Treatment of Anxiety Disorders: Implications for Medical Cost Offset

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Identification and amelioration of psychological factors that contribute to unnecessary medical service utilization and excessive diagnostic procedures is of the utmost importance in developing a more cost-effective health care system. Anxiety and its pathological expression represent one of the most crucial challenges facing our health care system.

The overall aim of this chapter is to acquaint the reader with an overview of anxiety disorders and their treatment. In so doing we will focus our review on addressing the following questions: (a) what are the direct and indirect costs of anxiety disorders?; (b) what are the fundamental features of anxiety that lead sufferers to seek medical services with such fervor?; (c) what is the available scientific evidence supporting the efficacy of existing empirically-supported treatments for anxiety disorders?; (d) what is the evidence that these treatments are effective when delivered in the real world as opposed to a research center?; (e) are there factors that predict treatment response?; and (f) what are the priorities for future research on treating anxiety disorders medical cost offset?

Costs of Anxiety Disorders

The costs of anxiety disorders are considerable. The high costs are due to several factors including their extremely high prevalence (Kessler, et al., 1994), their debilitating nature, and their chronicity when left untreated. Some costs of anxiety disorders cannot be quantified monetarily. These include the emotional suffering of the afflicted person and their loved ones as well as the overall lowering of one's quality of life. Specific data illustrating these non-monetary costs will be presented in the context of our discussion of specific anxiety disorders and their consequences. Several attempts have been made to estimate the monetary costs of anxiety disorders (Dupont, Rice, Shiraki, & Rowland, 1996; Greenberg, et al., 1999). Cost of illness studies typically divide the costs of an illness into direct costs such as those associated with providing both psychiatric and nonpsychiatric treatments, and indirect costs associated with loss of productivity among those suffering from the illness.

The most comprehensive study of the monetary costs of anxiety disorders was conducted by Greenberg et al. (1999) using data from both the National Comorbidity Study and supplemental data on nonpsychiatric medical costs from a large health maintenance organization (HMO). Like other cost-of-illness studies, costs were calculated using a prevalence-based human capital approach which estimates the annual costs of all individuals suffering from the illness within a given year regardless of when the condition was diagnosed. One of the more significant strengths of the study was the effort made to statistically control for extraneous demographic factors (e.g., age, education, number of children) that have been shown to relate to cost variables. Based on 1990 dollars, the total costs of anxiety disorders were estimated at 42.3 billion which translates into 63.1 billion in 1998 dollars. This translates into a per sufferer 1990 annual cost of $1542. The breakdown of the major cost categories are presented in Figure 1.

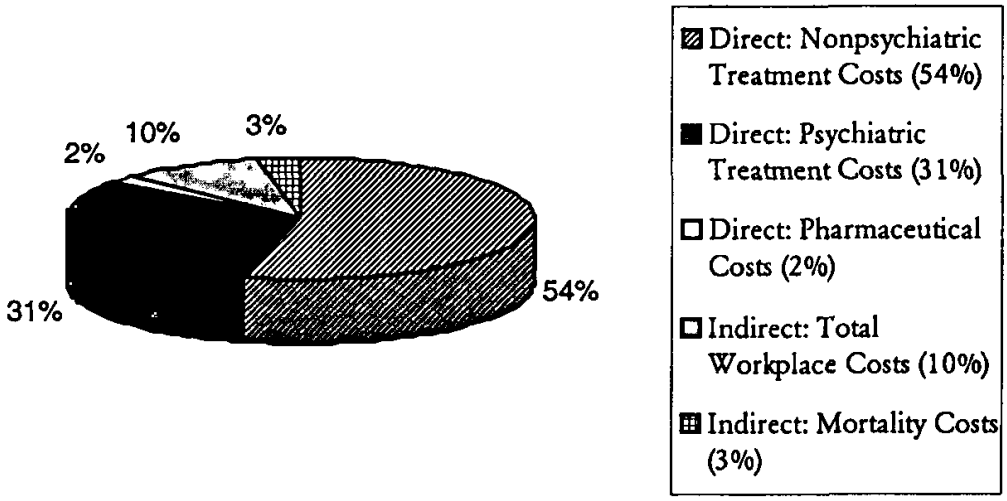

Figure 1. Breakdown of direct and indirect costs of anxiety disorders.

There are several compelling reasons to suggest that the 42.3 billion dollar cost estimate represents a significantly underestimate of the true financial burden of anxiety disorders. First, obsessive-compulsive disorder (OCD) - the most disabling of all the anxiety disorders - was not assessed in the National Comorbidity Study. Consequently, the Greenberg et al.cost estimates do not take into account the added costs associated with those suffering from OCD. Second, the NCS did not include people younger than 15 or older than 54. Third, legitimate cost categories such as the use of alternative medical practitioners, costs associated with secondary consequences of anxiety disorders (e.g., substance abuse), and other societal costs resulting from early onset anxiety disorders such as early school drop-outs, marital discord, etc. were not included in the Greenberg et al. cost estimates.

As seen in Figure 1, over half of the total estimated costs of anxiety disorders results from nonpsychiatric medical services. This fact has significant implications

for medical cost offset. Early identification of anxiety disorders and delivery of effective treatments are likely to result in a sizeable reduction of nonpsychiatric treatment costs.

Nature of Anxiety and Its Relationship to Medical Treatment Seeking

Anxiety has been conceptualized as an emotional response to anticipated threat consisting of physiologic, behavioral, and cognitive/subjective components. As a class, anxiety disorders share several common factors. These include: (a) activation of the sympathetic nervous system; (b) faulty threat perception; (c) attentional hypervigilance; (d) ruminative worry; and (e) safety-seeking behavior.

Sympathetic Activation

Most anxiety states produce an activation of the sympathetic nervous system. With this activation come numerous physiologic changes including increases in muscle tension, cardiac output, respiration, sweating, and vascular changes resulting in reduced blood flow. These physiologic effects of sympathetic activation have considerable adaptive significance from an evolutionary perspective (facilitating successful defensive response to potential threat). However, in the case of anxiety disorders, one's innate alarm mechanism is triggered in the absence of any objective threat. Consequently, the salient somatic perturbations associated with anxiety arousal are more likely to be experienced as highly aversive and sometimes even harmful, thus prompting anxiety sufferers to seek out medical evaluation and treatment.

Faulty Threat Perception

Faulty threat perception appears to be present in all the anxiety disorders. Cognitively-oriented theorists go one step further in asserting that faulty threat perception is the central cause of anxiety disorders; whereas biologically-oriented theorists argue instead that anxiety disorders are the result of abnormalities in one's neurobiology. A more lengthy discussion of this debate takes us too far a field from our major focus. Suffice it to say that regardless of its causal status, faulty threat perception is present in all the anxiety disorders. This has considerable implications for medical treatment seeking, since erroneous perceptions of threat are common among anxiety disorder sufferers.

It is likely that cognitive appraisal interacts significantly with physiologic activation to determine which features become the primary sources of medical concerns. For instance, the patient who perceives increased cardiac output as a sign of a potential heart problem is likely to seek out medical services; whereas one who perceives increased cardiac output as a benign consequence of anxiety will likely not. Similarly, one who interprets breathlessness associated with anxiety-induced hyperventilation as a sign of breathing difficulties is more likely to seek out medical service than someone who is aware that their breathlessness is a harmless consequence of over breathing in response to anxiety or stress.

Attentional Hypervigilance and Worry

The shift in focus of attention to threat cues is a well established feature of anxiety. Undoubtedly, this feature accomplishes an important function when faced with real danger - namely providing much needed information to facilitate preparatory action. In the case of anxiety disorders, attentional hypervigilance contributes to the maintenance of pathological anxiety by limiting available attentional resources for the cognitive processing of corrective threat disconfirming information. In many cases, attentional hypervigilance may exacerbate anxiety by serving as a perceptual amplifier thus resulting in heightened threat perception and ruminative worry. Even when the original threat focus is unrelated to one's physical health (e.g., work or relationship concerns), the resulting anxiety arousal may lead to secondary concerns related to the adverse medical consequences of anxiety, thus prompting the individual to seek out medical services.

Avoidance and Other Safety-Seeking Behavior

The previously mentioned physiologic and cognitive features of anxiety would be of little import if they were not of assistance in mobilizing escape or avoidance from potential threats. Defensive actions figure prominently in anxiety. More recently, attention has focused on other forms of safety-seeking behavior such as checking behaviors, reassurance seeking, use of companions, and use of physical aids (Kamphuis & Telch, 1998). Although some evidence suggests that safety-seeking behaviors may have short-term anxiety-reducing effects, several lines of evidence across multiple anxiety disorders now suggest that safety-seeking behaviors may play an important role in the maintenance of pathological fear reactions. This central feature of anxiety disorders has particular relevance for health care utilization and medical cost offset. Patients with anxiety disorders often use repeated visits to the emergency room or primary care physician as a safety behavior to cope with their anxiety. In the process, some patients will undergo multiple diagnostic work-ups that are both costly and often unnecessary. Several years ago we treated a panic disorder patient who experienced esophageal distress in response to his anxiety. At intake the patient had resorted to the safety behavior of pureeing all his food in a blender in order to cope with his fear that he would choke if he ate "regular" food. He had also undergone an amazing number of costly diagnostic work-ups over a span of about 18 months. Although treatment with benzodiazepines provided him some relief, his symptoms persisted and his functioning was significantly impaired. Exposure to interoceptive fear cues combined with graduated safety behavior fading resulted in a complete resolution of his symptoms and a return to normal functioning.

