SOMEWHERE OVER THE RAINBOW: RECOMMENDATIONS FOR THE DIAGNOSIS AND TREATMENT OF DEPRESSIVE MIXED STATES
Learning Objectives

• Impart the importance of screening for the presence of mixed features and family history of bipolar disorder in all patients presenting with symptoms of depression

• Improve identification of mixed features in patients presenting with symptoms of depression

• Optimize treatment strategies for patients with depressive mixed states
• Although categorical classifications may be useful for clinical practice, the overwhelming majority of the evidence points to a dimensional (spectrum) view of mood disorders

  • e.g., treatment response (antidepressant vs. mood stabilizing agent) and links with family history of BP

• Individuals with unipolar depression and "a little bit of mania" are more likely to have an eventual diagnostic conversion to bipolar disorder

References:
So You Think It's Unipolar Depression?

• Over one-third of unipolar patients are eventually re-diagnosed as bipolar

• As many as 60% of patients with BPII are initially diagnosed as unipolar

• Presence of even subthreshold (hypo)mania symptoms is strongly associated with conversion to bipolar disorder
  • Each (hypo)mania symptom increases risk by ~30%

Progression to Bipolar Disorder From MDD With Subthreshold Hypomania

N=550 individuals followed for >1 year (mean follow-up: 17.5 years) after a diagnosis of major depression at intake.

19.6% of patients converted to bipolar disorder during follow-up

N=550 individuals followed for >1 year (mean follow-up: 17.5 years) after a diagnosis of major depression at intake.

Clues Across The Spectrum

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<th>Symptoms</th>
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Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

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Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

Which Patients With Unipolar Depression Will Convert to Bipolar Disorder?

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A Rose By Any Other Name…

**Major depressive disorder** (unipolar depression)

**Bipolar disorder II**

**Bipolar disorder I**

**DSM-5 DIAGNOSIS**

- Depression
- Depression with subsyndromal mania
- Mixed states
- Mania with subsyndromal depression
- Mania

*Increasing #/severity of manic symptoms*  
*Increasing #/severity of depressive symptoms*

"With mixed features" if subthreshold (hypo)manic symptoms co-occur with depressive episodes

"With mixed features" if subthreshold depressive symptoms co-occur with manic episodes
Evolution of the DSM

• DSM-IV mixed episode
  • Diagnostic criteria for major depression and mania met at the same time

• DSM-5 mixed features specifier
  • Recognizes the presence of subthreshold (hypo)manic symptoms during a depressive episode
  • Specifier may be applied to major depressive disorder, bipolar II, or bipolar I

APA Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Text Rev. 2000;
APA Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013.
DSM-5 Mixed Features Specifier

• Full criteria for a MDE and ≥ 3 of these manic symptoms:
  – Elevated, expansive mood
  – Inflated self-esteem or grandiosity
  – More talkative than usual or pressure to keep talking
  – Flight of ideas or racing thoughts
  – Increase in energy or goal-directed activity (socially, at work or school, or sexually)
  – Increased or excessive involvement in activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, foolish business investments)
  – Decreased need for sleep

• Diagnosis may be complicated by comorbid conditions, including untreated ADHD, personality disorders, and substance abuse

APA Diagnostic and Statistical Manual of Mental Disorders. 5th ed. 2013.
Mixed Features: The Exception or the Rule?

Mixed Features Commonly Encountered in Adults With Both Major Depressive Disorder and Bipolar Disorder: The International Mood Disorders Collaborative Project

% of Individuals Who Met Criteria For Mixed Features During an Index Major Depressive Episode

- MDD: 26.0% (n=149)
- BP II: 34.0% (n=65)
- BPI: 33.8% (n=49)
Depression With Mixed Features (DMX)

Associated with:
- Family history of BP
- Suicidality
- Antidepressant-induced mania
- Young age of onset
- Long duration of illness
- Poor prognosis
- Severe depression
- Antidepressant resistance
- Females
- Comorbid anxiety
- Comorbid SUD
- Impulse control

The prognosis for depression with co-occurring (hypo)mania (DMX) is much **worse** than for pure unipolar depression or bipolar depression without mixed features

Symptoms Most Commonly Seen in DMX

- Irritability
- Distractibility
- Psychomotor agitation
- Racing/crowded thoughts
- Increased talkativeness
- Emotional lability
- Rumination
- Initial or middle insomnia
- Dramatic expressions of suffering
- Impulsivity
- Risky behaviors

Symptoms Most Commonly Seen in DMX

- Psychomotor agitation
- Racing thoughts/flight of ideas
- Irritability
- Distractibility
- Talkativeness
- Increased goal-directed activity
- Risky behavior
- Decreased need for sleep
- Inflated self-esteem
- Elevated mood

Frequency Among Patients With DMX

DMX Diagnostic Criteria

• Although irritability, distractibility, and psychomotor agitation are among the most common symptoms of DMX, they are excluded from DSM-5 mixed features criteria due to the overlap of these symptoms with other disorders (e.g., anxiety disorders) and between mania and depression.

