# Realistic Expectations and a Disease Management Model for Depressed Patients With Persistent Symptoms

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***Objective:*** To describe the efficacy of currently available treatments for depression in achieving remission and to highlight additional strategies for those patients who continue to experience persistent depressive symptoms in spite of optimal treatment.

***Data Sources:*** The authors reviewed the literature (electronic and hand searches) on the efficacy of current pharmacologic and psychotherapeutic antidepressant treatments and the utility of a chronic disease management model. A search of PubMed was conducted for English-language articles published from 1980 to 2005 using the keywords *depression treatments, outcome, course of illness*, and *treatment resistant depression*.

***Data Synthesis:*** Current treatments for depression leave a significant minority (20%–40%) of patients with persistent depressive symptoms. A disease management model that may be useful for major depressive disorder is described.

***Conclusions:*** The goal of treating depression to achieve remission, although ideal, is currently unattainable for many patients. The long-term care of patients with persisting depressive symptoms may be well served by adding a disease management component to the overall treatment strategy. Doing so may help to improve coping, interpersonal functioning, and quality of life.

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The purpose of this article is to explore additional ways of helping those depressed patients who continue to experience depressive symptoms and impaired functioning in spite of optimal antidepressant treatments. In current practice, the goals in treating major depressive disorder are to remove all signs and symptoms of depression, to restore occupational and psychosocial functioning, and to reduce the likelihood of relapse and recurrence.[1] As such, there has been a persistent call for raising the bar for outcome in the treatment of depression. The prevailing ethos is to "push" treatment in order to achieve full remission and not to be satisfied with partial response.[2–5]

There are excellent reasons for trying to achieve complete remission of depressive symptoms. The potential consequences of failing to achieve full remission are well documented and include an increased risk of relapse and treatment resistance,[6–8] continued psychosocial limitations,[9] decreased ability to work and decreased workplace productivity,[10] and increased cost for medical treatment.[10] Sustained depression may also worsen morbidity and mortality of other medical conditions.[11,12] Unfortunately, many patients do not respond completely or even partially to currently available treatments; their depressions appear refractory to remission. It is possible that there are "good prognosis" and "poor prognosis" forms of depression. Persistent residual symptoms may be markers for such poorly responsive types of depression.

Given the current rates of treatment efficacy in depression, how did these goals become so widely accepted? Are they realistic for all patients? Should we focus some of our energies on teaching patients effective ways of coping with depression as a chronic illness?

The mainstay of psychiatric treatment today is pharmacotherapy. The most common conceptual and treatment model is a biomedical one that emphasizes cure and eradication of disease; an active medical role for the physician; an acquiescent, passive role for the patient; and the implied promise of a medical solution for a medical problem. A number of converging forces have coalesced to reinforce the prominence of this model.

First, many depressed patients have not responded to the talking therapies. Psychotherapy usually takes time to show an effect, requires considerable therapist skill, is time-consuming, is expensive in the short term, and needs

active engagement by both therapist and patient. There is also a shortage of available psychotherapists trained to deliver evidence-based psychotherapies.

Second, the proliferation of pharmacotherapy outcome studies demonstrating significant efficacy for medications has led to efforts to identify and measure neurochemical substrates and receptor systems that may be involved in the pathophysiology of depression. Such knowledge has encouraged the notion that it is possible to fine-tune neurochemical processes with tailored chemical treatments to resolve psychiatric symptoms and illnesses. The seemingly more benign side effect profile of many of the newer antidepressants has reinforced the practice of beginning the treatment of depression with pharmacotherapy.

Third, spiraling health care costs over the past 20 years leading to managed care pressures have pushed psychiatrists in the United States into treating depression with potentially quicker, less expensive, and readily available drug treatments. Lowered reimbursement rates for psychotherapies, increased rates for medical management, and pressure to see more patients have also contributed to reinforce the emphasis on pharmacotherapy. This is particularly true when the treatment is provided by primary care physicians who lack training in psychotherapy and can only provide brief visit times.

