Depression: Diagnosis and Treatment

Jonathan Bolton MD
Center for Rural and Community Behavioral Health
University of New Mexico
Diagnosis
Depressive Syndromes (DSM V)

• Major Depressive Disorder
• Persistent Depressive Disorder (Dythymia)
• Premenstrual Dysphoric Disorder
• Substance-Induced Depressive Disorder
• Depression due to General Medical Condition
• Disruptive Mood Dysregulation Disorder
• Other Specified Depressive Disorder
Major Depressive Episode

- Depressed Mood *and/or*
- Loss of interest/pleasure (anhedonia)

- Weight loss/gain
- Insomnia/hypersomnia
- Psychomotor agitation/retardation
- Loss of energy
- Feelings of worthlessness, excessive guilt
- Diminished concentration
- Recurrent thoughts of death/suicide
Major Depressive Disorder

Symptoms of a Major Depressive Episode

Duration: \(\geq 2\) weeks

Depressed Mood and/or Anhedonia
(and \(\geq 4\) other symptoms)

A change from previous functioning

Not due to General Medical Condition,
Substance Use/Abuse
MDD Specifiers
• With anxious distress
• With mixed features
• With melancholic features
• With atypical features
• With psychotic features
  – Mood congruent
  – Mood incongruent
• With catatonia
• With peripartum onset
• With seasonal pattern
MDD

US lifetime prevalence: 16%
US 12 month prevalence: 6.6%

Degree of role impairment: 59% severe/very severe

Mean duration of an MDD episode: 16 weeks

52% were treated
42% of these were adequately treated
22% of total had adequate treatment

Kessler 2003
Risks for Depression

• Genetics
• Environment
• Situation
  – Loss
  – Role transition
• Medical illness
• History of trauma as a child
• Personality style/disorder (neuroticism)
• Drug abuse
Risks of Depression

Poor compliance with medical treatment

Cardiovascular
  1.8 RR for future CHD in depressed pt
  1.8 RR for hypertension
  Incr risk of CVA

Metabolic/Endocrine
  3.15 RR of depression leading to diabetes spectrum

Dementia
  Late life depression associated with dementia:
  All causes 1.85; Alzheimers 1.65; Vascular Dementia 2.5
Persistent Depressive Disorder (Dysthymia)

Amalgam of two DSM IV diagnoses:
Dysthymic Disorder + Chronic Major Depressive Episode

Depressed mood for >= 2 years
With >= 2 symptoms:
   Poor appetite/overeating
   Insomnia/hypersomnia
   Anergia
   Low self-esteem
   Poor concentration
   Feeling of hopelessness
Dysthymia

Dysthymia + Major Depressive Episode = ‘Double Depression’
Premenstrual Dysphoric Disorder

• Depressive Symptoms ($\geq 5$) associated with the majority of menstrual cycles over $\geq 12$ months

Primary Symptoms
$\geq 1$

• Marked affective lability
• Marked irritability/anger
• Marked depressed mood

Secondary Symptoms
$\geq 1$

• Anhedonia
• Difficulty with concentration
• Anergia
• Change in appetite
• Hypersomnia/Insomnia
• Sense of being overwhelmed
• Physical sx (breast tenderness, joint pain, bloating, weight gain)
Substance-Induced Depressive Disorder

• Depressive symptoms *persist* beyond the expected physiological effect.
• Onset of symptoms is *within one month* of last use.
• Types: Alcohol, phencyclidine, other hallucinogens, inhalants, opioids, sedative-hypnotics, amphetamine/other stimulants, cocaine, other.
• Differential Dx: Substance intoxication or withdrawal
Substance-induced Depressive Disorder

• Iatrogenic: due to prescribed medications
  – Interferon
  – Steroids
  – Betablockers
  – Isotretinoin/Accutane
  – Chemotherapy
Depression Due to General Medical Condition

• Prominent and persistent period of depressed mood and/or anhedonia

• Specifiers:
  – With depressive features
  – With Major Depressive-like features
  – With Mixed features
Depression Due to General Medical Condition

