Evaluating and Treating Depression in Primary Care

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Depressed Patients in Primary Care?
What percentage of antidepressant prescriptions are written by primary care providers?

A. 25%
B. 50%
C. 70%
D. 90%

Correct answer C
Depression in Primary Care

- 20% of patients presenting in primary care
- 2/3 of depressed patients present with somatic symptoms
- The number of patients receiving care for psychiatric illness in primary care settings is increasing.
- Primary care doctors write 62-70% of all prescriptions for anti-depressants.
Depression Facts

- The first episode usually occurs in the late teens or twenties but can occur at any time of life.
- The first episode is often precipitated by a stress or a loss. The degree of stress needed to precipitate an episode may go down over time.
- MDD is remitting and relapsing which means it will usually go away on its own (after 8-16 months) but often recurs.
- Each episode increases the risk of a subsequent episode.
- Non-recurrent late life depression may be different, more closely associated with dementia.
Medical Consequences of Depression

- Depression is a risk factor for heart disease (OR 4.5 for MI) and stroke.
- People who are depressed after a heart attack are 4 times more likely to die in the next year.
- Recurrent depression probably increases the risk for Alzheimer’s.
- Depression worsens the course of diabetes.
- Depression is a systemic illness—increases platelet aggregation, decreases beat to beat heart rate variability, causes increased immune system activation.
- Depression is associated with poorer self care.
Diabetes and Depression

- 4623 Primary care patients with type II diabetes followed for 5 years
- MDD associated with 1.36 greater risk for advanced microvascular complications (blindness, ESRD, amputation) and 1.24 for macrovascular complications (MI, stroke)
- Depression is associated with greater incidence, symptom severity, complications, disability, cost and mortality.
- The relationship between depression and diabetes is bidirectional.
- Depression activates the HPA axis, stimulates the sympathetic nervous system, increases inflammatory responses, and increases platelet aggregation.
- Depression impairs glycemic control through negative effects on adherence to diet, glucose monitoring, medication adherence, diet, and exercise.

Lin et al 2010
Differential Diagnosis of Depression

- Worried well
- Major depressive disorder
- Dysthymia (chronic mild depression)
- Bipolar depression
- Adjustment disorder
- Secondary depression (medical illness, substances or medications)
- Complicated grief
Major Depressive Episode

- Two weeks of depressed mood and/or loss of interest as well as 3-4 (total of 5):
  -- change in weight
  -- insomnia or hypersomnia
  -- Psychomotor agitation or retardation
  -- fatigue or loss of energy
  -- feelings of worthlessness or guilt
  -- decreased concentration or indecisiveness
  -- recurrent thoughts of death
- The symptoms cause clinically significant distress or impairment
Bipolar Depression

- Episodes of depression which may be identical to MDD plus episodes of mania or hypomania
- Sometimes hard to diagnose
- Bipolarity may emerge with antidepressant treatment
- Requires mood stabilizing medications
Bipolar Depression--clues

- BPI eat and sleep more, slow down
- BPII are more agitated
- Abrupt on set or termination of episodes
- Wired or agitated or anxious on ADs
- Improve on ADs but relapse
- Seasonal
- Family history of bipolar
- Post partum depressions
Secondary Depression

- The medical condition is a biological contributor, not just a stressor.
- Endocrine and brain disorders are most likely to cause depression.
- 50% of people with Parkinson’s disease get depressed.
- 33% of people with Alzheimer’s dementia get depression.
- 20-50% of people who have had a stroke suffer from post-stroke depression.
- Pancreatic cancer can present as depression.
Secondary Depression

- Most drugs of abuse can cause depression.
- Alcohol dependence often contributes to depression.
- Often difficult to determine which came first.
- Even brain stimulants can contribute to depression.
- B blockers, retinoic acid, interferon, chronic steroid use can all cause depression.
Screening

Two Question

“During the past month have you often been bothered by feeling down, depressed, or hopeless?”