Fourth, the pharmaceutical industry has strongly supported the biomedical model. The industry not only has discovered and brought to market an ever-expanding number of antidepressant agents, but has educated health care professionals and patients about the potential value of these agents in bringing about symptom reduction. Financial support for continuing medical education in the United States comes largely from drug companies and other commercial entities.[13]

On an individual level, both psychiatrists and patients have willingly embraced the biomedical model. For psychiatrists, at least in the United States, medical management of depression is more financially profitable than psychotherapy as it requires less time. Many patients hope that a medication will resolve their depressive symptoms without having to work at changing maladaptive cognitions, relationship styles, and ways of coping.

What do we do with patients who do not respond well to available treatments? Have we raised expectations too high, both for patients and for therapists? Are we at risk of overtreating patients, particularly with unproven polypharmacy, possibly harming them with unnecessary side effects or unrealistic expectations and at the same time contributing to rising health care expenditures? Are there other disease management options that we can provide for those with persistent and/or residual symptoms in addition to their ongoing antidepressant treatments?

Depression is a heterogeneous disorder and includes major and minor variations and acute, chronic, and recurrent forms, as well as forms with melancholic, atypical, and psychotic features. In this article, we focus on patients, whatever their form of depression, who have not responded well to currently available treatments and who continue to experience persistent problematic depressive symptoms. We reviewed the literature (electronic and hand searches) on the efficacy of current pharmacologic and psychotherapeutic antidepressant treatments and the utility of a chronic disease management model. A search of PubMed was conducted for English-language articles published from 1980 to 2005 using the keywords *depression treatments, outcome, course of illness*, and *treatment resistant depression*.

To address the question of treatment recommendations for this difficult-to-treat population,[14,15] we will provide an overview of (1) the long-term course of depression, (2) the effectiveness of current treatments, and (3) a model of chronic care and disease management.

## THE LONG-TERM COURSE OF MAJOR DEPRESSIVE DISORDER

Observational studies indicate that major depressive disorder tends to be a chronic disorder with high rates of relapse and recurrence as well as persistent functional impairment.[16] Many patients with major depressive disorder respond positively to treatment, but many others continue to experience residual symptoms and recurrences as well as persistent and/or intermittent impairment.[6,17–23]

A recent 8- to 11-year follow-up study of 69 patients with severe recurrent major depression at study intake found that recovery and relapse rates did not differ substantially from those in earlier studies despite high levels of antidepressant maintenance treatment, psychological therapies, and compliance.[24] Thirty percent of follow-up months were spent in an episode of depression, and 18% of patients never achieved asymptomatic status during the follow-up period.[25] Goldberg and Harrow[26] reported similar findings, with 37% to 53% of depressed patients having residual symptoms in a 10-year follow-up study.

These long-term follow-up studies indicate that 15% to 30% of patients with major depressive disorder have a favorable response to standard therapy, with remission of depressive symptoms and maintenance of a euthymic state. At the other extreme, 10% to 30% of patients go on to experience a chronic course characterized by continuous symptoms and functional impairment despite treatment. The remaining patients have an intermittent course characterized by remissions, subsyndromal symptoms, recurrences, and relapses. Even with improvement of clinical symptoms, however, psychosocial impairments can be significant and persistent.[27]

### Factors Associated With Recurrence and Chronicity

Several studies have shown that as the duration of recovery increases, the risk of recurrence decreases.[19,28,29]

Those who recover early (e.g., during the first 6 months of depression) have a better chance of avoiding subsequent relapses.[20,29] Factors associated with chronicity and recurrence include greater severity of depressive episodes, elevated stress, conflict and interpersonal dependency, family history of depression, emotional reliance, earlier age at onset, older age,[20,30] high neuroticism scores,[31,32] comorbid dysthymia,[33] comorbid nonaffective psychiatric illness such as substance use disorder or anxiety disorder,[34] comorbid nonpsychiatric medical disorders,[35] a history of multiple episodes of depression prior to the index episode of depression,[36] and the presence of psychosocial impairment.[37] Not all investigators have found clear predictors of chronicity. In their review, Riso et al.[38] found few consistent factors that related to chronicity of depression. There are contradictory findings across multiple studies that have examined the association between any particular clinical variable and the recurrence of major depressive disorder.

