Mental Health in Family Medicine 2013;10:175–81

Article

Ten ways to improve the treatment of depression and anxiety in adults

Boadie W Dunlop MD MS
Assistant Professor, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA

Kelly Scheinberg MD
Addiction Psychiatry Resident, Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA

Anne L Dunlop MD MPH
Associate Professor, Department of Family and Preventive Medicine, Emory University School of Medicine, and Emory School of Nursing, Atlanta, GA

ABSTRACT

Complaints of depression and anxiety are very common among adult patients seeking treatment in primary care settings, and primary care providers prescribe the majority of medications for these conditions. Psychiatrists are often asked to evaluate and manage patients with major depression or anxiety disorders who have not improved after treatment in primary care.

We highlight ten frequently overlooked aspects of the care of patients who present with depression and anxiety in primary care. Chief among these aspects is the consideration of a thorough differential diagnosis, particularly bipolar disorder, psychotic disorders, dementia and substance abuse, each of which requires specific treatment approaches. Additional considerations include avoidance of medications or doses that may aggravate anxiety symptoms and regular follow-ups to assess symptomatic and functional improvement. Finally, it is important to actively manage the treatment through dose escalation, switching medications or employing additional treatment components until remission is achieved.

Judicious use of benzodiazepine clonazepam and appropriate referrals to psychotherapy can contribute to optimal treatment outcomes.

Keywords: antidepressive agents, anxiety disorders, depressive disorder, medical errors, primary healthcare

Complaints of anxiety or depressed mood, both as presenting symptoms or as notable items on review of symptoms, are common among primary care patients. Mood and anxiety disorders are commonly comorbid with chronic conditions such as heart disease and diabetes, and their presence complicates treatment and worsens long-term outcomes.[1,2] Moreover, patients with untreated or undertreated mental health disorders are high users of medical services, often presenting with physical complaints that cannot be linked to a specific medical disorder.[3] As such, primary care providers prescribe the majority of medications for the management of depression and anxiety.[4] Unfortunately, treating mental health disorders in the primary care setting can be very challenging.[5] Under the usual time constraints, it is not feasible to cover all salient aspects of the patient's symptoms, prior episodes, treatments, current social and family function, and pertinent medical considerations. Although primary care clinicians do their best given time pressures and the range of conditions that warrant attention in any given healthcare encounter, it is possible that the evaluation and management of mental health disorders can fall short of the clinical ideal.

This article aims to elucidate ten of the most common missteps that, from a psychiatrist's perspective, occur in the diagnosis and treatment of patients with mood and anxiety disorders in primary care. We provide evidence-based and clinically

informed recommendations to enhance the care of patients experiencing depressed or anxious mood states (Table 1). We start from the basics; as with all of medicine, effective treatment begins with making an accurate diagnosis. A patient's complaint of 'I'm depressed' or 'I'm anxious' is simply where the assessment commences – additional information is *always* required for good care.[6] Once the diagnosis (or diagnoses – see below) are clarified, key aspects to the initiation and monitoring of treatment need to be implemented to optimise outcomes and prevent iatrogenic harm.

Consider a broad psychiatric differential diagnosis when assessing a patient with depressed or anxious mood

Major depressive disorder, panic disorder and generalised anxiety disorder are all commonly diagnosed in primary care, but other psychiatric disorders have similar presentations and require specific treatment considerations. Table 2 offers sample screening questions for these illnesses.

Bipolar disorder

Patients with bipolar disorder often seek care when in a depressed or anxious mood state. Antidepressant medications can precipitate mania or rapid cycling of mood states in these patients.[7] Patients who endorse symptoms of prior manic or hypomanic episodes should be referred to a psychiatrist. If elevated mood episodes are present in the absence of an alternative etiology (e.g. induced by illicit drug use or medical illness), bipolar disorder should be diagnosed and treatment with a mood stabiliser initiated; antidepressant medications should generally be avoided in these patients.

