A PATIENT-CENTERED APPROACH TO THE MANAGEMENT OF DEPRESSION

Achieving and Maintaining Remission in the Primary Care Setting

November 15, 2012
Boston, Massachusetts
Session 3: A Patient-Centered Approach to the Management of Depression: Achieving and Maintaining Remission in the Primary Care Setting

Learning Objectives

1. Develop strategies for effectively screening patients for depression within the boundaries of the primary care office visit.
2. Evaluate measurement-based care, specifically the APA guidelines, and strategies to address failure of initial antidepressant therapy.
3. Apply clinical data and guideline recommendations in creating an individualized, appropriate, and effective treatment plan.

Sloan Manning, MD
Adjunct Associate Professor
University of North Carolina
Chapel Hill, North Carolina
Co-Director, Mood Disorders Clinic
Moses Cone Family Practice Residency
Greensboro, North Carolina

Dr Manning is adjunct associate professor in the department of family medicine at the University of North Carolina at Chapel Hill. He also serves as co-director of the Mood Disorders Clinic at the Moses Cone Family Practice Residency in Greensboro, North Carolina. He earned his MD from the University of Mississippi Medical Center and completed his residency in family practice at Baptist Memorial Hospital in Gadsden, Alabama. He is board certified by the American Board of Family Practice, and is a member of both the American Academy of Family Physicians and the North Carolina Academy of Family Physicians.

Dr Manning is the founding editor of The Primary Care Companion to The Journal of Clinical Psychiatry, and has authored or co-authored more than 50 letters, articles, and editorials in a variety of journals, including Archives of Family Medicine, Bipolar Disorders, Comprehensive Psychiatry, Journal of Affective Disorders, Journal of Clinical Psychiatry, North American Clinics of Psychiatry, and The Journal of Family Practice. He is also a reviewer for the Journal of Affective Disorders.

His research interests include integrated somatic/mental health care systems in primary care, physician education in primary care psychiatry, and disorders of the bipolar spectrum, including their temperamental underpinnings and pharmacologic management. He was a member of the national coordinating council for the STABLE project, researching performance measures and quality improvement initiatives for bipolar treatment.

Roger S. McIntyre, MD, FRCPC
Professor of Psychiatry and Pharmacology
Head, Mood Disorders Psychopharmacology Unit
Toronto, Ontario, Canada

Dr McIntyre is currently professor of psychiatry and pharmacology at the University of Toronto and head of the mood disorders psychopharmacology unit at the University Health Network, Toronto, Canada. He is involved in multiple research endeavors that primarily aim to characterize the association between mood disorders and medical comorbidity. This research involves elucidating metabolic adverse events associated with the use of psychotropic medications, the impact of medical comorbidity on the course of mood disorders, and the effect of glucose homeostasis on neurocognition.

Dr McIntyre is a contributor to the Canadian Psychiatric Association (CPA) guidelines for the treatment of depressive disorders and the Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of bipolar disorder. He has published extensively in leading peer-reviewed journals and textbooks. Dr McIntyre is also a reviewer for many journals including the American Journal of Psychiatry, Biological Psychiatry, Journal of Clinical Psychiatry, and The New England Journal of Medicine, and serves as a grant reviewer for the National Institute of Mental Health.

He completed his MD at Dalhousie University and did his psychiatry residency training and fellowship in psychiatric pharmacology at the University of Toronto.
Faculty Financial Disclosure Statements
The presenting faculty reports the following:

Dr Manning has disclosed that he is a consultant for AstraZeneca, Eli Lilly, Lundbeck, PamLab LLC, and Takeda. He is also a member of the speakers’ bureaus for AstraZeneca and Eli Lilly.

Dr McIntyre has disclosed that he is a consultant for AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen-Ortho, Eli Lilly, Lundbeck, Merck, Organon, Pfizer, and Shire. He is a member of the speakers’ bureaus for AstraZeneca, Biovail, Bristol-Myers Squibb, Eli Lilly, Merck, and Pfizer and receives grant/research support from AstraZeneca, Eli Lilly, Janssen, Lundbeck, Pfizer, and Shire.

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Nathan Hamilton, PharmD-Clinical Support, has no financial relationships to disclose.

Ashley C. Lilly, MHA-Account Director, has no financial relationships to disclose.

