10:45 – 11:45am
Diagnosis and Management of Depression in Primary Care

SPEAKER
Cathy Frank, MD

THE DIAGNOSIS AND MANAGEMENT OF DEPRESSION IN PRIMARY CARE

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"When I give a lecture, I accept the fact that people look at their watches, but what I do not tolerate is when they look at it and raise it to their ear to find out if it stopped”
-Marcel Archard

No disclosures
Some somatic treatments will be discussed that are not-FDA approved for the treatment of depression. These treatments will be indentified.

The Diagnosis and Management of Depression in Primary Care
Learning Objectives

- Utilize simple, quick tools to screen for depression
- Understand how changes in DSM-5 affect the diagnosis and characterization of depressive disorders
- Compare and contrast treatment modalities including pharmacotherapy and CBT
Case Presentation

• 30 year WMF who comes complaining of malaise and vague abdominal discomfort. This is her third visit in three months for similar complaints. Lab work and PE are unremarkable.
• PMH: S/P tonsillectomy/ adenoidectomy
• Medications: Uses an IUD
• ROS: Anorexia without weight loss, fatigue, early morning awakening.

Case Presentation (con’t)

• Family History: Mother suffered from depression. Maternal aunt committed suicide in her 40’s
• Psychiatric History: Brief counseling in college after a break-up with boyfriend
• Substance Use: A glass of wine a night. Cannabis in college
• FURTHER INFORMATION NEEDED?
• SCREENING TESTS? DIAGNOSIS?

Clinical Features of Depression and Diagnostic Changes in DSM-5

DSM-4-TR CLASSIFICATION OF MOOD DISORDERS

Major Depressive Disorder (MDD): DSM-5 Criteria

• A ≥ 5 of the following for > 2 weeks; represent a change in functioning; > 1 must be: Depressed mood or anhedonia (loss of interest or pleasure)
  • Depressed mood (sad, empty, hopeless)
  • Anhedonia
  • Significant change in appetite/weight
  • Insomnia or hypersomnia
  • Psychomotor agitation or retardation
  • Worthlessness or excessive guilt
  • Impaired concentration, indecisiveness
  • Suicidality or recurrent thoughts of death

Major Depressive Disorder: DSM-5 Criteria (cont’d)

- B. Symptoms cause functional impairment or significant distress
- C. Symptoms are not due to the direct physiological effects of substances or due to another medical condition
- D. Symptoms are not better accounted for by a psychotic disorder such as schizoaffective, schizophrenia, etc
- E. There has never been a manic or hypomanic episode

New DSM-5 Nomenclature: MDD

- Changes in the diagnosis of Major Depressive Disorder
  - Qualifier related to bereavement has been excluded
  - Grief vs. MDD:
    - Grief is emptiness and loss vs. persistent depressed mood or anhedonia
    - Pangs of grief vs. persistent mood disturbance not tied to a specific thought
    - In grief, self-esteem is usually preserved
    - Grief generally has positive as well as negative emotions

New DSM-5 Nomenclature: MDD

- Changes in the diagnosis of Major Depressive Disorder; many new specifiers:
  - With mixed features: New qualifier can have “mixed” symptoms without qualifying as the diagnosis of bipolar disorder
  - With anxious distress
  - With mood-congruent or mood incongruent psychotic features
  - With melancholic, atypical, catatonia, peripartum onset, and seasonal pattern remain unchanged

Screening Mnemonic for MDD

- S Sleep disturbance: insomnia/hypersomnia
- I Interest in activities diminishes/anhedonia
- G Guilt for real or imagined transgressions
- E Energy is low or abnormally high
- C Concentration is impaired
- A Appetite disturbance: anorexia/hyperphagia
- P Psychomotor activity retarded/increased
- S Suicidal ideation/plan/intent/attempt

Two-Question Screening (PHQ-2)

1. During the past 2 weeks, have you often been bothered by feeling down, depressed, or hopeless?
2. During the past 2 weeks, have you often been bothered by having little pleasure in doing things?