Post-traumatic stress disorder

Patients with post-traumatic stress disorder (PTSD) often present with insomnia, anhedonia, poor concentration, irritability and isolation. Because PTSD may arise after events that people experience as highly shameful, patients may not spontaneously disclose prior traumatic experiences. It is therefore helpful to use direct inquiries as indicated in Table 2. Details of the event beyond those necessary for diagnosis are best addressed in a mental health setting. The best established treatment for PTSD is an exposure-based psychotherapy.[8]

Table 1 Key clinical recommendations

Recommendation	References
Consider a broad psychiatric diagnosis when assessing a patient with depressed or anxious mood, as misdiagnosis is frequent and negatively affects outcomes	12, 39
Make specific and appropriate referrals to specific forms of psychotherapy, such as IPT, CBT and PST	40, 41
Providing key educational messages at the beginning of treatment can enhance treatment adherence, particularly with regard to antidepressant medication use	14, 42
Early monitoring for adherence, treatment response and side effects can improve adherence and outcomes	18, 42, 43
Treat depression until remission in order to decrease relapse rate	20, 44, 45
Change treatment after 6 weeks if there is no or very minimal response to initial medication	22, 46
Evaluate every anxious or depressed patient for alcohol or drug abuse	29, 47

Key recommendations and supporting references for ways to improve clinical outcomes for patients with depression and anxiety disorders.
CBT = Cognitive Behavioral Therapy, IPT = Interpersonal Therapy, PST = Problem-solving Therapy.

Table 2 Sample screening questions for use in evaluating patients presenting with symptoms of anxiety or depression

Disorder	Sample Questions
Bipolar Disorder	Have you had a period of several days in a row in which you felt so happy or energetic that friends or family said you were acting hyper, talking too fast, or that you didn't seem to be your usual self? Have you had a period of a several days in a row where you felt you needed much less sleep than you usually do?
PTSD	Have you ever experienced an extremely frightening event in which you were abused, seriously hurt or nearly killed? Have you ever seen or heard of anything like that happening to someone you are close to? Do you have upsetting memories or dreams, or become upset when you encounter reminders of this event?
OCD	Do your everyday activities take a long time to complete? Why is that? Do you check things repeatedly, or need to wash your hands or clean things several times to put your mind at ease? Do you have to do things a certain number of times, or just the right way, in order to feel OK?
Psychotic disorders	Do you ever hear the voice of someone talking, but when you look there is nobody there? Have you ever felt that you were being watched or that there was a plot to harm you?

Obsessive-compulsive disorder

Patients with obsessive-compulsive disorder (OCD) often present with depression or anxiety. Obsessions and compulsions are unique in that patients nearly always have the perception that their ideas or behaviours are irrational; consequently they are often unwilling to volunteer information about these behaviours because of shame or embarrassment, making the diagnosis easy to miss. Treatment of OCD is highly challenging, as high doses of antidepressants for sustained periods of three to four months are necessary to determine efficacy.[9]

Psychotic disorders

It is not at all uncommon for psychotic patients to present with anxious or depressed mood, but hallucinations or delusions may not be elicited unless specifically asked about. Additionally, severely depressed patients may also develop nihilistic or derogatory delusions or hallucinations. Patients with psychotic symptoms should be referred to psychiatric specialty care whenever possible.

Bereavement, adjustment disorders, and minor depression

Bereavement and adjustment disorders are mood states that onset shortly after a negative life event. Minor depression is diagnosed when clinically important depressive symptoms emerge in the absence of a stressful life event, but the diagnostic and statistical manual (DSM) criteria for a major depressive episode are not met. All these conditions should initially be treated with psychotherapy (e.g. supportive behaviour therapy, cognitive behavioural therapy, group therapy) with medication reserved for specific symptoms (e.g. a sedative for short-term treatment of marked insomnia) or for patients who develop severe symptoms (e.g. suicidal ideation).[10,11]

Dementia

An early sign of several dementing disorders can be reduced emotion regulation. This deficit may take the form of impulsivity, irritability, depression or anxiety. Therefore, elderly patients presenting with mood symptoms should undergo a medical evaluation for primary cognitive disorders.