“During the past month have you often been bothered by little interest or pleasure in doing things”

96% sensitivity and 57% specificity for major depression
PATIENT QUESTIONNAIRE – PHQ-9

Patient Name: ___________________________  MRN ____________
Physician: _______________________________  Date: ____________

Over the last 2 weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>□</td>
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<td>Little interest or pleasure in doing things.</td>
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<td></td>
<td>Feeling down, depressed, or hopeless.</td>
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<td>3.</td>
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<td>Trouble falling/staying asleep, sleep too much.</td>
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<td>Feeling tired or having little energy.</td>
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<td>5.</td>
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<td>Poor appetite or overeating.</td>
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<td>6.</td>
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<td></td>
<td>Feeling bad about yourself – or that you are a failure or have let yourself or your family down.</td>
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<td>7.</td>
<td>□</td>
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<td></td>
<td>Trouble concentrating on things, such as reading the newspaper or watching television.</td>
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<td>8.</td>
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<td>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>
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<td>9.</td>
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<td></td>
<td>Thoughts that you would be better off dead or of hurting yourself in some way.</td>
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</tbody>
</table>

A. How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?
   - □ Not difficult at all  □ Somewhat difficult  □ Very difficult  □ Extremely difficult

B. In the past two years have you felt depressed or sad most days, even if you felt okay sometimes?
   - □ Yes  □ No

Symptoms _________  Severity Score _________
Myths About Depression

- It represents moral failure
- “I don’t have anything to be depressed about.”
- “I can just think (or pray) my way out of it.”
- It is a normal response to life’s trouble.
- It is a normal response to illness.
Is it Depression?

- The “normal” things most like depression are sadness, grief, and existential angst” although the distinction is often difficult to make.
- Clinical depression is often a perversion of normal sadness and grief which can impair true emotional healing.
- Fallacy of good reasons/human tendency to normalize
- Physical symptoms, social withdrawal, loss of interest, suicidal thoughts are warning signs
Treatment

- Medications
- Psychotherapy
- Support/Encouragement
- Education
- Exercise
What percentage of patients experience remission with an initial trial of an antidepressant?

A. 33%
B. 50%
C. 66%
D. 90%

Correct answer is A.
What percentage of patients (cumulatively) experience remission after 4 trials of antidepressants?

A. 40%
B. 60%
C. 80%
D. 100%

Correct answer is C
Medications

- Antidepressants vary more by side effects than by efficacy.
- 50-60% respond to a given medication, 33% experience complete remission.
- Antidepressants and psychotherapy are equally efficacious (with caveats.)
- Antidepressants plus psychotherapy may be more efficacious.
- Antidepressants treat more than depression!
Sequenced Treatment Alternatives to Relieve Depression STAR*D

- What do you do when patients fail their first anti-depressant trial?
- 5 year NIMH trial, N=4041
- Included patients in a primary care setting (who were no different in terms of symptom severity, illness variables or co morbidity)
- “Real world” patients with shared decision making (augmentation vs. switch, medications vs. therapy)
- Outcome measure was remission (HRS<7)
STAR*D

**Level I**  All patients take citalopram

**Level II**  Non-remitters or those who do not tolerate citalopram switch to bupropion, CBT, venlafaxine, sertraline or augment with bupropion, CBT, or buspirone

**Level III**  Switch to mirtazapine or nortriptyline or augment with lithium or T3

**Level IV**  Switch to tranylcypromine or venlafaxine and mirtazapine
STAR*D Level I--Citalopram

- Citalopram for 12-14 weeks.
- Remission rate of 28% with a mean dose of 41.8mg
- A majority responded by six weeks but many required up to 12 weeks.
- Associated with remission--white, female, employed, better educated, higher income
- Negatively associated with remission--longer episode, psychiatric or medical co morbidity, lower baseline function
STAR*D Level II—Switch or Augment

- Switch to bupropion 21% remission, switch to sertaline 18% remission, switch to venlafaxine 25% remission
- Augmentation with bupropion 29.7% remission, buspirone 30.1% remission Bupropion was better tolerated
- Remission rate 25%; 50%-55% after 2 sequential trials
- CBT was comparable but took longer. It had less adverse events.
STAR*D Level III

Switch to mirtazapine or nortriptyline or augment with lithium or T3

Remission Rates

- Mirtazapine 12%
- Nortriptyline 20%
- Lithium 16% (more adverse events)
- T3 25%

No significant difference
STAR*D Step IV

Tranylcypromine 7% remission
vs
venlafaxine/mirtazapine 14% remission
STAR*D

- Lower remission rates with each successive trial
- Remission rate of 53% after 2 trials and 81% after 4 trials
- Higher relapse rates with more refractory patients
- Remission is more durable than response
Basic Algorithm