- Neurological
  - CVA
  - Parkinson’s
  - Huntington’s
  - Multiple Sclerosis
  - TBI
- Endocrine
  - Hypothyroidism
  - Cushing’s

Other
- SLE
- Liver disease
Other Specified Depressive Disorder

• Recurrent Brief Depression
  – 2-13 days
  – At least once a month (not associated with menses)
  – For >12 months

• Short-duration Depressive Episodes
  – 2-13 days
  – >= 4 symptoms of MDE

• Depressive Episodes with Insufficient Symptoms
  – Depressed Affect + >=1 symptom of MDE
Demoralization

- Persistent inability to cope
- Feelings of hopelessness, helplessness, meaninglessness, subjective incompetence, low self-esteem
- Feel powerless to change
- Giving up-Given up (Engel)
- Less associated with anhedonia (MDE)
Mnemonic for Depression: ‘Sig E Caps’

• Sleep
• Interest
• Guilt
• Energy
• Concentration
• Appetite
• Psychomotor
• Suicidality
Screening Instruments

Self Report

PHQ-9
Beck Depression Inventory

Clinician-completed

Hamilton Depression Rating Scale
### Patient Health Questionnaire (PHQ-9)

**Name:** __________________________ **Date:** __________________

*Over the past 2 weeks, how often have you been bothered by any of the following problems? (use “✓” to indicate your answer)*

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half of days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead, or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**add columns:** □ + □ + □ + □

*(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card.)*

**Total:** □

- **0-4** remission
- **5-9** mild
- **10-14** moderate
- **15-19** moderately severe
- **20-27** severe
Treatment
Response, Remission, Recovery, Relapse, Recurrence
Treatment of Depression

• Somatic Treatments
  • Medications
  • ECT
  • Phototherapy
  • Vagal Nerve Stimulation
  • Transcranial Magnetic Stimulation

• Psychotherapy
  • Cognitive Therapy
  • Interpersonal Psychotherapy
Antidepressant Medication Classes

• Tricyclic Antidepressants (TCAs)
• Monoamine Oxidase Inhibitors (MAOIs)
• Serotonin-Specific Reuptake Inhibitors (SSRIs)
• Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
• Norepinephrine and Dopamine Reuptake Inhibitors (NDRIs)
• Serotonin Antagonist-Reuptake Inhibitors (SARIs)
• Alpha 2 Adrenergic Blockers
**Serotonin synthesis**

- tryptophan
  - \textit{tryptophan} hydroxylase
- 5-hydroxytryptophan (5-HTP)
  - \textit{aromatic aminoacid decarboxylase} (AADC)
- 5-hydroxytryptamine (5-HT, serotonin)

**Catecholamine synthesis**

- phenylalanine
  - \textit{phenylalanine hydroxylase}
- tyrosine
  - \textit{tyrosine hydroxylase} (TH)
- dihydroxyphenylalanine (DOPA)
  - \textit{aromatic aminoacid decarboxylase} (AADC)
- dopamine
  - \textit{dopamine beta hydroxylase} (DBH)
- norepinephrine
  - \textit{phenylethanolamine-N-methyl transferase} (PNMT)
- epinephrine
Sites of Antidepressant Drug Action
MDD Algorithm

SSRI

SSRI 2  Bupropion

Venlafaxine/Duloxetine

TCA  Mirtazapine

MAOI

ECT

Augmentation Agents

Atypical Antipsychotic  Thyroid hormone (T3)  Lithium

Dopamine agent: Stimulant, Pramipexole  L-methylfolate
Serotonin-Selective Reuptake Inhibitors

- Fluoxetine/Prozac (20-60 mg/d)
- Sertraline/Zoloft (50-200 mg/d)
- Paroxetine/Paxil (20-60 mg/d)
- Fluvoxamine/Luvox (50-200 mg/d)
- Citalopram/Celexa (20-40 mg/d)
- Escitalopram/Lexapro (10-20 mg/d)
Serotonin Syndrome