Make specific and appropriate referrals to psychotherapy

Just as there are specific medications, there are specific forms of psychotherapy. Patients with anxiety disorders in particular, benefit from cognitive behavioural therapy (CBT), in which they undergo exposure to their fears and gain mastery over them. There are several forms of effective psychotherapy for depression, including CBT and interpersonal therapy.[1] Non-specific 'supportive' therapy can help people in times of crisis or stress but is typically not efficacious for serious mental health disorders.[12] Family therapy or behavioural marital therapy can be effective when dysfunction in families or couples is a primary driver of the patient's depressive symptoms.[13] Providers should be aware of local therapists who practice evidence-based forms of treatment.

Be sure to frame expectations appropriately when initiating an antidepressant medication

Appropriate education for patients starting medication should include:

1 potential side effects
2 expected time frame for observing improvement (up to six weeks; twelve weeks for OCD)
3 the necessity of consistent daily dosing
4 the minimum duration of treatment (at least six months after remission).[11]

This instruction is crucial because non-adherence often occurs if the patient has unrealistic expectations and does not experience immediate relief, has uncomfortable initial (but usually temporary) side effects, or has resolution of symptoms early on and feels medication is no longer needed. A focused, brief education about these topics can enhance adherence and improve outcomes.[14]

For patients who experience agitation or increased anxiety upon starting an antidepressant, options include reducing the dose by half, adding a low dose benzodiazepine during the initial adjustment period or switching the patient to an alternative treatment. Any patients who report this kind of activation side effect should have a safety assessment as their risk for suicidal ideation is increased.[15]

Monitor adherence closely during the first month

Roughly half of all patients prescribed an antidepressant medication discontinue it within 30 days of initiation,[16] and at least one-third who start an antidepressant medication have low adherence.[17] A phone call to the patient one to two weeks after starting medication to inquire how they are doing can identify side effects, help correct any misunderstanding about the drug and increase medication adherence.[18] This contact is especially important in patients under the age of 25 as all antidepressants carry a black box warning about suicide risk for this age.[15]

Use caution in selecting the initial antidepressant dose for anxious patients

The usual starting doses for selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) were established primarily through studies of patients with major depression and may be too high for patients with significant levels of anxiety. Anxious patients may have increased anxiety, agitation or even panic attacks with standard starting doses. Starting at half the usual dose for four to six days before increasing to the typical starting dose can greatly improve tolerability and adherence.[19]

Do not be content with 'good enough'

Remission is defined as the near-complete absence of symptoms of the disorder and return to the patient's premorbid level of functioning. Achieving remission provides the best protection against future relapses[20] and requires regular re-evaluation and modification of therapy if indicated. In patients with only a partial response at six weeks of treatment, psychiatrists nearly always raise the dose of the antidepressant. Patients whose improvement plateaus at less than full recovery should continue to have their dose raised at three- or four-week intervals, unless tolerability concerns are present. Raising the dose can also be effective for patients

who previously demonstrated good response but now report some loss of benefit.[21] If an increase in dosage produces no additional benefit, it is usually best to augment the antidepressant with a second medication or psychotherapy. As a general rule, for partially responsive patients, an increase in dosage should be considered before augmenting with another medication.

Minimal improvement at six weeks requires a change in treatment

Except for PTSD and OCD (which should have eight and twelve week SSRI/SNRI treatment trials, respectively, before concluding efficacy), patients whose illness shows little improvement in depression or anxiety despite six weeks at a maximum-tolerated dose should be switched to an alternative medication or psychotherapy.[22] Failure of one SSRI does not preclude trial with a second SSRI, but two SSRI treatment failures should definitely lead to a medication switch with a different mechanism of action.[23]

Do not use bupropion as a first-line treatment for patients who have significant anxiety

Bupropion has features that both patients and doctors like – specifically, low rates of weight gain and sexual dysfunction. However, unlike the SSRIs and SNRIs, bupropion is not approved for the treatment of any anxiety disorder. It is often activating, which causes great discomfort for anxious patients.[24] Bupropion may be a reasonable choice for depressed patients without prominent anxiety, but for highly anxious patients it should usually be reserved as an augmentation agent after partial improvement with an SSRI or SNRI.

