Improving Diagnosis and Treatment Strategies for Major Depressive Disorder

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Disclosure

• Speakers Bureau—Acadia, Alkermes, Allergan, AstraZeneca, Janssen, Jazz, Lundbeck, Merck, Novartis, Otsuka, Pfizer, Shire, Sunovion, Takeda, Teva
• Consultant—Acadia, Alexza, Alkermes, Allergan, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly, Forum, Genentech, ITI, Janssen, Jazz, Lundbeck, Merck, Medivation, Mylan, Neurocrine, Novartis, Noven, Otsuka, Pfizer, Reckitt Benckiser, Reviva, Shire, Sunovion, Takeda, Teva, Valeant, Vanda
• Stockholder—Bristol-Myers Squibb, Eli Lilly, J & J, Merck, Pfizer (shares of common stock purchased > 10 years ago)
Outline

• New developments in diagnosis
• Screening and measurement-based care
• What do the guidelines say about treatment?
• Update on new branded antidepressants
• Augmentation strategies
Depression is a Common Diagnosis

- Depression is the most common diagnosis among patients seen by psychiatrists in the US¹
- Depression is a serious, chronic, disabling illness affecting more than 300 million people worldwide²
- Depression results in a substantial burden of disease to both the individual and society³
- Residual symptoms are common and cause significant psychosocial and occupational functional impairment⁴,⁵


Depressive Disorders in DSM-5 (2013)

- 296.99 (F34.8) Disruptive Mood Dysregulation Disorder
- 296.2x (F32.x) Major Depressive Disorder, Single Episode
- 296.3x (F33.x) Major Depressive Disorder, Recurrent Episode
- 300.4 (F34.1) Persistent Depressive Disorder (Dysthymia)
- 625.4 (N94.3) Premenstrual Dysphoric Disorder
- xxx.xx Substance/Medication-Induced Depressive Disorder
- 293.83 Depressive Disorder Due to Another Medical Condition
- 311 (F32.8) Other Specified Depressive Disorder (e.g. Recurrent Brief Depression)
- 311 (F32.9) Unspecified Depressive Disorder
**DSM-5: Major Depressive Disorder (MDD) - Specifiers**

- With anxious distress
- With mixed features
- With melancholic features
- With atypical features
- With mood-congruent psychotic features
- With mood-incongruent psychotic features
- With catatonia
- With peripartum onset
- With seasonal pattern (recurrent episodes only)

**MDD: Overview of Changes in DSM-5**

- Core mood criterion now includes hopelessness, potentially broadening the diagnosis
  - DSM-IV-TR “depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)” to DSM-5 “depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopelessly) or observation made by others (e.g., appears tearful)”

- DSM-5 allows for clinical judgment in distinguishing normal reactions to significant loss from a disorder in need of clinical attention (DSM-IV-TR had a carefully worded bereavement exclusion)

- New specifiers of MDD “with anxious distress” and “with mixed features” allow characterization of additional symptoms

- Elimination of NOS designations replaced with other specified disorder and unspecified disorder

MDD: DSM-5 Criteria

A. \( \geq 5 \) of 9 symptoms present for 2-week period and \( \geq 1 \) of the symptoms is either (1) depressed mood or (2) loss of interest/pleasure; other symptoms: change in weight/appetite, insomnia/hypersomnia, agitation/retardation observed by others, fatigue/loss of energy, worthlessness/guilt, inability to think/concentrate/make decisions, thoughts of death/suicide

B. Significant distress or impairment

C. Not attributable to the physiological effects of a substance or to another medical condition

D. Exclude schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders

E. There has never been a manic episode or a hypomanic episode

DSM-5 Major Depressive Episode

Mixed Features Specifier

- Can use this specifier for either major depressive disorder or bipolar disorder
- Full criteria are met for an MDE and \( \geq 3 \) of the following manic/hypomanic symptoms are present during the majority of days of the current or most recent episode of depression:
  - ↑ Mood; ↑ Self-esteem or grandiosity; ↑ Talkative/pressured speech; Flight of ideas/racing thoughts; ↑ Energy or goal-directed activity; ↑ Activities with high potential for painful consequences; ↓ Need for sleep (not insomnia)

Treatment of major depressive disorder with the mixed features specifier should likely be the same as for treatment of bipolar depression (ie, avoidance of antidepressant monotherapy)

MDD Mixed State Patients Are Different

• Younger age at onset
• Recurrent episodes
• Greater risk for suicidality
• More functional impairment, unemployment
• More alcohol/substance use comorbidity
• More cardiovascular disease
• Often follows a rapid cycling course


What Is Bipolar Depression?

