Published in final edited form as:

Depress Anxiety. 2005 ; 22(2): 59–67. doi:10.1002/da.20089.

RESULTS OF A NATURALISTIC LONGITUDINAL STUDY OF BENZODIAZEPINE AND SSRI USE IN THE TREATMENT OF GENERALIZED ANXIETY DISORDER AND SOCIAL PHOBIA

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Abstract

The past decade has brought major new developments in the psychopharmacologic management of generalized anxiety disorder and social phobia. We examined medication-prescribing patterns for the treatment of these anxiety disorders for 12 years to assess changes in patients' anti-anxiety psychotropic medication usage during that period of evolving practice guidelines. We examined psychotropic medication use in 305 patients with generalized anxiety disorder and 232 with social phobia enrolled in the Harvard/Brown Anxiety Disorders Research Project (HARP), a prospective, longitudinal study of anxiety disorders. Psychotropic treatment patterns seem to have remained relatively stable over 12 years with benzodiazepines the medications most commonly used for both generalized anxiety disorder and social phobia. Comparatively, selective serotonin reuptake inhibitor (SSRI) and venlafaxine usage as stand-alone medications for these disorders remained low throughout the follow-up period. At the 12-year follow-up, 24% of patients with generalized anxiety disorder and 30% of patients with social phobia were utilizing neither an SSRI/selective norepinephrine reuptake inhibitor (SNRI) nor a benzodiazepine. Treatment recommendations for use of SSRIs and venlafaxine in the management of generalized anxiety disorder and social phobia initially promulgated in 1998 had a modest impact on changes in psychopharmacologic practice 4–5 years later. Difficulties in the implementation of treatment guidelines are discussed.

Keywords

treatment guidelines; generalized anxiety disorder; social phobia; psychotropic drugs

INTRODUCTION

Epidemiological studies report lifetime prevalence rates of generalized anxiety disorder (GAD) and social phobia of 5.1% and 13.3% respectively, whereas the lifetime prevalence of any anxiety disorder is 24.9% [Kessler et al., 1994]. The treatment of a broad range of anxiety disorders has been revolutionized by the emergence of the selective serotonin reuptake inhibitor (SSRI) class of medications. Initially introduced as antidepressants, these medications have been demonstrated to exhibit efficacy in the treatment of anxiety

disorders. In a previous report based on this study sample, we reported a striking gap between pharmacologic guidelines for the treatment of panic disorder and the actual delivery of care, and that benzodiazepines remained the treatment of choice in actual clinical practice [Bruce et al., 2003].

This report examines changes in the use of psychotropic drugs for the treatment of GAD and social phobia over 12 years of follow-up, spanning approximately 7–8 years before and 4–5 years after the initiation of new psychopharmacologic guidelines to treat these disorders [Ballenger et al., 1998]. Although benzodiazepines have been used to treat anxiety associated with GAD and social phobia, SSRIs have been found to be effective in the treatment of social phobia [Liebowitz et al., 2002; Stein et al., 2002]. Additionally, venlafaxine, a serotonin and norepinephrine reuptake inhibitor (SNRI) [Montgomery et al., 2002; Rickels et al., 2000] has shown to be effective for the treatment of GAD. A distinct advantage of the use of selective serotonin agents is their capacity to also treat comorbid psychiatric disorders such as depression, obsessive compulsive disorder, panic disorder, and posttraumatic stress disorder that often accompany GAD and social phobia [Ballenger et al., 1998, 2001]. Benzodiazepines are not effective in the treatment of comorbid depression and may be associated with the induction of dysphoria, development of benzodiazepine dependency, and lethality in overdose when combined with alcohol. If not tapered gradually, benzodiazepines can induce withdrawal symptoms. Benzodiazepines are often associated with sedative side effects, which may be associated with mild cognitive impairment and falls in the elderly. A key advantage of benzodiazepines is their rapid onset of action and efficacy in reducing feelings of anxiety [Shader and Greenblatt, 1993].

SSRIs and venlafaxine are safe in overdose and carry a lower risk of causing physiological dependence, although abrupt termination of these agents is associated with a discontinuation syndrome characterized by dizziness, nausea, lethargy, and headaches [Haddad, 1998]. A disadvantage of the SSRIs and venlafaxine in treating anxiety symptoms is the delay in onset of anxiolytic effect that may last from several days to several weeks. Usage of SSRIs have also been associated with an increased incidence of sexual dysfunction [Clayton et al., 2002].

