

# Cognitive-Behavioral Therapy for the Treatment of Anxiety Disorders

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In this article, we consider the evidence supporting the range of applications of cognitive-behavioral therapy (CBT) for anxiety disorders, and we examine some of the complex issues encountered for the combination of pharmacologic and cognitive-behavioral treatment strategies. The available evidence supports CBT as an effective first-line treatment for anxiety disorders offering longer-term maintenance of treatment gains. There is also evidence that CBT is an effective strategy for pharmacotherapy nonresponders, a replacement strategy for patients who wish to discontinue their medications, and a standard strategy for pharmacotherapy patients who need to boost their treatment response. Relative to combination therapy, we review some of the conditions that may influence the longevity of treatment gains from CBT.  
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There is consistent evidence that cognitive-behavioral therapy (CBT) is an effective first-line strategy for the treatment of anxiety disorders. There is also evidence, particularly for the treatment of panic disorder, that CBT is an effective strategy for pharmacotherapy nonresponders, a replacement strategy for patients who wish to discontinue their medications, and a standard strategy for pharmacotherapy patients who need to boost their treatment response. In this article, we consider each of these applications of CBT and discuss some of the complex issues that are encountered for the combination of pharmacologic and cognitive-behavioral treatment strategies. Prior to considering these roles, however, it is important to first consider the nature of CBT interventions.

For the pharmacologic treatment of anxiety disorders, there is ample evidence that patients can improve on treatment with selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, benzodiazepines, and monoamine oxidase inhibitors.<sup>1,2</sup> These medications most likely exert their action by attenuating the anxiety elicited by the feared cues associated with each disorder (e.g., social interactions for patients with social anxiety disorder<sup>3</sup>), but in many cases, this attenuation of anxiety lasts only as long as medication is continued. With medication discontinuation, relapse is common (e.g., results in panic disorder<sup>2,4,5</sup>), al-

though relapse rates are reduced when treatment is maintained for a longer period before discontinuation.<sup>6</sup>

In contrast to pharmacotherapy, CBT is focused directly on eliminating exaggerated fears and the avoidance responses that help maintain anxiety disorders. In exposure-based procedures, patients repeatedly confront feared stimuli under controlled conditions, with the goal of dissipating (extinguishing) fears as patients acquire a sense of safety in the presence of these stimuli. The exact stimuli used depend on the disorder under treatment, and with specialization of protocols for each anxiety disorder, interventions are based on specific models of the core fears, avoidance behaviors, and cognitive biases thought to maintain each disorder. For example, models of panic disorder tend to emphasize the role of core fears of the somatic sensations of anxiety in motivating anticipatory anxiety, escalation of panic, and agoraphobic avoidance.<sup>7,8</sup> In contrast, models of social phobia focus on core fears of negative evaluation by others and the cognitive biases and avoidance patterns that prevent disconfirmation of these fears.<sup>9,10</sup> Obsessive-compulsive disorder (OCD) is defined by idiosyncratic fears (e.g., of contamination, harming others) that are linked to repetitive attempts to manage or “neutralize” these fears—the obsessions and compulsions that define the topography of the disorder.<sup>11</sup>

Despite differences in the models for each anxiety disorder, cognitive-behavioral treatments for these disorders have in common systematic attempts to provide conditions where patients can relearn a sense of safety in relation to feared cues. Some of this learning is engendered with psychoeducational interventions that provide patients with a new model for interpreting their ongoing anxiety experiences. Cognitive-restructuring interventions further this aim by helping patients learn to reevaluate their automatic assumptions about their fears. These interventions are

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hastened by a variety of self-monitoring and logical-evaluation exercises that encourage patients to test the accuracy of their assumptions in relation to ongoing experiences. Testing of assumptions also occurs as part of exposure interventions, which are used to help patients systematically relearn safety based on their own prospective experiences with their feared cues. For example, in panic disorder, treatment includes education about the source and nature of anxiety and panic symptoms, as well as the role of avoidance in maintaining fears and increasing disability.<sup>12</sup> Cognitive-restructuring interventions are aimed at helping patients eliminate catastrophic thoughts (e.g., “I will faint,” “What if I lose control?”) that intensify anxiety, with particular attention to the tendency to overestimate the probability of negative outcomes, or the degree of catastrophe should these outcomes occur.