Do not use alprazolam for generalised anxiety

Both patients and doctors appreciate the rapid relief that benzodiazepines provide from psychiatric symptoms. For most patients, however, the initial medication for anxiety should be an SSRI. Patients who continue to experience anxiety despite a maximum-tolerable dose of SSRI may benefit from augmentation with a benzodiazepine.[25] Of the benzodiazepines, alprazolam is particularly problematic due to its very short half-life and rapid onset of action, which makes its use highly reinforcing. Moreover, alprazolam can induce recurrent bouts of rebound anxiety that may intensify the anxiety experience, thus heightening the risk for increased frequency of use and potential dependence.[26] If it is determined that a benzodiazepine would be beneficial, long-acting agents such as clonazepam are strongly preferred.[25,27] Alprazolam is best reserved for patients who experience intense anxiety or panic attacks in infrequent, predictable situations, such as exposure to specific phobias (e.g. flying, claustrophobia). Benzodiazepines should generally be avoided in patients with a history of alcohol or drug abuse.[28]

Evaluate every anxious or depressed patient for alcohol or drug abuse

High anxiety or depressive emotional states are very distressing, leading some patients to self-medicate with alcohol or other substances before seeking help from a medical provider. Prescription medication treatment in such patients is unlikely to be effective without co-treatment of the substance-abuse problem.[29] Referral to specialty care is recommended. Quick screening tools for hazardous substance use are the Alcohol Use Disorders Identification Test[30] and the Drug Abuse Screening Test.[31]

Conclusion

Treating psychiatric conditions in the primary care setting is indeed a great and growing challenge. In the US, most patients receive at least some of their mental health treatment in a primary care setting, with roughly a third of all treated patients with a mental disorder receiving care solely through primary care.[32] Inadequacies of treatment for depression and anxiety disorders provided through primary care settings have been demonstrated across nations.[33,34] Many barriers impede the provision of adequate mental health treatment in primary care settings, including limitations on time, insurance restrictions,

patient-related factors and inability to obtain specialist consultation.[35]

These forces are placing an increasing responsibility on the primary care clinician to manage depressed or anxious patients who in the past may have been referred directly to psychiatric specialty care.

To assist clinicians and control treatment costs, stepped-care models[36] and specific treatment guidelines[10,37] have been developed for primary care management of psychiatric disorders. These tools provide support for decision-making by primary care clinicians but may neglect details of assessment and treatment that influence outcomes for mentally ill patients. Although psychiatric consultation can improve outcomes, the medical practice system or patient-related factors may limit the use of this intervention.[38] The recommendations provided in this paper reflect common revisions made by psychiatrists to the care of depressed and anxious patients treated in primary care, and are offered with the aim of improving treatment satisfaction for both the patient and clinician.