The purpose of this study was to examine the long-term use of SSRIs and benzodiazepines in patients with GAD and social phobia that were enrolled in the Harvard/Brown Anxiety Research Project (HARP). We sought to examine shifts in prescribing patterns of the SSRI medications, venlafaxine, and the benzodiazepines in response to the availability of newer pharmacologic agents in the 1990s and revised treatment guidelines [Ballenger et al., 1998, 2001].

This study served to extend our previously published findings in regard to panic disorder that found relatively little impact on clinical practice of newly developed treatment guidelines. Few naturalistic studies exist that have documented changes, if any, in the pattern of psychopharmacologic management of GAD or social phobia since the advent of the SSRIs in the mid-1980s. An earlier study from the HARP examined changes in pharmacologic treatment of GAD from 1989 to 1996 and found that nearly one third of the 1989–1991 intake sample of GAD patients were on no medication; in 1996, the percentage of GAD patients that were untreated pharmacologically was still 27% [Salzman et al., 2001].

In presenting this information, we seek to address the following questions. First, how have psychopharmacologic treatments of GAD and social phobia shifted from 1990 to 2002 since the advent of new pharmacologic treatment guidelines for the management of these anxiety disorders in 1998? Second, what factors seem to influence the choice of psychopharmacologic treatment for these anxiety disorder patients? Third, are there

temporal differences in the overall percentage of patients being treated pharmacologically for these anxiety disorders?

SUBJECTS AND METHODS

HARP is a prospective, naturalistic, longitudinal, multicenter study of adults with a current or past history of anxiety disorders. In total, 711 participants entered this study from over 30 clinicians' practices at 11 different clinical treatment facilities in the New England area. These methods are described in detail elsewhere [Keller et al., 1994]. Inclusion for participation included a past or current diagnosis of the following at intake: panic disorder with or without agoraphobia, agoraphobia without panic disorder, social phobia, or GAD. Participants must have been at least 18 years of age at intake, willing to participate voluntarily in the study, and had to sign a written consent form. Exclusion criteria consisted of the presence of an organic brain syndrome, a history of schizophrenia, or current psychosis at intake; otherwise, any comorbidity was allowed.

PROCEDURES

The present data derive from the structured diagnostic interview administered at intake (1989–1991) and subsequent semiannual and annual follow-up interviews over 12 years. The initial comprehensive evaluation assesses lifetime history using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM)-III-R Non-Affective Disorders, Patient Version (SCID-P), and the Research Diagnostic Criteria (RDC) Schedule for Affective Disorders-Lifetime (SADS-L). Items on the SCID-P and SADS-L were combined to create the SCALUP, a structured interview used to assess diagnoses at intake (available from M.B.K. upon request). The instrument yielded both present and past RDC diagnoses for affective disorders and DSM-III-R diagnoses for non-affective (including anxiety) disorders. Interviews conducted by trained research assistants usually took place in single sessions lasting 2–4 hr. Follow-up evaluations were conducted at 6-month intervals for the first 2 years, annually for years 3–7, and 6-month intervals for years 8–10 using the Longitudinal Interval Follow-up Evaluation-Upjohn (LIFE-UP) [Keller et al., 1987]. The LIFE-UP gathered weekly information about the presence of specific symptom criteria, psychiatric comorbidity, and psychosocial functioning. Additionally, information on pharmacologic treatment from the patients was collected every 6–12 months retrospectively for each week during the interval and included type of medication, average daily dosage, or whether patients were taking it as needed.

PSYCHIATRIC STATUS RATINGS

The LIFE-UP assesses psychopathology with a six-point Psychiatric Status Ratings (PSRs) that is scored for each week of the follow-up interval (Table 1). For example, a PSR of 6, the greatest severity of illness, requires full DSM-III-R criteria in addition to severely disrupted psychosocial or occupational functioning. A PSR of 5 requires meeting full DSM-III-R criteria with moderately disrupted psychosocial/occupational functioning. We considered a participant to have been remitted from social phobia or GAD if he/she experienced 8 consecutive weeks at PSR ratings of 2 or less. This definition of remission has been used widely in studies of affective and other disorders. Additionally, patients who remitted from an anxiety disorder were judged to have relapsed if their PSR score increased to a 5 or a 6 for 2 consecutive weeks.

