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MODULE 2

BIPOLAR DISORDER—CLASSIFICATION AND DIAGNOSIS

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MODULE 2
BIPOLAR DISORDER—CLASSIFICATION AND DIAGNOSIS

MODULE 2
BIPOLAR DISORDER—CLASSIFICATION AND DIAGNOSIS

- Part 1: Description of mood episodes

- Part 2: Diagnosis of bipolar disorder and major depressive disorder

- Part 3: Rating scales for bipolar disorder and major depressive disorder

Objectives

- To describe the three mood episodes defined by the DSM-5

- To characterize the disease course of bipolar disorder and major depressive disorder

- To explain the design of some clinical rating scales used to assess symptom severity and quality of life

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Bipolar Disorder : By the Numbers

PREVALENCE

- Lifetime prevalence up to **4.4%**

- **Equally common** among men and women

- Average age at onset is **20** for both men and women

(Bipolar Disorder)

COMORBIDITY

% of patients meeting DSM-IV criteria for comorbid disorders (lifetime):

- At least 1: **65%**

- At least 2: **42%**

- 3 or more: **24%**

(Bipolar I and Bipolar II Disorder)

ECONOMIC IMPACT

Estimated total economic burden **$151 billion**

- **$30.7 billion** in direct costs

- **$120.3 billion** in indirect costs

(Bipolar I and Bipolar II Disorder)

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Mood Episodes – the Building Blocks of Bipolar Disorder and Major Depressive Disorder

Major depressive episode

Manic episode

Hypomanic episode

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The Mood Chart

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Major Depressive Episode (MDE)

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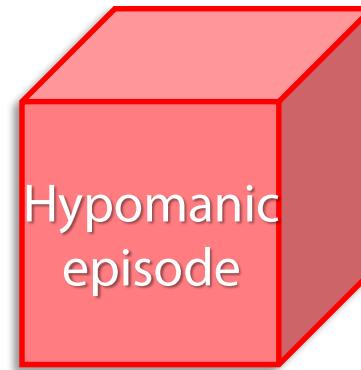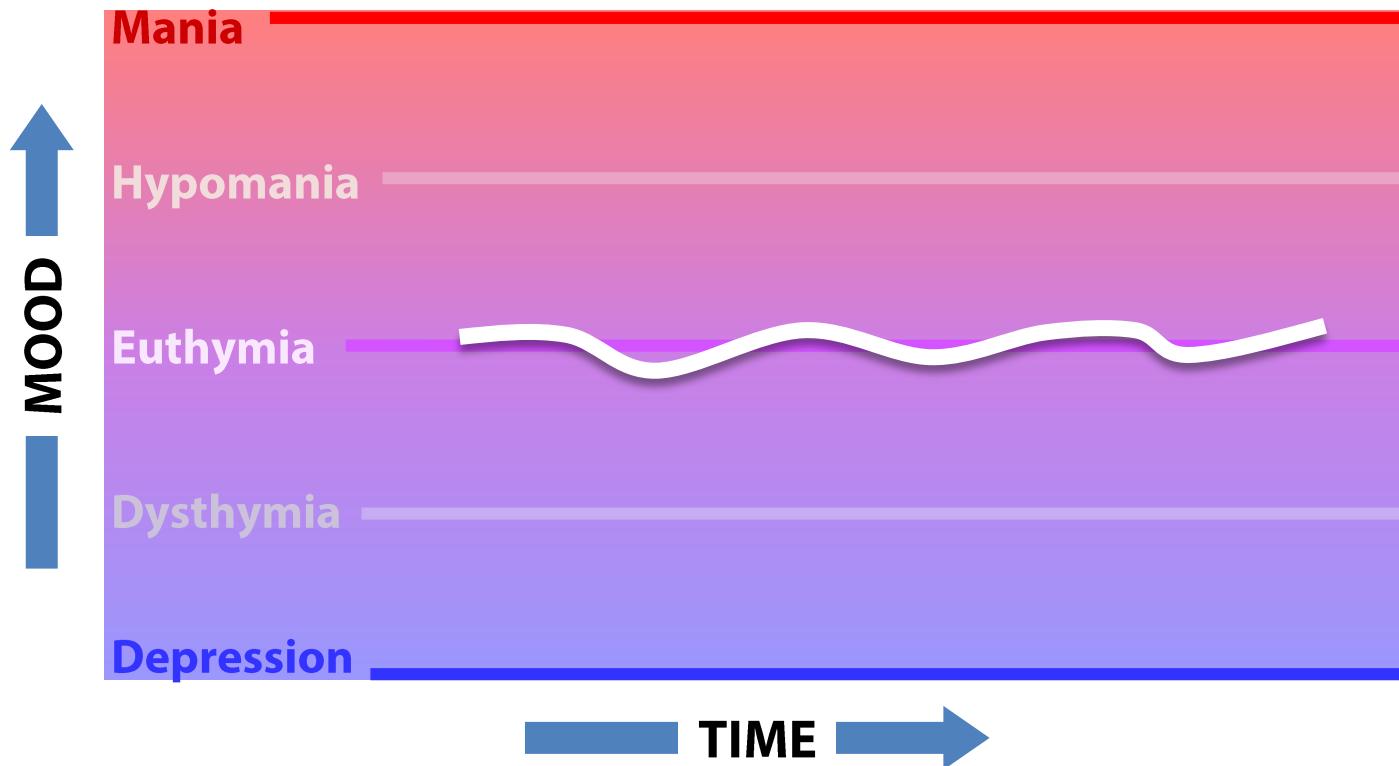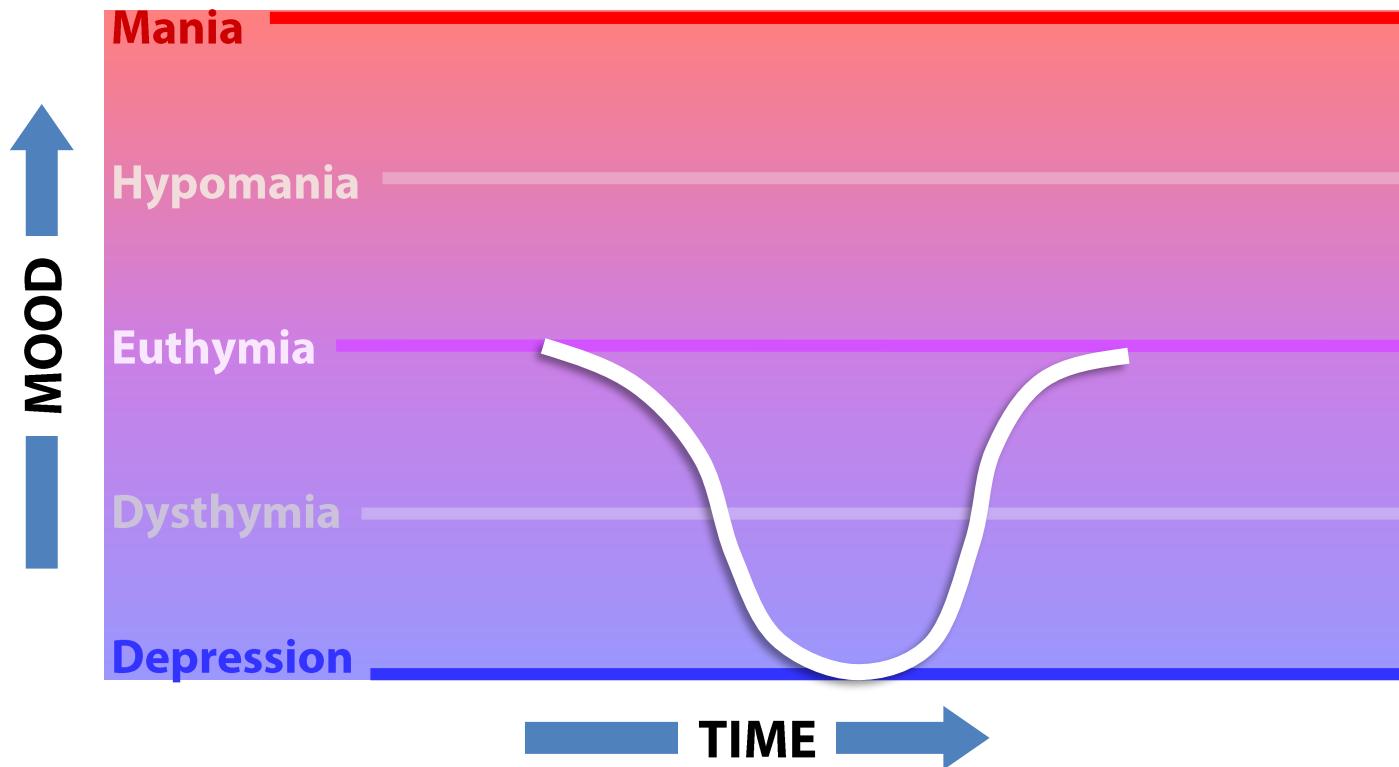
Major Depressive Episode (MDE)

