Bipolar Disorder: Developing a Cost Effective Management Program

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Summary
Bipolar disorder affects a significant number of people and is frequently missed by primary care providers. Patients may go years without proper treatment, which has significant impact on their ability to function in society and earn a living. Once identified, bipolar disorder is expensive to manage. Cost effective management should include early identification, use of evidence based therapy, and nonpharmacologic interventions such as psychotherapy and occupational rehabilitation.

Key Points
- Bipolar disorder is one of the most expensive behavioral health diagnoses for both individuals and their insurance providers.
- Sixth leading cause of disability.
- Bipolar disorder is frequently missed by primary care providers.
- Management requires a combination approach of medications and psychotherapy.
- Polypharmacy may be necessary to manage manic, depressive, and other symptoms.

BIPOLAR DISORDER (BPD) IS A BRAIN disorder spectrum characterized by extreme shifts in mood, energy, and functioning. This spectrum includes Bipolar I, Bipolar II and cyclothymia. In Bipolar I, the patient has had at least one manic or mixed episode. Sixty percent of patients with bipolar I will have concomitant substance abuse. They use alcohol or other substances to manage mood. With Bipolar II, the patient has had one or more depressive episodes and at least one hypo-manic episode. The hypo-manic episode may not be recognized by the patient or health care provider leading to a misdiagnosis of major depressive disorder. Symptoms of this BPD usually emerge in late adolescence or early adulthood. In cyclothymia, symptoms are milder, with a history of hypomanic episodes and periods of depression that do not meet the criteria for major depressive episodes. Exhibit 1 compares the two main types, Bipolar I and Bipolar II.

This severe and recurrent condition affects nearly two percent of the U.S. population. Thus, more than 2 million American adults are affected by BPD. In order to predict expenses, managed care groups should determine the incidence of BPD in their covered populations. For example, Medicaid populations have much higher percentages of patients with BPD because of high unemployment rates among these patients.

BPD is the most expensive behavioral health diagnosis for both individuals and their insurance providers. The total lifetime costs for patients with BPD have been estimated at $24 to $45 billion. Hospitalization is a significant portion of the direct costs

Exhibit 1: BPD: Types I and II

Bipolar I
- Diagnosis includes mania
- 40% of patients experience mixed states (mania and major depression)
- 60% of patients experience co-morbid substance abuse

Bipolar II
- Female to male ratio is 2:1
- Recurrent hypomania and major depression
- Higher rate of suicide attempts
- Diagnostic challenges
  Hypomania often not experienced as “abnormal”
  Prior hypomania often underreported
of this disease. Seventy five percent of BPD patients are hospitalized at least once. Outpatient treatment, prescription and treatment costs, and non-medical support costs account for the rest of the direct costs. Exhibit 2 illustrates the differences in direct costs between patients with BPD and the general medical outpatient. Overall, patients with BPD had twice as high costs. Of note, the BPD group had much higher emergency room visits. This may be because of running out of medications. Cost differences are also seen between BPD and other psychiatric disorders (Exhibit 3).

Lost productivity is the largest portion of indirect costs related to BPD. The unemployment rate among patients with BPD is very high. If these patients do have a job, work-related absenteeism and other occupational difficulties are common. Compared with people without BPD, these patients have a sevenfold increased likelihood of missing work.

BPD is ranked as the sixth leading cause of disability worldwide. Between 30 and 60 percent of persons with BPD do not regain full social or occupational functioning after the onset of illness. Six months after hospitalization for a manic episode, 43 percent of people are still unemployed, although many have mild to no symptoms. This would suggest that cost effective management of people with BPD should include some type of occupational rehabilitation.

Another significant indirect cost of BPD is the premature death. Up to 15 percent of individuals with BPD eventually commit suicide.