INTER-RATER RELIABILITY AND VALIDITY

Three studies have been conducted using participants already enrolled in HARP to assess inter-rater reliability, subject recall, and validity of the (LIFE-UP) PSRs used to assess the course of all disorders [Warshaw et al., 1994]. Assessment of inter-rater reliability of the

anxiety disorder PSRs and the other instruments found good to excellent reliability. The long term test–retest substudy conducted to assess the reliability of using subjects' retrospective recall to assess PSRs over 1 year found very good to excellent reliability for the anxiety disorders and for major depressive disorder. The separate external validity assessment comparing PSRs with other psychosocial measures found good concurrent and discriminant validity.

STATISTICAL ANALYSES

Statistical analyses were conducted using *SAS v6.07* [SAS Institute, 1990; Cary, NC], using PROC FREQ, PROC MEANS, PROC NPARIWAY, PROC T-TEST, PROC ANOVA, PROC LOGISTIC, AND PROC PHREG. All *t* tests conducted were two-tailed. Nonparametric tests (Z-scores) were conducted on data that was not normally distributed. Additionally, proportional hazards regressions using time-varying covariates were conducted to examine significant predictors of SSRI and benzodiazepine use over the 10-year follow-up period. These analyses allowed us to examine how variations within a predictor variable over time influenced the use of an SSRI or benzodiazepine. For example, for the participants who started using an SSRI during our period of observation, we designated the month the SSRI use started for that individual as month 0. Ratings were then assembled relative to that time, from 1 year before use of that SSRI until 1 year afterward. Proportional hazards regressions were also conducted for the patients whose illness was in recovery from anxiety disorder to examine if receiving various types of psychotropic treatment (SSRIs, benzodiazepines, monotherapy, or combined pharmacologic treatment) increased the likelihood of recovery.

RESULTS

At intake, 179 patients with GAD and 176 with social phobia were enrolled into the study. Most patients were Caucasian women with an average age of 40 years. Slightly under half were working full time at intake (45% GAD, 47% social phobia, respectively) and one in three had a college education or higher. Clinical characteristics of the intake sample are reported in Table 2. Patients with both GAD and social phobia exhibited a high rate of comorbid anxiety and major depressive disorders; a high rate of lifetime alcohol/substance use and dependency was also evident in both the GAD and social phobia patient samples. During the subsequent 12-year follow-up interval, an additional 126 patients experienced an onset of GAD, whereas 56 additional patients experienced an onset of social phobia during follow-up. We thus included in the analysis 305 patients with GAD and 232 patients with social phobia. All patients were receiving some form of treatment at study intake; this may have included psychotherapy without psychotropic medication management. Patients with comorbid diagnoses of both social phobia and GAD were counted and included in both diagnoses. This study did not make direct comparisons between these two disorders. The data presented in Tables 4 and 5 represents a mix of patients who entered the study with the disorder of interest and those who developed the disorder during the course of follow-up.

MEDICATION DOSES

Average doses of specific SSRIs, SNRIs, and benzodiazepines are reported in Table 3. The average daily dose at the 12-year follow-up is reported because some of the medications were not yet developed or approved at intake or in earlier follow-up years. Additionally, the proportion of patients taking benzodiazepines on an as-needed basis is reported. The average daily dose of benzodiazepine was within a modestly lower range than is typically prescribed, although there were large standard deviations in dose because some of the patients were taking extremely low or extremely high doses. For the SSRIs, the average doses were in a midlevel dosage range.

USE OF PHARMACOLOGIC AGENTS OVER FOLLOW-UP

Twelve-year use of SSRI/SNRI and benzodiazepines in patients with GAD and social phobia is reported in Tables 4 and 5. At intake, most participants with social phobia or GAD reported taking a benzodiazepine. Less than 20% reported using an SSRI and one third reported no SSRI or benzodiazepine treatment. Over the course of the 12-year follow-up, use of benzodiazepines remained relatively stable and was the most frequent medication class utilized. Examination of only SSRI/SNRI utilization indicated an increase during follow-up for both anxiety disorders, from 6% to 21% for GAD and from 8% to 22% for social phobia over the 12-year follow-up. Inspection of concomitant use of both SSRI/SNRI and benzodiazepines indicated an increase from week 1 post-intake to the 12-year follow-up in both the GAD and social phobia patient groups (12% to 24%, and 9% to 25%, respectively). At the 12-year follow-up, 24% of the patients with GAD and 30% of the patients with social phobia were not being treated with either a benzodiazepine or an SSRI/SNRI medication. This lack of treatment with either agent was consistent throughout the 12 years of follow-up. Comparison of those patients in episode of social phobia or GAD with the patients who improved and were not meeting full DSM criteria during follow-up indicated that being in episode did not markedly increase the overall use of either SSRIs or benzodiazepines. Additionally, comparing patients with GAD or social phobia at intake with those who subsequently developed GAD or social phobia during follow-up revealed no statistically significant differences in overall treatment patterns with SSRIs or benzodiazepines.