Exposure interventions provide patients with direct experiences to relearn safety in response to phobic cues by giving the patients opportunities to allow anxiety to dissipate through repeated controlled contacts with feared stimuli. For example, in the treatment of panic disorder, exposure includes both programmed experiences with the induction of feared bodily sensations (“interoceptive exposure,” e.g., hyperventilation, may be used to induce dizziness, numbness, tingling, hot flushes, and derealization) and *in vivo* exposure to feared situations when agoraphobic avoidance is present. Although anxiety reduction techniques such as relaxation training were once central to treatment efforts for a variety of disorders, they are now less routinely applied to disorders other than generalized anxiety disorder (GAD).<sup>13</sup>

### FACTORS INFLUENCING EXPOSURE OUTCOME

One of the notable features of CBT for the anxiety disorders is that it appears to have relatively strong maintenance of treatment gains,<sup>14–18</sup> although it is clear that additional strategies for relapse prevention are needed.<sup>19</sup> We have suggested that these strengths may be due to the systematic “unlearning” of fears and avoidance behaviors.<sup>3</sup> Accordingly, it is important to consider some of the factors influencing the durability of extinction learning that results from exposure-based treatments.

Advances in the animal laboratory have documented that extinction learning resulting from exposure is far from a passive process. Instead, it appears to be an active learning of a new meaning (“relative safety”) in relation to the original fear cue. The durability of this new learning depends on the context in which it is learned; after extinction training, memories of the original fear learning and the extinction learning appear to be in competition, with the dominant memory being determined by context. For example, Bouton and associates (for a review, see Bouton<sup>20</sup>) have provided compelling evidence that return of fear is likely when that fear was learned in context A, extinguished

in context B (e.g., a different cage or a scented room), and then reassessed in context A or in a brand new context, i.e., context C. In short, the durability of exposure-based learning appears to be dependent on the degree to which the “safety” learning is cued by subsequent stimuli. To create especially durable safety learning (resistance to relapse), efforts need to be devoted to enhancing the salience of learning during exposure.

Recent research has documented that extinction learning in humans appears to parallel findings from the animal laboratory. Specifically, Mystkowski and colleagues<sup>21–23</sup> demonstrated that return of fear following initial response to exposure treatment for spiders is more likely to occur when follow-up assessment occurs in a context different from the one in which subjects received treatment.

Moreover, there is increasing evidence that the success of exposure-based procedures is dependent on helping patients construct clear and unambiguous tests of fearful assumptions. For example, instruction to patients to direct attention to what is objectively occurring during exposure to phobic situations<sup>24</sup> and inhibition of the use of maladaptive coping behaviors (termed “safety behaviors”) enhance exposure outcome.<sup>25,26</sup> The notion of safety behaviors deserves additional comment. Wells et al.<sup>25</sup> raised the important question of why many socially phobic individuals do not improve from the social situations that they do attend (complete avoidance of social situations is rare). They assessed socially phobic patients and documented the wide use of subtle avoidance or coping behaviors designed to help them endure social events. The utilization of these safety behaviors (e.g., holding on to things, walking close to walls, and avoiding eye contact with others) appeared to inhibit learning of true safety in exposure (the individual believes, e.g., “I ‘survived’, but only because I averted my eyes”). Salkovskis et al.<sup>27</sup> replicated these findings in a panic disorder sample and found greater fear decline in patients who were encouraged to inhibit safety behaviors during an exposure session compared with patients who continued to use these behaviors.

Furthermore, recent evidence suggests that clinicians should encourage their patients to discard not only the use of safety behaviors but also their availability. Powers et al.<sup>28</sup> observed a 94% response rate for claustrophobic individuals who underwent exposure treatment to a small chamber with no safety behavior utilization. They found significantly lower response rates for those instructed to use safety behaviors during exposure (e.g., opening a small window to allow access to fresh air blown in by a small fan) and those who had these options available but were encouraged not to use them (response rates, 44% and 45%, respectively).

Distraction is another factor that may decrease the degree of safety learning from exposure.<sup>29</sup> For example, Telch and colleagues highlighted the negative effect of distraction in 2 recent studies in which they showed that claustrophobic persons who were instructed to engage in a

cognitive-load task during exposure showed significantly less fear decline compared with those who received the same duration of exposure without the distracting cognitive-load task (reference 30 and M. J. Telch, Ph.D.; D. V. Valentiner, Ph.D.; D. Ilai, Ph.D., et al., manuscript submitted).

