Chapter 4: Collaborative Care for Bipolar Disorder and PTSD

Introduction

The majority of patients in this study will have clinically significant depressive symptoms evidenced by a PHQ-9 score of 10 or more. Patients will then be assessed for bipolar disorder using the CIDI measure and for PTSD using the PCL-5. Following the initial assessment by the care manager, patients then will have a telepsychiatry diagnostic assessment by a psychiatrist. Patients will differ in their prior histories of bipolar disorder or PTSD, their treatment histories, their current treatments, their history of trauma, and in the extent of their medical and psychiatric comorbidities. Some patients will already be on active treatments (e.g., lithium or antipsychotics for patients with bipolar disorder, antidepressants for PTSD). Others may be receiving treatments of limited benefit (e.g., monotherapy with an antidepressant for bipolar patients, or benzodiazepines or other minor tranquilizers). Others may have had counseling but still meet criteria for current bipolar depression or PTSD. Some patients may have a long history of illness while others may be experiencing their first episode. Some patients will have significant co-occurring medical or psychiatric disorders such as panic disorder, substance use disorders, or chronic pain. Treatment with mood stabilizing medications or antipsychotic medications should occur in almost all patients with bipolar depression, whereas behavioral interventions are of benefit for all patients and may be especially important for patients with PTSD. Individuals with bipolar disorder who receive psychotherapy in addition to medications have better outcomes than those who receive medications alone (Miklowitz DJ et al. Psychosocial treatments for bipolar depression: a 1-year randomized trial from the Systematic Treatment Enhancement Program. Arch Gen Psychiatry 64: 419–426, 2007.) However, some patients have strong preferences for medications or behavioral interventions, and such treatment preferences should be incorporated in treatment planning whenever possible, for example, by combining behavioral interventions and medication treatments together.

Because of variation in each patient’s history and clinical circumstances, it is not possible to specify a treatment algorithm that will be a perfect fit for each patient. The treatment guidelines outlined in the next few pages provide general guidelines for treating patients with bipolar disorder and/or PTSD in primary care. Within these guidelines, the treatment team will have to use clinical judgment to ensure each patient has a treatment plan that is best suited for his or her clinical circumstances.

These guidelines are based on consensus statements and treatment guidelines for bipolar depression and for PTSD, and based on detailed discussions with key stakeholders including primary care physicians, psychiatrists, and patients with bipolar disorder from Federally Qualified Health Centers.

- Treatment recommendations by a consensus panel convened by the Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) (Bipolar Disorders 2009), and the British Association for Psychopharmacology (J Psychopharmacology 2009)
- Treatment Guidelines for Bipolar Disorder by the American Psychiatric Association
- International Psychopharmacology Algorithm Project (ipap.org)
- Institute of Medicine reports: Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment. Released June 20, 2014.

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The recommendations from these stakeholder interviews, consensus statements, and guidelines were adapted for the treatment of primary care patients with bipolar disorder by the study investigators.

The ultimate goals of treatment are **clinically significant reduction in symptoms** and **full return of psychosocial functioning** and **prevention of relapse and recurrence** of symptoms, although for some patients complete remission of symptoms is not possible and it is necessary to determine at what point the patient no longer benefits from additional adjustments to the treatment regimen. Recovery from PTSD is generally thought to be unlikely as long as the patient continues to experience the trauma (e.g., ongoing abuse in a relationship); however, an intervention to provide a safe environment is important. The effectiveness of psychotropic medications for treating PTSD symptoms for patients who remain in abusive or dangerous circumstances is uncertain.
Figure 4.1 Overview of the Collaborative Care Treatment Approach

Step 1: Engagement
- Introduce and Educate Patient on Collaborative Care

Step 2: Assessment and Treatment Planning
- Care Manager Assesses Patient
- Telepsychiatrist Assesses Patient
- Develop $T_x$ Plan
- Patient Willing To Initiate $T_x$ (Pharmacotherapy and/or Behavioral Activation) *