- Bipolar depression is defined by having Major Depressive Episodes (MDEs) and manic/hypomanic episodes
  - Bipolar type I is when there is a history of manic episodes
  - Bipolar type II is when there is a history of hypomanic episodes but no manic episodes
- On cross-sectional examination, the symptoms of an MDE are the same for both major depressive disorder and bipolar disorder
  - Easy to misdiagnose bipolar depression for major depressive disorder

Misdiagnosis of Bipolar Disorder and Bipolar Depression Is Common

- Up to 69% of persons with bipolar disorder are misdiagnosed initially
  - Mean 3.5 diagnoses and 4 clinicians before receiving the right diagnosis
- Comorbidity is common and can be confusing
  - 50%-70% have at least one comorbid psychiatric or mental condition
  - Examples include anxiety, substance use, obesity, CVD
- As many as 1 in 5 primary care patients who have clinically significant depressive symptoms and are receiving antidepressant treatment actually have bipolar I or bipolar II disorder

Incorrect Dx → incorrect prognosis and incorrect treatment

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Measurement-based Care (MBC) in the Treatment of Depression

- Components of MBC may include:\n  - Antidepressant dosage
  - Depressive symptom severity
  - Medication tolerability and safety
  - Adherence to treatment

- Steps of MBC include:\n  - Screening
  - Antidepressant selection based upon treatment history
  - Assessment-based medication management
  - Ongoing care

- MBC can also be used to:\n  - Monitor disease course and effects of treatment
  - Guide treatment change

Patient-reported Outcome Scales (PROS)

Patient Health Questionnaire-9 - PHQ-9

9 Items that assess the 9 DSM-IV criteria for MDD:\n- Anhedonia
- Depressed mood
- Sleep
- Feeling tired
- Appetite change
- Guilt or worthlessness
- Concentration
- Slowed down or restless
- Suicidal thoughts

**Patient-reported Outcome Scales (PROS)**

**PHQ-9**
- Scored 0 to 3 points per item (range 0 to 27)\(^1\)
- Severity of depression\(^1\):
  - 0–4 = minimal depression
  - 5–9 = mild depression
  - 10–14 = moderate depression
  - 15–19 = moderately severe depression
  - 20–27 = severe depression

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**Evidence of the Benefit of Measurement-Based Care: Clinical Outcomes in Measurement-Based Treatment (COMET) Study**
- 83 Physicians, 74 primary care sites
- Sites were randomized to treatment as usual vs measurement-based care (MBC)
- 642 Patients were randomized and evaluated at a 6-month follow-up assessment
- MBC condition: PHQ-9 completed monthly and information faxed to PCP
- Depression diagnoses based on PCP clinical evaluation
- Response rates (controlling for demographic variables): 67.0% vs. 59.7% (OR 2.02 [1.36–3.02], NNT = 14)

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Treatment Modalities for Acute MDD
Selection of initial treatment should consider clinical features, and patient preference and experience

Symptom severity
Co-occurring disorders
Psychosocial stressors
Patient preference
Prior treatment experiences

Pharmacotherapy
Psychotherapy
Electroconvulsive therapy
Complementary/alternative therapies
Combination therapy

Principles of pharmacotherapy

- Antidepressant is recommended as initial treatment for mild to moderate MDD, and definitely for severe MDD.
- Since effectiveness is similar across antidepressants, initial selection should largely be based on:
  - Anticipated side effects and their tolerability for the individual
  - Pharmacological properties of the medication such as half-life and drug interactions
  - Additional factors, such as prior medication response, cost and patient preference

First-line antidepressants

- An SSRI, SNRI, mirtazapine or bupropion is optimal for most patients

APA Pharmacotherapy Recommendations

- Mild to moderate MDD
  - Antidepressant is recommended as an initial treatment choice
- Severe MDD
  - Antidepressant definitely should be provided
- Antidepressant effectiveness is similar between and within classes
  - Response rates in clinical trials typically range from 50-75%
  - Initial selection should be based on:
    - Pharmacological properties
    - Safety and tolerability for the individual patient
    - Medication response in prior episodes
    - Cost
    - Patient preference

APA Guidelines: Reasons for Nonresponse

TABLE 9. Potential Reasons for Treatment Nonresponse

- Inaccurate diagnosis
- Unaddressed co-occurring medical or psychiatric disorders, including substance use disorders
- Inappropriate selection of therapeutic modalities
- Inadequate dose of medication or frequency of psychotherapy
- Pharmacokinetic/pharmacodynamic factors affecting medication action
- Inadequate duration of treatment
- Nonadherence to treatment
- Persistent or poorly tolerated side effects
- Complicating psychosocial and psychological factors
- Inadequately trained therapist or poor “fit” between patient and therapist

