxiety disorder. Early onset BD is associated with a more severe course of the illness and poor outcome. Children with pre-pubertal-onset of BD are reported as approximately 2 times less likely to recover than those with post-pubertal-onset. In addition, individuals with pre-pubertal-onset had more chronic symptoms, spent more follow-up time with subsyndromal mood symptoms, and had more polarity changes per year than those with post-pubertal-onset (Birmaher et al, 2009a; 2014; Carlson & Pataki, 2016; Diler, 2007; Holtzman et al, 2015).

Youth with BD show a continuum of symptom severity from subsyndromal to full syndromal with frequent mood fluctuations. Earlier studies in youth suggested high rates of chronicity of manic presentations, such as a 14% recovery after 6 months (Geller et al, 2000), and high rates of rapid cycling (50%) with almost no inter-episode recovery (Findling et al, 2001).

Naturalistic and follow-up studies have reported that 70% to 100% of youth with BD will eventually recover (e.g., show no significant symptoms for 2 months) from their index episode. However, up to 80% will experience recurrences (e.g., one or more recurrences in 2-5 years) despite ongoing treatment. In addition, analogous to findings for adults, the prospective course in these youths is characterized by mood fluctuations of varying intensities throughout 60% to 80% of the follow-up time, particularly depressive and mixed symptoms, and have frequent shifts in symptom polarity. During adolescence, there is a drastic increment in the rates of suicidal ideation and attempts and substance abuse. In addition, youth with BD show high rates of legal, social, familial, and academic problems (Birmaher et al, 2009a; 2014; Diler, 2007; Diler et al, 2019). A recent study evaluated more individualized course during a 9-year period identified four longitudinal mood trajectories:

- “Predominantly euthymic” course (24%)
- “Moderately euthymic” course (35%)
- “Ill with improving course” (19%), and
- “Predominantly ill” course (22%) (Birmaher et al, 2014).

Early identification of BD in youth is the key not only for mood stabilization but also to enable the child to follow a normative developmental path and prevent an unrecoverable loss in the child’s psychosocial development and education (Birmaher & Axelson, 2005).



[Click on the image to watch Dr. Birmaher talk about “What Happens Over Time with Youth Who Have Been Diagnosed With Bipolar Spectrum Disorders” \(36:06\)](#)

Early age of onset, long duration, low socioeconomic status, mixed or rapid cycling episodes, psychosis, subsyndromal mood symptoms, comorbid disorders, exposure to negative life events, high expressed-emotion, and family psychopathology are associated with worse course and outcome (Birmaher et al, 2009a; Diler, 2007).

Within each group, on average youths were euthymic 84%, 47%, 43%, and 12% of the follow-up time respectively. Better course was associated with older age at onset of mood symptoms, less lifetime family history of BD and substance abuse, and less history at baseline of severe depression, manic symptoms, suicidality, subsyndromal mood episodes, and sexual abuse (Birmaher et al, 2014). Interestingly, the fact that a subgroup of BD youths has a mainly euthymic course questions whether these subgroup needs lifetime treatment.

Individuals with BD and attention-deficit hyperactivity disorder showed functional recovery in 4 years in only 20% of cases (Biederman et al, 2004). However, it is now agreed that BD in youth is not characterized by ultra-rapid cycling or chronic mania but manifested by recurrent mood episodes—albeit more frequent than in adults with BD (Birmaher et al, 2009a).

ETIOLOGY AND RISK FACTORS

The single best predictor of BD in youth is family history. Twin and family studies have demonstrated that BD is a highly inherited illness with concordance between identical twins of about 70%; that is, 2-3 times that for non-identical twins. Current studies indicate that multiple genes are likely to be responsible for BD but so far, they have not been identified. Interested professionals may read Schulze's review (Schulze, 2010) or click [here](#) for a list of potential susceptibility genes (Ikeda et al, 2018).

Subthreshold manic or hypomanic episodes were a risk factor for the development of manic, mixed, or hypomanic episodes in the offspring of parents with BD (Axelson et al, 2015). Further longitudinal prospective analyses suggest that offspring of BD parents with mood lability, depression/anxiety, subsyndromal manic symptoms, and early-onset parental BD were at 50% risk to develop BD (Hafeman et al, 2016).

The above studies inform us about the risk factors for developing BD in offspring of parents with BD for the group as a whole. However, they do not tell us about the risk of developing BD for an individual child. To do this, a risk calculator has been developed recently (Hafeman et al, 2017b). If the calculator is externally validated it may become a useful tool for clinical practice and research.

Despite BD being an inherited illness, there are other biological, social or emotional variables which can either precipitate BD or serve as protective factors in people genetically predisposed (Bootsman et al, 2016; Diler et al, 2019; Pan et al, 2017). Research and clinical experience also suggest that trauma or stressful life events can trigger an episode of BD; however, many episodes occur without an obvious or identifiable cause. In brief, the etiology is multifactorial with complex interaction of biological vulnerabilities and environmental influences.

Recent advances in neuroimaging, such as magnetic resonance imaging (MRI) and functional MRI (fMRI), indicate that neural circuits involved in emotion processing and regulation in BD youth are different from healthy peers (Diler et al, 2013; 2014; Hafeman et al, 2017a; Singh et al, 2012). The reduced volume of the amygdala in adolescents with BD is one of the most consistent neuroimaging findings (Pfeifer et al, 2008). Neuroimaging findings in BD youth need to be taken with caution because of small samples and other confounding

“One of the overall goals of neuroimaging is to understand what differentiates children who are at risk for BD from other children. The ultimate goal is to identify neurobiological markers (physical differences in the chemistry and structure of the brain) for BD so that we can more effectively treat those who are at risk for developing it” (DelBello, 2012). Click on the picture below to watch Dr Leibenluft's talk about how brain imaging data is being combined with genetic research to understand BD and brain function (5:00)



factors such as subjects' different mood phases (e.g., depressed, hypomanic, euthymic) and the presence of comorbid disorders and medications.

BD youth display deficits in neurocognitive domains of attentional set-shifting, visuospatial memory, working memory, cognitive flexibility, and executive functions (Dickstein et al, 2016; Doyle et al, 2005; Pavuluri et al, 2006b). Neurocognitive deficits also differentiated BD from unipolar depressed youth (Murphy et al, 1999). Improvement of acute mood episode may accompany improvement in neurocognitive functioning (e.g., verbal and working memory); however, studies suggest that neurocognitive deficits may be independent of the child's mood state, can exist even when there are no signs of mania or depression, and may have long-term implications for reduced functional ability (Frias et al, 2017; Pavuluri et al, 2009).

COMORBIDITY

Comorbid disorders, particularly disruptive behavior disorders, attention deficit hyperactivity disorder, and anxiety disorders are very common. Presence of comorbid conditions adversely affect the clinical course of BD (Sala et al, 2014; Yen et al, 2016). The prevalence of comorbid disorders depends on the methods utilized for ascertainment and the sample studied (e.g., more common in clinical versus community, and in children versus adolescents—with more ADHD and oppositional defiant disorder in the former and more conduct and substance use disorders among the latter).

Presence of multiple comorbid conditions is very common in youth with BD and they adversely affect the course of the illness

CLINICAL PRESENTATIONS

The practice parameters for BD of the American Academy of Child and Adolescent Psychiatry recommends that clinicians should adhere to the DSM, including duration criteria (McClellan et al, 2007). There is consensus that children and adolescents can fulfill DSM criteria for BD-I and II. However, in fact, the majority of youth are diagnosed in the US with “other specified BD” because they do not meet the duration requirements for BD-I or II (Axelson et al, 2011b).

Although the presentation of BD is heterogenous, the most common symptoms across subtypes are increased energy, irritability, mood lability, distractibility, and increased goal directed activity (all approximately in 75% of cases); hallucinations and delusions are the least frequent (about 26% of cases) (Van Meter et al, 2016). Grandiosity and hypersexuality are the most specific symptoms but are not as common (57% and 32%, respectively).

Depression is usually the first mood episode observed in many youth with BD; however, a diagnosis of BD cannot be made before a history or presence of mania/hypomania. Careful assessment of current and past symptoms of mania/hypomania is necessary for all youth, especially in those who present with depression.

It is very important to evaluate whether mood and symptoms are abnormal, clearly different from the youth's usual mood and behavior, above and beyond the young person's developmental level, the context where the symptoms occur, and the extent to which the symptoms affect functioning.

Episodicity

Despite suggestions by some investigators that episodicity—*distinct periods* of abnormal mood and accompanying symptoms—is not needed to diagnose pediatric BD, most investigators, clinicians, and the AACAP guidelines recommend that episodicity be required for diagnosis (Leibenluft et al, 2003; McClellan et

al, 2007). In fact, it is suggested to focus on determining the presence of mood episodes first and then ascertain the extent to which manic/hypomanic symptoms are present during an identifiable time frame.

Irritability

“There now is substantial consensus that chronic irritability, regardless of explosiveness or severity, is not sufficient for a diagnosis of BD, in contrast with formulations that focused on rages or severe aggression. However, irritability is commonly present in youth with BD. Counting irritability as part of the diagnostic criteria for a manic or hypomanic episode requires that the irritability either begins or significantly increases in intensity *in conjunction with* the presence of accompanying manic symptoms.” (Goldstein et al, 2017).