Let us now turn to a brief examination of several specific anxiety disorders. Note that due to space limitations, we have chosen to focus only on generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder. These were selected for two major reasons. First, each of these disorders has been associated with significant non-psychiatric health care utilization; second, each has been the focus of

significant pharmacological and psychological treatment research. For readers who may be unfamiliar with these disorders, we provide a brief description of the nature and epidemiology, along with relevant data (when available) pertaining to health care utilization, short and long-term treatment efficacy, moderators of treatment outcome, and treatment effectiveness.

Generalized Anxiety Disorder

Defining Features and Epidemiology of GAD

Since its introduction as a diagnostic entity in DSM-III (American Psychiatric Association, 1980), generalized anxiety disorder (GAD) has undergone considerable transformation in terms of both its conceptualization and diagnostic criteria. GAD was first described as a residual diagnosis for those presenting with significant chronic anxiety that could not be better accounted for by a mood disorder or another anxiety disorder. As research on GAD progressed, recognition for the role of uncontrollable worry as a central feature of GAD increased. This led to a major shift in the conceptualization of GAD from a residual anxiety disorder category in DSM-III, to a bona fide anxiety disorder characterized by uncontrollable worry. GAD is currently diagnosed when the individual presents with excessive and uncontrollable anxiety and worry in multiple life spheres (e.g., relationships, finances, health, work performance, etc.) for a period of at least six months. The anxiety must be accompanied by at least three of the following symptoms: restlessness or feeling on edge, becoming easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, or sleep disturbance, and must result in significant impairment or distress (APA, 1994).

Approximately 5.1% of the general population will have GAD at some point during their lifetime, and women (6.6%) are twice as likely as men (3.6%) to suffer its effects (Kessler, McGonagle, Zhao, et al., 1994). Interestingly, GAD has the highest rate of comorbidity with any Axis I anxiety disorder or depression (23%), and ranks first as the principal anxiety disorder most likely to have a comorbid condition associated with it (82%; Moras & Barlow, 1992). The onset of GAD usually occurs early in life and it tends to run a fluctuating but chronic course in which symptoms become exacerbated during times of stress. It is unlikely to remit without treatment (Wittchen, Carter, Pfister, Montgomery, & Kessler, 2000; Yonkers, Dyck, Warshaw, & Keller, 2000).

Social and Economic Costs of GAD

GAD is associated with significant impairment in social and occupational functioning as well as increased health concerns (Wittchen, et al., 2000; Kessler, et al., 1994; Wittchen, Zhao, Kessler, & Eaton, 1994). While little is known about the monetary impact of GAD, the National Comorbidity Survey revealed that approximately half of those with GAD seek services in the primary care setting (Kessler, et al., 1994; Wittchen, et al., 1994). Moreover, patients with GAD often remain undiagnosed and untreated in these settings (Ormel, Koeter, van den Grink, & van

de Willige, 1991; Fifer, et al., 1994; Roy-Byrne, 1996; Zajecka, 1997). Due to its unremitting nature, the failure to identify and treat GAD in primary care may contribute to a markedly higher rate of health care utilization among this population.

Following depression, GAD is the most prevalent mental disorder found in the primary care setting (Barrett, Barrett, Oxman, & Gerber, 1988). Among patients high in health care utilization, 40% have a lifetime history of GAD, and 22% meet for a current GAD diagnosis (Katon, Von Korff, & Lin, 1990). Given the physical symptoms associated with GAD, these findings are not surprising. Moreover, physical complaints associated with chronic anxiety, may also drive up medical service seeking (Roy-Byrne, 1996). In a study by Wulsin, Arnold, and Hillard (1991), 23% of emergency room patients presenting with atypical chest pain met criteria for a current GAD diagnosis. In a study of 216 chest pain patients with normal coronary angiograms, 56% met diagnostic criteria for GAD (Kane, Harper, & Wittels, 1988). In addition to chest pain symptoms, individuals suffering from GAD often report symptoms of gastrointestinal discomfort. For example, among patients diagnosed with irritable bowel syndrome, 34-54% will suffer from GAD sometime in their lifetime; and 11 - 26% will meet for a current GAD diagnosis. Interestingly, among IBS patients with comorbid GAD, 80% report that their GAD symptoms preceded the onset of their irritable bowel symptoms (Lydiard, Fossey, Marsh, & Ballenger, 1993). Taken together, these findings indicate that GAD is associated with a variety of physical complaints likely to be presented in the primary care setting.

Efficacy of Current Treatments for GAD

Treatment research for GAD can be broadly divided into research investigating the efficacy of pharmacotherapy and psychotherapy. Among pharmacological treatments for GAD, benzodiazepines have been the most extensively investigated. However, buspirone and antidepressants have more recently become a focus of GAD treatment research (Ballenger, 1999).

Among psychosocial interventions, behavioral and cognitive-behavioral therapies (CBT) have been the most extensively investigated. However, a significant body of this research has focused on dismantling studies aimed at investigating the efficacy of the individual procedural components of CBT (Butler, Fennell, Robson, & Gelder, 1991; Barlow, Rapee, & Brown, 1992; Borkovec & Costello, 1993). Cognitive-behavioral treatments for GAD share much in common with CBT for other anxiety disorders. The major treatment procedures commonly used in CBT treatments for GAD include: (a) self-monitoring of anxiety-provoking situations; (b) applied relaxation; (c) coping desensitization; (d) cognitive-restructuring of anxiety-provoking cognitions; and (e) worry exposure. The overarching strategy with these treatments is to increase the patient's mastery to cope with stressful life situations.

A comprehensive meta-analysis of pharmacological and psychosocial treatments for GAD was conducted by Gould, Otto, Pollack, and Yap (1997). They included 35 controlled studies published from 1974 to 1996. Of these, 22 investigated pharmacological treatments, 11 investigated psychosocial treatments,

and two investigated combined pharmacological plus psychosocial treatments. Interestingly, only one of these studies directly compared pharmacotherapy to psychosocial interventions. Employing the same search procedures as Gould et al., a total of 18 additional controlled studies were identified from 1996 to the present. However, only two of these investigated psychosocial interventions.

Under the classification criteria used by Gould et al. (1997), five studies classified as CBT employed relaxation training alone or relaxation training in combination with biofeedback as the sole treatment. Because treatments that target anxiety reduction through relaxation strategies as their sole focus may lack therapeutic potency relative to a more comprehensive CBT approach, we have provided a further subdivision of the effects size analyses for psychosocial interventions. Effect sizes reported for CBT under the criteria used by Gould et al. will be referred to as *CBT–All Inclusive.* For purposes of this chapter, we have added an additional category that we will refer to as *CBT- Contemporary.* This includes only those studies in which the treatment included additional strategies (in addition to relaxation or biofeedback) targeting other facets of GAD (i.e., dysfunctional cognitions or pathological worry). Table 1 provides a breakdown of the number of studies in each category, the number of patients included in the studies, the average duration of treatment, and the average duration at follow-up assessment.

Treatment	Number of Studies	Total Number of Patients	Average Treatment Duration	Average Follow-up Duration
RX	22	3280	4.4 wks	N/A
CBT	11	590	8.1 wks	6 mo.
RX + CBT	2	132	8 wks	6 mo. (1 study)

Table 1. Specifications of treatment efficacy research for GAD.

Short-term Efficacy

As reported by Gould et al. (1997), both CBT and pharmacotherapy led to significant improvement in GAD symptoms; but neither treatment showed a clear advantage over the other. However, when effect size estimates were based on the subset of studies in which a more multifaceted CBT approach was used (CBT-Contemporary), effect sizes were slightly higher for CBT relative to pharmacotherapy (See Figure 2).

Gould et al. (1997) also examined treatment effects on depression and found that compared to pharmacotherapy, CBT yielded a significantly greater treatment effect (ES = 0.77 vs. .46). Among the pharmacological interventions, the greatest treatment effects were associated with benzodiazepines, followed by antidepressants, and buspirone (See Figure 2). Comparisons of attrition across the major treatment modalities revealed no significant difference in attrition between CBT (M = 10.6%) and pharmacotherapy (M = 15.2%); however, antidepressants were associated with the largest attrition rate (33.5%), which is likely attributable to medication side effects.

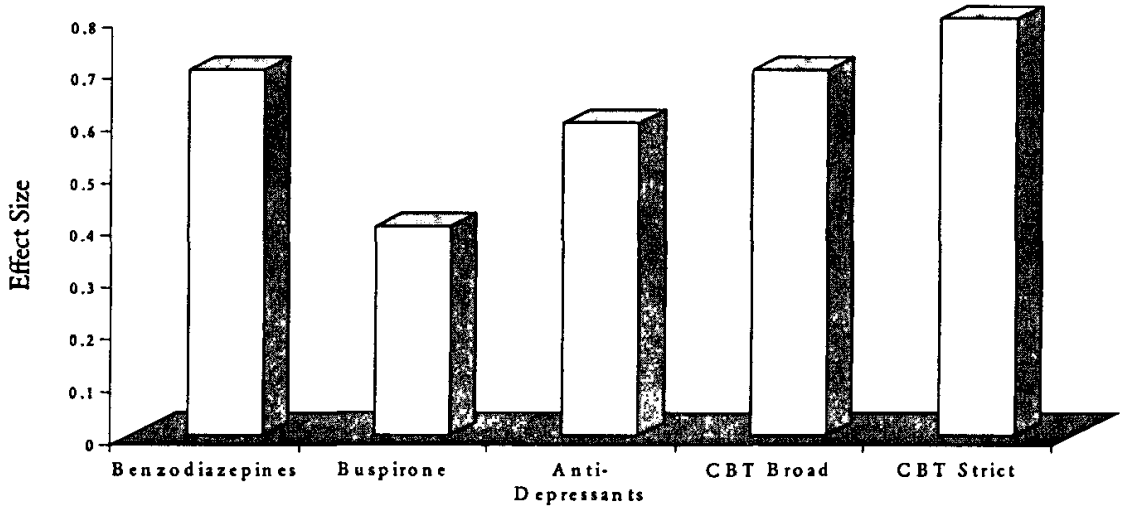

Figure 2. Short-term efficacy of treatments for GAD. Data from Gould et al. (1997).

