

Bipolar Disorders Children & Adolescents

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Depressive Disorders

Major Depressive Disorder: Depressed (or irritable mood in children and adolescents) or loss of interest/pleasure (anhedonia) plus other symptoms (total of at least 5).

1. **Depressed mood or irritable** most of the day, nearly every day, as indicated by either subjective report or observation made by others .
2. **Decreased interest or pleasure** in most activities, most of each day
3. **Significant weight change (5%) or change in appetite**
4. **Change in sleep**: Insomnia or hypersomnia
5. **Change in activity**: Psychomotor agitation or retardation
6. **Fatigue or loss of energy**
7. **Guilt/worthlessness**: Feelings of worthlessness or excessive or inappropriate guilt
8. **Concentration**: diminished ability to think or concentrate, or more indecisiveness
9. **Suicidality**: Thoughts of death or suicide, or has suicide plan

Depressive Disorders

Persistent Depressive Disorder (Dysthymia): 2-year h/o depressed mood most of the day for more days than not (1-year for children & adolescents with irritability instead of depressed mood) plus at least two of :

1. poor appetite or overeating
2. Insomnia or Hypersomnia
3. low energy or fatigue
4. low self-esteem
5. poor concentration or difficulty making decisions
6. feelings of hopelessness

Depressive Disorders

Other Specified Depressive Disorder

1. Recurrent Brief Depression:

Depressed mood and 4 other symptoms for 2-13 days at least 1/month for 12 consecutive months

2. Short-duration depressive episode (4-13 days):

Depressed affect and 4 other symptoms for 4-13 days

3. Depressive disorder with insufficient symptoms:

Depressed affect and at least 1 other symptom for at least 2 weeks

Unspecified Depressive Disorder:

Symptoms characteristic of depressive disorder but not meeting criteria or lack of information

Mood Disorder Prevalence and Impairment

Mood Disorder	Female	Male	Total	Severe Impairment
Major Depression or Dysthymia	15.9%	7.7%	11.7%	8.7%
Bipolar Disorder Type I or II	3.3%	2.6%	2.9%	2.6%
Any Mood Disorder	18.3%	10.5%	14.3%	11.2%

Kessler et al, JAACAP, 1010

Mood Disorder Prevalence and Impairment

Age	13-14	15-16	17-18	Total
Major Depression or Dysthymia	8.4%	12.6%	15.4%	11.7%
Bipolar Disorder Type I or II	1.9%	3.1%	4.3%	2.9%
Any Mood Disorder	10.5%	15.5%	18.1%	14.3%

Kessler et al, JAACAP, 1010

Mood Disorder Prevalence and Impairment

Age	9-10	11	12	13
Any Depressive Disorder	0.5%	1.95%	0.4%	2.6%

Costello JE, et al JAMA 2003

Subthreshold Depression & Outcomes

Study of 1006 17-18 y/o followed for up to 8 years

Looked at individuals who were:

- **Asymptomatic (n = 728; 72%)**
- **Subthreshold Depression (n = 73; 7.2%)**
- **Major Depression (n = 182; 18%)**

Evaluated them at 2 time periods:

- **Ages 18 – 21**
- **Ages 21 - 25**

Fergusson et al, Arch Gen Psych 2005

Subthreshold Depression & Outcomes

Ages 18 – 21 Years of Age

Outcome	Asymptomatic N = 728	Subthreshold N = 73	Major Depression N = 182
Major Depression	16.4%	27.4%	50%
Sought Treatment for Depression	6.7%	13.7%	32.4%
Anxiety Disorder	9.2%	13.7%	32.4%
Sought Treatment for Anxiety	2.5%	9.6%	13.2%
Suicidal Ideation	10%	20.6%	26.4%

Subthreshold Depression & Outcomes

Ages 21 – 15 Years of Age

Outcome	Asymptomatic N = 725	Subthreshold N = 72	Major Depression N = 179
Major Depression	15.7%	33.3%	39.1%
Sought Treatment for Depression	11%	26.4%	26.8%
Anxiety Disorder	14.2%	19.4%	31.3%
Sought Treatment for Anxiety	5.2%	13.9%	15.6%
Suicidal Ideation	10.2%	20.8%	16.2%

