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***Mood Instability and Cyclothymic Spectrum Mood Disorders: General***

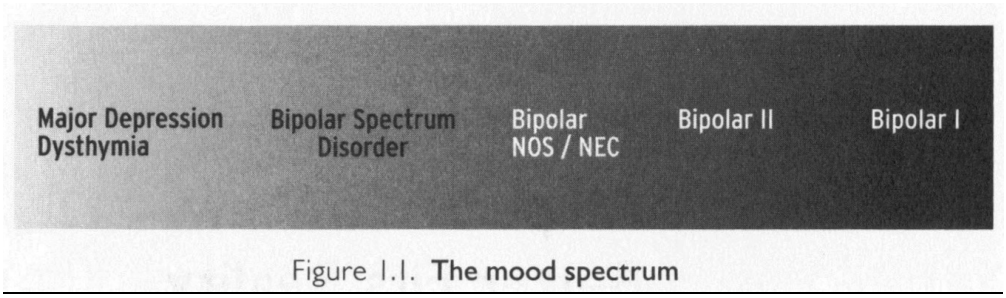
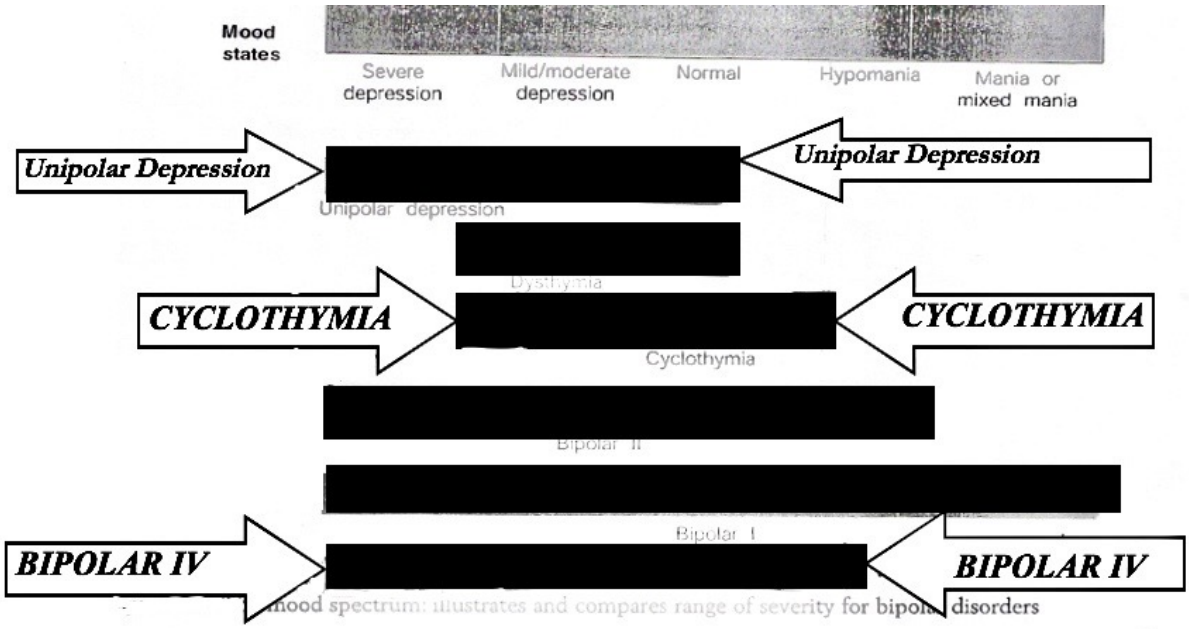
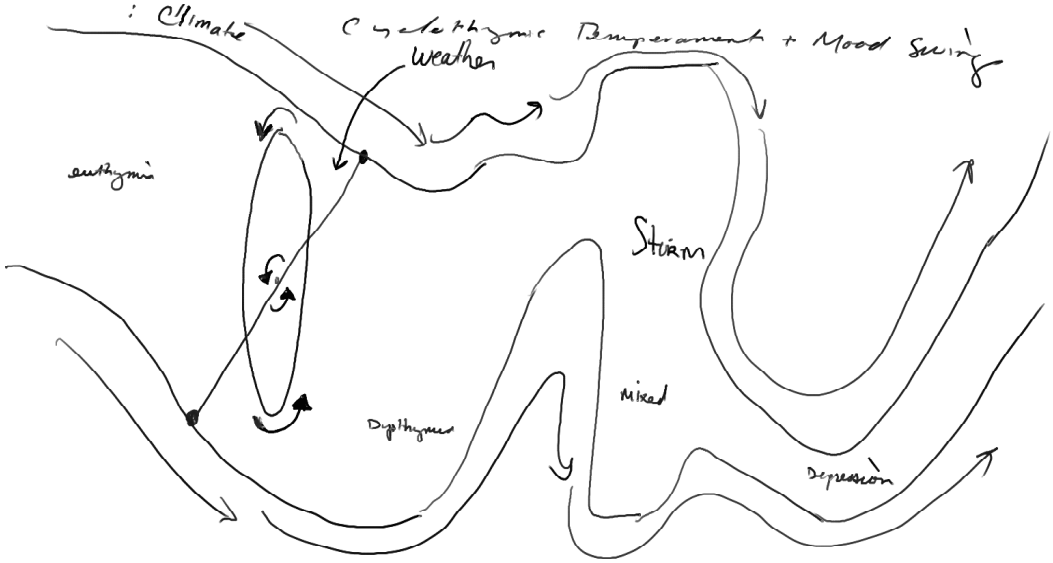



Figure 1.1. **The mood spectrum**




mood spectrum: illustrates and compares range of severity for bipolar disorders



- I prefer the term 'cyclothymia' (or 'cyclothymic') to 'bipolar' since it captures the essence of cycles or episodes of mood states and implies a spin to mood; it also deemphasizes the idea of two poles of mood problems (mania and depression) when in reality mood episodes can be a painful mix of various elements that doesn't fall neatly into one pole or another. For that reason, I also prefer the term 'polymorphic' to 'bipolar' (or even 'polychromatic'). That said, I'll stick to the more commonly used word "bipolar".
- Depression dominates bipolar spectrum disorders; upward shifts in mood can be subtle, fleeting, and easy to confuse with feeling better
- When depression is not just depression
    - What may seem for years to be unipolar depression can be discovered later to have been bipolar depression or more elegantly described as depression superimposed on a cyclothymic or hyperthymic temperament
    - 69-73% of patients with bipolar disorder are initially misdiagnosed
    - There is a 91% misdiagnosis rate in primary care settings
    - The most frequent misdiagnoses were unipolar depression (60%) followed by anxiety disorders (26%)
    - Roughly 30% (range 10-55%) of individuals presenting with depression have bipolar disorder, predominantly bipolar II disorder or bipolar disorder, not otherwise specified
    - 30% of patients with bipolar disorder seek help within 1 year of symptom onset (70% don't )
        - 33% had depressive symptoms first
        - 18% had mix of depressive and manic symptoms first
        - 24% had ***non-mood*** symptoms first (e.g., school problems)
    - 30% of misdiagnosed patients waited 10 years or more for correct diagnosis.
    - The average amount of time between symptoms and appropriate diagnosis is 8-17 years (Egeland, 1987, others, including STEP-BD data from 2005). To put this in perspective, correct re-diagnosis takes as much as three-fold longer than the 6-year recovery time for intravenous heroin addiction
    - Nearly 40% of patients with a history of unipolar major depression also had a history of subthreshold hypomania (Angst, AJP, 2010)
    - The earlier the age of onset of one's depression, the longer the delay to appropriate diagnosis.
        - 15-17 year delay if onset 12 or younger
        - 10-12 year delay if onset between 13-18
        - 2-6 year delay if onset between 19-29
        - 2-3 year delay if onset 30 or older
    - Misdiagnosed patients
        - Average of 4 doctors before correct diagnosis
        - More likely to receive antidepressants
        - Less likely to receive mood stabilizers
    - Untreated bipolar disorder is associated with decreasing time between mood episodes (Kraeplin, 1921 and Roy-Byrne et al, 1985): 4 years between first and second, 2-3 years between second and third, 2 years between third and fourth, 1 year between fourth and fifth
    - Some factors that increase the chance that a depression is really a bipolar (and not a unipolar) depression:
        - *family history of formal bipolar disorder in a first degree relative
        - *highly recurrent depressive episodes
        - *onset before age 20
        - *postpartum depression
        - at least 3 antidepressant trials
        - loss of response to antidepressant
        - atypical depression (hypersomnia, hyperphagia, rejection hypersensitivity, leaden paralysis)
        - hyperthymic when not depressed
    - Edvard Munch, describing what was likely a bipolar depression: "The second half of my life has been nothing but a struggle to keep myself upright. My path took me along the edge of an abyss, a bottomless pit…Every so often I left the path and threw myself into the commotion of life, amongst people. But I always had to return to the path along the abyss…My art was self-confession…in my case the fear of life is also a need…Without (it) I would be a ship without a helmsman."

## Bipolar depression: Characteristics

- Family history (mood or bipolar disorders)
- Early onset (more familial), multiple recurrences
- Anergic-retarded ("atypical"): classic
- Often postpartum, psychotic, or agitated
- Mixed-states misdiagnosed as simple depressive
- Hypomania: needs independent verification
- Most of morbidity (%-time ill) in bipolar disorder
- High co-morbidity (substance, anxiety) & disability
- High suicide risks (highest if mixed)
- High antidepressant demand (patients & clinicians)
- Antidepressants overused
- Mood-stabilizers & SGAs: underused & limited
- Costs: much higher than in UP depression

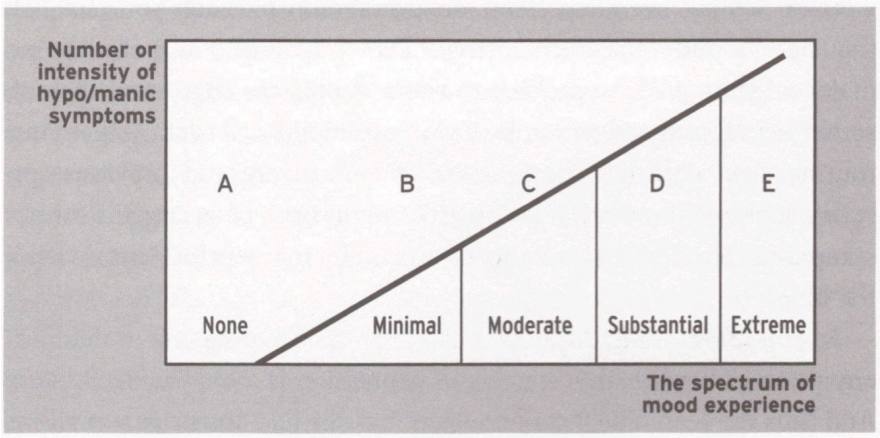



Figure 1.2. The continuum of hypomanic/manic symptoms among patients with mood disorders