APA Guidelines: Medication Strategies to Address Nonresponse to Treatment

- **Optimize** dose
- **Change** to another antidepressant
- **Augment** by adding depression-focused psychotherapy
- **Augment** by adding a non-MAOI antidepressant or a non-antidepressant medication such as lithium, thyroid hormone, or a second-generation antipsychotic
APA Guidelines: Risk Factors for Recurrence

<table>
<thead>
<tr>
<th>TABLE 10. Risk Factors for Recurrence of Major Depressive Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence of subthreshold depressive symptoms</td>
</tr>
<tr>
<td>Prior history of multiple episodes of major depressive disorder</td>
</tr>
<tr>
<td>Severity of initial and any subsequent episodes</td>
</tr>
<tr>
<td>Earlier age at onset</td>
</tr>
<tr>
<td>Presence of an additional nonaffective psychiatric diagnosis</td>
</tr>
<tr>
<td>Presence of a chronic general medical disorder</td>
</tr>
<tr>
<td>Family history of psychiatric illness, particularly mood disorder</td>
</tr>
<tr>
<td>Ongoing psychosocial stressors or impairment</td>
</tr>
<tr>
<td>Negative cognitive style</td>
</tr>
<tr>
<td>Persistent sleep disturbances</td>
</tr>
</tbody>
</table>


Does Switching Work?

- Non-responders to antidepressant monotherapy during acute treatment of major depression are often switched to a new antidepressant
- Meta-analyses evidence that switching was not superior to continuation

When Augmenting, Not All Agents Have the Same Level of Evidence or Recommendation for Use

<table>
<thead>
<tr>
<th>Adjunctive Agent</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>1</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>1</td>
</tr>
<tr>
<td>Risperidone</td>
<td>1</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>1</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>1</td>
</tr>
<tr>
<td>Bupropion</td>
<td>2</td>
</tr>
<tr>
<td>Lithium</td>
<td>2</td>
</tr>
<tr>
<td>Mirtazapine/mianserin</td>
<td>2</td>
</tr>
<tr>
<td>Modafinil</td>
<td>2</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>2</td>
</tr>
<tr>
<td>TCAe (e.g., desipramine)</td>
<td>2</td>
</tr>
<tr>
<td>Other antidepressants</td>
<td>3</td>
</tr>
<tr>
<td>Other stimulants (methylphenidate, etc.)</td>
<td>3</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>3</td>
</tr>
</tbody>
</table>

- **Level 1** = Meta-analysis with narrow confidence intervals and/or 2 or more RCTs with adequate sample size, preferably placebo controlled
- **Level 2** = Meta-analysis with wide confidence intervals and/or 1 or more RCTs with adequate sample size
- **Level 3** = Small-sample RCTs or nonrandomized, controlled prospective studies or case series or high-quality retrospective studies


Outline

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- Update on new branded antidepressants
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Three New Branded Antidepressants

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Vilazodone</th>
<th>Levomilnacipran</th>
<th>Vortioxetine</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Brand Name</td>
<td>Viibryd</td>
<td>Fetzima</td>
<td>Trintellix (Formerly Brintellix)</td>
</tr>
<tr>
<td>Initial Approval</td>
<td>2011</td>
<td>2012</td>
<td>2013</td>
</tr>
<tr>
<td>Mechanism</td>
<td>SSRI, partial agonist at 5-HT1A receptors</td>
<td>SNRI</td>
<td>SSRI, 5-HT3 receptor antagonism and 5-HT1A receptor agonism</td>
</tr>
<tr>
<td>Dosage</td>
<td>Recommended target dosage: 20 mg to 40 mg once daily with food. Start with 10 mg/d x 7 days, followed by 20 mg/d x 7 days, and then can increase to 40 mg/d.</td>
<td>Recommended dose: 40 mg to 120 mg once daily with or without food. Initiate dose at 20 mg/d x 2 days and then increase to 40 mg/d. Based on efficacy and tolerability, increase dose in increments of 40 mg at intervals of 2 or more days.</td>
<td>The recommended starting dose is 10 mg administered orally once daily without regard to meals. The dose should then be increased to 20 mg/d, as tolerated. Consider 5 mg/d for patients who do not tolerate higher doses.</td>
</tr>
<tr>
<td>Adverse Events (≥5% and 2x placebo)</td>
<td>Diarrhea, nausea, vomiting and insomnia</td>
<td>Nausea, constipation, hyperhidrosis, heart rate increase, erectile dysfunction, tachycardia, vomiting and palpitations</td>
<td>Nausea, constipation and vomiting</td>
</tr>
</tbody>
</table>