Depressed Adolescents Grown Up

- **Prospective Case-Control Study of 73 Depressed Adolescent compared with 37 controls**
- **Followed up 10-15 years after initial assessment**
- **Women 50.7%**
- **Age at intake 15.4**
- **Age at follow up 26**

Outcomes:

- **Suicide**
- **Suicide attempts**
- **Psychiatric diagnoses**

Depressed Adolescents Grown Up

Subjects	Depressed N = 73	Healthy N = 37
Completed Suicides	7.7%	0
Suicide Attempts In follow Up Period	37/73 (50.7%)	2/37 (5.4%)
Major Depression	49%	27%
Anxiety Disorder	19.2%	10.8%
Alcohol Dependence	27.4%	21.6%
Drug Dependence	17.8%	8.1%
Eating Disorder	9.6%	0
Antisocial Personality	6.8%	0

Predictors of Recurrence Young Adults

**274 subjects with adolescent-onset depression
who were assessed after age 24:**

- 1. 17% had age of onset < age 13**
- 2. 50% with duration of 1st episode <8 weeks**
- 3. 76% had only single episode of MDD < age 19**
- 4. 64% had 5-7 MDD symptoms; 36% had 8-9**
- 5. 79% had treatment of MDD in adolescence**
- 6. 23% had h/o suicide attempt during
adolescence**

Predictors of Recurrence Young Adults

Positive Associations:

- **Low levels of emotional reliance**
- **Single episode of major depression in adolescence**
- **Low levels of family members with recurrent major depression**
- **Low antisocial and borderline symptoms**
- **Positive attributional style (males only)**

Predictors of Recurrence Young Adults

Negative Associations:

- **Female gender**
- **Low levels of emotional reliance**
- **Multiple episodes of major depression in adolescence**
- **Higher levels of family members with recurrent major depression**
- **Elevated borderline symptoms**
- **Conflict with parents (females only)**

Bipolar Disorder in DSM-5

- Bipolar I disorder: manic episode(s) or mixed episode(s) plus MDE(s)
- Bipolar II disorder: hypomanic episode(s) and major depressive episode(s)
- Cyclothymia: hypomanic symptoms plus depressive symptoms
- Other Specified Bipolar and Related Disorder

Bipolar Disorder in DSM-5

Other Specified Bipolar and Related Disorder

1. Short-duration hypomanic episodes (2-3 days) and major depressive episodes
2. Hypomanic episodes with insufficient symptoms and major depressive episodes
3. Hypomanic episodes without prior major depressive episodes
4. Short-duration cyclothymia (less than 24 months)

Manic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally *and persistently increased goal-directed of activity or energy*, lasting at least 1 week and present most of the day, nearly every day (or any duration if hospitalization is necessary).

Manic Episode

B. During the period of mood disturbance and increased energy or activity, three (or more) of the following symptoms (four if the mood is only irritable) are present to a significant degree and represent a noticeable change from usual behavior:

Manic Episode

1. Inflated self-esteem or grandiosity
2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
3. More talkative than usual or pressure to keep talking
4. Flight of ideas or subjective experience that thoughts are racing

Manic Episode

5. Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. Increase in goal directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

Manic Episode

- C. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features
- D. No due to direct physiologic effects of a substance or a general medical condition

Hypomanic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood and abnormally *and persistently increased goal-directed of activity or energy*, lasting at least 4 consecutive days and is present most of the day, nearly every day.

Good Prognosis Associated With

- Short duration of manic episodes
- Advanced age of onset
- No comorbid psychiatric disorders
- No suicidal ideation
- No psychosis

Poor Prognosis

- Exposure to adversity (Trauma)
- No psychotherapeutic interventions
- Medication Non-Adherence
- Family Psychopathology
- Inter-episode Subsyndromal Symptoms
- **Earlier Age of Onset**

Age and Prognosis

STEP-BD: (Systematic Treatment Enhancement Program for Bipolar Disorder)

N = 983 Adults with BPAD

28% age of onset \leq 12

38% age of onset 13-18

34% age of onset $>$ 18

Age and Prognosis

STEP-BD: (Systematic Treatment Enhancement Program for Bipolar Disorder)

Younger age associated with:

- Faster cycling
- More depressed days
- More manic & depressive episodes
- Substance use
- Suicide attempts

Age and Prognosis

Age of onset & Treatment Delays:

N = 480 Adults with BPAD

<u>Age of Onset:</u>	<u>Years to 1st Treatment</u>
<12	16.8
13 – 18	11.5
19 – 29	4.6
30 +	2.6

Leverich et al. J Pediatr 2007

Course of Pediatric BPAD

COBY Study (Course & Outcome of Bipolar Youth Study)

N = 413 Youth ages 7 -17

BPAD I	244 (59%)	Age 12.8
BPAD II	28 (7%)	Age 14.8
BPAD NOS	141 (34%)	Age 11.9

Birmaher et al. Am J Psych 2009

Course of Pediatric BPAD

N = 413 Youth ages 7 -17

Recruitment

Outpatient = 68%

Inpatient = 14%

- Mean age at 1st symptoms 8.4 years
- Mean age at 1st DSM IV Episode 9.3 years
- BPAD II more likely than BPAD I or NOS to have depressive episode as index episode

Course of Pediatric BPAD

- Subjects interviewed every 39 weeks for 192 weeks
- Full recovery: 8 week with minimal or no mood symptoms
- Subsyndromic: some symptoms and impairment but not meeting full syndromic criteria
- Recovery from Index Episode: 81.4%
- Time to recovery from Index Episode 124 weeks

Course of Pediatric BPAD

- Recurrence after recovery from Index Episode-62.5%
- Median time to recurrence from Index Episode-71 weeks

Average of syndromal recurrences over 4 years

- 33% had 1
- 20% had 2
- 10% had 3

Course of Pediatric BPAD

Polarity of syndromal recurrences

- Major Depression 59%
- Hypomania 21%
- Mania 15%
- Mixed 5%

Course of Pediatric BPAD

Week-by-Week:

40% of weeks subjects asymptomatic

60% of weeks subjects symptomatic:

- 42% Subsyndromal
- 18% Syndromal
- More time with depressive/mixed symptoms than mania/hypomania

Course of Pediatric BPAD

Psychosis:

- 16% of participants at Index Episode
- 17% in Follow Up period

Course of Pediatric BPAD

Conversion from BPAD II or BP NOS

- 36% of subjects with BPAD II or NOS converted in follow up period (61/169)

Of these:

- BPAD II to BPAD I 25% (7/28)
- BP NOS to BPAD I 19% (28/141)
- BP NOS to BPAD II 18% (26/141)

Course of Pediatric BPAD

Chronic Symptoms

- (>75% of follow up period with some symptoms) occurred in 38% of subjects
- Mostly subsyndromal - depression

Duration of Illness

- Each year of illness duration decreased chance of 2-month recovery by 20%

BPAD is fundamentally a depressive disorder.

Course of Pediatric BPAD

COBY: Suggests that bipolar spectrum disorders in youth:

- Episodic disorders
- Characterized most often by subsyndromal episodes
- Less often characterized by syndromal episodes
- With mainly depressive and mixed symptoms
- With rapid mood changes

Fits with Adult BPAD which really is viewed as fundamentally a depressive disorder.

Bipolar Affective Disorder Diagnosis & Classification

- **2008 Study of 130 consecutively admitted bipolar children & adolescents**
- **Ages 3-17**
- **Mean of 11.6 years):**

Staton, et al. J Affective Disorders 2008

Bipolar Affective Disorder Diagnosis & Classification

98% had 2 or 3 of the following symptoms:

- Elation, grandiosity or racing thoughts**

97% had 5 or more of the 8 criteria when manic

90% had problematic distractibility-inattention

49% had rage attacks

Staton, et al. J Affective Disorders 2008

Diagnosis & Classification

- **Elation:**

Mood distinct from normative extremes of joy and excitement.

- **Grandiosity:**

Presence of extreme non-normative entitlement or self confidence.

- **Racing Thoughts:**

Inferred (in younger people) by recurrent periods of speech so rapid making it hard to comprehend or by flight of ideas.

Diagnosis & Classification

90% had Distractibility-Inattention: 3 of 5

- 1. Easily distracted**
- 2. Difficulty sustaining attention**
- 3. Careless mistakes**
- 4. Failure to finish tasks**
- 5. Problems organizing tasks/activities**

Excluded 4 other DSM 5 ADHD inattentive symptoms: (poor listening, avoiding work requiring sustained attention, loses things, forgetfulness).