Table 1.1. **Symptoms of bipolarity across the mood spectrum**

| Symptom | Point A | Point B | Point C | Point D | Point E |
|---|---|---|---|---|---|
| Distractability | No manic symptoms | Slightly unfocused | Notable difficulty staying on task | ADD could be invoked | Nonfunctional |
| Insomnia | No disturbance | 6 hours or less, sometimes broken | 4 hours or less, frequent awakenings | 2 hours or less, waking too early | Nights of no sleep at all |
| Grandiosity | No extremes of self-esteem | Pleased with accomplishments, abilities, prospects | "Life of the party," charismatic | Intrusively self-confident, irritating | Grandiose; "narcissistic," unshakeable beliefs in self |
| Flight of ideas | Nothing unusual | Many ideas about many things | Highly creative, making rapid connections | Experiencing many unrelated ideas at high speed | Psychotic disconnection of thought (highly tangential to loose) |
| Activity level | Unremarkable | Highly energetic, engaged | Multiple projects at quick pace | So many projects, not completing them, bouncing one to another | Constant motion, ineffectual |
| Speech | Normal prosody | Quick but not otherwise remarkable | Rapid speech, occasionally difficult to follow | Very rapid speech, losing most listeners | The proverbial "fire hose" |
| Impulsive risk | Safe or minimally risky behavior | Some choices regrettable and not thought through in advance | Increased risk taking, impulsive | Spending hundreds of dollars, increased "sex, drugs and rock-and-roll" | Spending sprees far beyond means; illegalities, dangerous choices |

- In patients with major depression, the variables associated with eventual re-diagnosis to bipolar depression include the following (together of which are associated with a 27-65% chance of progression to bipolar II); some of the following is overly technical:
    - Mood lability:
        - Mood lability refers to a pattern whereby moods shift frequently and/or suddenly from one mood state to another greater in intensity, duration, and/or frequency than would be expected by external life events
        - It appears to be a marker for affective dysregulation, which means poorly regulated feeling/mood states, even if the dysregulation is not impairing.
        - Often associated with other cyclothymic tempermental traits
        - Specificity is 86%; this means that 86% of those who are or have been experiencing formal mood lability are suffering from bipolar disorder and 14% are not
        - Sensitivity is 42%; this means that 42% of those who are not or have not been experiencing formal mood lability are NOT suffering from bipolar disorder and

58% are. This means that the presence of mood lability is more critical for the accurate re-diagnosis of unipolar depression to bipolar depression than the absence of mood lability for the ruling out of bipolar depression

- Four or more episodes of major depression
  - ¼ of patients with unipolar depression experienced no further mood episodes in a 13.5 year follow-up (Stephens and McHugh, 1991)
  - Patients with first unipolar major depressive episode are very likely to recover and be symptom-free at 12 year follow-up (Tohen, 1990)
  - Nearly all patients with bipolar disorder have a recurrent mood episode within 4 year follow-up (Tohen, 1990)
  - The usual natural history of bipolar illness is one episode per year (Kessing, 1998)
- Brief episodes of major depression (e.g., duration less than 3 months)
  - Average duration of untreated unipolar depression is 6-12 months
  - Average duration of untreated bipolar depression is 3-6 months
- Abrupt onset and cessation of mood episodes
- Onset of depression before age 25: 68% specificity, 71% sensitivity
  - New-onset depression in a child or young adult has a 50% chance of evolving into bipolar illness by age 30.
- Atypical depressive features
  - Depressed and/or irritable mood
  - Reactive mood—can lift under right circumstances
  - Hypersomnic-psychomotor retarded (which means oversleeping and slowed body movements; 88% specificity, 59% sensitivity)
  - Leaden paralysis
  - Interpersonal/rejection sensitivity
  - Carbohydrate craving
  - Phobic anxiety
  - Obsessive-compulsive features
  - Somatization (body aches, pains, concerns
  - Panic/sub-panic
  - Worse in evening (reversed diurnal variation)
  - Self-pity
  - Demandingness
  - Jealousy/suspiciousness
  - Ideas of feelings that reference that people or things are referring to you or focused on you or reaching out to you more than is likely given the evidence

- Response to antidepressants
  - Loss of response to an antidepressant, "tolerance" to antidepressants
    - 18% of patients with unipolar depression develop tolerance
    - 58% of patients with bipolar disorder develop tolerance
  - Lack of efficacy of three or more antidepressants
  - Worse or wired on antidepressants/pharmacological-induced hypomania: 100% specificity (no false positives); 32% sensitivity (many false negatives)
    - less than 1% of persons with unipolar (Akiskal, 2003; Ghaemi, 2004)
      - can't induce rapid cycling if unipolar
    - 20-50% of patients with bipolar disorder (Akiskal, 2003; Ghaemi, 2004)
      - can induce rapid cycling with increased frequency of mood episodes over time
    - Often mixed states
    - Subthreshold hypomania could be experienced more as irritability (Goldberg, Truman, 2003)

        - Subthreshold irritable hypomania could become chronic (El-Mallakh, Karippot, 2005)
        - Could lead to subsyndromal depressive or manic states (called roughening by Sachs, 1996)
- Hyperthymic personality or subthreshold hypomania/hyperthymia/cyclothymia
- Bipolar family history, particularly in a first degree relative: 98% specificity; 56% sensitivity
- Psychotic features: 85% specificity, 42% sensitivity
- Post-partum onset: 84% specificity, 58% sensitivity

| | | | | | | |
|---|---|---|---|---|---|---|
| How old were you when you first were depressed? *(circle one)* | As long as I can remember | Grade School | Middle School | High School | 18–24 | >24 |
| How many episodes of depression have you had? | One | 2–4 | 5–6 | >10 | | |
| Have antidepressants ever caused: *(circle all that apply)* | Excessive energy | Severe Insomnia | Agitation | Irritability | Racing thoughts | Talking a lot |
| How many antidepressants have you tried, if any? | None | 1 | 2 | 3 | >3 | |
| Has an antidepressant you took worked at first, then stopped working? | No | Yes | | | | |
| Do your esipsodes *start* gradually, or suddenly? | Gradually | Can't say | Suddenly | | | |
| Do your episodes *stop* gradually, or suddenly? | Gradually | Can't say | Suddenly | | | |
| Did you have an episode after giving birth? | No | Within 6 months | Within 2 months | Within 2 weeks | | |
| Are your moods much different at different times of year? | No effect of time of year | Yes, seasonal shifts | | | | |
| When you are depressed, do you sleep differently? | No | Sleep less | Sleep more | | | |
| When you are depressed, do you eat differently? | No | Eat less | Eat more | | | |
| When you are depressed, what happens to your energy? | Nothing | It varies a lot | Very low | Extremely low, can hardly move | | |
| In episodes, have you lost contact with reality? (delusions, people thought you were odd) | No | Yes | | | | |

Table 2.1. **Non-manic markers of bipolar disorder and their relative strengths**

| Relative strength | Variable |
|---|---|
| Strong | First-degree relative with reliable diagnosis of bipolar disorder<br>First episode of depression between ages 18–24<br>Postpartum depression<br>Highly recurrent episodes of depression<br>Ever psychotic (without drugs, etc.)<br>Transient hypomania/mania on antidepressant |
| Less strong | Very short episodes of depression, with rapid onset and offset<br>Antidepressant loss of response (a.k.a. "Prozac poop-out")<br>Having tried more than three antidepressants<br>Seasonality of mood<br>"Atypical depression" features when depressed: hypersomnic, hyperphagic, leaden anergy, mood reactivity |

Table 2.2. **The WHIPLASHED mnemonic**

| | |
|---|---|
| W | Worse or "wired" when taking an antidepressant |
| H | Hypomania, hyperthymic temperament, or mood swings by history |
| I | Irritable, hostile, or showing mixed features in depression |
| P | Psychomotor (retardation or agitation) |
| L | Loaded family history of affective illness (not necessarily just bipolar disorder) |
| A | Abrupt onset or termination of episodes |
| S | Seasonal or postpartum pattern of depression |
| H | Hyperphagia or hypersomnia |
| E | Early age of onset of depression |
| D | Delusions, hallucinations, or other psychotic features |

- Cyclothymic Temperament/Cyclothymia
    - Self-Administered Symptom Scale for detecting cyclothymic temperament (Akiskal et al, 2005: TEMPS-A Scale for Cyclothymic Temperament (Short Version))
        - My ability to think varies greatly from sharp to dull for no apparent reason
        - I constantly shift between feeling lively and sluggish
        - I get sudden shifts in mood and energy
        - The way I see things is sometimes vivid but at other times lifeless
        - My mood often changes for no reason
        - I go back and forth between being outgoing and being withdrawn from others
        - My moods and energy are either high or low, rarely in between
        - I go back and forth between feeling overconfident and feeling unsure of myself
        - My need for sleep varies a lot from just a few hours to more than 9 hours
        - I sometimes go to bed feeling great and wake up in the morning feeling life is not worth living
        - I can really like someone a lot and then completely lose interest in them
        - I am the kind of person who can be sad and happy at the same time
- Hyperthymic temperament/cyclothymic hyperthymia/hypomania
    - Characterized by the following possible patterns:
        - Morning
            - Early morning awakenings about 1-2 hours prior to normal waking time
            - Arising from sleep with racing thoughts
            - Arising from sleep increased activity or a burst of energy
        - Evening
            - Burst of energy and activity in the late evening and lasting into the early morning hours
        - Energy often used adaptively by cleaning, rearranging furniture, writing, painting, or engaging in other projects
        - These shifts may be followed by a brief period of sleep (which may be difficult to initiate because of racing thoughts, and then a resumption of activity
        - Mood may be elevated, expansive or irritable
        - In women, irritable mood is more common than elation, often giving rise to angry outbursts and damaging significant relationships
    - Hyperthymia/Hypomania Self-Administered Symptom Scale
        - Do you have periods of energy, activity, or ideas that come and go abruptly?
        - During these periods, are you
            - Productive
            - Creative
            - Frenetic but aimless and unproductive
        - During these periods, do you feel
            - Unconquerable
            - Convinced of your self-worth, talents and abilities
            - Positive about the future
            - Talkative?
            - Distinctly more social?
        - During these periods, do you feel that your thoughts are racing or that your mind is crowded with thoughts?
        - During these periods, do you need less sleep
        - During these periods, do you
            - Do things you later regret
            - Make plans that you find impossible to complete or follow through

        - Take on tasks that you suddenly lose interest in or find you are without the energy or desire to complete?
    - Are you particularly more depressed or lethargic immediately before or immediately following these periods of energy?
    - Does it feel like you "crash," needing much more sleep and with extreme lethargy>
    - What is your mood during these periods of energy and activity?
        - Elated?
        - Joyful?
        - Unrestrained with a sense of self-importance?
        - Distinctly or particularly irritable or agitated?
    - Do others notice your change in mood or energy

- MDQ Symptom Scale for Hypomania
    - Has there ever been a period of time when you were not your usual self and...
        - ... you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?
        - ... you were so irritable that you shouted at people or started fights or arguments?
        - ... you felt much more self-confident than usual?
        - ... you got much less sleep than usual and found that you didn't really miss it?
        - ... you were more talkative or spoke much faster than usual?
        - ... thoughts raced through your head or you couldn't slow your mind down?
        - ... you were so easily distracted by things around you that you had trouble concentrating or staying on track?
        - ... you had much more energy than usual?
        - ... you were much more active or did many more things than usual?
        - ... you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?
        - ... you were much more interested in sex than usual?
        - ... you did things that were unusual for you or that other people might have thought were excessive, foolish or risky?
        - ... spending money got you or your family in trouble?
    - If you checked YES to more than one of the above, have several of these ever happened during the same period of time?
    - How much of a problem did any of these cause you - like being able to work; having family, money or legal troubles; getting into arguments or fights?
    - Have any of your blood relatives (i.e. children, siblings, parents, grandparents, aunts, uncles) had manic-depressive illness or bipolar disorder?
    - Has a health professional ever told you that you have manic-depressive illness or bipolar disorder?
    - How big of a problem do you feel this is?
- Lifelong traits of hyperthymic temperament
    - Upbeat and exuberant; bubbly
    - Energy-driven; thrives on action
    - Self-reliant, self-assured, confident
    - Optimistic
    - Self-employed
    - Vivid
    - Versatile with broad interests
    - Active
    - Extraverted
    - Articulate and jocular
    - Verbally aggressive
    - Strong-willed
    - Risk-taking
    - Full of plans
    - Habitual short sleeper (6 hours or less)
    - Uninhibited and novelty/sensation-seeking
    - Breaking social norms
    - Generous and spendthrift
    - Overinvolved and meddlesome
    - Muted, highly adaptive version of mania at the trait level
- Signature temperament of leaders and famous people
- More frequent in families of persons with bipolar disorder (Chiaroni, 2004)
- Predictor of antidepressant-induced mania (Henry, 2001)