Long-term Efficacy

Of the 35 studies included in the meta-analysis of Gould et al. (1997), only 7 studies included follow-up assessments of six months or longer. The results indicate that treatment gains for CBT (all inclusive) were generally maintained at follow-up. When only contemporary CBT treatments are examined, the follow-up results are more encouraging with a trend toward continued improvement beyond posttreatment (See Figure 3). This is in sharp contrast to the one study that examined the long-term effects of a pharmacological treatment following medication discontinuation; not surprisingly, patients treated with diazepam alone lost much of their improvement at the treatment-free follow-up (Power, et al., 1990).

Clinical Significance of Treatment Effects

Do GAD patients receiving treatment show a level of improvement that is clinically significant? The best data available for addressing this question comes from a report by Fisher and Durham, (1999). Using clinical significance criteria established by Jacobson and Truax (1991), the authors examined end state recovery status for 20 psychosocial treatment comparisons groups across 6 studies. Across all 20 comparisons, including 17 different psychosocial interventions and CBT variants, they identified a 40% recovery rate, and when examining recovery rates atthe 6-month follow-up, they found that 50-60% of patients who received either CBT or applied relaxation achieved high endstate functioning (recovery status).

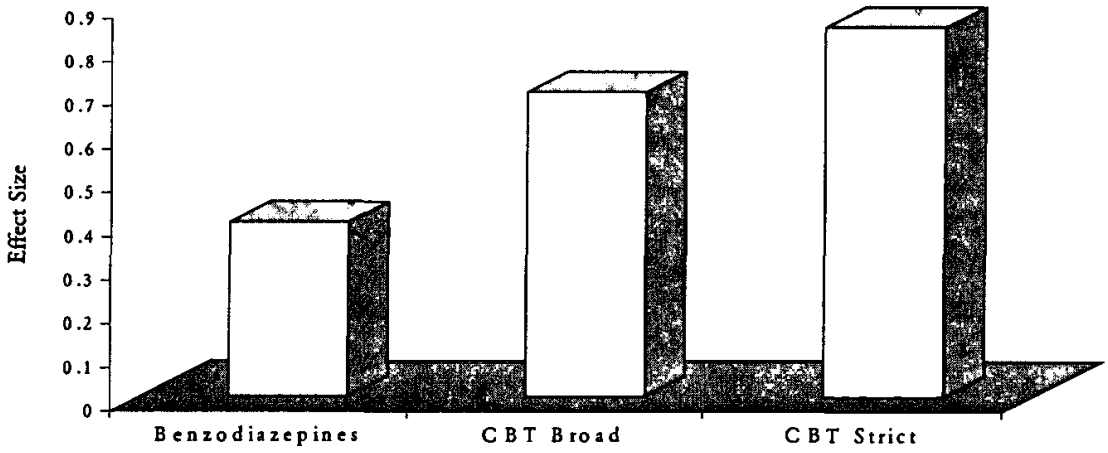

Figure 3. Long-term efficacy of treatments for GAD. Data from Gould et al. (1997).

Predictors of Clinical Response to Treatment in GAD

Data on predictors of clinical response among GAD patients are limited. In a five year, prospective, naturalistic follow-up study 167 GAD patients were assessed at intake and every 6-12 months for five years (Yonkers et al., 2000). Analysis of the cross-sectional data revealed that remission was less likely to occur in the presence of low overall life satisfaction, a cluster B or C comorbid personality disorder, and poor spousal or family relationships. Consistent with the Yonkers et al. report, the presence of comorbid personality disorders was also predictive of a poorer clinical response among 50% of GAD patients treated with pharmacotherapy (Mancuso, Townsend, & Mercante, 1994). Specifically, cluster B and C personality disorders as well as significant life dissatisfaction was associated with poorer outcome at the 16-week follow-up. In a study examining predictors of clinical response to cognitive therapy, Sanderson, Beck, and McGinn (1994) found patients diagnosed with a comorbid personality disorder were more likely to drop out of treatment.

Cost Effectiveness

We were unable to locate any data pertaining to the cost-effectiveness of the treatments for GAD. Given that the treatments for GAD resemble those for panic disorder, it could be argued that the findings on the cost-effectiveness of treatments for panic disorder described later in this chapter suggest that both medication and CBT are reasonably cost-effective in the short-term and that CBT is a more cost-effective treatment in the long-term. Of course, this conclusion is highly speculative and awaits research that directly examines the cost-effectiveness of treatments for GAD.

Treatment Effectiveness

No research was identified that investigates the transportability of GAD treatments from the research setting to the primary care or community mental health arena.

Obsessive-Compulsive Disorder

Nature & Epidemiology of Obsessive-Compulsive Disorder

Obsessive-Compulsive Disorder (OCD) is one of the most intense, chronic, and impairing forms of pathological anxiety. OCD is characterized by threatening and intrusive thoughts, images, or impulses that cause the individual extreme anxiety and distress. Individuals with OCD typically attempt to neutralize or suppress these obsessions with repetitive, ritualistic behaviors or compulsions. In a study looking at the classification of obsessions in OCD, Antony and colleagues (Antony, Downie, & Swinson, 1998) found that 68.7% of the sample of 182 OCD patients had aggressive obsessions (e.g., fear of harming oneself or another), 57% of OCD patients had contamination obsessions, 53.2% symmetry / exactness concerns, 30% had hoarding or saving obsessions, and 24% had religious (blasphemous) obsessions. Significantly, 34.1% had somatic concerns, which often involve fear of having contracted an infection or disease, or hypochondriacal conviction of being ill.

The compulsions are often linked logically to the obsession, as is the case with washing rituals triggered by contamination fears or checking behavior in response to obsessive fears of having left doors unlocked or stoves on. Other compulsions seem to have a more superstitious or "magical" link to an obsession, such as counting, repeating words, or ordering objects to avert some vague, dreaded outcome. OCD patients are often painfully aware that their obsessions and compulsions are "senseless," and often hide their symptoms for years before seeking treatment. They also commonly suffer depression, panic attacks, generalized anxiety and worry, and debilitating avoidance.

OCD was once considered rare. The Epidemiology Catchment Area (ECA) survey in 1984, however, found a 2.5% lifetime prevalence for the disorder in the U.S., with a slightly higher rate in women (Robins, Helzer, Weissman, & Orvaschel, 1984).. Mean age of onset is 17.5 years in males, and 20.8 in females (Rasmussen & Eisen, 1990). Notably, one third to one half of OCD patients first experience OCD symptoms in childhood, and the phenomenology of the disorder is nearly identical in children and adults (Rapoport, 1989). The disorder tends to be chronic without treatment, with a waxing and waning of symptoms throughout the lifespan (Antony et al., 1998).

Individuals with OCD often have psychiatric comorbidity. Nearly a third of OCD patients meet criteria for major depression upon diagnosis, while two-thirds report a history of depression (Rasmussen & Eisen, 1992). Comorbid anxiety disorders is also high: 30% of OCD patients have a simple phobia, 20% have social phobia, 15% are diagnosable with panic disorder (Rasmussen & Tsuang, 1986). Ten percent of women with OCD have a history of anorexia (Kasvikis, Tsakiris, Marks, & Basoglu, 1986), while 33% of bulimic women have a history of OCD (Hudson & Pope, 1987). There is also a strong association between OCD and tic disorders. The OCD prevalence among Tourette's patients is high: 30-60% (Leckman,

Peterson, Pauls, & Cohen, 1997). Approximately 5% of OCD patients have comorbid Tourette's syndrome (Rasmussen & Eisen, 1992), while many more report a history of tics (Leckman et al., 1997). Perhaps most relevant to medical utilization is the 8% rate of hypochondriasis among OCD patients, likely related to the previously noted somatic obsessions.

Non-Financial Costs of OCD

OCD sufferers often pay a large price tag with respect to emotional distress and impairment in social and occupational functioning. Given the large amount of time OCD sufferers spend on performing rituals and the often bizarre nature of the rituals (which motivates secrecy), it is not surprising that OCD patients find themselves socially isolated. A 1990 Gallup poll examining quality of life of OCD sufferers, found that 20% spent 5-8 hours a day engaged in rituals, and 13% spent over 17 hours a day during the most severe period of their disorder (Gallup Organization, 1990). Moreover, 48% had lost friends, 26% reported that their symptoms caused the end of their intimate relationship, and 57% reported difficulty making new friends. This is consistent with other studies reporting that 62% of OCD patients have difficulty maintaining a relationship (Calvocoressi, Lewis, Harris, Trufan, Goodman, McDougle, & Price, 1995), and that celibacy rates are high relative to other anxiety disorders (Steketee, Grayson, & Foa, 1987). Koran and colleagues compared quality of life issues in OCD patients to the general U.S. population and depressive or diabetic patients, and found social functioning and instrumental role performance to be significantly more impaired in the OCD sample (Koran, Thienemann, & Davenport, 1996).