At least five of these symptoms are required:
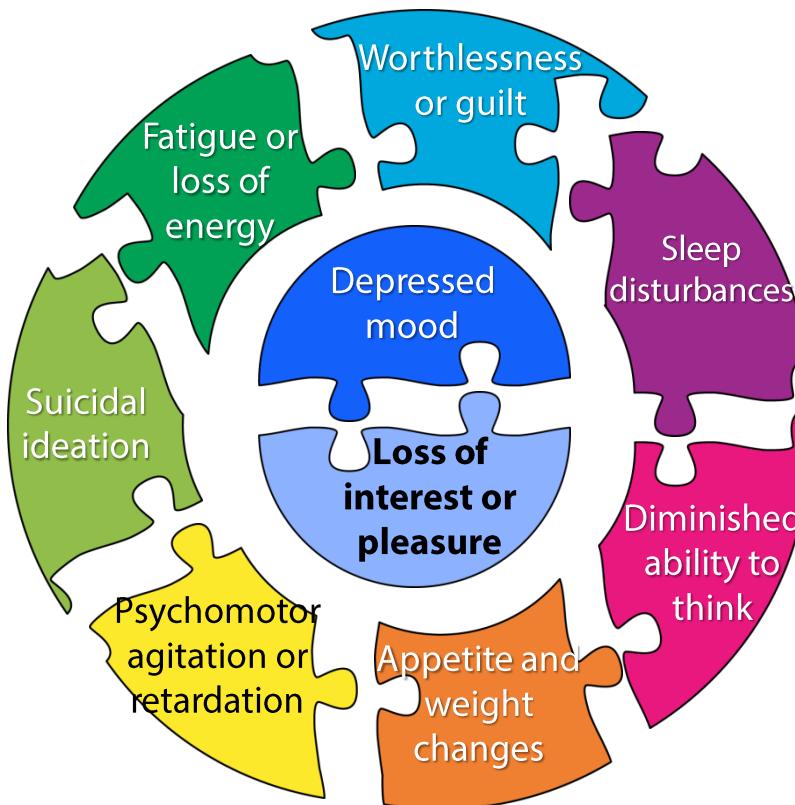
**At least one of the symptoms is either:**

Depressed mood

OR

**Loss of interest or pleasure**

Symptoms last ≥ 2 weeks

11 of 53

Major Depressive Episode (MDE)

Other causes ruled out:

- General medical condition

- Substance use

- Bereavement

COURSE

MDE

days to
weeks

≥4 months if
untreated

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Manic Episode

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Manic Episode

One core symptom required:

At least three of these required (four if mood is irritable):

Elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy

Pressured speech

Pleasurable activities with risky consequences

Flight of ideas

Distractibility

Increase in goal-directed activity

Inflated self-esteem

Decreased need for sleep

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Manic Episode

- Symptoms last ≥ 1 week, or any duration if hospitalized

  Impaired occupational or social function

- Average onset: early 20s

Other causes ruled out

- General medical condition

  Substance use

- Antidepressant treatment

COURSE

Manic episode

a few days → a few days to several months → **MDE** ~60% of cases

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Hypomanic Episode

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Hypomanic Episode

One core symptom required:

At least three of these required (four if mood is irritable):

Elevated, expansive, or irritable mood and abnormally and persistently increased activity and energy

Pressured speech

Pleasurable activities with risky consequences

Flight of ideas

Distractibility

Increase in goal-directed activity

Inflated self-esteem

Decreased need for sleep

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Hypomanic Episode

- Symptoms last ≥ 4 days

  Unequivocal change in function (observable by others)

- No marked impairment in occupational or social function

  Other causes ruled out

COURSE

MDE → 1-2 days → **Hypomanic episode** several weeks to months → **MDE** ~60%-70% of cases

or

Manic episode ~5%-15% of cases

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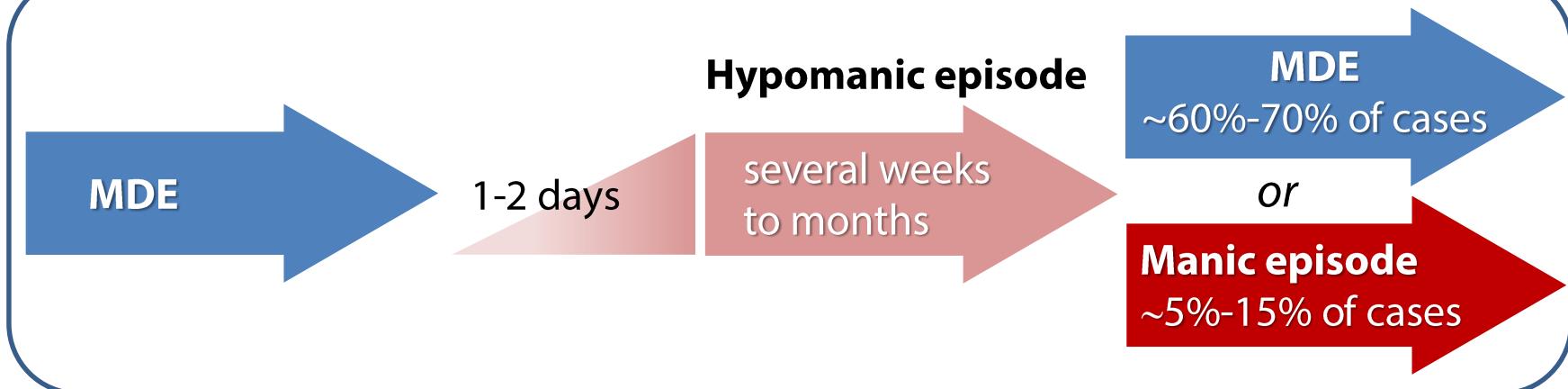
Mood Episode Spectrum

MANIC EPISODE	HYPOMANIC EPISODE	MAJOR DEPRESSIVE EPISODE
Period of abnormally elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy lasting at least one week with ≥3 symptoms (4 if irritable)	Same criteria as manic episode with:	≥5 symptoms during the same 2-week period with change in function

MANIC EPISODE

Period of abnormally elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy lasting at least one week with ≥3 symptoms (4 if irritable)

- Grandiosity
- Decreased need for sleep
- More talkative
- Distractibility
- Flight of ideas/racing thoughts
- Increase in goal-directed activity
- Excessive involvement in pleasurable activities with potential for painful consequence

HYPOMANIC EPISODE

Same criteria as manic episode with:

- Only four-day duration
- Associated with an "unequivocal change in functioning" (though need not be impairment in functioning, as with mania)
- If psychosis is present or hospitalization is needed, episode considered mania

MAJOR DEPRESSIVE EPISODE

≥5 symptoms during the same 2-week period with change in function

- Must include either depressed mood or anhedonia (or both)
- Appetite/weight change
- Insomnia/hypersomnia
- Psychomotor retardation
- Fatigue
- Worthlessness/guilt
- Impaired concentration
- Thoughts of death

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Key Takeaways

- Major depressive episodes are characterized by at least one core symptom of depressed mood or apathy, accompanied by at least four other symptoms of depression
- Manic episodes are characterized by at least one core symptom of persistently elevated, expansive, or irritable mood and abnormally and persistently increased goal-directed activity or energy, accompanied by:
    - at least 3 other symptoms of mania (if the mood is elevated or expansive)
    - at least 4 other symptoms of mania (if the mood is irritable)
- Hypomanic episodes are similar to manic episodes but are generally less severe

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BIPOLAR DISORDER—CLASSIFICATION AND DIAGNOSIS

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# Bipolar Disorder and Major Depressive Disorder

MOOD EPISODES

Major depressive episode

Manic episode
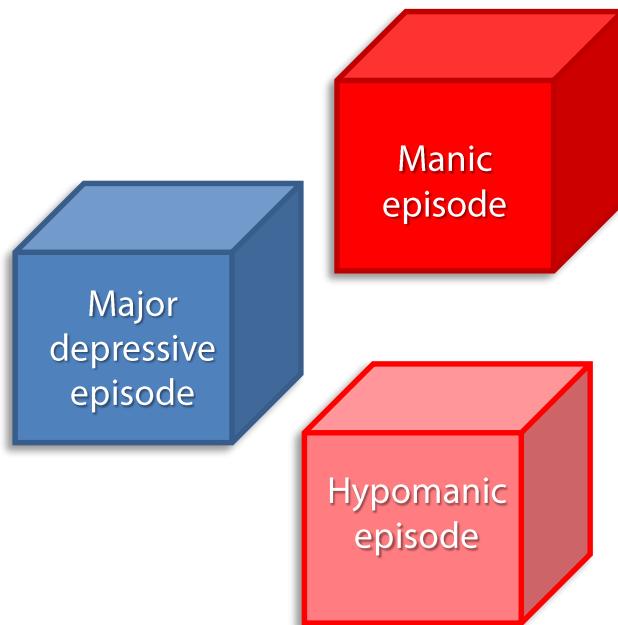
Hypomanic episode

CONSTITUTE…

Bipolar I Disorder

Bipolar II Disorder

Major Depressive Disorder (MDD)