It may be that factors influencing recovery are intrinsic to the depressive illness itself and less related to external circumstances or even to treatments received. Patients who respond to treatment early in the course of the depression are more likely to go on to a favorable long-term course.[20,39,40] In a treatment study of depressed inpatients, the 37% who had a good response to hospital treatment went on to do well over the follow-up period. Those who did not respond significantly while in the hospital continued to have a very low remission/response rate in spite of extensive multimodal treatments.[41] In medicine generally and in major depressive disorder specifically, patients who do not respond to an effective pharmacologic treatment have a lower probability of responding to a second or third treatment trial.[42] Goldberg and Harrow[26] also found that there was consistency in either persistence of morbidity or sustained remission. It cannot be assumed therefore that there is a cumulative effect of sequential therapies. Certain forms of major depressive disorder appear to be more or less responsive to treatment. It is not clear whether such responsiveness to treatment is associated with particular subtypes of depressive illness such as melancholic, atypical, or psychotic or with some as yet undetermined other variables.

## THE EFFECTIVENESS OF CURRENT TREATMENTS

Outcome for treatment of depression is classified in several ways. Response is most commonly thought of as significant improvement but not necessarily complete relief of symptoms.[43] Response is often defined as a greater than 50% decrease from baseline depression symptom scores on such instruments as the Hamilton Rating Scale for Depression (HAM-D)[44] or the Montgomery-Asberg Depression Rating Scale (MADRS).[45] Remission is defined as minimal or no residual symptoms, no longer meeting diagnostic criteria for depression and often quantified as a score equal to or less than 7 on the HAM-D.[46] There are other ways of defining outcome, but these definitions of response and remission are most commonly used in treatment outcome studies.[47,48] Nevertheless, even patients who meet HAM-D definitions for remission may continue to experience problematic depressive symptoms or difficulties in psychosocial functioning.[27,49]

Most treatment outcome studies of depression are efficacy rather than effectiveness trials. As such, they examine a homogeneous and unrepresentative sample of depressed patients. Outcome data from such studies most likely overestimate response rates.[50] For example, Keitner et al.[51] reported that only 27 (7%) of 378 responders to advertisements for depression treatment studies met eligibility criteria for participation in those studies. Similarly, Zimmerman et al.[52] found that 29 (8%) of 346 depressed outpatients would have qualified for participation in an antidepressant efficacy trial given the common exclusion criteria that are used in clinical trials.

### Treatment Options for Major Depressive Disorder

Options for the treatment of major depressive disorder usually include monotherapy with an antidepressant medication; psychosocial treatments (individual, family, or group therapy); combined pharmacotherapy and psychosocial treatment; substitution of one antidepressant for another; augmentation of an antidepressant with other agents such as lithium, thyroid hormone, or atypical antipsychotic agents; combination of antidepressants; electroconvulsive therapy (ECT); repetitive transcranial magnetic stimulation (rTMS); and vagus nerve stimulation.

***Pharmacotherapy.*** Used as monotherapy, available antidepressant medications are comparably effective for depressed patients, although any individual patient may respond preferentially to one antidepressant over another. Results of a pooled analysis comparing the efficacy of venlafaxine, fluoxetine, paroxetine, fluvoxamine, and placebo suggested that selective serotonin reuptake inhibitors (SSRIs) were significantly more efficacious than placebo in achieving remission rates while venlafaxine was significantly more effective than the SSRIs. Nonetheless, remission rates with SSRIs were only 35% and with venlafaxine only 45%, suggesting that at least 55% of patients failed to achieve remission.[53] A meta-analysis of data from 7 randomized, controlled antidepressant trials found response rates of 62% to 63% and a remission rate of 47% for bupropion and SSRIs in comparison to 51% and 36%, respectively, for placebo.[54] Tricyclic antidepressants have comparable remission and response rates. Amitriptyline may be slightly better than other tricyclic and heterocyclic antidepressants and may also have an "edge" in terms of efficacy over SSRIs but is less well tolerated.[55]