Financial Costs of OCD

The financial costs of OCD are considerable. Morbidity costs due to reduced work productivity are staggering. Steketee and colleagues found a 40% unemployment rate for OCD patients, and reduced income due to impairment (Steketee, et al., 1987). A survey of patient members of the OC foundation found that patients lost an average of two years wages due to their illness (Hollander, et al., 1996). In the most extensive cost analysis of OCD, Dupont and colleagues estimated the 1990 costs of OCD to be 8.4 billion. Approximately 70% or 6.2 billion of which was due to morbidity costs associated with lost productivity; whereas 25% or 2.1 billion was the estimated direct costs associated with providing treatment services. Mortality costs due to lost wages were estimated at 3% and were based on the assumption that 2% of all suicides are OCD-related. A final 1% included expenses for legal, and social services (DuPont, Rice, Shiraki, & Rowland, 1996). Frost and Steketee (1997) note that the DuPont et al. figures likely underestimate the overall costs of OCD since they are based on the percentage of anxiety disorder patients with OCD. However, it has been noted that certain costs of OCD may be higher than those for other anxiety disorders (Turner, Beidel, Spaulding, & Brown, 1995).

Health Care Utilization in OCD

There are several reasons why individuals with OCD might be expected to over-utilize medical services. Because OCD patients commonly have somatic obsessions, the disorder has similarities to hypochondriasis: both involve a fear of illness or contamination which is not delusional, but the belief resists explanation or reassurance (Barsky, 1992). This makes it likely that individuals with OCD will seek out medical services to alleviate their fears.

Based on data from the ECA 80% of OCD sufferers are treated as outpatients (80%), and of these, 40.4% saw a general physician an average of 4.6 times a year (Narrows, Regier, Rae, Manderscheid, & Locke, 1993). There is evidence that patients with OCD may present more often to medical *specialists*– particularly dermatologists for skin conditions related to excessive washing and infectious disease specialists (Rapoport, 1988). Rasmussen (1985) argues that individuals with undiagnosed OCD are likely to present themselves first to primary care physicians or dermatologists–and that the latter should be trained to diagnose the disorder. A study looking at the incidence of OCD in African Americans presenting for treatment of chronic pruritic conditions in an urban dermatology clinic found that 15% met criteria for OCD (Friedman, Hatch, & Paradis, 1993). Kennedy & Schwab (1997) conducted a survey of anxiety patients participating in drug trials in a university outpatient clinic to determine the number of primary care physicians and specialists seen in the last year. They found that of the 32 OCD patients, 28% had seen a physician in primary care, 28% in dermatology, 22% in internal medicine, 25% in cardiology, and 19% had seen an ear-nose-throat physician. The OCD patients saw significantly more dermatologists and cardiologists than individuals with panic disorder or GAD, or the general public. Surprisingly, only 3% of the OCD patients had seen a psychiatrist in the past year.

Treatment Efficacy Studies for OCD

As in the case for other anxiety disorders, both antidepressant medication and specific forms of psychosocial treatments have well-established clinical efficacy in the treatment of OCD. Given that one of the important brain regions affected in OCD–the basal ganglia–is served by seratonergic pathways, it is no surprise that the most widely studied and most effective drug treatment for OCD involve medications which inhibit the reuptake of serotonin. Clomipramine was the first medication to demonstrate clinical efficacy in the treatment of OCD. More recently, several SSRIs including fluoxetine, fluvoxamine, sertraline and paroxetine have all demonstrated clinical efficacy in placebo controlled clinical trials.

Based on a recent review (Greist, Jefferson, Kobak, Katzelnick, & Serlin, 1995) and literature search of journal publications from 1996-present using Psych-Info and MEDLINE, we found 34 controlled studies investigating treatment efficacy of seratonergic-acting medications, with 3,060 patients treated, an average treatment length of 9.2 weeks, and an average follow-up period of 18 months.

Among psychosocial treatments for OCD, the most widely investigated is a structured learning based treatment known as exposure and response prevention or ERP for short. The basic components of ERP are similar to those used in the behavioral treatment of other anxiety disorders. They include (a) thorough *assessment* of the nature, course, and prior treatment of the patient's OCD symptoms, specific information on the internal and external fear cues that trigger compulsions and avoidance behavior; (b) *education* about the disorder and anxiety reduction principles; (c) in-session imaginal and *in vivo exposure* to fear-provoking cues; (d) response prevention in which the patient is encouraged to refrain from engaging in the compulsion; and (e) daily *home practice of exposure and response prevention exercises.* Based on a recent review of studies through 1995 (Abramowitz, 1997) and a subsequent literature search, we found 16 controlled studies investigating the efficacy of ERP, with 376 participants treated, an average treatment length of 9.4 weeks, and an average follow-up period of 29 months.

Evidence for Short-term Efficacy

Research on effective pharmacological treatments for OCD has focused on the seratonin reuptake inhibitors clomipramine (CMI), fluoxetine, fluvoxamine, and sertraline. Greist and colleagues (1995) reported on the short-term efficacy of the four most widely studied medications (i.e., clomipramine, fluoxetine, fluvoxamine, and sertraline) using data from four, large, industry-sponsored randomized clinical trials conducted at 48 sites. The treatments were 10-13 weeks in length, and the results are based on intent-to-treat samples (Total N = 1,520). All four medications were significantly more effective than placebo. The effect sizes for the three medications are presented in Figure 4.

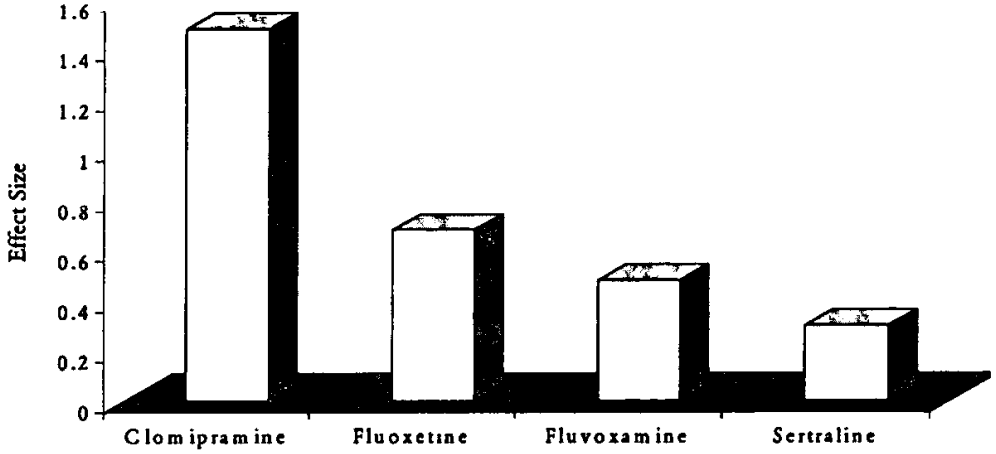

Figure 4. Effect sizes from 4 large industry sponsored randomized clinical trials. Data from Greist et al. (1995).

As seen in Figure 4, the effect size for clomipramine was significantly greater than those for the three SSRIs, which did not differ significantly from each other. The response rates based on clinician ratings of "improved" or "very much improved" was 60% for clomipramine, 38% for fluoxetine, 43% for fluvoxamine,

and 39% for sertraline. The authors suggested that the apparent superiority of clomipramine in these studies may be a subject selection artifact in which non-responders from the earlier clomipramine study were entered as subjects in the latter SSRI studies. The fact that they were previously non-responsive to clomipramine may have decreased the likelihood that they would be responsive to another SRI medication. Regardless, all four medications provide significant short-term benefit for OCD sufferers. Several other SSRI medications under investigation are paroxetine and citalopram (Mundo, Bianchi, & Bellodi, 1997). Several controlled studies have tested the efficacy of adding seratonin-enhancing drugs (such as buspirone and clonazepam), and dopamine antagonists (such as haloperidol and risperidone), to SRI regimens with some promising results (McDougle, Epperson, Pelton, Wasylink, & Price, 2000).

Evidence for the short-term efficacy of psychosocial treatment for OCD comes mostly from randomized clinical trials of exposure and response prevention (ERP). In a review of 12 ERP treatment outcome studies (N=330), 83% of treatment completers were classified as responders at posttreatment based on clinician ratings (Foa & Kozak, 1996). Depicted in Figure 5 are data examining the short-term efficacy of clomipramine, SRI medications combined, and ERP come from a meta-analysis of 32 clinical trials in OCD published between 1975 and 1995 (Abramowitz, 1997).