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Bipolar I Disorder

- One or more manic episodes

60%-70% of manic episodes occur before or after an MDE

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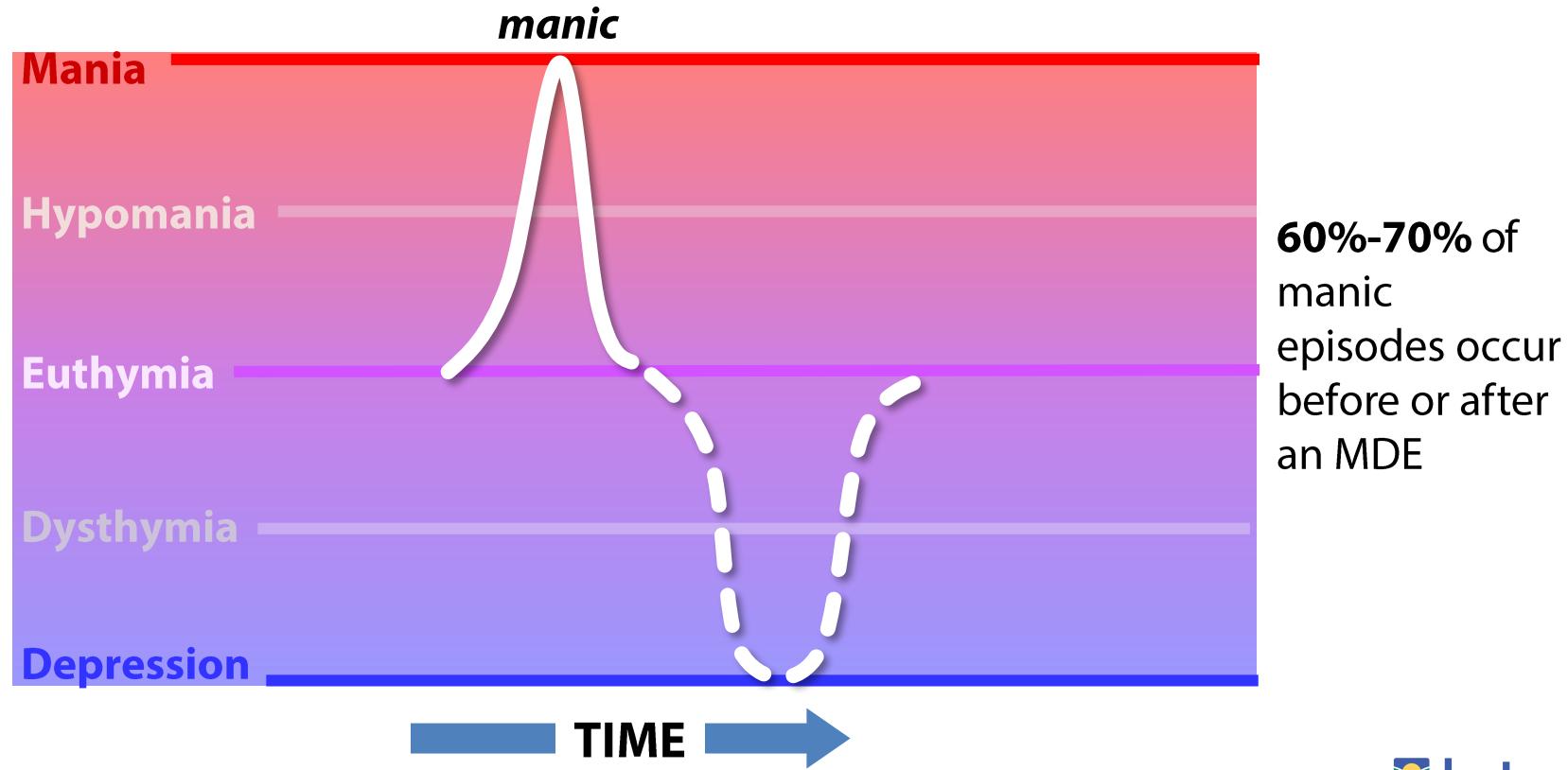
Bipolar II Disorder

- One or more major depressive episodes
- At least one hypomanic episode
- No history of manic episodes

60%-70% of hypomanic episodes occur before or after an MDE

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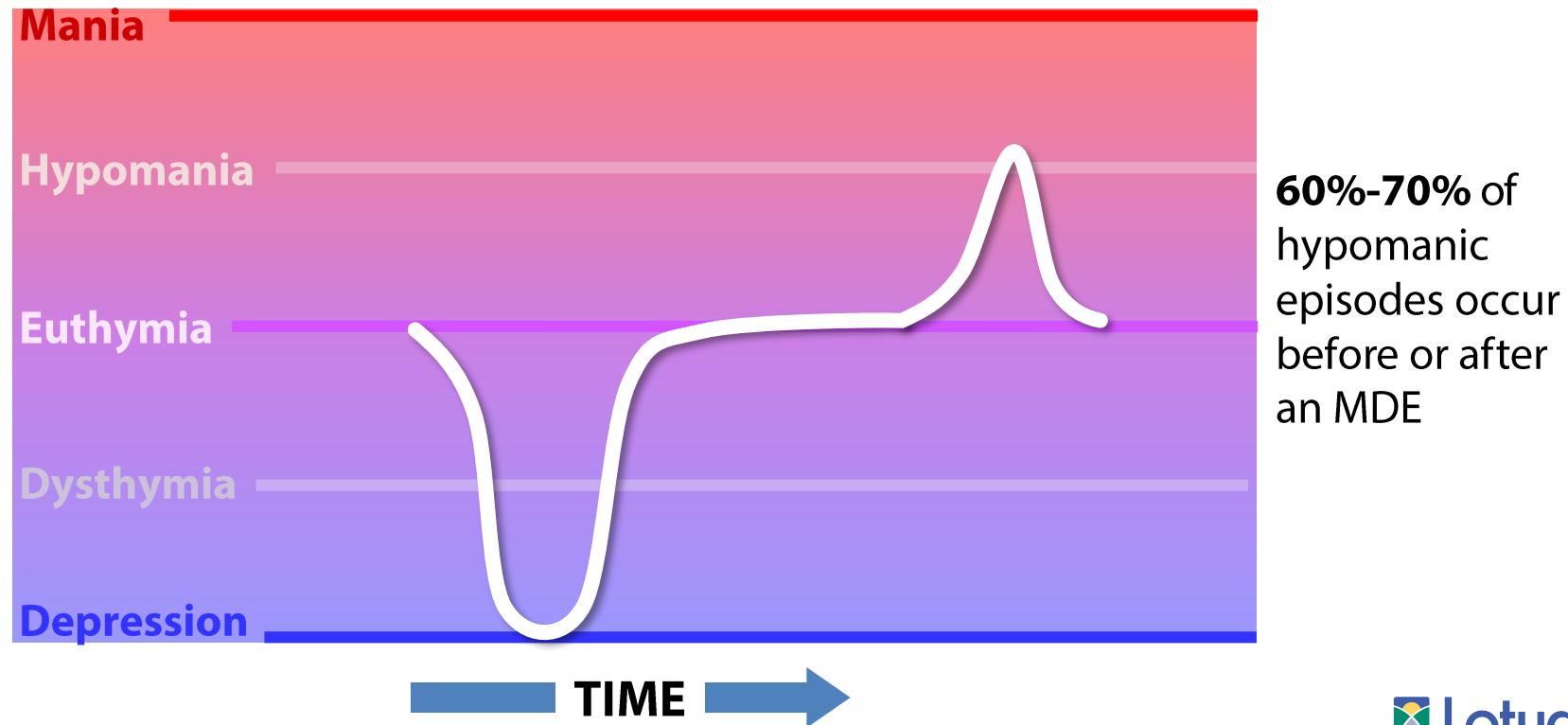
Specifier: Rapid Cycling

- Can apply to bipolar I disorder or bipolar II disorder
- Four or more mood episodes within a 12-month period
- Episodes can occur in any combination and order

