Management of Treatment-Resistant Depression: Psychotherapeutic Perspectives

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Treatment-resistant depression is a heterogeneous condition that occurs within a psychosocial milieu. The impact of prior pharmacologic interventions may have been adversely affected by a poor therapeutic alliance, low social support, life stress, or chronic adversity and cognitive or personality factors such as neuroticism or pessimism. This article considers the psychosocial factors that predispose to treatment-resistant depression and the psychotherapeutic principles thought to be helpful in both shorter- and longer-term treatment plans. We focus on the interpersonal, cognitive, and behavioral forms of treatment that constitute the depression-focused psychotherapies, which have been studied in major depressive disorder. Also discussed are modifications in treatment planning necessary to take into account the complexity of treatment-resistant depression.
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Treatment-resistant depression is a heterogeneous entity, defined by the lack of satisfactory clinical response to multiple treatments that should have worked, including the failure of the processes that usually result in spontaneous remission. Even without specific interventions, up to 80% of a group of depressed people will remit within 2 years. Thus, resistant depressions arise because of the futility of both specific and nonspecific therapeutic elements. Psychosocial factors are often implicated in antidepressant nonresponse.[1] The challenge for the therapist trying to help a person "stuck" in an episode of treatment-resistant depression is to identify factors that might be maintaining the depressive state and to implement alternate treatment strategies. Interventions that aim to help depressed people better cope with their manifold psychosocial difficulties therefore hold some promise for meaningful benefit, even when multiple antidepressant medications have failed. This article will review the psychosocial correlates of treatment-resistant depression and relevant cognitive, behavioral, and interpersonal treatment approaches.

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PSYCHOSOCIAL CORRELATES OF ANTIDEPRESSANT NONRESPONSE

Nonspecific elements account for between 50% and 75% of the "therapeutic activity" of an initial antidepressant trial.[2] Consequently, the failure of nonspecific therapeutic factors is an important component of treatment resistance. Placebo-expectancy response rates are highest for those with more acute, less severe, and less complex depressive disorders.[3] Factors that decrease the probability of response to a placebo-expectancy intervention include chronicity of the index episode, presence of complicating medical and psychiatric comorbidities, and higher initial levels of symptom severity.[3] A strong therapeutic alliance increases the probability of response to all types of treatment.[4] Difficulty developing such an alliance therefore is an important risk factor for treatment resistance.

The ability to adhere to treatment represents another general correlate of responsiveness. The ubiquity of nonadherence is often underappreciated by physicians, and in one series, one third of antidepressant nonresponders had not adhered to pharmacotherapy.[5] It is likely that a history of multiple prior treatment failures engenders a pessimism that further increases the likelihood of nonadherence.[1] Other factors that decrease the likelihood of response to various treatment interventions include poor social support, long-standing marital discord, and a constellation of problematic personality traits commonly referred to as "neuroticism."[1] Neuroticism refers to a stable or long-standing pattern of heightened emotional and physiologic reactivity that is associated with an increased risk of both anxiety and

depressive disorders. A closely linked set of cognitions, sometimes called "dysfunctional attitudes," that predispose the distressed person to experience excessively negative thoughts about self, world, and future also have been implicated in nonresponse to a variety of treatments.[6,7]

The interpersonal world of the depressed patient is often compromised by the additive or interactive impact of these various risk factors across months or years of persistent symptoms. For example, the consequences of adverse life events are increased by low social support and cognitive distortions or neuroticism.[1] Conversely, impaired performance in vocational and social roles resulting from a sustained depressive syndrome increases the likelihood of experiencing negative life events (e.g., being fired or demoted by the demanding boss or "cheated on" by the neglectful spouse). Although most loved ones and friends will "stand by" the depressed person, the gloomy despair, negative focus, irritability, and tendency to complain often keep significant others at a distance. Phone calls go unreturned, invitations are declined, and social gatherings are avoided. Caring others may offer what appears to be perfectly good advice, only to be told "yes . . . but," or ". . . it won't make a difference." Most would-be helpers experience this type of response as frustrating or even punishing. Eventually, even a dedicated friend may stop trying to help. It does not take months to establish such a pattern. In a study of hospitalized depressed patients, negative changes in the treating psychiatrists' verbal and nonverbal behavior were observed over the course of only 4 weeks of unsuccessful treatment.[8]

Human beings, like all other vertebrates, are "creatures of effect" in that a variety of positive reinforcers or rewards increase the likelihood of certain thoughts and behaviors. Conversely, the lack of reinforcement, or extinction, will eventually reduce the likelihood of operant (reinforcement-seeking) behavior. One correlate of a persistent, intractable dysphoria is a reduction in the depressed person's capacity to experience pleasure. Decreased hedonic capacity represents a profound liability, specifically reducing the likelihood that the intractably depressed patient will try to access the various rewards that help to make life worth living.