- Back to cyclothymic temperament
    - Symptoms may include:
        - Self-esteem
            - shaky self-esteem alternating between lack of self-confidence and overconfidence; present in 75% of patients
            - Extraversion alternating with introversion; present in 50% of patients
        - Sleep and energy
            - Increased sleep alternating with decreased need for sleep; present in 75% of patients
            - Lethargy/sluggishness alternating with good energy/liveliness
            - Energy usually high or low with little in between degrees.
            - Restlessness
            - Decreased verbal output alternating with talkativeness
        - Concentration
            - Periods of mental confusion alternating with periods of sharpened creative thinking; present in 50% of patients
            - Unevenness in quantity and quality of work; present in 75% of patients
            - Sharp/intense perceptions alternating with dulled or lifeless perceptions.
            - Racing thoughts, which may manifest itself in spurts of creativity, such as writing verses
        - Mood
            - Sudden shifts in mood or energy out of nowhere
            - Mood often changes for no reason
            - Mood usually high or low with little in-between
            - Feel all emotions intensely.
            - Depressive or irritable mood predominates; present in 50% of patients
            - Explosive, aggressive outbursts; present in 50% of patients
            - Unexpected tearfulness alternating with excessive punning and jocularity
        - Other
            - Repeated shifts in work, study, interest, or future plans; present in 50% of patients
            - Buying sprees, extravagance, or financial disasters; present in 75% of patients
            - Drug or alcohol abuse; present in 50% of patients
            - Unexplained promiscuity or extramarital affairs; present in 40% of patients
            - Joining new movement with enthusiasm, rapidly changing to disillusionment; present in 25% of patients.
            - Often start things and lose interest in them
            - Often have a strong urges to do outrageous things.
    - Formal cyclothymia is define as the subthreshold oscillation of hypomanic (aka, hyperthymic) and depressive (aka dysthymic) periods for at least 2 years (1 year in youth), the presence of numerous periods with hypomanic (or hyperthymic) symptoms and numerous periods with depressive symptoms that do not meet criteria for a hypomanic episode or a major depressive episode; not without symptoms for more than 2 months at a time
    - 50% of folks with cyclothymic temperament will subsequently develop bipolar I or II
    - Other data suggest 33-88% progress to bipolar II
    - 6% of population may have cyclothymic temperament
    - May serve as the reservoir of bipolar genes and perhaps of greatness in human societies
- Bipolar depressive symptoms
    - Clients often suffer chronically from subsyndromal depressive symptoms and the concomitant functional impairment even in the absence of a frank mood episode.
    - Clients typically spend more time struggling with depressive symptoms than with symptoms of mania or hypomania. Depressive relapses four times more likely than hypomanic or manic relapses.

- In bipolar I, patients (studied over 10 years) spent three to five times more days depressed than they spent hypomanic or manic
- In bipolar II, patients (studied over 10 years) spent nine times more days depressed than they spent hypomanic
- When projected across a lifetime, people with bipolar disorder will "lose" 15 years to depression
- Subsyndromal depressive symptoms are associated with functional impairment in work, home and relationships
- Bipolar depression is more difficult to treat than mania; in patients with bipolar I, it takes twice as long to treat bipolar depression to remission as it does to treat mania; bipolar depression is also more likely to be associated with a greater likelihood of treatment resistance, as reflected by failure to remit across at least 1 year of continuous treatment

- The Bipolar II Spectrum
  - Most common expression of bipolarity
  - May be more common than major depressive disorders
  - Involves episodes of depression, periods of normal mood, and episodes of hypomania lasting 1 or more days (if the duration criterion, currently set at 4 days minimum, is loosened).
  - Often involves anxiety, irritability, and rejection sensitivity
  - Benazzi:
    - Depression with two manic-like symptoms present in 72% of patients with bipolar II and 42% of patients with unipolar depression
    - Depression with three manic-like symptoms
      - present in 47% of patients with bipolar II and 7.6% of patients with unipolar depression
      - in a follow-up of 563 patients, present in 50% of patients with bipolar II
    - Overlaps with cyclothymia, borderline personality disorder, atypical depression, agitated ("pseudo-unipolar") depression.
  - General
    - 30-57% of adults with bipolar disorders
      - More common in adult women
      - 57% in 908 patients, 14,328 visits over 7 years in 7 sites (4 in the US and 3 in Europe; Hamshere, 2005), 57% of visits by patients with hypomania met criteria for mixed episode.
    - 20-85% of youth with bipolar disorders (e.g., 82% Dilsaver, 2005)

- Hypomania
    - Relatively consistent change in character and neurovegetative symptoms over at least 1-4 days (formally 4 days)
    - Symptoms of the more sunny or euphoric aspects of hypomania include:
        - Often, symptoms feel good and adaptive
        - Carefree and cheerful
        - High energy
        - Vitality
        - Less need for sleep
        - Sharper senses
        - Creative thinking
        - Overconfident
        - Overly optimistoc
        - Overinvolvement in new projects, activities
        - Talkative
        - Overly gregarious
        - People-seeking
        - Heightened sexual drive and behavior
        - Spending sprees
        - Increased consumption of coffee, cigarettes, and alcohol
        - Increased laughter, joking, and puns
        - Often recurrent
        - Impairing or causing significant distress
        - Cognitive errors
            - Positive fortune-telling
            - Overrelying on luck
            - Underestimating risk or danger
            - Disqualifying the negative
            - Overvaluing the positive
            - Overvaluing immediate gratification
            - Misinterpreting others' intentions

Table 2.3. **The Bipolarity Index**

| | Episode characteristics (DSM symptoms) |
|---|---|
| 20 | Prominent euphoria or grandiosity |
| 15 | Mixed state with full manic and full depressed symptoms |
| 10 | Hypomania, cyclothymia, or manic after antidepressant (within 12 weeks) |
| 5 | Hypomanic after antidepressant, or subthreshold hypomania, psychotic or postpartum depression |
| 2 | Recurrent unipolar depression or ever psychotic |
| | **Family history** |
| 20 | At least one first-degree relative with clear bipolar disorder (BD) |
| 15 | • Second-degree relative with clear BD or<br>• First-degree relative with depressions and behavioral evidence suggesting BD |
| 10 | • First-degree relative recurrent depressions or schizoaffective disorder or<br>• Any relative with clear BD or recurrent depressions with behaviors suggesting BD |
| 5 | • First-degree relative with a substance use disorder or<br>• Any relative with possible bipolar disorder |
| 2 | • First-degree relative with possible recurrent depressions or<br>• First-degree relative with anxiety (including PTSD or OCD), eating disorder, or ADD/ADHD |
| | **Age of onset (first depression)** |
| 20 | 15–19 years old |
| 15 | Less than 15 or between 20 and 30 |
| 10 | 30–45 |
| 5 | After age 45 |
| | **Course of illness and associated features** |
| 20 | Recurrent, distinct manic episodes separated by at least two months of full recovery |
| 15 | Same as above but hypomanic; or same but or incomplete recovery between episodes |
| 10 | • Any substance use disorder (except nicotine/caffeine) or<br>• Psychotic only during mania or<br>• Legal issues when manic |
| 5 | • More than three prior episodes of depression or<br>• Recurrent hypomania but with incomplete recovery between episodes or<br>• Borderline PD; anxiety (including PTSD and OCD); eating disorder; hx of ADHD or<br>• Gambling or other risky behaviors or<br>• Behavioral evidence of perimenstrual exacerbation of mood symptoms |

*continued*

| | |
|---|---|
| 2 | • Baseline hyperthymic temperament when not manic or depressed or<br>• Marriage three or more times (including to the same individual) or<br>• Starting a new job and changing it within a year, twice or more or<br>• More than two advanced degrees |
| | **Response to treatment** |
| 20 | • Full recovery within four weeks of treatment with a mood stabilizer |
| 15 | • Full recovery but within 12 weeks, or relapse within 12 weeks of stopping treatment or<br>• Switch to manic or mixed within 12 weeks of starting an antidepressant or increasing the dose |
| 10 | • Worsening dysphoria or mixed during antidepressant Rx (not akathisia, anxiety, sedation) or<br>• Partial response to one or two mood stabilizers or<br>• ntidepressant-induced new or worsening rapid cycling |
| 5 | • Three antidepressants with no response or<br>• Switch to hypomania or mania with antidepressant withdrawal |
| 2 | • Near-complete response to antidepressant withdrawal within a week |

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## The Bipolar Spectrum Diagnostic Scale

(Used by permission of Dr. Nassir Ghaemi, Oct. '02; additional history from developer Dr. Ron Pies, June '03 )

The BSDS is a test for subtle versions of bipolar disorder. Before you start this test, you should know that it will not give you a "yes or no" answer as to whether you have bipolar disorder.

Put a check after each sentence in the paragraph above that accurately describes you.

Some individuals noticed that their mood and/or energy levels shift drastically from time to time _____ .
These individuals notice that, at times, they are moody and/or energy level is very low, and at other times, and very high_____.
During their " low" phases, these individuals often feel a lack of energy, a need to stay in bed or get extra sleep, and little or no motivation to do things they need to do_____ .
They often put on weight during these periods_____ .
During their low phases, these individuals often feel "blue," sad all the time, or depressed_____ .
Sometimes, during the low phases, they feel helpless or even suicidal _____ .
Their ability to function at work or socially is impaired _____ .
Typically, the low phases last for a few weeks, but sometimes they last only a few days _____ .
Individuals with this type of pattern may experience a period of "normal" mood in between mood swings, during which their mood and energy level feels "right" and their ability to function is not disturbed _____ .
They may then noticed they marked shift or "switch" in the way they feel _____ . Their energy increases above what is normal for them, and they often get many things done they would not ordinarily be able to do _____ .
Sometimes during those "high" periods, these individuals feel as if they had too much energy or feel "hyper" _____ .
Some individuals, during these high periods, may feel irritable, "on edge," or aggressive _____.
Some individuals, during the high periods, take on too many activities at once _____.
During the high periods, some individuals may spend money in ways that cause them trouble_____ .
They may be more talkative, outgoing or sexual during these periods _____ .
Sometimes, their behavior during the high periods seems strange or annoying to others _____ .
Sometimes, these individuals get into difficulty with co-workers or police during these high periods _____ .
Sometimes, they increase their alcohol or nonprescription drug use during the high periods _____ .

After you have read this passage, please decide which of the following is most accurate:

This story fits me very well, or almost perfectly_____ .
This story fits me fairly well_____ .
This story fits me to some degree, but not in most respects_____ .
This story doesn't really describe me at all_____ .

Another Symptom Scale (greatly overlaps with scale above)

## Hypomania/Mania Symptom Checklist (HCL-32)

(Journal of Affective Disorders 2005, Angst and colleagues)

At different times in their life everyone experiences changes or swings in energy, activity and mood ("highs and lows" or "ups and downs"). The aim of this questionnaire is to assess the characteristics of the "high" periods.