*Example for rapid cycling with mixed features:*
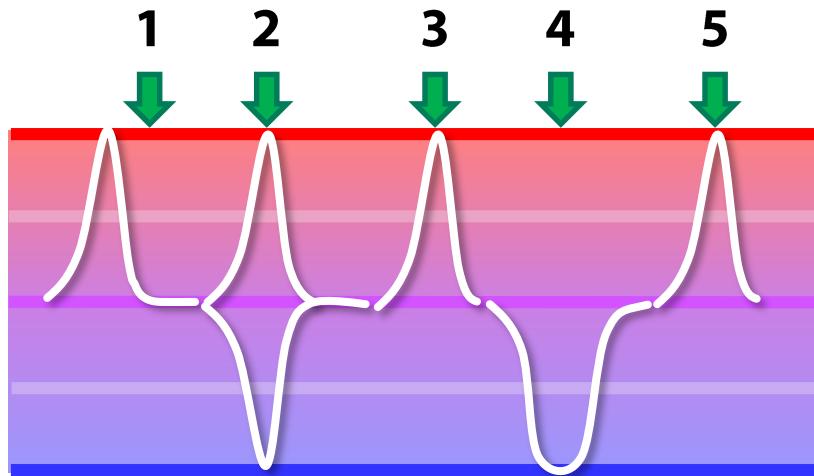
Example for rapid cycling :
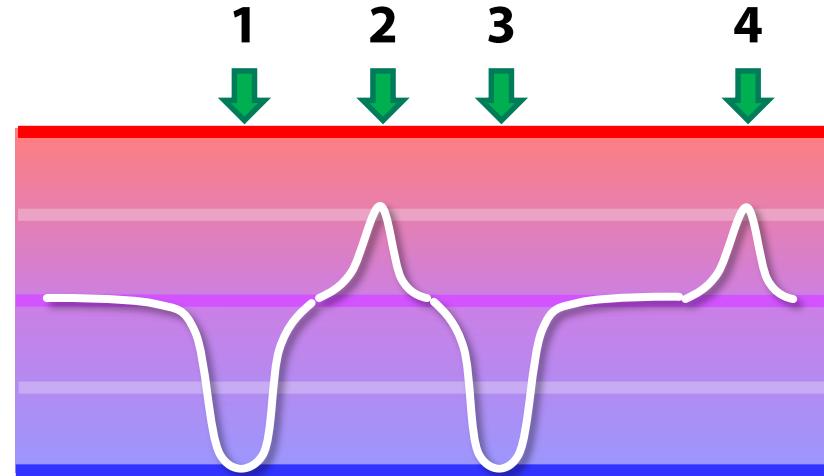
12 months

12 months

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- Other Specified Bipolar and Related Disorder
- Unspecified Bipolar and Related Disorder

"The Bipolar Spectrum"

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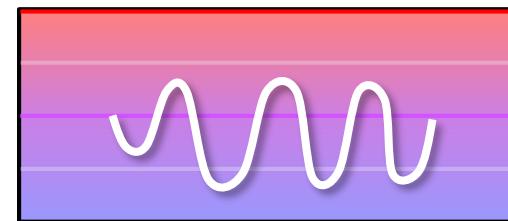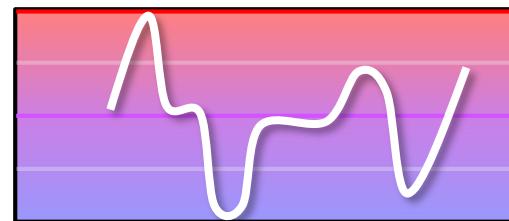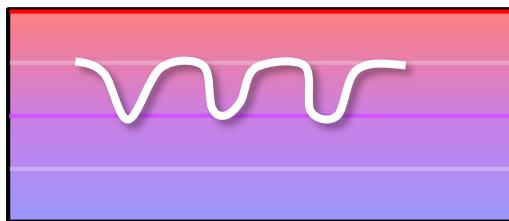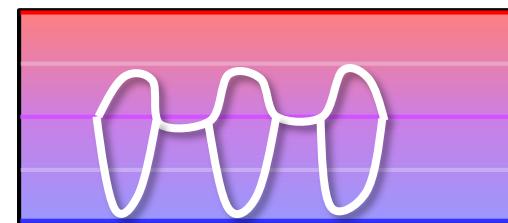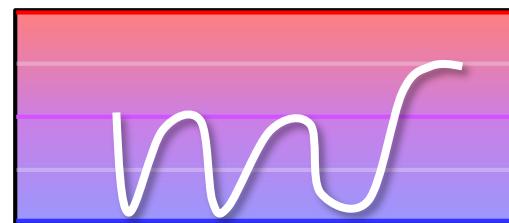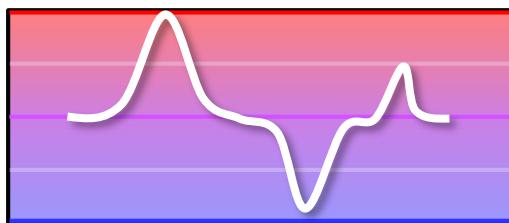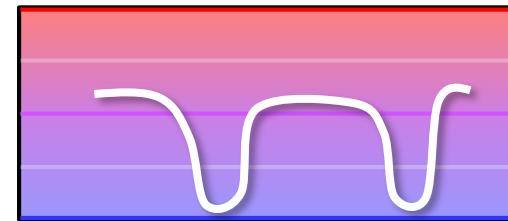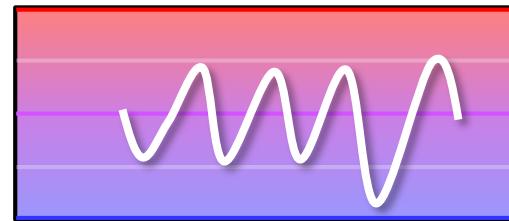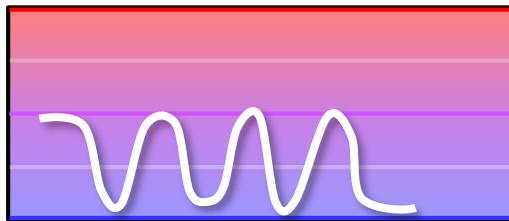
Major Depressive Disorder

- One or more major depressive episodes
- No manic or hypomanic episodes

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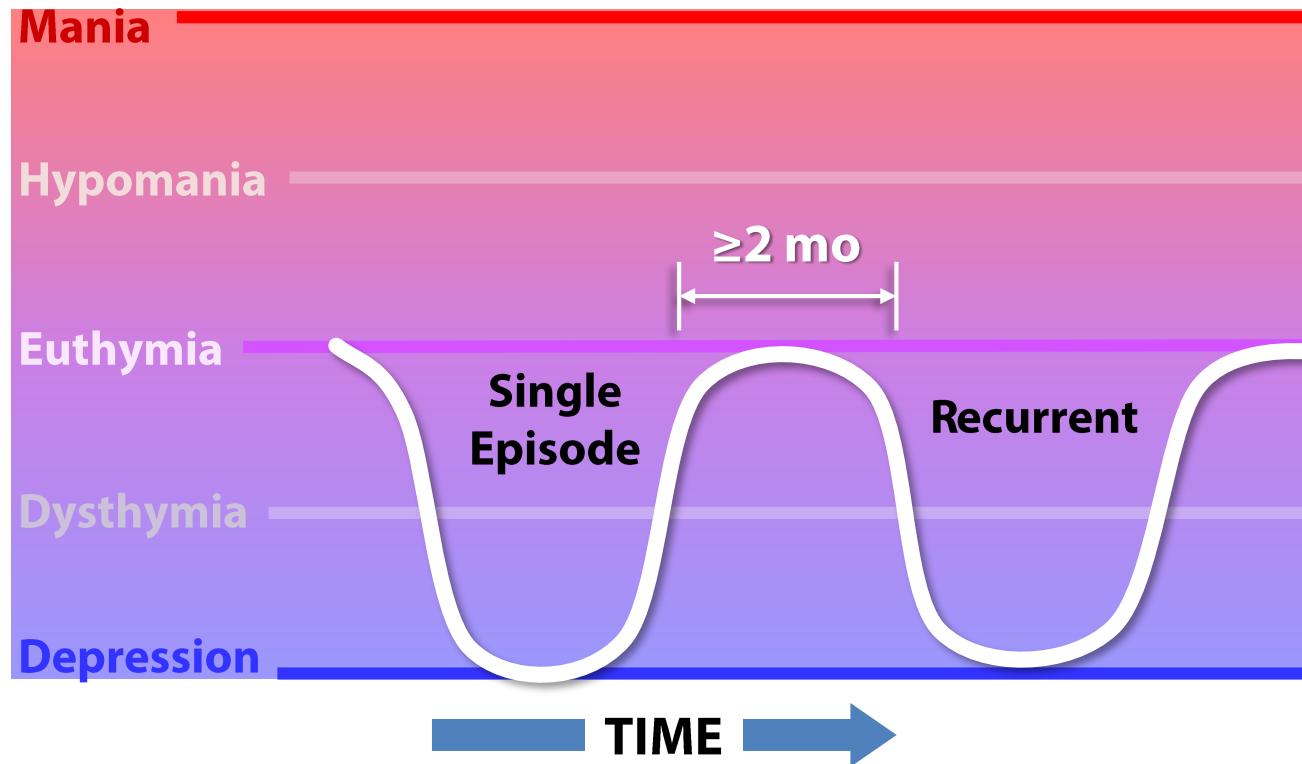
Bipolar Depression Versus Major Depressive Disorder

