Outcomes and Cost Effectiveness of Collaborative Care Disease Management Approach in Depression Patients

Roueen Rafeyan, MD
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Summary
There are many reasons why it is important for managed care systems to ensure adequate treatment of depression in their patients. The best chance for achieving and maintaining remission of symptoms occurs when the patient is treated early in the disease process with combination therapy and has complicating comorbid conditions adequately treated. Because the majority of depression is treated in the primary care setting, managed care should consider implementing some type of integration of behavioral health into primary care to improve the outcomes and cost effectiveness of depression treatment.

Key Points
• The impact of major depression on patients, families, and society can be devastating.
• Depression is frequently associated with and may negatively impact medical disorders.
• Depression may result in structural and functional changes in the brain.
• Comorbid anxiety, substance abuse, and chronic pain can complicate treatment of depression and must be addressed.
• Integration of behavioral health into primary care management can improve outcomes and reduce overall costs.

IN ANY GIVEN YEAR, 19 MILLION AMERICAN adults, 9.5 percent of the population in the United States, suffer from depressive disorders. The incidence rate of depression among the general population is 17 to 24 percent. In females, the incidence rate is closer to 24 percent. The average age of onset 50 years ago was 29 but today is 14.5 years.

There is an urgency to treat this disease for several reasons. When untreated, this may be a fatal disease. Those suffering from major depression may experience suicide rates of 10 to 15 percent.

Depression is the leading cause of disability in the U.S. By 2020, it is projected that depression will be the leading cause of disability worldwide. Depression leads to lowered work productivity. Presenteeism, low performance while at work transformed to lost workday equivalents, is a major issue for employers. Thirty to 67 percent of the workplace costs of depression are related to presenteeism. Physicians should ask their patients about work functioning to determine treatment efficacy.

Absenteeism related to depression is also a major employer issue. Patients with painful physical symptoms of depression miss an average of 9.4 days per month, while patients with depression but not pain miss 4.5 days of work. Depression also affects families. As shown in the STAR*D trial, remission of a mother’s depression has a positive impact on both mothers and their children (Exhibit 1). Unsuccessful treatment of a mother’s depression can lead to depression, anxiety, and behavior issues in her children. Depression has a significant effect on health scores, especially when the patient has another chronic disease. The most impact on health scores is seen with the combination of diabetes and depression. It is very difficult to control diabetes and other chronic diseases in the depressed patient.

There is also a relationship between depression and stroke. Depression increases the risk of stroke significantly. It also increases the risk of stroke mortality. Patients with five or more depressive symptoms at baseline had increased risk of stroke mortality. Stroke patients have an increased risk of developing depression. Post-stroke depression independently
increases risk of death by 13 percent.\textsuperscript{9}

There are similar findings in a relationship between depression and cardiovascular disease. The prevalence of depression is increased between 15 and 25 percent in coronary artery disease, acute myocardial infarction (MI), angina, and heart failure.\textsuperscript{10} Depressed patients have an increased risk for MI, cardiac death, and mortality from all causes.\textsuperscript{11} Depression post-MI is associated with a fourfold increase in risk of mortality in the six months after the MI.\textsuperscript{12}

Another urgent reason to treat depression is that repeated episodes of depression are associated with functional and structural changes in the brain.\textsuperscript{13} Aggressive, early, and sustained treatment might prevent the disease from becoming chronic with eventual neuronal damage and chronic progressive neurodegenerative disease.\textsuperscript{14} The first few episodes of depression in an individual may be caused by psychosocial stressors – loss of job, spouse, etc (Exhibit 2).\textsuperscript{15} After three episodes, the patient has greater than a 90 percent chance of another relapse. After about the fifth or sixth episode, depressive episodes continue without psychosocial stress. It appears that this is due to changes in the brain with atrophy in certain areas.