1. First of all, how are you feeling today compared to your usual state?

2. Compared to other people, my average level of activity energy and mood

is generally rather stable and even | is generally higher | is generally lower | has frequent periods of ups and downs

3. Please try to remember a period when you were in a "high" state (while not using drugs or alcohol). In such a state:

- I need less sleep
- I feel more energetic and more active
- I am more self-confident
- I enjoy my work more
- I am more sociable (make more phone calls, go out more)
- I want to travel and/or do travel more
- I tend to drive faster or take more risks when driving
- I spend more money/too much money
- I take more risks in my daily life (in my work and/or other activities)
- I am physically more active (sport etc.)
- I plan more activities or projects.
- I have more ideas, I am more creative
- I am less shy or inhibited
- I wear more colorful and more extravagant clothes/make-up
- I want to meet or actually do meet more people
- I am more interested in sex, and/or have increased sexual desire
- I am more flirtatious and/or am more sexually active
- I talk more
- I think faster
- I make more jokes or puns when I am talking
- I am more easily distracted
- I engage in lots of new things
- My thoughts jump from topic to topic
- I do things more quickly and/or more easily
- I am more impatient and/or get irritable more easily
- I can be exhausting or irritating for others
- I get into more quarrels
- My mood is higher, more optimistic
- I drink more coffee
- I smoke more cigarettes
- I drink more alcohol
- I take more drugs (sedatives, anti-anxiety pills, stimulants)

A Scale for Adolescents

## Mood Disorder Questionnaire-Adolescent Version

Has there ever been a time for a week or more when your adolescent was not his/her usual self and…

| | Yes | No |
|---|---|---|
| …felt too good or excited? | | |
| …was so irritable that he/she started fights or arguments with people? | | |
| …felt he/she could do anything? | | |
| …needed much less sleep? | | |
| …couldn't slow his/her mind down or thoughts raced through his/her head? | | |
| …was so easily distracted by things | | |
| …had much more energy than usual? | | |
| …was much more active or did more things than usual? | | |
| …had many boyfriends or girlfriends at the same time? | | |
| …was more interested in sex than usual? | | |
| …did many things that were foolish or risky? | | |
| …spent too much money? | | |
| …used more alcohol or drugs? | | |

If you checked Yes to more than one of the above, have several of these ever happened to your adolescent during the same period of period of time?

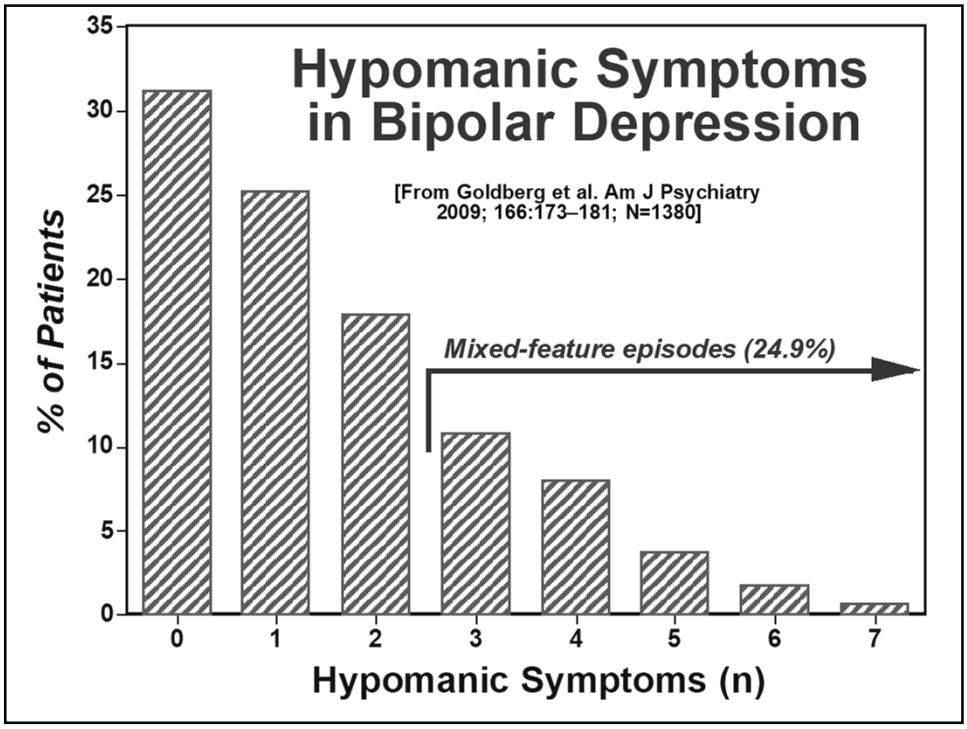
How much of a problem did any of these cause your adolescent—like school problems, failing grades, problems with family and friends, legal troubles (no problem, minor problem, moderate problem, or serious problem)?

- Mania, proposed enrichment of DSM-IV symptomatologic criteria (per Akiskal)
    - Euphoria—which can easily shift to irritability or hostility
        - Indeed, clinical experience dating back to Kraeplin suggest that irritability and aggressive behavior are more important components of manic episodes in many patients
        - Euphoric mania represents a minority of manic episodes
    - Psychomotor agitation
        - Restlessness
        - Inner agitation
            - Feelings of unprovoked rage
            - Easily provoked and enraged when provoked
        - Inner anxiety
        - Can feel like bursting inside, like a violent force is smashing through one's body
    - Boundless energy
    - Grandiose self-esteem
    - Pressure of speech—flight of ideas
        - In "flight of ideas", the content of the ideas and somehow the pattern of thoughts are reflected in the content and pattern of the speech itself.
        - In "racing thoughts", the patient may repeat monotonous laments, but the great energy involved in these depressive lamentations and in this speech denote the mixed depressive-manic nature of this symptoms. In some cases, there is a certain degree of pressured speech. The ideas come and go rapidly as if they were hunting each other or continuously overlapping without any link between them
        - Crowded thoughts
        - Can feel unrelentingly painful and oppressive
        - Often more intense at night and cause insomnia
        - Depressive ruminations are different: only a few thoughts carry the anxieties and fears of the patient and they are constantly present or recur frequently; the patient complains of their content but not of their course.
    - Heightened perceptions
    - Marked distractibility of attention
    - Little need for sleep
    - Increased risk-taking—squandering money
    - Social disinhibition
    - Lechery
    - Denial—loss of insight—impaired judgment
- Mixed mood states (also see dimensional conceptualizations)
    - Technically, this is when someone is experiencing full criteria for both a major depressive episode and either a hypomanic or manic episode at the same time; this is a categorical approach.
    - Informally, it is when someone is experiencing a mood episode that has some combination of symptoms from both depression and hypomania/mania; this is a dimensional approach, preferred by many including McElroy et al, 1992 and 1995, Bauer et al, 1994, Perugi et al, 1997, and below.
        - Some authors use the concept of "mixed depressive state" or "agitated depression" to describe "soft" mixed states defined by a depressive state associated with manic or hypomanic symptoms (Akiskal et al, 2005; Benazzi, 2002; Koukopoulos and Koukopoulos, 1999)
        - Suppes et al, 2005: mixed hypomania is common
        - Akiskal and Benazzi, 2005: dysphoric hypomania
    - Mixed states are common, difficult to treat, potentially severe, and may carry a high risk of suicide
    - Mixed states are heterogenous in their phenomenology, such that the rates reported in studies vary from 14%-67%
    - 60% of manias and hypomanias are elated/euphoric, but 40% are dysphoric
    - Henry et al, 2007, using a dimensional model (compared to a categorical model based on DSM-IV) identified 3 clusters of mixed episodes, all of which included equivalent degrees of sadness:
        - Depressive cluster
            - Clients exhibited emotional hypo-reactivity
            - Inhibition in cognitive processes and psychomotor activity
            - Frequency of emotions in the previous week, in decreasing order:
                - Sadness
                - Anxiety
                - Panic
                - Irritability
                - Anger
                - Joy
                - Exaltation (~0)
            - Formal diagnostic breakdown
                - 83.3% met formal (DSM-IV) criteria for pure major depressive episode

            - 9.5% met formal criteria for major depressive episode with manic symptoms
            - 7.2% met formal criteria for mixed episode
            - 0 met formal criteria for hypomania or mania
    - Hypomanic/manic cluster
        - Clients exhibited emotional hyper-reactivity
        - Excitation in cognitive processes and psychomotor activity
        - Frequency of emotions in the previous week, in decreasing order:
            - Irritability
            - Exaltation
            - Anxiety
            - Sadness
            - Joy
            - Anger
            - Panic
        - Formal diagnostic breakdown
            - 0 met formal criteria for pure major depressive episode
            - 0 met criteria for major depressive episode with manic symptoms
            - 9.5% met formal criteria for mixed episode
            - 90.5% met formal criteria for hypomania or mania
    - Mixed cluster
        - Clients exhibited emotional hyper-reactivity
        - Excitation in cognitive processes and psychomotor activity
        - Frequency of emotions in the previous week, in decreasing order:
            - Anxiety
            - Sadness
            - Irritability
            - Panic
            - Anger
            - Joy
            - Exaltation
        - 9.2% met formal criteria for pure major depressive episode
        - 47.4% met formal criteria for major depressive episode with manic symptoms
        - 18% met formal criteria for mixed episode
        - 25% met formal criteria for hypomania or mania
- Historical concepts of mixed states:
    - Weygandt, 1899: "it is very common, both in the manic and in the depressive episodes of manic-depressive or circular insanity, for there to be not only periods of time which are mostly without symptoms, but also, often, hours or days when the symptoms switch to the opposite pole. So, during a manic episode, euphoria can suddenly change into a deeply depressive mood, while the other symptoms of exaltation, such as hyperkinesia and hyperactivity, distractibility and excitability, logorrhea (excessive talking), and flight of ideas, persist; or after a month-long depression, suddenly a smile can be observed on the face of the patient and the depressive mood can change for hours or days into a high or manic mood, but without any change in psychomotor behavior, in the inhibition or, sometimes, in the severe stupor. Less common, but actually frequent enough if observation is careful, is a temporary change in psychomotor behavior while the affective aspects of the psychosis continue without any change; the patients remain euphoric, but the manic excitability changes into a psychomotor inhibition. Instead of tireless hyperactivity, the patients stay in bed, show slowness of movement and little or no mutism. In patients with the phenomenological picture of depression with stupor, one can sometimes observe a change to mild excitability, agitation and an urge to speak lasting for hours or days, while the depressive mood continues."
    - Kraeplin, 1900's: described 6 mixed states, from manic states with dysphoric features to depressive states with some agitation. He defined mood states as starting from excitement or inhibition of cognitive processes, mood and psychomotor activity (volition, per Kraeplin).
- Symptoms:
    - Unrelenting dysphoria or irascibility and instability
    - Irritability
        - Irritable-hostile depression (Benazzi, Akiskal, 2005) as distinct from but similar to agitated depression and borderline personality disorder.
        - ~60% of patients with bipolar disorder suffered irritability versus ~37% of unipolar depressed patients (Benazzi, Akiskal, 2005).
        - 62% of patients with bipolar disorder suffered from anger attacks versus 26% of unipolar depressed patients (Perlis, 2004)

- Severe agitation—may be goal-directed (as opposed to the hyperarousal, inner tension, fidgeting, or pacing in the absence of goal-directedness seen in agitated depression); may exist on a backdrop of psychomotor retardation
- Anhedonia (feeling that nothing is pleasurable)
- Pressured speech
- Refractory free-floating anxiety (very common) with panic attacks
- Unendurable or intense sexual excitement
- Intractable insomnia
- Suicidal thoughts/obsessions (14-26% versus 0-7% in pure mania)
- "Histrionic" demeanor yet with genuine expressions of intense suffering
- Racing thoughts amidst extreme fatigue
- Grandiosity
- Persecutory delusions
- Confusion
- Examples of behaviors associated with mixed states
  - Depressed and having an affair (or with other types of hypersexuality)
  - Actively considering suicide with building a vacation in Europe
  - Engaging in spending sprees, even shoplifting, during a depressive episode
  - Telling jokes with morbid themes or joking about one's suicidal thoughts
  - Panic states lasting hours or days driven by intense restlessness and irritable mood
  - Depressed mood with severe insomnia due to racing thoughts

- Often pre-morbid depressive temperament
- May arise from the intrusion of an affective episode into an opposite affective temperament or one with a high degree of chronic instability such as the cyclothymic temperament.