Major depressive episodes may look the same for different disorders
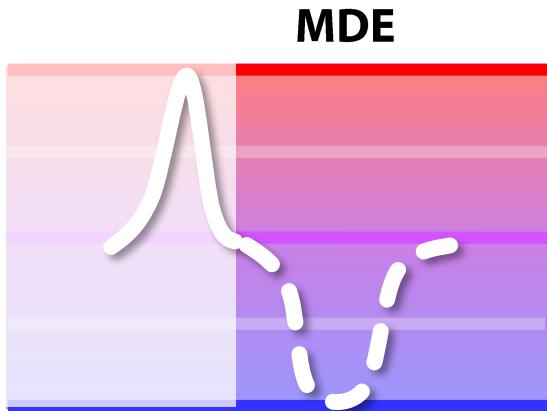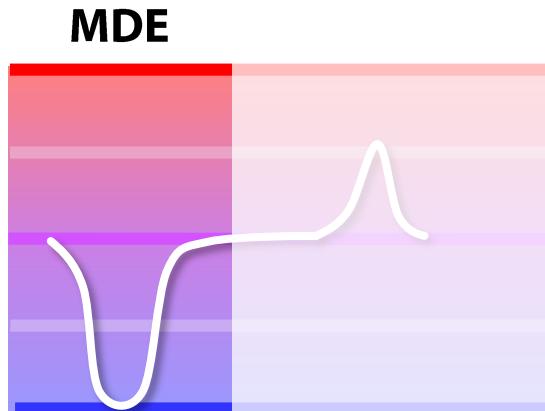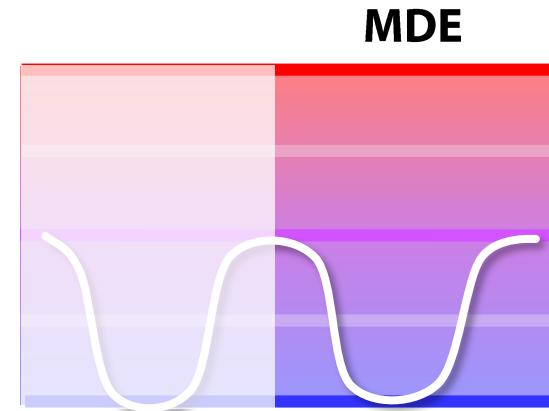
**MDE**   **MDE**   **MDE**

Bipolar I disorder   Bipolar II disorder   Major depressive disorder

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Bipolar Disorder versus Major Depressive Disorder
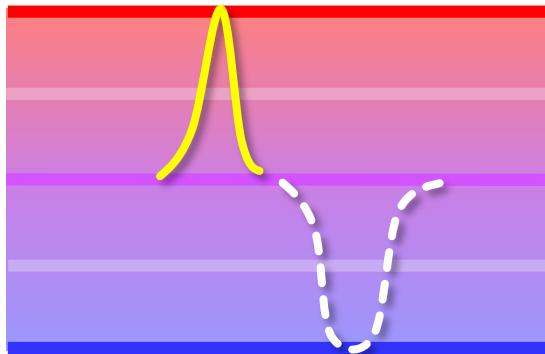
One or more manic episodes

One or more MDEs; at least one hypomanic episode
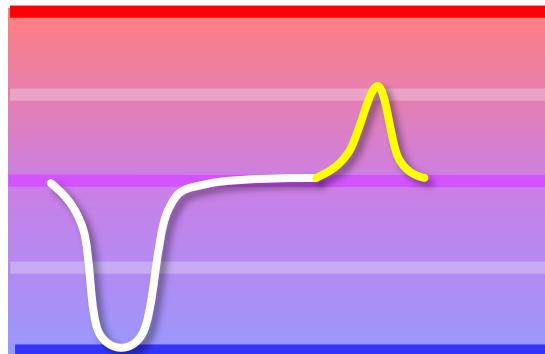
NO MANIC episodes
NO HYPOMANIC episodes

Bipolar I disorder

Bipolar II disorder

Major depressive disorder

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Specifier: Mixed Features
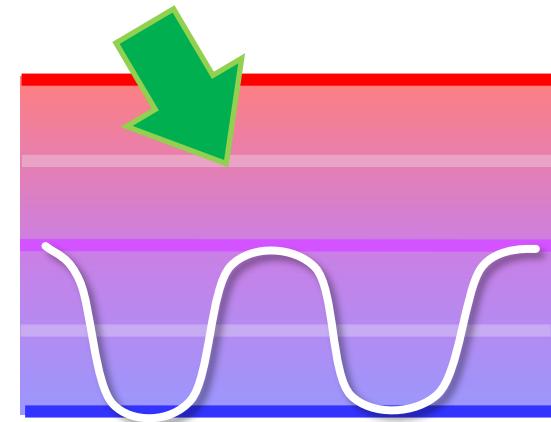
• Can apply to bipolar I, bipolar II, and major depressive disorder
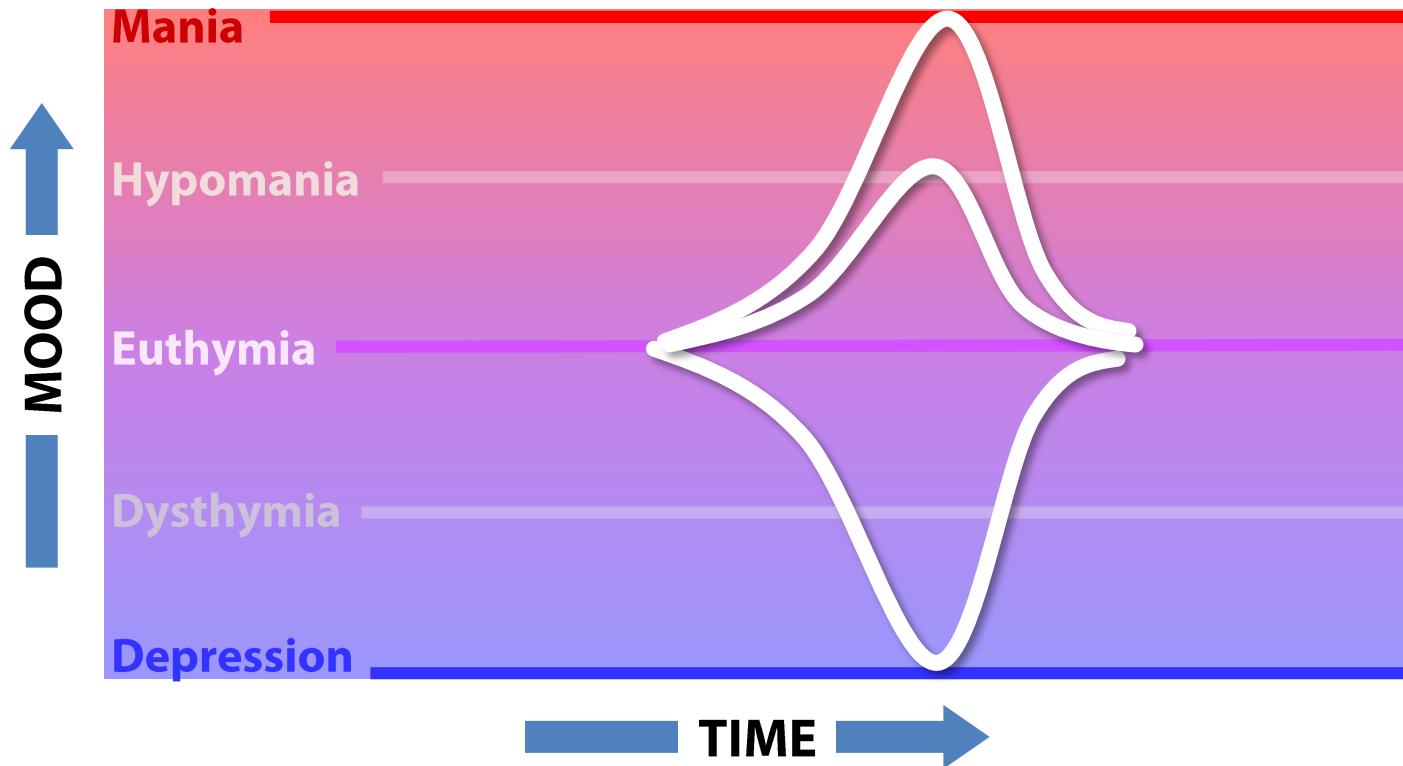
Specifier: Mixed Features

MANIC EPISODE + **MDE**

Manic or hypomanic episode with mixed features	Depressive episode with mixed features
• Full criteria for a manic or hypomanic episode are met	• Full criteria for a depressive episode are met
• Meet 3 of the criteria for a depressive episode during a majority of days	• Meet 3 of the criteria for a manic or hypomanic episode during a majority of days

If the full criteria for both mania and depression are met simultaneously then the diagnosis should be manic with mixed features

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Key Takeaways

- Bipolar I disorder requires one or more manic episodes. MDEs are common, but not required for diagnosis.

- Bipolar II disorder requires at least one MDE and at least one hypomanic episode.

- Other specified bipolar and related disorder and unspecified bipolar and related disorder encompass a complex range of symptomatology that can be considered a "bipolar spectrum."

- Major depressive disorder requires one or more MDEs and the absence of manic and hypomanic episodes.

- The specifier "mixed features" can apply to both bipolar disorder and major depressive disorder and describes an episode that has both manic or hypomanic and depressive symptoms.