It is important to remember that irritability is part of the diagnostic criteria for many other disorders such as oppositional defiant, major depressive, generalized anxiety, and post-traumatic stress disorders and is frequently present in youth with other psychiatric diagnoses such as ADHD and pervasive developmental disorders. Therefore, irritability has low specificity for BD; it can be considered as an analogous to fever or pain in physical illness, which suggests that “something is wrong” (Kowatch et al, 2005). On the other hand, the absence of episodes of irritability may decrease the likelihood of BD.

In contrast to episodic irritability, the chronic presence of this symptom has been recently conceptualized as the core feature of a new condition: “disruptive mood dysregulation disorder,” also known as temper dysregulation disorder with dysphoria and severe mood dysregulation (see [Chapter E.3](#) of the e-Textbook) .

Subthreshold Presentations

Subthreshold or subsyndromal presentations are those in which the young person appears to show significant manic symptomatology but do not meet the criteria for BP-I or BP-II disorders, for example the duration requirements. Follow-up studies (e.g., Birmaher et al, 2009a; DelBello et al, 2007) have shown that the most common presentation of BD is subsyndromal, particularly with mixed and depressive symptomatology. For example, the COBY study showed that during 60% of the 4-years of follow-up, children and adolescents with BD experienced mood symptoms and 40% of the time were subsyndromal (Birmaher et al, 2009a). Furthermore, subsyndromal symptoms were accompanied by significant psychosocial difficulties and increased the risk of suicidality, legal problems, and substance abuse. In addition, about 50% of youth with the COBY definition of “other specified BD” converted into BD-I or II later on, especially if they had family history of mania or hypomania (Axelson et al, 2011b). The above findings indicate the need for early recognition and treatment of subsyndromal symptomatology. Based on the COBY study data allowed to build and validate a risk calculator which predicted the 5-year risk of conversion from subthreshold mania to BD-I/II with 71% discrimination (Birmaher et al, 2018).

Bipolar Depression

Similar to in adults, depressive episodes are the most common manifestation of BD in children and adolescents—both in frequency and duration

Chronic irritability was associated with ADHD, oppositional defiant disorder, and major depressive disorder rather than BD. Episodic irritability was associated with increased risk to develop BD and anxiety (Leibenluft et al, 2006)

[Click here](#) to view an expert panel discussion including Gabrielle Carlson (US), Samuele Cortese (UK), Robert Findling (US), Benjamin Goldstein (Canada), Carmen Moreno (Spain), Andrea Cipriani (UK), and Michael Ostacher (US) about the diagnosis and irritability in youth with BD (58:55)

About 50% of the youth with BD-NOS, particularly those with a family history of mania or hypomania, converted into BD-I or II during follow up (Axelson et al, 2011b).

(Birmaher et al, 2009a). The COBY study reported that during naturalistic follow-up most recurrences after the index episode were major depressive episodes (60%), followed by hypomanic (21%), manic (15%), and mixed (5%) across all subtypes (Birmaher et al, 2009a). However, depression is commonly underdiagnosed. Bipolar depression tends to be more severe, has more mixed manic symptoms and self-harm behaviors (Diler et al, 2017a), higher comorbidity with oppositional defiant disorder, conduct disorder and anxiety disorders (Uchida et al, 2015), and increased risk for psychosocial impairment and suicide than unipolar depression (Wozniak et al, 2004). Careful monitoring of developmental progression of mood symptoms is critical because:

- Many adolescents experience depression first, before the emergence of mania
- The presence of subsyndromal manic symptoms during depression significantly increases the risk for progression to a manic episode (Diler et al, 2017b), and
- If the manic symptoms are ignored, the course of the illness is likely to be recurrent with progressively more severe and refractory episodes of both mania and depression (Geller & Luby, 1997).

Preschool and Preadolescence Presentations

It is reported that mood lability (e.g., rapid mood variation with several mood states within a brief period of time, which appears internally driven without regard to the circumstances) and irritability/anger, are more characteristic of childhood-onset rather than adolescent-onset mania. Adolescents with BD, relative to children with BD, have more adult-like manic symptomatology (e.g., more typical and severe manic and depressive symptomatology) (Birmaher et al, 2009c).

Given the emotional and cognitive developmental stage of preschool children (aged from 3 to 7 years), questions have been raised regarding the validity of manic symptoms such as grandiosity and elation at this age. In parallel, the AACAP guidelines suggest that clinicians *should be cautious* when making BD diagnoses in children younger than 6 (McClellan et al, 2007). Few studies suggest that preschool children may suffer from BD.

DIFFERENTIAL DIAGNOSIS

It is important for clinicians to have a working knowledge of normative cognitive, behavioral, and affective development and cultural norms so that they can determine whether certain behavior is normative or pathological at the child's stage of development. It is difficult to diagnose BD in youth given the variability in the clinical presentation, high comorbidity, overlap of symptoms with other psychiatric disorders, effects of development on symptom expression, children's difficulties in verbalizing their emotions, and the potential effects of medications. Presence of past and current mania/hypomania should be a part of every child psychiatric assessment (please see Tables 1 and 2). Clinicians must be cautious about attributing symptoms to mania or hypomania unless they show a clear temporal association with the abnormally elevated, expansive and/or irritable

In comparison with adolescent-onset BD, childhood-onset BD manifest itself with more subsyndromal presentations, rapid mood changes and not well defined grandiose ideation. Also, children with BD have a higher familial loading for mood disorders and a different pattern of comorbid disorders than adolescent-onset BD. In contrast, adolescent-onset BD is associated with more severe and more "classic" (e.g., adult-like) mood symptomatology (Birmaher et al, 2009c).

Clinicians should carefully observe whether the symptoms of the comorbid disorder disappear or persist while children with BD are euthymic and whether symptoms associated with BD worsen during the mood episode.

mood. For example, substance use can complicate the clinical picture of BD, but the essential feature of a drug-induced mood disorder is the onset of symptoms in the context of drug use, intoxication, or withdrawal. Both substance use and BD can co-exist (e.g., dual diagnosis). However, mood symptoms that start before or persist longer than a month after cessation of drug use can be considered as the primary disorder (APA, 2013). Furthermore, chronic symptoms such as hyperactivity or distractibility should not be considered evidence of mania unless they clearly intensify with the onset of abnormal mood. Prolonged presentations of non-specific manic-like symptoms that do not change in overall intensity should raise the possibility of an alternative psychiatric diagnosis (Birmaher & Axelson, 2005; Diler et al, 2019).

The presence of psychotic symptoms calls for differential diagnoses with other psychiatric disorders such as schizophrenia. In that case onset is usually insidious and the patient lacks the engaging quality of mania. The following

Table E.2.1 Bipolar disorder versus disruptive behavior disorder

- If the behavior problems only occur while the child is in the midst of an episode of mania or depression, and the behavior problems disappear when the mood symptoms improve, the diagnoses of oppositional or conduct disorder should not be made.
- If a child has “off and on” oppositional or conduct symptoms or these symptoms only appear when the child has mood problems, the diagnosis of BD (or other disorders such as recurrent unipolar depression or substance abuse) should be considered.
- If the child had oppositional behaviors before the onset of the mood disorders, both diagnoses may be given.
- If a child has severe behavior problems that are not responding to treatment, consider the possibility of a mood disorder (bipolar and non-bipolar depressions), other psychiatric disorder (e.g., ADHD, substance abuse), and/or exposure to stressors.
- If a child has behavior problems and a family history of bipolar, consider the possibility that the child has a mood disorder (unipolar major depression or BD disorder).
- If a child has behavior problems and is having hallucinations and delusions consider the possibility of BD disorder. Also consider the possibility of schizophrenia, use of illicit drugs/alcohol, or medical/neurological conditions.

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Table E.2.2 Bipolar disorder versus attention deficit hyperactive disorder (ADHD)

Suspect the presence of bipolar disorder in a child with ADHD if:

- The “ADHD” symptoms appeared later in life (e.g., at age 10 years old or older)
- The symptoms of “ADHD” appeared abruptly in an otherwise healthy child
- The ADHD symptoms were responding to stimulants and now are not
- The “ADHD” symptoms come and go and tend to occur with mood changes
- A child with ADHD:
 - Begins to have periods of exaggerated elation, grandiosity, depression, no need for sleep, inappropriate sexual behaviors
 - Has recurrent severe mood swings, temper outbursts, or rages
 - Has hallucinations and/or delusions
 - Has a strong family history of BD in his or her family, particularly if the child is not responding to appropriate ADHD treatments.

Birmaher B. *New Hope for Children and Adolescents with Bipolar Disorders*. New York: ©Three Rivers Press, 2004, reproduced with permission.

characteristics would favor a BD diagnosis: good affective contact, transient rather than persistent speech incoherence and poverty of content, good response to mood stabilizers, and family history of BD. However, the first episode of mania can present with severe thought disorder and hallucinations making the differential diagnosis between schizophrenia and BD difficult. In these cases a careful and ongoing follow-up helps to clarify the diagnosis (Diler, 2007; Diler et al, 2019).