Summarizing a cognitive perspective on maximizing learning from exposure, Wells et al.<sup>25</sup> recommended active elucidation of patients' feared catastrophes and the perceived likelihood of these catastrophes, identification of safety behaviors linked to catastrophic fears, construction of the exposure in a manner that allows testing and disconfirmation of feared catastrophes, elimination (or reversal) of safety behaviors during exposure, and active processing (discussion) of what was learned from the exposure. In addition, research on contexts underscores the importance of varying the context of exposure procedures to provide durable learning of safety in response to feared cues.<sup>20</sup>

## COMBINING COGNITIVE-BEHAVIORAL THERAPY AND PHARMACOTHERAPY

### Acute Outcome Findings

The efficacy of short-term CBT is reflected by a wealth of studies from the last several decades. Much of this research is summarized in a series of meta-analytic reviews that describe the strength of CBT interventions relative to an alternative treatment, most notably pharmacotherapy.<sup>31-36</sup> These studies provide consistent evidence that CBT offers equivalent efficacy to medications, with evidence for superiority over medications that ranges from a subtle edge for panic disorder<sup>33</sup> to more pronounced effects for the treatment of posttraumatic stress disorder (PTSD).<sup>35</sup>

However, the conclusions brought by meta-analytic reviews are necessarily broad and can raise questions about the equivalence of patients seen across studies. Are the patients randomized in CBT studies the same as those randomized in pharmacotherapy studies, so that it is fair to compare the results across studies? Moreover, what about the allegiance effects that are not uncommon in the field, in which results in a trial appear to be influenced by the treatment under study most favored by the investigators (for examples in the treatment of depression, see references 37 and 38)? Fortunately, these challenges to meta-analytic results are nicely addressed by large-scale studies, often using multiple sites (some specializing in CBT and some in pharmacotherapy) and randomly assigning the same cohorts of patients to either modality of treatment. These large studies have in general reflected the broader conclusions offered by meta-analytic reviews. CBT tends to be found to be as effective as medication at acute outcome assessments, with differences between active treatments often not reaching significance but sometimes showing a subtle edge for CBT as reflected by studies of panic disorder,<sup>14</sup> GAD,<sup>39</sup>

and OCD<sup>40</sup> and sometimes showing a subtle advantage for pharmacotherapy as reflected by the Heimberg et al.<sup>41</sup> multicenter study of social phobia.

A number of these studies are also noteworthy for providing a perspective on the additive value of combined pharmacotherapy and CBT. Overall, it appears that the addition of programmed exposure can extend pharmacologic treatment gains for a variety of disorders, but there is less evidence for the advantage of adding pharmacologic treatment to comprehensive cognitive-behavioral programs.<sup>42</sup> For example, in a study of panic disorder, Barlow et al.<sup>14</sup> compared the efficacy of CBT, imipramine, and their combination in a large sample (N = 312) of panic disorder patients at 4 sites. Patients were randomly assigned to receive CBT, imipramine, imipramine plus CBT, CBT plus placebo, or pill placebo. Treatment outcome was assessed at 3 different stages (12 weeks of acute treatment, 6-month treatment continuation phase, and 6-month treatment-free follow-up). All 4 active treatments resulted in marked acute improvements that were significantly greater than those observed for the pill-placebo condition. No differences were observed between imipramine and CBT. The combination treatment did outperform CBT on several measures, but failed to outperform CBT plus placebo, indicating that the increased efficacy of adding imipramine to CBT at the acute treatment outcome was accounted for by the nonspecific effects associated with pill taking.

Power et al.<sup>40</sup> observed a similar pattern of findings in a treatment comparison study of GAD. They randomly assigned 113 patients to placebo, diazepam, CBT, CBT plus diazepam, or CBT plus placebo. The CBT-plus-diazepam condition showed greater pretreatment-to-posttreatment changes on the Hamilton Rating Scale for Anxiety<sup>43</sup> compared with diazepam alone, but did not outperform the CBT-alone condition. However, response rates revealed only an advantage of active treatment over placebo, with no differences among the active treatment conditions. Examination of the response rates at 6-month follow-up mirrored the results at posttreatment. Specifically, there was no significant advantage of combined treatment with CBT plus diazepam compared with CBT alone, although CBT (offered alone or in combination) appeared superior to diazepam alone.