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- Part 1: Description of mood episodes

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Rating Scales for Bipolar Disorder and Major Depressive Disorder

- Severity of depression, mania, and anxiety symptoms

- Function and Quality of Life scales

- Other rating scales and diagnostic scales

Rating scales for severity of depression, mania, and anxiety symptoms

- Montgomery-Åsberg Depression Rating Scale (MADRS)
- Children's Depression Rating Scale-Revised (CDRS-R)
- Clinical Global Impressions – Severity of Illness (CGI-S)
- Clinical Global Impression–Bipolar Version–Severity of Illness (CGI–BP–S)
- Young Mania Rating Scale (YMRS)
- Quick Inventory of Depressive Symptomatology (Self-Report, 16-Item) (QIDS-SR$_{16}$)
- Hamilton Rating Scale for Anxiety (HAM-A)

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Montgomery-Åsberg Depression Rating Scale (MADRS)

- Consists of 10 items that are core depression symptoms

- Contains items rated on 0-6 (no abnormality to severe)

- Frequently used in clinical trials

- Requires existing diagnosis of a disorder with depressive symptoms

6   **Most severe**

5

4

3

2

1

0   **None/absent**

1) Apparent sadness
2) Reported sadness
3) Inner tension
4) Reduced sleep
5) Reduced appetite
6) Concentration difficulties
7) Lassitude (apathy)
8) Inability to feel
9) Pessimistic thoughts
10) Suicidal thoughts

Total score range **0-60**

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Children's Depression Rating Scale-Revised (CDRS-R)

- Consists of 17 items that measure the presence and severity of depression symptoms in children (6-12 years)

- The items are rated on a scale from 1 to 5, 1 to 6, or 1 to 7

Most severe

5
4
3
2
1

None/absent

ITEMS (rated on a scale of 1 to 5)

4) Sleep disturbance

5) Appetite disturbance

16) Listless speech

Most severe

6
5
4
3
2
1

None/absent

ITEMS (rated on a scale of 1 to 6)

1) Impaired schoolwork

8) Irritability

9) Excessive guilt

14) Excessive weeping

17) Hypoactivity

Most severe

7
6
5
4
3
2
1

None/absent

ITEMS (rated on a scale of 1 to 7)

2) Difficulty having fun

3) Social withdrawal

6) Excess fatigue

7) Physical complaints

10) Low self-esteem

11) Depressed feelings

12) Morbid ideation

13) Suicide ideation

15) Depressed facial affect

Total score range **17-113**
≥40 indicates depression

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Clinical Global Impressions – Severity of Illness (CGI-S)

- One of the most widely used brief assessment tools in psychiatry

- Raters compare patient to all previous similar patients

Severity of Illness
Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?
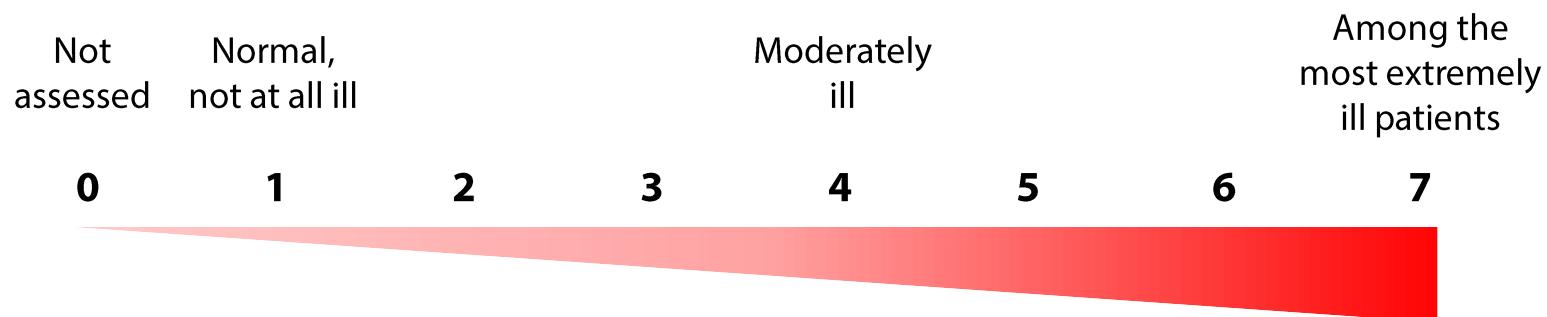
Not assessed	Normal, not at all ill		Moderately ill			Among the most extremely ill patients
0	1	2	3	4	5	6	7

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# Clinical Global Impression–Bipolar Version–Severity of Illness (CGI–BP–S)

Severity of illness

	Normal, not ill	Minimally ill	Mildly ill	Moderately ill	Markedly ill	Severely ill	Very severely ill
Mania							
Depression	1	2	3	4	5	6	7
Overall bipolar illness							
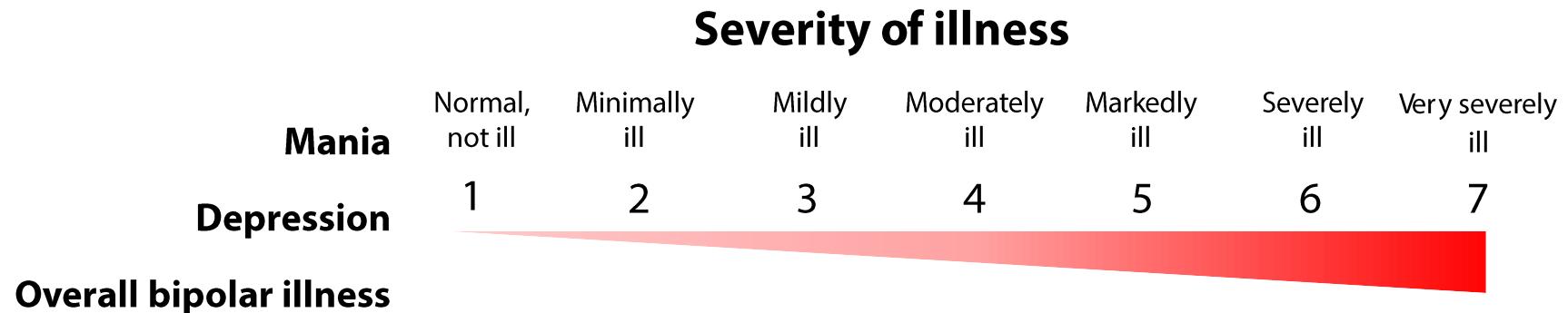
Young Mania Rating Scale (YMRS)

- 11-item scale designed to evaluate severity of manic symptoms
- Most frequently used scale for mania
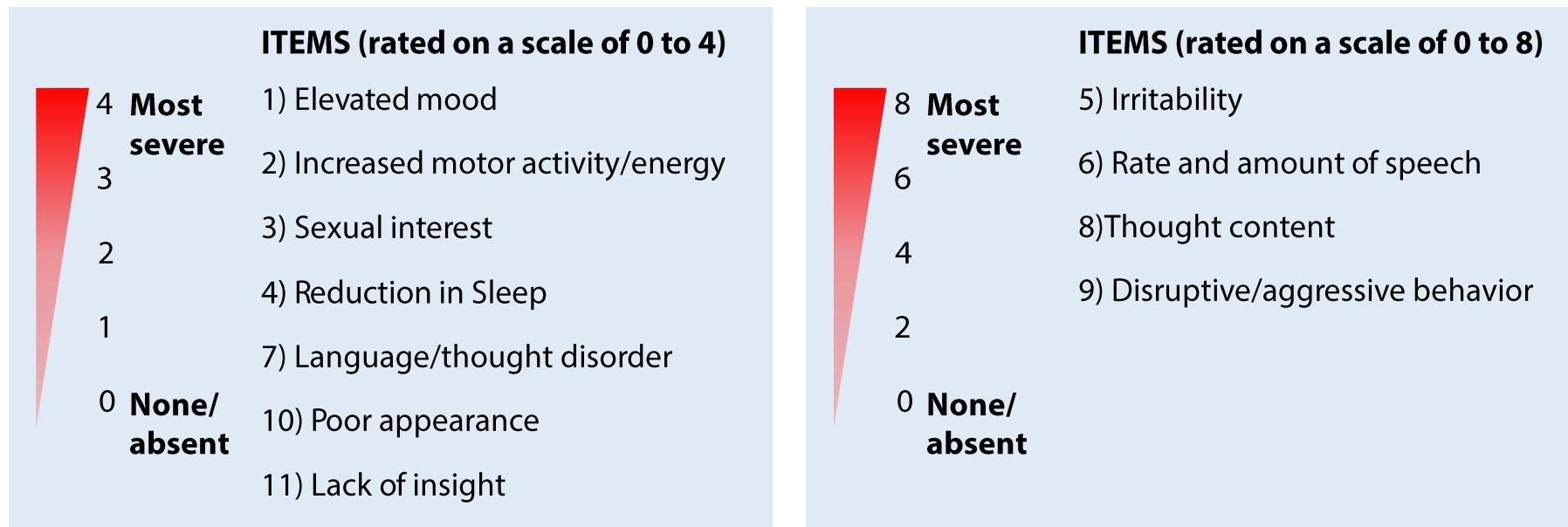
ITEMS (rated on a scale of 0 to 4)