Since the advent of biological psychiatry there has been the tendency to view anhedonia as a consequence of an internal or endogenous dysfunction of brain function. However, sustained stress can cause an anhedonic-like state. This process is illustrated by the results of experimental studies utilizing the learned helplessness paradigm, in which the animal's hedonic capacity is measured by the willingness to work for various concentrations of sugar water. Rodents typically find a 0.7% solution of sugar water to be sufficiently rewarding to maintain a high rate of operant behavior (e.g., bar-press responses). After exposure to chronic stress, however, the rodents will not work for such moderate reinforcers and often require extremely high reinforcer concentrations.[9] Parallel changes in appetitive behavior have been demonstrated following a loss of social dominance in studies of free-ranging primates.[10] Thus, it is plausible that external stressors that result in decreased reinforcer salience may underpin the depressed person's conviction of "why bother . . . it won't make a difference."

The mental world of the depressed person is marked by preoccupation with negative memories and intrusive negative thoughts about self, world, and future as well as the loss of the subtle positive bias that enables the nondepressed person to overlook everyday life's innumerable small affronts and disappointments. Depressed mood "primes" such negative thinking, which in turn usually elicits deeper levels of dysphoria. The suffering person's sense of personal responsibility may have an excessively internal focus (guilty) and/or shift to bitter recriminations of others' conduct (hostility). In either case, there is the tendency to view problems as insurmountable and all-encompassing and to view oneself as incapable of effective problem-solving. The depressed person's sense of hopelessness thus is continually reinforced by a distorted but unshakable view of a harsh and gloomy reality.

The resulting behavioral state of diminished social activity, decreased hedonic capacity, increased solitary time, and negative cognitive focus describes the phenomenological world of treatment-resistant depression patients.[1] The perceived hopelessness should never justify therapeutic nihilism, however, and each of the characteristics described above can be operationalized as potential targets for behavioral, cognitive, or interpersonal interventions. Nevertheless, it is important for the therapist to recognize that, after numerous treatment failures, it is unlikely that there will be a rapid or dramatic response to any novel intervention except, perhaps, electroconvulsive therapy (ECT) (if the patient has never received this treatment). Such recognition may help the therapist begin to build a new therapeutic alliance with the treatment-resistant patient based on more modest, but accurate, expectations.

EVIDENCE THAT PSYCHOTHERAPY WORKS

Much of the evidence about the effectiveness of newer antidepressants comes from studies either supported by or directly conducted by the manufacturers of those medications. A large portion of these studies form the basis of a U.S. Food and Drug Administration (FDA)-mandated evaluation of safety and efficacy, which is necessary to lead to approval for use (sales) in the United States. It is the current standard for such studies to include placebo control groups. Therefore, by the time a new antidepressant is introduced to the U.S. market, there is already convincing evidence that the new treatment works, at least in comparison to placebo. Since psychotherapy is not manufactured nor protected by patents, there are no comparable corporate research and development funds to sponsor research.

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Moreover, a pill-placebo group is not an adequate control group for psychotherapy research. As a result, there will never be the weight of evidence supporting the efficacy of psychotherapy that can be marshaled for antidepressant pharmacotherapy. Nevertheless, a sizeable number of comparative studies have examined cognitive, behavioral, and interpersonal therapies in relatively uncomplicated (without severe personality problems or a large number of comorbidities) groups of depressed outpatients, and, in aggregate, 4 conclusions can be drawn (see the Depression Guideline Panel[11] or Rush and Thase[12] for detailed reviews).