- Start with an SSRI or Bupropion, titrate to an appropriate dose and wait 4-8 weeks.
- For a partial response raise dose or augment or wait
- For no response switch medications
- Consider a tricyclic, monamine oxidase inhibitor, ECT, TMS, VNS, DBS
- SSRI non response is not predictive of failure of another SSRI but can also change to bupropion or an SSNRI
- Always consider psychotherapy
Augmentation
SSRI or venlafaxine or duloxetine
+ 
buproipion and/or mirtazapine

Any anti-depressant
+ 
lithium, T3, buspirone, aripiprazole, quitiapine, lamotrigine

Psychotherapy
Dosing Strategies

- “Wait and see dose”—a potentially therapeutic dose
- Titration—how you get there
- Maximum dose—dose after which you augment or change if it is not effective
- Speed of action vs. dose/side effects
- “Proving the medicine a failure”
Medication Resistance

- Consider the adequacy of the medication trial.
- Reassess the diagnosis.
- Consider psychiatric and medical co-morbidities.
- Assess compliance.
- Consider pharmacokinetics.
- Is medication contributing to depression?
When to Stop Medications?

- Most people should be treated for 8-12 months after remission.
- After 8-12 months treatment is to prevent a new episode.
- Anxiety may re-emerge quickly.
- Factor in patient preference, number of episodes, severity of episodes, efficacy of medication, side effects.
How to Stop Medications

Discontinuation Symptoms (DS) vs. Re-emergence of psychiatric symptoms

- Fluoxetine has minimal DS
- Venlafaxine, paroxetine, and duloxetine have significant DS
- Taper as slowly as one increment a month in order to monitor for returning symptoms
Psychotherapy

- Either as primary treatment or with medications
- Cognitive behavioral therapy and interpersonal therapy are evidence based
- Other therapies probably work
- Evidence is good for time-limited, directive psychotherapy that focuses on current problems and changing current behavior.
- Feeling Good by David Burns
Education/Resources

- Feeling Good by David Burns
- Darkness Revealed by William Styron
- Night Falls Fast by Kay Redfield Jamison
- An Unquiet Mind by Kay Redfield Jamison
- The Noonday Demon by Andrew Solomon
- Ordinary People
- Mr. Jones
Supporting People with Depression

- Encourage proper treatment
- Decrease stigma
- Encourage social interaction
- Watch for signs of danger
- People with depression should push themselves but not too much
How much more do non-generic antidepressants cost compared to generics?

A. 10 times more
B. 50 times more
C. 75 times more
D. 100 times more

Correct answer is C.
High Value Care

Consumer Reports “Best Buy” Antidepressants

- Citalopram
- Sertraline
- Fluoxetine
- Bupropion
- Escitalopram
SSRIs

First choice for patients with anxiety. Good side effect profile. Often inexpensive.

- Fluoxetine—activating, very long half life, CYP2D6 inhibitor, cheap
- Paroxetine—short half life, discontinuation symptoms, sedating, anticholinergic, cheap
- Sertraline—longer titration in some patients, cheap
- Citalopram—tires some, cheap, may cause arrhythmias
- Escitalopram—can start at therapeutic dose, may be better tolerated, tires some
SSRI Side Effects

--GI
--Anxiety

--Headache
--Sexual side effects (delayed orgasm, decreased libido)

• Bleeding
• SIADH/hyponatremia
• Osteoporosis—Two fold increased risk of clinical fragility fracture, increased odds of falling, lower mineral density of the hip
• Monitor for suicidal thoughts
**Dosing SSRIs**

- **Sertraline**—start at 25-50mg, wait at 100mg or 50mg, max. at 200mg
- **Fluoxetine**—start at 5mg, 10mg, or 20mg, wait at 20mg or 40mg, max at 60-80mg
- **Paroxetine**—start at 10mg or 20mg, wait at 20mg or 40mg, max at 60mg
- **Citalopram**—start at 10-20mg, wait at 40mg or 20mg, max at 40mg*
- **Escitalopram**—start at 5mg or 10mg, wait at 10mg or 20mg, max at 20mg
- **Fluvoxamine**—start at 50mg, wait at 200mg, max at 300mg

*20 mg for those over 60, hepatic insufficiency, cardiac problems*
Venlafaxine (Effexor)

- SNRI (more norepinephrine reuptake inhibition at 225mg and higher)
- Indications for MDD, GAD, panic disorder and social phobia
- Dosing--venlafaxine XR—start at 37.5mg or 75mg, wait at 75mg, 150mg, or 225mg, max at 225mg but has been used up to 375mg and 450mg
- Discontinuation syndrome, sweating, GI, HTN
Duloxetineine (Cymbalta)