If “no” to both, patient is unlikely to have MDD
If “yes” to either, proceed with a more detailed assessment

Premenstrual Dysphoric Disorder

- 20 years of research have now defined this disorder
- Essential feature is the experience of mood symptoms that occur repeatedly during the premenstrual phase of the cycle and remit around the onset of menses or shortly thereafter.
- Symptoms may increase approaching menopause
- Symptoms cease after menopause


DSM-5, APA, 2013
New DSM-5 Nomenclature

**Premenstrual Dysphoric Disorder (PMDD)**
- In the majority of menstrual cycles, ≥ 5 symptoms in the week before the onset of menses; improve with a few days after the onset of menses; become minimal or absent in the week post menses. At least 1 symptom must be MOOD:
  - Marked affective lability
  - Marked irritability/anger/interpersonal conflict
  - Marked depressed mood, hopelessness
  - Marked anxiety, tension, and or feeling keyed up or on edge.
- PLUS, ≥5 of the following: decreased interest; difficulty concentrating; lethargy; appetite change, feeling overwhelmed; hyper/hyposomnia; breast tenderness, joint or muscle pain, bloating, weight gain

**Persistent Depressive Disorder**
- A new DSM-5 diagnostic entity
- A consolidation of Dysthymic Disorder & chronic Major Depression
  - A. Depressed mood for most of the day, more days than not, as indicated by either subjective account or observation by others, for at least 2 years
  - B. Presence while depressed of ≥2: poor appetite or overeating; insomnia or hypersomnia; low energy or fatigue; low self esteem; poor concentration or difficulty making decisions; hopelessness

**Persistent Depressive Disorder**
- During the two year period, never without symptoms of the mood symptoms for more than two months at a time
- There has never been a manic or hypomanic episode nor cyclothymia
- Not better accounted for by a psychotic disorder
- Not due to a substance or general medical condition
- Must cause clinical distress or impairment

**Epidemiology of Major Depression**
- **LIFETIME PREVALENCE**
  - Women: 10-20%
  - Men: 7-12%
  - Adolescents: 5%
- **ONSET:**
  - Peak age onset 20’s
  - MDD can occur at ay age

**Epidemiology of Other Depressive Disorders**
- **LIFETIME PREVALENCE**
  - PMDD: 1.8%-5.8%
  - Persistent Depressive: 12-Month prevalence 0.5-1.5%
- **ONSET**:
  - PMDD: Can occur at any age,
  - Persistent Depressive Disorder: Usually early onset in childhood, Teens, or young adults
Prevalence of Depression as a Concomitant Condition

- Cancer: 0-38%¹
- Diabetes: 33%²
- Post-partum: 15%³
- Post stroke: 29%⁴
- Post MI: 20%⁵,⁶


Common Comorbid Conditions with Major Depressive Disorder

- Panic Disorder: 48%
- PTSD: 50%
- Social Anxiety: 52%
- GAD: 62%
- OCD: 42%
- Alcohol Dep: 15%
- Anorexia nervosa: 71%
- Borderline PD: 10%


Suicide

- MDD: 15% lifetime suicide risk ¹
- In the U.S., a suicide every 15 minutes ¹
- World Wide rate every 40 seconds ²
- Always ask about suicidal thoughts:
  - Plan
  - Intent
  - Weapon availability

¹ American Foundation for Suicide Prevention; ²: WHO 9/2014

Risk Factors for Suicide

**EPIDEMIOLOGIC:**
- Older age
- Caucasian/Native American
- Male gender
- Living alone

**STATISTICAL:**
- Family history of suicide
- History of attempts
- Physical illness
- Pain

**Acute Risk Factors**
- Moderate to severe depression
- Psychosis
- Mania
- Severe to moderate anxiety
- Substance abuse within the last month
- Hopelessness
- Global insomnia
- Anhedonia
Differential Diagnosis of Depressed Mood

• Bipolar disorders are the most commonly missed diagnoses. Use of Mood Disorder Questionnaire (MDQ)
• Think Bipolar Disorder if:
  ▫ Refractory depression
  ▫ Younger age of onset of depression
  ▫ Family history of Bipolar Disorder
  ▫ Presentation of depression with decreased need for sleep, increased energy, increase in goal directed activity
  ▫ Previous history of psychosis
  ▫ Hypomanic/manic response to antidepressants