First, depression-focused psychotherapies (i.e., cognitive, interpersonal, and behavioral therapies), typically provided across 8 to 16 weeks, are significantly more effective than waiting-list or minimal-contact control conditions.[11,12]

Second, depression-focused therapies typically produce response rates comparable to those found with antidepressant medications in randomized clinical trials.[11,12]

Third, there is no compelling evidence that one form of depression-focused psychotherapy is superior to another.[11] It has been suggested that cognitive therapy may have more enduring effects following termination of therapy,[12] but the 1 controlled trial directly comparing cognitive therapy and interpersonal therapy did not reveal any advantage for the cognitive therapy condition across a 24-month follow-up.[13]

Fourth, the addition of cognitive therapy or interpersonal therapy to ongoing pharmacotherapy increases the likelihood of remission for patients with chronic,[14] severe recurrent[15] or resistant,[1,16] or partially treatment-responsive[17] depressive syndromes. Treatment-resistant depression thus represents an important indication for combining psychotherapy and pharmacotherapy.

IMPLEMENTING A DEPRESSION-FOCUSED PSYCHOTHERAPY

Reviewing Past Treatment History

Although it is helpful to view a change in treatment as a fresh start, it is both foolish and disrespectful not to take into account what has been learned about a particular patient during prior treatment trials. A first order of business is to ensure that reasonable somatic treatment alternatives have not been overlooked. For example, the treatment plan should take into account that ECT, tricyclic antidepressants (TCAs), lithium augmentation, and monoamine oxidase inhibitors (MAOIs) have a better established likelihood of helping the treatment-resistant depression patient than psychotherapy.[18] This would be particularly true if the patient has pronounced melancholic (ECT or TCAs) or reverse neurovegetative (MAOIs) features.

A second goal is to elicit from the patient some appraisal of what has and has not been helpful in past treatment collaborations. Often, treatment-resistant depression patients will report that their therapist was a nice person or obviously wanted to help them, but that talking about problems just did not help. Not uncommonly, the treatment-resistant depression patient will attribute the failure to gain objective benefit despite months of work with a kind and qualified therapist as further evidence of intractable personal shortcomings ("She tried her best, but I just didn't have what it takes to make use of therapy."). If there are specific complaints (e.g., "He just didn't seem to understand" or "She didn't seem to listen to me"), it may be helpful to encourage the patient to be watchful for the same problem and to bring this up if it is happening again. Although the new therapist cannot guarantee "smooth sailing," he or she can promise to be open to feedback about the process of therapy.

Assessing Treatment Goals and Monitoring Outcomes

Many chronically depressed patients have difficulty focusing on specific problems and, instead, are overwhelmed by the totality of their difficulties. Therapists may introduce a new model of intervention by helping the patient to operationalize a problem list that, in turn, will serve as a guide to treatment.

Decreased activity and diminished participation in pleasurable or rewarding activities are almost invariant problems for the treatment-resistant depression patient. One approach to operationalization is to establish the functional relationship between variations in mood and activity level. Cognitive and behavior therapists typically use a daily activity schedule[19] to begin prospective monitoring of depressed mood (usually rated on a 1-to-10 scale) and activities, which are recorded on an hour-by-hour basis. Such an assignment can provoke the first strain on development of an effective alliance if the treatment-resistant depression patient cannot see the relevance of mood and activity monitoring. For example, patients will sometimes agree to try the assignment but will not follow through. If so, the therapist should respond nonjudgmentally and accept responsibility for assigning homework without recognizing that the patient was not ready to complete it. The therapist might then help the patient to fill out the past 24 hours on the activity schedule during the session, underscoring examples of relationships between periods of inactivity and low mood.

The therapist also can help to operationalize the signs and symptoms of the patient's depressive syndrome. More conventional paper-and-pencil assessments can be used to quantify global symptom burden and to monitor response to treatment prospectively. The most commonly used self-report measure is the Beck Depression Inventory (BDI),[20] which is heavily weighted by self-ratings for negative cognitions. The more recently introduced Inventory for Depressive Symptomatology (IDS)[21] has the advantage of more balanced coverage of the DSM-IV syndromal criteria for depressive disorders. For most treatment-resistant depression patients, regular completion of the BDI or IDS will be the first time that a clinician has regularly assessed

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the outcome of treatment. We prefer to have patients keep track of their symptom status week by week using a graph. Beyond monitoring the impact of treatment, these inventories can be used to provide details about specific symptoms that may be addressed in therapy.

Beyond documenting a global syndrome severity score, it is important to identify specific troublesome symptoms, such as insomnia, panic attacks, or generalized anxiety. These symptoms, which reflect increased central nervous system arousal as well as subjective cues of threat or dread, may warrant the use of more traditional behavioral interventions such as relaxation training or stimulus control strategies.