Suggested Reading List


Session 3
10:45 AM - 12:00 PM
A Patient-Centered Approach to the Management of Depression: Achieving and Maintaining Remission in the Primary Care Setting

Speakers:
Sloan Manning, MD
Roger S. McIntyre, MD, FRCPC

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Off-Label/Investigational Discussion: In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

A Patient-Centered Approach to the Management of Depression:

Achieving and Maintaining Remission in the Primary Care Setting

Drugs Referenced in Symposium

- Aripiprazole
- Bupropion
- Buspirone
- Citalopram
- Duloxetine
- Escitalopram
- Lithium
- Milnacipran
- Mirtazapine
- Nortriptyline
- Olanzapine
- Quetiapine
- Risperidone
- Sertraline
- Triiodothyronine
- Venlafaxine

Please indicate the approximate number of patients that you see each week with depression

1. None
2. 1 to 10
3. 11 to 20
4. 21 to 30
5. 31 to 40
6. 41 to 50
7. 51 to 60
8. ≥60

Which of the following is a realistic goal for a patient undergoing treatment for MDD?

1. ≥75% reduction in depression score
2. 50-74% reduction in depression score
3. 25-49% reduction in depression score
4. <25% reduction in depression score
Which of the following is not an appropriate first-line switch in a patient who has failed an SSRI?

1. Escitalopram
2. Duloxetine
3. Buspirone
4. Mirtazapine
5. Bupropion

Which of the following can most reliably be performed in the confines of the modern 15-minute office visit?

1. 9-item Patient Health Questionnaire
2. 17-item Hamilton Depression Rating Scale
3. Montgomery-Asberg Depression Rating Scale
4. Quick-Inventory of Depressive Symptomatology – Self Report

Which of the following statements is true regarding antidepressant response at 2 weeks?

1. Assessing response at two weeks likely does not yield clinically meaningful information
2. Symptom improvement at two weeks is highly predictive of overall treatment response
3. No symptom improvement at two weeks is highly predictive of overall treatment failure
4. Assessing for improvement at two weeks is only useful in severely depressed patients

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The Status Quo

- Physicians fail to recognize depression in 30-50% of patients
- Only 50% of patients receive minimally adequate pharmacologic treatment
- Less than 10% receive minimally adequate psychotherapy visits

Healthy People 2020: Mental Health Goals

- Several Healthy People 2020 goals pertain to depression:
  - Increase the proportion of primary care facilities that provide mental health treatment onsite or by paid referral
  - Reduce the proportion of persons who experience major depressive episodes
  - Increase the proportion of adults aged 18 and older with major depressive disorder (MDD) who receive treatment
  - Increase depression screening by primary care providers


Challenging the Traditional Model

- A plurality of trials have evaluated collaborative care models for depression
- Two 2012 systematic reviews evaluated a total of 69 randomized trials of collaborative care1,2
  - Consistently more effective than traditional model
    - Higher response to treatment
    - Higher remission rates
    - Improved treatment adherence
    - Improved quality of life and functional status


The DIAMOND Model

- DIAMOND
  - Depression Initiative Across Minnesota, Offering a New Direction
  - Designed by the Institute for Clinical Systems Improvement (ICSI)
  - Payment redesign targeted to realign incentives
- DIAMOND model included 80 primary care practices; 7 health plans

The DIAMOND Model

- Consists of four processes:
  - Standardized assessment and monitoring (PHQ-9)
  - Registry for tracking patients
  - Stepped care for intensifying and changing treatment
  - Measures to prevent relapse
- Introduces two new players:
  - Care manager for follow-up, coordination
  - Consulting psychiatrist for recommendations

The DIAMOND Model: Outcomes at Six Months

- % of Patients Achieving Remission
  - Primary Care: 6%
  - Behavioral Health Clinics: 8%
  - DIAMOND Clinics: 26%

Grand Challenges in Global Mental Health: The Burden of Depression

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**Multidimensionality of Mood Disorders**

- The prevalence and epidemiology of psychiatric and medical comorbidities in mood disorders is high.
- Stress sensitive medical disorder prevalent.
- Cardiometabolic disorders most common specific cause of premature mortality.


**Relative Risk of Cardiovascular and Overall Mortality from the Nurses Health Study**


**Adiposity, Inflammation and Depression**


**Increased Inflammation Predicts Higher HAM-D Scores & Treatment Resistance**


**Body Mass Index: Impact on Antidepressant Response**


**CBT & Inflammation: Symptom, and Neurobiological Marker Improvement**

Remission is the Goal

% Reduction in Score

- Remission ≥75%
- Response 50% - 74%
- Partial Response 25% - 49%
- Nonresponse <25%

Remission also defined as attainment of a virtually asymptomatic status (17-item Hamilton Depression Rating Scale [HDRS] score ≤7) for at least two consecutive weeks.