- Abdominal pain
- Diarrhea
- Elevated blood pressure
- Delirium
- Myoclonus
- Increased motor activity
- Irritability/Hostility
- Mood change

- Hyperpyrexia
- Cardiovascular Shock
- Death
Norepinephrine and Serotonin Reuptake Inhibitors (SNRIs)

- Venlafaxine/Effexor (75-225 mg/d; Extended Release)
- Duloxetine/Cymbalta (60-120 mg/d)

- Side Effects
  - Weight gain, sexual dysfunction, headaches, GI, elevated
  - blood pressure
  - Discontinuation Syndrome
Norepinephrine and Dopamine Reuptake Inhibitor (NDRI)

• Buproprion/Wellbutrin
  SR 150-450 mg/d
  XL 300 mg/d

Side effects
• Seizures (caution in eating disorders, h/o seizure do)
Alpha 2 Adrenergic Blockers

- Mirtazapine/Remeron (15-45 mg/d)

  Side Effects: Sedation, weight gain
Tricyclic Antidepressants (TCAs)

- Imipramine/Tofranil
- Amitriptyline/Elavil
- Clomipramine/Anafranil
- Doxepin/Sinequan
- Desipramine/Norpramin
- Nortriptyline/Pamelor
- Protriptyline/Vivactil
- Maprotiline/Ludiomil
- Amoxapine/Asendin
- Trimipramine/Surmontil
Monoamine Oxidase Inhibitors (MAOIs)

- Phenelzine/Nardil (45 -90 mg/d)
- Tranylcypromine/Parnate (30-60 mg/d)
- Isocarboxazid/Marplan (30-60 mg/d)

Effective antidepressants (third-line)

Side effects: weight gain, orthostasis, sexual dysfunction, dry mouth, headache, insomnia/somnolence
Risks: lethal in overdose; hypertensive crisis, stroke.

Drug-Drug Issues:
Food/drink with Tyramine (hypertensive crises)
meperidine/Demerol and SSRIs (Serotonergic Syndrome)
Stimulants, cold remedies (hypertensive crisis)
Phenylalanine → Tyrosine → Tyramine

Tyramine can be broken down by MAO A to HPA.

Tyramine-rich diet can lead to catecholamine release (DA, NE, EP) and ultimately to Hypertensive Crisis.

Diets high in tyramine include:
- Aged cheese
- Dry Sausage
- Beer/Red wine
- Fava beans
- Smoked fish
- Liver
Augmentation Strategies

- Lithium (600-1200 mg/d)
- Thyroid hormone (T3) (12.5-50 mcg/d)
- Dopamine agonists
  - Stimulant
  - Pramipexole/Mirapex (0.25-5 mg/d)
- Antipsychotic
  - Aripiprazole (2.5-10 mg/d)
  - Olanzapine (+ Fluoxetine) (6/12.5-12/50 mg/d)
- L-methylfolate/Deplin (7.5-15 mg/d)
- TCAs
<table>
<thead>
<tr>
<th>STEP</th>
<th>TREATMENT</th>
<th>REMISSION RATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Citalopram</td>
<td>36.8%</td>
</tr>
<tr>
<td>2</td>
<td><strong>Switch:</strong> Bupropion, CT, Sertraline, Venlafaxine</td>
<td>30.6%</td>
</tr>
<tr>
<td></td>
<td><strong>Augment:</strong> Bupropion, Buspirone, CT</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><strong>Switch:</strong> Mirtazapine, Nortriptyline</td>
<td>13.7%</td>
</tr>
<tr>
<td></td>
<td><strong>Augment:</strong> lithium, thyroid hormone</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><strong>Switch:</strong> Tranylcypromine, Venlafaxine + Mirtazapine</td>
<td>13.0%</td>
</tr>
</tbody>
</table>
STAR 0 Study Results Demonstrate Limited Rates of Remission with Current Antidepressant Medications

*Determined by QIDS-SR 16 Rating Scale