Although the BDI provides a fair glimpse into the patient's perceptions about self, world, and future, cognitive therapists sometimes expand assessment to include the Dysfunctional Attitude Scale[22] or the Automatic Thoughts Questionnaire.[23] These scales are strongly state-dependent, but they still can be used to provide some estimation of the relevance of cognitive distortions to the patient's problems. The stress-diathesis model suggests that the most relevant cognitive distortions are those that accompany negative events. In one study by our group,[24] patients who presented with the combination of life stress and a high level of cognitive distortion were highly responsive to cognitive therapy, whereas patients with a similar level of distortions but no recent adversity were not. The latter patient group may have been suffering from depressive ruminations, a more autonomous type of cognitive distortion associated with melancholia. Such patients may benefit from alternate behavioral strategies, such as distraction or thought-stopping.

Later in the course of therapy, cognitive therapists will use the Daily Record of Dysfunctional Thoughts form[19] to help the patient begin to evaluate the interplay between mood, behavior, and automatic negative thoughts. A variety of cognitive strategies are then used to "test" the accuracy of negative thoughts and consider more rational alternatives.[19]

We have found another self-report scale, the Inventory of Interpersonal Problems (IIP),[25] to provide a helpful description of the patient's perceived level of social support and difficulties. Not surprisingly, high scores on the IIP also may be used as proxy for Axis II pathology. The state dependence of this measure and its utility for monitoring treatment response have not yet been fully established. Nevertheless, as perceptions of one's social support system can have important prognostic implications, further study of the IIP appears worthwhile.

Interpersonal therapists use an assessment of interpersonal difficulties as a parallel strategy.[26] This assessment, typically completed during 1 or 2 sessions, links the onset and course of the depressive disorder to one or more of the following areas: unresolved grief, role transition, role disputes, and social deficits.[26] These thematic areas are sufficiently broad to apply to virtually all depressed patients, and it is not uncommon for the treatment-resistant depression patient to be "plagued" by social deficits and multiple interpersonal adversities, such as the death of a child, disability of a spouse, loss of employment, or economic decline. As in cognitive-behavioral therapy, the interpersonal therapist can next elicit feedback to reinforce the collaborative nature of treatment (e.g., "Does this description make sense to you? Can you think of anything that we've overlooked?")

Shaping the Treatment Context and Setting Reasonable Expectations

One strategic benefit of a comprehensive assessment is that it serves as the vehicle to establish a shared context for therapy. The therapist can present the results of the evaluation in a broad narrative, such as "We've found that your depression is accompanied by a substantial amount of anxiety. You also have large amounts of solitary time, which is usually filled with worry and negative thinking. Over the course of the depression, it appears that you've become more distant from your friends and loved ones. I'm also concerned that you have lost confidence in your, and your doctor's, ability to solve your problems. This has become a vicious cycle—and the worse you feel, the less you have been able to do to help yourself." This case formulation can then be translated into an operationalized problem list.

Once a shared case formulation is established, the model of treatment is presented in a manner tailored to the patient's problem list. It is useful to provide a realistic estimate of the duration of treatment and the likelihood of benefit. ("Based on past experiences, I think that there's at least a 50:50 chance that this therapy can make a significant difference. Of course, the results of treatment research studies do not directly tell us about your chances, but most studies do find 40% to 60% response rates, even for chronic depression. I would like to recommend that we agree to a 12-week contract to work together, which should give the therapy a fair chance to help. Together, we'll keep track of your progress, and if it's not helping, we will make changes. How do you feel about giving it a chance?")

Psychoeducation

One commonality of the depression-focused psychotherapies is the use of explicit patient education about depression and its various risk factors and treatments. This strategy is called psychoeducation. Once the initial expectations for treatment are established, psychoeducation may also address the nature of treatment resistance. We prefer to use a combination of the medical or illness model to help to normalize the patient's condition and the rehabilitation model to convey the progressive and pragmatic nature of the intervention.[1] Most patients will know of someone who has benefited from physical therapy after a knee or back injury, so this metaphor has some general appeal. Moreover, the findings of recent neuroimaging studies can be

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utilized to illustrate how depression alters brain metabolism and the activity of the "circuitry" that underpins emotional expression. Thus, the preoccupation with negative thinking can be linked to increased paralimbic blood flow, and difficulty initiating action or following through with demanding tasks can be attributed to decreased metabolism in the dorsolateral prefrontal cortex. In this way, the activities of therapy are presented as methods that help to compensate for, or cope with, alterations in brain function.