APA MDD Treatment Guidelines:
“The goal of acute phase treatment for major depressive disorder, insofar as possible, is to achieve remission and a return to full functioning and quality of life.”


Definition of Outcomes

- Response (without remission)
  - 50% decrease in baseline depression scores
- Remission
  - HAM-D score ≤7 (also referred to as HDRS)
  - QIDS-SR score ≤5

QIDS-SR=Quick Inventory of Depression Symptomology – Self-Report
QIDS-C30: 30-item Inventory of Depressive Symptomatology – Clinician-Rated Scale

Causes of Non-Remission in Major Depressive Disorder

- Failure to establish the diagnosis
- Absence of measurement-based care
- Complex illness presentations
- Absence of early improvement

Evidence-Based Treatment Options

- SSRIs (fluoxetine, paroxetine, etc)
- SNRIs (duloxetine, venlafaxine)
- NRIs (bupropion)
- 5HT2 antagonists (trazodone)
- Atypical antipsychotics (aripiprazole, quetiapine, etc)
- Noradrenergic antagonist (mirtazapine)
- TCAs (amitriptyline, nortriptyline, etc)
- MAOIs (phenelzine)
Other Treatment Options

- Buspirone
- Folate
- Inositol
- Lamotrigine
- Lithium
- Melatonin
- Omega-3 fatty acids
- Pindolol
- Psychostimulant (e.g., modafinil)
- S-adenosyl methionine (SAM-e)
- St. John’s wort
- Testosterone
- Thyroid hormone

Non-Drug Therapy/Procedures

- Acupuncture
- Deep brain stimulation (DBS)
- Electroconvulsive Therapy (ECT)
- Light therapy
- Psychosurgery
- Psychotherapy
- Transcranial Magnetic Stimulation (TMS)
- Vagus Nerve Stimulation (VNS)

Tools to Assess Response & Remission

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<tr>
<th>Measure</th>
<th>Time to complete (min)</th>
<th>Patient/clinician rated</th>
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<td>PHQ-9</td>
<td>&lt;2</td>
<td>Patient</td>
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<td>HDRS-17</td>
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<tr>
<td>BDI</td>
<td>5–10</td>
<td>Patient</td>
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<tr>
<td>HDRS-7</td>
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<td>Clinician</td>
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<tr>
<td>SDS</td>
<td>1–2</td>
<td>Patient/clinician</td>
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CANMAT Recommendations for Incomplete Response to an Initial Antidepressant

First line switch
- Duloxetine
- Escitalopram
- Milnacipran*
- Mirtazapine
- Sertraline
- Venlafaxine

First line add-on
- Aripiprazole
- Lithium
- Olanzapine
- Risperidone

Optimization

- Adequate adherence
  - ≈20% of TRD is attributable to nonadherence → underestimate
  - ≈1/3 of patients are nonadherent to antidepressant therapy
- Adequate dose
- Adequate duration
Treatment Strategies

- Options
  - Optimization
  - Augmentation
  - Combination
  - Switching

Case #1: “Debbie”

- 35-year-old WF
- Works in call center for major credit card company
- Medical History: HTN (HCTZ 25 mg QD), seasonal allergic rhinitis
- Social History: +Tobacco (1/2 ppd), +EtOH (1-2 beers/wk)
- Family History: Son (ADHD), mother (treated with antidepressants), sister (substance abuse in high school)
- Psychiatric History:
  - Onset of depressive symptoms at age 25 after husband’s affair; now divorced x 6 yrs
  - Previously has taken four antidepressants:
    - Paroxetine (max dose 20 mg; weight gain, sexual adverse effects; duration of tx=4-6 months)
    - Bupropion (max dose 150 mg; headache, agitation)
    - Escitalopram (currently on 20 mg x 3 months; experiencing mild orgasmic delay)

Case: “Debbie”

Diagnosis

- Debbie:
  - MDD “Difficult to treat”
    - Failed three separate pharmacologic approaches
    - Bipolar disorder ruled out
  - Most difficult symptoms:
    - Insomnia
    - Irritability

Are We Reassessing Too Late?
Early Improvement at 2 Weeks Predicts Response

- Early improvement at 2 weeks (N=4284)
- No improvement at week 2 (N=2263)

- Early Improvement: 20% score reduction from baseline on the HDRS-17 within 2 weeks of treatment