Inadequate or inappropriate treatment is likely to increase BPD cost of care and has a negative economic impact on the patient. Persons with BPD

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**Exhibit 2: Health Plan Treatment Costs: BPD vs. General Medical Outpatients**

<table>
<thead>
<tr>
<th></th>
<th>BPD (n=1346)</th>
<th>General Medical Outpatients (n=1346)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpt Mental Health</td>
<td>$3,430</td>
<td>$1,264</td>
</tr>
<tr>
<td>Inpt Mental Health</td>
<td>$1,038</td>
<td></td>
</tr>
<tr>
<td>Psych Rx</td>
<td>$3,227</td>
<td>$2,930</td>
</tr>
<tr>
<td>Prim Care Visits</td>
<td>$2,410</td>
<td></td>
</tr>
<tr>
<td>Other Spec Visits</td>
<td>$2,177</td>
<td></td>
</tr>
<tr>
<td>ER Visits</td>
<td>$2,177</td>
<td></td>
</tr>
<tr>
<td>Outpt Radiol/Labs</td>
<td>$2,177</td>
<td></td>
</tr>
<tr>
<td>Other Rx</td>
<td>$2,177</td>
<td></td>
</tr>
<tr>
<td>Other Svcs</td>
<td>$2,177</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$3,346</td>
<td>$1,462</td>
</tr>
</tbody>
</table>

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**Exhibit 3: Medicaid HMO Study**

<table>
<thead>
<tr>
<th>Any Psychiatric Disorder</th>
<th>Carve-Out Costs</th>
<th>Drug Costs</th>
<th>Medical Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>$3,430</td>
<td>$1,264</td>
<td>$1,038</td>
<td></td>
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<tr>
<td>$3,227</td>
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<td>$2,177</td>
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<td>$2,177</td>
<td></td>
</tr>
</tbody>
</table>
usually see several physicians and spend, on average, more than eight years seeking treatment before receiving a correct diagnosis.\(^9\)

Misdiagnosis occurs because primary care physicians (PCP) are not always knowledgeable about or comfortable managing patients with BPD.\(^10\) Because patients do not always acknowledge prior episodes of mania, it can be difficult for a PCP to distinguish major depression from BPD. In one survey, 41 percent of PCPs did not screen patients with major depression for BPD.\(^10\) Targeting PCPs knowledge on BPD is one way managed care can improve treatment for their covered populations. Ninety four percent of PCPs in this survey said they would use a brief BPD screening instrument if it were available.\(^10\)

BPD is managed with various pharmacologic therapies, psychotherapy, and behavioral therapies. Management requires both acute and chronic management and may require agents for both manic and depressive symptoms. The various pharmacologic therapies used for acute mania management are outlined in Exhibit 4. Lithium is most commonly used to manage acute mania. Anticonvulsants such as carbamazepine, valproic acid, and lamotrigine are slightly less effective alternatives for managing acute mania. These agents are more effective in patients who rapidly cycle between mania and depression. Atypical antipsychotics at low doses are also used for managing mania. The new generation atypical antipsychotics offer tolerability benefits over conventional antipsychotics. Compared with 1st-generation antipsychotics, 2nd generation antipsychotics improve medication-adherence behavior, quality of life, and subjective tolerability.\(^11,12\)

Typical antidepressants are used to manage acute depression but can increase cycling between depression and mania in BPD. Other agents are sometimes used to manage depressive episodes. Some which have been studied are quetiapine, olanzapine/fluoxetine combination, and lamotrigine.\(^13-14\) Exhibit 5 compares the efficacy of the various agents for the treatment of BPD.\(^15\)

After diagnosis, management of BPD often falls short of treatment guidelines. In an analysis of hospitalized persons with BPD, five in six were discharged from hospital with medications inconsistent with national treatment guidelines. In a study of outpatients with BPD, one third were not receiving mood stabilizers. In a Med-Cal analysis of persons diagnosed with BPD, 58 percent did not receive a mood stabilizer in the first year after diagnosis. Direct health care costs were significantly higher for those who did not use mood-stabilizing agents during that first year.\(^9\)

There are many challenges in managing mania. Some of these include medication tolerability, poor acceptance of treatment or insight into illness, transition between treatment setting (inpatient vs. outpatient), management of other symptoms such as agitation and insomnia, transition to longer-term treatment, and adherence.