Differential Diagnosis of Depressed Mood (continued)

• Persistent Depressive Disorder
• Premenstrual Dysphoric Disorder
• Cyclothymia
• Bereavement
• Adjustment disorder
• Depression due to a general medical condition
• Substance induced mood disorder
• Schizoaffective Disorder
• Dementia

Differential Diagnosis of Depressed Mood (cont’d)

• Depressive Disorder Due to Another Medical Condition:
  ▫ Neurological
    ▪ Parkinson’s disease
    ▪ Post-stroke
    ▪ Multiple sclerosis
    ▪ CNS tumors
  ▫ Endocrine
    ▪ Hypothyroidism, Hyperthyroidism
  ▫ Infectious
    ▪ AIDS, Meningitis, Encephalitis
  ▫ Cancer
    ▪ Pancreatic CA, Small cell lung CA

TREATMENT OF MAJOR DEPRESSION, PERSISTENT DEPRESSIVE DISORDER, AND PMDD
Treatment of Major Depression

Most patients require evidence-based Psychotherapy and somatic treatment

Psychotherapy of Major Depression and Persistent Depressive Disorder

Treatment of Major Depression

- Evidence-Based Psychotherapies:
  - Cognitive-Behavioral Therapy (CBT)
  - Mindfulness-Based Cognitive Therapy
  - Behavioral Activation (BA)
  - Interpersonal Therapy

Cognitive Behavioral Therapy (CBT)

- An evidence-based psychotherapy in which the therapist helps the patient identify and correct distorted and maladaptive beliefs about self or others
- Focuses on the here and now without ignoring the past
- Short term treatment on average 8-12 sessions

Psychopharmacology

Response Rates in MDD

- 10-20% of patients do not tolerate an initial antidepressant trial
- 25-35% of patients who complete an adequate trial of an antidepressant do not obtain remission

Thase ME, Rush, AJ. J Clin Psychiatry. 1997; 58 (Suppl. 1)
Pharmacotherapy of Depression

- All antidepressants are equally effective for the treatment of depression
- Choice of an antidepressant is based on:
  - Prior response
  - Response of first degree relatives
  - Comorbid medical and psychiatric illnesses
  - Drug-drug interactions
  - Adverse effects
  - Cost
  - Ease of administration

Pharmacotherapy of MDD/PDD

<table>
<thead>
<tr>
<th>SELECTIVE SEROTONIN REUPTAKE INHIBITORS</th>
<th>SEROTONIN MODULATORS</th>
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<tbody>
<tr>
<td>Citalopram (Celexa)</td>
<td>Nefazadone (Serzone)</td>
</tr>
<tr>
<td>Fluoxetine (Prozac)</td>
<td>Trazodone (Desyrel)</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>Vilazodone (Viibryd)</td>
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<tr>
<td>Fluvoxamine (Luvox)</td>
<td>Vortioxetine (Brintellix)</td>
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<tr>
<td>Paroxetine (Paxil, Paxil CR)</td>
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<td>Sertraline (Zoloft)</td>
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Pharmacotherapy of MDD/PDD

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<tr>
<th>SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITORS</th>
<th>ATYPICAL ANTIDEPRESSANTS</th>
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<tbody>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>Bupropion (Wellbutrin)</td>
</tr>
<tr>
<td>Venlafaxine (Effexor)</td>
<td>Mirtazapine (Remeron)</td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
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<tr>
<td>Levomilnacipram (Fetzima)</td>
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Pharmacotherapy of MDD/PDD

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<tr>
<th>HETEROCYCLIC ANTIDEPRESSANTS</th>
<th>MAO INHIBITORS</th>
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<tbody>
<tr>
<td>Amitriptyline</td>
<td>Phenelzine</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Tranylcypromine</td>
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<tr>
<td>Desipramine</td>
<td>Selegiline</td>
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<tr>
<td>Doxepin</td>
<td>Isocarboxazid</td>
</tr>
<tr>
<td>Imipramine</td>
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<tr>
<td>Nortriptyline</td>
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SELECTIVE SEROTONIN REUPTAKE INHIBITORS