Case: Approach to Treatment for MDD

- Make diagnosis
- Choose reasonable intervention
- Follow through with intervention
  - Measurement-based approach with:
    - Set visit schedule
    - Regular monitoring of symptom improvement, side effects, medication adherence
    - Set dose titration and treatment algorithm
    - Use of critical decision points
**Are We Reassessing Too Late?**
Early Improvement at 2 Weeks Predicts Response

- Early improvement at week 2 (N=4284)
- No improvement at week 2 (N=2263)

- 53% went on to have a stable response
- 89% did not go on to have a stable response

Lack of improvement in first 2 weeks of treatment may indicate that changes in management should be considered

Early improvement: 30% score reduction from baseline on the HAM-D-17 within 3 weeks of treatment. Follow-up response determined at wk 4-8.


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**Treating Depression in the “Real World”**

- **Remission**, not response, is the goal
- Should first treatment fail, either switching or augmenting is reasonable
- For most patients, remission requires repeated trials of “sustained, vigorously-dosed” antidepressant medication
- Likelihood of remission substantially decreases after two adequate treatment trials, suggesting need for more complicated regimens and psychiatric consultation


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**Strategies for Refractory Depression**

- **Switch** to a different antidepressant (within class or across classes)
- **Augment** the treatment regimen with a non-antidepressant agent
- **Combine** the initial antidepressant with a second antidepressant
- **Psychosocial Intervention**
  - Manual-Based Therapy (e.g., Cognitive Behavioral Therapy)
  - Family-Focused Therapy (FFT)
  - Psychoeducation/Bibliotherapy
  - Others


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**STAR*D Treatment Strategies and Options**


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**STAR*D Cumulative Remission Rates**


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**STAR*D Clinical Study Results Remission Rates (HAM-D-17≤7)**

Remission Rates in STAR*D – Level 1
Citalopram

STAR*D: Level 2 Medication Switch
Citalopram to Bupropion-SR, Sertraline, or Venlafaxine-XR

Non-STAR*D-evaluated Medication Switch
SSRI to Duloxetine

STAR*D: Level 2 Switch
Cognitive Therapy Versus Medication

STAR*D: Level 3 Medication Switch
Mirtazapine or Nortriptyline

STAR*D: Level 4 Medication Switch
Tranylcypromine or Mirtazapine Combined With Venlafaxine-XR
STAR*D: Level 2 Medication Augmentation
Bupropion-SR or Buspirone

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<tr>
<th>Medication</th>
<th>% Achieving Remission</th>
<th>HDRS-17</th>
<th>QIDS-SR-16</th>
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<tbody>
<tr>
<td>Bupropion-SR</td>
<td>30%</td>
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<tr>
<td>Buspirone</td>
<td>39%</td>
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N=656
P=NS among groups

STAR*D: Level 3 Medication Augmentation
Lithium or Triiodothyronine

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<th>% Achieving Remission</th>
<th>HDRS-17</th>
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<td>Lithium*</td>
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<tr>
<td>Triiodothyronine</td>
<td>25%</td>
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Non-STAR*D-Evaluated Augmentation
Adding Atypical Antipsychotics to SSRIs

<table>
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<th>Remission</th>
<th>Discontinuation for Adverse Events</th>
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<tr>
<td>Remission rate 30.7% vs. 17.2% for placebo</td>
<td>OR: 2.00 (95% CI 1.69-2.37)**</td>
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<tr>
<td>Adverse event discontinuation rate 9.1% vs. 2.3% for placebo</td>
<td>OR: 3.91 (95% CI 2.68-5.72)**</td>
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NNT = 9
NNH = 17

• Augmentation with an atypical antipsychotic is also a first-line CANMAT strategy not evaluated in STAR*D
• Meta-analysis at left includes trials of augmenting initial SSRI failure with select* atypicals
• Remission measured via changes in HDRS-17 scores

Summary and Conclusions

• Depression is under-recognized and under-treated in current primary care practice
• Adequate screening can be performed within the confines of the modern office visit
• Remission is an achievable treatment goal
• Early (2 week) follow-up may predict response
• Algorithm-guided care improves patient outcomes

Which of the following is a realistic goal for a patient undergoing treatment for MDD?

1. ≥75% reduction in depression score
2. 50-74% reduction in depression score
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Post-test
Which of the following is not an appropriate first-line switch in a patient who has failed an SSRI?

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Which of the following can most reliably be performed in the confines of the modern 15 minute office visit?

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Questions & Answers