Things You Think You Know, That May Not Be True in the Diagnosis and Treatment of Depression

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Belief 1
Antidepressants Have Been Proven Effective for the Patients Treated in Our Practice

The Rhode Island MIDAS Project

• MIDAS = Methods to Improve Diagnostic Assessment and Services
  • Research assessments integrated into routine clinical practice
    – Structured Clinical Interview for DSM-IV (SCID)
    – Structured Interview for DSM Personality (SIDP-IV)
    – Schedule for Affective Disorders and Schizophrenia (SADS) (extracted HAM-D)

Generalizability of Treatment Research

Unique opportunity to apply inclusion and exclusion criteria used in efficacy trials to the patients treated in routine clinical practice.

Generalizability of Treatment Research

FIGURE 1. Impact of Sequential Application of Exclusion Criteria on the Number of 346 Depressed Outpatients Who Would Have Qualified for Participation in an Antidepressant Efficacy Trial

Patients in the MIDAS Project

- 1500 psychiatric outpatients
- 596 principal diagnosis of DSM-IV MDD or bipolar depression
  - 399 (67%) female; 197 (33%) male
  - Mean age = 38.2 years (SD = 12.0)
  - 89% white
  - 11% < high school; 66% high school or GED; 23% graduated college

Exclusion Due to Bipolarity or Psychosis

- 59 (9.9%) of the 596 patients had DSM-IV bipolar I or bipolar II depression
- Of the remaining 537 patients, 34 (5.7%) had psychotic features
  - approximately 1/6 patients would be excluded due to bipolarity or psychosis

Application of Remaining Exclusion Criteria to Patients Treated in Clinical Practice

- 503 outpatients with nonbipolar, nonpsychotic depression
- Exclusion criteria of 39 published studies applied

Results

- The percentage of patients that would have been excluded ranged from 0% to 95.0% (mean = 65.8%)
- In approximately half of the studies more than 70% of the depressed patients would have failed to qualify for the efficacy study
Other Studies Applying Inclusion/Exclusion Criteria to Clinical Patients with MDD

<table>
<thead>
<tr>
<th>Author</th>
<th>No. with MDD</th>
<th>% Who Would Qualify</th>
</tr>
</thead>
<tbody>
<tr>
<td>van der Lem</td>
<td>1597</td>
<td>20–25</td>
</tr>
<tr>
<td>Wisniewski</td>
<td>2855</td>
<td>22</td>
</tr>
<tr>
<td>Zetin</td>
<td>276</td>
<td>11</td>
</tr>
</tbody>
</table>

Other Studies Applying Inclusion/Exclusion Criteria to Clinical Patients with MDD

- Mean extracted 21-item HAM-D = 20.4 (SD = 6.0)
- At the 2 most common cutoffs of 20 on the 21-item HAM-D and 18 on the 17-item HAM-D, 47.3% and 44.5%, respectively, would have been excluded

Taking a Closer Look at Symptom Severity

**TABLE 1. Commonly Used Psychiatric Inclusion and Exclusion Criteria in 170 Antidepressant Efficacy Trials**

<table>
<thead>
<tr>
<th>Exclusion criterion</th>
<th>All studies (N) (%)</th>
<th>Studies during 1999-2007 (n=114)</th>
<th>Studies during 2010-2014 (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity scale score below the cutoff</td>
<td>170 (1000)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity scale score above the cutoff</td>
<td>14 (0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic disorder and current psychotic features</td>
<td>13 (0.8)</td>
<td>51 (45.1)</td>
<td></td>
</tr>
<tr>
<td>Subscale severe and persistent</td>
<td>52 (46.0)</td>
<td>45 (80.4)</td>
<td></td>
</tr>
<tr>
<td>Significant suicidal ideation</td>
<td>12 (10.2)</td>
<td>48 (85.7)</td>
<td></td>
</tr>
<tr>
<td>History of suicide attempt(s)</td>
<td>16 (14.0)</td>
<td>19 (33.9)</td>
<td></td>
</tr>
<tr>
<td>Significant homicidal ideation or violence risk</td>
<td>16 (14.0)</td>
<td>12 (21.4)</td>
<td></td>
</tr>
<tr>
<td>Other nondepressivensubstance use disorders</td>
<td>49 (43.6)</td>
<td>43 (76.1)</td>
<td></td>
</tr>
<tr>
<td>Episode duration too long</td>
<td>18 (15.8)</td>
<td>16 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Episode duration too short</td>
<td>46 (41.4)</td>
<td>37 (66.1)</td>
<td></td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>76 (68.2)</td>
<td>49 (87.5)</td>
<td></td>
</tr>
<tr>
<td>Cyclothymic disorder</td>
<td>23 (20.2)</td>
<td>23 (41.1)</td>
<td></td>
</tr>
<tr>
<td>Borderline personality disorder</td>
<td>42 (37.5)</td>
<td>20 (35.7)</td>
<td></td>
</tr>
<tr>
<td>Items 1 of the Hamilton Rating Scale below the cutoff</td>
<td>23 (20.2)</td>
<td>10 (17.9)</td>
<td></td>
</tr>
<tr>
<td>Any Axis I disorder</td>
<td>24 (21.1)</td>
<td>22 (39.3)</td>
<td></td>
</tr>
</tbody>
</table>