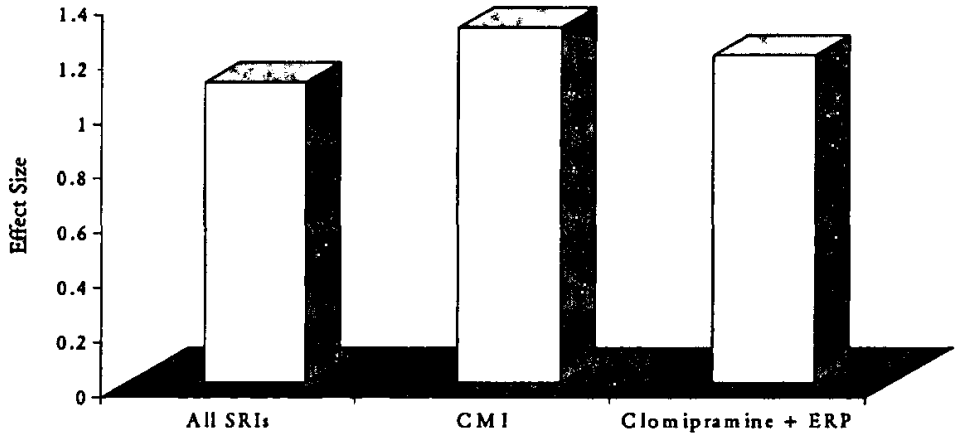

Figure 5. Short-term efficacy of treatments for OCD. Data from Abramowitz (1997).

These data suggest that in the short-term, behavioral and pharmacological treatments are of comparable clinical efficacy. The validity of meta-analytic results, however, rests upon the individual studies used in the analyses–some of which have significant methodological limitations. To address this problem, Foa and colleagues began a large, multisite, randomized control trial in 1990 at a cognitive-behavioral-oriented site and a pharmacologically-oriented site. They are comparing the short- and long-term efficacy of four treatments: clomipramine (CMI) alone, ERP alone, CMI plus ERP, and pill placebo. The treatment phase was 12 weeks, with a 6-month, no-treatment follow-up. Preliminary results suggest an acute response

rate for ERP which is similar to the meta-analysis: 84.6% for the 61 completers, and 61.1% for the 83 intent-to-treat sample (Kozak, Liebowitz, & Foa, 2000).

Long-term Efficacy

Although the SSRIs provide effective short-term treatment for OCD, few studies have examined the long-term efficacy of pharmacological treatments. One study by Ravizza and colleagues followed 130 subjects for 2 years following a 6-month treatment with clomipramine, fluoxetine, or fluvoxamine (Ravizza, Barzega, Bellino, Bogetto, & Maina, 1996). During the follow-up, subjects continued with the same dosage, continued with half the dose, or discontinued the medication. No differences were found in outcome between full and half dosages, and continuation of medication was significantly more effective than discontinuation. The relapse rates were equally high for all three pharmacological treatments when the patients discontinued medication altogether: 76.9% for clomipramine, 80.0% for fluoxetine, and 84.6% for fluvoxamine. A more recent review of the effects of discontinuation of SSRI medications indicates that approximately 80% of successfully-treated OCD patients relapse once medication is discontinued (Ravizza, Maina, Bogetto, Albert, Barzega, & Bellino, 1998).

In contrast to pharmacotherapy, treatment gains for ERP are largely maintained after treatment completion. In a review of 16 ERP studies with 376 participants and a mean follow-up period of 29 months, 76% continued to be much improved or very much improved on the CGI at follow-up (Foa & Kozac, 1996). The multi-site study by Kozac and colleagues (Kozac, Liebowitz, & Foa, 2000) provides additional evidence of the superior long-term durability of ERP to pharmacotherapy. Preliminary results of relapse rates at the 3-month follow-up are presented below. As seen in Figure 6, ERP whether given alone or in combination with medication is associated with a low rate of relapse, whereas most patients treated with clomipramine alone relapse following discontinuation of medication.

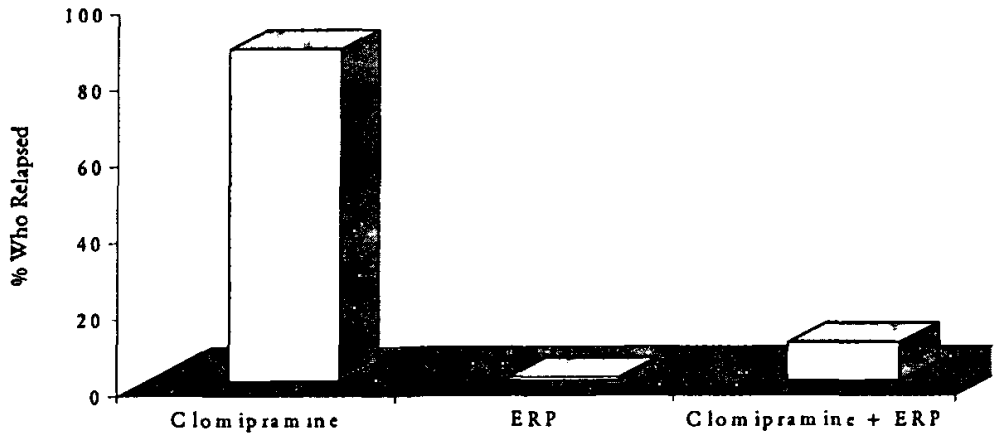

Figure 6. Relapse following discontinuation of treatment. Data from Kozak et al. (2000).

Are the Symptom Changes Clinically Meaningful?

The effect sizes for pharmacological and psychological interventions for OCD clearly indicate significant gains with these treatments. The improvements in symptoms and global functioning ratings at posttest are at least one standard deviation better in the treated groups than in the control groups. It is difficult to tell from the efficacy data, however, whether such a difference *is clinically significant*: does the treatment meet improvement standards desired by the patients and their clinicians? To answer this question with regards to ERP, Abramowitz (1998) compared the posttreatment functioning of OCD patients from 16 outcome studies with 9 samples from the general public (mostly university students not screened for OCD) who were administered OCD symptom measures in 6 studies. The author found that at posttest, although treated patients were not symptom-free, they were functioning at a level more similar to the normative sample than to untreated OCD patients up to 5 months after treatment.

Predictors of Treatment Outcome

A number of factors have been investigated as predictors of outcome in the treatment of OCD, including comorbid Axis I and II disorders, pre-treatment OCD severity, and treatment adherence to ERP homework. Although early studies suggested that Axis I comorbidity predicted poor outcome, the evidence to date is equivocal. Many studies have looked at depressed *mood* as a treatment predictor with mixed results (see Steketee, Henninger, & Pollard, 2000, for review). Steketee and colleagues found that pre-treatment major depression predicted poor outcome following 16 weeks of ERP (Steketee, Henninger, & Pollard, 2000), but comorbid depression was not found to affect treatment outcome in several medication trials (Goodman, et al., 1989). Steketee and colleagues also examined comorbid anxiety disorders and found that GAD was related to drop-out rates and poorer outcome at follow-up, while social phobia was not (Steketee, Henninger, & Pollard, 2000). Other studies have not found comorbid anxiety to moderate the effects of behavioral treatments for OCD (Stekeetee & Shapiro, 1995) or pharmacotherapy (Orloff, Battle, Baer, & Ivanjack, 1994).

There is stronger evidence that Axis II comorbidity predicts a less favorable outcome for both ERP and pharmacotherapy. Borderline and avoidant personality disorder were found to predict poor outcome in the treatment of OCD with CMI (Baer & Jenike, 1992) and fluvoxamine (Cottraux, Mollard, Bouvard, & Marks, 1993), while schizotypal personality disorder predicted poor outcome in several SSRI studies (Jenike, Baer, & Carey, 1986; Ravizza, Barzega, Bellino, Bogetto, & Maina, 1995). Personality disorders also predicted poor outcome with ERP treatments in several studies (AuBuchon & Malatesta, 1994; Cottraux et al., 1993), although they did not in one study (Steketee, Henninger, & Pollard, 2000).).

Although overall pre-treatment OCD severity has not been found to predict treatment outcome in either the psychosocial or pharmacological treatments (O'Sullivan, Noshirvani, Marks, Monteiro, & Lelliott, 1991; Steketee, 1993), the

data is mixed regarding the predictive value of specific symptoms (see Kozac, et al., 2000). A positive predictor of outcome in the behavioral treatment of OCD is treatment compliance, particularly with homework assignments (Araujo, Ito, & Marks, 1996; Keijsers, Hoogduin, & Schaap, 1994; O'Sullivan, et al., 1991).

Do Treatment Effects Generalize to the Real World?

Some argue that efficacy data gathered through RCT studies may exaggerate the true effectiveness of treatments. The therapists in RCTs are often highly trained in the treatment approach, while private clinicians may have difficulty effectively using the treatment manual. Researchers also commonly exclude the more severe patients with comorbid diagnoses in order to obtain a homogenous experimental group, while many of the eligible patients may refuse randomization to placebo conditions (creating a "self-selected" group). Thus the treated patients in RCT studies may not be representative of the typical outpatient seen in private practice. To determine whether ERP efficacy data generalizes to the real world of clinical practice, Franklin and colleagues compared outcome data from 4 RCTs with data from 110 outpatients with OCD seen at a university-based anxiety research clinic on a fee-for-service basis (Franklin, Abramowitz, Kozak, Levitt, & Foa, 2000). No outpatients were excluded for comorbidity, concomitant or past treatment, age, or OCD severity. The results provided strong support for the effectiveness of ERP. Pre-post change in symptom scores yielded comparable, clinically significant improvement in both the RCT and clinic groups. The pre- to posttreatment size was 3.26 for the clinic sample, in comparison to 3.88 and 2.31 from two of the RCT studies. The effect sizes for the other RCT outcome studies were significantly lower, possibly related to the less-intensive approach used in these two studies. Thus, the limited available data support the efficacy of ERP when delivered in a non-research setting.