• Some argue that these 3 particular symptoms are the defining features of DMX and that excluding them will lead to misdiagnosis and dangerous treatment strategies.

  • Imagine if we excluded psychosis as a diagnostic feature of schizophrenia?

Non-DSM Criteria for DMX

• Do not exclude agitation, irritability, or distractibility
  • Benazzi criteria
  • Koukopoulos criteria
  • Research-based diagnostic criteria
• Consider family history
• Consider age of onset of depression

Non-DSM Criteria for DMX

4X as many cases of DMX identified using research-based diagnostic criteria

Non-DSM Criteria for DMX

- All patients identified as DMX will indeed have DMX

**HOWEVER,**
- Only 5.1% of individuals who have DMX will be identified
- ~95% at risk of receiving inappropriate treatment

Which is potentially more detrimental?
Misdiagnosing someone who is "pure unipolar" as DMX?

or

Treating unidentified DMX with antidepressants?

Consequences of Misdiagnosis/
Inappropriate Treatment

- Years (often a decade or more) of unnecessary suffering
- Treatment resistance?
- Reduced likelihood of responding to eventual appropriate mood stabilizer treatment
- Treatment-emergent activation syndrome (TEAS)
- Suicidality
Treatment Resistance

• Patients with DMX are less likely to respond to treatment-as-usual for major depressive disorder

• Diagnostic conversion from unipolar to bipolar is significantly related to treatment resistance
  • As many as two-thirds of patients whose diagnosis is converted from unipolar to bipolar disorder are treatment resistant

• Approximately half of patients with treatment-resistant "unipolar" depression may actually be bipolar

• Repeated exposure to antidepressants may lead to resistance to mood stabilizers and poorer outcomes in patients without "pure unipolar" depression
  • It may also be that patients with more antidepressant trials were always going to be resistant

Treatment-Emergent Activation Syndrome (TEAS)

- Over 20% of patients may experience TEAS related to antidepressants
- Most common with serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs)
- Hypothetically related to high noradrenergic potency
- The presence of even minor, subthreshold (hypo)mania during a depressive episode increases the risk of TEAS

(Hypo)mania
Agitation
Anxiety
Panic attacks
Irritability
Hostility/aggression
Impulsivity
Insomnia
Suicidality

Higher Risk of TEAS

- TCA or SNRI use
- Absence of antimanic mood stabilizer
- Genetic factors
- Comorbid alcoholism
- Female gender + comorbid anxiety disorder
- Bipolar I > bipolar II
- History of antidepressant-induced mania
- Mixed depression
- Low TSH with TCA use
- Hyperthymic temperament

TSH: thyroid-stimulating hormone.

DMX and Suicidality

• Non-euphoric (hypo)manic symptoms (including psychomotor agitation, impulsivity, irritability, and racing/crowded thoughts) combined with depressive symptoms (i.e., DMX) = recipe for suicidality

• Presence of mixed features increases risk of suicidality by 4X in both unipolar and bipolar depression

• DMX may underlie the connection between antidepressant use and suicidality
  • Most notably in the pediatric population, in which DMX is often the rule rather than the exception
  • Both young age of onset of depression and DMX symptoms indicate bipolarity

One of the Most Important Questions to Ask Any Patient With Depression

Any manic/hypomaniac symptoms and/or family history of bipolar disorder?

Every patient. Every time.
DMX and Family History

• Family history of BP
  • 4X higher in DMX than in "pure" unipolar depression
  • Highly associated with patients who have 2+ (hypo)manic symptoms during major depressive episodes (MDEs)
  • As common in DMX as in BP
  • Supports the idea of DMX as a "soft" bipolar disorder and a dimensional rather than a categorical view of mood disorders

Prieto ML et al. J Affective Disord 2015;172:355-60;
Tools for Assessing DMX

See APPENDIX for more details on each assessment tool

• Bipolar Depression Rating Scale (BDRS)
  • Clinician-administered assessment of current symptoms

• Mini International Neuropsychiatric Interview (MINI)
  • Patient self-report assessing current (hypo)manic symptoms