**Symptom Severity and Generalizability: Changes Over 20 Years**

Inclusion cutoff on symptom severity scale

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Change</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAM-D-17 &gt; 22</td>
<td>44.0% vs 17.5%</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>MADRS &gt; 25</td>
<td>76.2% vs 25.0%</td>
<td>&lt; .01</td>
</tr>
</tbody>
</table>

*P < .05

Studies of Vortioxetine: An Extreme Example

12 studies of vortioxetine
26 nonvortioxetine trials
Inclusion cutoff on MADRS > 25
  vortioxetine studies: 11/12 (91.7%)
  nonvortioxetine studies: 8/26 (30.8%)

European Medicines Agency Guideline for Antidepressant Medication

• “Though some of the earlier studies may be done in hospitalized patients, the majority of the database should be in out-patients for better generalizability of study results.”
• “Clinical trials will usually recruit patients, who are moderately ill, as it is difficult to demonstrate an effect in mildly ill patients.”
• Demonstration of efficacy “in moderately ill patients is considered sufficient for a registration package to get a license for ‘Treatment of Episodes of Major Depression’”
• What is the logic?

Implications

• Raises questions about the generalizability of AETs
  – Should antidepressants only be approved and marketed for the narrow range of patients in whom they are proven effective?
• What about STAR*D?

FDA’s Code of Federal Regulation (21CFR201.57)

• Revised April 1, 2015
• A product label “should identify those characteristics that are important for understanding how to interpret and apply the study results. The description thus should identify important inclusion and exclusion criteria... For example, the description should discuss enrollment factors that exclude subjects prone to adverse effects, the age distribution of the study population, a baseline value that results in a study population that is more or less sick than usual...” (italics added)


FDA’s Code of Federal Regulation (21CFR201.56)

• Chapter on labeling requirements
• A product’s labeling “must be updated when new information becomes available that causes the labeling to become inaccurate, false, or misleading”
• Information contained in the present report warrants a modification to the labels of recently approved antidepressants as they have only been established as effective for a narrow range of severity of depression

Implications for Future

• Personalized medicine

STAR*D = Sequenced Treatment Alternatives to Relieve Depression.
Advisory Board Meeting
October, 2018

- Review of 3 Multicenter Trials of Medication X
- RESPONSE RATE

<table>
<thead>
<tr>
<th></th>
<th>Dose A</th>
<th>Dose B</th>
<th>Dose C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>52.6*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 2</td>
<td>48.8</td>
<td>50.3</td>
<td>56.5*</td>
</tr>
<tr>
<td>Study 3</td>
<td></td>
<td>53.2*</td>
<td></td>
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</table>

Genetic Abnormality

<table>
<thead>
<tr>
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<th>Dose A</th>
<th>Dose B</th>
<th>Dose C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>65.6*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 2</td>
<td>58.8*</td>
<td>60.3*</td>
<td>68.5*</td>
</tr>
<tr>
<td>Study 3</td>
<td></td>
<td>63.2*</td>
<td></td>
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Normal Genetic Test

<table>
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<th></th>
<th>Dose A</th>
<th>Dose B</th>
<th>Dose C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>41.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 2</td>
<td>38.8</td>
<td>40.3</td>
<td>46.5*</td>
</tr>
<tr>
<td>Study 3</td>
<td></td>
<td>43.2</td>
<td></td>
</tr>
</tbody>
</table>

Perspectives

- Company
- Clinician/Patient
- Regulatory agency
- Health insurance company

Belief 2

Early Response to Antidepressants = Placebo Response

Evolution of the Delayed Antidepressant Hypothesis

- Columbia group (mid 1980s)
  - Lack of drug-placebo differences in first 3 weeks of treatment
  - Pattern analysis
- Modern era studies demonstrating early onset of efficacy

Onset of Action of Antidepressants: A Meta-Analysis

- 47 placebo-controlled studies with weekly ratings
  - 74 cohorts on active medication (> 5000 patients)
  - 47 cohorts on placebo (> 3400 patients)
- All studies used same outcome measure (HAM-D)