Choosing Among Medications for MDD

- What is the likelihood of success (response, remission)?
  - Number needed to treat (NNT) is used to describe this
  - The lower the NNT, the better

- What is the likelihood of encountering problematic adverse effects?
  - Number needed to harm (NNH) is used to describe this
  - These are very different from drug to drug
  - The higher the NNH, the better

- A caveat: if an individual patient prefers one medication over the other, the above does not matter
LHH: Vilazodone 40 mg/day is 3.4 times more likely to result in a therapeutic response than a discontinuation because of an AE.
Levomilnacipran – NNT, NNH, LHH?

Figure 1 NNT for response/remission, NNH for adverse events where incidence with levomilnacipran ≥ 5% and ≥ 2 times the rate for placebo as identified in product labelling (3), and NNH for discontinuation because of an adverse event, with 95% CI, for pooled short-term studies comparing levomilnacipran vs. placebo. AE, adverse event; D/C, discontinuation; NNH, number needed to harm; NNT, number needed to treat.
LHH: Vortioxetine 5–20 mg/day is 5.1 times more likely to result in a therapeutic response than a discontinuation because of an AE.
### NNT Response and NNH D/C AE

![Graph showing NNT and NNH for various antidepressants](Image)

- **Vilazodone**
- **Duloxetine**
- **Duloxetine**
- **Escitalopram**
- **Levomilnacipran**
- **Sertraline**
- **Venlafaxine**
- **Vortioxetine**

**Number Needed to Treat or Harm vs. Placebo**

### LHH

**Table 4**

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>NNT vs. placebo for response (prior to rounding)</th>
<th>NNH vs. placebo for discontinuation because of an adverse event (prior to rounding)</th>
<th>LHH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine</td>
<td>5.7</td>
<td>24.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>6.7</td>
<td>30.7</td>
<td>4.6</td>
</tr>
<tr>
<td>Levomilnacipran</td>
<td>9.8</td>
<td>18.2</td>
<td>1.8</td>
</tr>
<tr>
<td>Sertraline</td>
<td>5.3</td>
<td>6.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>5.7</td>
<td>7.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Vilazodone</td>
<td>8.0</td>
<td>26.1</td>
<td>3.3</td>
</tr>
<tr>
<td>Vortioxetine</td>
<td>8.4</td>
<td>42.7</td>
<td>5.1</td>
</tr>
</tbody>
</table>

**NNH** – number needed to harm.

**NNT** – number needed to treat.

**LHH** – likelihood to be helped or harmed.
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Real-World Determinants of Adjunctive Antipsychotic Prescribing for Patients with MDD and Inadequate Response to Antidepressants

• Online survey (N=411, physicians in USA and Europe)
• 24% physicians considered adding an antipsychotic, 13% actually prescribed it (4,018 adult MDD patients)
• Physicians reserve antipsychotics for more severe illness and greater functional impairment, and those who had already failed a number of treatment options
• Symptoms such as depressive features, anxiety, psychotic symptoms, and irritability also prompted physicians to prescribe antipsychotics

Physician’s Reasons for Deciding to Prescribe an Adjunctive Antipsychotic


Physician’s Reasons for Not Prescribing an Adjunctive Antipsychotic

**Physician’s Indication of the Preferred Symptoms for Prescribing Antipsychotics for Patients with MDD**

![Bar chart showing the percentage of physicians indicating preferred symptoms for antipsychotic prescription.]

**FDA-Approved Augmentation Strategies Responder Rates (≥ 50% ↓ Rating Scale Total Score From Baseline)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percentage Responders on Medication</th>
<th>Percentage Responders on Antidepressant Alone</th>
<th>Number Needed to Treat (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole 2-20 mg/d</td>
<td>37.4%</td>
<td>22.5%</td>
<td>7 (5-11)</td>
</tr>
<tr>
<td>Brexpiprazole 1-3 mg/d</td>
<td>23.2%</td>
<td>14.5%</td>
<td>12 (8-26)</td>
</tr>
<tr>
<td>Olanzapine-Fluoxetine Combination (6-18/25-50 mg/d)</td>
<td>38.7%</td>
<td>29.4%</td>
<td>11 (7-30)</td>
</tr>
<tr>
<td>Quetiapine-XR 300 mg/d</td>
<td>58.3%</td>
<td>46.3%</td>
<td>9 (5-24)</td>
</tr>
</tbody>
</table>