Results of the largest effectiveness study conducted to date (Sequenced Treatment Alternatives to Relieve De-

pression [STAR*D]), which studied 2876 outpatients with major depressive disorders treated with citalopram in psychiatric and primary care settings, reported a remission rate of 28% to 33% (depending on the outcome measure used) and a response rate of 47%.[56] These results are consistent with the majority of earlier outcome studies.

Response to antidepressants is less than optimal for a considerable proportion of depressed patients.[57] One third fail to experience sufficient improvement despite adequate treatment.[58] Although algorithm-guided treatment of major depression was found to be more effective than treatment as usual, substantial symptoms and functional impairment persisted even among the responders.[59]

***Psychotherapy.*** A review of controlled, double-blind trials for outpatients with mild to moderate depression comparing medications, psychotherapy, and control conditions reported that remission rates (defined as a score of ≤ 7 on the HAM-D or ≤ 5 on the Raskin Depression Scale) were 46% for medications, 46% for psychotherapy (cognitive-behavioral therapy and/or interpersonal therapy), and 24% for control conditions. Medication and psychotherapy were comparable to each other and significantly better than the control condition.[60]

A meta-analysis of psychotherapy for depression reported similar response rates for cognitive-behavioral therapy (50%), interpersonal psychotherapy (IPT) (52%), and behavioral therapy (55%),[1] even for patients with moderate to severe depressions.[61] Patients who respond to psychotherapy are frequently left with residual symptoms that are associated with relapse and suboptimal psychosocial functioning.[62] Similar to monotherapy with antidepressant medications, psychotherapy results in a response/remission rate that clusters around 50%.

Some recent developments in the field of psychotherapy for depressive disorders do demonstrate promise. First, a growing body of evidence indicates that the delivery of cognitive and behaviorally based therapies, during either the acute or continuation phase of treatment, may help to protect against relapse and recurrence better than maintenance antidepressant medication taken alone.[8,63–65]

A second development concerns the modification of therapy procedures in order to better target residual depressive symptoms and other risk factors for relapse. Segal and colleagues[66] have developed Mindfulness-Based Cognitive Therapy, a group treatment that teaches patients to distance themselves from negative cognitions rather than modify thought content through accuracy testing. Another modified form of cognitive-behavioral therapy, called well-being therapy,[63] incorporates cognitive strategies to help patients enhance well-being along 6 dimensions.[67]

Finally, IPT for depression has been associated with a delayed but positive effect on quality of interpersonal and social functioning,[68,69] which may provide additional protection against relapse and recurrence beyond symptom remission.

***Pharmacotherapy and psychotherapy combinations.*** In spite of the prevalence of its use, relatively few studies have investigated the efficacy of the combination of pharmacotherapy with psychotherapy. Results have been conflicting,[70] with some studies supporting the superiority of combined therapy[64,71–75] while others not.[76–78] A meta-analysis of 12 studies of combination treatment versus psychotherapy alone and 5 studies of combination treatment versus drug therapy alone showed effect sizes of 0.01 and 0.17, respectively.[79] The effectiveness of combination treatment seems to be clearest for the chronic and the most severely depressed subgroup of patients.[80] A study of sertraline and/or IPT for patients with dysthymic disorder found that, while there was no significant difference between the effectiveness of sertraline alone and its combination with IPT, the combination treatment was associated with lower dropout rates and lower utilization of health and social services.[81]

In another study of depressed patients that compared psychotherapy with and without pharmacotherapy, the advantage of combining antidepressants with psychotherapy was equivocal. Patients appeared to favor the combined treatment, but both therapies were equally efficacious in reducing depressive symptoms.[82] The addition of family therapy to pharmacotherapy improved outcomes for patients with at least moderate depressive symptoms at hospital discharge, even though remission (16%) and improvement (29%) rates overall were quite low.[41] In summary, studies that support combining medication and psychotherapy still leave a substantial percentage of patients (40%–50%) unremitted from their illness.