Weekly Reduction in HAM-D Scores on Medication (n = 5158) and Placebo (n = 3418)

<table>
<thead>
<tr>
<th>Week #</th>
<th>Medication</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.5</td>
<td>3.6</td>
</tr>
<tr>
<td>2</td>
<td>3.3</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>2.1</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>6</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Total change</td>
<td>13.0</td>
<td>9.0</td>
</tr>
</tbody>
</table>

Drug-Placebo Separation on the HAM-D over the Course of a 6-Week Trial

Meta-Analyses of Onset of Action of SSRIs

- 25 placebo-controlled studies using the HAM-D
  - Active medication (2260 patients)
  - Placebo (1623 patients)
- Difference between active drug and placebo
  - Week 1: 1.07 points
  - End of 6 weeks: 3.30 points

Meta-Analyses of Onset of Action of SSRIs in the Treatment of OCD

- 17 placebo-controlled studies 8 to 24 weeks in duration
  - 12 trials 10 or 12 weeks in duration
  - 3275 participants overall
- Difference between active drug and placebo on Y-BOCS
  - Week 2: 0.91 points
  - End of 12 weeks: 3.30 points (approximated from figure)
  - More than half of the improvement by the end of treatment was evident at 4 weeks

Clinical Implications

Setting patient expectations

Belief 3

Relapse Means the Drug Stopped Working
(The “Poop-out” Effect)
The Clinical Scenario

• "The medication stopped working"
• Why?

Treatment Responders

• True Drug Responders
• Responders to nonspecific effects of treatment (placebo responders)

Relapse during Continuation Treatment

• Relapsers during continuation phase
  – True drug responders during acute phase
  – Placebo responders during acute phase

Quitkin’s Formulas

• Estimated the percentage of relapse during continuation treatment attributable to initial placebo response
  • Acute phase study
    – 6 weeks
    – Imipramine vs phenelzine vs placebo
  • Continuation phase
    – 6 weeks
    – Majority of relapse attributable to initial placebo response


Data Needed to Apply Quitkin’s Formulas

• Acute Phase
  – Medication response rate
  – Placebo response rate
• Continuation phase
  – Relapse rate in medication responders continued on medication
  – Relapse rate in placebo responders continued on placebo

Design of Continuation Studies

• Placebo Substitution
• Extension
Placebo Substitution Design

Open-label Acute Phase (6–12 weeks)
responders
Double-blind Continuation Phase (6–12 months)
medication responders
Continue Active Medication Placebo

Extension Design

Double-blind Acute Phase (6–12 weeks)
responders to active or placebo
Double-blind, stay on the same medication, Continuation Phase (6–12 months)
medication responders placebo responders

Continuation Studies Using Extension Design

- Claghorn and Feighner (1993): paroxetine
- Detke et al (2004): paroxetine, duloxetine (2 doses)

Duration of Acute and Continuation Phases

<table>
<thead>
<tr>
<th>Authors</th>
<th>Acute Phase (weeks)</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anton et al</td>
<td>6</td>
<td>52</td>
</tr>
<tr>
<td>Claghorn and Feighner</td>
<td>6</td>
<td>52</td>
</tr>
<tr>
<td>Detke et al</td>
<td>8</td>
<td>26</td>
</tr>
<tr>
<td>Montgomery et al</td>
<td>6</td>
<td>20</td>
</tr>
</tbody>
</table>

Relapse Rates during Continuation Phase

<table>
<thead>
<tr>
<th>Author</th>
<th>Active Medication</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anton et al</td>
<td>8.6%</td>
<td>25.3%</td>
</tr>
<tr>
<td>Claghorn and Feighner</td>
<td>9.6%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Detke et al—paroxetine</td>
<td>5.7%</td>
<td>29.3%</td>
</tr>
<tr>
<td></td>
<td>duloxetine 80</td>
<td>5.7%</td>
</tr>
<tr>
<td></td>
<td>duloxetine 120</td>
<td>9.3%</td>
</tr>
<tr>
<td>Montgomery et al</td>
<td>4.1%</td>
<td>22.8%</td>
</tr>
<tr>
<td>Total—All studies</td>
<td>7.4% (39/522)</td>
<td>24.1% (56/232)</td>
</tr>
<tr>
<td>SSRI studies</td>
<td>7.9% (13/164)</td>
<td>24.0% (25/104)</td>
</tr>
</tbody>
</table>