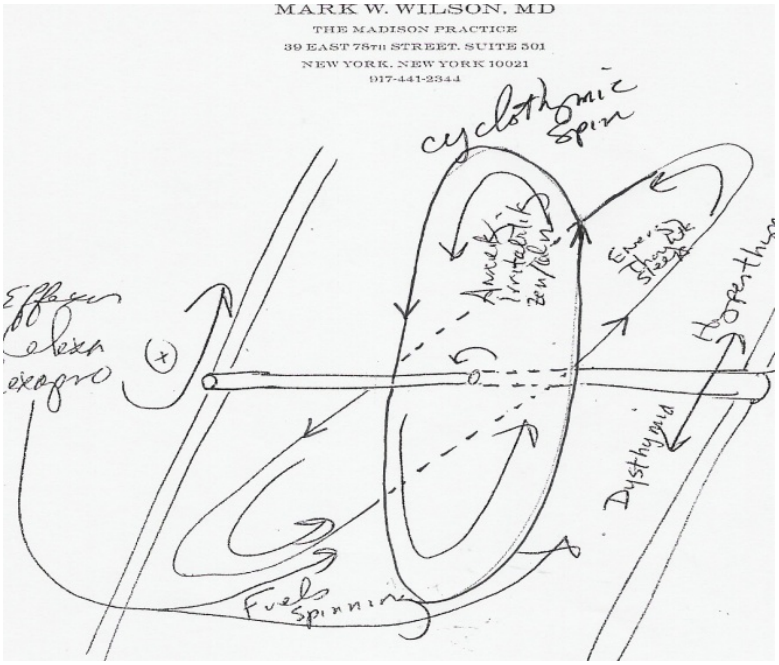


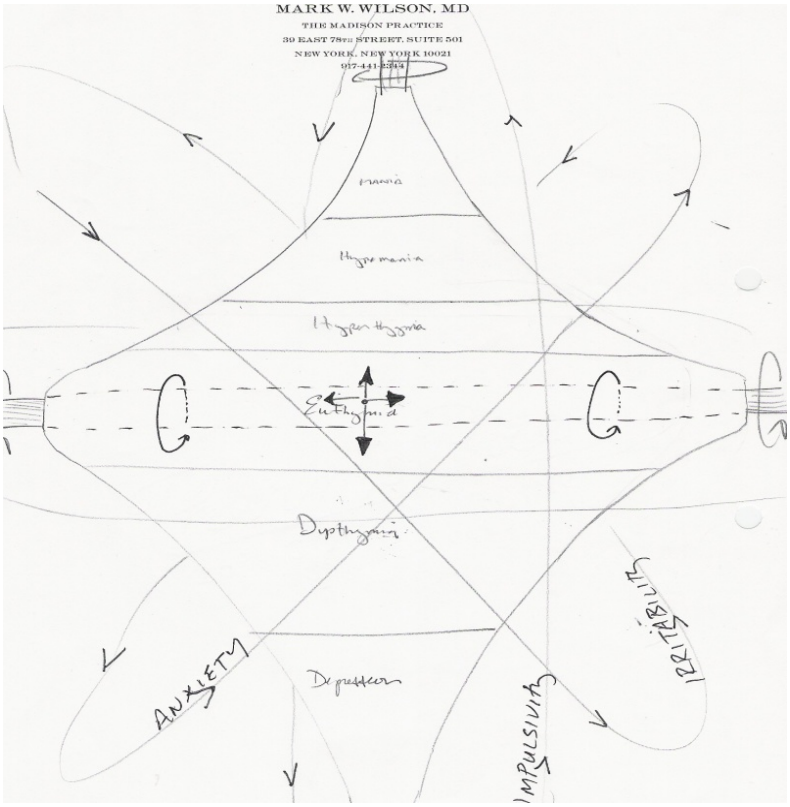
- Risk of recurrence after a single manic or mixed episode - a systematic review and meta-analysis
  Lars Vedel Kessing, Per Kragh Andersen, Maj Vinberg
  *Bipolar Disorders 2018, 20 (1): 9-17*
  **OBJECTIVES:** For the first time to estimate the risk of recurrence among patients with a single manic/mixed episode by systematically reviewing prior studies on cohorts of adults, and cohorts of children and adolescents, respectively.
  **METHODS:** A systematic literature search up to August 2017 was carried out including studies in which < 25% of the participants were estimated to have had a mood episode that required pharmacological treatment prior to the index manic or mixed episode at inclusion.
  **RESULTS:** Three studies including a total of 293 adult patients with a single manic or mixed episode and three studies of children and adolescents including 126 patients were identified. In the adult studies, 31%, 40% and 42% experienced recurrence after recovery within 1 year, 59% after 2 years, and 58% after 4 years, respectively. In the studies on children and adolescents, 40% and 52% experienced recurrence after recovery within 1 year, 30% and 60% after 2 years and 64% and 67% after 4 to 5 years, respectively. Results from meta-analyses showed a 1-year rate of recurrence of 35% (95% confidence interval [CI]: 30-41%) in adults, and in adolescents/children, a 1-year rate of recurrence of 48% (95% CI: 38-58%), a 2-year rate of 46% (95% CI: 33-60%) and a 4-5-year rate of recurrence of 65% (95% CI: 52-77%; as data from different studies were included at 1, 2 and 5 years, rates of recurrence did not increase steadily with time).
  **CONCLUSIONS:** The rate of recurrence is high among adults as well as children and adolescents. It is important that clinicians and patients as well as relatives are well informed about these high risks when deciding to start maintenance treatment or not following onset of a single manic or mixed episode.
- Rapid cycling
  - More than four mood episodes in one year; as the number of episodes increases, the duration decreases and eventually stabilizes after 4-6 episodes
  - Frequently presents late in the course of the illness (or early, in child bipolar disorder)
  - Can last as long as 2-4 years.
  - May be a severe phase of the illness rather than a subtype.
  - May be early prsentation of illness in youth.
  - Recovery rates (Schneck, 2004):
    - 40% if no rapid cycling
    - 15% if rapid cycling
  - Predominantly in patients with bipolar II (30.3% versus 6% in bipolar I)
  - Prevalence 13-56%
    - women have rates of 70% (range 58%-92%); women > men
  - Associated with premorbid cyclothymia, depressive first episodes, more severe suicide attempts, more frequent hospitalizations; Mackinnon, 2005: rapid mood switches in familial bipolar disorder associated with 75% rate of sucidal ideation, 38% history of suicidal behavior, higher risk of panic disorder; female gender and early age of onset increased risks.
  - Episodes consist of more severe depression, less severe mania, and fewer psychoses than non-rapid cycling bipolar
  - Often with prior history of rapid cycling, substance abuse, and childhood physical and/or sexual abuse
  - Often with family history of bipolar disorder, depression, and substance abuse
  - In adults, rapid cycling resolves within 2 years in 80% of patients (Coryell)
  - In children and adolescents:
    - rapid cycling in 46-87%
      - ultrarapid cycling in 10-30%
      - ultradian cycling in 77%
      - 50% with no inter-episode recovery)
    - more than twofold increase over adults.
- Psychosis (hallucinations and delusions)
  - Present in 50% of adult patients
- Proposed definition of bipolar spectrum disorder (Ghaemi, Ko, and Goodwin, 2001)
  - A. At least one major depressive episode
  - B. No spontaneous hypomanic or manic episodes
  - C. Either of the following, plus at least two items from criterion D, or both of the following plus one item from criterion D, or neither and six of the items from criterion D:
    - A family history of bipolar disorder in a first degree relative
    - Antidepressant-induced mania or hypomania
  - D.
    - Hyperthymic personality (at baseline, nondepressed state)
    - Recurrent major depressive episodes (>3)
    - Brief major depressive episodes (on average, < 3 months)
    - Atypical depressive symptoms (DSM-IV-TR criteria)
    - Psychotic major depressive episodes

- Early age at onset of major depressive episode (< age 25 yo)
- Postpartum depression
- Antidepressant wear-off (acute but not prophylactic response)
- Lack of response to 3 or more antidepressant treatment trials

- Of adults diagnosed with unipolar depression per DSM-IV at an outpatient clinic, 47% were diagnosable with bipolar spectrum disorder
- In a study of patients with treatment-refractory unipolar depression (per DSM-IV), 52% were diagnosable with bipolar spectrum disorder.

- Dimensional conceptualizations




- Major depression, unipolar
- Major depression with or alternating with
  - Dysthymia: double depression
  - Cyclothymic temperament: bipolar II-b mixed state; typically non-psychotic

        - Irritability, anxiety, agitation, mood/energy/sleep/focus swings common
    - Cyclothymic disorder, and atypical depressive features: bipolar IV disorder subtype or pseudo-unipolar depression
        - Irritability, anxiety, agitation, mood/energy/sleep/focus swings common
        - 50-70% of patients with borderline personality disorder meet criteria for bipolar spectrum disorders
    - Hyperthymic temperament: bipolar IV disorder subtype or hyperthymic depression or excited depression or pseudo-unipolar depression
        - Irritability, anxiety, agitation common
        - often males in their 50's whose life-long drive, ambition, high energy, confidence, and extroverted interpersonal skills helped them advance in life, to achieve success in a variety of business domains and/or political life
    - Medication-induced mixed states: bipolar III-b mixed states
        - Consists of hyperthymia, hypomania, mania, or depression caused by medication
        - Suggests vulnerability to and high risk of bipolar disorder or cyclothymia
        - increasingly seen following the overzealous treatment of psychomotor retarded, seemingly unipolar depressions arising from a stable hyperthymic temperamental background without hypomanic episodes
        - Common features
            - Family history of bipolar disorder
            - Habitual short sleep—less than six hours per day
            - Cheerful, optimistic personality style
            - Extraverted and sociable
            - Tendency to become irritable easily
            - Unrelenting sadness and irascibility
            - Recurrent depressions
            - Agitation against a background of psychomotor retardation
            - Extreme fatigue with racing thoughts
            - Panic
            - Insomnia
            - Suicidal obsessions and impulses
            - Unendurable sexual excitement
            - Histrionic countenance with genuine expressions of intense suffering
            - Abuse of stimulants and alcohol
    - Hypomania(s): bipolar II disorder
    - Hypomania and underlying cyclothymia: bipolar II-1/2 disorder
        - Consists of periods of
            - Bipolar depression or double depression
            - Cyclothymic/bipolar dysthymia
            - Cyclothymia/bipolar hyperthymia
            - Bipolar hypomania
            - Euthymia
    - Protracted hypomania: bipolar I-1/2 disorder
    - Mania(s): bipolar I disorder
        - Consists of periods of
            - Bipolar depression or double depression
            - Cyclothymic or bipolar dysthymia
            - Cyclothymic or bipolar hyperthymia
            - Bipolar hypomania
            - Bipolar mania
            - Euthymia
- Dysthymia temperament/dysthymia: unipolar, cyclothymic or bipolar dysthymia
    - Overlaps with dysphoria from borderline personality disorder
- Hyperthymic temperament/hyperthymia
    - Borderland between extraversion and hypomania.
    - Creativity common and heritable in familial bipolar disorder (and to a lesser extent in ADHD).
    - Common in bipolar disorder, men > women
    - Associated with more frequent manic switches
    - Irritable temperament could be variation of hyperthymia
        - common in bipolar disorder
        - associated with higher risk of psychotic features
        - associated with higher frequency of manic episode at the start of the illness.
- Cyclothymic temperament/cyclothymia
    - Borderland between normal mood swings and bipolar disorder
    - Consists of periods of
        - Hyperthymia
        - Dysthymia
        - Euthymia
    - Common in bipolar disorder
    - Associated with higher co-morbidity
    - Overlaps with intermittent explosive disorder (highly co-morbid with mood, anxiety and substance use disorders)
- Mania, unipolar/hypomania unipolar
    - Consists of periods of
        - Hypomania and/or mania
        - Euthymia
- Bipolar 1/2 disorder
    - AKA schizobipolar disorder; similar to schizoaffective disorder, bipolar type.