Diagnosis & Classification

49% had rage attacks

Rage Attacks:

- 1. Severe anger with psychomotor agitation and/or verbal or physical aggression**
- 2. Lasting at least 20 minutes**
- 3. Occurring at least twice/week**
- 4. For majority of weeks in past year**

Staton, et al. J Affective Disorders 2008

Diagnosis & Classification

53% had ultradian cycling (Ultradian rhythms are recurrent periods or cycles repeated throughout a 24-hour circadian day)

22% had chronic mania or chronic simultaneous mixed manic condition

Rages increased with age in boys and decreased in age with girls

Depression worsened with age in this sample

Diagnosis & Classification

Conclusions:

Recurrent or chronic simultaneous presence of any two symptoms of elation, grandiosity or racing thoughts and a total of 5 DSM manic symptoms will identify nearly all clinically referred bipolar children & adolescents

Staton, et al. J Affective Disorders 2008

Prognosis of Childhood-Onset Bipolar Disorder

2007 Study of 480 adult outpatients with BPAD

- **Mean age 42.5 years**
- **Childhood onset (≤ 12 years of age) 14%**
- **Adolescent onset (13-18) 36%**
- **Early adulthood (19-29) 32%**
- **Late adulthood (after age 30) 19%**

Leverich et al. J of Pediatrics 2007

Prognosis of Childhood-Onset Bipolar Disorder

Patient assessed retrospectively and also for a 1-year prospective period.

A. Duration of illness onset to 1st treatment

- Childhood onset - 17 years**
- Adolescent onset – 11.5 years**
- Early adulthood – 4.6 years**
- Late adulthood – 2.6 years**

Prognosis of Childhood-Onset Bipolar Disorder

B. Parental history of bipolar disorder:

- **Childhood onset – 47%**
- **Adolescent onset – 37%**
- **Early adulthood – 21%**
- **Late adulthood – 17%**

C. Parental history of depression:

- **Childhood onset – 52%**
- **Adolescent onset – 43%**
- **Early adulthood – 29%**
- **Late adulthood – 25%**

Prognosis of Childhood-Onset Bipolar Disorder

D. Physical abuse as a child:

- **Childhood onset – 36%**
- **Adolescent onset – 22%**
- **Early adulthood – 15%**
- **Late adulthood – 12%**

E. Sexual abuse as a child:

- **Childhood onset – 31%**
- **Adolescent onset – 20%**
- **Early adulthood – 11%**
- **Late adulthood – 10%**

Prognosis of Childhood-Onset Bipolar Disorder

1-year prospective outcomes:

Patients with childhood & adolescent onset:

- **More days manic (51 versus 35/39)**
- **More days depressed (162, 139, 108, 128)**
- **More mood episodes (5.4, 4.1, 2.6, 2.8)**
- **More severe depression and mania**

Stimulant Use in Youth at Risk for Bipolar Disorder

Original Study done in late 1960's

**75 boys age 6-12 with ADHD treated with
methylphenidate:**

MAX Subjects (N = 17):

**Additional irritability, oppositionality, conduct,
anxiety/depression**

MIN Subjects (N = 58) had ADHD

Stimulant Use in Youth at Risk for Bipolar Disorder

**Followed up at ages 21 – 23 and evaluated to
BPAD diagnosis and looked at prior response to
stimulants**

MAX Subjects (N = 17)

2 hypomania; 1 cyclothymia for 17.6%

MIN Subjects (N = 58)

1 mania, 4 hypomania, 5 cyclothymia for 17.2%

(Carlson et al. J Child & Adol Psychopharm 2009)

Stimulant Use in Youth at Risk for Bipolar Disorder

**Of the 13 subjects who developed BPAD:
Response to Stimulant (compared with whole
sample) :**

77% positive response (69%)

15% mixed response (15%)

8% bad response (4%)

No difference in:

**Dose or response; Duration of treatment (3
years); or use of thioridazine (17%)**

Stimulant Use in Youth at Risk for Bipolar Disorder

Conclusions:

- 1. ADHD boys with symptoms suggesting childhood mania do not respond differently to methylphenidate than boys without such symptoms.**
- 2. No evidence that methylphenidate precipitates young adult bipolar disorder in susceptible individuals.**

(Carlson et al. J Child & Adol Psychopharm 2006)