ASSESSMENT

Psychiatric Interviews

It is necessary to evaluate the *frequency, intensity, number, and duration* (FIND) when assessing mood episodes. The most widely used interviews in BD studies are the Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children—Present and Lifetime version (K-SADS-PL) (available for free at <https://www.pediatricbipolar.pitt.edu/resources/instruments>) and the Washington University KSADS (WASH-U-KSADS). However, these interviews are lengthy and time-consuming, are mainly used for research purposes, and require training of the interviewer. Thus, symptom checklists for BD and depressive disorders based on the DSM criteria are also useful (please see the “Child and Adolescent Bipolar Spectrum Assessment Report” in the appendix).

Clinician-Based Rating Scales

Two clinician-based rating scales are currently used for the assessment of manic symptoms and their severity in youth, the *Young Mania Rating Scale* (YMRS;) (Young et al, 1978) and the *KSADS Mania Rating Scale* (KSADS-MRS) (available online at the above link for the K-SADS). A recent study found that the YMRS is not a valid measure for BD in youth (Youngstrom et al, 2015).

Youth, Parent, and Teacher Rating Scales

Parental reports appear to be more accurate in identifying mania than youth or teacher reports (Youngstrom et al, 2015). The *General Behavior Inventory* (GBI) (Youngstrom et al, 2008), the parent version of the YMRS (P-YMRS), the parent version of the *Mood Disorder Questionnaire* (MDQ) (Wagner et al, 2006a), and more recently the *Child Mania Rating Scale, Parent Version* (CMRS-P) (Pavuluri et al, 2006a) have been shown to have appropriate psychometric properties and can be useful to screen for BD symptoms in youth.

The Parent MDQ has the lowest reading level and most translations into other languages but is no longer in the public domain (the self-rating version for adolescents is available [here](#)). The parent GBI-10 has the most research data, is sensitive to treatment effects, but has the highest reading level (it may be available from the author [Eric Youngstrom](#)). It has been suggested that the parent CMRS -10 (Henry et al, 2008) is the most specific instrument for screening of BD in youth and has a teacher version. A list of instruments and scales used in BD in youth can be found [here](#).

Other parent-reported instruments have been used to screen dimensional psychopathology in youth such as the *Child Behavior Checklist* (CBCL), but these instruments are not specific or useful for *ruling in* mania (Diler et al, 2009). On

the other hand, the CBCL or its subscales (e.g., sum of its aggression, attention, and anxiety/depression subscales—CBCL-dysregulation profile, formerly proposed as the “bipolar profile”) may reflect symptom severity, comorbidity, or functional impairment and low scores may be helpful in ruling out mania (or any psychopathology) (Diler et al, 2007; Youngstrom et al, 2005b).

Mood Timelines or Diaries

These instruments, which use school years, birthdays, and holidays as anchors, can help children, parents and clinicians to visually represent the course of their mood, identify events that may have triggered symptoms, and to examine the relationship between treatment and response. Many of these instruments use colors or ratings from 0-10 to chart daily changes in mood along with significant stressors, illnesses, and treatments. We include in the appendix an example of these tools (the [Mood & Energy Thermometer](#)) developed at the inpatient child and adolescent bipolar services at the University of Pittsburgh. Readers can also click [here](#) to access other instruments for mood charting. Mobile devices are also increasingly used to monitor youth’s self-report sleep and mood changes.

Other Areas

Psychosocial Functioning

It is imperative to obtain information from multiple informants to accurately assess changes in functioning, which should be measured against what would be the expected level of functioning for a child given their culture, age and intellectual capabilities.

Level of Care

Clinicians should also evaluate the appropriate intensity and setting of care (e.g., outpatient versus inpatient or partial hospitalization). The level of care will depend on factors such as the severity of mood symptoms, the presence of suicidal, homicidal symptoms, and risk for lethality, psychosis, substance dependence, agitation, child’s (and parents’) adherence to treatment, parental psychopathology, and family environment.

Medical Conditions

The presence of medical conditions that may trigger or worsen mood symptoms should be assessed. No biological or imaging tests exist for the diagnosis of BD. However, thyroid functioning (e.g., TSH) and whole blood count, B12, folate, iron levels can be obtained when a first mood episode of BD is identified (see below additional lab tests that may be necessary before or during medication treatment). A more detailed organic work-up may be required if a first episode psychosis is considered in differential diagnosis (see [Chapter H.5](#) of the e-Textbook).

TREATMENT

The treatment of BD has three stages: acute, continuation, and maintenance. The goal of the acute phase is to control or ameliorate the acute symptoms that are affecting the child’s psychosocial functioning and well-being or endangering the

Mood time lines (mood monitoring) instruments should be user (child) friendly and can be modified (according to the child’s age, culture and interests) to increase compliance.

Team approach

Psychiatrists, psychologists, behavioral and developmental pediatricians, social workers, school counselors and teachers, and many other professionals who are involved in treating the child should work together as a team so optimal care can be attained in the medical, educational, family, and social domains. It is very important to consider the parents, the child, and the school as a part of this team and include them in decision making.

child's life. Continuation treatment is required to consolidate the response during the acute phase and avoid relapses. The main goal of the maintenance phase is to avoid new episodes or recurrences. The choice of pharmacological, psychosocial, or combined (pharmacological and psychosocial) treatment for each of these stages depends on the severity, phase of illness, subtype of BD, chronicity, comorbid disorders, child's age, family and patient preference and expectations, availability of experts in psychotherapy, family and environmental circumstances, and family psychopathology.

PSYCHOEDUCATION

Psychoeducation and support start in the assessment phase and are indicated in every phase of treatment. Family members and the patient should be informed about the causes, symptoms, course, and different treatments, and the risks associated with each treatment option as opposed to no treatment. The patient and family should be prepared for what is likely to be a recurrent and often chronic illness with frequent fluctuations in the child's mood, and the importance of good adherence to treatment. This will require a good deal of time. In addition, restoration of hope and reversal of demoralization for the child and parents and case management (e.g., negotiation with school and parents about reasonable expectations) may be necessary (Birmaher & Axelson, 2005; Diler et al, 2019).

Sleep hygiene and routine are important, especially because sleep deprivation leads to worsening of symptoms (please see Table E.2.3), thus ensuring a stable circadian rhythm is important.

Acute Treatment

The current evidence is derived from open-label, retrospective analyses, case reports, and RCTs that are summarized in more detail in [McClellan et al \(2007\)](#), and (Liu et al, 2011). There are very few studies targeting prepubertal children ([Geller et al, 2012](#)), bipolar depression, and the treatment of bipolar depression in the context of comorbid disorders such as anxiety and ADHD.

In order to avoid unnecessarily high dosages and increasing the risk of side effects and poor adherence to treatment, unless the child is too agitated, acutely suicidal, and/or psychotic, it is recommended to start with a low dose and increase dosage slowly, according to response and side effects. In general, and until further studies suggest otherwise, dose of anticonvulsants and SGAs, as well as target blood levels of lithium and some of the anticonvulsants, are similar to those in adults with BD. However, it is possible that children and adolescents may need higher lithium blood concentrations, close to 1 mEq/dl ([Geller et al, 2012](#)), because it seems that, relative to adults, children and adolescents have lower ratios of brain-to-serum lithium concentration (Birmaher & Axelson, 2005).

PHARMACOTHERAPY

Acute Manic/Mixed Episodes

The effectiveness of monotherapy with lithium, valproate, carbamazepine and second generation antipsychotics (risperidone, aripiprazole, quetiapine, olanzapine, asenapine, ziprasidone, and cariprazine) are broadly comparable in

A balanced daily schedule maintained through practical lifestyle habits, such as regular sleep patterns and consistent daily routines may improve BD symptoms while irregular sleep patterns may induce mood episodes.

To assist with psychoeducation, dedicated [associations](#) and several other websites and books are available including: Depression and Bipolar Support Alliance (DBSA) [Guide for BD](#), and against [stigma](#).

When planning treatment in each phase, it is very important to take into account [quality of life issues for youth](#) with BD that would consider:

- Cultural differences and expectations
- Meaningful relationships with family, peers, mentors, coaches, and teachers
- Optimal academic performance
- Optimal occupational performance as it pertains to endeavors such as music, art, dance, athletics
- Other personally rewarding areas from which the youth derives a sense of competency, mastery, and pleasure.

Table E.2.3 Sleep hygiene. Tips from the American Sleep Association.***Maintain a regular sleep routine***

- Go to bed at the same time. Wake up at the same time. Ideally, your schedule will remain the same (+/- 20 minutes) every night of the week.

Avoid naps if possible

- Naps decrease the “sleep debt” that is so necessary for easy sleep onset.
- Each of us needs a certain amount of sleep per 24-hour period. We need that amount, and we don’t need more than that.
- When we take naps, it decreases the amount of sleep that we need the next night – which may cause sleep fragmentation and difficulty initiating sleep, and may lead to insomnia.

Don’t stay in bed awake for more than 5-10 minutes.

- If you find your mind racing, or worrying about not being able to sleep during the middle of the night, get out of bed, and sit in a chair in the dark. Do your mind racing in the chair until you are sleepy, then return to bed. No TV or internet during these periods! That will just stimulate you more than desired.
- If this happens several times during the night, that is OK. Just maintain your regular wake time, and try to avoid naps.

Don’t watch TV or read in bed.

- When you watch TV or read in bed, you associate the bed with wakefulness.
- The bed is reserved for two things – sleep and hanky panky.