- Prevalence of bipolar disorder
    - ***9.5 million adults, 4.4% of the population***, suffers from bipolar spectrum disorders, ~45% of which suffer from bipolar II disorder (where folks suffer from depression predominantly and, to a lesser extent, hypomania (which might exist as irritable states); the number doubles if one includes more subtle bipolar spectrum disorders

- WHO ranks bipolar disorder as the 14th highest cause of disease burden within high income countries, and the 19th within low- and middle-income countries.
- 1996: 6th leading cause of disability in developed nations worldwide.
- Prevalence of bipolar disorder in adults
  - Bipolar I
    - 1% per NCS replication, 2007 and Kessler et al, 2006
    - 0.4-1.6% per DSM-IV
    - 0.6% 12-month prevalence per NCS replication
  - Bipolar II
    - 0.5% per DSM-IV
    - 1.7% per Kessler
    - 0.8% 12-month prevalence per NCS replication
  - Bipolar spectrum (***including*** I, II, ***AND*** 'not otherwise specified')
    - 4% per Kessler
    - 2-5% per Goodwin and Ghaemi
    - 5-7% per Akiskal
    - 8.3% is highest estimate
  - Other estimates
    - Lifetime incidence of mania (and therefore bipolar I disorder in particular) is 1%
    - 1-4.4% (0.82% worldwide based on strict critereria)
    - 0.7% in young adults 19-23 yo (Lewinsohn, 1993)
    - Elderly adults
      - Overall rate: 0.08-5% (with most studies falling in the range of 0.1-1%)
      - Overall rate in the outpatient psychiatry population: 2-8%
      - Overall rate in the inpatient psychiatry population: 5-20%
      - 3.2% of Kraeplin's original group of 900 patients (from which he studied what was then called manic-depressive illness) required their first hospitalization at age 65 or older
      - 2.1% (new onset) in adults aged 60-65
      - 1.1% (new onset) in adults aged 65-80
- Lifetime prevalence of all psychotic disorders 3-3.5%
  - 0.12% for bipolar I disorder *with* psychotic features
  - 0.12% for bipolar I disorder *without* psychotic features
  - 0.35% for depression *with* psychotic features
  - 0.42% for substance-induced psychotic disorders
  - 0.32% for schizoaffective disorder
  - 0.87% for schizophrenia
- Youth
  - It is estimated that there are 2,072,000 youth under 13 with bipolar disorder in the US
    - prevalence range of 1-9%
  - Narrowly defined: 0.1-1.1%
  - Broadly defined: 2.4-6.7%
  - **Risk of bipolar disorder in offspring (2010)**
    - **No parent with bipolar disorder (2,239,553 youth)**
      - **0.48%**
    - **1 parent with bipolar disorder (11,995 youth)**
      - **4.4% so 95.6% do NOT go on to develop bipolar disorder)**
    - **2 parents with bipolar disorder (83 youth)**
      - **24.9% (so 75% do NOT go on to develop bipolar disorder)**
  - National Comorbidity Survey—Adolescent Supplement, 10,123 US adolescents, 13-18 years
    - I or II:
      - Total 2.6%
      - Female 3.3%
      - Male 2.6%
      - 13-14 1.9%
      - 15-16 3.1%
      - 17-18 4.3%
  - Carlson and Kashani, 1988:
    - 0.6% prevalence of mania in 14-16 yo's
    - Rates rose to 13.3% depending on whether duration and severity criteria were accounted for
    - Lewinsohn et al, 1995: community survey in adolescents
      - prevalence of bipolar disorder is 1%
        - 0.1% had mania
        - most had hyperthymia or cyclothymia

        - an additional 5.7% with subthreshold symptomatology
    - Lewinsohn, 1993, 1995; youth aged 14-18
        - 1-1.4% prevalence of bipolar disorder (primarily bipolar II and cyclothymia)
        - BUT ADDITIONAL 5.7% prevalence of bipolar disorder, not otherwise specified
            - or 4.5% prevalence of subsyndromal bipolar disorder
    - Duffy, 1998
        - Children of lithium-responding parents: 4.76% bipolar I, 0% bipolar II, 14.3% bipolar spectrum; less symptom severity and more benign course
        - Children of lithium non-responding parents: 0% bipolar I, 6.6% bipolar II, 13.3% bipolar spectrum
    - Egeland et al, 2003
        - 2.9% bipolar I, 2.9% bipolar II, 2/3 had onset > 13 yo
    - Meyer, 2004
        - 9.4% bipolar I, 9.4% bipolar II, onsets all in adolescence and adulthood
- Age of onset
    - Average age of onset 17.37 yo
    - Overall 65.2% at 18 yo or younger (Perlis et al, 2004; NDMDA study), ~1/3 at younger than 13
    - 61% prior to 20 yo or younger per another study
    - Other data:
        - 27.7% ages 2-12; 14% per Leverich et al 2007
            - 2 yo—0.1%
            - 3 yo—0.2%
            - 4 yo—1%
            - 5 yo—3%
                - 5 yo or younger—5% per NDMDA survey
            - 6 yo—2.2%
            - 7 yo—2.5%
            - 8 yo—3.5%
            - 9 yo—3%
            - 10 yo—4.4%
                - 10 yo or younger—10-20% per other study; 0.3-0.5% per Goodwin and Jamison, 1990; Kraeplin, 1921; Loranger and Levine, 1978)
            - 11 yo—2.3%
            - 12 yo—5.5%
        - 37.5% ages 13-18
            - 13 yo—7%
            - 14 yo—5.4%
            - 15 yo—6.7%
            - 16 yo—6.5%
            - 17 yo—6.5%
            - 18 yo—5.4%
        - 12.1% ages 19-21
            - 19 yo—4.5%
                - 10 yo to 19 yo—21% per other data
                    - 10-14 yo: 14% of total (per NDMDA survey)
                    - 13-18 yo: 37% per STEP-BD
                    - 15-19 yo : 28% of total (per NDMDA survey)
                - Prior to age 19 yo:
                    - 66% per STEP-BD study
                    - 55.3% per Perlis
                    - 20% report symptoms beginning before age 19, though symptoms often include depression and hyperactivity (with manic episodes beginning later)
        - 20-29 yo: 32%
            - 20 yo—4.6%
            - 21 yo—3%
            - 22.7% ages 22 on
                - 30-39 yo: 18%
                - 50-59 yo: 8%
    - Age ranges from other studies:
        - In pediatric bipolar disorder (Geller, 2000, 2001, 2002, 2004 and 2006; Bromet, 2005)
            - 7.3-9.3 yo overall; some research suggests 5-6 yo
            - ~11 yo for bipolar II
- Course
    - Kraeplin (in the time before adequate treatments were discovered): "the duration of individual attacks is extremely varied. There are some which last only eight to fourteen days, indeed we sometimes see that states of moodiness or

excitement…do not continue in these patients longer than one or two days or even only a few hours. For the most part, however, a simple attack usually lasts six to eight months. On the other hand, the cases are not at all rare, in which an attack continues for two, three, or four years, and a double attack (can) double that time. I have seen manias, which even after seven years, indeed after more than ten years, recovered, and a state of depression, which after fourteen years recovered.

- Kraepilin noted that the time between episodes could be years, even decades. Among 703 "intervals" that he studied in his patients, Kraeplin found one case in which forty-four years separated one episode of illness from the next.
- In 1942, the average duration of a mood disorder in bipolar disorder was 6.5 months (before adequate treatment was discovered)
- 1980 study of 434 patients
  - ~28% of folks with bipolar disorder (50% of those with bipolar I disorder) first experience a manic episode followed by a depressive episode then by a free interval (the MDI pattern); the MDI pattern appears to be far more responsive to prophylactic treatment than the DMI pattern below.
  - 25% of folks with bipolar disorder first experience depression followed by mania or, more often, hypomania and then by a free interval (DMI pattern); 78% of those with DMI pattern have bipolar II
  - 20% were rapid cyclers (see below)
  - 19% had a continuous circular course with long cycles
  - The remainder had irregular patterns
- If untreated, and in the days before treatment was available, mood episodes tended to recur more and more frequently as patients aged.
- If untreated, the average duration of a manic episode is 3 months
- If untreated, the average duration of a bipolar depressive episode is 6-13 months
- Number of episodes of illness in sixty-six patients with bipolar disorder

| Number of episodes | Percentage of patients |
|---|---|
| 1 | 8 |
| 1-3 | 29 |
| 1-4 | 26 |
| >7 | 37 |

- The median number of episodes is nine
- The average female patient, if untreated or undertreated, can lose nearly 9-14 years of life, activity, and health
- Cigarette smoking associated with rapid cycling and greater severity of bipolar disorder.
- In adults, a history of childhood abuse (reported in 48.3% of veterans with bipolar disorder in Brown, 2005) is associated with co-morbid post-traumatic stress disorder, panic disorder, depression, alcohol use disorders, and suicide attempts.
- 30% of 171 adult patients with bipolar disorder met criteria for metabolic syndrome. 49% met criterion for abdominal obesity, 41% for high triglycerides, 48% for low HDL, 39% for high blood pressure, 8% for high fasting glucose or antidiabetic medication use (Fagiolini, 2005).
- Persistent symptoms worsens prognosis
- Anxiety symptoms worsen prognosis; risk of relapse increases by
  - 1.55 fold if one anxiety disorder
  - 2.07 fold if social anxiety disorder
  - 2.17 fold if two or more anxiety disorders
  - 2.45 fold if PTSD

- Co-morbid disorders (some of these disorders can also mimic or be confused with bipolar disorder as well)
  - ~94% with 6 or more other lifetime diagnoses per NCS-R; overall, 55-90% with co-morbid disorders in other studies
  - General medical issues (prevalence)
    - Smoking 54-68%; 2-3X increased risk
    - Hypertension 35-61%; 2-3X increased risk
    - Metabolic syndrome 30-49%; 1.5-2X increased risk
    - Dyslipidemia 23-38%; </=3X increased risk
    - Obesity 21-49%; 1-2X increased risk
    - Diabetes 8-17%; 1.5-2X increased risk
  - Alcohol and substance abuse and dependence:
    - 10-30% in teens
    - 21-70% in adults
    - Weiss et al, 2005: 48% have substance use disorder (current or past); ¾ with recover
  - Anxiety
    - Overall
      - 40-93% of people with bipolar disorder also have an anxiety disorder.

