Bridging the Gaps in Recognition and Management of Comorbid Depression

A Pocket Guide for Recognition and Treatment of Comorbid Depression

- Based on collaborative best practices in primary care and managed care
- Intended to bridge treatment and management decisions to reduce fragmentation in patient care
- Developed through expert consensus

Sponsored by PRIME through an educational grant from Wyeth
Position Statement

Current evidence suggests that there is a coexistence of major depressive disorder (MDD) and chronic medical illnesses. While it seems intuitive that the onset of chronic illness might lead to MDD, a large body of research suggests that MDD may actually be a risk factor for the development of several chronic illnesses, including cardiovascular disease and cancer. Additionally, several studies have suggested that treatment with antidepressants and psychotherapy is effective in treating MDD in patients with chronic illness, as well as improving outcomes and quality of life in these patients. In order to recognize and effectively manage comorbid depression, practitioners in primary care and managed care settings convened a meeting to identify and resolve barriers. The output of this consensus meeting is this pocket guide. The purpose of this pocket guide is to assist the practitioner in identifying and managing patients with chronic medical illness and comorbid MDD, and as a result, improve the care of these patients.

Comorbid MDD

- Biological mechanisms may link depression and many medical illnesses
- Depression may adversely impact the course of medical illness
- The presence of MDD in the patient with chronic medical illness may lead to:
  - Increases in health care utilization
  - Lost productivity in both the work and home setting
  - Functional disability
- Early identification and treatment of depression in the medically ill can improve outcomes and quality of life
• Patients with concomitant MDD and medical illness may have higher rates of morbidity and mortality than those not affected with concomitant MDD and medical illness.
Consensus Panel to Address Comorbid Depression in Managed Care and Primary Care

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Some Chronic Medical Conditions Associated with Increased Rates of MDD
<table>
<thead>
<tr>
<th>Coronary artery disease</th>
<th>Cancer</th>
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<tbody>
<tr>
<td>Congestive heart failure</td>
<td>HIV/AIDS</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>Chronic pain</td>
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<tr>
<td>Diabetes mellitus</td>
<td>Substance abuse disorders</td>
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<tr>
<td>COPD Nicotine dependence Asthma Obesity</td>
<td>Chronic fatigue syndrome</td>
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<tr>
<td>CKD (including ESRD)</td>
<td>Fibromyalgia</td>
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<tr>
<td>Alzheimer’s disease</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>Arthritic conditions</td>
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</table>
Recognition of Comorbid Depression

**Coronary Artery Disease**
- 17%–27% of patients with CAD have MDD
- Depression has been associated with a 1.5- to 2-fold increase in the risk for onset of CAD
- Depression predicts increased morbidity and mortality in patients with existing CAD
- Post-MI patients with depression have higher mortality
- Treatment of MDD with SSRIs appears to be safe and effective in patients with CAD*

**Type 2 Diabetes**
- As many as 10%–25% of patients with type 2 diabetes may have MDD
- Depression is an independent risk factor for the development of type 2 diabetes
- Depression is associated with poor medication adherence and glycemic control, increased health care costs and disability, worsening of vascular complications, and higher rates of death
- Treatment of MDD appears to be effective in type 2 diabetes but may not improve glycemic control*

**Cerebrovascular Disease**
- 14%–19% of patients who have had a stroke also have MDD
- Depression impacts stroke recovery through effects on activities of daily living and cognition
- Poststroke mortality is increased in those with depression
- Treatment of MDD in stroke appears to be beneficial and may enhance functional status and survival*

**Cancer**
- 22%–29% of patients with cancer have MDD
- Depression may result from diagnosis of cancer and subsequent physical decline, use of antineoplastic drugs, and cytokines associated with large tumor burden
- Presence of comorbid depression is associated with poor prognosis and increased morbidity
• Treatment of MDD may improve psychological distress but has not been shown to affect survival*

**Chronic Pain**

• 30%–54% of patients with chronic pain have MDD
• Severity and duration of pain are worse in those with depression
• Treatment for MDD may improve pain through complementary mechanisms*

*Presently available therapies may not be specifically FDA-approved for the treatment of MDD in the patient with chronic medical illness. Practitioners should use clinical judgment and weigh the risks and benefits of therapy for such patients.
Diagnosis of MDD

Diagnostic Criteria for 296.2x, Major Depression, Single Episode

At least 5 symptoms must be present for at least a 2-week period, and symptoms #1 or #2 must be present:

1. Depressed mood
2. Diminished interest or pleasure in all or almost all activities
3. Significant change in weight or appetite
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness or excessive guilt
8. Diminished ability to concentrate
9. Recurrent thoughts of death and suicidal ideation, or suicide attempt

Source: DSM-IV-TR.

Questions to Assist in the Diagnosis of Depression

Over the past 2 weeks:

Were you depressed or down, most of the day, nearly every day?

Were you much less interested in or much less able to enjoy those things you used to enjoy most of the time?

Was your appetite decreased or increased nearly every day? Did your weight decrease or increase without trying intentionally? Did you have trouble sleeping nearly every night?

Did you talk or move more slowly than normal or have you been fidgety, restless or had trouble sitting still almost every day?

Did you feel tired or without energy almost every day? Did you feel worthless or guilty almost every day?

Did you have difficulty concentrating or making decisions almost every day?
Did you repeatedly consider hurting yourself, feel suicidal, or wish that you were dead?

Did these symptoms cause significant problems at home, work or school, or socially in some other important way?