For the treatment of OCD, Franklin and colleagues<sup>39</sup> randomly assigned 122 OCD patients to clomipramine, exposure with response prevention (ERP), clomipramine plus ERP, or pill placebo. The treatment phase lasted 12 weeks, with a 6-month, no-treatment follow-up. At posttreatment, all active treatments outperformed placebo. In addition, ERP, either alone or in combination with clomipramine, was associated with a more favorable acute response compared with clomipramine alone and placebo. However, there was no advantage of the combination treatment over ERP alone. Again, the findings at 6-month follow-up mirrored those at posttreatment.

Similar findings were reported by van Balkom et al.<sup>44</sup> and Cottraux et al.,<sup>45</sup> as both studies reported no advantage of combination treatment for OCD. However, more promising findings were reported by Hohagen et al.<sup>46</sup> They randomly assigned 58 patients to receive either ERP plus fluvoxamine or ERP plus placebo. The treatment phase lasted 8 weeks, and assessment was conducted at posttreatment only. Analyses of response rates at posttreatment revealed an advantage of ERP plus fluvoxamine over ERP plus placebo.

Evidence for combination treatment in social phobia is limited to a trial conducted in a primary care setting that provided only limited evidence for an advantage for combined treatment.<sup>47</sup> This study, however, was marked by much more subtle effects for exposure therapy than are typical in the literature.<sup>32</sup>

### Issues in Combined Treatment

Emerging evidence has been reported for possible deleterious effects of combination treatment strategies, once medications are discontinued. The strongest evidence for this effect comes from the treatment of panic disorder and is informed by 2 large-scale studies, one investigating imipramine treatment<sup>14</sup> and one investigating alprazolam treatment.<sup>48</sup> In both of these studies, there was evidence that once medication was withdrawn, not only were advantages of combined treatment lost, but outcome tended to suffer relative to CBT alone. There is also recent evidence for a similar effect in the treatment of social phobia. Haug et al.<sup>49</sup> examined the longer-term outcome of patients in the Blomhoff et al.<sup>47</sup> trial. Over time, medication discontinuation was common, and over the follow-up interval, the combined treatment condition lost its advantage so that it was no longer distinguishable from CBT alone. The loss of treatment maintenance effects with combined treatment is especially worthy of concern because it is the longer-term maintenance of treatment gains that gives CBT a particular cost-benefit advantage relative to medication.<sup>32,33,50</sup>

To understand the potential nature of longer-term deleterious effects of combined treatment, it is helpful to return to the consideration of extinction context effects, this time focusing on the role of internal cues. As noted, research suggests that "safety learning" from exposure procedures (extinction) is dependent on the context of the learning. These findings also extend to internal cues such as drug or emotional state. As demonstrated in the animal laboratory, changes in internal state (such as anxiety reduction from a benzodiazepine) appear to be a powerful enough context that adequate safety learning from exposure (extinction) is achieved only in that context.<sup>51</sup> When the internal drug state is changed, return of fear is more likely.

This effect was recently demonstrated in humans in the treatment of fears of spiders.<sup>23</sup> Internal state was manipulated by the blind ingestion of either caffeine or placebo, and fear reduction was tested under congruent (caffeine extinction and caffeine testing or placebo extinction and placebo

testing) and incongruent (caffeine extinction and placebo testing or the reverse) conditions. Exposure treatment was effective, and no difference between conditions was evident immediately at posttreatment. However, follow-up testing 1 week later revealed that patients tested under the incongruent condition had greater return of fear. Again, these results are consistent with animal studies; return of fear was more likely when the internal state was changed between exposure (extinction) training and later assessment.

Inspection of the studies by Barlow et al.,<sup>14</sup> Marks et al.,<sup>48</sup> and Haug et al.<sup>49</sup> reveals results fully in line with extinction studies. As compared with the durability of treatment effects in CBT alone, loss of efficacy was greater when patients originally received CBT in the context of medication treatment and then later discontinued medication treatment. It is important to note that these effects were far more evident in the studies by Barlow et al.<sup>14</sup> and Marks et al.,<sup>48</sup> and it is possible that discontinuation-related symptoms from medication taper may have hastened relapse, i.e., patients were confronted by both a change in medication context and the possible emergence of medication taper symptoms. In addition, it is not clear whether these effects play a greater role in panic disorder and social phobia; interference effects were not evident in studies of OCD,<sup>45</sup> but many of these patients continued taking medications and therefore context effects may have been attenuated.