- Koukopoulos, et al, Perugi, and Akiskal have all suggested a link between anxiety and bipolar disorder
- Bipolar disorder with co-morbid anxiety associated with:
  - Earlier age onset bipolar disorder
  - More frequent and/or severe cycles
  - Diminished quality of life
  - Heightened levels of suicidality
  - Poor or delayed treatment response
- In children, anxiety disorders linked with worsened prognosis of bipolar disorder, at least in the medium term

- Agoraphobia
  - 6-62% in McIntyre et al, 2006
- Panic disorder
  - 17-38% (5 times more likely than in general population) versus 10-14% in unipolar depression
  - May co-aggregate in families with bipolar disorder, perhaps related to chromosome 18q
  - Bipolar with co-morbid panic associated with:
    - Greater number and severity of depressive episodes
    - Greater suicidal ideation
    - More medication side effects
    - Longer time to remission
- Social phobia
  - 4-37% in McIntyre et al, 2006
  - 22% in another study
  - May also co-aggregate in families with bipolar II disorder and may be 5 times more likely in folks than in the general population.
- Generalized anxiety disorder

Table 3.1. **Comparison of GAD and bipolar disorder criteria**

| Generalized Anxiety Disorder (DSM) | Bipolar Disorders (Patient Experience) |
|---|---|
| *Cognitive*<br>• worry<br>• difficulty concentrating | *Cognitive*<br>• anxiety, agitation (in mixed states)<br>• distractibility |
| *Energy*<br>• keyed up, on edge<br>• restlessness, tension<br>• easily fatigued<br>• difficulty falling/staying asleep | *Energy*<br>• motor agitation<br>• restlessness<br>• extreme fatigue (depressed phases)<br>• extreme insomnia (manic/mixed phases) |
| *Mood*<br>• irritability | *Mood*<br>• dysphoria, irritability |

  - 18-27% versus 9.7% in unipolar depression
  - 2-43% in McIntyre et al, 2006
- OCD
  - 2-39% in McIntyre et al, 2006
  - May co-aggregate and may be 5 times more likely (22%) in folks with bipolar disorder than in the general population
  - Bipolar with co-morbid OCD associated with:
    - Higher rates of suicidal ideation and attempts
- Post-traumatic stress disorder

Table 4.3. **Comparison of PTSD, bipolar disorder, and borderline disorder**

| Domain | PTSD | Bipolar | Borderline |
|---|---|---|---|
| Stable/ unstable | Unstable experience<br>Transient paranoia or dissociation<br>Affective instability | Unstable mood<br>Transient paranoia<br>Affective instability | Unstable sense of self<br>Transient paranoia or dissociation<br>Affective instability |
| Anger | Intense anger | Intense anger | Intense anger |
| Relationships | Unstable relationships | Unstable relationships | Unstable intense relationships |
| Suicidality | Suicide risk | Suicidal ideation or attempts | Recurrent suicidal behavior |
| Impulsivity | Substance use, impulsive avoidance | Impulsive spending, sex, drug use, risk behaviors | Impulsive spending, sex, drug use, risky behaviors |
| Attachment | Normal attachment range, at least prior to trauma | Normal attachment range, at least prior to onset | Abandonment fear<br>Chronic emptiness |
| Onset | After trauma | After mood changes | Interpersonal |
| Symptom duration | Hours to a day with each intrusive recall | Technically >4 days | Hours to a day |

    - 5-40% in McIntyre et al, 2006
- Anxiety co-morbidity in pediatric bipolar disorder
    - Up to 90% with anxiety; anxiety often precedes the onset of mood disorder (e.g., Dickstein, 2005; Masi, 2001)
        - 35% in children
        - 50% in teens
    - 19-52% of kids with panic disorder have co-morbid bipolar disorder (Biederman, 1997; Birmaher, 2002)
    - 56% of children and adolescents with bipolar disorder have multiple anxiety disorders.
    - 52% of children and adolescents with panic disorder have bipolar disorder
- Borderline personality disorder

Table 4.2. **Other features of borderline and bipolar disorders**

| Domain | Borderline | Bipolar |
|---|---|---|
| *Age of onset* | Childhood; disturbances should be noted even before puberty and strongly shortly thereafter | 18–24 with relatively normal premorbid mood, relationships, function |
| *Family history* | Substance use and trauma | Bipolar or very high-functioning relatives |
| Episode precipitants | Common, usually interpersonal, with rapid symptom onset thereafter | Largely independent of psychosocial events |

- Disruptive behavior disorders (ADHD, ODD, conduct disorder)
    - 75-93% in children
    - 60% in teens
    - Adults
        - 6-21.2% in adults vs. 3.5% in adults without bipolar disorder
        - STEP-BD, 2007: 9%
        - NCS-R: 21.2%
            - In adults with ADHD: 19.4% (4.5-47%) have bipolar disorder vs. 3.1% in adults without ADHD
        - Higher rates in those with onset of bipolar disorder less than 18 yo
        - Earlier age of onset of mood disorder in those with comorbid ADHD
        - Duration of wellness in folks with bipolar disorder in last two years before diagnosis:
        - 4 mo in those with ADHD
        - ~11 mo in those without ADHD
    - Life time course of bipolar disorder
        - Presence of ADHD
            - 60% with alcohol abuse
            - 45% with drug abuse

- 42% with > 20 mood episodes
- 46% with lifetime suicide attempt(s)
- 43% with lifetime violent behavior(s)
- 45% with lifetime legal problem(s)
- Absence of ADHD
- 40% with alcohol abuse
- 25% with drug abuse
- 30% with > 20 mood episodes
- 32% with lifetime suicide attempt(s)
- 20% with lifetime violent behavior(s)
- 20% with lifetime legal problem(s)

- Medical illnesses
- Obesity
- Osteoarthritis
- Sleep apnea
- Metabolic syndrome
- Hypercholesterolemia
- Hypertriglyceridemia
- Hypertension
- Insulin resistance/diabetes—risk of diabetes is tripled
- Risk of heart attack increased two to fourfold
- Risk of death from heart attack increased two to fourfold
- Risk of stroke doubled
- Increased need for stroke rehabilitation
- Risk of dementia doubled
- Worse control of diabetes
- Standardized mortality rates four-eightfold higher with onset 34 yo and younger

- Gender
- Women are more likely to have dysphoric or mixed mania and rapid cycling.
- Women may be more responsive to lithium.
- Oral contraceptives may have mood stabilizing properties in women with bipolar disorder, though there are reports of oral contraceptives exacerbating mood problems.
- Reproductive dysfunction in women with bipolar disorder
- Joffe, 2006
- Early-onset menstrual cycle dysfunction reported in 34.2% of women with bipolar disorder, 24.5% of women with unipolar depression, and 21.7% of healthy women
- Rasgon, 2005, 25 women, aged 18-45, over 2 years
- 10 on Depakote, 6 on lithium, 5 on atypical antipsychotics (alone or combo???)
- 41.% reported oligomenorrhea (low bleeding in periods) BUT 40% reported same oligomenorrhea PRIOR to medications
- Over time, all subjects exhibited a decrease in luteal phase progesterone and an increase in free testosterone.
- Depakote was associated with an increase over time in total testosterone but otherwise no more likely to be associated with oligomennorhea.
- Rasgon, 2003: 17 women with bipolar disorder, followed over 3 months, all with meds for bipolar, 35% on oral contraceptives
- 59% had long (>29 days) menstrual cycle length
- 18% with oligomenorrhea (low bleeding in periods)
- Menstrual abnormalities preceded the onset of bipolar disorder in many
- Pregnancy/post-partum
- The pregnancy period can sometimes confer protective effects on the course and expression of bipolar disorder, although it more often exacerbates the course and expression of bipolar disorder.
- 14% of depressed women whose FIRST psychiatric presentation was within the 1st postpartum month convert to a bipolar disorder diagnosis within 15 years
- Women with bipolar disorder are most likely to present with depressive or mixed episodes during pregnancy
- Major depressive disorder 41.3%
- Mixed states 38.1%
- Hypomania 11.1%
- Mania 9.6%
- Women with bipolar disorder in pregnancy have increased risk of
- smoking
- substance use

- obesity
- cesarean section
- preterm delivery

- Recurrence risk for bipolar disorder is 37-60% in the post-partum period, increased to 85.5% in those who discontinue their mood stabilizing medications
  - Wesello, 2017

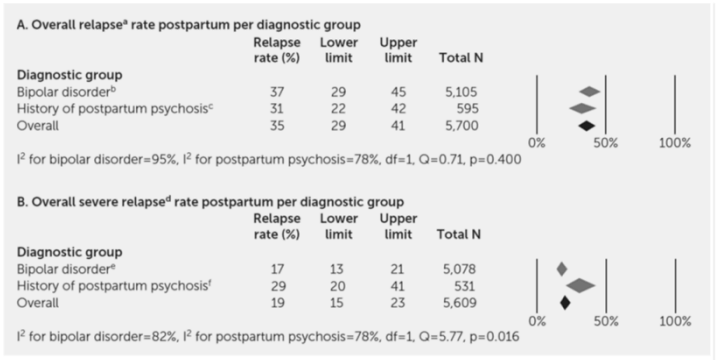
## UPDATE: LITHIUM OR LAMOTRIGINE IN PREGNANCY

- Data from the population-based Danish Registry
- N=55 women treated with lamotrigine and n=59 treated with lithium
- Post delivery 4 women taking lamotrigine (7.3%) and 9 (15.3%) taking lithium required hospitalization; Fishers exact=0.20
- Indices of women treated with lamotrigine suggest they had greater illness (eg. more hospitalizations; concurrent treatment)
- Note clearance of both agents increases greatly in pregnancy

Wesello, 2017, J Affective Disorders, Vol 218; pp. 394-397

  - Wesseloo, et al, 2016
    - 33% of women at high risk experience of post-partum relapse
    - Continuation of prophylactic medication during pregnancy is highly protective for maintaining mood stability post-partum
    - For those with a history of post-partum psychosis may have less risk of relapse if prophylaxis is started immediately after birth

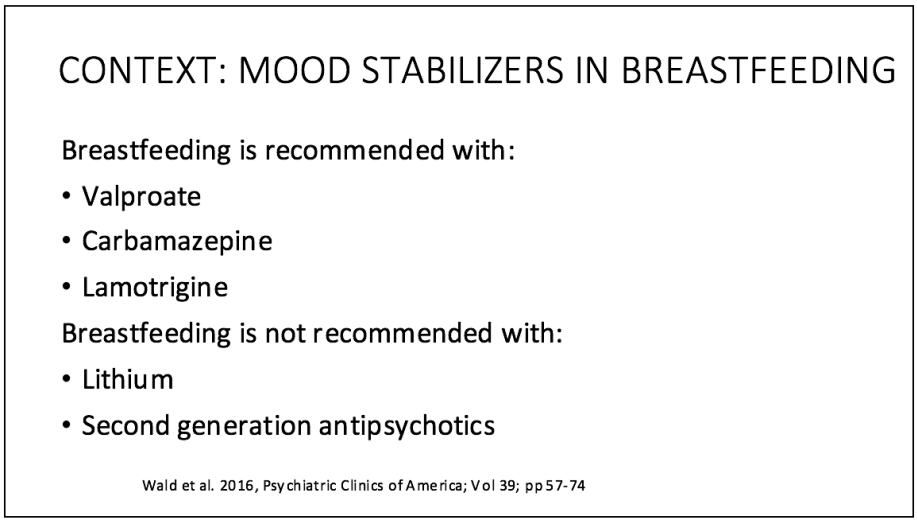
## CONTEXT: RISK OF POSTPARTUM RELAPSE IN WOMEN WITH BIPOLAR DISORDER OR PRIOR POSTPARTUM PSYCHOSIS




Wesseloo, Kamperman, Munk-Olsen, Pop, Kushner, Bergink, AJP, 2016; Vol 173: pp 117-127; Relapse occurred in 23% of women with bipolar illness who took medication in pregnancy and 66% who did not

  - Viguera et al, 2007
    - 71% risk of at least one recurrence
    - Among those who discontinued treatment
      - Twofold increased risk of recurrence
      - Time to first recurrence more than fourfold shorter
      - Time to recurrence was 11-fold shorter after abrupt vs. gradual discontinuation
      - Proportion of weeks ill during pregnancy fivefold greater
      - Recurrence, other:
        - Depressive or mixed episodes in 74%
        - Hypomania or manic episodes in 26%
        - Occurred in first trimester 47% of time
  - Relapse during pregnancy is significantly higher (50-60%) when mood stabilizer treatment is stopped before or during pregnancy.