REFERENCES

1 Egede LE. Disease-focused or integrated treatment: diabetes and depression. *Medical Clinics of North America* 2006;90:627–46.
2 Barth J, Schumacher M and Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosomatic Medicine* 2004;66:802–13.
3 Katon W, Kleinman A and Rosen G. Depression and somatization: a review Part I. *American Journal of Medicine* 1992;72:127–35.
4 Mark TL, Levit KR and Buck JA. Datapoints: psychotropic drug prescriptions by medical specialty. *Psychiatric Services* 2009;60:1167.
5 Eisenberg L. Treating depression and anxiety in primary care. *New England Journal of Medicine* 1992;326:1080–3.
6 Mojtabi R and Olfson M. Proportion of antidepressant prescribed without a psychiatric diagnosis is growing. *Health Affairs* 2011;30:1434–42.
7 Ghaemi SN, Wingo AP, Filkowski MA *et al*. Long-term antidepressant treatment in bipolar disorder: meta-analyses of benefits and risks. *Acta Psychiatrica Scandinavica* 2008;118:347–56.
8 Institute of Medicine. *Treatment of Posttraumatic Stress Disorder: an assessment of the evidence*. National Academies Press: Washington, DC, 2008.
9 American Psychiatric Association. *Practice guideline for the treatment of patients with obsessive-compulsive disorder*. American Psychiatric Association: Arlington, VA, 2007.
10 National Institute for Health and Clinical Excellence. *Depression: the treatment and management of depression in adults, including adults with a chronic physical health problem*. NICE clinical guidelines 90 and 91, National Collaborating Centre for Mental Health: London, 2009.
11 Anderson I, Ferrier I, Baldwin R *et al*. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2000 British Association for psychopharmacology guidelines. *Journal of Psychopharmacology* 2008;22:343–96.
12 American Psychiatric Association. *Treating Major Depressive Disorder: a quick reference guide*. American Psychiatric Association: Washington, DC, 2010, pp. 1–28.
13 Baucom D, Shoham V, Mueser K *et al*. Empirically supported couples and family interventions for marital distress and adult mental health problems. *Journal of Consulting and Clinical Psychology* 1998; 66:53–88.
14 Mundt JC, Clarke GN, Burroughs D *et al*. Effectiveness of antidepressant pharmacotherapy: the impact of medication compliance and patient education. *Depression and Anxiety* 2001;13:1–10.
15 Stone M, Laughren T, Jones ML *et al*. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. *BMJ* 2009339: b2880.
16 Olson M, Marcus S, Tedeschi M *et al*. Continuity of antidepressant treatment for adults with depression in the United States. *American Journal of Psychiatry* 2006;163:101–8.
17 Cooper C, Bebbington P, King M *et al*. Why people do not take their psychotropic drugs as prescribed: results of the 2000 National Psychiatric Morbidity Survey. *Acta Psychiatrica Scandinavica* 2007;116:47–53.
18 Dietrich A, Oxman T, Williams J *et al*. Re-engineering systems for the treatment of depression in primary care: cluster randomized controlled trial. *BMJ* 2004;329:602.
19 Ninan PT, Dunlop BW. *Contemporary Diagnosis and Management of Anxiety Disorders*. Handbooks in Health Care: Newtown PA, 2006, pp. 47.
20 Rush AJ, Kraemer HC, Sackeim HA *et al*. ACNP Task Force. Report by the ACNP Task Force on response and remission in major depressive disorder. *Neuropsychopharmacology* 2006;31:1841–53.
21 Schmidt ME, Fava M, Zhang S *et al*. Treatment approaches to major depressive disorder relapse. Part 1: dose increase. *Psychotherapy and Psychosomatics* 2002;71:190–4.
22 Adli M, Baethge C, Heinz A *et al*. Is dose escalation of antidepressants a rational strategy after a medium-dose treatment has failed? *European Archives of Psychiatry and Clinical Neuroscience* 2005;255:387–400.
23 Rosso G, Rigardetto S, Bogetto F *et al*. A randomized, single-blind, comparison of duloxetine with bupropion in the treatment of SSRI-resistant major depression. *Journal of Affective Disorders* 2012;136: 172–6.
24 Papakostas GI, Stahl SM, Krishen A *et al*. Efficacy of bupropion and the selective serotonin reuptake