Cost effectiveness

Although the benefits of effectively treating OCD are clear, only one study has examined the costs associated with providing behavioral therapy to OCD patients. Turner and colleagues found in their survey of behavior therapists that OCD cost significantly more to treat than other anxiety disorders: the mean cost per OCD case was $4,370, compared to $2,695 for social phobia, for example (Turner, Beidel, Spauling, & Brown, 1995). This was due to the increased number of sessions typically required for treating OCD: 46.4 hours, compared with a mean of 20.7 hours for the other anxiety disorders. Given the substantial impairment, healthcare utilization, and other economic costs associated with obsessive-compulsive disorder, such a price for effective treatment may well be cost-effective in the long term.

Panic Disorder

Defining Features and Epidemiology

Panic disorder is a debilitating anxiety disorder characterized by recurring unexpected episodes of intense fear (panic attacks) coupled with persistent

apprehension surrounding the attacks. The panic-related apprehension manifests in one or more of the following ways: (a) persistent worry about future attacks; (b) unrealistic concern about the consequences of having a panic attack (e.g., heart attack, insanity, social humiliation); or (c) changes in behavior to cope with the fear of panic e.g., avoidance of situations that might trigger an attack (American Psychiatric Association, 1994).

Panic disorder affects approximately 3% of the general population and is about twice as prevalent among women(Kessler, et al., 1994).

Social and economic costs of panic disorder

Panic disorder is associated with significant impairment. A recent study showed that the quality of life of individuals suffering from panic disorder is comparable to those suffering from major depression (Candilis, et al., 1999). Compared to the general population, patients with panic disorder show higher prevalence rates of chronic medical conditions (e.g., hypertension, migraine headaches, thyroid disease) (Rogers, et al., 1994). Other medical conditions that are more frequently observed in patients suffering from panic disorder include mitral valve prolapse and cardiorespiratory disorders, such as asthma and chronic obstructive pulmonary disease (Gorman, et al., 1988; Karajgi, Rifkin, Doddi, & Kolli, 1990; Weissman, Markowitz, Ouellette, Greenwald, & Kahn, 1990; Zandbergen, et al., 1991).

Panic disorder is frequently associated with comorbid psychiatric problems such as alcohol abuse, drug abuse, and suicide (Markowitz, Weissman, Ouellette, Lish, & et al., 1989). It has been demonstrated that approximately 70% of patients with panic disorder have at least one comorbid Axis I or Axis II disorder (Brown & Barlow, 1992; Sanderson, Di Nardo, Rapee, & Barlow, 1990). Emotional and physical health ratings of patients with panic disorder are presented in Table 2.

Domain	%
Health	
Poor Physical Health	35
Poor Emotional Health	38
Psychiatric Problems	
Alcohol Abuse	27
Other Drug Abuse	18
Attempted Suicides	20
Work Impairment	
Full-Time Employed	55
Unemployed	25
Financially Dependent	27

Table 2. Impared quality of life in panic disorder. Data from Markowitz et al. (1989) and Massion et al. (1993).

In addition to health and emotional impairment, panic disorder often contributes to significant impairment in occupational functioning. Massion, Warshaw, and Keller (1993) reported a fourfold rate of unemployment (relative to the national average) among patients with panic disorder. Not surprisingly, their results also revealed increased financial dependency (e.g., receiving disability or welfare) among patients with panic disorder relative to the general population.

Healthcare Utilization

Given the adverse effects of panic disorder on health and quality of life, it is not surprising that the disorder is associated with increased use of medical services. Data from the Cross National Collaborative Study indicated high utilization rates of specialists such as cardiologists, neurologists, and primary care physicians, as well as outpatient mental health clinics and psychotherapists (Leon, Olfson, & Portera, 1997). The results further showed that 48% of patients with panic disorder were seen by a non-mental health care provider. The estimated mean expenditure for a panic episode was $3,393 (Leon, et al., 1997). Table 3 presents data on the utilization of medical services among those afflicted with panic disorder.

	% Using Service	Median Number of Visits
General Medical Sector		
Cardiologist	20.6	2.0
Neurologist	13.4	2.0
Other specialists	31.2	3.5
Any of the above	47.2	9.5
Primary Care Physicians	70.4	7.0
General practitioner	67.8	4.5
Outpatient clinic	13.9	14.0
Mental Health Sector		
Outpatient	47.9	26.0
Community mental health	12.9	12.0
Psychotherapist or counselor	44.3	24.0

Table 3. Utilization of medical services in panic disorder. Data from Leon et al. (1997).

Treatment Efficacy

The most extensively researched approaches to the treatment of panic disorder are pharmacotherapy and cognitive-behavioral therapy (CBT). Several classes of pharmacological agents have been extensively investigated and proven beneficial in the treatment of panic disorder. These consist of several classes of antidepressants including TCAs such as Imipramine, MAOIs such as Phenelzine, and the SSRIs such as Paroxetine; as well as several classes of anxiolytics such as the high potency BZs such as Alprazolam and the non-BZ anxiolytic Buspirone.

Most research on psychosocial treatments for panic disorder has focused on cognitive-behavioral interventions. These treatments focus on providing patients specific training in identifying internal and external cues that trigger panic and assisting the patient in learning techniques to eliminate their faulty emotional responding to these cues. Specific procedural components included in contemporary cognitive-behavior therapy for panic disorder include: (a) education about the nature and physiology of panic and anxiety; (b) breathing retraining designed to assist patients in learning to control hyperventilation; (c) cognitive restructuring aimed at teaching patients to identify and correct faulty threat perceptions that contribute to their panic and anxiety; (d) interoceptive exposure aimed at reducing patients' fear of harmless bodily sensations associated with physiological activation; and (e) fading of maladaptive defensive behaviors such as avoidance of external situations (Barlow, Craske, Cerny, & Klosko, 1989; Clark, et al., 1994; Margraf, Barlow, Clark, & Telch, 1993; Telch, et al., 1993).

Since 1974, approximately 44 controlled clinical trials have been published investigating the efficacy of pharmacotherapy in the treatment of panic disorder, and an additional 24 controlled studies have examined the efficacy of CBT for panic disorder. Moreover, we found 12 controlled trials that investigated combined medication plus psychological treatment. Table 4 presents a summary of these studies.

Treatment	Number of Studies	Number of Patients	Duration of Treatment, Weeks	Length of Follow-Up, Weeks
TCAs	17	25-1168	6-28	0-24
BZs	13	25-1168	5-32	
SSRIs	14	55- 367	8-16	
CBT	24	18- 312	1-16	0-48
RX + CBT	12	21- 312	12-28	0-72

Table 4. Summary of treatment efficacy research in panic disorder.

Short-term Efficacy

In the last decade, the efficacy of treatments for panic disorder has been systematically reviewed in several meta-analytic studies (Gould, Otto, & Pollack, 1995; Clum, Clum, & Surls, 1993). Gould, Otto, and Pollack compared the efficacy of pharmacological, cognitive-behavioral, and combined pharmacological and cognitive-behavioral treatments in a meta-analysis of 43 controlled studies that included 76 treatment conditions. The clinical trials included in this study were conducted between 1974 and 1994. The short-term efficacy data are depicted in Figure 7. The results showed that all three modalities were effective in reducing the prominent features of the disorder as evidenced by the large average effect size. A comparison of the treatment modalities revealed an advantage of CBT alone over medication and the combination treatment (effects sizes (ES), 0.88, 0.47, and 0.56 respectively). CBT also yielded the smallest attrition rates (5.68%), indicating that is it is better tolerated than pharmacotherapy alone (average attrition rate of 19.8%) or combined medication plus CBT (average attrition rate of 22%).

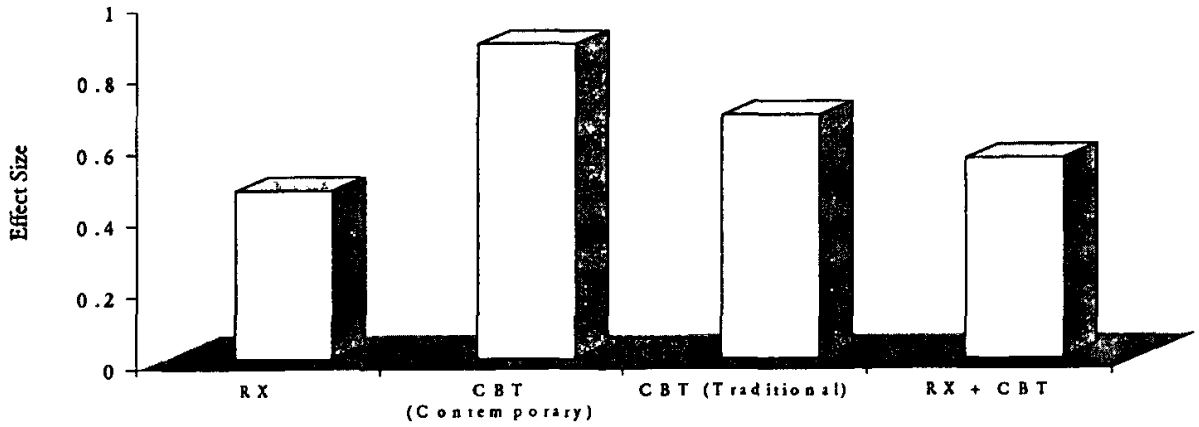

Figure 7. Short-term efficacy for CBT, medication, and their combination. Data from Gould et al. (1995).