- Postpartum period (especially the first 6 weeks)
    - Very high risk time for depression, mania, and/or psychosis.
    - The post-partum period increases the risk of relapse in bipolar disorder to 67-82%, although prophylactic mood stabilizer treatment with lithium several weeks before delivery or immediately post-partum greatly reduces the rate of relapse two- to five-fold.
    - The risk of post-partum psychosis is 5% in women with bipolar disorder (100-fold higher than 0.05% risk present in the general population).
- Lithium appears to be a relatively safe option for pregnant women, although it is associated with an increased risk of cardiovascular malformations, such as Ebstein's anomaly (see below).
- Valproic acid use in the first trimester is associated with 3-8% risk of spina bifida, and there may be long-term behavioral sequelae of prenatal exposure
- Tegretol is associated with a 0.5% risk of spina bifida as well as elevated risks of craniofacial anomalies and microcephaly
- Reproductive safety and risk of teratogenicity for tiagabine and gabapentin are currently unknown.
- Lamotrigine does not appear to be teratogenic
- Calcium channel blockers and omega 3 fatty acids may be safe options
- Folate at 1-4 mg/day may help decrease the risk of neural tube defects
- Postpartum psychosis occurs in 1/1000 women in the general population but in 1/5-1/3 of women with bipolar disorder; postpartum psychosis occurs within the first 24-48 hours postpartum
- Starting lithium before delivery reduces relapse rates from 50% to 10%
- Breast feeding




    - Lithium used to be contraindicated during nursing but more recent evidence suggests levels in breast milk and infants are low with little to no significant adverse effects in infants
    - Depakote and Tegretol are compatible with nursing

- Teratogenicity
    - Background rates of birth defects 2-6%, depending on the study
    - Most organs formed in first trimester
    - Neural tube closes by 5 weeks
    - Brain is formed during all three trimesters (and continues to grow til age 27
    -

Pediatric Bipolar Disorder—see separate handout

Mortality and Suicide risk

- Morbidity and mortality from medical illnesses
    - Higher risk for cardiovascular disease, violence, and alcohol and drug abuse, all of which add to the mortality risk of this condition.
    - The specific standard mortality rate for cardiovascular deaths are 2.5-2.7 times that of the general population.
    - 2.5-2.7 fold increase in risk of all cause mortality
- Suicide risk
    - Virginia Woolf: "Dearest, I feel certain I am going mad again. I feel we can't go through another of these terrible times. And I shan't recover this time. I begin to hear voices, and I can't concentrate. So I am doing what seems the best thing to do."
    - General
        - Approximately 30,000 people die annually by suicide in the United States; in 2004, 32,439 people took their lives.

- Suicide is the
- 3rd leading cause of death internationally in those under the age of 44 yo
- 3rd leading cause of death in 10-19 yo's
- 4th leading cause of death in children
- 7th leading cause of death in the United States, resulting in more deaths annually than HIV disease
- 10th leading cause of death for persons aged 14-64
- 11th leading cause of death across all age groups
- In Germany in the year 2000, suicide killed more people than did traffic accidents, drugs, and violence together, and around 60% of those suicides were related to depression
- 66% of those with depression contemplate suicide; 15% will actually commit suicide
- National suicide rate: 12.87/100,000
    - This represents an increase of 31% from 9.8/100,000 in 1957
    - Beginning in 1987, the rate begin to decline and has continued to do so ever since
    - Prozac was introduced to the American market in 1988
    - The rate in Denmark is 20/100,000

- Bipolar disorder is a dangerous illness; the completed suicide rate is 10-20 times the rate in the general population; somewhere between 8-20% of patients complete suicide; one review of 30 reports published between 1936 and 1988 showed that 19% of the deaths of 9389 persons studied were caused by suicide
- 25-58% of individuals with bipolar disorder attempt suicide at some time during their illness; in one study, 16% of those with unipolar depression attempted suicide, 34% of those with bipolar II disorder, and 24% of those with bipolar I disorder
- The lethality of suicide attempts is 2.5-fold higher in bipolar vs. unipolar disorder.
- Lifetime completed suicide rate is 18.9% (average from 30 studies from 1936-1988, range 8-50% in other studies)
- In the 30 months after a patient's first bipolar depressive episode, 40% of patients engaged in dangerous suicidal behaviors and 18% attempted suicide
- Mortality rates from suicide
    - 15-30 fold higher than those without psychiatric illness; rate in unipolar depression is 20-fold higher than those without psychiatric illness
    - Of those individuals with bipolar disorder who *attempted* suicide, untreated individuals had close to 30 times the risk of dying from suicide compared to treated individuals
    - Chen and Dilsaver, 1996:
        - 29.2% in bipolar disorder
        - 15.9% in unipolar major depression
        - 4.2% in all other DSM III Axis I disorders combined
        - Odds ratio of suicides in bipolar compared with unipolar 2.0
    - Angst, 2002: suicide risk in bipolar disorder
        - 29.2-fold higher if untreated
        - 6.4-fold higher if treated

- In bipolar disorder, risk factors include:
    - Acute depression, especially when there is hopelessness, turmoil, global insomnia, anhedonia, anxiety, panic
    - Mixed episodes and/or cycling within an episode
    - Substance abuse
    - Nicotine dependence
    - Adult or child sexual abuse
    - Suicidal ideation
    - Past suicide attempts
    - Aggression, impulsivity
    - Personality disorders
    - Co-morbid medical illnesses
    - History of suicide attempts (either personal or familial)
    - First episodes requiring hospitalization
    - First episodes in general
    - Time immediately after hospital admission and immediately after discharge
    - Higher number of episodes

Other

- Recurring (relapsing and remitting) disorder
- Estimated annual societal cost ranges from $10-45 billion with another $26 billion salary equivalent los/year
- ~50 lost workdays/year/patient; 180 million last workdays/year overall

Biology (see separate handout)

History, general treatment strategies and other issues/aspects of bipolar disorder (see handout)

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Some thoughts on borderline personality disorder, a syndrome that overlaps symptomatically with Bipolar II disorder:

From NAMI:

# Borderline Personality Disorder

- Overview
- Treatment
- Support
- Discuss

Borderline personality disorder (BPD) is a condition characterized by difficulties in regulating emotion. This difficulty leads to severe, unstable mood swings, impulsivity and instability, poor self-image and stormy personal relationships. People may make repeated attempts to avoid real or imagined situations of abandonment. The combined result of living with BPD can manifest into destructive behavior, such as self-harm (cutting) or suicide attempts.

It's estimated that 1.6% of the adult U.S. population has BPD but it may be as high as 5.9%. Nearly 75% of people diagnosed with BPD are women, but recent research suggests that men may be almost as frequently affected by BPD. In the past, men with BPD were often misdiagnosed with PTSD or depression.

# Symptoms

People with BPD experience wide mood swings and can display a great sense of instability and insecurity. Signs and symptoms may include:

- Frantic efforts to avoid being abandoned by friends and family.
- Unstable personal relationships that alternate between idealization—"I'm so in love!"—and devaluation—"I hate her." This is also sometimes known as "splitting."
- Distorted and unstable self-image, which affects moods, values, opinions, goals and relationships.
- Impulsive behaviors that can have dangerous outcomes, such as excessive spending, unsafe sex, substance abuse or reckless driving.
- Suicidal and self-harming behavior.
- Periods of intense depressed mood, irritability or anxiety lasting a few hours to a few days.
- Chronic feelings of boredom or emptiness.
- Inappropriate, intense or uncontrollable anger—often followed by shame and guilt.
- Dissociative feelings—disconnecting from your thoughts or sense of identity, or "out of body" type of feelings—and stress-related paranoid thoughts. Severe cases of stress can also lead to brief psychotic episodes.

Borderline personality disorder is ultimately characterized by the emotional turmoil it causes. People who have it feel emotions intensely and for long periods of time, and it is harder for them to return to a stable baseline after an emotionally intense event. Suicide threats and attempts are very common for people with BPD. Self-harming acts, such as cutting and burning, are also common.

# Causes

The causes of borderline personality disorder are not fully understood, but scientists agree that it is the result of a combination of factors:

- **Genetics.** While no specific gene has been shown to directly cause BPD, studies in twins suggest this illness has strong hereditary links. BPD is about five times more common among people who have a first-degree relative with the disorder.
- **Environmental factors.** People who experience traumatic life events, such as physical or sexual abuse during childhood or neglect and separation from parents, are at increased risk of developing BPD.
- **Brain function.** The way the brain works is often different in people with BPD, suggesting that there is a neurological basis for some of the symptoms. Specifically, the portions of the brain that control emotions and decision-making/judgment may not communicate well with one another.

# Diagnosis

There is no single medical test to diagnose BPD, and a diagnosis is not based on one sign or symptom. BPD is diagnosed by a mental health professional following a comprehensive psychiatric interview that may include talking with previous clinicians, medical evaluations and, when appropriate, interviews with friends and family. To be diagnosed with BPD, a person must have at least 5 of the 9 BPD symptoms listed above.

# Treatment

A typical, well-rounded treatment plan includes psychotherapy, medications and group, peer and family support. The overarching goal is for someone with BPD to increasingly self-direct her treatment plan as a person learns what works as well as what doesn't.

- **Psychotherapy**, such as dialectical behavioral therapy (DBT), cognitive behavioral therapy (CBT) and psychodynamic psychotherapy, is the first line of choice for BPD.
- **Medications** are often instrumental to a treatment plan, but there is no one medication specifically made to treat the core symptoms of emptiness, abandonment and identity disturbance. Rather, several medications can be used off-label to treat the remaining symptoms. For example, mood stabilizers and antidepressants help with mood swings and dysphoria. Antipsychotic medication may help control symptoms of rage and disorganized thinking.
- **Short-term hospitalization** may be necessary during times of extreme stress, and/or impulsive or suicidal behavior to ensure safety.

# Related Conditions

BPD can be difficult to diagnose and treat—and successful treatment includes addressing any other disorders somebody might have. A person with BPD may have additional conditions like:

- Anxiety disorders, such as PTSD.
- Bipolar disorder.
- Depression.
- Eating disorders, notably bulimia nervosa.
- Other personality disorders.
- Substance use disorders.

# Diagnostic criteria for 301.83 Borderline Personality Disorder

**These criteria are obsolete.**
**DSM Criteria**
**DSM Version**
DSM IV - TR
**DSM Criteria**

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

(1) frantic efforts to avoid real or imagined abandonment.
Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.

(2) a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation

(3) identity disturbance: markedly and persistently unstable self-image or sense of self

(4) impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, Substance Abuse, reckless driving, binge eating).
Note: Do not include suicidal or self-mutilating behavior covered in Criterion 5.

(5) recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior

(6) affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days)

(7) chronic feelings of emptiness

(8) inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)

(9) transient, stress-related paranoid ideation or severe dissociative symptoms

**DSM Version**
DSM IV
**DSM Criteria**

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