inhibitors in the treatment of major depressive disorder with high levels of anxiety (anxious depression): a pooled analysis of 10 studies. *Journal of Clinical Psychiatry* 2008;69:1287–92.
25 Dunlop BW and Davis PG. Combination treatment with benzodiazepines and SSRIs for comorbid anxiety and depression. *Primary Care Companion to the Journal of Clinical Psychiatry* 2008;10:222–8.
26 Chinouard G. Issues in the clinical use of benzodiazepines: potency, withdrawal, and rebound. *Journal of Clinical Psychiatry* 2004;65(Suppl 5):7–12.
27 Herman J, Brotman A and Rosenbaum J. Rebound anxiety in panic disorder patients treated with shorter-acting benzodiazipines. *Journal of Clinical Psychiatry* 1987;48(Suppl):22–8.
28 Longo L and Johnson B. Addiction: Part I. Benzodiazepines-side effects, abuse risk and alternatives. *American Family Physician* 2000;61:2121–8.
29 Levin FR, Mariani J, Brooks DJ *et al*. A randomized double-blind, placebo controlled trial of venlafaxine-extended release for co-occurring cannabis dependence and depressive disorders. *Addiction* 2013; 108(6):1084–94.
30 Saunders J, Aasland O, Babor T *et al*. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. II. *Addiction* 1993;88:791–804.
31 Skinner H. The drug abuse screening test. *Addictive Behaviors* 1982;7:363–71.
32 Wang PS, Delmer O, Olfson M *et al*. Changing profiles of service sectors used for mental health care in the U.S. *American Journal of Psychiatry* 2006; 163:1187–98.
33 Young AS, Klap R, Sherbourne CD *et al*. The quality of care for depressive and anxiety disorders in the United States. *Archives of General Psychiatry* 2001; 58:55–61.
34 Van Os TW, van den Brink RH, van der Meer K *et al*. The care provided by general practitioners for persistent depression. *European Psychiatry* 2006;21: 87–92.
35 Cunningham PJ. Beyond parity: Primary care physicians' perspectives on access to mental health care. *Health Affairs* 2009;28:w490–501.
36 Franx G, Oud M, de Lange J *et al*. Implementing a stepped care approach in primary care: results of a qualitative study. *Implementation Science* 7:8.
37 Institute for Clinical Systems Improvement (ICSI). *Major depression in adults in primary care*. Institute for Clinical Systems Improvement: Bloomington, MN, 2011.
38 Conradi HJ, deJonge P, Kluiter H *et al*. Enhanced treatment for depression in primary care: long-term outcomes of a psycho-educational prevention program alone and enriched with psychiatric consultation or cognitive behavioral therapy. *Psychological Medicine* 2007;37:849–62.
39 Mitchell A, Vaze A and Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. *The Lancet* 2009;374(9690):609–19.
40 Butler A, Chapman J, Forman E *et al*. The empirical status of cognitive-behavioral therapy: A review of meta-analyses. *Clinical Psychology Review* 2006; 26: 17–31.
41 de Mello MF, de Jesus Mari J, Bacaltchuk J *et al*. A systematic review of research findings on the efficacy of interpersonal therapy for depressive disorders. *European Archives of Psychiatry and Clinical Neuroscience* 2005;255:75–82.
42 Williams JW Jr, Gerrity M, Holsinger T *et al*. Systematic review of multifaceted interventions to improve depression care. *General Hospital Psychiatry* 2007;29:91–116.
43 Vergouwen CM, Bakker A, Katon WJ *et al*. Improving adherence to antidepressants: a systematic review of interventions. *Journal of Clinical Psychiatry* 2003;64:1415–20.
44 Dunlop BW, Holland P, Bao W *et al*. Recovery and subsequent recurrence in patients with recurrent major depressive disorder. *Journal of Psychiatric Research* 2012;46:708–15.
45 Paykel E, Ramana R, Cooper Z *et al*. Residual symptoms after partial remission: an important outcome in depression. *Psychological Medicine* 1995;25: 1171–80.
46 Quitkin FM, McGrath PJ, Stewart JW *et al*. Chronological milestones to guide drug change: when should clinicians switch antidepressants? *Archives of General Psychiatry* 1996;53:785–92.
47 Young MA, Fogg LF, Scheftner WA *et al*. Interactions of risk factors in predicting suicide. *American Journal of Psychiatry* 1994;151:434–5.

ADDRESS FOR CORRESPONDENCE

Boadie Dunlop, 1256 Briarcliff Road NE, Building A, 3rd Floor, Atlanta, GA 30322. Email: bdunlop@emory.edu

Submitted 11 June 2013
Accepted 8 September 2013