Step 3: Treatment to Target
- Initiate $T_x$
- Adjust $T_x$ or Consider Referral for Specialty Care
- Patient Optimally Responding to $T_x$?
  - No
    - Case Review: Will Patient Benefit From Further $T_x$ Adjustment?
      - Yes
      - No

Step 4: Maintenance and Relapse Prevention
- Develop Maintenance Plan
- Develop Relapse Prevention Plan

Note: *All bipolar patients should have pharmacotherapy. Those who decline medication may have BA, but should proceed to ‘Engagement’ steps until ready to initiate pharmacotherapy.
Options for Treatment of Bipolar Disorder and PTSD in Primary Care
In general, active treatment is recommended unless the patient is unwilling to take medications or participate in behavioral interventions.

Watchful Waiting
In some situations, active treatment may not be initiated immediately, in which case, watchful waiting (with self-management and symptom monitoring) is recommended. If the patient is not willing to enter active treatment, the CM will conduct symptom monitoring and self-management support and use motivational interviewing to enhance engagement every two weeks, re-assessing readiness to engage in active treatment. Once the patient is willing to enter active treatment, it is recommended that the patient initiate active treatment.

Treatment Considerations
Treatment is generally initiated in the primary care clinic in collaboration with the patient’s PCP. For some patients, this will be their first treatment episode, whereas other patients may have prior treatment trials or may have recently started on medications by their primary care provider. The first choice to be made is whether to offer medication, behavioral activation or both. Mood stabilizing medications are recommended for all patients with bipolar disorder including those who are euthymic because maintenance medications can prevent recurrence. As such, behavioral activation alone without medication is not a preferred treatment plan for patients with bipolar disorder and should be avoided whenever possible.

Initial Treatment Choice for Patients with Bipolar Disorder
Patients with bipolar disorder should consider use of a bipolar maintenance medication such as those listed in Table 6.1 in Chapter 6. Patients should be asked about current maintenance medication treatments and doses they are taking for bipolar disorder. Behavioral Activation can be combined with medications as part of the initial treatment plan or, if not initially used, can be added subsequently.

Patients with bipolar disorder not currently receiving maintenance treatment
Patients who are not currently receiving maintenance treatment should begin treatment with the PCP reviewing the mood stabilizing medication options in Table 6.1 (Chapter 6) with patients, and select a medicine consistent with the patient’s prior experiences and current treatment goals. Patients who have previously responded to one of these medications and are not currently taking that medication might consider restarting on the previously beneficial medication. Patients who have previously failed or not tolerated an adequate trial of one of these medications should consider an alternative medication.

Patients with bipolar disorder currently receiving maintenance treatment
Maintenance treatment may differ from treatment of acute bipolar depression in some patients. However, in many patients, intensification of maintenance treatment may be the first step in treating a bipolar depressive episode. For example, a patient with bipolar disorder treated with lithium may have a maintenance dose resulting in a serum lithium level of 0.6mEq/L – a first step in treating bipolar depression may be to increase the lithium dose to reach a serum level of 1.0 mEq/L. Prior response to mood stabilizing medications and antipsychotic medications should be assessed. Increasing maintenance medications within the limits in the Psychotropic Medication Table (chapter 6, table 6.1) can be the first step in intensifying treatment for an acute episode of bipolar depression.
**Initial Treatment Choice for Patients with PTSD**

Both psychotropic medication and Behavioral Activation are efficacious for PTSD. Behavioral activation if not used initially can be added to or can replace pharmacotherapy if the initial treatment targets are not met (International Psychopharmacology Algorithm Project [IPAP] *Post-traumatic stress disorder (PTSD) algorithm notes (2005)*, page 11. retrieved from ipap.org/ptsd/). Patients who have a preference for behavioral interventions may be started on Behavioral Activation as their initial treatment.