In the most ambitious clinical trial to date, Barlow, Gorman, Shear, and Woods (2000) compared the efficacy of CBT, Imipramine, and their combination in a large sample (N=312) of carefully diagnosed panic disorder patients at four sites. A noteworthy aspect of this trial was the teaming up of investigators with different therapeutic expertise, thus controlling for allegiance effects. Patients (N = 312) were randomly assigned to one of five treatment conditions: (a) CBT; (b) Imipramine; (c) Imipramine plus CBT; (d) CBT plus placebo; or (e) pill placebo. Treatment efficacy was evaluated at three different stages: 12 weeks of acute treatment, six-month treatment continuation phase, and 6 month treatment-free follow-up. The acute response rates are shown in Figure 8. After acute treatment all four active treatments showed marked improvements that were significantly greater than those observed for the pill placebo condition. Results at the six-month treatment-free follow-up are reported below.

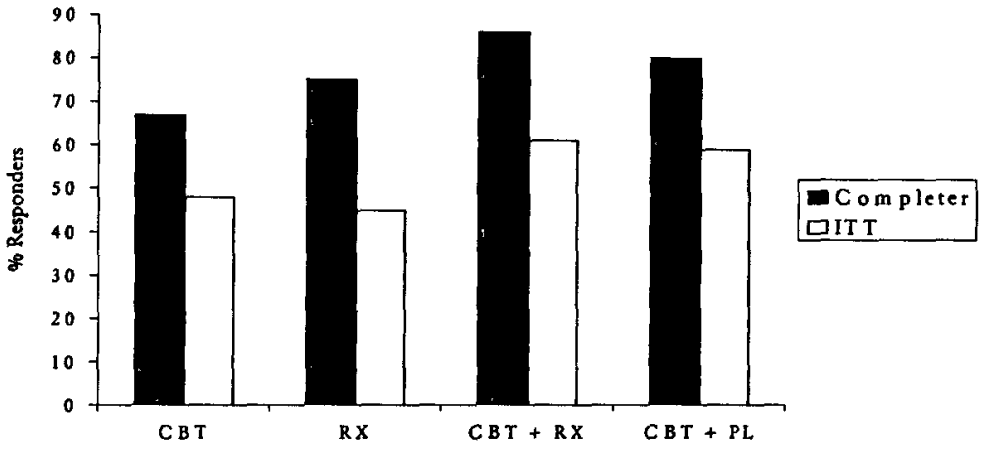

Figure 8. Completer and intent-to-treat (ITT) analysis of short-term response rates from most definitive randomized clinical trial. Data from Barlow et al. (2000).

Long-term Efficacy

In order to evaluate the long-term treatment efficacy, Gould et al. (1995) calculated mean posttreatment to follow-up effects sizes of studies using a minimum follow-up period of six months. Posttreatment to follow-up effect sizes are presented in Figure 9. The mean effect size among pharmacological interventions was 0.46, indicating considerable relapse after discontinuation of treatment. The small effect sizes that were observed for CBT (ES = 0.06) and for the combination treatment (ES = 0.07) suggest that CBT results in significantly greater maintenance of treatment gains relative to medication treatments.

A similar pattern was observed in the study by Barlow et al. (2000). CBT alone and CBT plus placebo were superior to placebo after no-treatment follow-up. Contrary to expectation, the combination of Imipramine plus CBT was significantly less effective than CBT alone or CBT plus pill placebo. Response rates at no-treatment follow up are presented in Figure 10.

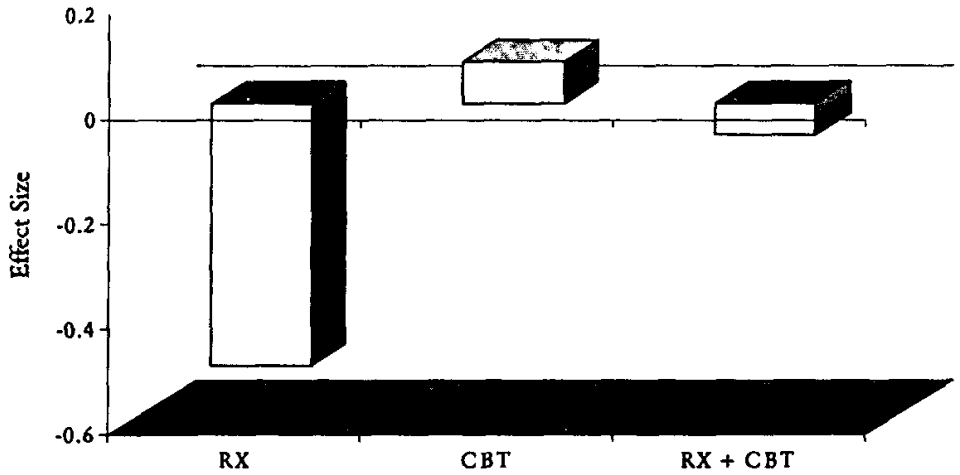

Figure 9. Long-term efficacy for CBT, medication, and their combination. Data from Gould et al. (1995).

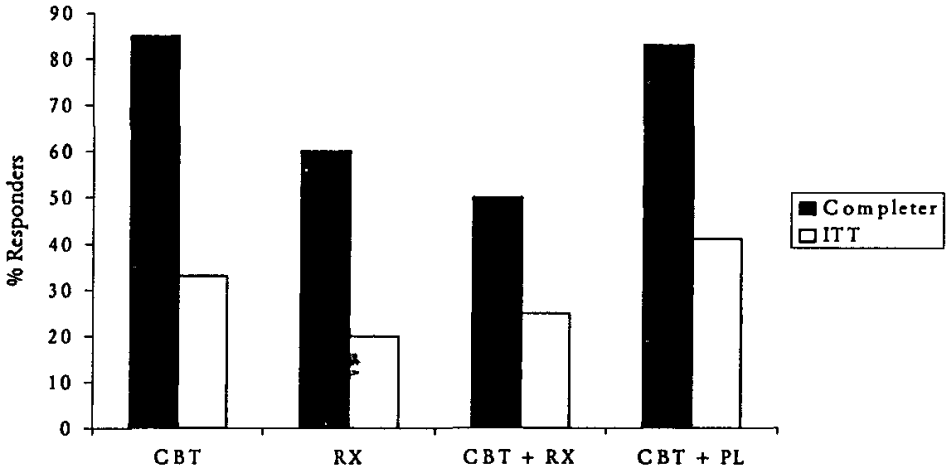

Figure 10. Completer and intent-to-treat (ITT) analysis of long-term response rates from most definitive randomized clinical trial. Data from Barlow et al. (2000).

Quality of Life

Few studies have directly evaluated the impact of interventions for panic disorder on patients' quality of life. Telch, Schmidt, Jaimez, Jacquin, and Harrigton, (1995) examined changes in quality of life following eight weeks of CBT administered in a group format. Participants who had received CBT showed more improvement in the domains of work functioning, social functioning, and family functioning compared to wait-list controls. These gains were maintained at a 6-month follow-up.

Improvement in quality of life is not restricted to CBT treatments. Jacobs, Davidson, Gupta, and Meyerhoff (1997) found that panic patients treated with clonazepam showed significant gains in quality of life relative to placebo-treated patients. Moreover, they showed that improvement in quality of life was directly related to improvement in panic symptoms.

Predictors of Clinical Response

Incidence of treatment non-response and relapse suggests that there are factors that moderate the efficacy of existing interventions. Cowley, Flick, and Roy-Byrne (1996) conducted follow-up interviews with panic disorder patients up to 60 months after completion of treatment. Consistent with previous findings (e.g., Warshaw, Massion, Shea, Allsworth, & Keller, 1997), level of agoraphobia proved to be the strongest predictor of overall improvement. In addition, the presence of major depression or Axis-II comorbidity at pre-treatment predicted a less favorable clinical response.

Several other studies have demonstrated an association between Axis-II comorbidity and poorer treatment outcome (e.g., Pollack, Otto, Rosenbaum, & Sachs, 1992). However, results of a recent study by Telch, Kamphuis, & Schmidt (2001) showed that Axis-II comorbidity no longer predicted level of improvement after controlling for baseline differences in panic disorder symptom severity.

Schmidt and Telch (1997) observed a relationship between panic patients perceived physical health and clinical response to CBT. Immediately following treatment, 71% of patients who perceived their physical health at intake as good met recovery criteria, compared to only 35% of those who perceived their health as poor. At a six-month no-treatment follow-up, 67% of those who perceived their physical health as good met composite recovery criteria compared to only 33% of those who perceived their health as poor.

Finally, Schmidt and Woolaway-Bickel (2000) found that patients' adherence to CBT as measured by therapist ratings predicted a more favorable response to CBT.

Treatment Effectiveness

Efficacy research is conducted under controlled circumstances. This has led to reservations regarding the generalizability of findings from randomized clinical trials. For example, it has been argued that the study samples might not be representative of the clinical population encountered in the community. Also, the utilization of treatment manuals in clinical trails is not as frequently observed in clinical practice.

To date, little attention has been given to the question of whether efficacy data from panic treatments delivered in the context of randomized clinical trials can be generalized to "real world" clinical practice. Fortunately, preliminary findings are promising. Wade, Treat, and Stuart (1998) compared the results of a 15-session CBT protocol in a community mental heath center (CMHC) to the results of two CBT efficacy studies. Pre-to post treatment changes as well as longer term follow-up findings observed in the CMCH sample were comparable to those observed in the two controlled efficacy studies (Stuart, Treat, & Wade, 2000).