Weight Gain?
Short-term Weight Gain from RCTs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percentage Gaining ≥ 7% Bodyweight on Medication</th>
<th>Percentage Gaining ≥ 7% Bodyweight on Antidepressant Alone</th>
<th>Number Needed to Harm (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine-Fluoxetine Combination</td>
<td>40.4%</td>
<td>2.3%</td>
<td>3 (3-3)</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>5.2%</td>
<td>0.6%</td>
<td>22 (15-48)</td>
</tr>
<tr>
<td>Quetiapine-XR</td>
<td>5.2%</td>
<td>1.7%</td>
<td>29 (18-79)</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>3.9%</td>
<td>2.0%</td>
<td>52 (ns)</td>
</tr>
</tbody>
</table>


Akathisia?

Figure 2. Akathisia (Major Depressive Disorder): Absolute Risk Increase (ARI) and Number Needed to Harm (NNH) vs placebo

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Rate on antipsychotic n/N (%)</th>
<th>Rate on placebo n/N (%)</th>
<th>ARI (95% CI)</th>
<th>NNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>92/371 (24.8)</td>
<td>10306 (4.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>65/543 (12.4)</td>
<td>7411 (1.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine Extended Release</td>
<td>3/627 (0.5)</td>
<td>3/200 (1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine-Fluoxetine Combination</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Somnolence?**

Figure 4. Somnolence (Major Depressive Disorder): Absolute Risk Increase (ARI) and Number Needed to Harm (NNH) vs placebo

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Rate on antipsychotic n/N (%)</th>
<th>Rate on placebo n/N (%)</th>
<th>ARI (95% CI)</th>
<th>NNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quetiapine Extended-Release</td>
<td>10/267 (3.7)</td>
<td>11/300 (3.6)</td>
<td></td>
<td>5 (5, 6)</td>
</tr>
<tr>
<td>Olanzapine-Fluoxetine Combination</td>
<td>24/510 (16.3)</td>
<td>27/442 (6.2)</td>
<td></td>
<td>10 (7, 16)</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>30/643 (4.7)</td>
<td>24/111 (2.5)</td>
<td></td>
<td>24 (17, 42)</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>23/371 (6.2)</td>
<td>14/306 (4.6)</td>
<td></td>
<td>43 (95% CI)</td>
</tr>
</tbody>
</table>

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**FDA-Approved Augmentation Strategies Discontinuation Because of an AE**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percentage D/C AE on Medication</th>
<th>Percentage DC A/E on Antidepressant Alone</th>
<th>Number Needed to Harm (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole 2-20 mg/d</td>
<td>3.8%</td>
<td>1.5%</td>
<td>43 (24-225)</td>
</tr>
<tr>
<td>Brexpiprazole 1-3 mg/d</td>
<td>2.6%</td>
<td>0.7%</td>
<td>53 (30-235)</td>
</tr>
<tr>
<td>Olanzapine-Fluoxetine Combination (6-18/25-50 mg/d)</td>
<td>11.6%</td>
<td>2.6%</td>
<td>12 (9-18)</td>
</tr>
<tr>
<td>Quetiapine-XR 300 mg/d</td>
<td>15.4%</td>
<td>2.3%</td>
<td>8 (6-12)</td>
</tr>
</tbody>
</table>

FDA-Approved Augmentation Strategies
LHH: Response Vs. D/C AE

<table>
<thead>
<tr>
<th>Medication</th>
<th>NNT Response</th>
<th>NNH D/C AE</th>
<th>LHH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole 2-20 mg/d</td>
<td>7 (5-11)</td>
<td>43 (24-225)</td>
<td>6.1</td>
</tr>
<tr>
<td>Brexpiprazole 1-3 mg/d</td>
<td>12 (8-26)</td>
<td>53 (30-235)</td>
<td>4.4</td>
</tr>
<tr>
<td>Olanzapine-Fluoxetine Combination (6-18/25-50 mg/d)</td>
<td>11 (7-30)</td>
<td>12 (9-18)</td>
<td>1.1</td>
</tr>
<tr>
<td>Quetiapine-XR 300 mg/d</td>
<td>9 (5-24)</td>
<td>8 (6-12)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Summary

• Changes in DSM-5 allow for specifiers, including Mixed Features (MF)
• Distinguishing MDD from MDD-MF or Bipolar Depression will impact treatment choice
• Measurement-Based Care can improve outcomes
• Switching vs. augmentation in the face of inadequate response remains a conundrum
• New antidepressants and augmentation strategies provide additional choices and can be characterized using NNT, NNH, and LHH
Questions?

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