Estimated Percentage of Relapse Attributable to Loss of Placebo Effect

<table>
<thead>
<tr>
<th>Model</th>
<th>Point Estimate</th>
<th>Lower Limit of 95% CI</th>
<th>Upper Limit of 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusive Model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRI</td>
<td>159%</td>
<td>96%</td>
<td>225%</td>
</tr>
<tr>
<td>All AOs</td>
<td>186%</td>
<td>147%</td>
<td>228%</td>
</tr>
<tr>
<td>Independent Model</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRI</td>
<td>81%</td>
<td>34%</td>
<td>128%</td>
</tr>
<tr>
<td>All AOs</td>
<td>110%</td>
<td>78%</td>
<td>143%</td>
</tr>
</tbody>
</table>

AD = antidepressant
Discussion and Conclusions

• Most of the “poop-out” effect can be attributed to loss of initial placebo response
• Limitations
  – Small number of studies
  – Generalizability of controlled studies

Belief 4

The Greatest Problem in the Diagnosis of Bipolar Disorder is its Underdiagnosis

Is Bipolar Disorder Underrecognized?

Studies of Underdiagnosis of Bipolar Disorder

• Albanese et al (2006)
• Angst et al (2010)
• Angst et al (2011)
• Benazzi (1997)
• Ghaemi et al (2000)
• Ghaemi et al (1999)
• Hantouche et al (1998)
• Manning et al (1997)
• Mantere et al (2008)
• McCombs et al (2007)

Methods

• Participants
  – 700 psychiatric outpatients
  • 58.3% female
  • Mean age 39.9 years
• Measures
  – Self-report of prior diagnosis of bipolar disorder
  – SCID
  – FH-RDC

Diagnosis of Bipolar Disorder

• Self-report of prior bipolar diagnosis 20.7%
• SCID diagnosis of bipolar disorder 12.9%
• SCID confirmation of prior diagnosis 43.4%

FH-RDC = Family History Research Diagnostic Criteria.
Agreement between SCID and Self-Report of Prior Bipolar Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>SCID Bipolar Diagnosis (&quot;Gold Standard&quot;)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
</tr>
<tr>
<td>Self-reported Prior Dx of Bipolar D/O</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>63</td>
</tr>
<tr>
<td>No</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
</tr>
</tbody>
</table>

But What about Validity?

Family History of Bipolar Disorder in First-Degree Relatives

<table>
<thead>
<tr>
<th></th>
<th>SCID Bipolar A</th>
<th>Previous Bipolar-Not Confirmed B</th>
<th>Not Bipolar C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relatives at Risk</td>
<td>Bipolar Disorder</td>
<td>Morbid Risk</td>
<td>Relatives at Risk</td>
</tr>
<tr>
<td></td>
<td>326</td>
<td>8.0%</td>
<td>345</td>
</tr>
</tbody>
</table>

3-group $X^2 = 27.1, P < .001$
$A > C X^2 = 27.3, P < .001$
$A > B X^2 = 6.34, P < .02$
$B = C X^2 = 1.21, ns$

Why is Bipolar Disorder Overdiagnosed?

- "Campaign" to improve diagnostic recognition

Clinical Implications of Overdiagnosing Bipolar Disorder

- Overtreatment with mood stabilizer agents
- Overprescription of medications generally
- Overexposure to medication side effects
- Never-ending search for the "magic pill"
- Undertreatment with psychotherapy

Belief 5

It is a Burden to Measure Outcome in Clinical Practice
Measuring Outcome: Not the Standard of Care in the Treatment of Depression

- Survey of 314 psychiatrists
  - 6.5% use scales almost all the time
  - 11.4% use scales frequently
  - 21.3% sometimes use scales
  - 60.8% rarely or never use scales
- Survey of 340 UK psychiatrists
  - 11.2% use scales routinely
  - 30.5% use scales occasionally
  - 58.2% never use scales

Using Scales to Assess Outcome Including Remission Status

- Impractical to use the HAM-D or MADRS in clinical practice
- Use of a self-report scale
  - Consider patient time
  - Clinically Useful Depression Outcome Scale (CUDOS)

Major Advantages of the CUDOS

- Covers the DSM-IV symptom criteria
- Assesses psychosocial function and quality of life
- < 2 minutes to complete
- < 10 seconds to score
- Can be used to determine remission
- Free

Patient Acceptability of Scale Completion Study 1

- 50 depressed outpatients in ongoing treatment
- Completed CUDOS, measure of perceived burden and acceptability
  - 98% none-minimally burdensome to complete
  - 94% willing to complete at every visit