• Clinically Useful Depression Outcome Scale with DSM-5 Mixed (CUDOS-M)
  • Patient self-report assessing current (hypo)manic symptoms

• Hypomania Checklist (HCL-32)
  • Patient self-report that screens for lifetime (hypo)manic symptoms
The Old View:
A Trace of Depression Means Treat With an Antidepressant

- Mania
- Mania with subsyndromal depression
- Depression with subsyndromal mania
- Depression

Mixed States

Antidepressant
The New View:
A Trace of Mania Means Treat With an Antipsychotic

Antipsychotic

Mixed States

Mania with subsyndromal depression

Depression with subsyndromal mania

Mania

Depression
Issues With Existing Treatment Guidelines for DMX

- Any existing guidelines (and FDA approvals) for mixed bipolar disorder refer to DSM-IV criteria (co-occurring threshold-level MDE + threshold-level mania)
  - Recommendations are to treat as mania
- A diagnosis of MDD implies the use of unipolar depression treatment guidelines
  - Possibly ineffective and potentially harmful
- Treatment guidelines for bipolar depression are likely the most applicable to DMX
  - Many are not up to date with the latest clinical trial data (i.e., atypical antipsychotics with mood-stabilizing properties)
- Very few studies have yet to focus specifically on DMX

Bipolar Spectrum-Based First-Line Monotherapy Treatment Recommendations

Depression

Depression with subsyndromal mania

Mixed states

Increasing #/severity of manic symptoms

Mania with subsyndromal depression

Increasing #/severity of depressive symptoms

Unipolar depression?

Bipolar disorder?

Does it matter in terms of choosing the best treatment?

Only those patients with essentially NO symptoms of (hypo)mania should be considered for antidepressant monotherapy

Antidepressant

Atypical Antipsychotic

Mood Stabilizer

Treatment Algorithm for Depression Without Mixed Features

Treatment Algorithm for Depression With Mixed Features (DMX)

1. MDE with subsyndromal hypomania
   - Evaluate whether antidepressant may be exacerbating mixed features; discontinue/taper antidepressant if deemed ineffective
     - Yes
       - Patient on antidepressant monotherapy?
         - Yes
           - Initiate atypical antipsychotic with evidence of efficacy in DMX*
             - Therapeutic response?
               - Yes
                 - Consider ECT and novel/experimental options
               - No
                 - No
                   - No
                     - Add antidepressant
                       - Therapeutic response?
                         - Yes
                           - Continue as maintenance therapy
                         - No
                           - Consider ECT and novel/experimental options
     - No
       - Add or switch to mood stabilizer or switch to different atypical antipsychotic
         - No
           - Therapeutic response?
             - Yes
               - Continue as maintenance therapy
             - No
               - Consider ECT and novel/experimental options

*Asenapine, lurasidone, olanzapine, quetiapine, and ziprasidone have each shown some efficacy in treating DMX

# Atypical Antipsychotics

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<tr>
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<th>Evidence of Efficacy in DMX</th>
<th>FDA-Approved for BP Depression</th>
<th>FDA-Approved for BP Mania</th>
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Asenapine in DMX

Figure 1. Improvement in Depressive Symptoms as Assessed by Least Squares Mean Change From Baseline in MADRS Total Scores

Error bars indicate standard error.

*P<.05 vs placebo.
†P<.05 vs olanzapine.

Abbreviations: LOCF = last observation carried forward, LS = least squares, MADRS = Montgomery-Asberg Depression Rating Scale.

Asenapine in Mania With Depressive Symptoms (DSM-5 Specifier)

Improvement of depressive symptoms at Week 3

Cut-offs used to define depressive symptom severity in patients with ≥3 depressive features: mild (score ≥1 for MADRS items and ≥2 for PANSS items), moderate (score ≥2 MADRS, ≥3 PANSS), and severe (score ≥3 MADRS, ≥4 PANSS) symptoms; remission defined as MADRS ≤12; post hoc analysis.

Lurasidone in Bipolar Depression With Hypomanic Symptoms (DSM-5 Specifier)

MADRS responder rates (6-week LOCF-endpoint): groups with and without subsyndromal hypomania

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<tr>
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<th>Lurasidone</th>
<th>Placebo</th>
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<tr>
<td>Subsyndromal hypomania (baseline YMRS ≥4)</td>
<td><strong>51.2</strong></td>
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<td>Subsyndromal hypomania (score of ≥2 for 2 or more YMRS items)</td>
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<td><strong>31.1</strong></td>
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Change from baseline in YMRS score groups with and without subsyndromal hypomania

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<td><strong>0.3</strong></td>
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**p<0.01

Lurasidone Efficacy in DMX: Montgomery-Åsberg Depression Scale (MADRS)

Mean daily dose of lurasidone was 36.2 mg/day.