4 **Most severe**

3

2

1

0 **None/ absent**

1) Elevated mood

2) Increased motor activity/energy

3) Sexual interest

4) Reduction in Sleep

7) Language/thought disorder

10) Poor appearance

11) Lack of insight

ITEMS (rated on a scale of 0 to 8)

8 **Most severe**

6

4

2

0 **None/ absent**

5) Irritability

6) Rate and amount of speech

8) Thought content

9) Disruptive/aggressive behavior

Total score range **0-60**

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Quick Inventory of Depressive Symptomatology (Self-Report, 16-Item) (QIDS-SR$_{16}$)

- Validated depression rating scale
  - Requires existing diagnosis of a disorder with depressive symptoms
- Self-reported versions use clearly stated criteria ("anchor points") for ratings
  - Estimates of frequency and severity
- One score for each of the nine DSM-IV-defined symptoms for MDE
- Contains items rated on 0-3 (no symptoms present to severe)

3 **Most severe**

2

1

0 **None/ absent**

| Select highest score from 1-4 | 1) Falling asleep
2) Sleeping during the night
3) Waking up too early
4) Sleeping too much |

5) Feeling sad

| Select highest score from 6-9 | 6) Decreased appetite
7) Increased appetite
8) Decreased weight (within the last 2 weeks)
9) Increased weight (within the last 2 weeks) |

10) Concentration/decision making

11) View of myself

12) Thoughts of death or suicide

13) General interest

14) Energy levels

| 15) Feeling slowed down
16) Feeling restless | Select highest score from 15 or 16 |

Total score range **0-27**

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Hamilton Rating Scale for Anxiety (HAM-A)

- Used for patients who have already been diagnosed

- 14-item scale relies on patient subjective report

- Contains items rated on 0-4 (none to very severe)
  - Performed by clinician

4 **Very severe**

3

2

1

0 **None**

Anxious mood	Somatic general (sensory)
Tension	Cardiovascular symptoms
Fears	Respiratory symptoms
Insomnia	Gastrointestinal symptoms
Intellect	Genitourinary symptoms
Depressed mood	Autonomic symptoms
Somatic general (muscular)	Behavior at interview

Total score range **0-56**

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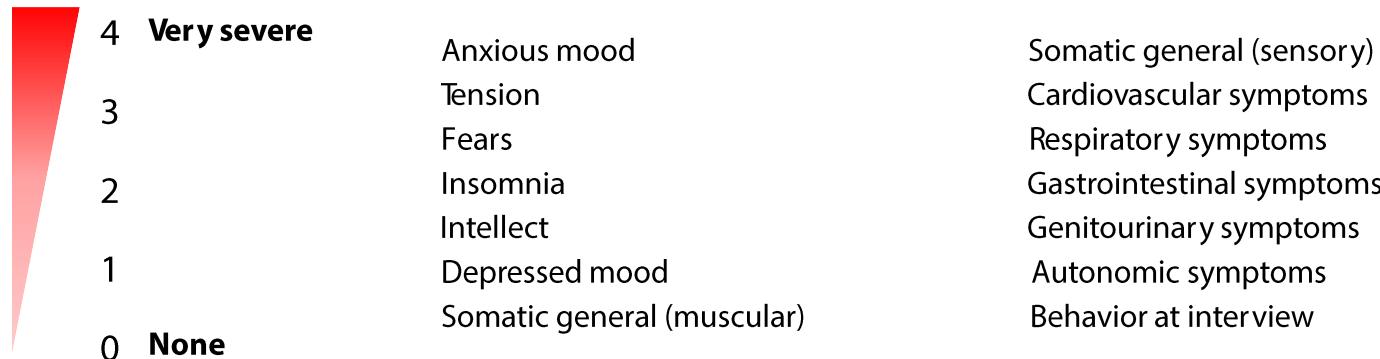
Rating Scales for Function and Quality of Life

- Sheehan Disability Scale (SDS)

- Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF)

Sheehan Disability Scale (SDS)

- Self-report measure

- Commonly used

- Shows sensitivity to treatment

10   **Extremely**

9

8   **Markedly**

7

6

5   **Moderately**

4

3

2   **Mildly**

1

0
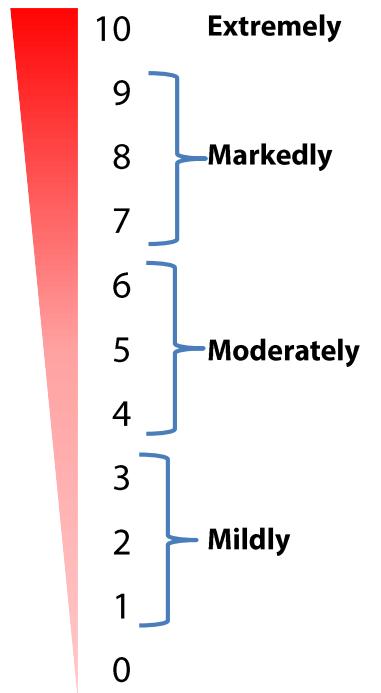
Disability subscales

- **Work:** The symptoms have disrupted your work…

- **Social life:** The symptoms have disrupted your social life…

- **Family life:** The symptoms have disrupted your family life/home responsibilities…

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Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF)

Taking everything into consideration, during the past week how satisfied have you been with your…

1   **2**   **3**   **4**   **5**

Very Poor   **Very good**
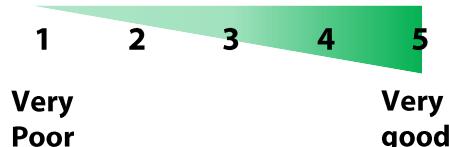
…physical health?   …ability to function in daily life?

…mood?   …sexual drive, interest, and/or performance?*

…work?   …economic status?

…household activities?   …living/housing situation?*

…social relationships?   …ability to get around physically without feeling dizzy or falling?

…family relationships?   …your vision in terms of ability to do work or hobbies?*

…leisure-time activities?   …overall sense of well-being?

Summed to yield raw score (range of 14 to 70)

*If satisfaction is very poor, poor, or fair on these items, please underline the factors associated with lack of satisfaction.

…medication? (If not taking any, leave blank)

…overall life satisfaction and contentment?

Stand-alone items, not included in total score

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Other Rating Scales for Bipolar Disorders and MDD[*]

- **Bipolar Depression Rating Scale (BDRS)**

   20 items capture key elements of bipolar depression with scores ranging from 0-60

- **Hamilton Rating Scale for Depression, 17 item (HAM-D$_{17}$)**

   17 items assess severity of depression with scores ranging from 0-42

- **Bech-Rafaelsen Mania Scale (MRS)**

   11 items assess severity of mania symptoms with scores ranging from 0-44

[*] Not used in clinical trials of Latuda® (lurasidone HCl) for the treatment of bipolar I depression

Diagnostic Scales for Bipolar Disorders and MDD*

- **Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)**

  Widely used diagnostic interview with separate modules to diagnose various disorders

- **Mini-International Neuropsychiatric Interview (MINI)**

  - Short diagnostic interview with separate modules to diagnose various disorders

  - Used to confirm diagnosis of Bipolar I Disorder in Latuda® (lurasidone HCl) trials

* Not used in clinical trials of LATUDA for the treatment of bipolar I depression

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Rating Scales for Safety Assessments

- Columbia-Suicide Severity Rating Scale (C-SSRS)

Involuntary Movements Assessment Scales

- Abnormal Involuntary Movement Scale (AIMS)

- Barnes Akathisia Rating Scale (BAS or BARS)

- Simpson Angus Scale (SAS)

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Columbia-Suicide Severity Rating Scale (C-SSRS)

SUICIDAL IDEATION

SEVERITY SUBSCALE
5-point scale (1 = wish to be dead,
5 = active suicidal ideation with
specific plan and intent)

INTENSITY SUBSCALE
5 items (frequency, duration,
controllability, deterrents, reason)
5-point scale

1   2   3   4   5

Least
severe

Most
severe
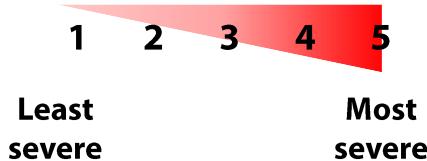
SUICIDAL BEHAVIOR

BEHAVIOR SUBSCALE
Actual, interrupted, and aborted attempts
Preparatory acts or behavior
Suicidal behavior present
Yes/No responses, plus number of attempts

LETHALITY SUBSCALE
Assesses actual and potential lethality and medical
damage associated with actual suicide attempts