Proportional hazards regressions with time-varying covariates were conducted to examine predictors of SSRI and benzodiazepine use in patients with GAD and social phobia. The results indicated that comorbid major depressive disorder was a significant predictor of SSRI use during follow-up. Patients with GAD and comorbid major depressive disorder were more than twice as likely to start taking an SSRI than were those without major depressive disorder (risk ratio [RR] = 2.30; $P < .0001$) after covarying for other anxiety disorders and demographic variables. Similarly, patients with social phobia and comorbid major depression were nearly twice as likely to begin SSRI treatment compared to those patients with social phobia and no major depressive disorder (RR = 1.85; $P < .001$).

Interestingly, patients with social phobia and comorbid major depressive disorder were significantly more likely to start taking a benzodiazepine during follow-up than were patients with social phobia without comorbid major depressive disorder (RR = 1.43; $P < .03$) after covarying for other anxiety disorders and demographic variables. Other comorbid conditions, such as alcohol/substance use disorders and additional comorbid anxiety disorders, did not significantly predict SSRI or benzodiazepine use in patients with GAD or social phobia.

PHARMACOLOGIC TREATMENT AND CLINICAL COURSE

Proportional hazard regressions analyses were conducted to determine if types of psychotropic treatment improved rates of recovery in patients with GAD and social phobia. Overall, the patients who recovered were no more likely to be taking an SSRI the week before recovery nor were they more likely to be receiving a benzodiazepine the week before recovery. Further, results indicated that patients who recovered were no more likely to be receiving combination treatment (SSRIs and benzodiazepines) the week before recovery. Finally, analyses examining the intensity of treatment, including dose and whether the patients were taking a medication as needed, were conducted to see if there were any effects on clinical outcome. Again, the patients whose disorder recovered were no more likely to be receiving higher doses of benzodiazepines or SSRIs or to be taking a benzodiazepine as needed the week before recovery than were those whose illness had not recovered.

DISCUSSION

The findings of this 12-year longitudinal study of anxiety disorders demonstrate that recommended guidelines for the treatment of social phobia and GAD promulgated in 1998 have had a relatively limited impact on the actual delivery of care in our patient sample by the end of the 12-year follow-up. This may reflect a delay in the filtering down of treatment guidelines into actual clinical practice. These results are consistent with a previously published report from HARP that also demonstrated this gap for the psychopharmacologic treatment of panic disorder [Bruce et al., 2003]. Our results also extend and confirm initial findings from a previous report on pharmacologic treatment patterns of GAD [Salzman et al., 2001]. The findings are of particular importance in that a significant percentage of the patients followed in this study continued to meet full criteria and symptoms of their anxiety disorders after several years of treatment [Bruce et al., 2005] and that at 12-year follow-up, almost one third of patients with social phobia and one fourth of patients with generalized anxiety disorder were not being treated with either an SSRI/SNRI or a benzodiazepine.

Despite the large sample size and the number of years patients were followed, limitations of our study included the following. First, minority patients were underrepresented. Second, we did not have direct access to medication records and relied on patient self-report as to the medications and dosages they were receiving. Third, the study population was a New England sample and may not have reflected national treatment patterns. Because patients recruited for this study were all receiving treatment at the time of intake, it could be argued that rates of treatment utilization are even lower in the community than the results presented from this study. Fourth, HARP is an observational study of anxiety disorders, and by design, HARP observes but does not manipulate the treatment received by subjects. Treatment effects in the HARP study are thus difficult to discern in that some severely ill patients were being treated more intensely whereas others might have dropped out of treatment altogether, therefore washing out any effects that may exist.

Although our results indicate that those patients who recovered from either social phobia or GAD were no more likely to be taking SSRIs or benzodiazepines (or their combination) before recovery, the lack of treatment effects on clinical course outcome was not unexpected. It is therefore difficult to discern potential treatment effects for a number of reasons, including our findings of lower doses of medication for the anxiety disorders, inadequate length of time on medications, or self-selective biases that make treatment seem to have negative effects because there is no experimental control over treatment.