*\(p<0.05\); **\(p<0.01\); ***\(p<0.001\).

Lurasidone Efficacy in DMX: Young Mania Rating Scale (YMRS)

Lurasidone Efficacy in DMX: Hamilton Anxiety Rating Scale (HAM-A)

Mean Change From Baseline

Placebo (n=100)  Lurasidone (n=108)

BL mean = 16.7  BL mean = 17.0

-9.9***  -5.4

***p<0.001

Lurasidone Efficacy in DMX: Sheehan Disability Scale (SDS)

Mean Change From Baseline

Placebo (n=100)  Lurasidone (n=108)

BL mean = 20.5

-6.4

BL mean = 19.9

-11.2***

***p<0.001

Lurasidone Efficacy in DMX: Suicide and TEAS

Efficacy of Olanzapine Monotherapy in the Treatment of Bipolar Depression With Mixed Features

Quetiapine Efficacy in DMX: Clinical Global Impression (CGI-BD)


**p=0.002
Quetiapine Efficacy in DMX: MADRS

Quetiapine Efficacy in DMX: YMRS

Ziprasidone Monotherapy for DMX: Improvement in Depressive Symptoms

Ziprasidone Monotherapy for DMX: No Improvement in Manic Symptoms

Tolerability of Atypical Antipsychotics

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<th>SEDATION</th>
<th>WEIGHT GAIN</th>
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Patients on atypical antipsychotics should be regularly monitored for side effects, including BMI.
Mood Stabilizers for DMX

- No mood stabilizer is actually approved for use in depression of any kind (unipolar, mixed, bipolar)

- There are some data for the efficacy of lamotrigine or valproate for bipolar depression

- Lithium is well known for its anti-suicide effects; however, neither lithium nor carbamazepine monotherapy is recommended for the treatment of bipolar depression

---

Antidepressant Monotherapy for DMX?

• No
• Don't
• Seriously, just don't do it

• Antidepressant monotherapy should probably NOT be used in patients with even the slightest hint of (hypo)mania (or a family history of bipolar disorder)

• You will most likely not know if your depressed patient has ever had any (hypo)manic symptoms and/or family history of bipolarity unless you ask
  
  • Every patient. Every time.

• Any patient on antidepressant monotherapy should be regularly monitored for response and emergence of hypomania
Combination Therapy

• The treatment of DMX may require a combination of medications
• Common combinations for BP depression include:
  • Atypical antipsychotic + mood stabilizer
  • Atypical antipsychotic + antidepressant
    • Olanzapine-fluoxetine combination in particular
  • Mood stabilizer + antidepressant
• The combination of olanzapine or risperidone and carbamazepine is not recommended; always check the safety of any particular combination
• If an antidepressant is prescribed for DMX, it should be used in conjunction with a mood-stabilizing agent (atypical antipsychotic or mood stabilizer)
• It is questionable whether adding an antidepressant to a mood stabilizer or an atypical antipsychotic has any therapeutic benefit

Olanzapine-Fluoxetine Combination in the Treatment of Bipolar Depression With Mixed Features


Response defined as ≥ 50% reduction in the MADRS total score and < 2 concurrent manic/hypomaniac symptoms (measured by the YMRS)

No significant benefit from adding fluoxetine to olanzapine
No Faster Recovery From Mixed Depression in Bipolar Disorder When Antidepressants Are Added to Mood Stabilizers (STEP-BD)

Kaplan-Meier Curve for Time to Recovering/Recovered by Antidepressant Use

355 STEP-BD entrants with major depression + 1 or more manic symptoms

Other Adjunctive Pharmacological Treatment Strategies

- Modafinil/armodafinil
  - Stimulants may worsen symptoms (including irritability, agitation, and TEAS) in patients with DMX

- Pramipexole
- Folic acid
- Inositol
- Ketamine
- N-acetyl cysteine

- Omega-3 fatty acids
- Ramelteon
- Celecoxib
- Topiramate for weight management
- Benzodiazepines (short-term) for anxiety and agitation

Nonpharmacological Interventions

• Electroconvulsive therapy (ECT)
• Transcranial magnetic stimulation (TMS)
• Sleep deprivation
• Individual or group psychoeducation
  – Focus on early warning signs of relapse
• Interpersonal and family therapy
• Cognitive behavioral therapy

Summary

• Not all patients with depression should be given an antidepressant.

• The inappropriate overprescribing of antidepressants may contribute to drug-induced (hypo)manic episodes, treatment resistance, suicidality, and overall poor quality of life for many patients suffering from depression.