Treatment for depression includes biological inter-
ventions (antidepressants), psychological interventions (psychotherapy), and social interventions. Social interventions help the patient get out of problem social situations such as an abusive marriage. The biopsychosocial approach, which combines all of these interventions, is the most effective.

The goal of depression treatment is to achieve remission (no symptoms) and keep the patient in remission. Patients who reach remission have functional ability equivalent to those without depression. Those who only respond to treatment (~50 percent reduction in symptoms) are as functionally impaired as those who do not respond to treatment.

Unfortunately, many patients receive inadequate treatment. Some studies have shown that about 50 percent of patients with major depression receive some type of treatment but only 22 percent receive adequate treatment.16

The best rate of recovery for depression patients is during the first six months of symptoms.17 After that, it becomes more difficult for patients to recover.

Clinicians may think their patients are responding well to medications but without the use of validated tools like the Hamilton Depression scale, it may be impossible to tell if the patient has achieved remission.

Different depression symptoms respond differently to medications. Emotional symptoms tend to improve more than physical symptoms, especially pain. Improving painful symptoms greater than 50 percent increases the likelihood of remission. Additionally, the fewer symptoms a patient has remaining after treatment, the longer the time till relapse (231 weeks versus 68 weeks).18

The STAR*D trial examined the effectiveness of various antidepressants in achieving remission. Forty-three percent of the study sites in this trial were in primary care. This trial used a stepped approach. The remission rates and the regimens at each step are shown in Exhibit 3.19 This trial illustrates that the remission rate declines with each additional step in therapy. Unfortunately, only about one-fourth of patients will achieve remission with the first treatment chosen.

Noncompliance is an important reason for suboptimal treatment outcomes. Seventy-five percent of antidepressants are discontinued by month four. Patients frequently report that the medication was not

### Exhibit 3: STAR*D Trial Results19

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<thead>
<tr>
<th>Step</th>
<th>Regimens</th>
<th>Remission Rates</th>
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<tbody>
<tr>
<td>Step 1</td>
<td>Citalopram 40 mg/day</td>
<td>25.4%</td>
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<tr>
<td>Step 2</td>
<td>Switch to either Bupropion SR, Sertraline, Venlafaxine XR, Cognitive behavioral therapy (CT), CT + Citalopram, Citalopram + Bupropion SR, or Citalopram + Buspirone</td>
<td>25.1%</td>
</tr>
<tr>
<td>Step 3</td>
<td>Switch to either Mitrazepine, Nortriptyline, Lithium + Bupropion SR, Sertraline, Venlafaxine XR, or Citalopram</td>
<td>17.8%</td>
</tr>
<tr>
<td>Step 4</td>
<td>Switch to Tranylcypromine or Mitrazepine + Venlafaxine XR</td>
<td>10.1%</td>
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### Exhibit 4: Interventions to Reduce Noncompliance

- Educate patients regarding the disease and treatment options.
- Discuss common side effects of the antidepressant medication openly with patients.
- Reassure patients that other medication options will be explored in case of side effects.
- Emphasize that these medications need to be taken on a daily basis to be effective.
- Reassure patients that antidepressant medications are not addicting and they do not cause end-organ damage.
- Share with patients that continued treatment with medication has a neuro-protective effect.
effective after a week, made them feel worse, or they stopped because they felt better. Some interventions to reduce noncompliance are shown in Exhibit 4.

Management of patients who are not responding to treatment includes reconsidering the diagnosis and referring the patient to a psychiatrist. It may require case management, involving pharmacists to monitor medication compliance, and more aggressive pharmacotherapy.

One option for more aggressive therapy is to add a second-generation antipsychotic agent to target dopamine, which is not targeted by most antidepressants. The second-generation antipsychotics which are FDA approved for add-on therapy in depression are aripiprazole, olanzapine in combination with fluoxetine, and quetiapine. Adding these agents can lead to a quick improvement in depression scores.