Our data indicates that comorbid major depression was a significant predictor of SSRI use during follow-up in both the GAD and the social phobia patient cohorts. Conversely, additional comorbid anxiety disorders and alcohol/substance abuse disorders did not significantly predict SSRI or benzodiazepine use in either patient cohort.

At a practical level, the findings may indicate that SSRIs have a significant set of side effects for many patients such that they choose to discontinue them. A recent review of pooled studies of 6,299 primary care patients indicated that 36–43% of the patients taking an SSRI reported sexual dysfunction [Clayton et al., 2002]. Another study indicated that discontinuation of SSRIs in patients with panic disorder has been attributed to adverse side effects 52% of the time; by comparison, adverse side effects secondary to benzodiazepines were responsible for medication discontinuation in only 7% of cases [Cowley et al., 1997]. Clearly, the issue of adverse effects associated with antidepressant usage remains a highly important public health concern that bears on the usage of these medications for the treatment of anxiety disorders [Cheeta et al., 2004].

Our findings indicate that benzodiazepine use for the anxiety disorders studied remained relatively constant over the 12-year interval examined. Consistent with this finding, Uhlenhuth et al. [1999] reported a negligible decrease in the overall frequency of expert recommendations for benzodiazepines as a first-line treatment for panic disorder over a 5-year interval in the 1990s. Romach et al. [1995] have presented data on clinical aspects of chronic use of alprazolam and lorazepam and found these benzodiazepines to be clinically appropriate maintenance therapy for chronic psychiatric conditions. For many patients, it is possible that SSRIs do not afford the rapid symptomatic relief provided by benzodiazepines. Patients in the general population may also differ from those encountered in the research studies that established the efficacy of the SSRIs in the treatment of anxiety disorders. The high rate of comorbidity with other psychiatric disorders in patients with anxiety disorders contributes to the complexity of the problem. Our findings highlight the need for more refined prospective study of the appropriate role for benzodiazepine medications, with or without concomitant use of SSRI/SNRI medications, in the GAD and social phobia patient populations.

In addition to the need for more empirical data to support treatment recommendations, specific treatment guidelines for the treatment of anxiety disorders and algorithms to aid in decision making may not have been disseminated adequately into community practice. Individual clinicians may experience treatment guidelines as overly idealized and overly intrusive, limiting the clinician's creativity and feeling for his or her specific patient [Ferrier et al., 1996; Lomas et al., 1989]. Another source of resistance to treatment guidelines may be the perception that they are not grounded in clinically pertinent evidence-based data, as may be the case with long-term benzodiazepine usage [Cabana et al., 1998; Dugan and Cohen, 1998].

The findings of this study highlight the problem of utilizing evidence-based pharmacologic treatment of psychiatric disorders in actual clinical practice. Some recommendations still support the use of benzodiazepines as first-line treatments for these disorders [Romach et al., 1995; Shader and Greenblatt, 1993]; assessment of the optimal role for benzodiazepines in the treatment of these disorders awaits the development of more refined empirically based algorithms. Several authors have examined this problem and suggested strategies for addressing this issue. Mellman et al. [2001] have highlighted different levels of treatment guidelines and examined barriers to implementation including the necessity for collaboration between practicing clinicians and researchers as well as issues related to healthcare public policy. Practical measures to facilitate the development of the translational process that can move clinical research findings into actual clinical practice have been outlined by Roy-Byrne et al. [2003].

The findings of our naturalistic, longitudinal study suggest that recommended pharmacologic treatment guidelines for GAD and social phobia published in 1998 have not yet been implemented fully in actual practice up to 5 years later. This finding is consistent with recently published articles examining trends in the outpatient treatment of anxiety disorders [Olfson et al., 2004; Stein et al., 2004]. Although our study has focused on pharmacologic treatment, there is evidence from earlier studies from HARP that empirically supported psychosocial treatments for anxiety disorders were also being markedly underutilized [Goisman et al., 1993, 1999], demonstrating the ubiquity of the public health problem of inadequate treatment of anxiety disorders in clinical practice.