***Medication switching strategies.*** A common clinical practice for patients not responding to an adequate trial of an antidepressant is to switch them to another antidepressant. A number of studies have evaluated the effectiveness of SSRIs in nonresponders to other agents. These studies enrolled 10 to 53 patients, usually in an open-label trial. Response rates ranged from 29% to 82%, with an average response rate of 54.3%.[83] Thirty to sixty percent of SSRI nonresponders may benefit from switching to a dual reuptake inhibitor such as venlafaxine[84] or bupropion.[5] Although a number of switching strategies are available,[85] none achieve remission in the majority of cases. Similar results were found in the largest study of switching strategies to date (STAR*D). Seven hundred twenty-seven depressed outpatients who had not remitted with or could not tolerate citalopram were switched, randomly, but unblinded and without a placebo control group, to other antidepressants. Remission rates in patients switched to bupropion were 21.3%; to sertraline, 17.6%; and to venlafaxine, 24.8%.[86]

***Medication augmentation strategies.*** Another common practice is to use thyroid hormone to augment an antidepressant medication when it is not completely effective. A review of comparative trials of $T_3$ augmentation in

  

refractory depression reported an average response rate of 57%.[87] Lithium augmentation in refractory depression has similar results, with a reported average response rate of 46%.[87] It is striking that in a review of augmentation strategies,[88] the response rate hovers around 50%. Another augmentation strategy is the recent trend of using atypical antipsychotic agents to augment antidepressants, particularly for patients with treatment-resistant depressions. Very few studies have tested this practice using randomized trials and meaningful numbers of subjects.[58] One double-blind study of 28 patients with randomly assigned treatments found a response rate of 60% for olanzapine augmentation of fluoxetine.[89] Another small open-label study of 8 patients also reported significant benefit for risperidone augmentation.[90] A small (N = 20) open-label study of ziprasidone augmentation found a response rate of 50% and a remission rate of 25% in the intent-to-treat analysis.[91]

A retrospective chart review of the effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmenting agents for treatment-resistant depressions found an overall response rate of 65% and no significant difference in effectiveness between any individual agent.[92]

A recent report from the STAR*D studies described depressed outpatients who had not remitted with citalopram and were randomly assigned, but unblinded and without a placebo control group, to augmentation with bupropion (N = 565) or buspirone (N = 286) for 12 weeks. Remission rates in these patients were 29.7% with bupropion augmentation and 30.1% with buspirone augmentation.[56]

***Combining antidepressants.*** Combining approved antidepressants for patients not responding to a standard course of treatment with 1 antidepressant medication has become increasingly common in spite of the lack of rigorous testing.[84] Of the 27 studies of combination therapy published, 22 were open-label trials with small sample sizes. Of the 5 randomized controlled trials combining antidepressants, 3 involved mianserin, which is not U.S. Food and Drug Administration–approved for the treatment for depression.[93]

In one recent study, 39 inpatients with nonpsychotic unipolar depression were randomly assigned to 6 weeks of treatment with fluoxetine, desipramine, or their combination. Remission rates for the combined treatment group were significantly better than with either agent alone when measured by the MADRS (53.8%), but not the HAM-D (30%–80%). In either case, 46% to 60% of the patients did not achieve remission with a combination of norepinephrine and serotonin reuptake inhibitors.[94]

***Electroconvulsive therapy.*** Electroconvulsive therapy is an effective, short-term treatment for major depressive disorder and is arguably more effective than drug therapy for many patients.[95] There is, however, limited evidence from randomized clinical trials for the efficacy of ECT in the subgroup of patients who are most likely to receive it, namely older patients or those with treatment-resistant depressions. The effectiveness of ECT in community settings is also not as high as has been reported in research studies. Prudic et al.[96] reported remission rates from 30.3% to 46.7% (response rate of 63.7%), depending on outcome criteria used, and a relapse rate of 64.3%. Sixty percent of patients with or without medication-resistant depressions responded (60% improvement in MADRS scores) to a course of bilateral ECT.[97]