Do not drink caffeine

- The effects of caffeine may last for several hours after ingestion. Caffeine can fragment sleep, and cause difficulty initiating sleep. If you drink caffeine, use it only before noon.
- Remember that soda and tea contain caffeine as well.

Avoid inappropriate substances that interfere with sleep

- Cigarettes, alcohol, and over-the-counter medications may cause fragmented sleep.

Exercise regularly

- Exercise before 2 pm every day. Exercise promotes continuous sleep.
- Avoid rigorous exercise before bedtime. Rigorous exercise circulates endorphins into the body which may cause difficulty initiating sleep.

Have a quiet, comfortable bedroom

- Set your bedroom thermostat at a comfortable temperature. Generally, a little cooler is better than a little warmer.
- Turn off the TV and other extraneous noise that may disrupt sleep. Background “white noise” like a fan is OK.
- If your pets awaken you, keep them outside the bedroom.
- Your bedroom should be dark. Turn off bright lights.

If you are a “clock watcher” at night, hide the clock.***Have a comfortable pre-bedtime routine***

- A warm bath, shower
- Meditation, or quiet time

non-psychotic manic/mixed episodes (Findling & Ginsberg, 2014; Liu et al, 2011), although less so than in adults (Goldstein et al, 2017). Recent studies suggest that SGAs may be more efficacious than the traditional mood stabilizers (i.e, lithium and anticonvulsants) but it should be kept in mind that youth are extra-sensitive to the metabolic side effects of SGAs (Liu et al, 2011).

Interested readers may visit the US [clinical trials website](#) and search for ongoing studies of BD in youth.

Partial Responders and Non-Responders

In patients who do not respond to the initial monotherapy or who do not tolerate the medication, clinicians can try to:

- Stop mood *destabilizing* medication (e.g., antidepressants)
- Optimize the current treatment
- Switch to a different mood stabilizer, or
- Combine the monotherapy with other treatment options.

While it is ideal to use the lowest dose of medication possible to minimize side effects, some patients may require higher amounts. In addition, some researchers recommend short-term adjuvant medications during the acute phase of monotherapy. For example, lorazepam and clonazepam sometimes are temporarily used for the management of acute agitation or insomnia (Birmaher & Axelson, 2005), monitoring the possibility of behavioral disinhibition caused by these medications. Despite limited research supporting its efficacy, some youth with BD may benefit from melatonin. For combined medication treatment, it is suggested that using two mood stabilizers with different mechanism of action—such as lithium or an anticonvulsant—with a SGA may be more effective than monotherapy (Liu et al, 2011).

Hypomania

There are no studies in children and adolescents that specifically address the treatment of hypomania. Until research becomes available, for those youth whose hypomanic symptoms significantly impair their function, similar treatments to those described for mania are recommended.

Bipolar Depression

Youth with bipolar depression spend substantial amounts of time burdened by depressive symptoms or major depression that significantly impair their psychosocial functioning and increase the risk for suicide. However, there are few studies in youth with bipolar depression. The FDA has approved the combination of olanzapine and fluoxetine for bipolar depression in youth aged 10-17 years. In a RCT of monotherapy with lurasidone, depressive symptoms significantly decreased in children and adolescents with bipolar depression. Long-term treatment with lurasidone 20 mg/day was found effective in reducing depressive symptoms over one year and the FDA has approved lurasidone for 10-17 year-olds (DelBello et al, 2017). In contrast to findings in adults, a RCT reported that quetiapine XR was not superior to placebo in youth with BD-I/II (Findling et al, 2014b). In the absence of more research data for young people, treatment strategies can be extrapolated from evidence obtained in adults. This includes using lithium, lamotrigine, valproate, cariprazine, or a combination of anticonvulsant or an SGA

If a child does not respond to treatment at any stage, factors associated with non-response need to be considered, such as:

- Misdiagnosis
- Poor adherence to treatment
- Presence of comorbid psychiatric and medical conditions, and
- Ongoing exposure to negative events (family conflict, abuse, etc.).

with an antidepressant (Earley et al, 2019; Nivoli et al, 2011).

An open-label study with omega-3 fatty acids showed minimum to modest improvement in depression symptoms in bipolar youth with good tolerance (Wozniak et al, 2007). Light therapy may be considered for subjects with recurrent seasonal depression. Transcranial Magnetic Stimulation has also been suggested in a few small studies but needs to be further evaluated (Birmaher & Axelson, 2005; Goldstein et al, 2017).

Electroconvulsive therapy (ECT) may be useful for severely impaired adolescents with manic or depressive episodes of BD-I if other treatments are either not helpful or cannot be tolerated (McClellan et al, 2007).

Treatment of Comorbid Conditions

BD in youth usually presents with comorbid conditions that may worsen the prognosis. It is recommended to use the most effective medications and psychosocial treatments for each specific comorbid disorder and treatment for each comorbid disorder should begin sequentially. Sometimes medications for BD may also be effective for the other psychiatric disorder (Birmaher & Axelson, 2005; McClellan et al, 2007).

In general, before treating the comorbid disorder(s), it is recommended to first stabilize the symptoms of BD, especially if the child's comorbid symptoms (e.g., ADHD, behavior problems) appear to be secondary to the mood disorder (mania, depression, or both) (Birmaher & Axelson, 2005; Diler et al, 2019). If the comorbid conditions cannot be attributed to BD or do not improve after the symptoms of mania/hypomania subside, treatment for both the BD and the comorbid conditions is indicated, especially if they have comorbid substance use. If available, psychosocial treatments should be tried before adding new medications.

Amphetamine and methylphenidate preparations and atomoxetine are treatment options for ADHD. For comorbid anxiety disorders, cognitive-behavioral therapy can be tried first. Because selective-serotonin reuptake inhibitors (SSRIs) are effective in treating anxiety disorders, for those with severe anxiety who did not respond to therapy, SSRIs can be tried with caution in combination with a mood stabilizer.

Monitoring Pharmacotherapy and Clinical Concerns

Because all psychotropic drugs can cause important adverse effects, a careful risk-benefit analysis is needed (and should be discussed with the parents and youth) when initiating pharmacologic treatment. Click [here](#) to access the US FDA website to review updated information about the safety of psychotropic medications.

The list of prescription drugs that interact with psychotropic medications is long and should be checked prior to prescribing any new medication. There are [several websites](#) and smart phone applications (e.g., Micromedex Drug Information by Thomson Reuters or Medscape) that provide updated information on drug interactions.

A *pregnancy test* should be performed in all post-menarche females at baseline and whenever sexual activity is a possibility during follow-up (many of the medications for BD are teratogenic). Urine drug screen may be ordered

in adolescents at baseline and then as necessary. Height and weight (e.g., body mass index—BMI), vital signs, and waist circumference should be recorded at each visit. Keep in mind that laboratory tests are not a replacement for clinical evaluation (e.g., physical exam, family history of cardiac, diabetes, and thyroid diseases) and it is important to review signs and symptoms of potential adverse events with patients and their families as well as emphasize the need to contact the prescribing physician if symptoms occur (e.g., rash with lamotrigine and other anticonvulsants).

Tables E.2.4 and E.2.5 summarize common side effects from mood stabilizers and gives general monitoring guidelines based on recommendations from FDA package inserts and typical practice from our BD clinic and research center.

Lithium

The target serum level of lithium in acute treatment is 0.8 to 1.2mEq/L, to be reduced to 0.6 to 0.8mEq/L once euthymia has been achieved. Lithium has a narrow therapeutic window (blood levels between 0.6 and 1.2 mEq/L) and severe lithium toxicity can cause permanent renal and neurological damage or even death. Dose should be titrated for each individual because tolerability varies among patients and some individuals will be symptomatic at lower blood levels, although initial symptoms of toxicity usually do not manifest until blood levels are above 1.5 mEq/L.

Patient and parents should be informed about symptoms associated with lithium toxicity (e.g., dizziness, clumsiness, unsteady gait, slurred speech, coarse tremors, abdominal pain, vomiting, sedation, confusion and blurry vision, behaving like a drunk person). If a patient has difficulty taking fluids or having excessive fluid loss (e.g. nausea, vomiting, diarrhea, febrile illness), lithium dose should be reduced or temporarily held until regular fluid intake is resumed. If other symptoms of lithium toxicity occur in addition to gastrointestinal distress, referral for immediate evaluation is necessary (Birmaher & Axelson, 2005; Diler et al, 2019). Blood levels should be obtained as early as 5-7 days after each dose increase, and immediately if clinical symptoms of toxicity occur. In addition, other baseline laboratory tests such as those for thyroid and kidney functioning are necessary at baseline and during follow up (please see Tables E.2.4 and E.2.5). Patients should be counseled to maintain adequate hydration during vigorous exercise or on hot days, and avoid major changes in salt, caffeine or fluid intake. In addition, they must notify physicians and pharmacists that they are taking lithium, and not to take substances that interact with lithium. Common non-prescription drugs and substances that can elevate lithium levels include most non-steroidal anti-inflammatory drugs (acetaminophen does not), alcohol and marijuana. Caffeine tends to lower lithium levels (Birmaher & Axelson, 2005).