Having established the relevance of a rehabilitation model of intervention, some final guidelines of therapy can be introduced (Table 1). To summarize, these include the following: therapy will involve homework, the impact of therapy on symptoms will be monitored, no aspect of therapy is intended to be too hard or demanding, change may be slow, and things could get frustrating. A final assumption is that when change is too slow or not possible, acceptance of disability may have liberating effects.

Table 1. Suggested Guidelines for Psychotherapeutic Intervention for Treatment-Resistant Depression[a]

The therapy relationship should be collaborative and centered around the goal of teaching new skills to improve coping with a chronic illness. The therapist must pair core therapeutic skills (eg, empathy and understanding) with the ability to appropriately select specific, targeted interventions (eg, relaxation training, activity scheduling, problem-solving, or cognitive restructuring).
The therapist may make judicious use of examples from other medical models in which rehabilitative interventions are used to enhance the outcome of a chronic disorder (eg, poststroke rehabilitation, pain management, or orthopedic rehabilitation).
The therapist may express cautious optimism that problems can be addressed with varying degrees of success. However, it is important to be understanding of the patient's pessimism and elicit feedback from the patient about what has not worked well in the past.
Establish stepwise, short-term goals specifically addressing life problems and/or symptoms. Use graded tasks or intermediate assignments to approach more daunting or potentially overwhelming problems.
Meet frequently and, if necessary, shorten sessions to enhance learning and retention. Keep sessions active and avoid the "silent treatment." Obtain feedback at beginning and end of treatment sessions so that patient's reactions to therapy can be monitored and promptly addressed. Be vigilant concerning subtle affective and behavioral reactions within sessions as an in vivo source of feedback.
Use homework assignments and in-session rehearsal to facilitate development of new coping skills. It is important to avoid implicit criticisms about difficulties in therapy, such as homework noncompliance. The therapist must address his or her own dysfunctional cognitions blaming the patient for "not wanting to get better."
Involve spouse or significant others to provide psychoeducation and enhance alliance with family members.
Establish intermediate and long-term goals as symptomatic improvement and short-term goals are accomplished.
Do not terminate therapy until the patient has achieved a remission and sustained it for at least 4 to 6 months.

[a]Reprinted, with permission, from Thase and Howland.[1]

Critical Therapist Skills

Therapists working with treatment-resistant depression patients need to be more active within sessions than traditional therapists, and they must assume a more directive posture. At times, the effective therapist will use the same skills as competent coaches and personal trainers.[1] However, such a directive stance must not come at the expense of the core qualities of empathy, respect, and genuineness. Not uncommonly, a novice therapist learning a depression-focused psychotherapy will put the techniques ahead of therapeutic alliance, to the detriment of the working relationship.

One essential directive skill is the ability to maintain control of the pacing and time management of each individual session. This can be accomplished by setting a pattern or agenda from the initial sessions onward. In cognitive therapy, the agenda includes (1) a weekly status report, (2) review of homework, (3) 1 or 2 "modules" of therapeutic activity, (4) feedback, and (5) a new homework assignment.

Some depressed people with extensive prior experience in therapy may find a more directive therapist or imposition of such structure to be disquieting or even aggravating. They may be used to therapy as the place to be comforted by the opportunity to ventilate and have an implicit "contract" that the therapist will permit them to speak at length about their disappointments and grievances. It is the therapist's job to recognize this unspoken violation of expectations and to use the opportunity to engage the patient in a dialogue about the collaborative nature of therapy. The therapist might introduce the problem as follows: "There seems to be some tension between us right now, like we're competing for air-time. Have you noticed it too?" This should open the door to a frank discussion of what was helpful and not helpful about the past therapies. The new therapist should acknowledge the value of traditional therapies and validate that it is not easy to change therapists. Nevertheless, the change in therapy approaches also can represent a new opportunity for overcoming the depression. During this interchange the therapist has the opportunity to demonstrate openness to the patient's concerns, as well as respect for the patient's point of view. The exchange might also elicit negative cognitions, such as "How can she understand my problems if I can't tell my story in detail?" or "Dr. B will never be able to understand me the way that Dr. A did."