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**Exhibit 4: Pharmacologic Strategies: BPD Management**

**Mood stabilizers for treatment of BPD manic episodes**
- Lithium
- Anticonvulsants such as valproic acid, carbamazepine, and lamotrigine

**Atypical antipsychotics for BPD acute manic episodes**
- Aripiprazole
- Ziprasidone
- Quetiapine
- Olanzapine
- Risperidone

**For treatment of BPD depressive episodes**
- Quetiapine
- Olanzapine/Fluoxetine Combination
- Lamotrigine

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**Exhibit 5: Bipolar Disorder: Summary of Efficacy Evidence from Recent Clinical Trials\(^15\)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mania Monotherapy</th>
<th>Mania Combination Therapy</th>
<th>Depression</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium (Li)</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Divalproex (DVPX)</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Carbamazepine (CBZ)</td>
<td>++</td>
<td>ND</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Lamotrigine (LTG)</td>
<td>ND</td>
<td>+</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Olanzapine (OLZ)</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Risperidone (RIS)</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>ND</td>
</tr>
<tr>
<td>Quetiapine (QTP)</td>
<td>++</td>
<td>+/-</td>
<td>HD</td>
<td>ND</td>
</tr>
<tr>
<td>Ziprasidone (ZIP)</td>
<td>++</td>
<td>+/-</td>
<td></td>
<td>ND</td>
</tr>
<tr>
<td>Aripiprazole (ARP)</td>
<td>ND</td>
<td>ND</td>
<td></td>
<td>++</td>
</tr>
</tbody>
</table>

* = number of adequately powered, randomized, controlled trials
+/-. = number of equivocal, randomized, controlled trials
ND = no data
Adherence to maintenance treatment is important to maintaining a stable mood in BPD. Some of the factors known to influence adversely affect adherence with BPD therapy include younger age, single marital status, male gender, lower educational level, hypo–manic denial, psychosis, co–morbidity substance abuse, medication adverse effects, and unfavorable personal attitudes towards treatment. There are several methods for assessing adherence with BPD therapy (Exhibit 6). Combinations of methods have most commonly been used in studies.

Nonadherence can be intentional or unintentional. Patients can overuse medications in a misguided attempt at speeding recovery or because they misunderstand the directions. Underuse can also occur because of forgetfulness, misunderstanding directions, stretching supply due to costs, and adverse effects.

Psychotherapy can be combined with medication to maintain the patient. Randomized trials showed the value of structured forms of psychotherapy as adjuncts to mood stabilizers. These structured forms include cognitive–behavioral therapy, interpersonal and social rhythm therapy, family–focused therapy, and group psychoeducation. Combining psychotherapy with medication maintenance can delay recurrences, stabilize symptoms, and improve medication adherence. Exhibit 7 summarizes the interventions that can improve medication adherence. Specific adherence strategies include once–daily dosing if possible, use of adherence–enhancing aids (e.g., weekly pill boxes, daily mood charting), asking family members to supervise medication use, monitoring medication blood levels closely, and using depot antipsychotics if appropriate in treatment regimen. Besides medication adherence, optimizing treatment of BPD requires the use of medications with broad spectrum of efficacy as these may be effective for treatment of comorbid disorders. Polypharmacy may be required to manage symptoms. Sleep disturbances, anxiety/psychosocial stressors, and comorbid conditions can destabilize mood and need to be managed appropriately. Educate of the patient and their significant others is important to long term mood control. The course of this illness may change over time so patients need to be continuously monitored.

Conclusion
Optimizing outcomes in patients with BPD requires selection of agents known to be efficacious for BPD as a primary therapeutic agent. Polypharmacy may be necessary, but should be supported by evidence–based guidelines. Treatments should be customized based upon prior response, patient preference, comorbidities, and co–prescribed medications. Medication adherence has to be monitored on a continuous basis.

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References
8. American Psychiatric Association. Practice guideline for the treatment of pa-