For patients with PTSD, the initial medication choice is often an antidepressant medication, *usually a selective serotonin reuptake inhibitor (SSRI)* (see Chapter 6). Patients who have previously responded to an antidepressant from a different class should be restarted on the previous antidepressant whenever possible. Patients who have previously failed or not tolerated an adequate trial of an SSRI will be considered for an alternative antidepressant (see below). For patients with comorbid PTSD and bipolar disorder, the choice of psychotropic medications will differ, as most patients with bipolar disorder should receive a mood stabilizing medication (see above and *Antidepressant use in Bipolar Depression*, page 7).

Antidepressants should be started at low doses and titrated to a therapeutic dose over a period of 4-6 weeks. See table 6.1 (Chapter 6) for recommended titration schedules. If patients cannot tolerate a particular treatment (i.e., intolerable side effects even with careful titration and clinical management), consider switching to an alternative antidepressant or Behavioral Activation after 2-4 weeks. Strategies for managing common side effects of antidepressants are outlined in Chapter 6.

Patients with severe sleep disturbance or nightmares may be offered prazosin, an alpha-1-adrenergic antagonist (see table 6.1 for dosing) or for sleep disturbance without nightmares, a low dose of trazodone, a sedating antidepressant medication (e.g, 25-50mg QHS).

**Evaluating treatment response**

An adequate trial of treatment will depend on the initial treatment selected. For Behavioral Activation, the trial would consist of at least 6-8 sessions.

An adequate trial of medication for *bipolar disorder* means that patients have completed a four-week trial at sufficient dose (see Table 6.1 in Chapter 6). Initial response to medications used to treat bipolar depression usually occurs within four weeks. If there is *no response* to treatment after 4-6 weeks of treatment at a therapeutic dose, an alternative plan should be initiated. If there is a *partial response* by weeks 4-6, a continued trial (8-10 weeks) of the medication at a full therapeutic dose is recommended.

An adequate trial of medication for PTSD may take 12 weeks, however, adjustments or changes to treatment may be indicated sooner. If a patient has *no improvement* after 4-6 weeks on a therapeutic dose, an alternate treatment should be initiated. If a patient has a partial response by weeks 4-6, a full trial (12 weeks) of the antidepressant at a full therapeutic dose is recommended.
- Patients who have had a full response to initial treatment (see Chapter 3 for definition of response) should proceed to relapse prevention planning (see Maintenance and Relapse Prevention Planning below) and maintenance treatment.
- Patients who do not have a full response to initial treatment should be discussed in the weekly caseload consultation with the consulting psychiatrist. At this time, the consulting psychiatrist may make a recommendation for an alternate treatment plan or see the patient for a telemedicine psychiatric consultation visit.

**Patients with sub-optimal response to initial treatment**
For patients who have had insufficient benefit on an initial treatment course, evaluate and assess new treatment courses, which may include:

- Increasing the dose of psychotropic agents to maximum dose and measure serum level if indicated, such as with lithium therapy.
- Replacing one (or more, if applicable) medications with alternate medications not currently used by the patient.
- Combination of psychotropic medication and Behavioral Activation
- Re-assessing concurrent substance use and treat substance use disorder if present
- Consider augmenting treatment (see below).
- Consider referral to specialty mental health care, particularly for patients who have failed at least two psychotropic medication trials and BA, or for:
  - Psychosis
  - Significant worsening and/or non-response despite three steps of treatment
  - Treatment during pregnancy
  - Specialized treatments for comorbid psychiatric disorders (for example, severe mood or anxiety disorders, substance use disorders, personality disorders). Such specialized treatments may include specialized psychotherapy (cognitive behavioral therapy, dialectical behavior therapy, etc.), or specialty substance abuse treatment such as a residential treatment program
  - Other types of evidence-based psychotherapies for PTSD not available in primary care such as cognitive processing therapy or prolonged exposure

Patients who have failed an adequate trial of a first-line medication should be considered for a trial of a different medication. The choice of the second agent may vary depending on the clinical circumstances (psychiatric consultation can be helpful with this decision). For patients with bipolar disorder, consider a medication from a different class. For example, if the first trial was with an antipsychotic medication such as quetiapine, then the second trial might involve a medication from another class such as lithium or lamotrigine. For patients with PTSD the second medication may be from the same or a different class.