Depression has a high comorbidity with many conditions such as anxiety disorders which can complicate treatment. High anxiety levels are associated with higher suicide risk and reduced remission rates. Patients with high levels of anxiety frequently utilize medical services. Anxiety needs to be addressed with aggressive treatment. Short-term use of benzodiazepines, along with antidepressant medication, is recommended for these patients. Patients can be referred for individual therapy; cognitive behavioral therapy (CBT) is most effective in the setting of co-morbid anxiety.

Although frequently missed in clinical interviews, substance abuse and dependence significantly impacts the effectiveness of depression treatment. Some type of substance abuse screening should occur in all patients with depression and those who are positive should be referred for treatment of their substance issues. These patients need to be educated that treating depression and anxiety in the presence of active drug or alcohol abuse is minimally effective and at times dangerous. Clinicians need to avoid getting frustrated with patients who have repeated substance abuse relapses. Addiction is a chronic disease and requires lifelong treatment.

Pain is yet another complicating factor. Chronic pain frequently results in depression and exacerbates existing depression. Depressive symptoms lower pain threshold and result in exaggerated pain response. Improvement of pain symptoms increases the odds for remission. Aggressive treatment of depressive symptoms will allow for better pain management and reduce utilization of medical services. Tricyclic and serotonin norepinephrine reuptake inhibitor (SNRIs) antidepressants are most effective for these patients. Because of their safety and tolerability profile, the SNRIs are preferred.

Optimizing outcomes in depression requires examining how mental health care is currently delivered. Seventy percent of all primary care visits have psychosocial drivers. Fifty percent of all mental health care services are delivered by a primary care provider (PCP). Sixty-seven percent of all psychoactive agents and eighty percent of antidepressants are prescribed by PCPs. Mental health outcomes in primary care treated patients are currently only slightly better than spontaneous recovery.

One way to improve the delivery of mental health care is to integrate primary care and behavioral health practices. There are numerous benefits of integration. Some of the benefits include improved recognition of mental health disorders, improved PCP skills in medication prescription practices, and

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<th>Model</th>
<th>Desirability</th>
<th>Attributes</th>
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<tbody>
<tr>
<td>Separate Space and Mission</td>
<td>-</td>
<td>Traditional BH Specialty Model</td>
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<tr>
<td>1.1 Referral Relationship</td>
<td>+</td>
<td>Preferred provider/ limited information exchange</td>
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<td>Co-location</td>
<td>++</td>
<td>On-Site BH Unit/ Separate Team</td>
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<td>Collaborative Care</td>
<td>+++</td>
<td>On site/shared cases w/BH Specialist</td>
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<td>Integrated Care</td>
<td>+++</td>
<td>BHC as PC Team Member</td>
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increased use of behavioral interventions by PCPs. Integration has been shown to improve depression remission rates, self-management skills for patients with chronic conditions, clinical outcomes compared with treatment in either sector alone, and patient adherence and retention in treatment.

Initially, integrating behavioral health increases costs but overall results in reduced costs. Integration adds $264.00 per case of depression treated in primary care. The treatment success rate and overall patient adherence to treatment doubles with this expenditure. The result of integration is a positive cost-effectiveness index of $491.00 per case of depression treated.20

Integration can occur on a continuum (Exhibit 5). The most desirable is to have a behavioral health clinician as part of the primary care team.

The hallmarks of a successful primary care behavioral health service include timely access for PCPs, behavioral health care by all PCPs, the use of behavioral health interventions more frequently by PCPs, and the service is provided as part of the health care process. The behavioral health service should be viewed as a form of primary care delivered to all appropriate patients.

Conclusion
Depression has a major impact on patients, families, employers, managed care, and society. Effective management to achieve remission and prevent long-term brain changes requires a biopsychosocial approach and addressing complicating comorbidities. When seeking to improve depression outcomes in their patient population, managed care should consider integration of behavioral health services into primary care delivery. JMCM

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References