POTENITAL LETHALITY

2   Likely to result in death

1   Likely to result in injury, but
    not likely to cause death

0   Not likely to result in death
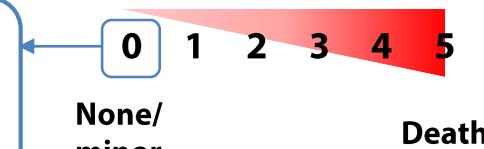
0   1   2   3   4   5

None/
minor

Death

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Abnormal Involuntary Movement Scale (AIMS)

FACIAL AND ORAL MOVEMENTS

1. Muscles of facial expression
2. Lips and perioral area
3. Jaw
4. Tongue

4 Severe
3
2
1
0 None

EXTREMITY MOVEMENTS

5. Upper (arms, wrists, hands, fingers)
6. Lower (legs, knees, ankles, toes)

TRUNK MOVEMENTS

7. Neck, shoulders, hips

GLOBAL JUDGMENTS

8. Severity of abnormal movements
9. Incapacitation due to abnormal movements
10. Patient's awareness of abnormal movements

4 Aware, severe distress
3
2
1
0 No awareness

DENTAL STATUS

11. Current problems with teeth and/or dentures
12. Does patient usually wear dentures?
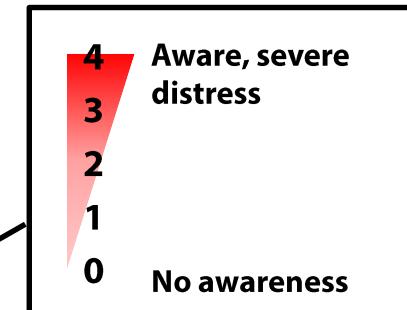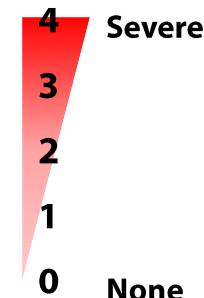
No (0) / Yes (1)

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Reproduced and adapted from Sunovion Pharmaceuticals Inc. as a self read training module

Barnes Akathisia Rating Scale (BAS or BARS)

1. OBJECTIVE

0 = normal, occasional fidgety movement of limbs

1= presence of characteristic restless movements

2 = observed phenomena, present for at least half the observation period

3 = constantly engaged in characteristic restless movements

3   **Severe**

2

1

0   **None**
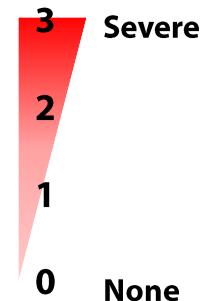
2. SUBJECTIVE

Awareness of Restlessness

0 = absence

1 = nonspecific sense

2 = aware, and/or complains of inner restlessness aggravated specifically by being required to stand still

3 = awareness of intense compulsion to move most of the time and/or reports strong desire to walk or pace most of the time

Distress Related to Restlessness

0 = no distress

1 = mild

2 = moderate

3 = severe

3. GLOBAL CLINICAL ASSESSMENT OF AKATHISIA

0 = absent; 1 = questionable; 2 = mild; 3 = moderate; 4 = marked; 5 = severe

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Simpson Angus Scale (SAS)

10-item instrument to evaluate the symptoms of parkinsonism

1. GAIT
2. ARM DROPPING
3. SHOULDER SHAKING
4. ELBOW RIGIDITY
5. FIXATION OF POSITION OR WRIST RIGIDITY
6. LEG PENDULOUSNESS (ability to swing freely in a hanging position)
7. HEAD DROPPING
8. GLABELLA* TAP
9. TREMOR
10. SALIVATION

4 Severe
3
2
1
0 None

4 21 or more blinks
3 16-20 blinks
2 11-15 blinks
1 6-10 blinks
0 0-5 blinks
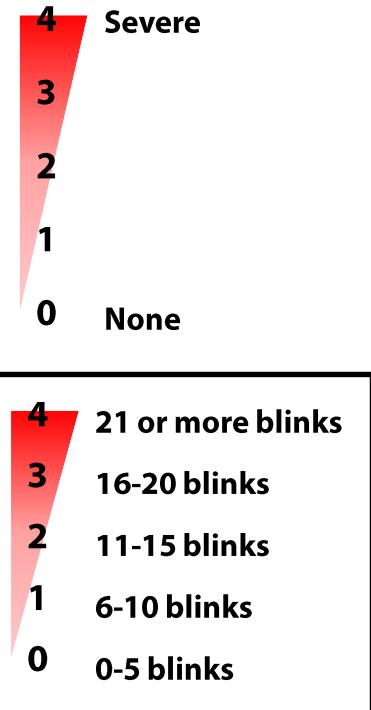
 * The region between the eyebrows and above the nose

Key Takeaways

- The following scales were used to assess depressive symptoms in the Latuda® (lurasidone HCl) clinical trials in bipolar depression
  - Montgomery-Åsberg Depression Rating Scale (MADRS)
  - Clinical Global Impression–Bipolar Version–Severity of Illness (CGI–BP–S) depression scale
  - Quick Inventory of Depressive Symptomatology (16-Item) (Self-Report) (QIDS-SR$_{16}$)
- The MADRS was used for the primary efficacy in the clinical trials
- The CGI-BP-S was used as the key secondary efficacy endpoint in the clinical trials
- The Young Mania Rating Scale (YMRS) measured severity of mania symptoms and was a secondary endpoint in the clinical trials
- The Sheehan Disability Scale (SDS) and Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF) were used to measure quality of life satisfaction in the clinical trials

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Module 2: Bipolar Disorder-Classification and Diagnosis

GLOSSARY

Akathisia -   motor restlessness characterized by muscular quivering (e.g., the urge to move the limbs, especially the legs), the inability to sit still, and a feeling of inner restlessness

anhedonia -   absence of pleasure from the performance of acts that would normally be pleasurable

comorbidity -   a concomitant but unrelated pathological or disease process

dysthymia -   a chronic but typically less severe form of depression

euthymia -   normal mood

glabella -   the region between the eyebrows and above the nose

hypomania -   a less severe form of mania

mania -   abnormally elevated mood

parkInsonism -   any of a group of nervous disorders similar to Parkinson's disease, marked by muscular rigidity, tremor, and impaired motor control

perioral -   of or relating to the tissues around the mouth prevalence· the total number of cases of a disease in a given population at a specific time

psychomotor -   of or relating to movement or muscular activity associated with mental processes; can manifest, for example, as the inability to sit still and being restless, or conversely, as a slowing down in movements and speech

Module 2: Bipolar Disorder-Classification and Diagnosis

REFERENCE

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Text Rev. Washington, DC: American Psychiatric Association; 2013.

Barnes TRE. A rating scale for drug-induced akathisia. Brit 1 Psych/at. 1989;154:672-676.

Bech P, Rafaelsen OJ, Kramp P, Bolwig TG. The Mania Rating Scale: scale construction and inter-observer agreement. Neuropharmacology. 1978;17(6) :430-431. Berk M, Malhi GS, Cahill C, et al. The Bipolar Depression Rating Scale (BORS): its development, validation and utility. BipolarDisord. 2007;9:571-579.

Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmaco/ Bull. 1993;29:321-326. Guy W, ed. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: U.S. Department of Health, Education, and Welfare; 1976.

Hamilton M. The assessment of anxiety states by rating. Brit 1 Med Psycho/. 1959;32(1):50-55.

Hamilton M. A rating scale for depression. 1 Neural Neurosurg Psychiat. 1960;23:56-62.

Merikangas KR, Akiskal HS, Angst J, et al. lifetime and 12-month prevalence of bipolar spectrum disorder in the national comorbidity survey replication. Arch Gen Psychiatry. 2007;64:543-552.

Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Brit J Psychiat. 1979;134:382-389.

Posner K, Brown GK, Stanley B, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multi site studies with adolescents and adults. Am 1 Psychiatry. 2011;168:1266-1277.

Rush AJ, Trivedi MH, Ibrahim HM, et al. The 16-item Quick Inventory of Depressive Symptomatology (QIDS), Clinician Rating (QIDS-C), and Self-Report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biol Psychiatry. 2003;S4:S73-583.

Sheehan DV, Harnett-Sheehan K, Raj BA. The measurement of disability. Int Clin Psychopharm. 1996;11(Suppl 3):89-95.

Sheehan DV, lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.1.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. 1998;59(suppl 20):22-33.

Simpson GM, Angus JWS. A rating scale for extrapyramidal side effects. Acta Psychiat Scand. 1970; 212:11-19.

Spearing MK, Post RM, Leverich GS, Brandt D, Nolen W. Modification of the Clinical Global Impressions (CGI) scale for use in bipolar illness (BP): the CGI-BP. Psychiat Res. 1997;73:159-171.

Spitzer RL, WilliamsJBW, Gibbon M, First MB. The Structured Clinical Interview for DSM-I11-R (SCID). I: History, rationale, and description.Arch GenPsychiatry.1992;49:624--629.

Stahl SM. Stahl's Essential Psychopharmacalogy: Neuroscientific Basis and Practical Applications. 3rd ed. New York, NY: Cambridge University Press; 2008.

Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Brit J Psychiat. 1978;133:429-435.