### Additional Strategies for Combination Treatment

Fortunately, there is evidence that some of the beneficial effects of CBT on long-term course can be maintained if CBT is reinstated or ongoing at the time of medication discontinuation and thereafter. This evidence comes primarily from studies of the application of CBT to benzodiazepine discontinuation difficulties. Discontinuation of benzodiazepine treatment of panic disorder has been linked with symptoms as severe as or more severe than those pretreatment, and discontinuation failure is common.<sup>5,52</sup> Benzodiazepine discontinuation appears to expose patients to taper-emergent withdrawal symptoms as well as the re-emergence of panic disorder. These events appear to occur in patients who have a high degree of fear of the associated somatic sensations and who are particularly vigilant to the possible return of symptoms.<sup>53</sup> Given this model, CBT that focuses on interoceptive exposure combined with cognitive restructuring has the potential to (1) decrease conditioned fears of somatic sensations and the tendency to catastrophically misinterpret these sensations, (2) provide patients with coping skills for managing the severity of panic sensations, and (3) provide patients with skills for minimizing withdrawal symptoms.<sup>53</sup>

Accordingly, we emphasized these treatment goals in the application of CBT to benzodiazepine discontinuation difficulties. In a sample of 33 outpatients with panic disorder who had been treated with high-potency benzo-

diazepines (alprazolam or clonazepam) for a minimum of 6 months, we examined the efficacy of 2 taper conditions: a slow-taper condition with physician support and a slow-taper condition with support plus 10 sessions of group CBT.<sup>54</sup> Patients undergoing the slow taper-alone program showed a high rate (75%) of discontinuation failure, as compared with a 24% failure rate among patients receiving adjunctive CBT. Moreover, patients successfully discontinuing benzodiazepines had lower levels of distress than they did prior to taper, and most patients in the CBT program (77%) remained benzodiazepine free at 3-month postdiscontinuation follow-up.

This initial report was followed by 2 additional trials. Hegel et al.<sup>55</sup> reported the success of CBT in an open trial of patients initially treated with or switched to a panic suppression dose of alprazolam. After a 2-week panic-free stabilization period, patients began a 12-week CBT program modeled after that of Barlow and Craske,<sup>12</sup> and then at week 4 of treatment began to taper their alprazolam medication. Three patients were lost to follow-up; of the remaining patients, 80% were able to discontinue their benzodiazepine medication and 76% were panic free at the end of the treatment period. These results were maintained over time, with 85% of the sample panic free at a 12-month follow-up evaluation (80% remained off alprazolam).

Similar results were reported by Spiegel et al.<sup>56</sup> in a randomized trial of patients first treated with a panic-suppressing dose of alprazolam, then randomized to a very slow taper program alone or a taper program combined with 12 weeks of CBT. Consistent with findings indicating that a very gradual taper program can enhance acute taper success,<sup>57,58</sup> 80% of the taper-alone group and 90% of the taper plus CBT group achieved alprazolam discontinuation. However, dramatic effects were obtained over a 6-month follow-up period; during this time, only half of the subjects in the taper-alone group were able to stay alprazolam free, compared with all of the patients who received the CBT program.

Additional study has extended this application of CBT to SSRI discontinuation. In a case series, Whittal and associates<sup>59</sup> documented improved clinical outcome in conjunction with a successful SSRI discontinuation in the context of a brief program of group CBT; these outcomes were maintained at a 3-month follow-up assessment. Likewise, in a small randomized trial, Schmidt and associates<sup>60</sup> reported dramatic improvement, with over 75% of patients meeting criteria for high endstate functioning, in patients who failed to respond fully to SSRI treatment, with no significant difference in outcome between patients who were randomly assigned to maintain or discontinue their SSRIs during the course of CBT.

In sum, studies of medication discontinuation in patients with panic disorder provide a model for improving longer-term outcome for combination treatment. When CBT is continued during the course of taper and the medication-

free period that follows, there is evidence of continued maintenance of treatment gains. Hence, CBT should be considered for initial application or reinstatement when patients are considering medication discontinuation. This issue is particularly important given the high rates of medication noncompliance that have been documented for the affective disorders.<sup>61-63</sup>