Acknowledgments

Contract Grant sponsor: Wyeth-Ayerst Laboratories; Grant sponsor: NIMH; Grant number: MH51415

The Harvard/Brown Anxiety Disorder Research Program is conducted with the participation of the following investigators: M.B. Keller, M.D. (Chairperson); M.T. Shea, Ph.D. (Veterans Administration Hospital, Providence–Brown Medical School); J. Eisen, M.D., K. Phillips, M.D., R. Stout, Ph.D. (Butler Hospital–Brown Medical School); S.E. Bruce, Ph.D., R.B. Weisberg, Ph.D., M.G. Warshaw, M.S.S., M.A. (Brown Medical School); R.M. Goisman, M.D. (Massachusetts Mental Health Center–Harvard Medical School); A. Massion, M.D. (University of Massachusetts Medical Center); M.P. Rogers, M.D. (Brigham and Women’s Hospital–Harvard Medical School); C. Salzman, M.D. (Massachusetts Mental Health Center–Harvard Medical School); G. Steketee, Ph.D. (Boston University School of Social Work); K. Yonkers, M.D. (Yale University School of Medicine); I. Goldenberg, Psy.D.; G. Mallya, M.D. (McLean Hospital–Harvard Medical School); T. Mueller, M.D. (Butler Hospital–Brown Medical School); F. Rodriguez-Villa, M.D. (McLean Hospital–Harvard Medical School); R. Vasile, M.D. (Beth Israel Deaconess Medical Center–Harvard Medical School); C. Zlotnick, Ph.D. (Butler Hospital–Brown Medical School); and E. Fierman, M.D. Additional contributions from: P. Alexander, M.D. (Butler Hospital–Brown Medical School); J. Curran, M.D.; J. Cole, M.D. (McLean Hospital–Harvard Medical School); J. Ellison, M.D., M.P.H. (Harvard Pilgrim Health Care–Harvard Medical School); A. Gordon, M.D., S. Rasmussen, M.D. (Butler Hospital–Brown Medical School); R. Hirschfeld Ph.D. (University of Texas, Galveston); J. Hooley, D.Phil. (Harvard University); P. Lavori, Ph.D. (Stanford University); J. Perry, M.D. (Jewish General Hospital–McGill University School of Medicine, Montréal); L. Peterson (Midcoast Medical Group, Rockport, ME); J. Reich, M.D., M.P.H.; J. Rice, Ph.D. (Renard Hospital–Washington University School of Medicine); H. Samuelson, M.A. (Brigham and Women’s Hospital); D. Shera, M.S. (Harvard School of Public Health); N. Weinshenker, M.D. (New Jersey Medical School); M. Weissman, Ph.D. (Columbia University); and K. White, M.D. This investigation was supported in part by Wyeth-Ayerst Laboratories, through its Global Research Program on Anxiety and Depression and by the NIMH (grant MH51415).

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TABLE 1**Psychiatric status rating scale for generalized anxiety disorder and social phobia**

Generalized anxiety disorder	Code	Social phobia
Experiences worry more days than not, accompanied by at least six of 18 DSM-III-R symptoms of GAD, and these symptoms cause a major disruption in functioning.	6	Full criteria and phobic avoidance grossly interferes with the person's normal routine, or with usual social activities, or with relationships with others.
Experiences worry more days than not, accompanied by at least six of 18 DSM-III-R symptoms of GAD, but these symptoms cause no major disruption in functioning.	5	Meets full criteria for social phobia without gross interference in functioning.
Experiences worry and anxiety more days than not, but only has three to five symptoms of GAD	4	Meets all criteria for social phobia EXCLUDING criterion E (interference, or marked distress about having the fear).
OR		
Has at least 6 symptoms of GAD and does not experience worry and anxiety more days than not.		
Has only three to five symptoms of GAD and does not experience worry and anxiety more days than not.	3	Meets criterion A (fear) and criteria B and G (exclusionaries). Fails more than 1, but less than all of criteria C, D, E, and F (DSM-III-R).
Experiences only occasional worry and anxiety, and may or may not be bothered by one or two symptoms of GAD.	2	Meets criterion A (fear) and criteria B and G (exclusionaries) only. Fails all other criteria for DSM-III-R social phobia.
None of the above.	1	None of the above.