Patient Acceptability of Scale Completion Study 2

- 50 depressed outpatients in ongoing treatment
- Completed CUDOS, BDI, measure of perceived burden and acceptability
  - CUDOS took less time to complete (64% vs 12%)
  - CUDOS less burdensome to complete (50% vs 10%)
  - Prefer to complete to monitor treatment (40% vs 14%)

The Future of Measurement-Based Care

- Internet
- Outcometracker.org
Acceptance of Web-Based and Paper Assessment

<table>
<thead>
<tr>
<th>Question</th>
<th>Paper (%)</th>
<th>Web (%)</th>
<th>About the Same (%)</th>
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</thead>
<tbody>
<tr>
<td>Less Time to Complete</td>
<td>10.3</td>
<td>62.1</td>
<td>27.6</td>
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<tr>
<td>Question</td>
<td>79.3</td>
<td>0.0</td>
<td>20.7</td>
</tr>
<tr>
<td>Prefer to Complete</td>
<td>0.0</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Safer and More Secure</td>
<td>0.0</td>
<td>51.7</td>
<td>48.3</td>
</tr>
<tr>
<td>More Accurate</td>
<td>0.0</td>
<td>47.4</td>
<td>52.6</td>
</tr>
</tbody>
</table>


Financial Considerations

Cost – free
Billing – computer testing (96103)
Standardized testing report

Belief 6

It Does Not Matter Which Depression Scale You Use in Clinical Practice

Measuring Outcome When Treating Depression

- Using a depression scale is like using a scale to measure weight (or a thermometer to measure fever)

Desirable Features of a Self-Report Depression Outcome Scale

- Brief/acceptable to patients
- Covers all DSM-IV diagnostic criteria for MDD
- Reliable (internal consistency; test-retest reliability)
- Valid indicator of symptom severity
- Indicator of remission status
- Assesses psychosocial function and quality of life
- Assesses suicidal thoughts
- Sensitive to change
- Easy to score
- Inexpensive

4 Self-Report Depression Scales Assessing DSM-IV / DSM-5 MDD Criteria

- QIDS
  - Quick Inventory of Depression Symptomatology
- PHQ-9
  - Patient Health Questionnaire
- CUDOS
  - Clinically Useful Depression Outcome Scale
- BDI-II
  - Beck Depression Inventory-II

Comparison of Self-Report Scales

<table>
<thead>
<tr>
<th>Free</th>
<th>CUDOS</th>
<th>QIDS</th>
<th>PHQ-9</th>
<th>BDI-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brief (easily completed at every visit)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Indicates overall symptom severity</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Assesses each MDD symptom individually</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Indicates remission status</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Assesses psychosocial function</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Assesses quality of life</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>Assesses suicidal thoughts</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Sensitive to change</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
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<td>Easy to score</td>
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<td>✓</td>
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</tr>
</tbody>
</table>

Treatment Selection and Severity of Depression

- Mild depression: Medication or psychotherapy
- Moderate depression: Medication or psychotherapy
- Severe depression: Medication

Prevalence of Severity Subtypes According to Different Measures of Depression

Patients
- 245 depressed outpatients in ongoing treatment in the Rhode Island Hospital outpatient practice

Methods
- Evaluated with the 17-item HAM-D
- Completed the CUDOS, PHQ-9, and QIDS

Definitions
- Severity categorization based on the scale developers’ recommended thresholds

Prevalence of Severity Subtypes According to Different Measures of Depression

<table>
<thead>
<tr>
<th>Scale</th>
<th>Mild (%)</th>
<th>Moderate (%)</th>
<th>Severe (%)</th>
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<tbody>
<tr>
<td>HAM-D</td>
<td>30.2</td>
<td>43.3</td>
<td>24.9</td>
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<td>CUDOS</td>
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<td>45.9</td>
<td>19.0</td>
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<td>PHQ-9</td>
<td>7.4</td>
<td>21.3</td>
<td>69.3</td>
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<td>QIDS</td>
<td>12.8</td>
<td>33.5</td>
<td>52.9</td>
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## Summary

1. Limited evidence of the efficacy of antidepressants for the majority of patients seen in clinical practice
2. Onset of action of antidepressants is sooner than had been previously thought
3. Relapse does not necessarily mean medicine stopped working
4. Overdiagnosis of bipolar disorder is more common than underdiagnosis
5. The biggest obstacle in measuring outcome is the clinician
6. Not all measures of depression are created equally

## Practical Take-Aways

- When initiating antidepressants tell patients that medication often begins to work in the first week or two of treatment
- Be as concerned, if not more concerned, with the overdiagnosis of bipolar disorder as with its underdiagnosis
- It is more difficult to undo an overdiagnosis of bipolar disorder than its underdiagnosis
- Measuring outcome in the treatment of depression should be done at every visit