Adapted from Sheehan DV, et al. *J Clin Psychiatry*. 1998;59(Suppl 20):22-33, with permission from the authors.
**Tools to Assist in Diagnosing and Assessing the Impact of Depression**

A Helpful Mnemonic to Remember the Key Signs and Symptoms of Depression

<table>
<thead>
<tr>
<th>SIG-E-CAPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>S- Sleep disturbance</td>
</tr>
<tr>
<td>I- Loss of interest</td>
</tr>
<tr>
<td>G- Guilt out of proportion</td>
</tr>
<tr>
<td>E- Loss of energy</td>
</tr>
<tr>
<td>C- Concentration difficulties</td>
</tr>
<tr>
<td>A- Loss of appetite</td>
</tr>
<tr>
<td>P- Psychomotor retardation or agitation</td>
</tr>
<tr>
<td>S- Suicidal ideation</td>
</tr>
</tbody>
</table>

**Montgomery-Åsberg Depression Rating Scale (MADRS)**

Measures the effect of treatment on depression severity, on a continuously graded scale from 0 to 6, with 0 indicating normal or near-normal, and 6 indicating severely affected. Symptoms included within the assessment are:

- Apparent sadness
- Reported sadness
- Inner tension
- Reduced sleep
- Reduced appetite
- Concentration difficulties
- Lassitude
- Inability to feel
- Pessimistic thoughts
- Suicidal thoughts
Each symptom is rated according to the degree to which it is present.

Goals of treatment according to MADRS

- < 14 response
- < 10 remission

Hamilton Rating Scale for Depression (HAM-D)

Rating scale used widely by clinicians and in clinical research to assess 17 factors related to depression

- Psychological anxiety
- Somatic anxiety
- Loss of insight
- Depressed mood
- Work and interests
- Insomnia early
- Insomnia middle
- Insomnia late
- Loss of libido
- Agitation
- Hypochondriasis
- Psychomotor retardation
- Suicide
- Guilt
- Somatic symptoms
- Weight loss
- Gastrointestinal symptoms

Higher scores indicate more severe depression.

Goals of treatment according to HAM-D

- \( \leq 12 \) response
- \( \leq 7 \) remission


Clinical Global Impression – Improvement (CGI-I)

CGI-I requires the clinician to rate how much the patient’s illness has improved or worsened relative to a baseline state. It compares the condition of the patient’s illness at baseline to the condition of the patient’s illness at the time of the evaluation, and is rated from 1 to 7.

<table>
<thead>
<tr>
<th></th>
<th>Very Much Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Much Improved</td>
</tr>
<tr>
<td>3</td>
<td>A Little Improved</td>
</tr>
<tr>
<td>4</td>
<td>No Change</td>
</tr>
<tr>
<td>5</td>
<td>A Little Worse</td>
</tr>
<tr>
<td>6</td>
<td>Much Worse</td>
</tr>
<tr>
<td>7</td>
<td>Very Much Worse</td>
</tr>
</tbody>
</table>
In using the CGI-I to assess a patient’s current clinical state, the goal should always be to achieve a score of 1. Scores of greater than 1 should prompt a re-evaluation and/or a potential change to the patient’s current therapeutic regimen.

### Treatment of Comorbid MDD

#### Selective Serotonin Reuptake Inhibitors (SSRIs)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>20–40 mg daily</td>
</tr>
<tr>
<td>Escitalopram oxalate</td>
<td>10–20 mg daily</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20–80 mg daily; 90 mg weekly</td>
</tr>
<tr>
<td>Fluvoxamine maleate</td>
<td>50–300 mg daily in divided doses</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>20–50 mg daily; 25–62.5 mg daily of CR product</td>
</tr>
<tr>
<td>Sertraline</td>
<td>50–200 mg daily</td>
</tr>
</tbody>
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#### Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine</td>
<td>40–60 mg daily</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75–225 mg daily in divided doses</td>
</tr>
<tr>
<td>Venlafaxine XR</td>
<td>75–225 mg daily</td>
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</table>

#### Other Agents

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>200–450 mg daily in divided doses</td>
</tr>
<tr>
<td>Bupropion SR</td>
<td>150–400 mg daily in divided doses</td>
</tr>
<tr>
<td>Bupropion XL</td>
<td>150–450 mg daily</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>15–45 mg daily</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>300–600 mg daily in divided doses</td>
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**NOTES**

*For better tolerability, patients should initially be started on the lowest dose of the antidepressant, and titrated slowly at weekly intervals to an optimal therapeutic response.*

*Geriatric patients may require a dose adjustment due to increased sensitivity to the effects of antidepressants.*
Because of adverse effects and drug interactions, tricyclic antidepressants and monoamine oxidase inhibitors are generally not recommended as first- or secondline therapy in patients with comorbid medical illness.

St. John’s Wort (Hypericum perforatum) has not been demonstrated to be effective for the treatment of major depression and is not approved for this use.
Initiating Treatment and Assessing Response

Educate and discuss disease state and preconceived notions regarding depression.

Administer MADRS or HAM-D:

a. If MADRS ≥ 22 or antidepressant therapy
b. Many patients may benefit from psychotherapy

Advise patient that antidepressant therapy may take 4-6 weeks to deliver meaningful response.

Provide patient follow-up:

a. At week 2 to assess adherence
b. At week 4 to assess drug effectiveness

If patient is clearly improved, with the goal of:

If patient is only partially improved:

a. First consider titrating dose,
b. Consider adding psychotherapy

If patient is not improved at all after 8 weeks of therapy, consider changing to another antidepressant:

a. Consider augmentation
b. Consider psychiatric referral

MONITOR THROUGHOUT FOR TREATMENT-EMERGENT SUICIDALITY OR MANIC/HYPOMANIC SYMPTOMS

GOAL OF TREATMENT SHOULD ALWAYS BE REMISSION
References for Further Information

National Institute of Mental Health
www.nihm.nih.gov

National Alliance on Mental Illness
www.nami.org

American Psychiatric Association
www.psych.org