Anticonvulsant Mood Stabilizers

These medications have neurological, cognitive, and gastrointestinal side effects that can usually be managed by dose adjustments. Dose increases should be gradual and periodic blood tests are suggested (see Table E.2.5) to monitor the blood level of many of them and for rare but serious side effects (e.g., hepatic failure, pancreatitis, thrombocytopenia). It is very important that patients and

It is very important to pay a close attention to patients' own description of what the important side effects are and what the side effects mean to them. For example, a patient may become noncompliant with lithium (without telling the doctor), because of weight gain, acne or tremor.



Click on the picture to visit the US FDA website to view updated information about the safety of psychotropic medications.

Table E.2.4 Side effects of mood stabilizers and routine laboratory monitoring before and during pharmacotherapy (Birmaher & Axelson, 2005).

	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Lithium	<ul style="list-style-type: none"> • Polyuria • Polydipsia • Tremor • Weight gain • Nausea • Diarrhea • Hypothyroidism • Cognitive dulling • Sedation, • Leukocytosis 	<ul style="list-style-type: none"> • New onset or exacerbation of acne or psoriasis • Bradycardia • Hair loss • ECG changes (T-wave flattening) 	<ul style="list-style-type: none"> • Kidney, brain damage and death (due to acute toxicity) • Decreased renal function • Pseudotumor cerebri • Extrapyramidal symptoms • Movement abnormalities • Nystagmus • Seizures • Hyperparathyroidism • Sinus node dysfunction • Arrhythmias 	<ul style="list-style-type: none"> • BUN • Creatinine • Urinalysis • TSH, Free T4 • CBC • Electrolytes • Calcium, Albumin • Weight 	<ul style="list-style-type: none"> • Lithium level • BUN • Creatinine • Urinalysis • Calcium • Albumin • Weight 	<ul style="list-style-type: none"> • Each¹ dose change & every 3-6 months and PRN • Every 3-6 months 	<ul style="list-style-type: none"> • 24-hour urine for protein and creatinine clearance if proteinuria, marked polyuria or change in serum creatinine
Valproate	<ul style="list-style-type: none"> • Weight gain • Tremor • Nausea • Diarrhea • Cognitive dulling • Sedation, fatigue • Ataxia • Dizziness 	<ul style="list-style-type: none"> • Serum transaminase elevation • Alopecia • Elevated testosterone • Polycystic ovary syndrome • Rash • Hair loss 	<ul style="list-style-type: none"> • Hepatic failure • Thrombocytopenia • Pancreatitis • Severe dermatological reactions • Myelosuppression • Anticonvulsant hypersensitivity syndrome 	<ul style="list-style-type: none"> • CBC with differential & platelet count • AST, ALT • Lipase • Weight • Menstrual history 	<ul style="list-style-type: none"> • Divalproex level • Platelet Count • AST, ALT • Weight • Menstrual history 	<ul style="list-style-type: none"> • Each¹ dose change and PRN • Every 2weeks x2, then q • every month x2, then every 3-6 months 	<ul style="list-style-type: none"> • Risk of hepatic failure is highest in first 6 months of treatment • Repeat lipase if pancreatitis suspected

BMI: body mass index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.
¹Initially, regular blood tests are required to check serum level. Once a desired and stable level is achieved, the other tests are to check serum levels and other parameters (e.g., renal and thyroid function).

Table E.2.4 (Continuation)							
	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Carbamazepine	<ul style="list-style-type: none"> Nausea, vomiting Clumsiness, dizziness Nystagmus Sedation Blurred vision, diplopia, photosensitivity Cognitive dulling Ataxia CYP450 enzyme-induction (increased clearance of drugs metabolized by hepatic cytochrome system, including oral contraceptives) 	<ul style="list-style-type: none"> Hyponatremia Rash Confusion Leukopenia 	<ul style="list-style-type: none"> Serious dermatological reactions Agranulocytosis Aplastic anemia Atrioventricular block, arrhythmias Hepatitis Renal dysfunction Anticonvulsant hypersensitivity syndrome 	<ul style="list-style-type: none"> CBC with differential & platelet count AST, ALT Sodium 	<ul style="list-style-type: none"> Carbamazepine level CBC with differential & platelet count AST, ALT Sodium 	<ul style="list-style-type: none"> 1 & 3-4 weeks¹ after dose change and PRN With blood levels after dose change and then every 3-4 months 	<p>Check labs if unexplained fever, sore throat, lymphadenopathy or severe fatigue</p>
Lamotrigine	<ul style="list-style-type: none"> Dizziness Ataxia Headache Tremor Blurred vision, diplopia, 	<ul style="list-style-type: none"> Rash Nausea, vomiting Ataxia Cognitive dulling Confusion 	<ul style="list-style-type: none"> Serious dermatological reactions Anemia Anticonvulsant hypersensitivity syndrome 	<ul style="list-style-type: none"> CBC with differential & platelet count AST, ALT 	<ul style="list-style-type: none"> Lamotrigine level is not suggested but may guide treatment CBC with differential & platelet count AST, ALT 	<ul style="list-style-type: none"> Every 3-6 months 	<p>Clear instruction should be given about how to avoid skin rash (e.g., avoiding sun burn, not changing lotion, shampoo, or detergent) and when/how to reach doctor when rash occurs</p>

BMI: body mass index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.

¹Initially, regular blood tests are required to check serum level. Once a desired and stable level is achieved, the other tests are to check serum levels and other parameters (e.g., renal and thyroid function).

Table E.2.4 (continuation)

	Common	Uncommon	Rare	Baseline tests	Follow-up tests	Test frequency	Comments
Antipsychotics	<ul style="list-style-type: none"> Weight gain Postural hypotension Extrapyramidal symptoms Dizziness Sedation 	<ul style="list-style-type: none"> Hyperglycemia, hypercholesterolemia, increased triglycerides, diabetes Hyperprolactinemia Rash Photosensitivity Nausea, diarrhea, dyspepsia, constipation Elevated serum transaminases Urinary difficulties Sexual dysfunction Cognitive dulling 	<ul style="list-style-type: none"> Tardive dyskinesia Neuroleptic malignant syndrome Seizure Hepatic failure 	<ul style="list-style-type: none"> Glucose Triglycerides, total cholesterol, HDL, LDL AIMS Height, weight, BMI, waist circumference EKG (for ziprasidone) 	<ul style="list-style-type: none"> Glucose Triglycerides, total cholesterol, HDL, LDL AIMS Other tests as necessary (e.g., EKG) Height, weight, BMI, waist circumference 	<ul style="list-style-type: none"> Every 3-6 months and PRN 	

BMI: body mass index; BUN: blood urea nitrogen; TSH: thyroid stimulating hormone; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CBC: complete blood count; HDL: high density lipoprotein; LDL: low density lipoprotein; AIMS: Abnormal Involuntary Movement Scale; PRN: as needed.

family members are aware of the initial symptoms of serious side effects and how to contact the doctor if they occur. However, it is controversial whether this reduces the risk of serious adverse events.

There is a warning issued by the US FDA in 2008 about the risk for increased suicidality associated with use of anticonvulsant medications (Arana et al, 2010). Although other studies do not report an increased suicide risk with anticonvulsants, patients (and families) should be informed about this risk and strategies to deal with it discussed.

Valproate has been associated with polycystic ovary syndrome. Baseline menstrual history and a gynecological consultation in any female who develops significant changes in her menstrual cycle and/or hirsutism while on this medication is required.

Carbamazepine induces the metabolism of other medications (e.g., oral contraceptives) as well as its own metabolism and may decrease the blood level and reduce its effectiveness and that of other medications.

Oxcarbazepine, an analogue of carbamazepine, may not induce hepatic enzymes and does not require blood level monitoring, but may cause other side effects such as dizziness, nausea, somnolence, diplopia, fatigue, and rash.

Lamotrigine is usually well tolerated, with relatively low risk for weight gain and sedation. However, particularly when the dose is increased rapidly, it may cause serious dermatological reactions such as *Stevens-Johnson syndrome* or *toxic epidermal necrolysis*. Treatment should be suspended immediately if a new rash appears. Also, lamotrigine should be reinitiated from the starting dose of 12.5 or 25 mg/day if it is stopped for 5 days or more. The rate of serious dermatological reactions may be reduced by current dosing recommendations, that is, to prescribe small amounts with gradual escalation (e.g., 25 mg/day in ≥ 12 years old adolescents with dose increases of 25 mg every two weeks given in a twice a day regime until 100 mg/day is reached), especially if valproate is used concomitantly (lamotrigine dose increases should be halved when in this combination because of a synergistic drug interaction with valproate which increases lamotrigine levels); this increases the risk of rash significantly. Note that it may take 6 to 8 weeks to achieve a therapeutic level because of this slow titration schedule.

Weight loss has been reported with **topiramate** when combined with SGAs (e.g., to counterbalance the weight gain side effect of SGAs). However, topiramate is not recommended for mood symptoms of BD.

SGAs

There are common side effects of SGAs as listed in Table 5, but there are differences between them, such as in extrapyramidal symptoms, prolactin secretion, and weight gain. Olanzapine and risperidone are associated with higher weight gain while lurasidone and ziprasidone with lower. The metabolic effects (e.g., increased weight, glucose and lipids) of SGAs are of substantial concern especially when they are used in youth over extended periods. Research suggests that weight gain is greater in youth relative to adults and in those in a SGA and mood stabilizer combination (Correll et al, 2010). See Table E.2.5) Click [here](#) to access practical monitoring tables.