- SSNRI
- Indications for MDD, GAD, fibromyalgia, diabetic peripheral neuropathy, chronic musculoskeletal pain
- Dosing--start at 20mg or 30mg, wait at 60mg, max at 90mg or 120mg
- More expensive generic
- Discontinuation syndrome, sweating, GI
Tricyclic Antidepressants

- Norepinephrine and serotonin reuptake inhibitors (vary in how much)
- May be better for severe or treatment resistant depression
- Caution with cardiac patients
- Treats chronic pain
- Nortriptyline and desipramine have less side effects than amitriptyline and imipramine
- Lethal in overdose
- Metabolized by 2D6
Bupropion (Wellbutrin)

- Norepinephrine, dopamine reuptake inhibitor
- Activating, with less sedation, weight gain, and sexual side effects
- Less used for anxiety disorders, may increase anxiety
- Lowers seizure threshold, dose related—use with caution in patients with seizure risk
Bupropion--Dosing

- IR-225-450 mg in 3 divided doses, maximum 150mg/dose
- SR 100mg, 150mg or 200mg BID. Second dose at 4pm to avoid insomnia.
- XL 150mg, 300mg, or 450mg once a day in the morning.
Mirtazapine (Remeron)

- Alpha 2 antagonist
- Dosing--start at 7.5mg or 15mg, wait at 30mg or 45mg, max 45mg
- May be more sedating at lower doses
- Causes weight gain and sedation (so used when those are beneficial)
- Minimal sexual side effects
- Mixes well with other antidepressants
Vilazodone (Viibryd)

- SSRI plus 5HT1A agonist (like buspirone)
- Must be taken with food
- Dosing—10mg for 1 week, 20 mg for 1 week, then 40mg.
- SSRI side effect profile, may have less sexual side effects
- Minimal weight gain
Selegeline (EMSAM)

- MOAI (A and B in the brain, B in the gut)
- Transdermal patch
- 6mg, 9mg, 12 mg
- Side effects include site reaction, headache, dry mouth
- Tyramine free diet at doses over 6 mg
- Many drug interactions. Must wash out other antidepressants prior to starting
Aripiprazole (Abilify)

- Partial agonist at D-2 plus α1 blockade
- 2.5-5 mg for MDD
- FDA indication for augmenting an antidepressant in MDD
- Usually not sedating
- Less metabolic side effects, some patients will still have weight gain
- Some patients will have akathisia, restlessness, anxiety
- Minimal EPS
Vortioxetine (Brintellix)

- SSRI, 5-HT1A agonist, 5-HT 3 and 5-HT7 antagonist
- Start at 10 mg, can increase to 20 mg
- Non-generic
- GI side effects
Levomilnacipran (Fetzima)

- SNRI, enantiomer of milnacipran (Savella)
- @0 mg for two days then 40 mg. Maximum dose 120 mg.
- Side effects include GI, flushing, sexual side effects
### Morning or Night?

<table>
<thead>
<tr>
<th>Morning</th>
<th>Night</th>
<th>Doesn’t Matter</th>
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<tbody>
<tr>
<td>Fluoxetine</td>
<td>paroxetine</td>
<td>sertraline</td>
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<tr>
<td>Venlafaxine</td>
<td>duloxetine</td>
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<td></td>
<td>citalopram</td>
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<td>escitalopram</td>
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</table>

“If it makes you sleepy, move it to night. If it interferes with your sleep, move it to the morning.”

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**Image Description:**
- The image features a serene night scene with a person walking on a path under a moonlit sky, symbolizing the connection between bedtime and sleep patterns.
Complementary and Alternative Treatments

- St John’s Wort
- SAMe
- Omega 3 fatty acids
- Exercise
Antidepressants and Suicide

<table>
<thead>
<tr>
<th>Age range (y)</th>
<th>Drug-placebo difference in number of cases of suicidality per 1000 patients treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-related increases</td>
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<tr>
<td>&lt;18</td>
<td>14 additional cases</td>
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<tr>
<td>18-24</td>
<td>5 additional cases</td>
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<tr>
<td>Drug-related decreases</td>
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<tr>
<td>25-64</td>
<td>1 fewer case</td>
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<tr>
<td>≥65</td>
<td>6 fewer cases</td>
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</tbody>
</table>

From reference 9.

Bridge, S. Suicide prevention, targeting the patient at risk. Australian Family Physician. 35(5): 2006