Another important issue centers around the widespread belief that depression involves aggression turned inward and that an effective therapy must help the patient "get to the bottom" of the problem. Again, the rehabilitative model can be invoked to illustrate that therapies do not have to address a core problem directly to have beneficial results. If it is clear that there are profound early traumas or long-standing and complex issues with caregivers that continue to trouble the patient, the therapist can suggest that such long-standing difficulties may be better dealt with from a position of greater strength, once the patient has begun to gain greater mastery over the depressive symptoms. Importantly, the goal is not to minimize the patient's issues but,

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rather, to present an alternate hypothesis, namely, that helping is not synonymous with uncovering.

As noted earlier, therapists also need to avoid the trap of becoming too focused on techniques and strategies. Cognitive interventions, for example, have some risk of provoking the perception of criticism (i.e., the patient may hear the therapist saying something like "Your thinking is distorted"). This is a particularly common problem for patients with early-onset, chronic depressions, who often have high, trait-like levels of interpersonal sensitivity. In this context, a brilliant interpretation intended to clarify that the patient had distorted thoughts about the therapist's intentions, however accurate, is usually less helpful than a simple refocus on the collaborative nature of therapy. The therapist's use of humor, while potentially endearing or disarming, can similarly elicit cognitions about being mocked or ridiculed. Sometimes there is no substitute for humility and a sincere apology ("I'm sorry—I'm concerned that I've unintentionally offended you with something that I've said. Would you mind sharing with me your thoughts about what's going on between us, right now?").

Involving Significant Others

Having caring loved ones or friends is a major asset. Moreover, significant others not uncommonly feel left out of their loved one's therapy and, perhaps, may be concerned that they are being villainized in the process. Inviting the significant others to participate in the psychoeducation, providing educational videos or pamphlets, and, on occasion, even enlisting significant others to help with homework assignments as co-therapists are reasonable methods to enhance social support.

Enhancing Medication Adherence

When past nonadherence has been identified as a potential problem, it is a legitimate use of therapy time to address medication-taking behavior. Perhaps surprisingly, this could begin by asking the patient to list the advantages or "pros" of not taking one's medication. Commonly listed advantages include the perceived freedom of not having to remember to take medication, the notion that taking medication reinforces the sense of being ill, and relief of annoying medication-related side effects.[27]

It is useful for the therapist to accept that nonadherence is essentially a normal behavior. From this perspective, adherence is viewed as a newly learned skill or one that is influenced by positive reinforcement, response inducements (such as the simplicity of the medication schedule or the convenience of the medication bottle[s], i.e., next to one's toothbrush), or prompts (a wristwatch alarm).

Nonadherent acts also can be directly linked to effectively laden cognitions. Not taking one's medication can be an indirectly punitive act ("I'll show you..."), as well as a provocative test ("Let's see if he/she is really keeping track of this"). Obviously, the more complex the patient's past history with various caregivers, the greater the likelihood that the act of taking medication will have additional (and often unspoken) meanings.

Managing the Course of Therapy

The depression-focused psychotherapies are conducted in both individual and group formats and typically range from 10 to 16 weeks in duration. Individual sessions are typically 45 to 60 minutes in length, whereas group sessions are usually 90 to 120 minutes long. Ideally, we would recommend twice-weekly sessions early on to facilitate the process of therapy. Perhaps even more frequent sessions would be helpful,[28] but economic considerations usually make this impossible. We prefer to continue with twice-weekly sessions until the patient has achieved at least a 50% reduction in symptom severity, shifting to weekly sessions thereafter. If the patient has not obtained significant symptom relief by the eighth week (i.e., 16th session), a careful evaluation of the continued indications for psychotherapy, as well as possible alternatives, should be undertaken.

In our experience, a successful course of acute-phase, focused psychotherapy for treatment-resistant depression typically lasts 4 to 6 months. It appears that patients who do not remit fully may benefit from less frequent, continuation-phase sessions over the next 6 to 9 months.[29] The utility of this longer-term model of preventive treatment will be further tested in the National Institute of Mental Health (NIMH)-funded nationwide study of treatment-resistant depression, known as Sequenced Treatment Alternatives to Relieve Depression (STAR*D).[30]

SUMMARY

The newer depression-focused psychotherapies are relevant and potentially valuable strategies for patients with treatment-resistant depression. Although there are virtually no well-controlled studies of cognitive, behavioral, and interpersonal strategies of treatment-resistant depression, a systematic approach to operationalizing problems, defining short-term goals, enhancing self-management of symptoms such as anxiety and insomnia, and improving interpersonal problem-solving skills has great promise to complement and enhance the wide variety of pharmacotherapy strategies for treatment-resistant depression.

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

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