**Optimizing Medication Treatment**
Confirm that the patient is on optimal dose of the first medication for a sufficient duration (see above). For bipolar disorder, consider adding a second medication from a different class. For example, if the patient is already taking lamotrigine (anticonvulsant) at optimal dose and has not achieved full response then add a medication from another class – for example either lithium (mood stabilizer) or quetiapine (antipsychotic), but not another anticonvulsant such as divalproex. Quetiapine, lurasidone, and olanzapine are antipsychotic medications. Fluoxetine is an antidepressant and is used in combination with olanzapine. Lamotrigine is an anticonvulsant medication. Lithium is a mood stabilizing medication in its own class. For PTSD, patients who...
have failed an adequate trial of a first-line antidepressant medication (usually an SSRI) should be considered for a trial of another antidepressant, either from the same or a different class (SSRI, SNRI, or mirtazapine). See Chapter 6 (table 6.1) for details on these medications.

Augmentation Strategies
In general, augmentation strategies are not preferable as first step treatments in primary care because they require closer clinical monitoring, more complex drug regimens, and often greater expense to the patient. There are, however, times when a patient has had a partial response to an initial medication and augmentation with another medication is clinically indicated. The consulting psychiatrist can be helpful with making this decision and with providing guidance on specific augmentation strategies. For example, augmentation strategies for PTSD may be especially useful for a patient who has had a good general response but has specific residual symptoms. In these situations, the choice of an augmenting agent is based on the nature of the residual symptoms.

Recommended augmentation strategies for bipolar disorder include:
- Adding lithium to lamotrigine, or adding lamotrigine to lithium
- Adding an antipsychotic agent such as lurasidone to lithium

Recommended augmentation strategies for PTSD include:
- General partial response: prazosin, clonidine, or an atypical antipsychotic medication.
- Persistent insomnia or nightmares: An alpha-1-adrenergic antagonist, such as prazosin; a low dose of a sedating antidepressant medication, such as trazodone (i.e., 25-50mg QHS) or mirtazapine (7.5-15mg QHS).
- Severe comorbid depression or anxiety: Combination of the initial antidepressant (typically SSRI or SNRI) with a psychotropic medication with a different mechanism of action [mirtazapine, bupropion (for patients with severe comorbid depression), or an atypical antipsychotic medication].

Antidepressant use in Bipolar Depression
Use of antidepressants, such as SSRIs (i.e. fluoxetine) and SNRIs (i.e. venlafaxine), which are often the first-line treatments for patients with PTSD, in treating bipolar depression is controversial. The STEP-BD study, a large comparative effectiveness study of bipolar depression treatment showed that adding an antidepressant to mood stabilizing medication did not lead to clinically significant improvements in bipolar depression. Additionally, use of the SNRIs such as venlafaxine, was associated with greater likelihood of developing hypomanic or manic symptoms. However, some studies have shown antidepressants such as fluoxetine may benefit patients with bipolar disorder who are stabilized and receiving maintenance treatment, particularly in those with Bipolar II Disorder. Current guideline recommendations on the use of antidepressants in bipolar disorder include (from the ISBD Consensus recommendations on antidepressant use in bipolar disorder, Pacchiarotti, et al. AJP 2013;170:1249-1262):
- Antidepressants may be used for acute bipolar depression treatment when there is a history of previous positive response to antidepressants
- Adjunctive antidepressants for acute bipolar I or II depression should be avoided if 2 or more concomitant manic symptoms are present, or if psychomotor agitation or rapid cycling are present
- Antidepressant monotherapy should be avoided in bipolar I disorder
Patients started on antidepressants should be closely monitored for signs of hypomania or mania
Antidepressants should be avoided in patients with predominantly mixed states and in individuals with high mood instability

Additional treatments to be considered during the program
Even when patients have been referred for specialty mental health care (i.e., additional psychotherapy or substance use treatment), they continue to work with the treatment team. The CM follows them with regular (at least monthly) telephone calls and keeps the patient’s regular PCP apprised of the patient’s progress.