Click [here](#) to see the FDA approval status and quality of research evidence for mood stabilizers and lithium.

If a patient exhibits significant weight gain, a more thorough investigation of metabolic status and a re-evaluation of the risk-benefit ratio of continuing with the current SGA are indicated. As mentioned above, consultation with a pediatrician and nutritionist and referral to a weight management clinic is advisable to manage weight gain or risk for metabolic syndrome before considering adjunct medications. Available data suggest that adjunct metformin (and lifestyle interventions) may be helpful in some adults and adolescents (Morrison et al, 2002; Prahara et al, 2011; Walkup & Cottingham, 2017; Zheng et al, 2019). In addition, although rare, the SGAs may cause extrapyramidal symptoms, tardive dyskinesia and neuroleptic malignant syndrome, and the youth needs to be evaluated at baseline and routinely for abnormal movements. Baseline EKG is not a routine test but may be necessary to rule out cardiac problems including QT prolongation if there is history of cardiac problems in the child or family or if ziprasidone or concomitant stimulant use is considered.

Antidepressants

In youth, selective serotonin reuptake inhibitors (SSRIs) may be helpful for the treatment of bipolar depression, but some youth on SSRIs experience manic switch. SSRIs and other antidepressants can trigger mania, hypomania, mixed episodes or rapid cycling, particularly when used without concomitant mood stabilizer treatment. About 5-10% of youths being treated with SSRIS/SNRIs may become disinhibited (Carlson & Mick, 2003). These symptoms should not be confused with hypomanic and manic symptoms. The disinhibition subsides 1-2 day after discontinuing the antidepressants. Families and youth should be informed about risks versus benefits of using antidepressants (including the warnings of US and British regulatory agencies about the small—1 to 3 per 100 persons—but significant increased risk for suicide with antidepressants) and, in addition to suicidality, close attention should be paid to possible increases or onset of agitation and serotonin syndrome (especially when combined with lithium). A safety plan including how to manage these risks should be discussed with the

Table E.2.5 Parameters in monitoring second-generation antipsychotic use.

Parameter	At the beginning				Quarterly	Annually	Every 5 Years
	Baseline	4 weeks	8 weeks	12 weeks			
Personal history	✓						
Family history	✓						
Weight (BMI)	✓	✓	✓	✓	✓		
Waist circumference	✓				✓		
Blood pressure	✓			✓		✓	
Fasting blood glucose	✓			✓		✓	
Fasting lipid profile	✓			✓			✓

youth and the family and, if indicated, the SSRIs or other antidepressants should be started in small doses, after stabilization of manic or hypomanic symptoms with mood stabilizers (Birmaher and Axelson, 2005). Tricyclic antidepressants should not be used since there is no evidence that they are clinically effective and are very toxic on overdose, an ever-present risk in depressed adolescents.

PSYCHOSOCIAL TREATMENTS

Supportive psychotherapy is necessary for all BD youth and their families. Specific psychosocial treatments have been developed to help with psychoeducation, manage acute manic and depressive symptoms, improve coping skills and adherence to treatment, and manage comorbid conditions. In addition, they may help with preventing recurrences. Parents are engaged in their youth's therapy and referred to treatment if necessary (Birmaher & Axelson, 2005). Also, psychosocial treatments that have been found efficacious for the treatment of comorbid conditions such as oppositional behaviors, substance abuse, and anxiety disorders are indicated before initiating pharmacotherapy for these conditions. Thus far, there are several lines of overlapping psychosocial therapies for BD youth and their families, designed to fit specific age groups and methods of intervention:

Child and Family Focused Cognitive Behavior Therapy

These therapies were specifically designed for 8-18 year-olds (West et al, 2007). In addition to focusing on the identified child, it includes intensive work with parents to support them in developing an effective parenting style and to meet their own therapeutic needs. It integrates the principles of reward-based CBT with interpersonal psychotherapy, with an emphasis on empathic validation. It consists of 12, 60-minute weekly sessions over 3 months dealing with multiple domains—individual, family, peer, and school. The key components are summarised by the acronym RAINBOW (West et al, 2007):

- **R**outine,
- **A**ffect regulation,
- **I** can do it,
- **N**o negative thoughts and live in the now,
- **B**e a good friend/balanced lifestyle for parent,
- **O**h—how can we solve this problem, and
- **W**ays to get support.

Data from open studies and a RCT suggest this therapy is associated with improvement in functioning, mood symptoms, and treatment adherence (Weinstein et al, 2015; West et al, 2014).

Multi-Family Psychoeducation Groups and Individual Family Psychoeducation

Fristad et al (Fristad, 2006) has developed multi-family psychoeducation groups and individual family psychoeducation as adjunctive treatments for bipolar and depressive spectrum youth. The goals are to increase knowledge and understanding of BD and its treatment, improve management of symptoms

and associated conditions, improve communication and problem-solving skills, and increase the child and family's sense of support in dealing with the illness, emphasizing psychoeducation on the role of medication and coping strategies. It consists of 24, 50-minute individual sessions, 20 are manual-driven and 4 are to be used for crisis management or additional practice.

Family Focused Therapy

Miklowitz et al (2011) developed a manualized version of family focused therapy specifically for adolescents with BD. It has the primary goal of reducing symptoms through increased awareness of how to cope with the disorder, of decreasing levels of familial expressed emotion, and of improving family problem-solving and communication skills. It has three treatment components: psychoeducation, communication enhancement training, and problem-solving skills training. In a 2-year randomized control trial, compared to an enhanced treatment group, adolescents who received this therapy recovered earlier from depression, spent less time in depressive episodes, and reported lower depression severity scores. However, a more recent randomized trial failed to show advantages of intensive psychotherapy combined with best-practice pharmacotherapy vs. brief psychotherapy and pharmacotherapy (Miklowitz et al, 2014).

Dialectical Behavior Therapy

Goldstein et al (2007) adopted dialectical behavior therapy—a treatment initially designed for adults with borderline personality disorder—for the treatment of adolescents. The adapted intervention consists of 6 months of weekly 60-minute sessions followed by another 6 months of bimonthly sessions. A RCT showed that adolescents receiving dialectical behavior therapy demonstrated less severe depressive symptoms and greater likelihood of improvement in suicidal ideation when compared with psychosocial treatment as usual (Goldstein et al, 2015).

Interpersonal and Social Rhythm Therapy

Hlastala et al (2010) adapted interpersonal and social rhythm therapy for adolescents with BD. They suggest that psychosocial stressors precipitate or exacerbate bipolar episodes through their ability to disrupt social and sleep routines. The emphasis is on addressing interpersonal functioning deficits and managing affective symptoms to reduce their negative influence on psychosocial functioning. A pilot study of 16 to 18 sessions over 20 weeks reported significant improvements in manic, depressive, and general psychiatric symptoms.

Recent studies have started to explore the potential benefit of early psychosocial intervention to ameliorate or even prevent the onset and progression of symptoms in youth at high risk for BD. Goldstein and colleagues modified interpersonal and social rhythm therapy for the adolescent offspring of parents with BD who had not yet developed BD. An open study showed that it was feasible and acceptable for this group and detected an improvement in sleep and circadian patterns (Goldstein et al, 2014). A RCT suggested some benefits in a treatment group (Goldstein et al, 2018).



Click on the picture to visit the AACAP's resource center to access reading materials such as "facts for families" and "frequently asked questions" and to watch a short interview with Dr Birmaher

CONTINUATION AND MAINTENANCE TREATMENT

Relatively few studies have examined continuation and/or maintenance treatment of BD in youth. Available evidence in consensus guidelines varies (Parker et al, 2017). During the continuation phase of treatment, which starts soon after the acute treatment of depression or mania/hypomania to prevent relapse and recurrence, clinicians usually continue the effective treatment interventions that helped the acute mood episode. After the acute treatment, clinicians should focus on treating the “syndromal” or “subsyndromal” mood symptoms because these symptoms increase the risk of relapse. To prevent relapses, the medications that helped during the acute phase need to be continued *for at least 6-12 months*. One recurrent mood episode may suggest increasing the maintenance phase to 12-24 months; subsequent recurrent episodes would require discussion with family and youth about longer duration of medication treatment for prevention of further episodes. Thus, the duration of treatment will usually depend on the severity and length of the illness, comorbid conditions that impair functioning, mood swings, exposure to stress, availability of psychosocial interventions at home and school, parental psychopathology, social supports, and other family and social circumstances.

Lithium, lamotrigine (especially for depression), SGAs and, to a lesser extent, valproate, are effective in preventing new episodes in adults. In youth, lithium and divalproex appear to be similarly effective (e.g., Findling et al, 2019).

While the optimal duration of psychosocial treatments for pediatric BD has not been established, continuing psychosocial interventions for subthreshold mood symptoms may be helpful (Miklowitz et al, 2011). It is reasonable to provide ongoing psychosocial support, crisis management and therapy booster sessions as appropriate (Birmaher & Axelson, 2005; Goldstein et al, 2017).