TABLE 2

Clinical characteristics of patients with generalized anxiety disorder and social phobia at intake

Characteristic	Generalized anxiety disorder	Social phobia
Total <i>n</i>	179	176
Comorbid anxiety disorders, <i>n</i> (%)		
Panic disorder	18 (10)	15 (9)
Panic disorder with agoraphobia	75 (41)	64 (36)
Social phobia	58 (32)	—
Generalized anxiety disorder (GAD)	—	58 (33)
Simple phobia	34 (19)	36 (20)
Obsessive compulsive disorder	33 (18)	28 (16)
Posttraumatic stress disorder	16 (9)	19 (11)
Major depressive disorder (MDD)	70 (39)	62 (35)
Lifetime alcohol/substance use/dependency	38 (21)	66 (38)
Global assessment scale score, mean (std)	52.98 (11.47)	52.83 (11.35)
Length of intake episode (years), mean (std)	16.13 (13.58)	17.83 (12.72)
Age of first onset (years), mean (std)	19.31 (14.95)	13.20 (7.74)

TABLE 3

Doses of benzodiazepines, SSRIs, and SNRIs in patients with generalized anxiety disorder and social phobia at 12-year follow-up*

Psychotropic medication	Generalized anxiety disorder		Social phobia	
	Average dose mg	% taking on daily basis	Average dose mg	% taking as needed (PRN)
Benzodiazepines				
Clonazepam ($n = 36^a, 22^b$)	1.57	94	1.84	14
Alprazolam ($n = 33, 15$)	2.00	79	1.12	40
Lorazepam ($n = 7, 6$)	2.80	71	2.20	17
Diazepam ($n = 6, 5$)	13.00	83	16.67	40
SSRI/SNRIs				
Fluoxetine ($n = 19, 18$)	39.47	100	40.78	0
Paroxetine ($n = 17, 8$)	26.47	100	27.50	0
Sertraline ($n = 10, 5$)	102.50	100	115.00	0
Venlafaxine ($n = 6, 8$)	172.00	100	182.13	0

* Average dose was calculated using all patients, including those taking medications on an as-needed schedule. Only medications with $n \geq 10$ or more are shown.

^a Number of patients with generalized anxiety disorder receiving medication.

^b Number of patients with social phobia receiving medication.

TABLE 4

Use of benzodiazepines, SSRIs, and SNRIs in patients with generalized anxiety disorder over 12 years of follow-up

Follow-up year (n)	SSRI/SNRI only (%)	Benzodiazepine only (%)	SSRI/SNRI + benzodiazepine (%)	Neither (%)
1 week after intake (188)	12 (6)	93 (49)	23 (12)	60 (32)
1 (187)	12 (6)	85 (45)	23 (12)	67 (3)
2 (176)	8 (5)	82 (47)	16 (9)	70 (40)
3 (175)	8 (5)	76 (43)	26 (15)	65 (37)
4 (165)	11 (7)	70 (42)	23 (14)	61 (37)
5 (159)	15 (9)	60 (38)	28 (18)	56 (35)
6 (156)	16 (10)	61 (39)	27 (17)	52 (33)
7 (152)	14 (9)	56 (37)	30 (20)	52 (34)
8 (143)	14 (10)	51 (36)	30 (21)	48 (34)
9 (141)	16 (11)	45 (32)	39 (28)	41 (29)
10 (135)	17 (13)	43 (32)	40 (30)	35 (26)
11 (114)	21 (18)	35 (31)	31 (27)	24 (24)
12 (97)	20 (21)	31 (32)	23 (24)	23 (24)

TABLE 5

Use of benzodiazepines, SSRIs, and SNRIs in patients with social phobia over 12 years of follow-up

Follow-up year (n)	SSRI/SNRI only (%)	Benzodiazepine only (%)	SSRI/SNRI + benzodiazepine (%)	Neither (%)
1 week after intake (170)	14 (8)	80 (47)	16 (9)	60 (35)
1 (168)	14 (8)	67 (40)	16 (10)	71 (42)
2 (51)	12 (8)	63 (42)	13 (9)	63 (42)
3 (138)	11 (8)	60 (43)	17 (12)	50 (36)
4 (131)	10 (8)	47 (36)	22 (17)	52 (40)
5 (126)	15 (12)	44 (35)	20 (16)	47 (37)
6 (123)	14 (11)	36 (29)	26 (21)	47 (38)
7 (119)	13 (11)	33 (28)	27 (23)	46 (39)
8 (111)	16 (14)	30 (27)	26 (23)	39 (35)
9 (104)	12 (12)	24 (23)	30 (29)	38 (37)
10 (100)	17 (17)	21 (21)	30 (30)	32 (32)
11 (87)	15 (17)	18 (21)	28 (32)	26 (30)
12 (76)	17 (22)	17 (22)	19 (25)	23 (30)