Additional treatments that may be considered by the CM or the treatment team at any stage in the treatment course include:
- referrals to self-help groups such as Alcoholics Anonymous and Narcotics Anonymous,
- referrals to support groups run by the Depression and Bipolar Support Alliance (DBSA), Alzheimer’s Association, ALANON, or caregiver support groups,
- referrals to other community resources,
- referrals to specialty services such as a chronic pain clinic

Each CM should develop and maintain a local resource list for such referrals.

Maintenance and Relapse Prevention
The goal for treatment is remission (see Chapter 3), however, for some patients complete remission of symptoms is not possible and it is necessary to determine at what point the patient no longer benefits from additional adjustments to the treatment regimen. For patients experiencing full response to treatment, or for patients who have reached the maximum benefit from treatment, the emphasis shifts from adjusting treatment to maintaining the clinical benefits achieved and preventing clinical deterioration (or relapse, for patients who are in remission). At this point the frequency of CM follow-up will decrease from every two to every four weeks. Information about adherence and symptoms will continue to be fed back to the patient’s providers and patients will be assessed for deterioration or relapse. If patients experience worsening of their clinical condition, care will be stepped up to treatment adjustment, which typically involves a treatment plan similar to the treatment that led to the maximum benefit. If no relapse occurs, the level of care will remain at the step where the patient responded. This phase will continue until the patient has had a total of 52 weeks of treatment after randomization to receive Collaborative Care.
## Troubleshooting: What to Do if Patients Don’t Improve as Expected

### Table 4.1 Solutions to Common Problems

<table>
<thead>
<tr>
<th>Common problem</th>
<th>Possible Solution</th>
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| **1. Wrong diagnosis**                              | • Reconsider diagnosis and differential diagnosis  
• Consider psychiatric consultation                                                                                                         |
| **2. Insufficient dose**                            |                                                                                                              |
• Increase dose                                                                                                                                      |
| **3. Insufficient length of treatment**             |                                                                                                              |
• Support and encourage patient to stay on medication for a full trial (12 weeks for antidepressant medications; four weeks for mood stabilizers) at a therapeutic dose. |
| **4. Problems with adherence**                      |                                                                                                              |
• Try to understand the patient’s perspective and concerns  
• Address barriers to adherence and problem-solve together                                                                                   |
| **5. Side effects**                                 |                                                                                                              |
(Remember: side effects may be amplified psychologically) | • Wait and reassure patient - the body often gets used to them (e.g., GI side effects from SSRIs or SNRIs)  
• Reduce dose  
• Treat side effect(s)  
• Change medication  
• See “Strategies for Managing Side Effects” – [Chapter 6, table 6.2](https://sharepoint.washington.edu/uwpsychiatry/SPIRIT/Pages/default.aspx) |
| **6. Other complicating factors**                   |                                                                                                              |
• a. psychosocial stressors / barriers  
• b. medical problems / medications  
• c. psychological barriers (low self-esteem, guilt, unwillingness to let go of “sick” role)  
• d. active substance abuse  
• e. other psychiatric problems | • Address problems directly  
• Consider adding behavioral interventions  
• Psychiatric case review  
• Consider telepsychiatry follow-up                                                                                                         |
| **7. Treatment is not effective** despite adequate trial of medication at adequate dose** |                                                                                                              |
• Psychiatric case review for treatment adjustment                                                                                               |