### **Inadequate Response to Pharmacotherapy**

CBT also can be used successfully for patients who have failed to respond adequately to pharmacotherapy. In 2 open studies of patients with panic disorder,<sup>64,65</sup> we found benefit for brief CBT applied to patients who had failed adequate previous trials of medication. In addition, in a small pilot study of the application of CBT to PTSD in a refugee population, we found that CBT offered significant benefit to patients who had failed to respond to a combination of SSRI and benzodiazepine treatment.<sup>66</sup> It is important to note that there is also evidence that patients with panic disorder who fail to respond to CBT can achieve benefit from medications,<sup>67</sup> although there are suggestions that these patients may also benefit from continued CBT.<sup>68</sup>

## **ISSUES IN THE APPLICATION OF CBT**

### **Psychiatric Comorbidity**

A number of studies suggest that CBT is effective despite the presence of comorbid major depression. For example, during treatment of panic disorder,<sup>69,70</sup> and possibly PTSD,<sup>71,72</sup> patients with comorbid depression appear to improve at rates similar to those of their nondepressed counterparts. Treatment of OCD in patients with comorbid depression leads to significant benefit, albeit at a lower magnitude than for less depressed patients with OCD.<sup>73,74</sup> There is also some evidence that comorbid depression improves with treatment of anxiety conditions.<sup>18,75,76</sup> However, in some<sup>77</sup> but not all<sup>78</sup> cases, additional CBT interventions may be necessary for treatment of depression.

Improvements also appear to extend to other comorbid conditions. For example, in a study of a 16-session protocol for treatment of panic disorder, Tsao et al.<sup>70</sup> found generalization of benefit to associated conditions (depression, GAD, and specific phobia, but not social phobia) so that comorbid diagnoses fell from 60.8% at pretreatment to 37.3% at posttreatment, with maintenance of these effects during 6-month follow-up. Similar results have been reported for benefit to comorbid conditions in the cognitive-behavioral treatment of GAD.<sup>79</sup>

### **Treatment Acceptability and Effectiveness**

In bridging the gap between success in clinical trials and success in treatment in the community, issues of treatment acceptability, tolerability, transportability, and affordability become paramount. Each of these issues will be considered in turn.

**Table 1. Dropout Rates in Controlled Trials as Represented by Mean Percentages in Meta-Analytic Reviews**

Disorder	Dropout Rate (%)
Generalized anxiety disorder <sup>34</sup>	
CBT	10.6
Benzodiazepines	13.1
Antidepressants	33.5
Social anxiety disorder <sup>32</sup>	
CBT	10.7
Benzodiazepines	12.0
Antidepressants	10.3
Panic disorder <sup>33,36</sup>	
CBT	5.6
Benzodiazepines	13.1
Non-SSRI antidepressants	25.4
SSRIs	19.9
Obsessive-compulsive disorder <sup>31</sup>	
CBT	16.7
Antidepressants	20.5
Posttraumatic stress disorder <sup>35</sup>	
CBT	19.0
Pharmacotherapy	38.0

Abbreviations: CBT = cognitive-behavioral therapy, SSRI = selective serotonin reuptake inhibitor.

There is evidence that CBT is an acceptable treatment as judged by patient preference. For example, Hofmann et al.<sup>80</sup> examined reasons potential participants refused randomization in a large multicenter trial of panic disorder conducted at sites known for their specialization in CBT or pharmacotherapy. Whereas 34% of the individuals refused participation due to concerns over imipramine treatment, less than 1% refused participation due to concerns about CBT. Examination of treatment preference among clinical patients presenting for treatment at an anxiety disorders program also supports the notion that CBT compares well to pharmacotherapy for treatment preference, with evidence of approximately equal rates of preference of CBT and pharmacotherapy.<sup>81</sup>

Perspectives on treatment tolerability are informed by studies of dropout and patient preference. Dropout rates in controlled clinical trials provide an index of the potential acceptability and tolerability of treatments offered. As summarized in Table 1, results of meta-analytic studies suggest that CBT is easily as tolerable as medication alternatives; that is, once patients opt to be treated in a clinical trial, the likelihood of successful delivery of CBT is high. Part of the tolerability of CBT may come from its relatively quick onset of initial beneficial effects, well within the time frame of antidepressant treatments for panic. For example, studies of CBT for panic disorder indicate improvements as early as the second session, with evidence of incremental improvement thereafter.<sup>82</sup>

With evidence that CBT for anxiety disorders is both an acceptable and tolerable treatment, questions arise regarding whether the treatments utilized in research settings can be transported successfully to community settings. Recent benchmarking studies, in which treatment effects observed

in clinical practice were compared with the effects observed in randomized controlled clinical trials, suggest they can. For example, Wade and colleagues<sup>83,84</sup> found comparable short-term and long-term response rates for a 15-session CBT protocol for panic disorder in a community mental health center. Similarly, Lincoln et al.<sup>85</sup> examined outcomes for 217 unselected patients with social phobia who were treated by 57 therapists in 4 clinics. Posttreatment results for this sample were comparable to those found in controlled efficacy studies.