***Repetitive transcranial magnetic stimulation and vagus nerve stimulation.*** Repetitive transcranial magnetic stimulation may have similar effectiveness to ECT.[98] A recent study comparing the efficacy of ECT versus rTMS for major depression reported a remission rate of 30% for each therapy and a response rate of 60% to rTMS and 55% to ECT.[99] Repetitive transcranial magnetic stimulation resulted in a 36% remission rate and a 44% response rate in patients with treatment-resistant depression.[100]

Vagus nerve stimulation has been approved as an adjunctive option for treatment-resistant depression. An open-label trial reported a 42% response rate and a 22% remission rate after 2 years.[101]

## Maintenance Treatment

Long-term maintenance treatment is recommended for those persons who have remitted or recovered from the acute phase of the depression. Most continuation and maintenance treatment studies focus only on those patients who have remitted or recovered as a result of acute phase treatments. Pharmacotherapy may be supplemented with psychotherapy or psychotherapy may be used by itself after a course of pharmacotherapy to reduce the likelihood of recurrences. Such treatments, while helpful in reducing recurrence rates in treatment-responsive patients, still do not prevent relapses in up to 40% of patients over a 1- to 2-year follow-up period.[8,102–105] Furthermore, tachyphylaxis or tolerance to the effects of the antidepressants may develop in those who do recover.[106–108]

In summary, there appears to be a ceiling effect in our ability to treat those forms of major depressive disorder that are not readily responsive to currently available treatments including augmentation, switching, and combined treatment strategies. Remission rates for these more difficult to treat forms of depression range between 25% and 50%. Although many forms of depression are amenable to the various treatment options reviewed, there may be a subtype of depression experienced by a significant minority of depressed patients (20%–40%) that is not responsive to current treatments. Continued attempts to treat these patients to remission may be demoralizing to patients and ultimately counterproductive. Table 1 presents an overview of estimated response and remission rates for the acute treatment of major depressive disorder based on the stud-

**Table 1. Estimated Efficacy of Acute Treatments for Major Depressive Disorder[a]**

| Treatment | Response (%) | Remission (%) |
|---|---|---|
| Pharmacotherapy | 50–65 | 28–47 |
| Psychotherapy | 50–58 | 30–48 |
| Combined pharmacotherapy/psychotherapy | 29–72 | 16–40 |
| Medication switching | 29–82 | 18–25 |
| Medication augmentation | 0–75 | 0–30 |
| Combining antidepressants | 27–92 | 34–40 |
| Electroconvulsive therapy | 53–80 | 27–56 |
| Repetitive transcranial magnetic stimulation | 0–57 | 0–45 |
| Vagus nerve stimulation | 31–44 | 15–27 |
| Placebo | 30–51 | 10–36 |

[a]Rates are derived from references cited in the article under the corresponding section headings. The rates are not comparable with each other, as they were not derived from the same population and the methodological rigor of the studies varied greatly.

ies reviewed in this article. These rates are not comparable to each other, as they are based on studies with different patient populations and methodologies. Nonetheless, they provide a framework for setting realistic expectations of treatment outcome.

While it is acknowledged that treatments for major depressive disorder are not sufficiently effective for many patients, this conclusion tends to be used as the basis for encouraging new trials of somatic or combination treatments in order to increase the likelihood of remission. Such options may be reasonable for those patients who want to continue to pursue more complete symptom resolution. Current evidence, however, suggests that newer treatments as well as older ones are limited in their effectiveness. Further, the course of the more severe forms of depressive illness has remained mostly unchanged despite the introduction of new treatments.[109] It may make better clinical sense, therefore, to help patients with persistent symptoms to cope more effectively with the reality of their illness even as various treatments continue. There may well be certain forms of depression that do not remit in spite of optimal treatment trials. It might be more productive and helpful to conceptualize patients with poor or incomplete response to antidepressant treatments as suffering from a chronic medical condition similar to other chronic conditions such as diabetes, arthritis, asthma, and chronic pain. Chronic disease management models are already available for many chronic medical disorders and to a degree have been adapted for some depressed patients. We suggest that for patients with persistent depression, such a disease management approach, in combination with ongoing antidepressant therapy, is the optimal treatment course.