- Better tolerated
- No orthostatic hypotension
- GI distress as SE
- +/- Sexual Side effects
- First line choice for anxiety

BUPROPION (Wellbutrin)

- No primary anxiety tx
- ADHD Off Label
- Activating
- Low sexual side effects
- Neuropathy Off label
- Smoking cessation
**TRAZODONE (Desyrel)**
- Priapism as SE
- Orthostatic Hypotension as SE
- Sedation as SE
- Less efficacy

**DULOXETINE (Cymbalta)**
- GAD
- HOT FLASHES Off label
- DIABETIC NEUROPATHY
- OA
- MUSCULOSKELETAL PAIN

**VENLAFAXINE (Effexor)**
- Fibromyalgia Off label
- Neuropathy Off label
- Hot flashes Off label
- Headache/BP side effect
- ? Tx resistant depression

**DESVENLAFAXINE (Pristiq)**
- GI distress
- Dizziness
- Diaphoresis
- Same benefits as Effexor?

**VILAZODONE (Viibryd)**
- GI: nausea, constipation
- Insomnia
- Pulmonary HTN in newborn
- Relative risk in women of childbearing age

**MIRTAZPINE (Remeron)**
- Increased appetite
- Weight gain
- Fatigue
- Somnolence
- ? More side effects at lower doses
- Less sexual side effects
LEVOMILNACIPRAN (Fetzima)

- GI Symptoms
- HTN
- Increased HR
- Diaphoresis
- Contraindicated with glaucoma

Monoamine Oxidase Inhibitors (MAOI)

- Very effective for depression and anxiety
- Limited use due to risk of hyperadrenergic crisis
- Reserved for:
  - Refractory patients
  - Patients with atypical depression
  - Pt’s with limited use of other medications
  - Pt able to comply with tyramine-free diet and drug restrictions

Current Treatment Strategies

- Step 1: Monotherapy with SSRI, SNRI or buproprion. PMDD responds preferentially to SSRI (always 1st line choice) or SNRI
- Step 2: Monotherapy with an agent other than used in Step 1 if no response 3-6 weeks
- Step 3: Monotherapy with agent other than Step 1 or 2 or ECT or TMS
  - If partial response in Step 3: Consider augmenting strategies

GUIDELINES FOR LENGTH OF DEPRESSION THERAPY

Nature of MDD is Recurrence

- Likelihood of future episodes increases with each episode.
- One episode: Likelihood of another 50-60%
- Two episodes: Likelihood of another 75%
- Three episodes: Likelihood of another 90%

American Psychiatric Assoc Practice Guidelines for Treatment of MDD, 3rd edition

Length of Therapy for MDD

- Factors in determining length of therapy in the maintenance phase include:
  - Severity of episode
  - Frequency of episodes
  - Presence of psychosis
  - Presence of suicidal behavior
  - Family history of a mood disorder

Length of Therapy for MDD

- If single episode of MDD:
  - Treat for 9-12 months
  - Maintain the dose of the antidepressant that it took to make the patient well
  - Taper the dose when discontinuing therapy

- Recommend Maintenance Treatment if:
  - 3 or more episodes of MDD
  - 2 or more episodes or MDD plus one or more of the following:
    - Family history of a mood disorder
    - Onset of MDD < 20 years or > 60 years
    - Severe episodes
    - Recurrence of MDD within 1 year of discontinuing an antidepressant

Kupfer DJ et al. Arch Gen Psychiatry 1992; 49: 769

Electroconvulsive Therapy (ECT)

- The most effective known treatment for major depression
- Safer than many antidepressants
- Treatment of choice for:
  - Refractory depression
  - Depression in pregnancy
  - Psychotic depression
  - Severe suicidality
  - Catatonia
  - Malnutrition due to MDD

Neuromodulation

Transcranial Magnetic Stimulation (TMS)

- FDA approved if failed 1 trial of antidepressant
- Noninvasive
- No general anesthesia
- No induced seizure
- MRI-strength pulsing magnetic field
- Tolerable and low risk