Cost-Effectiveness

In addition to treatment efficacy and tolerability, treatment costs should be considered in the overall evaluation of the utility of a treatment. Margraf and Schneider (1995) reported an 81% decrease in healthcare costs associated with anxiety symptoms over 3 years following a 15-session cognitive behavioral treatment for individuals with panic disorder. They concluded that for every dollar spent on the treatment, 5.6 dollars were saved in healthcare costs. In their meta-analyses of interventions for panic disorder, Gould, Otto, and Pollack, (1995) compared the expenses for CBT to those for pharmacological treatment. Their findings indicated that Imipramine and group-administered CBT were the most cost-effective interventions. The total cost over a 12-month period was approximately $600 for Imipramine and group CBT, compared to a total yearly cost of approximately $1400 for individual CBT.

Otto, Pollack, and Maki (2000) examined whether the cost estimates provided by Gould et al. (1995) were representative of treatments as they are delivered in the community. Otto et al. argued that previous estimates might have been colored by the controlled conditions evident in clinical trials (e.g., sample characteristics, manualized treatment). Using an outpatient clinic sample, the authors calculated

the average visit costs, medication costs, and alternative treatment costs per patient for both the acute treatment phase as well as for a one-year interval. As shown in Figure 11, CBT was the most cost-effective intervention for the acute phase ($518) as well as for a one-year interval ($523). Pharmacological treatment was shown to be more cost-effective than individual CBT during the acute phase (Costs $839, $1357, respectively). However, the cost for individual CBT was 59% of the cost for pharmacological treatment for a one-year interval.

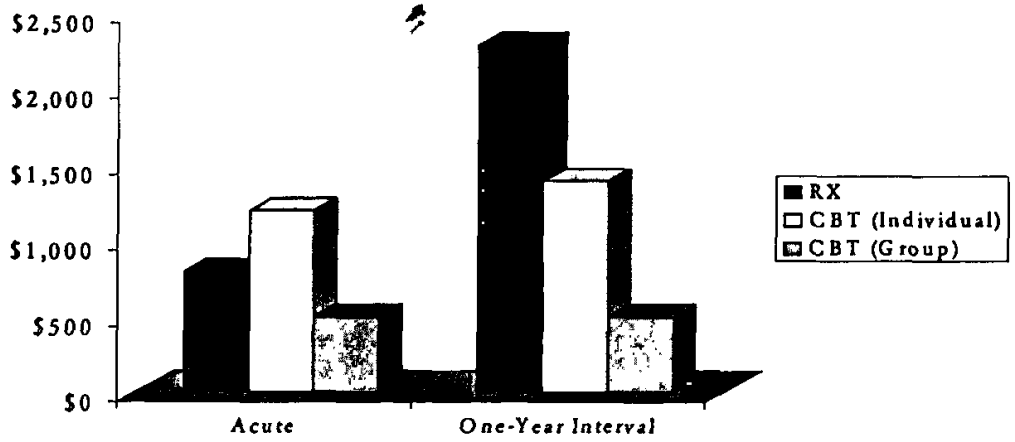

Figure 11. Cost of treatment. Data from Otto et al. (2000).

Otto et al. (2000) also estimated cost-benefit ratios for each treatment modality. The cost-benefit ratio was calculated by dividing the total cost of the intervention by the change in clinical status as measured by clinicians' ratings of global improvement. The findings matched the pattern observed for cost estimates, indicating superiority for group CBT for both the acute phase and one-year interval. Figure 12 presents the cost-effectiveness ratios for each treatment modality.

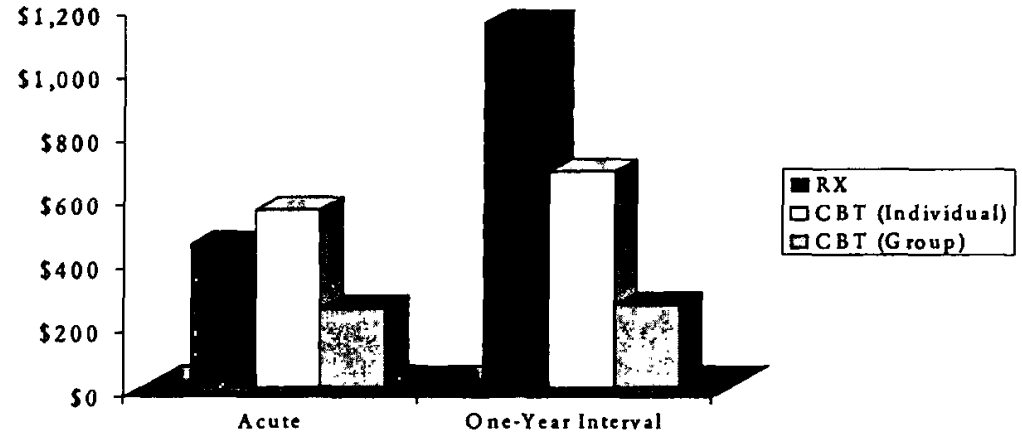

Figure 12. Cost-benefit ratios for each treatment modality. Data from Otto et al. (2000).

Comments: Future Directions

Despite the extensive treatment literature with respect to anxiety disorders, there is a striking paucity of research addressing various issues relevant to medical cost offset. In this next section, we discuss potential areas for future research.

Improving on Existing Treatments

The empirically-supported treatments currently available for anxiety disorders consist of multiple procedural elements such as education, cognitive restructuring, relaxation training, and exposure to fear cues. For the most part, there is a lack of data on the relative contribution of these procedural elements on treatment outcome. Can our existing treatments be trimmed? Dismantling studies are needed to assist in the challenge of designing more streamlined interventions without sacrificing treatment potency.

We also have much to learn about how to optimally deliver existing empirically-supported treatments. Issues surrounding the optimal sequencing of procedural elements, treatment dosing, individual versus group delivery, self-help versus therapist-assisted delivery, and the value of booster sessions have yet to be delineated.

Identifying Predictors of Clinical Response

Our review revealed that progress has been made in the identification of variables that predict patients' clinical response to existing treatments. For instance, we know that panic disorder patients with accompanying agoraphobia respond less favorably to either pharmacotherapy or CBT. Unfortunately, the treatment moderator analyses to date have yet to identify moderators of *differential* treatment response. In other words, little progress has been made in our ability to match patients to different treatments as a way of optimizing clinical response. Developing effective treatment matching algorithms hold much promise for medical cost offset.

Expanding the Range of Outcome Measures

In preparing this chapter it soon became apparent that we have virtually no data yet available on how treatment efficacy relates directly to medical cost offset. Given the staggering non-psychiatric medical costs associated with anxiety disorders, we might conclude on logical grounds that treatments that results in clinically significant improvement in anxiety symptoms should lead to reductions in health care utilization thus producing a considerable positive effect on medical cost offset. This argument is strengthened when one considers both the early age of onset and the chronicity of most anxiety disorders. However important questions remain. What is the relationship between symptom reduction and medical cost offset? What is the minimum level of symptom reduction necessary to produce medical cost offset? What is the relative effect of different treatment modalities (e.g., pharmacotherapy versus CBT) on medical cost offset? These and other questions can only be answered by clinical investigators incorporating a broader range of outcome indices in their analyses. These include both direct and indirect treatment costs, psychiatric

and non-psychiatric comorbidity, earnings data, work absenteeism, work productivity, and quality of life indices including family outcome indices.

Developing Empirically-Supported Interventions for Managed Care

The availability of empirically-supported treatments for anxiety disorders does not insure that patients will seek them out. Indeed, evidence suggests that only about 27% of adults with a diagnosed anxiety disorder will receive treatment for it (Kessler et al., 1994). Consequently, more effective screening strategies need to be developed in primary care settings so that anxiety disorders can be identified and appropriately treated. Managed care organizations have great potential to offer integrated physical and mental health services to their members. However, these organizations are unlikely to provide more effective screening and treatment for anxiety disorders in the absence of incentives to do so. When one considers that membership in any one managed care organization is often short-lived, there exists little incentive for the organization to offer science-based integrated health care that is cost-effective for the organization and society in the long-term. Mechanisms for overcoming this structural impediment need to be developed and implemented.

Concluding Remarks

Anxiety disorders are debilitating and chronic conditions that represent a major challenge to our health care system. The costs of anxiety disorders– both monetary and non-monetary – to the patient, family, and society are staggering. Two decades of research have demonstrated that pharmacotherapy, CBT, and their combination are all markedly effective in the short-term, but cognitive-behavioral treatments have demonstrated a clear advantage with respect to durability of treatment gains. Contrary to expectation, there appears to be growing evidence that combining medication and psychosocial interventions does not lead to greater improvements than psychosocial treatment alone. Findings from effectiveness studies – although limited in number – provide preliminary support that the treatment gains observed in controlled randomized clinical trials seem to also hold when these treatments are delivered in the "real-world." Although some progress has been made in the identification of factors that predict clinical response to treatment, there has been little progress in developing strategies for matching treatments to patient characteristics. Finally, there is a shocking absence of data on the effects of treating anxiety disorders on subsequent health care utilization and medical cost offset. This state of affairs requires creative new research directions integrating methods from psychology, psychiatry, primary care medicine, economics, epidemiology, and health policy research.

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