## CHRONIC CARE AND DISEASE MANAGEMENT

Disease management models have been used successfully in the treatment of a number of chronic medical conditions including chronic fatigue syndrome,[110] diabetes,[111–113] arthritis,[114,115] chronic pain,[116,117] and asthma.[118,119] The goal of disease management with such chronic diseases is to help patients focus on their well-being in spite of their illness.[114] A sense of wellness may be achieved by fulfilling a number of tasks including pursuing medical management of the condition; maintaining, changing, or creating meaningful behaviors or roles; and dealing with the emotional sequelae of having a chronic condition.[120] Patients appear to have better outcomes when they have an active and central role in managing their illness.[111]

Self-management skills are a core component of disease management and include education, problem-solving, decision-making, cognitive symptom management (relaxation, distraction, reframing), exercising, finding and utilizing resources, forming partnerships with health care providers, and setting up and carrying out an action plan.[114,115] Self-management programs have been found to be helpful for patients with arthritis,[114] chronic pain,[121] diabetes,[122] and asthma.[119] Self-management skills can be taught in a 6-session course.[119]

An important aspect of disease management is therapy to help patients accept the reality of their condition by focusing less on symptoms and more on functioning and quality of life. Patients who received this type of acceptance and commitment therapy had fewer sick days and used fewer medical treatments, in spite of experiencing the same level of pain as, for example, patients who received treatment as usual.[116] The disease management model is also likely to be applicable to psychiatric patients who have incomplete response to currently available treatments with a variety of disorders such as schizophrenia, bipolar disorder, and anxiety disorders.[123]

### Depression Management

A variety of approaches have been proposed to support coping with persistent depressive symptoms. Even though the importance of learning to cope with depressive symptoms has been recognized for some time,[124,125] these programs still have as their ultimate goal the reduction or elimination of depression.[126] A meta-analysis of 20 studies using a psychoeducational coping format found it to be beneficial.[127] A more recent systematic review and meta-analysis of randomized controlled trials of disease management programs for depression found that these programs had a significant effect on improving depression severity, patient satisfaction, and treatment compliance.[128] Two open-label studies using this approach with patients who have unipolar, chronic, and treatment-refractory depressions have also shown improvement in symptom burden and dysfunctional attitudes.[129,130]

Enhanced sense of mastery has been found to be related to an improved sense of well-being and quality of life. In contrast, the absence of well-being may create conditions of vulnerability to future adversities. Recovery

  

from any illness is postulated to lie not just in alleviating the negative but also in engendering the positive.[67] Well-being therapy, developed from these principles, focuses on environmental mastery, personal growth, purpose in life, autonomy, self-acceptance, and positive relations with others.[63,131] Mindfulness-Based Cognitive Therapy, another preventive treatment approach, teaches patients how to "decenter" and disengage from automatic cognitive processing patterns that are linked to relapse.[103]

Disease management programs for depression have been found to be effective in increasing patients' satisfaction with treatment, improving symptoms, and improving compliance with recommendations.[126] Patients with chronic, recurrent major depression were satisfied with the care they received from their primary care physicians in spite of incomplete symptom resolution and substantial side effects from medications.[132] Patients accepted the incomplete resolution of their depression, in part due to the continuing support of their family doctor.