CULTURAL PERSPECTIVES

Many professionals do not have access to non-English scientific literature and we largely don't know how BD youth around the world is being diagnosed and treated. Historically, several factors have made the diagnosis of bipolar disorder in childhood difficult. These include lack of awareness, diagnostic confusion, clinical bias against the diagnosis of mania in children, low prevalence, symptom overlap between bipolar disorder and other more common childhood-onset psychiatric disorders, developmental constraints, and variability in clinical presentation.

Stigma remains a big problem. Many clinicians around the world are still skeptical about persistent non-episodic manic symptoms, ultra-rapid mood cycling, and BD diagnosis in preschool children (Diler, 2007). However, a meta-analysis of epidemiological studies suggests that rates of BD-I in youth in the US and outside the US are similar (Van Meter et al, 2011).

Formal training in child psychiatry exists in only a few countries and countries where it actually exists have shortages of child psychiatrists (e.g., there are around 150 doctors trained in child psychology and psychiatry in China and 100 in Japan). In addition, trained allied mental health professionals, such as social workers, clinicians, nurses, and case workers are lacking in many countries (Diler, 2007).

In 1959, Shingawa described mania in youth in Japan as “Tendencies of hypomania, rash and frivolous words and behavior, appearance of problem behavior, and change from introversion to extroversion during periods of remission, lead on to ultimate transition into a positive personality exhibiting activeness, cheerfulness, and extroversion as a new stable personality upon cessation of the biphasic fluctuations.”

Using different diagnostic classification systems also have clinical implications. Professionals who use the ICD tend to give one diagnosis whereas multiple comorbid diagnoses, especially in youth with BD, are almost the rule when using the DSM. With some exceptions (e.g., the Chinese classification of psychiatric disorders), clinicians and researchers around the world use the DSM and not the ICD to diagnose BD in children but it is not known if the expression of some manic symptoms is different or if some symptoms are more or less often present in some cultures (Diler, 2007).

There are case reports or studies of BD in youth around the world dating back to the 1900s. Case series of adolescent onset BD appeared in the local psychiatric literature more than 100 years ago in China. Several case reports of children and adolescents with BD appeared in the Japanese literature in the 1950s, including a 10-year old child treated with ECT for depression and mania (Diler, 2007). However, in many countries, research in BD followed the increase in this diagnosis in the US, initially through case reports, but more recently they include epidemiologic, high-risk offspring studies, and biological (e.g., genetic, neuroimaging) studies that report findings similar to those in the US (Van Meter et al, 2011; Diler, 2007). In contrast with US findings, research studies from India—that examined bipolar youth who had never been on medication—found relatively lower ADHD comorbidity. However, the course was similar, i.e., high rates of recovery followed by relapses (Diler, 2007).

Some countries report less traditional treatments. For example, in China the first steps are to normalize the child's social environment, regulating the balance between active exercise/playing and mental stimulation (e.g., by reducing overstimulation from TV, movies, and video games) as well as providing the child with freshly prepared food (limiting the intake of sugar, dairy, foods rich in salicylic acid, and food preservatives) and supplementation with zinc and iron. Some clinics in China may prescribe psychiatric medications while others may consider acupuncture and herbal remedies. In India the practice at the inpatient services is to admit children with their caregivers who stay with the children during the entire hospitalization. Data from clinicians and researchers around the world would progress or even challenge our understanding of pediatric BD and help us integrate cultural and geographical aspects of this condition (Diler, 2007).

CONCLUSION

Despite the controversies, it is clear that, taking into account the developmental stage, it is possible to diagnose BD in children and adolescents. However, diagnosis may be cumbersome, especially in younger children and those with comorbid disorders (e.g., ADHD). Pediatric BD is associated with severe psychosocial consequences and increased risk for suicidality and substance abuse, stressing the need for prompt identification and treatment.

BD in youth is not limited to a few countries but a global problem. Clinicians around world are encouraged to share their experiences through case reports or clinical studies. This will help to incorporate cultural aspects of clinical presentations. Compared to 15 or 20 years ago, we now know more about effective screening and diagnosis, and there are more data to guide medication treatment as well as psychosocial interventions. However, most of the treatment studies focus

Click [here](#) to view international variations in the diagnosis of childhood onset bipolar disorder

on the acute phase. More research is needed in the acute treatment of bipolar depression and of comorbid conditions, such as ADHD and anxiety disorders. We also need to learn more about treatment of subsyndromal presentations and on how to prevent recurrences.

High risk studies are important for identifying early presentations that can guide prevention. Preliminary studies investigating disease and treatment specific biomarkers are promising, but longitudinal studies (combined with ecological monitoring using mobile sensors) in larger samples are needed to better understand core pathophysiological processes and individualized treatment/prevention options in youth with and at-risk for BD.

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Pieter Bruegel the Elder - The Peasant Dance

Appendix E.2.1

Name: _____

MOOD and ENERGY THERMOMETER

Please circle one or more of the below numbers FROM EACH COLUMN that reflects your mood & energy levels reflecting your day. You can circle more than one number if your mood/energy changes during the day.

E
L
E
V
A
T
E
D

/
U
P

D
E
P
R
E
S
S
E
D

/
D
O
W
N

+10 SUPER ELEVATED Have constant excitement and feel super happy, and have no control over self & cannot be calmed down at all & cannot function at all & someone needs to be present to monitor safety.
+9 EXTREMELY ELEVATED Have extreme excitement and feel extremely happy, non-stop giggling & laughing, and cannot control self & cannot be calmed down & function poorly.
+8 SEVERELY ELEVATED-almost all day
+7 SEVERELY ELEVATED- less than 50% of the day Feel very happy & giggling & laughing, and can control self only briefly & very difficult to calm down & don't function well.
+6 MODERATELY ELEVATED-almost all day
+5 MODERATELY ELEVATED- less than 50% of the day Feel cheerful/optimistic much more than usual/baseline (out of proportion) & some difficulty to control self & some difficulty to calm down & don't function as good as before.
+4 MILDLY ELEVATED-almost all day
+3 MILDLY ELEVATED-less than 50% of the day Feel cheerful and optimistic more than usual/baseline & others may notice it, but can calm down & function ok.
+2 SLIGHTLY ELEVATED-almost all day long
+1 SLIGHTLY ELEVATED- less than 50% of the day Feel a little bit more cheerful and optimistic, but others don't notice & function ok.



+10 SUPER ENERGETIC Have constant motor excitement, non-stop moving around, and cannot control self & cannot slow down at all & cannot function at all & someone needs to be present to monitor safety.
+9 EXTREMELY ENERGETIC Have motor excitement, non-stop moving around, and cannot control self & cannot slow down & function poorly.
+8 SEVERELY ENERGETIC -almost all day
+7 SEVERELY ENERGETIC- less than 50% of the day Have excessive energy & constantly moving and pacing about, and can control energy only briefly & very difficult to slow down & don't function well.
+6 MODERATELY ENERGETIC -almost all day
+5 MODERATELY ENERGETIC-less than 50% of the day Feel energetic and hyper much more than usual/baseline (out of proportion) & restless/pace & some difficulty to control energy & some difficulty to slow down & don't function as good as before.
+4 MILDLY ENERGETIC-almost all day
+3 MILDLY ENERGETIC-less than 50% of the day Feel energetic and hyper more than usual/baseline & others may notice it, but can easily slow down & function ok.
+2 SLIGHTLY MORE ENERGY-almost all day long
+1 SLIGHTLY MORE ENERGY-less than 50% of the day Feel a little bit more energetic than usual, but others don't notice a change & function ok.

<h3>OK MOOD</h3>
-1 SLIGHTLY DOWN- less than 50% of the day Feel a little depressed and cheerless, but others don't notice a change & function ok.
-2 SLIGHTLY DOWN-almost all day
-3 MILDLY DOWN - less than 50% of the day Feel depressed and cheerless more than usual & enjoying things and having fun is somewhat difficult & others may notice a change, but can brighten up & function ok.
-4 MILDLY DOWN -almost all day
-5 MODERATELY DOWN - less than 50% of the day Feel depressed and cheerless (out of proportion) much more than usual & enjoying things and having fun is more difficult & some difficulty to brighten up & don't function as good as before.
-6 MODERATELY DOWN -almost all day
-7 SEVERELY DOWN- less than 50% of the day Feel very depressed & cheerless & gloomy, and don't enjoy things and don't feel like having fun & very difficult to brighten up & don't function well.
-8 SEVERELY DOWN -almost all day
-9 EXTREMELY DOWN (life is not worth living) Have extreme depression and feel very miserable, have psychic pain ("I cannot stand it"), and cannot control self & cannot be down & function poorly.
-10 AT THE LOWEST POINT Have constant painful sadness and feel very numb & empty & don't want to live & cannot function at all & someone needs to be present to monitor safety.