The utility of a treatment is also determined by its cost-effectiveness. In their meta-analyses of panic disorder and social phobia, Gould and colleagues<sup>32,33</sup> compared CBT with pharmacologic treatment in terms of expenses. They found that group-administered CBT was the most cost-effective intervention, followed by individual CBT and then by medication. Acknowledging that these estimates may be colored by the controlled conditions evident in clinical trials, Otto et al.<sup>50</sup> calculated the cost of treatments for panic disorder as they are delivered in clinical practice. Taking into account average visit costs, medication costs, and alternative treatment costs per patient, they confirmed that group CBT was the most cost-effective intervention during the acute phase of treatment (\$518) as well as for a 1-year interval (\$523). While pharmacologic treatment was more cost-effective than individual CBT during the acute phase (costs were \$839 and \$1357, respectively), individual CBT was significantly more cost-effective over a 1-year period. More specifically, the cost of individual CBT was 59% of the cost for pharmacologic treatment for the 1-year interval. A similar pattern of results was evident for the cost-benefit ratio, as defined by the cost per unit increase on the clinicians' ratings of global improvement.<sup>50</sup>

#### **TREATMENT DISSEMINATION: UNDERUTILIZATION OF CBT**

Despite the promise of CBT for anxiety disorders, there is evidence indicating the underutilization of these methods in clinical practice. In a longitudinal study of anxiety patients receiving care in the northeastern United States, Goisman et al.<sup>86</sup> documented that only a small minority of anxious patients receive CBT interventions. These data join a broader literature indicating that empirically supported pharmacologic and psychosocial treatments for anxiety disorders are underutilized in specialty clinic and primary care settings<sup>86-88</sup> and that few patients receive an adequate "dose" of psychotherapy when they present for treatment.<sup>89</sup> Clearly, a major goal for students of CBT is to expand the application of these empirically supported interventions in clinics across the country. Until that occurs, clinicians must decide how to best utilize limited resources relative to the efficacy of CBT as a first-line treatment, an option for treatment resistance, a combination treatment, or a replacement strategy for medication.

## FUTURE DIRECTIONS

A final issue concerning the treatment of anxiety disorders is the prevention of new cases. As noted, comprehensive cognitive-behavioral models have been developed to explain the acquisition and maintenance of anxiety disorders,<sup>7,9</sup> including hypotheses about the cognitive and behavioral patterns that may put patients at risk for these disorders. If these models are accurate, then a potential exists for prevention strategies. The treatment of panic disorder provides an illustrative example in which the role of fears of anxiety sensations (anxiety sensitivity) has received attention as a predictor of panic in response to biological provocation procedures, as well as ongoing stress.<sup>90,91</sup> In addition, these fears appear to be an effective predictor of relapse,<sup>92</sup> and a reduction of these fears mediates the improvement in panic disorder symptoms achieved during CBT.<sup>93</sup> Using the presence of fears of anxiety sensations and occasional panic attacks as a marker of risk, Gardenswartz and Craske<sup>94</sup> recently examined the efficacy of a 5-hour workshop to prevent the onset of panic disorder. Elements of treatment included education about the nature and etiology of panic and agoraphobia, cognitive restructuring, exposure to feared somatic sensations (interoceptive exposure), and instructions for in vivo exposure to avoided situations. Six-month follow-up data were available for 121 participants who were randomly assigned to this preventive workshop or to a wait list. Results provided clear support for the preventive model: 13.6% of the wait-list group developed panic disorder compared with only 1.8% of those attending the prevention workshop. Given the emotional, social, and economic costs of panic disorder and its treatment, further investigation of such preventive strategies is encouraged.<sup>95</sup>

*Drug names:* alprazolam (Xanax and others), clomipramine (Anafranil and others), clonazepam (Klonopin and others), diazepam (Valium and others), imipramine (Tofranil and others).

*Disclosure of off-label usage:* The authors have determined that, to the best of their knowledge, imipramine is not approved by the U.S. Food and Drug Administration for the treatment of panic disorder.

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