We are in the process of piloting an adjunctive depression management program for patients and their family members. Families are included because of evidence highlighting the importance of the family environment for the course and outcome of depression.[133,134] The family sessions are based on the McMaster approach to families.[135] The focus is on education, support, role allocation, communications, and problem solving by the family. Individual sessions use cognitive-behavioral techniques. The focus is on setting realistic expectations, coping, developing healthy lifestyle habits, improving self-awareness, becoming more active, and rediscovering meaning in one's life. Phase 1 of the program includes 6 individual sessions, 4 family sessions, and 4 telephone contacts over 16 weeks. Phase 2 includes 4 individual sessions, 2 family sessions, and 8 telephone contacts over an 8-month maintenance period. We emphasize that this is an adjunctive service and is not meant to replace ongoing treatments for depression.

### Changing Paradigms: From Symptom Elimination to Symptom Management

It may be useful for certain difficult-to-treat patients to focus less on eliminating depressive symptoms and more on learning to function better in spite of them. With a disease management model, the main thrust is to acknowledge the difficult nature of the depressive illness, to remove blame from the patient and clinician for not meeting expected response criteria, to set realistic expectations, and to help promote better psychosocial functioning even in the face of persisting symptoms. The critical element when implementing such an approach is a judicious balance between maintaining hope for improvement without setting unrealistic expectations.

A disease management model for nonresponsive depressive symptoms should include adjunctive individual interventions, family interventions, and brief telephone contacts. Telephone contacts have been found to be helpful in the follow-up management of a number of chronic conditions.[136,137] Appropriate evidence-based treatments for the treatment of depression should continue concurrently even while patients and their significant others are shown how to cope more effectively with persisting symptoms. Components of such an intervention should encompass elements found to be helpful in the management of other chronic, remitting and relapsing disorders. These include education about the etiology, course of the illness, and various treatment options; cognitive reframing, not only of negative expectations but also of unrealistic goals that may lead to premature discouragement; coping skills training; family/social support system enhancement; graded exercise and relaxation training; dietary counseling; and, for those interested, spiritual guidance.

It is important to reemphasize that a disease management model is not nihilistic. Acceptance of the reality of a chronic illness does not mean the abandonment of hope for improvement.

## CONCLUSIONS

The field of psychiatry has come a considerable distance in terms of its ability to provide many effective treatments for major depressive disorder. In our therapeutic enthusiasm and desire to provide optimal help for patients, however, we should not neglect the needs of patients for whom our current advances in treatment are insufficient. For some patients, treatment may need to be thought of as the long-term management of a recurrent or chronic disorder that may not remit.[138] The development of a therapeutic approach that focuses on coping with the chronicity of some forms of depression may prove useful for both patients and therapists. Patients can feel empowered to take a more active role in the management of their depression even while continuing to participate in concurrent treatment trials. The potential for acquiring a sense of control and effectiveness, in contrast with feelings of passivity and helplessness, may at the very least improve a patient's morale.

A treatment approach that sets realistic expectations can also be of value to therapists. Therapists may feel pressured to escalate treatment in a more and more aggressive manner in an attempt to achieve an elusive remission. Having an alternate therapeutic perspective may provide the therapist with sufficient structure and sense of helpfulness to encourage ongoing treatment trials without resorting to unproven and potentially problematic measures. The goal should be to maximize coping in such a way as to help patients accept their current reality while also fostering hopefulness. Such adjunctive disease management programs should be tested in randomized clinical

trials focusing on quality of life, interpersonal functioning, and coping skills as primary outcome goals, rather than resolution of depressive symptoms. The therapeutic challenge is to maintain a sense of hopefulness about the likelihood of improved quality of life, morale, and interpersonal relationships without setting unrealistic expectations of the elimination of symptoms.

*Drug names:* bupropion (Wellbutrin and others), buspirone (BuSpar and others), citalopram (Celexa and others), desipramine (Norpramin and others), fluoxetine (Prozac and others), olanzapine (Zyprexa), paroxetine (Paxil, Pexeva, and others), quetiapine (Seroquel), sertraline (Zoloft and others), venlafaxine (Effexor), ziprasidone (Geodon).

*Disclosure of off-label usage:* The authors of this article have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this article.

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