<h3>OK ENERGY</h3>
-1 SLIGHTLY TIRED- less than 50% of the day Feel a little bit tired, but others don't notice a change & function ok.
-2 SLIGHTLY TIRED-almost all day
-3 MILDLY TIRED-less than 50% of the day Feel more tired and less active than usual/baseline & others may notice it, but can be active during the day & function ok.
-4 MILDLY TIRED-almost all day
-5 MODERATELY TIRED-less than 50% of the day Feel very tired & slowed down than usual/baseline (out of proportion) & have considerably less energy to do things & less active & spend more time than usual to rest & don't function as good as before.
-6 MODERATELY TIRED-almost all day
-7 SEVERELY TIRED- less than 50% of the day Have excessive tiredness & very difficult to move around & spend very long time to rest & physical activity is limited to few & don't function well.
-8 SEVERELY TIRED-almost all day
-9 EXTREMELY TIRED Feel like drained and worn out & almost no physical activity and cannot move around & function poorly.
-10 NO ENERGY AT ALL Have constant motor retardation, and cannot move arms or legs & cannot function at all & someone needs to be present to monitor safety.



DAILY SCHEDULE...

TODAY.. What time did you

a. wake up? _____

b. have breakfast? _____

c. have dinner? _____

Diler RS. Mood and Energy Thermometer. Child and Adolescent Bipolar Services (CABS)-2009 Western Psychiatric Institute and Clinic, Pittsburgh, PA.

Appendix E.2.2

Child and Adolescent Bipolar Spectrum Assessment Report																																																											
Assessment date & informant & interviewer & consensus MD:																																																											
Identification:																																																											
Previous inpatient tx (Dates/Mood @ admission/Diagnoses & Medications):																																																											
Age of onset of any mood symptoms: Longest euthymic mood over the past 12 months & since mood symptoms started: Change/temporal relation between (hypo)manic and depressive episodes:																																																											
Age of onset of hypomanic: _____ & manic episodes: _____	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th colspan="4" style="text-align: center; padding: 5px;">DSM-5 Manic Symptoms</th> </tr> <tr> <th style="font-size: small;">(F): Full, significant part of the day for ≥4 days, (S): Subthreshold, at least ≥4 hours/day or multiple brief episodes (N): Not present</th> <th style="font-size: x-small;">Current episode</th> <th style="font-size: x-small;">Past history</th> <th style="font-size: x-small;">#</th> </tr> </thead> <tbody> <tr> <td style="font-size: x-small;">Elevated/Expansive mood</td> <td></td> <td></td> <td style="text-align: center;">1 JA</td> </tr> <tr> <td style="font-size: x-small;">Irritability</td> <td></td> <td></td> <td style="text-align: center;">2</td> </tr> <tr> <td style="font-size: x-small;">Increased goal-directed activity</td> <td></td> <td></td> <td style="text-align: center;">3 JA</td> </tr> <tr> <td style="font-size: x-small;">Motor hyperactivity</td> <td></td> <td></td> <td style="text-align: center;">4</td> </tr> <tr> <th colspan="4" style="font-size: x-small; text-align: center;">Sx Associated with A Elevated/Irritable Mood & Increased Activity/Energy</th> </tr> <tr> <td style="font-size: x-small;">Inflated self-esteem, grandiosity</td> <td></td> <td></td> <td style="text-align: center;">1</td> </tr> <tr> <td style="font-size: x-small;">Decreased need for sleep</td> <td></td> <td></td> <td style="text-align: center;">2</td> </tr> <tr> <td style="font-size: x-small;">More talkative, pressured to keep talking</td> <td></td> <td></td> <td style="text-align: center;">3</td> </tr> <tr> <td style="font-size: x-small;">Flight of ideas or racing thoughts</td> <td></td> <td></td> <td style="text-align: center;">4</td> </tr> <tr> <td style="font-size: x-small;">Distractibility</td> <td></td> <td></td> <td style="text-align: center;">5</td> </tr> <tr> <td style="font-size: x-small;">Increased goal-directed activity or psychomotor agitation</td> <td></td> <td></td> <td style="text-align: center;">6</td> </tr> <tr> <td style="font-size: x-small;">Risky/dangerous behaviors done for pleasurable reasons</td> <td></td> <td></td> <td style="text-align: center;">7</td> </tr> </tbody> </table>			DSM-5 Manic Symptoms				(F): Full, significant part of the day for ≥4 days, (S): Subthreshold, at least ≥4 hours/day or multiple brief episodes (N): Not present	Current episode	Past history	#	Elevated/Expansive mood			1 JA	Irritability			2	Increased goal-directed activity			3 JA	Motor hyperactivity			4	Sx Associated with A Elevated/Irritable Mood & Increased Activity/Energy				Inflated self-esteem, grandiosity			1	Decreased need for sleep			2	More talkative, pressured to keep talking			3	Flight of ideas or racing thoughts			4	Distractibility			5	Increased goal-directed activity or psychomotor agitation			6	Risky/dangerous behaviors done for pleasurable reasons			7
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Total number of manic episodes: _____ & total number of hypomanic episodes: _____																																																											
Duration of manic episodes: (first: _____ / most recent: _____ / most severe: _____ / regular: _____)																																																											
Early signs/symptoms of mania/hypomania:																																																											
Individual/personal description of manic/hypomanic periods:																																																											
Presence of SIB/SI/SA and H/HA during mania:																																																											
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Response to med trials:																																																											
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Medical Concerns:																																																											
DIAGNOSIS & JUSTIFICATION:																																																											
RECOMMENDATIONS FOR TREATMENT & FOLLOW UP:																																																											
Strengths of the patient:																																																											

Rasmussen D, Iler, MD. Child and Adolescent Bipolar Spectrum Services (B-CADSS), Western Psychiatric Institute and Clinic of University of Pittsburgh Medical Center. "Assessment Report Form." 2019.

Appendix E.2.3

Joseph M Rey & Rasim Somer Diler

SELF-ASSESSMENT EXERCISES

(Only one answer is correct)

E.2.1 Which one of these factors increases the risk of bipolar disorder the most?

- A** Having a father with bipolar disorder
- B** Having a mother who abuses alcohol
- C** History of sexual abuse
- D** Having had a previous major depressive episode
- E** A personal history of aggressive behavior

E.2.2 The main difference between bipolar-I and bipolar II is that:

- A** Bipolar I cannot be diagnosed until the individual is a young adult
- B** Bipolar-II lacks full-blown manic episodes
- C** Bipolar-I has rapid cycles
- D** Bipolar-II does not have major depressive episodes
- E** Episodes are longer I bipolar-II

E.2.3 A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy level, which lasts most of the day, nearly every day, meets criteria for a manic episode if it:

- A** Lasts four or more days
- B** Lasts seven or more days
- C** Lasts more than 14 days
- D** Has a grandiose content
- E** Has a sexualized content

E.2.4 Janet is 13 years of age. In the 4 to 5 years prior to her visit, multiple mental health evaluations and treatments had been undertaken; however, little clinical improvement had been noticed. She had been diagnosed with ADHD. Her current assessment was triggered by her behavior the previous 10 days: not sleeping at all, spending the nights cleaning her room, she had unrealistic projects like becoming a rock star, was unable to remain seated, could not concentrate, was irritable, and spoke non-stop, but there was no suggestion of hallucinations or delusions. Nevertheless, she was so disturbed that she was admitted to hospital. Which one of the following would be your first management?

- A** Observing the child
- B** Individual psychotherapy
- C** Methylphenidate
- D** A second generation antipsychotic
- E** Mindfulness therapy

E.2.5 *Irritability is a very common symptom in children and adolescents. However, it is suggestive of a bipolar disorder only if it:*

- A** Is explosive or severe
- B** Responds to lithium treatment
- C** Happens after school
- D** Begins or significantly increases in intensity in conjunction with the presence of other manic symptoms
- E** Does not respond to behavioral management

E.2.6 *An adolescent, who was being treated with antidepressants because of suffering from major depression, developed mania. Which of these interventions would you implement first?*

- A** Start treatment with lithium
- B** Start treatment with a second generation antipsychotic
- C** Admit to hospital
- D** Stop antidepressants
- E** Lower the antidepressant dose

E.2.7 *The target blood level for lithium in the acute treatment of bipolar disorder should be (mEq/L):*

- A** 0.4 to 0.7
- B** 0.8 to 1.1
- C** 1.2 to 1.4
- D** 1.5 to 1.8
- E** 1.9 to 2.3

E.2.8 *A key criterium for the diagnosis of bipolar depression is:*

- A** The presence of biological symptoms (melancholia)
- B** Early morning waking
- C** Mood congruent delusions
- D** History of mania
- E** Suicidal thoughts

E.2.9 *Comorbid disorders are very frequent in youth with bipolar disorder. In general, management wise, it is recommended to first:*

- A** Clarify which one is the primary disorder
- B** Treat both disorders concurrently
- C** Treat the condition that is likely to show a quicker response (e.g., ADHD)
- D** Treat the comorbid condition
- E** Stabilize the bipolar symptoms

E.2.10 *The US FDA issued a warning in 2008 about the risk for increased suicidality associated with the use of anticonvulsant medications. Subsequently some other studies did not report an increased suicide risk with these drugs. How would you deal with this in relation to patients and families? I would:*

- A** Not prescribe anticonvulsants
- B** Not tell anything.
- C** Only tell this to the parents but not the child
- D** Inform them about this risk and discuss strategies to deal with it
- E** Tell them this fear is unfounded

A.2.1 Answer: A

A.2.2 Answer: B

A.2.3 Answer: B

A.2.4 Answer: D

A.2.5 Answer: D

A.2.6 Answer: D

A.2.7 Answer: B

A.2.8 Answer: D

A.2.9 Answer: E

A.2.10 Answer: D