• If there are any symptoms of (hypo)mania or a family history of bipolar disorder, an antipsychotic with mood-stabilizing properties may be the best option.

• You will not know if a depressed patient has (hypo)manic symptoms or a positive family history of bipolar disorder unless you ask! Every patient. Every time.
APPENDIX
## Bipolar Depression Rating Scale (BDRS)

Clinician-administered assessment of **current** symptoms

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<tr>
<th>Severity of Disturbances to:</th>
<th>Mood</th>
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</tbody>
</table>
Mini International Neuropsychiatric Interview (MINI)

Patient self-report assessing **current** (hypo)manic symptoms

Since you have been experiencing your current manic episode, have you almost every day had times when:

<table>
<thead>
<tr>
<th>Points</th>
<th>No</th>
<th>Yes</th>
<th><strong>1</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You felt sad, empty, tearful, down, or depressed?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You were less interested in most activities?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You had less pleasure doing the activities you used to enjoy?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You were slowed down in your speech, thoughts, or movements?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You had fatigue?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You felt without energy?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>5a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You had feelings of worthlessness?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>5b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You felt excessively guilty?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>You wished you were dead, considered hurting yourself, made plans to commit suicide or attempted suicide?</td>
<td>NO</td>
<td>YES</td>
<td></td>
</tr>
</tbody>
</table>

**TOTAL =**

- IF THE TOTAL NUMBER OF POINTS IS EQUAL TO OR GREATER THAN 3, THE PATIENT PRESENTS A PROBABLE (HYPOMANIC) MANIC EPISODE WITH MIXED FEATURES

### Clinically Useful Depression Outcome Scale With DSM-5 Mixed Features (CUDOS-M)

**Patient self-report assessing current (hypo)manic symptoms**

<table>
<thead>
<tr>
<th>Frequency of each symptom during the prior week</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>Not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statement</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>I felt so happy and cheerful, it was like a high</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I had many brilliant, creative ideas</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I felt extremely self-confident</td>
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<tr>
<td>I slept only a few hours but woke full of energy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My energy seemed endless</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I was much more talkative than usual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I spoke faster than usual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>My thoughts were racing through my mind</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I took on many new projects because I felt I could do everything</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I was much more social and outgoing than usual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I did wild, impulsive things</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I spent money more freely than usual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I had many more thoughts and fantasies about sex</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### Hypomania Checklist (HCL-32)

Patient self-report that screens for **lifetime** (hypo)manic symptoms

<table>
<thead>
<tr>
<th>HCL-32</th>
<th>HCL-32 (continued)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I need less sleep</td>
<td>I am more flirtatious and/or I am more sexually active</td>
</tr>
<tr>
<td>I feel more energetic and more active</td>
<td>I talk more</td>
</tr>
<tr>
<td>I am more self-confident</td>
<td>I think faster</td>
</tr>
<tr>
<td>I enjoy my work more</td>
<td>I make more jokes or puns when I am talking</td>
</tr>
<tr>
<td>I am more sociable (make more phone calls, go out more)</td>
<td>I am more easily distracted</td>
</tr>
<tr>
<td>I want to travel and/or do travel more</td>
<td>I engage in lots of new things</td>
</tr>
<tr>
<td>I tend to drive faster or take more risks when driving</td>
<td>My thoughts jump from topic to topic</td>
</tr>
<tr>
<td>I spend more money/too much money</td>
<td>I do things more quickly and/or more easily</td>
</tr>
<tr>
<td>I take more risks in my daily life (in my work and/or other activities)</td>
<td>I am more impatient and/or get irritable more easily</td>
</tr>
<tr>
<td>I am physically more active (sport etc.)</td>
<td>I can be exhausting or irritating for others</td>
</tr>
<tr>
<td>I plan more activities or projects</td>
<td>I get into more quarrels</td>
</tr>
<tr>
<td>I have more ideas, I am more creative</td>
<td>My mood is higher, more optimistic</td>
</tr>
<tr>
<td>I am less shy or inhibited</td>
<td>I drink more coffee</td>
</tr>
<tr>
<td>I wear more colorful and more extravagant clothes/make-up</td>
<td>I smoke more cigarettes</td>
</tr>
<tr>
<td>I want to meet or actually do meet more people</td>
<td>I drink more alcohol</td>
</tr>
<tr>
<td>I am more interested in sex, and/or have increased sexual desire</td>
<td>I take more drugs (sedatives, anti-anxiety pills, stimulants)</td>
</tr>
</tbody>
</table>